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## Nerve Conduction Velocity of Sciatic Nerve in High Fat Diet Induced Obesity in Rats: Effect of Corn Oil and Omega 3 Fatty Acids Supplement

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**Abstract: Background:** Obesity is a major susceptibility factor leading to the development of various conditions of the metabolic syndrome. In obese rats, slowing of motor nerve conduction velocity was observed. Fatty acids metabolism disturbance is very important in the occurrence of peripheral neuropathy. The aim of this work is to consider the role that balanced diets high in omega 6&9 PUFA (corn oil) or supplying rats with omega 3, play in modulating the impaired nerve function in obese rats. **Methods:** Thirty two adult male albino rats were randomly assigned to receive normal chow (NC) (n=8) or high fat diet HFD (n=24), for 12 weeks. After 12 weeks, body weight and body mass index(BMI) were measured and the NC group(n=8) continue their normal chow diet, **Group 1 (NC)** and served as a control group and the obese rats were randomly divided into 3 groups, 8 rats each: **Group 2:** Ob + HFD group, they continue their high animal fat diet, **Group 3:** Ob+HFD + corn oil group, they are obese rats received high fat diet containing corn oil and **Group 4:** Ob + HFD + Omega 3 group, they are obese rats, fed high animal fat diet supplemented with omega 3 (0.4 g/kg) daily. After five weeks, the final body weight was measured and BMI was calculated and blood samples were collected for measuring fasting plasma glucose level, insulin level and homeostasis model assessment of insulin resistance (HOMA-IR) test were evaluated. Plasma cholesterol, triglycerides and free fatty acids (FFAs) were measured. The rats were then killed and sciatic nerves were carefully dissected for measuring the nerve conduction velocity (NCV). Superoxide dismutase activity (SOD), malondialdehyde (MDA) and tumor necrosis factor alpha (TNF $\alpha$ ) were estimated in the nerve tissue of the 4 groups. **Results:** The results of this study showed a significant increase of body weight (gm) and BMI (kg/m<sup>2</sup>) in high fat diet group ( $p < 0.05$ ) after 12weeks of the start of the diet when compared to the control group (NC). There were significant elevations in the final weight (gm) and BMI (kg/m<sup>2</sup>), a significant elevation in insulin level ( $\mu$ IU/l) and HOMA-IR test, a significant increase in nerve malondialdehyde (MDA), and tumor necrosis factor alpha (TNF $\alpha$ ) and a significant decrease in superoxide dismutase activity (SOD) and nerve conduction velocity (NCV) (m/s) after 5weeks of high fat diet in (Ob+HFD) group, when compared to NC group. Changing diet composition for 5weeks in Ob+ HFD+corn oil and Ob+HFD+omega 3 groups, did not induce any significant variation in body weight, BMI, or fasting blood glucose level as compared to Ob+HFD group. Insulin level ( $\mu$ IU/l) and HOMA-IR test were significantly decreased in Ob+ HFD+corn oil and Ob+HFD+omega 3 groups compared to Ob+HFD group. Plasma cholesterol levels (mg/dl), triglycerides (mg/dl), and free fatty acids (FFA) (mmol/l) were significantly decreased after 5weeks diet in Ob+ HFD+corn oil or Ob+HFD+ Omega 3 groups when compared to mean values of Ob+HFD group. Tissue malondialdehyde (MDA) and tumor necrosis factor alpha (TNF $\alpha$ ) were significantly decreased but superoxide dismutase (SOD) activity was significantly increased in Ob+HFD+corn oil and Ob+HFD+omega3 groups compared to Ob+HFD. NCV(m/s) in Ob+HFD+ corn oil group was significantly increased compared to Ob+ HFD and their values in Ob+HFD+ corn oil group showed no significant variation as compared to NC group. While there was a significant increase in NCV in Ob+ HFD+Omega 3 group as compared to Ob+ HFD group, there was still a significant decrease compared to NC group. **Conclusion:** The results of this study may have important clinical and speculative implications. Corn oil or omega 3 supplementation may be effective in obesity induced neuropathy. The mechanism of their effects is multifactorial including improving insulin sensitivity, correction of dyslipdemia, reducing oxidative stress and an anti-inflammatory effect. This possibility should be carefully considered and examined in future trials of essential fatty acid supplementation.

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**Key words:** nerve conduction velocity, obesity, oxidative stress, inflammation, corn oil, omega3, insulin resistance.

### 1. Introduction

Obesity is a pathological condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and/or increased health

problems [1]. Obesity is a major susceptibility factor leading to the development of various conditions of the metabolic syndrome. A recent study from the World Health Organization approximates that,

globally, 1.6 billion adults are overweight with at least 400 million adults classified as obese [2].

In obese rats, slowing of motor nerve conduction velocity was observed. Obese Zucker rats develop neural deficits independently of hyperglycemia [3]. Evidence for the development of neuropathic changes at the prediabetic stage, prior to development of overt hyperglycemia and diabetes mellitus, is emerging from both clinical [4] and experimental [5] studies. The pathophysiologic basis of this relationship is not well understood. A number of pharmacological agents that showed promise in animal studies have been withdrawn from clinical trials because of a lack of efficacy or adverse side-effects [6].

The induction of obesity may be performed in animals by neuroendocrine, dietary or genetic changes. [7]. High-fat diet (HFD)-fed rats with alimentary obesity and hyperinsulinemia, develop nerve conduction velocity deficit, therefore, represent an ideal model for evaluating effects of changing dietary composition on manifestations of neuropathy[8]. The contributions of insulin resistance, hypertriglyceridemia and/or increased nonesterified fatty acids (NEFA), and hypercholesterolemia to this condition remain unknown [9].

Fatty acids metabolism disturbance is very important in the occurrence of peripheral neuropathy. Low plasma omega-6 and omega-3 fatty acids levels were associated with accelerated decline of peripheral nerve function with aging [10]. Evidence has emerged suggesting that both omega-6 and omega-3 fatty acids are also important for peripheral nerve health and function [11].

The administration of unsaturated fatty acids especially omega-3 has gained considerable attention recently. The effect of omega-3 fatty acid on the treatment of coronary arteries atherosclerosis has been shown [12]. Consumption of Omega-3 fatty acids in animal models could be effective in restoring nerve conduction velocity [13]. Also, omega 6&9 poly unsaturated fatty acids (PUFA) supplied from corn oil has also been reported to be beneficial in systemic diseases, such as hypertension [14], cardiovascular disease [15] and cancer [16], however, little is known about the possible benefits that dietary omega-3 or omega 6&9 may have for the nerve conduction disorders in obesity. In this study, we propose that the lipid changes associated with obesity might partially explain the reported neural dysfunction. We consider the role that balanced diets high in omega 6&9 (corn oil) or supplying rats with omega 3, can have in modulating the impaired nerve function in obese rats.

## 2. Material and methods

### Experimental animals and groups

Thirty two adult male albino rats of body weight 80-100 gm, 3 to 4 weeks old, were included in this study. The rats were supplied by the Animal House Unit of Kasr Al-Ainy, Faculty of medicine, Cairo University, housed in cages at room temperature with normal light & dark cycle. The rats were randomly assigned to receive normal chow; control group (NC) [16] (n=8), and HFD [17] (n=24), for 12 weeks. The composition of the different experimental diets used is shown in table 1.

**Table 1:** The composition of experimental diets

Ingredients Contents (g/kg diet)	HFD (animal fat)	HFD (animal fat) +corn oil	Control diet (NC)
Carbohydrates			
-Corn starch	100	100	480
-Sucrose	100	100	100
Fats			
- Soybean oil	50	50	50
- Animal fat	500	300	120
- Corn oil		200	
Protein			
- Casein	190	190	190

This study was carried out in the Physiology and Biochemistry Departments, Faculty of Medicine, Cairo University. After 12 weeks, the rats were classified into:

**Group 1:** they are the normal rats, received normal chow and served as normal control. They continued free access to laboratory rat chow and tap water and received 4 mL of normal saline through gavage daily for another 5 weeks (NC). The HFD-fed rats were divided into 3 groups, 8 rats each:

**Group 2:** Ob + HFF group, they are obese rats those continue their high animal fat diet and received 4 mL of normal saline through gavage for 5 weeks.

**Group 3:** Ob +HFD+ corn oil group, they are obese rats, received high fat diet. In this group of rats, corn oil was administered as 20% of the diet, replacing same percent of animal fat and received 4 mL of normal saline through gavage daily. Corn oil contains high omega 6&9 polyunsaturated fat [18]. FA analysis of corn oil showed that corn oil contained mono unsaturated fatty acids (27.576%), poly unsaturated fatty acids (PUFA) (57.36%), omega 6 (58%) and omega 9 (28%), fatty acids in the percent shown in table 2 [19].

**Table 2:** The fatty acid analysis of corn oil

	Saturated fatty acids	MUFA	PUFA	Omega 3	Omega 6	Omega 9
<b>Corn oil</b>	12.948	27.576	57.36	1	58	28

Values are expressed as weight percent (%) of total fat.

**Group 4:** Ob + HFD + Omega 3 group, they are obese rats, fed high fat diet rich in saturated animal fat for 5 weeks and received omega 3 (0.4 g/kg BW) daily through gavage [20]. Each Omega-3 capsule contains Fish Oil (Omega-3 Docosahexaenoic acid DHA 12%, eicosapentaenoic acid EPA 18%) 999 mg, Vitamin E 1 mg, Gelatin (food grade) 371 mg  $\alpha$  alpha tocopherol is included in the capsule to avoid auto-oxidation.

#### **Weight measurements:**

All rats were weighed in grams and naso-anal lengths were measured in cm at the end of the 12-week study and at the end of the 5 weeks of different diet trial. The body mass index (BMI) was calculated (by dividing the body weight in kilograms by the length in meters squared) [21] at the end of the study period (after 12 weeks of NC and HFD and after 5 weeks of corn oil or omega 3 supplementation).

Rats were fasted overnight for at least 6 hours and blood samples were obtained by introducing a fine heparinized capillary tube at the inner canthus of the eye into the venous plexus. The blood samples were delivered into centrifuge tubes to which anticoagulant was added then centrifuged at 10,000 rpm for 20 minutes and plasma was separated and stored at -70°C for measuring fasting blood glucose level, insulin level and HOMA-IR test were evaluated. Plasma cholesterol, triglycerides and FFAs were measured. The rats were then killed and sciatic nerves were carefully dissected for measuring of nerve conduction velocity, tissue superoxide dismutase activity (SOD), malondialdehyde (MDA) and tumor necrosis factor alpha (TNF $\alpha$ ).

#### **Biochemical measurements**

##### **Measurement of fasting plasma glucose level**

Plasma glucose in blood samples was measured using oxidase- peroxidase method [22].

##### **Measurement of plasma insulin**

Plasma insulin levels were analyzed using enzyme-linked immunosorbent assay ELISA (Dako, Carpinteria, CA) according to the manufacturer's instructions [23].

##### **HOMA-IR test**

To estimate insulin resistance, the homeostasis model assessment for insulin resistance (HOMA-IR: insulin resistance index) [24] was used, calculated as the product of fasting insulin (in  $\mu$ IU) and fasting glucose (in mmol/l) divided by 22.5. A lower index indicates greater insulin sensitivity.

##### **FFA detection**

FFA was measured in plasma samples using Free Fatty Acid Quantification Kit supplied by Abcam USA according to manufacturer guide [25].

#### **Measurement of lipid**

Plasma total cholesterol was assayed as described by Siedel *et al.* [26], while the protocols of Jacobs and Van Denmark [27] was adopted for the determination of triglycerides (TAG).

#### **Measurement of MDA**

To measure the MDA concentration, 100 mg of sciatic nerve tissue in 1 mL PBS, pH 7.0 was homogenized with micropestle in microtube. 20 % TCA was added to nerve homogenate to precipitate the protein, and centrifuged. Supernatants were collected and thiobarbituric acid (TBA) solution was added to the supernatants. After boiling for 10 minutes in water bath, the absorbance was measured. Concentration of MDA in supernatants of nerve homogenate was calculated using the standard curve [28].

#### **Measurement of SOD activity**

Superoxide dismutase (SOD) activity in nerve homogenate was measured through the inhibition of nitroblue tetrazolium (NBT) reduction by O<sub>2</sub><sup>-</sup> generated by the xanthine/xanthine oxidase system. One SOD activity unit was defined as the enzyme amount causing 50% inhibition in 1 mL reaction solution per milligram tissue protein and the result was expressed as U/mg protein [29].

#### **Measurement of TNF- $\alpha$**

TNF- $\alpha$  was measured by in nerve tissues using ELISA (quantikine R&D system USA) according to the manufacturer's instructions [30].

#### **Nerve conduction velocity measurements:**

##### **Electrophysiological Recording:**

The Sciatic nerve was mounted in a nerve chamber designed for recording of action potential from isolated nerve. It contains 15 stainless wire electrodes. The nerve was dissected free without any muscles remnants. About 2 cm of the nerve was positioned over the electrodes and embedded in paraffin oil to maximize signal amplitude and prevent drying. The proximal part of the nerve was stimulated by 2 platinum stimulating hook electrodes and the recording electrode was placed 1 to 2 cm apart from the stimulating one.

Electrophysiological measurements were performed using an AD instruments Power Lab 4/25 stimulator and Bio AMP amplifier followed by a computer assisted data analysis. Sciatic nerves were stimulated with square wave pulses of 200  $\mu$ sec duration at 1-10 volts for conduction velocities. Conduction velocity is measured by dividing the distance between the stimulating and recording electrodes by latent period, which is the time elapsed between the application of stimulus until the peak of the maximum compound action potential (CAP) [31].



**Statistical analysis:**

Data were analyzed using the statistical package SPSS version 15. Values were expressed as mean + standard deviation (SD). Comparisons between groups were done using analysis of variance (ANOVA) with multiple comparisons post hoc test in normally distributed quantitative variables while non para metrical Mann- Whitney test was used for non normally distributed quantitative variables. *P*-values less than 0.05 were considered as statistically significant [32].

**3. Results****Effect of 12 weeks of HFD on body weight and BMI in rats:**

The results of this study showed a significant increase of body weight (gm) and BMI ( $\text{kg/m}^2$ ) in high fat diet group ( $p < 0.05$ ) when compared to control group (NC) after 12 weeks of the start of the diet, indicating presence of obesity in HFD group (Table 3, Figures 1,2).

**Effect of 5 weeks of HFD (without supplementation) on body weight and BMI:**

The results reported a significant elevation in the mean values of final weight measurements (gm) and BMI ( $\text{kg/m}^2$ ) in rats after 5 weeks of high animal fat diet (Ob+HFD), when compared to corresponding values of normal chow group (NC). (Table 4, Figures 3,4)

**Effect of 5 weeks of HFD on plasma glucose, insulin, HOMA-IR in obese rats:**

Table 5 and figures 5-7 show that HFD yielded an insignificant elevation in the mean value of fasting blood glucose level (mmol/l), while there was a significant elevation in insulin level ( $\mu\text{IU/l}$ ) and HOMA-IR test after 5 weeks of HFD compared to NC group. This reflects the effect of HFD on induction of insulin resistance.

**Effect of 5 weeks of HFD on cholesterol levels, triglycerides and free fatty acids.**

When observing levels of plasma cholesterol levels (mg/dl), triglycerides (mg/dl), and free fatty acids (mmol/l) after 5 weeks of high animal fat diet (Ob+HFD) in table 6 and figures 8-10, the present results recorded a significant elevation in their plasma levels compared to NC group, denoting the effect of obesity and HFD on dyslipidemia and elevation of plasma lipid levels.

**Effect of 5 weeks of HFD on oxidative stress and inflammation:**

Our results recorded a significant increase in nerve tissue malondialdehyde (MDA), and tumor necrosis factor alpha ( $\text{TNF}\alpha$ ) and a significant decrease in superoxide dismutase activity (SOD) after 5 weeks of high animal fat diet in obese rats compared to NC group (Table 7, Figures 11-13). This reflects

impairment of antioxidant activity and the effect of HFD in obese rats on elevation oxidative stress and increased the inflammatory marker.

**Effect of 5 weeks of HFD on nerve conduction velocity in obese rats:**

Interestingly, the current results recorded a significant decrease in nerve conduction velocity (NCV) (m/s) after 5 weeks of high animal fat diet (Ob+HFD), compared to values recorded from normal chow group of rats (NC) ( $p < 0.05$ ) (Table 8, Figure 14).

**Effect of changing diet composition in obese rats on different parameters: Ob+ HFD+corn oil versus Ob+HFD+ Omega 3:**

When observing the values of final body weight (gm) and BMI measurements ( $\text{kg/m}^2$ ) in rats after changing diet composition for 5W, we can observe that there was no significant variation in these values in Ob+HFD+ corn oil group or in Ob+HFD+omega 3 groups compared to values recorded in Ob+HFD group (Table 4 and Figures 3&4).

Furthermore, as shown in table (5) and figures (5-7) there was no significant variation in fasting blood glucose level in Ob+HFD+ corn oil and Ob+HFD+ Omega 3 group compared to Ob+HFD group. As regarding the mean values of fasting insulin level ( $\mu\text{IU/l}$ ) and HOMA-IR test after 5 weeks there was no significant variation between Ob+HFD+corn oil group when compared to Ob+HFD+Omega 3, however, the plasma levels of these parameters in the Ob+HFD+ corn oil and Ob+HFD+ Omega 3 groups were significantly decreased when compared to Ob+HFD. Thus, these results reflect that changing the formula of diet from HFD only to addition of corn oil or of omega 3 to HFD improved insulin sensitivity and decreased the exposure to insulin resistance condition.

When observing levels of plasma cholesterol levels (mg/dl), triglycerides (mg/dl), and free fatty acids (mmol/l) after 5 weeks diet (Ob+HFD+ corn oil or Ob+HFD+ Omega 3), table 6 and figures 8, 9 & 10 show no significant change in the mean values recorded between these 2 groups, but the mean values of these parameters in the 2 groups were significantly decreased when compared to mean values recorded in Ob+HFD group. This indicates that the corn oil or omega3 protected against dyslipidemia.

When nerve tissue malondialdehyde level (MDA), superoxide dismutase activity (SOD) and tumor necrosis factor alpha level ( $\text{TNF}\alpha$ ) were estimated after 5 weeks of high corn oil diet (Ob+HFD+ corn oil), or high fat diet supplemented with omega 3 (Ob+HFD+Omega 3) in male rats, it can be observed that there was no significant variation in mean values of MDA, SOD activity or  $\text{TNF}\alpha$  in Ob+HFD+ corn oil group compared to

Ob+HFD+ Omega 3 group, but the 2 groups showed significantly decreased tissue malondialdehyde and (MDA) and tumor necrosis factor alpha (TNF $\alpha$ ) levels and significantly increased superoxide dismutase activity (SOD) when compared to Ob+HFD (Table 7, Figures 11-13).

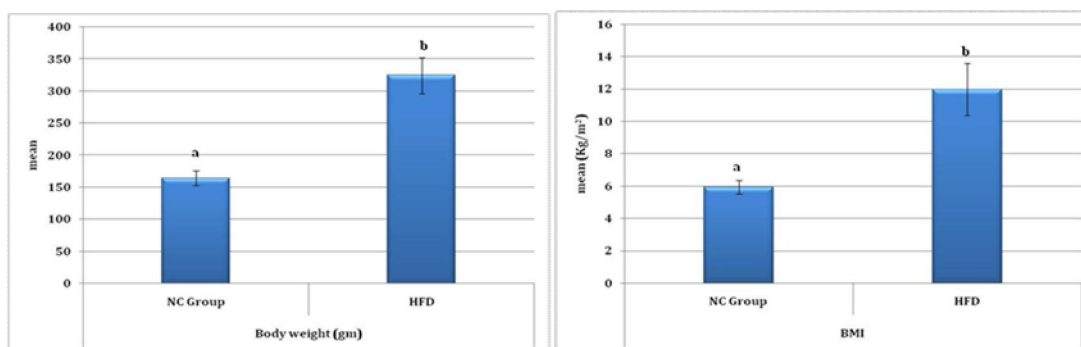
Regarding NCV(m/s) values, both in Ob+HFD+ corn oil and Ob+ HFD+Omega 3 groups, there was a significant increase compared to Ob+HFD and their values in Ob+HFD+ corn oil group showed no significant variation as compared to control group. In contrast in Ob+ HFD+Omega 3 group, there was a significant decrease in values of this group as compared to the control group and Ob+HFD+ corn oil (Table 8, Figure 14).

**Table 3:** Body weight measurements (gm) and body mass index (Kg/m<sup>2</sup>) in rats after 12weeks of normal chow (NC) (n=8), high animal fat diet (HFD)(n=24), in male rats.

	NC Group	HFD group
Body weight (gm) Mean $\pm$ SD	163.88 $\pm$ 11.52 <sup>a</sup>	324.25 $\pm$ 28.07 <sup>b</sup>
BMI (Kg/m <sup>2</sup> ) Mean $\pm$ SD	5.93 $\pm$ 0.40 <sup>a</sup>	11.69 $\pm$ 1.09 <sup>b</sup>

Results with different letters in the same raw are significant ( $p < 0.05$ )

Results with the same letter in the same raw are insignificant ( $p > 0.05$ ).



**Figure 1:** Body weight measurements (gm) and **figure 2:** body mass index in rats after 12weeks of normal chow(NC) (n=8), high animal fat diet (HFD)(n=24), in male rats.

Results with different letters are significant ( $p < 0.05$ ) Results with the same letter are insignificant ( $p > 0.05$ ).

**Table 4:**Final body weight measurements (gm) and body mass index(Kg/m<sup>2</sup>) in rats after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (Ob+HFD+Omega 3) in male rats.

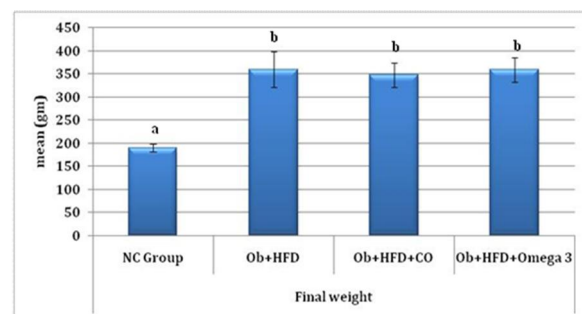
	NC group	Ob +HFD	Ob+ corn oil	Ob+HFD +Omega 3
Final weight (gm) Mean $\pm$ SD	189.50 $\pm$ 8.50 <sup>a</sup>	359.38 $\pm$ 38.53 <sup>b</sup>	347.25 $\pm$ 25.76 <sup>b</sup>	358.13 $\pm$ 26.16 <sup>b</sup>
BMI (kg/m <sup>2</sup> ) Mean $\pm$ SD	5.93 $\pm$ 0.40 <sup>a</sup>	11.96 $\pm$ 1.62 <sup>b</sup>	11.70 $\pm$ 0.55 <sup>b</sup>	11.90 $\pm$ 0.43 <sup>b</sup>

(n=8)

Results are mean  $\pm$  SD.

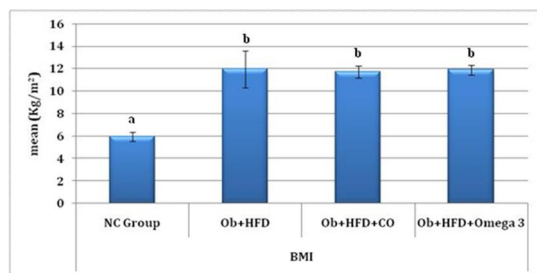
Results with different letters in the same raw are significant ( $p < 0.05$ )

Results with the same letter in the same raw are insignificant ( $p > 0.05$ ).



**Figure 3:** Final body weight measurements (gm) in rats after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats.

(n=8) -Results with different letters are significant ( $p < 0.05$ )-Results with the same letter are insignificant ( $p > 0.05$ ).



**Figure 4:** Body mass index (kg/m<sup>2</sup>) in rats after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats.

n=8

Results with different letters are significant ( $p < 0.05$ )

Results with the same letter are insignificant ( $p > 0.05$ ).

**Table 5:** Fasting plasma glucose level (mmol/l), insulin level(μIU/l) and HOMA-IR test after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet rich in polyunsaturated fatty acids(Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats.

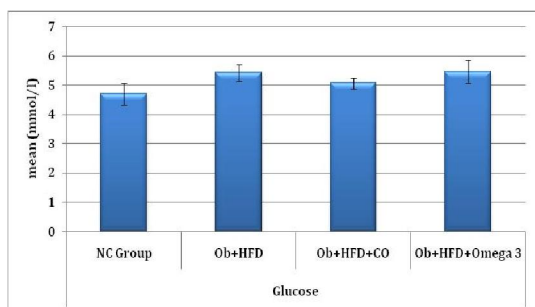
	NC group	Ob+HFD	Ob+HFD +corn oil	Ob+HFD + Omega 3
Glucose mmol/l	4.69 ± 0.37	5.41 ± 0.30	5.05 ± 0.18	5.45 ± 0.39
Insulin μIU/l	11.64 ± 0.78 <sup>a</sup>	20.59 ± 1.20 <sup>b</sup>	11.68 ± 0.74 <sup>a</sup>	11.55 ± 0.76 <sup>a</sup>
HOMA-IR	2.43 ± 0.26 <sup>a</sup>	4.95 ± 0.40 <sup>b</sup>	2.63 ± 0.23 <sup>a</sup>	2.80 ± 0.31 <sup>a</sup>

(n=8)

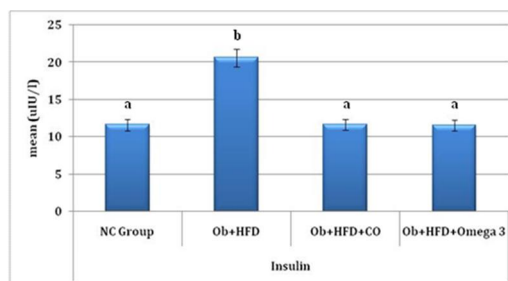
Results are mean ± SD.

Results with different letters in the same raw are significant ( $p < 0.05$ )

Results with the same letter in the same raw are insignificant ( $p > 0.05$ ).



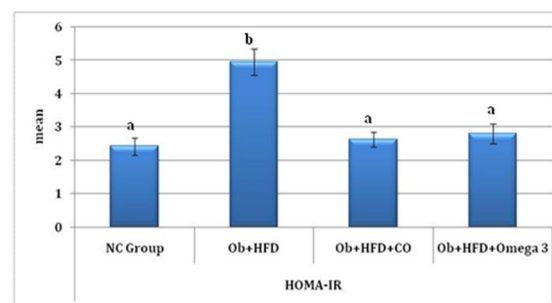
**Figure 5:** Fasting plasma glucose level (mmol/l) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet rich in polyunsaturated fatty acids ( Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats. Results in the different groups are insignificant to each other ( $p > 0.05$ ).



**Figure 6:** Insulin level(uIU/l) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet rich in polyunsaturated fatty acids(Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats.

Results with different letters are significant ( $p < 0.05$ )

Results with the same letter are insignificant ( $p > 0.05$ ).



**Figure 7:** HOMA-IR test after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet rich in polyunsaturated fatty acids(Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats.

Results with different letters are significant ( $p < 0.05$ )

Results with the same letter are insignificant ( $p > 0.05$ ).

**Table 6:** Plasma cholesterol levels (mg/dl), triglycerides (mg/dl), and free fatty acids (mmol/l) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (Ob+HFD+Omega 3) in male rats.

	NC group	Ob+HFD	Ob+HFD +corn oil	Ob+HFD + Omega 3
Cholesterol mg/dl	128.79 ± 2.86 <sup>a</sup>	188.44 ± 6.3439 <sup>b</sup>	140.86 ± 5.36 <sup>c</sup>	153.11 ± 2.00 <sup>c</sup>
Triglycerides mg/dl	72.43 ± 6.92 <sup>a</sup>	105.75 ± 2.80 <sup>b</sup>	84.53 ± 1.84 <sup>a</sup>	81.25 ± 1.64 <sup>a</sup>
FFA mmol/l	0.17 ± 0.04 <sup>a</sup>	0.52 ± 0.04 <sup>b</sup>	0.24 ± 0.02 <sup>a</sup>	0.27 ± 0.02 <sup>a</sup>

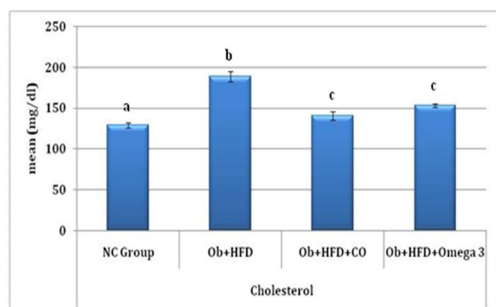
(n=8)

Results are mean ± SD.

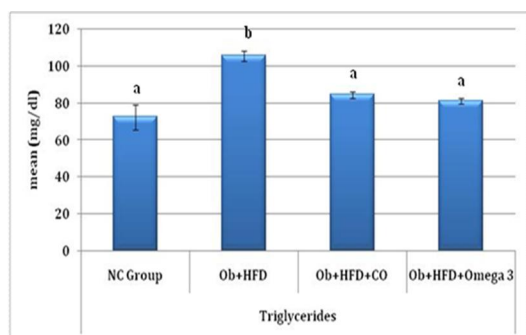
Results with different letters in the same are significant ( $p < 0.05$ )

Results with the same letter in the same raw are insignificant ( $p > 0.05$ ).

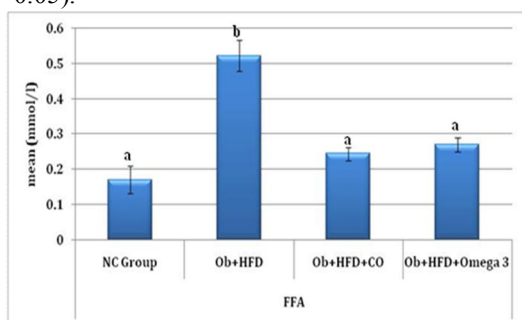




**Figure 8:** Plasma cholesterol levels (mg/dl) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (Ob+HFD+Omega 3) in male rats. Results with different letters are significant ( $p < 0.05$ ) Results with the same letter are insignificant ( $p > 0.05$ ).



**Figure 9:** Plasma triglycerides (mg/dl) after 5weeks of normal chow (NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (Ob+HFD+Omega 3) in male rats. Results with different letters are significant ( $p < 0.05$ ). Results with the same letter are insignificant ( $p > 0.05$ ).



**Figure 10:** Plasma free fatty acids (mmol/l) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (Ob+HFD+Omega 3) in male rats. Results with different letters are significant ( $p < 0.05$ ). Results with the same letter are insignificant ( $p > 0.05$ ).

**Table 7:** Tissue malondialdehyde level (MDA), superoxide dismutase activity (SOD) and tumor necrosis factor alpha level (TNF $\alpha$ ) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats.

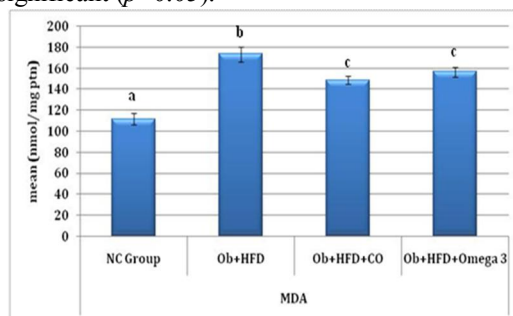
	NC group	Ob+HFD	Ob+HFD +corn oil	Ob+HFD + Omega 3
MDA nmol/mg ptn	111.36 $\pm$ 5.51 <sup>a</sup>	173.10 $\pm$ 7.07 <sup>b</sup>	148.51 $\pm$ 3.93 <sup>c</sup>	156.30 $\pm$ 4.84 <sup>c</sup>
SOD activity U/mg ptn	2.03 $\pm$ 0.17 <sup>a</sup>	0.45 $\pm$ 0.02 <sup>b</sup>	1.26 $\pm$ 0.15 <sup>c</sup>	1.60 $\pm$ 0.26 <sup>c</sup>
TNF $\alpha$ pg/ml	112.15 $\pm$ 2.07 <sup>a</sup>	234.89 $\pm$ 4.78 <sup>b</sup>	187.79 $\pm$ 4.62 <sup>c</sup>	207.23 $\pm$ 5.03 <sup>c</sup>

(n=8)

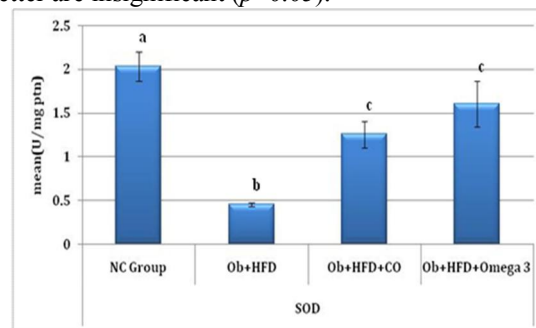
Results are mean  $\pm$  SD.

Results with different letters in the same raw are significant ( $p < 0.05$ )

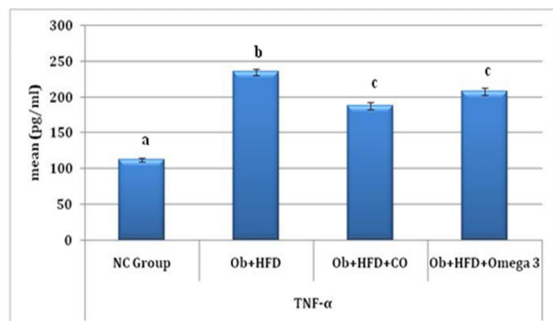
Results with the same letter in the same raw are insignificant ( $p > 0.05$ ).



**Figure 11:** Tissue malondialdehyde (MDA) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats. Results with different letters are significant ( $p < 0.05$ ). Results with the same letter are insignificant ( $p > 0.05$ ).



**Figure 12:** Tissue superoxide dismutase activity (SOD) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats. Results with different letters are significant ( $p < 0.05$ ). Results with the same letter are insignificant ( $p > 0.05$ ).



**Figure 13:** Tissue tumor necrosis factor alpha (TNF $\alpha$ ) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+HFD+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats.

Results with different letters are significant ( $p < 0.05$ ). Results with the same letters are insignificant ( $p > 0.05$ ).

**Table 8:** Nerve conduction velocity (NCV) (m/s) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats.

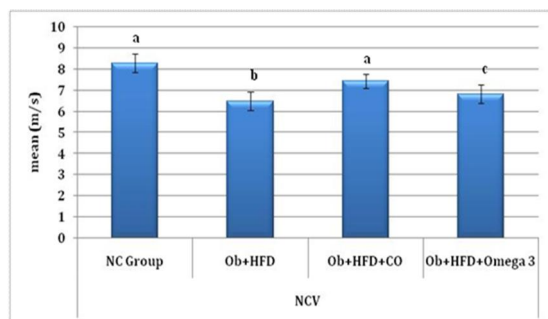
	NC group	Ob +HFD	Ob+HFD +corn oil	Ob+HFD + Omega 3
NCV m/s	8.28 $\pm$	6.49 $\pm$	7.85 $\pm$	7.22 $\pm$
Mean $\pm$ SD	0.44 <sup>a</sup>	0.43 <sup>b</sup>	0.33 <sup>a</sup>	0.43 <sup>c</sup>

(n=8)

Results are mean  $\pm$  SD.

Results with different letters in the same raw are significant ( $p < 0.05$ )

Results with the same letter in the same raw are insignificant ( $p > 0.05$ ).



**Figure 14:** Nerve conduction velocity (NCV) (m/s) after 5weeks of normal chow(NC), high animal fat diet (Ob+HFD), high corn oil diet (Ob+corn oil), or high fat diet supplemented with omega 3 (HFD+Omega 3) in male rats.

Results with different letters are significant ( $p < 0.05$ ) Results with the same letter are insignificant ( $p > 0.05$ ).

#### 4. Discussion:

Obesity is a strong risk factor for developing dyslipidemia [33,34], diabetes mellitus [35], fatty liver [36], cardiovascular (CV) diseases such as heart failure (HF) and coronary heart disease (CHD) [37].

Feeding of (HFD) to rats was proved to be a useful model of putative effects of dietary fat in humans [38]. In the present study, obesity was induced in rats by using a high fat diet. Obesity was induced in 12 weeks. The weight of rats fed HFD was significantly more than that of rats fed the normal diet. Rat models are therefore useful tools for inducing obesity as they will readily gain weight when fed high-fat diets [39]. Many workers were able to induce obesity in rats using different formulas of high fat diets [40-42].

An evidence for insulin resistance was recorded in the present study. Although fasting blood glucose levels were not significantly different between NC rats and Ob+HFD fed rats, insulin levels were significantly increased in Ob+HFD fed rats compared to NC rats and HOMA-IR test showed a significant increase in Ob+ HFD fed rats compared to NC rats. In agreement with our results, Oltman *et al.* [3] reported that obese Zucker rats are insulin resistant. Also Davidson *et al.* [43] reported that the obese Zucker HFD fed rats were not hyperglycemic; however, they were insulin resistant.

In contrast, Watcho *et al.* [8] and Obrosova *et al.* [44] reported that a 16-week HFD feeding resulted in a modest (14.5%) increase in non-fasting blood glucose concentrations compared with the mice fed NC which they described as being consistent with increased serum insulin concentrations as well as insulin resistance and impaired glucose utilization previously described in this model [45]. Moreover, Ishii *et al.* [46] reported that after 16 weeks of age, the group on a standard diet showed an increase in serum glucose levels and a decrease in serum insulin levels compared with high fat diet fed rats. Unexpectedly, in the group on the high-fat diet, they observed a suppressed of the progression of hyperglycemia and hypoinsulinemia. This might be explained in part by different animal species, variable duration of diet or by measuring non fasting blood glucose level.

We can see from these results that HFD fed obese rats developed insulin resistance, but did not developed diabetes or hyperglycemia.

It was also recorded from the results of this study that HFD in obese rats resulted in dyslipidemic changes as illustrated by increasing serum levels of triglycerides, total cholesterol, free fatty acids as compared to control; a finding in accordance with that of Woo *et al.* [47], and Kamal and Mohamed [48].

Dyslipidemic changes occurs in obesity may be due to the increased triglycerides content of the liver

due to increased influx of excess non esterified fatty acids (NEFAs) into the liver[49]. Lipid alterations affect the structure and function of the nerve membrane and have been considered as contributory factors to oxidative stress in obesity [50].

In the present study, it was found that nerve MDA level was significantly elevated with a significant decrease in the enzyme superoxide dismutase activity in HFD fed obese rats compared to NC rats and this was an indication for increased oxidative stress in these obese rats. Increased production of reactive oxygen species as well as reduced antioxidant defense mechanisms have been suggested to play a role in both humans and animal obesity induced pathology [51,52].

Interestingly, oxidative stress, the key metabolic abnormalities previously thought to be caused primarily by high glucose and shown to contribute to diabetic neuropathy, clearly manifest in this Ob+HFD model of pre-diabetic neuropathy characterized by insulin resistance in the absence of overt diabetes or hyperglycemia.

In this study, our obese rats also developed nerve disorder, demonstrated as NCV slowing. The finding that rats fed a high fat diet develop indices of neuropathy is consistent with studies of obese Zucker rats [3, 53], and also with clinical studies in which pre-diabetes and impaired glucose tolerance have been associated with an early-onset neuropathy [54, 55]. It was previously suggested that impaired glucose tolerance can directly cause nerve injury [56], however, it appears that NCV slowing is simply a covariant with other factors related to obesity.

This study shows that velocity of sciatic nerve conduction in obese rats could depend on dietary fat modification. The addition of omega 3 to high animal fat diet or consumption of corn oil rich in omega 6&9 PUFA in addition to animal fat was associated with increased sciatic nerve conduction velocity in obese rats, whereas high animal fat diet in obese rats caused a significant slowing of sciatic nerve conduction velocity. In addition, we found that omega 6&9 PUFA supplemented food (corn oil) induced a significant improvement of nerve conduction velocity compared to the enriching food with omega 3. These data show that omega 3 enrichment or corn oil could be associated with improved nerve conduction velocity in obese rats.

The present study provides evidence of the therapeutic efficacy of omega 6&9 PUFA and omega 3 on NCV deficits, in the model of neuropathy associated with obesity. It should be noticed that the improvement in NCV was not associated with weight reduction. As seen from the results of the present study, there is no significant change in final body weight or BMI between the obese groups fed HFD

with animal fat, corn oil or supplemented with omega 3 fatty acids.

Some previous studies suggested an association between insulin resistance, compensatory hyperinsulinemia, and peripheral neuropathy in human. Also, higher insulin resistance was independently associated with the presence of cardiac autonomic neuropathy (CAN) in Korean type 2 diabetes mellitus (T2DM) patients [57].

In the present study it was shown that either omega 3 or corn oil supplementation was associated with improved insulin sensitivity and decreased blood insulin level and this may play a role in improving nerve conduction, however the exact mechanism for this relation is not clear and needs further investigations.

One study provides evidence that insulin receptor substrate (IRS) proteins are expressed in the dorsal root ganglia (DRG) and could play an important role in the ability of insulin to support peripheral neurons. Elevated serine phosphorylation of IRS proteins reported in their study to be a major contributing mechanism underlying the effect of insulin resistance on neurons [58].

Insulin resistance is an important risk factor for endothelial dysfunction, and impairment of vascular function of epineurial arterioles precedes nerve dysfunction in obese normoglycemia Zucker rats [59]. It has been shown that improving insulin sensitivity improves vascular resistance in obese Zucker rats [60].

We can see from the results of the present study that dyslipidemia may be a contributing factor to reductions in peripheral nerve conduction velocity. This dyslipidemia was shown to be mostly corrected by dietary supplements and this correction appears to play a role in improvement of nerve conduction velocity, may be in part by a normalization of fatty acid composition of nerve membrane and eicosanoid synthesis, which is depressed in neuropathy and/or by a direct effect on incorporation of these fatty acids into the plasma membranes [61]. By changing membrane properties, omega 6&9 or omega 3 PUFA can modify the activity of transmembrane enzymes, such as Na,K- Atpase, which is implicated in the propagation of nerve impulses[62].

Our findings are consistent with studies showing that high dietary intake of fatty acids prevents the development and clinical progression of nerve conduction deficits in diabetic animals as well as in the general human population [63,11]. In diabetic rats, the administration of linoleic acid, an n-6 fatty acid, improved sciatic NCV [11]. In patients with generalized peroxisomal disorders, congenital diseases with impaired myelinogenesis, the administration of the n-3 fatty acids, DHA,

significantly improved myelin formation alleviating the symptoms in these patients [64].

PUFA are the major structural components of the neuronal membrane phospholipids [65] and therefore, their structural and chemical characteristics influence membrane functions, such as the activity of membrane bound proteins, signal transduction and also neurotransmission [66-68]. It was also reported that supplementation with sunflower oil, which contains high quantity of linoleic acid, restored NCV in diabetic rats, and this effect was accompanied by a modification of phospholipid fatty acid composition in nerve membranes [10].

In particular, the electrophysiologic effect of the omega-3 fatty acids seems to be the result of specific modulation of ion currents, particularly of the voltage-dependent sodium current and of the L-type calcium currents across sarcolemmal phospholipids membranes [68].

Mammals synthesize the long chain PUFA from linoleic acid [18:2(n-6)] and  $\alpha$ -linolenic acid [18:3(n-3)], which are the 2 precursors of (n-6) and (n-3) fatty acids families provided by the diet. Specific enzymes, desaturases and elongases, are involved in this pathway, but the conversion of precursors to long chain PUFA is generally low in humans. Consequently, the decrease in bioavailability of PUFA, affects the fatty acid composition of membrane phospholipids (PL) with repercussions on membrane protein functionality [69], eicosanoid production [70, 71], and peroxisome proliferator-activated receptor (PPAR) regulation [72,73].

It was suggested that the rate-limiting nature of  $\omega$ -6-desaturation contributes to the development of neuropathy. By passing the rate-limiting step by using gamma-linolenic acid (GLA) may have desirable effects and anti-inflammatory effects [74]. Because essential fatty acids (EFAs) and their metabolites are exceptionally important in both the structure and function of nerves [75], it seemed possible that neuropathy might be particularly responsive to PUFA supplementation.

An important observation in the results of this study is that omega-6 fatty acids, supplied by corn oil, appear to have a beneficial effect on peripheral nerve function than omega-3 fatty acids, requires consideration. In fact, omega-6 PUFAs are generally more highly represented in the nerve membrane than omega-3 fatty acids and have major effects of excess than the n-3 fatty acids [76].

The beneficial effects of omega 6&9 or omega 3PUFA may at least partially be related to inhibition of oxidative stress in peripheral nerve as evidenced in the present results by improving the antioxidant enzyme superoxide dismutase activity and decreasing oxidative stress marker MDA.

Oxidative stress is closely linked to upregulation of 12/15-lipoxygenase (12/15LO), an enzyme converting arachidonic acid to 12-Hydroxyeicosatetraenoic acid (12(S)-HETE), 15(S)-HETE, and a number of derivatives of these acids. These lipid-like compounds undergo spontaneous lipid peroxidation, which leads to induction of oxidative nitrosative stress, activation of mitogen-activated protein kinases (MAPKs), and proinflammatory response [77, 78]. MAPK activation has been demonstrated to play an important role in peripheral diabetic neuropathy [79, 80].

It was demonstrated that reducing oxidative stress in epineural vessels improved vascular relaxation to acetylcholine as well as NCV [52, 81-83]. The increase in superoxide in the aorta of high fat fed rats is likely due to increased NAD(P)H oxidase activity and/or expression, which has been linked to increased activity of angiotensin in obesity [84].

Finally, the results of the present study show that diet supplemented with omega 3 or PUFA rich in omega 6&9 fatty acids induce an anti-inflammatory effect as indicated by decreased TNF alpha content in the sciatic nerve of the obese rats.

Evidence for the importance of low grade inflammation in diabetic neuropathy is also emerging from both experimental and clinical studies [85,86].

Our results are in agreement with Ferrucci *et al.* [87] and Kapoor and Huang [88] who reported from their studies that n-3 PUFAs and the gamma linolenic acid (GLA), an n-6 fatty acid, have been shown to have significant anti-inflammatory properties. PUFAs inhibit the production of proinflammatory cytokines, i.e., IL-1 $\beta$ , IL6 and tumor necrosis factor-alpha by activating transcription factors, such as the peroxisome proliferator-activated receptors and nuclear factor kB [89]. As inflammation is one of the main pathophysiologic processes involved in peripheral polyneuropathy, it could be extremely relevant in progression of axonal damage [90].

Studies in normal volunteers indicate that omega-3 fatty acid supplementation reduced the ability of monocytes to produce IL-1 $\beta$  upon stimulation with endotoxin. The effect was most pronounced 10 weeks after stopping the supplementation and suggests prolonged incorporation of omega-3 fatty acids into a pool of circulating monocytes [91]. The capacity of the monocytes from these donors to synthesize IL-1 $\beta$  returned to the pre-supplement level 20 weeks after ending supplementation. Similar results were observed for IL-1 $\alpha$  and TNF [92].

Previous studies suggested that in patients affected by peripheral neuropathy, a supplementation with PUFA may positively influence the axonal degeneration of the nerve [10].



**Conclusion**

The results of this study have important clinical and speculative implications. Based on our findings, we suggest that corn oil or omega 3 supplementation may be effective in treatment of obesity induced neuropathy. The mechanism of their effects is multifactorial including improving insulin sensitivity, correction of dyslipidemia which could reflect on fatty acid composition of the nerve membrane structure and function, reducing oxidative stress and an anti-inflammatory effect. This possibility should be carefully considered and examined in future trials of essential fatty acid supplementation.

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## Impact of Uncertainties in Formation Thickness on Parameters Estimated from Well Testing Part 1: Gas Reservoirs

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**Abstract:** Well testing is of great importance in petroleum engineering, to have a kind of firsthand knowledge and estimating formation permeability, wellbore damage/ skin, etc. These parameters are further required to estimate production rate from a well and at the same time gives an idea of its productivity. These reservoir related parameters calculation is strongly dependent on formation thickness. Any uncertainty in formation thickness leads to ambiguous results, which in turn influences further reservoir development studies. This study focuses on analyzing the impact of such uncertainties and highlighting their effect on the resulting estimations, while considering cases of gas, oil and multiphase flow reservoirs one by one. The obtained results in case of gas reservoir shows that uncertainty in formation thickness has strong influence on well test estimated data.

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**Keywords:** Gas reservoir testing; thickness uncertainty; payzone uncertainty

### 1. Introduction

Conducting well test is of prime concern in the petroleum industry to check the potential of a reservoir (Shahin and Al-Awadly, 2011). Usually when it is conducted the drilled well do not have sufficient facilities to handle produced fluid(s), which can be harmful to the living organisms, vegetation and the soil itself, due to which sometimes different methods have to be adopted to reduce such disadvantages, like, decomposing the produced hydrocarbons (Okoro, Agrawal and Callbeck, 2012). Keeping in view such drawbacks, well test data need to be analyzed critically to rule out the chances of repeating such jobs.

Reservoir thickness has strong influence on test data interpretation and can be measured by using well logs, coring techniques, etc. These methods have their own limitations thus owing to different range of uncertainties in formation thickness estimation. According to Siemek et al. (Siemek and Nagy, 2004) in-accuracy in reservoir thickness can range from  $\pm 5\%$  to  $\pm 60\%$ . While estimating, parameters based on conducted well test or in other words, during well test analysis, thickness plays a significant role in calculating different formation properties. This paper thus focuses on analyzing such variations and their extent on calculated results in case of gas reservoir.

### 2. Parameters Affected by Formation Thickness

Formation thickness (F.H), in term of petroleum engineering or production geology can be described as a thickness of oil or gas formation, from where they are produced. F.H directly and indirectly

affects number of parameters and the following parameters have been included in this study:

Permeability can be determined by using the following equation (Lee, Rollins and Spivey, 2003).

$$k = 162.6 \frac{B_{g,avg} \cdot \mu_{g,avg}}{m h} \quad (1)$$

Further the radius of investigation, i.e., the distance from the well to which the pressure transient has moved can be estimated (Lee, Rollins and Spivey, 2003) by using equation (2).

$$r_i = \left( \frac{kt}{948 \phi \mu c_t} \right)^{0.5} \quad (2)$$

Similarly the drainage area can be calculated (Lee, Rollins and Spivey, 2003) by using equation (3) through by using the value of radius of investigation obtained by using eq.(2).

$$A = \pi r_i^2 \quad (3)$$

The influence of uncertainty in formation thickness can be analyzed indirectly (Lee, Rollins and Spivey, 2003; Chaudhry, 2003) by using the following equation (4) and further details can be found as discussed by Lee et al. (Lee, Rollins and Spivey, 2003) and the effective wellbore radius can be calculated by using the following equation (Lee, Rollins and Spivey, 2003; Chaudhry, 2003).

$$s = 1.151 \left[ \frac{b}{m} - \log \frac{k}{\phi \mu_{g,avg} c_{t,avg} r_w^2} + 3.23 \right] \quad (4)$$

$$r_{wa} = r_w e^{-s} \quad (5)$$

**3. Case Study**

The following set of data (table 1) has been used to analyze the effect of formation thickness uncertainty on above discussed parameters:

Table 1. Gas reservoir and well data

h (ft)	59
$\phi$ (%)	23
$B_{g,avg}$	0.59
$C_{t,avg}$ (psia <sup>-1</sup> )	$69.78 \times 10^{-6}$
$\mu_{g,avg}$ (cp)	0.0313
m	0.212
b	1.427
t(hrs)	50
$r_w$ (ft)	0.254

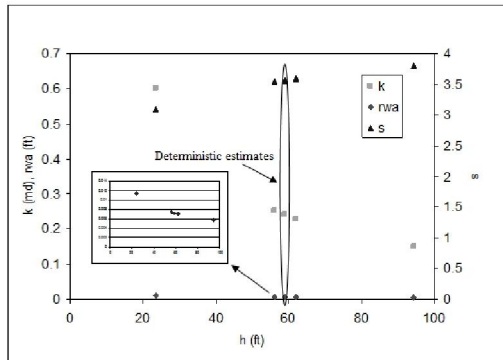


Figure 1. Influence of F.H uncertainty on permeability, effective wellbore radius and skin

Considering 59 ft as the deterministic values, uncertainties have been incorporated and the resulting formation thickness estimations are given in table 2. These set of formation thickness values are used to calculate the effect of F.H on formation permeability, skin, radius of investigation, drainage area and effective well bore radius.

Table 2. Deterministic and uncertainty incorporated values of formation thickness

h,ft (Deterministic value)	h,ft (including uncertainty)
59	23.6
	56.05
	61.95
	94.4

**4. Results and Discussion**

The obtained results using equations (1) to (5) are shown in the following figures 1 and 2:

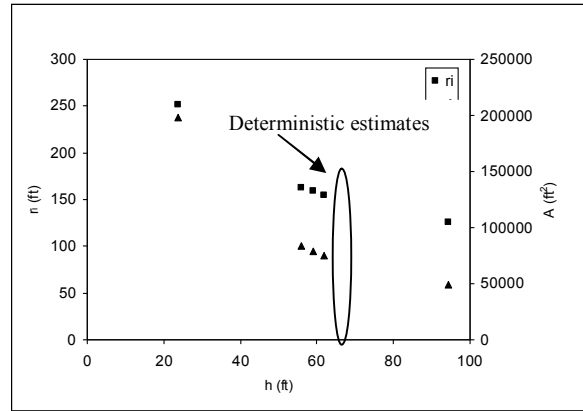


Figure 2. Effect of uncertainty in payzone thickness on radius of investigation & drainage area

The obtained results show that, inverse relationship exists between F.H and permeability, effective wellbore radius ( $r_{wa}$ ), radius of investigation & drainage area. While, a direct relationship exist between variation in F.H and formation damage. i.e., as the formation thickness increases skin increases.

Further, the % deviation in the estimated parameters based on uncertainty with reference to deterministic values has been calculated using the following equation and the obtained results are shown in figure (3).

$$\% \text{ Deviation} = \frac{\text{Deterministic value} - \text{Uncert. value}}{\text{Deterministic value}} \times 100 \quad (6)$$

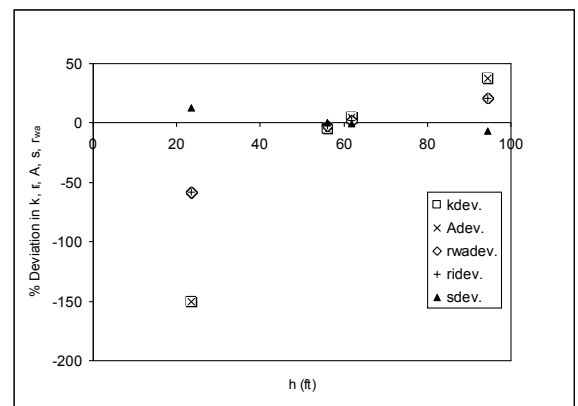


Figure 3. Percentage deviation in estimated parameters with reference to deterministic values

The above figure shows that the pessimistic and optimistic values of formation thickness based on uncertainty have highest and same deviation in



calculated permeability and drainage area values (-150% to 4.76%). Similarly, comparatively it has lesser and similar effect on radius of investigation and effective wellbore radius (-58.11% to 2.4). The obtained results also show that the degree of uncertainty in F.H has least influence on skin values, with a deviation of -0.68% to 12.87%.

## 5. Conclusion

The uncertainty in formation thickness affects all other estimated reservoir parameters. This study shows that these variations can be significant, especially in case of permeability, in particular. Which is a very crucial parameter, because of its usage in reservoir deliverability analysis and fluid dynamics studies. Therefore, uncertainty in formation thickness should be dealt with great care to cope with sources of errors in a better manner during gas reservoir exploitation.

## 6. Nomenclature

A	area
b	intercept
$B_g$	gas formation volume factor
$C_t$	total compressibility
h	formation thickness
k	permeability
m	slope
$r_i$	radius of investigation
$r_w$	wellbore radius
$r_{wa}$	effective wellbore radius

s	skin
t	time
$\phi$	porosity
$\mu$	viscosity

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## Impact of Uncertainties in Formation Thickness on Parameters Estimated from Well Testing Part 2: Oil Reservoirs

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**Abstract:** Formation thickness is of vital significance in estimating different reservoir parameters in oil reservoirs. Any error or uncertainty in formation thickness can contribute as tremendous source of error while estimating different parameters based on well testing, like, permeability, radius of investigation, etc. In this second part of the study, a pressure-buildup test has been analyzed, while incorporating the uncertainties in formation thickness. The effect of these uncertainties has been included in different calculations like, permeability, skin-factor, radius of investigation, wellbore storage, etc. The results show that the uncertainty in formation thickness affects all the aforementioned parameters, though the degree of influence can be different.

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**Keywords:** Oil reservoir; interpretation uncertainty; uncertainty impact

### 1. Introduction

As discussed previously in Part 1 of the paper (Zahoor and Khan, 2012), based on literature survey conducted by Siemek et al. (Siemek and Nagy, 2004), uncertainty in measured value of formation thickness (F.H) or pay zone (P.Z) can range from  $\pm 5\%$  to  $\pm 60\%$ . Furthermore, in previous study conducted by us (Zahoor and Khan, 2012) well test data of a gas reservoir was analyzed while taking into account such uncertainties, while here the study has been extended to oil reservoirs.

In this study, a pressure-buildup test conducted after a single constant rate flow has been analyzed while incorporating uncertainty in P.Z thickness value into effective oil permeability, radius of investigation, drainage area and skin-factor.

### 2. Incorporating Uncertainty in Formation thickness into Various Parameters

Payzone or formation thickness directly influences the permeability which in-turn effects other parameters calculated based on well test (Chaudhry, 2004; Chaudhry, 2003). This can be explained with the help of a flow chart as shown in figure (1), along with the equations selected from the work accomplished by Lee et al. (Lee, Rollins and Spivey, 2003) to be used for their estimation during this study.

### 3. Analyzing the Impact of P.Z Uncertainty on Welltest data Interpretation

The following set of data has been used to analyze the effect of formation thickness uncertainty on above discussed parameters, as given in table 1.

**Table 1:** Oil reservoir description and well parameters

Reservoir and Fluid Properties	
	1.132 cp
	39 %
$B_o$	1.24 RB/STB
$p_{thr}$	1647 psia
$P_{wf}$	1187 psia
$h_{deterministic}$ value	107 ft
$C_t$	$20.4 \times 10^{-6}$ psia <sup>-1</sup>
$m$	98.76 psia/cycle
$t$	67 hours
$q_o$	489 Stb/day
$r_w$	0.254 ft

From the deterministic value, using the minimum and maximum possible percentage uncertainty, the resulting values of payzone thickness becomes; 42.8, 101.65, 112.35 and 171.2 ft, which has been used to estimate different parameters calculated from well testing.

### 4. Results and Discussion

The obtained results using above mentioned data (table 1) and equations expressed in flow chart (figure 1) are shown in figures 2 and 3.

This study shows that, decrease in formation thickness gives a resulting stimulation effect, as reflected by decrease in “s-factor”, shifting it to negative value from higher positive. Further, it is noticed that the relationship between formation thickness and the estimated parameters in case of oil

reservoir, is the same as in case of gas reservoirs(Zahoor and Khan,2012) and can be summarized as follows (table 2):

Table 2: Influence of F.H on various parameters under consideration

Parameter	Payzone thickness
Permeability, Radius of investigation, drainage Area, effective wellbore radius	Inverse
Skin-factor	Direct

Furthermore, in terms of magnitude the extent can be different in case of gas and oil reservoirs, but still the relative change is same, as

shown in figure (4) in case of “s” estimation (even though the deterministic value of formation thickness is different in both cases, i.e., 59 ft(Zahoor and Khan,2012) and 107 feet respectively). The relative change is calculated by using the following equation:

$$\text{Relative change} = \frac{S_{\text{based on max.F.H}} - S_{\text{based on min.F.H}}}{S_{\text{based on max.F.H}}}$$

The obtained relative change value in case of oil and gas reservoirs has also been plotted in figure (4) against their respective maximum formation thicknesses (94.4 ft in case of gas reservoir(Zahoor and Khan,2012) and 171.2 ft in case of oil reservoir).

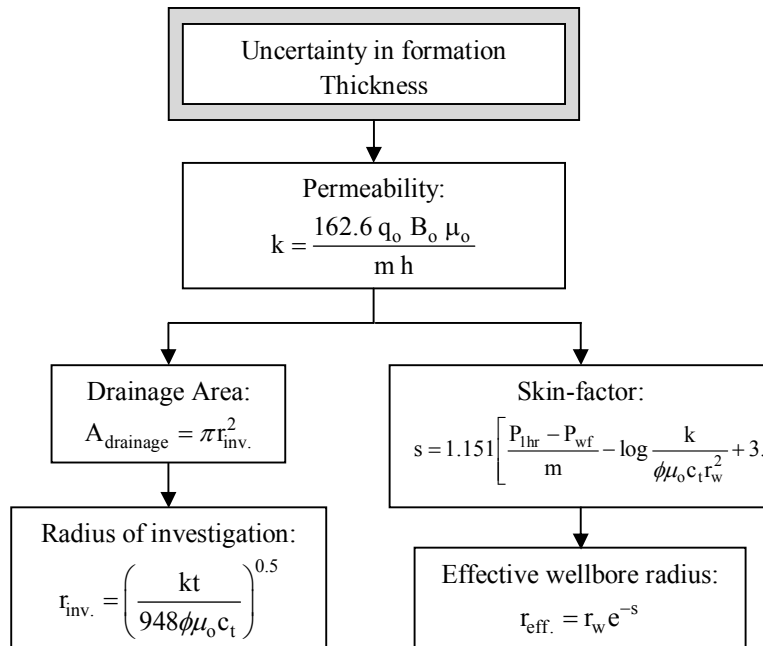


Figure 1: Flow chart and stepwise calculation procedure of calculating different F.H dependent parameters

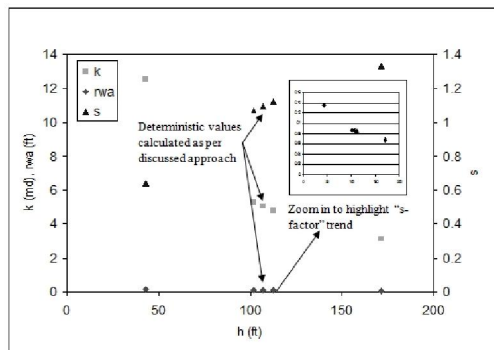


Figure 2. Estimated k,  $r_{wa}$  and s-factor based on deterministic value and including degree of uncertainty in formation thickness

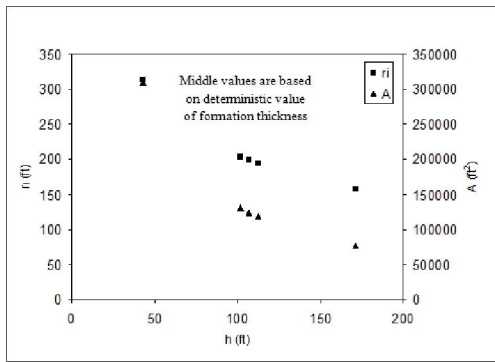


Figure 3. Estimations of “ $r_i$ ” and “A” based on different values of payzone/ formation thickness

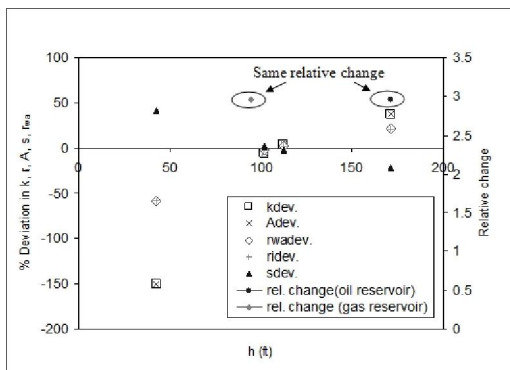


Figure 4: Estimated percentage deviation and relative change in “s”

### 5. Conclusions and Recommendations

Uncertainty in formation thickness measurement affects various parameters taken into account, during this study. So, special care should be taken in decreasing the magnitude of inaccuracy in formation thickness measurements to have more reliable results, based on which further reservoir studies can be conducted.

Further it can also be concluded that if uncertainty in payzone thickness significantly effects the well test data interpretations in case of single phase flow, then the study should be further extended

to multiphase flow reservoirs which are also commonly encountered.

### 6. Nomenclature

A	area
$B_o$	oil formation volume factor
$C_t$	total compressibility
h	formation thickness
k	permeability
m	slope
p	pressure
$q_o$	oil flow rate
$r_{inv.}$	radius of investigation
$r_w$	wellbore radius
$r_{eff.}$	effective wellbore radius
s	skin
t	time
	porosity
	viscosity

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## Error Generated due to Inaccuracy in Payzone Thickness While Interpreting Multiphase Flow Buildup Well Test Data

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**Abstract:** While performing reservoir related studies either conducted by an engineer or a production geologist, one have to deal with number of uncertainties arising from different sources based on the manner by which different properties required to be used as an input while evaluating buildup well test data. Out of the required input parameters, payzone thickness have a kind of key significance, as most of the well test estimated data is directly or either indirectly depend on it. Most of the petroleum reservoirs have multiphase flow, so in this study buildup test data for multiphase flow have been analyzed while incorporating the payzone thickness uncertainty.

[Zahoor M. K., Khan A. **Error Generated due to Inaccuracy in Payzone Thickness While Interpreting Multiphase Flow Buildup Well Test Data.** *Life Sci. J* 2012;9(4):478-479] (ISSN: 1097-8135).  
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**Keywords:** multiphase fluid reservoir; multiphase well test data; payzone uncertainty

### 1. Multiphase Flow Buildup Test Data Interpretation

In our previous studies (Zahoor and Khan,2012<sup>1</sup>;Zahoor and Khan,2012<sup>2</sup>) effect of uncertainties in formation thickness values on well test data interpretation for gas and oil reservoirs have been discussed. Here the study is extended to reservoirs producing multiphase flow. In a reservoir whether it is declared as gas or oil producing formation, encountering multiphase flow is a common phenomenon. In case of gas reservoirs; flow of gas, water and gas condensate might exists at a time and similarly as a general practice gas and water is produced with oil as a main stream in case of oil reservoirs. After drilling upto or through the pay, well test is conducted to have a prime knowledge of reservoir behavior, expected fluids flow rate and other fluid and reservoir properties. Payzone thickness has great significance in performing fluid in place calculations and also to estimate/predict various reservoir properties. Today, different techniques are available in the industry to measure payzone thickness as accurate as possible. But due to different limitations of these techniques accuracy of the measured value ranges between five to sixty percent, which has also been used in earlier research(Zahoor and Khan,2012<sup>1</sup>;Zahoor and Khan,2012<sup>2</sup>;Siemek and Nagy,2004). Here a research has been conducted to analyze the effect of such uncertainty on buildup test data interpretations, conducted on a well producing, gas, oil and water.

In this study, the methodology proposed by Perrine (Perrine,1956) has been adopted, because of vast acceptability in such cases and has also been discussed number of time in the literature. Briefly, the respective approach can be described as below and

further details can be found in literature(Lee, Rollins and Spivey,2003;Bourdarot,1996;Jun and Minglu,2011).

Effective fluid (gas, oil and water) permeabilities can be calculated by using the following equations (1-3):

$$k_g = \frac{162.5(q_{gt} - q_o R_s \times 10^{-3})B_g \mu_g}{m h} \quad (1)$$

$$k_o = \frac{162.5q_o B_o \mu_o}{m h} \quad (2)$$

$$k_w = \frac{162.5q_w B_w \mu_w}{m h} \quad (3)$$

While the total mobility and skin can be estimated by using eqs. (4 & 5).

$$\lambda_{total} = \frac{162.6[q_o B_o + q_w B_w + (q_{gt} - q_o R_s \times 10^{-3})B_g]}{m h} \quad (4)$$

$$s = 1.151 \left[ \frac{(p_{thr} - p_{wf})}{m} - \log \left( \frac{\lambda_{total}}{\phi c_r r_w^2} \right) + 3.23 \right] \quad (5)$$

### 2. Mutliphase Fluid Flow Properties and Well Data: A Case Study

The following is the well test and fluid properties used in this study, as mentioned in table 1:

Table 1: Parameter used for analysis

$q_{gt}$	1332 MScf/d
$q_o$	1595 Stb/d
$q_w$	409 Stb/d
$R_s$	240 Scf/Stb



$\mu_o$	0.524 cp
$\mu_g$	0.0166 cp
$\mu_w$	0.313 cp
$B_o, B_g, B_w$	1.214, 1.579, 1.008
$C_o, C_g, C_w$	0.0001, 0.00041, $9.8 \times 10^{-6}$ psi <sup>-1</sup>
$\phi, h$ (deterministic)	0.198 %, 55 ft
$P_{wf}, p_{1hr}$	1656, 1888 psia
$S_g, S_w$	12.5, 38.2

### 3. Results and Discussion

The obtained results based on the above mentioned methodology are given in table 2, while incorporating uncertainty in formation thickness.

Table2. Effect of pay zone uncertainty on well test Interpretation

h	$k_g$	$k_o$	$k_w$	$\lambda_{total}$	s
<i>1. Uncertainty due to core analysis</i>					
49.5	0.67	27.1	3.45	103.1	-3.2
55	0.6	24.4	3.1	92.8	-3.12
60.5	0.54	22.2	2.8	84.3	-3.07
<i>2. Uncertainty due to log analysis</i>					
44	0.75	3.56	3.9	116	-3.23
55	0.6	24.25	3.11	92.8	-3.13
66	0.5	20.4	2.6	77.3	-3.03
<i>3. Uncertainty arising from geological interpretation</i>					
22	1.5	61.13	7.8	232	-3.58
55	0.6	24.45	3.1	92.8	-3.13
88	0.37	15.3	1.9	58	-2.891

The obtained results show that the as the thickness increases, effective permeability of the fluids flowing in a reservoir decreases. As the mobility or total mobility is strongly based of these effective permeabilities, so as a result it also decreases. The same is the case with formation damage or skin. The negative sign with the skin factor "s", shows stimulation, so in this cases the stimulating effect decreases with the increase in payzone thickness.

### 4. Conclusions and Recommendations

Inaccuracy in formation thickness measurement (IFTM) has strong influence on set of information derived from multiphase flow well test data (IMWTD). Generally, on most of the calculated parameters included in this study and earlier studies conducted by us (Zahoor and Khan, 2012<sup>1</sup>; Zahoor and Khan, 2012<sup>2</sup>), IFTM has inverse effect, i.e., as IFTM decreases, most of the significant parameters value, increases.

These set of studies show that uncertainty in formation or payzone thickness should be handled

carefully to have better well test data interpretation and also the time to conduct such tests should be reduced, especially in the cases where there is lack of surface facilities to handle and process the produced fluids in an appropriate manner.

### 5. Nomenclature

B	formation volume factor
$c_t$	total compressibility
g, o, w	subscripts: gas, oil and water
h	formation thickness
k	permeability
m	slope
p	pressure
$p_{wf}$	wellbore flowing pressure
q	flow rate
$Q_{gt}$	total gas produced
$r_w$	wellbore radius
sskin	
$\phi$	porosity
$\mu$	viscosity

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## Water Quality Assessment of Taleghan River

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**Abstract:** There are several factors influencing the water quality based on its usage. The quality of drinking water is of the vital concern for human health and life. An essential attempt has to be done to develop a water quality index (WQI) corresponding with different conditions and characteristics of the relevant river or water body such as geographical, hydrological, discharge rate and pollution sources. The index is not specifically focused on human health or aquatic life regulations. However, a water index based on some very important parameters can determine a simple indicator of water quality. In the present study, the Taleghan water quality has been evaluated by available NSF water quality index. Subsequently, the nine present NSF parameters' weights have been changed and modified using the analytical hierarchy process (AHP) method as well as experts' opinions in the field in a way to satisfy local conditions. In the newly developed WQI, more weights are given to relation with these parameters it can be said that the factors like dissolved oxygen (Do), fecal coliform (F.c) and biological oxygen demand (BOD) when compared with NSF-WQI.

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**Keywords:** Water Quality; NSF Index; Talegan River; Iran

### 1. Introduction

The access to "closer and cleaner drinking water" is still a distant dream for about one-sixth of humanity on this planet (Harvey et al., 2002; Smedley and Kinniburgh, 2002). It is predicted that this increasing scarcity, and competition over water resources in the first quarter of the 21st century will dramatically change the way we value and use water (Mroczek, 2005; Maqbool et al., 2011). Assessment of surface water quality can be a complex process undertaking multiple parameters capable of causing various stresses on overall water quality.

The requirement of water in all forms of lives, from micro-organisms to man, is a serious problem today because many water resources have been reached to a point of crisis due to unplanned urbanization and industrialization (Singh et al., 2002; Dixit and Tiwari, 2008). Water quality degradation through different sources as well as different monitoring methods have been widely considered in the literature (Ali et al., 2004; Nakane and Haidary, 2010; Bhatnagar and Sangwan, 2009; Taseli, 2009; Najafpour et al., 2008; Joarder et al., 2008; Rene and Saidutta, 2008; Monavari and Guieysse, 2007; Jeong et al., 2010). Surface waters are most exposable to pollution due to their easy accessibility for disposal of wastewaters (Samarghandi et al., 2007). The consumption of different contaminants present in various industrial and agricultural sectors through biodegradation, or toxicity resistance to these pollutants by the microbial communities can provide

information about pollutant exposure, metabolic diversity and the potential source of contamination and the potential for the ecosystem natural attenuation, thus may be a practical indicator of the water quality (Monavari and Guieysse, 2007). Both the anthropogenic influences such as urban, industrial and agricultural activities increasing exploitation of water resources as well as natural processes, such as precipitation inputs, erosion, weathering of crustal materials, degrade surface waters and damage their use for drinking, industrial, agricultural, reaction or other purposes (Jarvie et al., 1998; Simeonov et al., 2003; Mahvi et al., 2005; Nouri et al., 2008; Karbassi et al., 2008). Rivers play a major role in assimilation or transporting the municipal and industrial wastewater discharge constitutes a constant polluting source, whereas surface run off is a seasonal phenomenon, largely affected by climate within the basin (Singh et al., 2004; Karbassi et al., 2007; Karbassi et al., 2008; Najafpour, 2008). Due to increasing problem of deterioration of river water quality, it is necessary to monitor the water quality in order to evaluate the production capacity (Mishra et al., 2009).

Over the past few years, a number of different tests have been developed to determine the organic content of wastewater (Sawyer et al., 1994). Many environmental indices have recently been suggested by different organizations and institutes, so that at the last decade of the 20th century much interest has been created to improve control water quality indices.

One of the methods that has led to an improvement over the old indices is the comparison of these indices with each other. In this regard, the first comparison among quality indices of water was conducted by Ott in 1971; he compared two indices which had been created by Landor and Deninger and revised the quality indices in USA. Two indices which were presented by them belong to general and particular consumption indices. Such research has also been conducted in European countries. Brokel and Helmond proved through the results of their research about environmental indices that around 30 indices can be applied throughout the world to classify water quality. They showed that all indices include between 3 to 72 variables which have been selected from NH<sub>4</sub>+N, PO<sub>4</sub> + P, NO<sub>3</sub>+N, PH and total solid (Ramirez and Solano, 2004).

In Iran water quality indices are under consideration too, such as the research conducted by Tajrishi and Norouzian in 1998 using a fuzzy classification technique on the Karoon and Dez rivers whereby these rivers were zoned qualitatively (Norouzian, 1998; Parvizi et al., 2004).

## 2. Material and Methods

To analyze and interpret the kinds of parameters measured along the range of a river, there are various mathematical methods that are used such as water quality index. It is one of the simplest methods with wide applications. In this method a considerable amount of data resulting from measurements of water quality are converted to a single and dimensionless number in a rated scale with interpreted quality and conception.

In general, water quality indices are divided into many methods (Sobhani, 2003), and the public indices is one of these methods which ignores the kind of water consumption in the evaluation process, NSF WQI, is among public indices (Ott, 1978) (Horton, 1965).

Among the public water quality indices, NSF is the most applicable index in this regard. On the other hand, the parameters considered in this index are mostly the parameters that are measured in the river water quality monitoring programs and environmental assessment (Zandberg and Hall, 1988).

### NSF Water Quality Index:

A Water Quality Index for the United States of America was developed by the National Sanitary Foundation (NSF) in 1970 to monitor the variation trend in river water quality. It has been used throughout the USA by the executive agencies. This index represents the general water quality status of monitoring stations using 9 quality parameters. This index has the capability of being estimated using

existing data from water quality parameters, if data for some parameters are lost. Parameters that are required for this index are as follows: fecal coliforms, BOD<sub>5</sub>, turbidity, pH, TSS, D<sub>0</sub>%, NO<sub>3</sub>, PO<sub>4</sub> and ΔT. Measured parameters according to the sub-index of each of them are achieved on conversion curves. Then, to estimate the final index the following equations are used (NSF, 2003):

$$NSFWQI = \sum_{i=1}^n W_i q_i$$

q<sub>i</sub>= Sub-index of each parameters

W<sub>i</sub>= Weighting factor

n= Number of sub-indices

Table one shows the ranking criteria of NSF water quality index and, in Table two, the weights of the water quality parameters are presented.

According to the book Field Manual for Water Quality Monitoring, the National Sanitation Foundation surveyed 142 people representing a wide range of positions at the local, state, and national level about 35 water quality tests for possible inclusion in an index. Nine factors were chosen and some were judged more important than others, so a weighted mean is used to combine the values so that field measurements could be converted to index values, respondents were asked by questionnaire to graph the level of water quality (0 through 100) corresponding to the field measurements (e.g., pH 2-12). The curves were then averaged and are thought to represent the best professional judgment of the respondents.

When test results from fewer than all nine measurements are available, we preserve the relative weights for each factor and scale the total so that the range remains 0 to 100.

Taleghan with about 1300 square kilometers in area 36 degrees 12 minutes north latitude and 50 degrees is 47 minutes North West of Tehran and part of Alborz province (Figure 1).

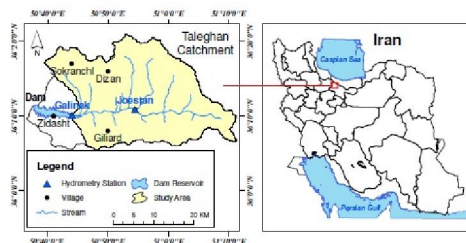


Figure 1. Location of Taleghan Watershed

In this study, sampling was done from 6 local streams in the study area. In order to consider the effect of flow quantity on the amount of different

parameters, sampling was done in two year (August 2008 until July 2010).

In Figure 3 the values of the final index for each station have been shown separately based on measuring results in the water considered, after the calculate with NSF modeling.

### 3. Results

In this study, sampling was done from 6 local streams in the study area. In order to consider the effect of flow quantity on the amount of different parameters, sampling was done in two year (August 2008 until July 2010).

In Figure 3 the values of the final index for each station in each season have been shown separately based on measuring results in the water considered, after the calculate with NSF modeling.

### 4. Discussions

Due to the lack of expert study and inspection of the water quality of most rivers of Iran, using water quality indices for particular consumption is considered as a simple method for the primary recognition of river water quality. Due to qualitative evaluation along the river, all the urban wastewater of Taleghan city enters the Taleghan River at stations 5 and 6. But river water is appropriate for drinking water and agricultural consumption at all stations is good. According to the aforementioned issues, to improve the river water quality it is necessary that the relevant authorities build a wastewater treatment plant for Taleghan city and, because of reduction in the dissolved oxygen downstream of the agriculture complex, manufacturing re-aeration structures such as concrete

spill ways in the river can contribute to promote its power of self-purification.

This table is based on an average of two years of design

Quality	Value
Very good	90-100
Good	70-90
Medium	50-70
Bad	25-50
Very bad	0-25

Table 1- Water quality value

Water Quality Factors and Weights	
Factor	Weight
Dissolved oxygen	0.17
Fecal coliform	0.16
pH	0.11
Biochemical oxygen demand	0.11
Temperature change	0.10
Total phosphate	0.10
Nitrates	0.10
Turbidity	0.08
Total solids	0.07

Table 2- Importance rate and parameters weight in NFSWQI (NSF water quality index ranking).

Table 3- Water Quality monitoring along with Taleghan River

Table 4- Water quality index (NSF result)

Table 3- Water Quality monitoring along with Taleghan River

Season	Station	Water Quality index									Total result
		T	DO	NO <sub>3</sub>	Turbidity	FC	pH	BOD	PO <sub>4</sub>	TS	
Summer	1	93	59	95	73	91	92	15	75	53	72
	2	81	74	95	75	82	86	12	96	56	74
	3	67	72	95	73	70	85	16	94	55	66
	4	93	71	95	67	63	82	25	95	56	68
	5	93	58	95	60	55	88	40	92	48	69
	6	89	57	93	58	45	84	7	96	49	63
Fall	1	93	73	95	82	99	67	13	97	46	75
	2	93	71	94	78	91	68	7	98	51	73
	3	85	73	91	77	78	69	10	96	55	64
	4	89	59	92	76	65	58	20	98	50	66
	5	81	60	87	73	58	57	9	97	46	62
	6	89	71	91	70	49	54	18	96	47	64
Winter	1	93	56	91	56	99	90	11	95	67	74
	2	93	59	71	65	99	86	28	94	53	73
	3	89	60	67	62	80	84	12	96	57	68
	4	85	56	67	29	69	85	9	97	57	62
	5	85	42	86	24	63	84	23	98	50	61
	6	89	45	63	5	54	84	6	96	52	55
Spring	1	93	56	93	45	82	83	7	94	79	70

	2	85	55	92	35	82	79	11	98	68	67
	3	89	54	90	37	67	82	14	98	70	66
	4	89	59	89	33	60	79	10	98	70	64
	5	89	52	87	27	56	80	11	96	67	62
	6	89	40	66	24	46	76	7	95	68	55

Table 4- Water quality index (NSF result)

Station	Spring	Summer	Fall	Winter
1	Good	Good	Good	Good
2	Medium	Good	Good	Good
3	Medium	Medium	Medium	Medium
4	Medium	Medium	Medium	Medium
5	Medium	Medium	Medium	Medium
6	Medium	Medium	Medium	Fair

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## Comparison of serum calcium, total protein and uric acid levels between hypertensive and healthy pregnant women in an Iranian population

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**Abstract:** The objective of this study was to compare serum calcium, total protein, and uric acid levels between hypertensive and healthy pregnant women. In this cross-sectional study, 100 healthy and 48 hypertensive pregnant women with singleton pregnancy who were at  $\geq 28$  weeks of gestation were included and serum calcium, total protein, and uric acid levels were compared between these two groups. Hypertensive group consisted of 28 subjects with mild preeclampsia, 17 with severe preeclampsia. Mean ( $\pm$ SD) serum calcium level was 7.88 ( $\pm$ 0.94) mg/dl (range, 6.94-8.82) in hypertensive and 8.28 ( $\pm$ 0.77) mg/dl (range, 7.51-9.05) in control group ( $P = 0.01$ ). Mean ( $\pm$ SD) serum total protein level was 6.023 ( $\pm$ 0.91) gr (range, 5.32-7.14) in hypertensive and 6.13 $\pm$ 0.77 (5.36-6.9) in control group ( $P > 0.05$ ). Mean ( $\pm$ SD) level of serum uric acid was 5.32 ( $\pm$ 1.41) mg/dl (range, 3.91-6.73) in hypertensive and 4.55 ( $\pm$ 1.14) mg/dl (range, 3.41-5.09) in control group ( $P = 0.001$ ). Mean serum Ca level was significantly lower in hypertensive pregnant women in comparison with healthy ones. Considering this factor in prenatal care is important.

[Azin Alavi, Keramat Allah Jahanshahi, Samie Karimia, Nasim Arabzadea, Soghra Fallahi. **Comparison of serum calcium, total protein and uric acid levels between hypertensive and healthy pregnant women in an Iranian population.** *Life Sci J* 2012;9(4):485-488] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 73

**Keywords:** Calcium; Uric acid; Pregnancy; Hypertensive disorder

### 1. Introduction

Hypertensive disorders in pregnant women are one of the major factors that cause high risk pregnancy and fetal and maternal morbidity. These disorders are most seen in primiparas and are reported in 10% of pregnancies. Early diagnosis of these disorders is a way of reducing maternal and neonatal morbidity/mortality (1-8). Epidemiological evidence suggests changes in the metabolism of calcium (Ca) as a responsible factor in the path physiology of preeclampsia. Hence, decreased in Ca intake may result in progression of preeclampsia to eclampsia (5, 6, 9).

There have been efforts to recognize a useful laboratory test to predict prognosis of hypertensive women in pregnancy. In a meta-analysis by Thangaratnam et al. on the level of uric acid during pregnancy, it was concluded that this factor is not an accurate predisposing factor. This finding agrees with the data reported by Cnossen et al. (10, 11). In another study, it was noted that severe preeclampsia and eclampsia were accompanied by decreased levels of serum Ca and total protein and on the other hand increased level of serum phosphorus (5). Likewise, lower serum Ca and higher uric acid levels were reported in pregnancy-induced hypertension (PIH) compared to normotensive women (6). A significant correlation between serum Ca and hypertension has

been shown in PIH (7). It has been reported that patients with high risk pregnancies (e. g., risk of progressive hypertension and those with low amounts of dietary Ca) can benefit from Ca supplementation (8). Regarding the aforementioned data we decided to measure the serum levels of Ca, total protein, and uric acid in a sample of hypertensive women in pregnancy.

### 2. Material and Methods

This cross-sectional study was done at Shariati Hospital, Bandar-Abbas, southern of Iran. One-hundred healthy pregnant women were entered into the study and were compared to 48 hypertensive pregnant women. All subjects were at 28 weeks of gestation or more at the time of entry and the subjects of the two groups were matched regarding age and parity and BMI. All cases had singleton pregnancy. Exclusion criteria were overt and/or gestational diabetes mellitus, nephropathy, glomerulopathy, and history of hypocalcaemia.

Hypertension was defined as blood pressure (BP) over 140/90 mmHg which was measured in two separate occasions six hours apart. Hypertensive women were categorized as following. Preeclampsia is defined as blood pressure (BP) of at least 140/90 mmHg after 20th week of gestation accompanied by proteinuria of at least 300 mg per 24 hours in previously normotensive women. The patients with

systolic blood pressure  $\geq 160$  mmHg or diastolic blood pressure  $\geq 110$  on two occasions with proteinuria equal or more than 2 grams in 24 hour urine sample or any of severe preeclampsia's criteria including oliguria (urine volume less than 500 cc per 24h), Thrombocytopenia (platelet count less than 100000), raised liver enzymes; aspartate aminotransferase (SGOT)  $> 50$  U/L or alanine aminotransferase (SGOT)  $> 60$  U/L, epigastric pain, pulmonary edema, visual or brain function disturbance or intrauterine growth restriction of the fetus were considered as severe preeclampsia. Eclampsia is recognized by occurrence of seizure in preeclampsia that is not correlated with other causes. Predesigned checklists were used to gather required data. The checklist had two parts. The first part consisted of questions regarding age, gravidity, gestational age, underlying disease, cause of admission, and history of hypertension. The second part included data regarding results of measuring serum levels of Ca, total protein, uric acid, complete blood count (CBC), fasting blood glucose (FBS), and urine analysis which these blood samples were performed in third trimester of pregnancy ( $\geq 28$  weeks of gestation) at time of admission before termination of pregnancy. All subjects were followed up for 48 hrs after delivery. Analysis of data was done using the SPSS Software for Windows (Ver. 16.0). The quantitative data were compared between the two

studied groups by the student t-test. Significant level was set as  $P < 0.05$ .

### 3. Results

Mean ( $\pm$ SD) age of control group was 26.6 ( $\pm 6.73$ ) years and in hypertensive this figure was 27.96 ( $\pm 6.25$ ) years. The oldest subject in control group had 43 years of age and in hypertensive had 44 years of age. The two groups were not different in terms of their mean age (Table 1). Mean ( $\pm$ SD) gestational ages in control group and hypertensive were 38.37 ( $\pm 2.12$ ) weeks and 36.06 ( $\pm 4.46$ ) weeks, respectively ( $P = 0.008$ ). In hypertensive group, 28 subjects (53.9%) had preeclampsia, 17 subjects (32.7%) had severe preeclampsia, and three subjects (0.97%) were diagnosed by eclamptic. Mean ( $\pm$ SD) blood platelet levels in control group and hypertensive were  $229 \times 10^3$  ( $\pm 72.3 \times 10^3$ ) vs.  $191 \times 10^3$  ( $\pm 80.5 \times 10^3$ ) ( $P = 0.005$ ). Mean ( $\pm$ SD) hemoglobin levels were 11.61 ( $\pm 1.99$ ) g/dl in control group and 11.85 ( $\pm 1.32$ ) g/dl in hypertensive (Table 1). Mean ( $\pm$ SD) serum Ca levels in control group and hypertensive were 8.28 ( $\pm 0.77$ ) mg/dl and 7.88 ( $\pm 0.94$ ) mg/dl, respectively ( $P = 0.01$ ). Table 3 presents the measured laboratory indices in the two groups. This study demonstrated very significant correlation between serum uric acid level and type of hypertensive disorder ( $p < 0.05$ ).

**Table 1.** Mean serum calcium, protein and uric acid to separate the blood disorder

Groups	Control	Mild preeclampsia	Severe preeclampsia	Eclampsia	P value
Number	100	8.28 $\pm$ 7.6	6.13 $\pm$ 5.1	4.54 $\pm$ 4.2	
Serum Ca levels (mg/dl)	28	7.88 $\pm$ 6.1	6.28 $\pm$ 4.5	5.04 $\pm$ 4.6	0.01
Total protein (gr/dl)	17	7.86 $\pm$ 6.6	6.15 $\pm$ 4.8	5.30 $\pm$ 4.5	NS
Serum uric acid level (mg/dl)	3	7.30 $\pm$ 6.7	5.63 $\pm$ 4.7	7.26 $\pm$ 5.2	0.001

Data are shown as mean $\pm$ SD; NS: Not significant (Pvalue  $> 0.05$ )

### 4. Discussions

In this study serum Ca, total protein and uric acid levels in healthy pregnant women (100 cases) and hypertensive pregnant women (48 cases) were measured and compared. Considering that mean of gestational age in control group was 38.37 ( $\pm 2.12$ ) weeks and in hypertensive group was 36.06 ( $\pm 4.46$ ) weeks, it can be concluded that pregnant women of this region postpone prenatal care for near the end of pregnancy except those who have disorders like hypertension. Serum Ca level difference was statistically significant between the two groups. Most studies on this issue confirm that high serum Ca level

in pregnancy can lead to decreased incidence of preeclampsia (1, 5-7, 12-16). Multiple interventional studies have assessed the effect of Ca by prescribing variant types of Ca included diets in pregnant women. It has been noted that such dietary regimens can be effective in reducing BP and hypertensive disorders (8, 17-19). Ca supplements (1.5-2 gr as cacarbonate) have been prescribed for prevention of pregnancy disorders and their benefits have been proven in some investigations (20, 21). A study that reviewed 12 clinical trials also demonstrated that Ca supplements can lead to reduction in PIH in comparison with placebo (22). Other study

demonstrated that serum Ca level in healthy pregnant women did not have any statistically significant difference in comparison with pregnant women who suffered from hypertensive disorders and low level of Ca could not be the cause of hypertension and related disorders in pregnancy (10, 23-26). One of the causes might be diet consisting of calcium and territorial condition of Iran. The condition is sunny and the diet include dairy. A clinical trial consisted of 4589 nullipar pregnant women in 13-21 gestational age showed that Ca has no more effect rather than placebo on PIH (27). Mehri et al.(28) and Eini et al. (29) established that serum Ca level has no obvious difference in hypertensive women compared to healthy ones and Ca included dietary regimens cannot prevent from progression of preeclampsia. Vancho et al. reported that Ca included regimens are not useful for diminishing the severity of preeclampsia if the Ca level is not low as enough for presence of preeclampsia (30). Positive effect of mother's serum Ca in breastfeeding ability amelioration has also been mentioned (9). We found that serum total protein cannot be a predictive factor for preeclampsia incidence, because its difference in the two groups was not significant. This observation is similar to that of Salari et al. study (23). But this result was in contrast to Shahverdi et al. finding (5). Difference observed with respect to serum uric acid level between the two groups was significant and its level was higher in hypertensive women. In Almasganj et al. study, that serum uric acid level in healthy pregnant women was compared with hypertensive pregnant women, similar result was found. Significant lower platelet count in hypertensive women is the result of thrombocytopenia in patient with PIH. Abbasnik et al. carried out a study and compared blood platelet levels in preeclampsia and healthy pregnant women. They demonstrated that platelet level was obviously higher in healthy women than preeclampsia patients (31). Due to our findings we can conclude that serum Ca level in patients with hypertensive disorders is lower than healthy pregnant women and this result showed that hypocalcaemia can accompanied by hypertensive disorders during pregnancy. According to most studies, dietary regimens which include Ca can prevent hypertensive disorders, so administration of Ca supplements can minimize these disorders. Considering there are not enough studies assessing serum total protein levels and there was no difference between the two groups regarding this factor, serum total protein level cannot be a strong predictive factor to diagnose hypertensive disorders during pregnancy. Our study and another study (6) showed that uric acid levels are high in hypertensive patients. But Thangaratinam et al. (32) concluded from a meta-

analysis that uric acid level measurement in pregnant women is not a strong predictive factor. Different references declared that serum Ca level diminishes during the third trimester of pregnancy (1). On the other hand there is a rising necessity of Ca during this trimester. Considering high prevalence of preeclampsia in our country(33) and especially in our study area, Bandar-Abbas- Iran special attention to nutritional conditions of pregnant women seems warranted. According to what mentioned in this article and necessity of special attention on this issue, we suggest:

1. Prospective studies with larger sample size and finding more factors for earlier diagnosis of hypertension in pregnancy.
2. Special attention to nutritional condition in pregnant women particularly in geographical regions that prevalence of malnutrition is high.
3. Educating pregnant women about nutrition during pregnancy and informing them about probable risks of inappropriate diet.

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## FACTS devices stabilizer design by using Genetic Algorithms

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**Abstract:** Stability of power system is an important issue and should be considered and improved. Flexible AC Transmission Systems (FACTS) can be used to improve power system stability. Stability enhancement can be improved via damping of low frequency oscillations (LFO). Static Synchronous Series Compensator (SSSC) can be used for LFO damping. In this paper SSSC is used to damp out LFO and a supplementary stabilizer based on SSSC is designed. Genetic Algorithms (GA) is used to adjust the parameters of the proposed stabilizer.

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**Keywords:** Low Frequency Oscillations, Static Synchronous Series Compensator, Supplementary Stabilizer, Genetic Algorithms

### 1. Introduction

With the practical applications of converter-based flexible AC transmission system (FACTS) controllers [1] such as the static synchronous compensator (STATCOM) [2], static synchronous series compensator (SSSC) [3] and unified power-flow controller (UPFC) [4], modeling and analysis of these FACTS controllers in power-system operation and control is of great interest. Power-flow calculations are fundamental to the operation, planning and control of power systems. In recent years, significant work has been done in the modeling of the FACTS controllers in power flow and optimal-power-flow studies [5–12].

SSSC is a voltage-sourced converter-based series compensator and was proposed within the concept of using converter-based technology uniformly for shunt and series compensation, as well as for transmission angle control. It has been successfully applied in power systems. In this paper, SSSC is used to increase power system stability. A supplementary stabilizer is equipped based on SSSC. The parameters of the proposed stabilizer are tuned by using PSO.

### 2. Static Synchronous Series Compensator (SSSC)

SSSC is one of the most important FACTS devices. It is installed in series with transmission line. This device has a voltage source converter serially connected to a transmission line through a transformer. It is necessary an energy source to provide a continuous voltage through a condenser and to compensate the losses of the VSC. A SSSC is able to exchange active and reactive power with the transmission system. But if our only aim is to balance the reactive power, the energy source could be quite small. The injected voltage can be controlled in phase

and magnitude if we have an energy source that is big enough for the purpose. With reactive power compensation only the voltage is controllable, because the voltage vector forms 90° degrees with the line intensity. In this case the serial injected voltage can delay or advanced the line current. This means that the SSSC can be uniformly controlled in any value, in the VSC working slot.

The Static Synchronous Series Compensator (SSSC) uses a VSC interfaced in series to a transmission line, as shown in the Figure 1. Again, the active power exchanged with the line has to be maintained at zero hence, in steady state operation, SSSC is a functional equivalent of an infinitely variable series connected capacitor. The SSSC offers fast control and it is inherently neutral to sub-synchronous resonance.

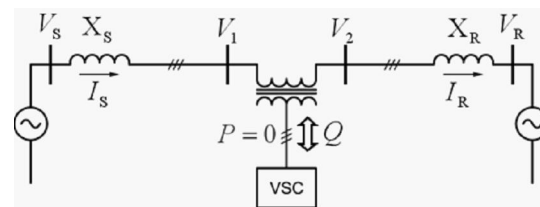


Figure 1: SSSC - A VSC interfaced in series to a transmission line

As mentioned, Static Synchronous Series Compensator (SSSC) is placed in the group of series connected FACTS devices. As shown in Figure 2, SSSC consists of a voltage source inverter connected in series through a coupling transformer to the transmission line. A source of energy is required for providing and maintaining the DC voltage across the DC capacitor and compensation of SSSC losses. Figure 3 shows the model of SSSC which consists of a series connected voltage source in series with

impedance. This impedance represents the impedance of coupling transformer. The SSSC when operated with an appropriate DC supply (an energy source and/or sink, or suitable energy storage) can inject a component of voltage in anti-phase with the voltage developed across the line resistance, to counteract the effect of the resistive voltage drop on the power transmission.

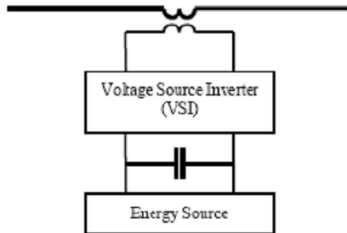


Figure 2: basic configuration of SSSC

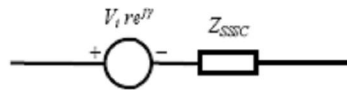


Figure 3: equivalent circuit of SSSC

**3. Test system**

A multi machine power system installed with SSSC is considered as case study. The proposed system is shown in figure 4. The SSSC is installed in line 4 and system data can be found in [13].

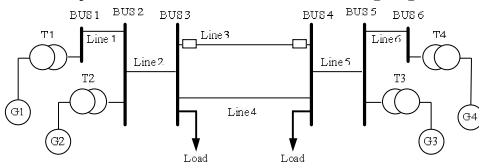


Figure 4: power system installed with SSSC in line 4

**4. Power system stabilizer**

An AVR (without supplementary control loops) can weaken the damping provided by the damper and field windings. This reduction in the damping torque is primarily due to the voltage regulation effects inducing additional currents in the rotor circuits that oppose the currents induced by the rotor speed deviation  $\Delta\omega$ . Adding supplementary control loops to the generator AVR or FACTS devices is one of the most common ways of enhancing both small-signal (steady-state) stability and large-signal (transient) stability. The Stabilizer can be used to add damping signal to the SSSC, where the output signal of the stabilizer is used as an additional input ( $v_{stab}$ ) to the SSSC. The stabilizer input signal can be either the machine speed deviation,  $\Delta\omega$ , or its acceleration power. The stabilizer is modeled by the nonlinear system depicted in Figure 5.

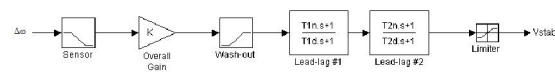


Figure 5: Conventional stabilizer

The model consists of a low-pass filter, a general gain, a washout high-pass filter, a phase-compensation system, and an output limiter. The general gain  $K$  determines the amount of damping produced by the stabilizer. The washout high-pass filter eliminates low frequencies that are present in the  $\Delta\omega$  signal and allows the stabilizer to respond only to speed changes. The phase-compensation system is represented by a cascade of two first-order lead-lag transfer functions used to compensate the phase lag between the excitation voltage and the electrical torque of the synchronous machine.

**5. Genetic Algorithms**

Genetic Algorithms (GA) are global search techniques, based on the operations observed in natural selection and genetics. They operate on a population of current approximations-the individuals-initially drawn at random, from which improvement is sought. Individuals are encoded as strings (Chromosomes) constructed over some particular alphabet, e.g., the binary alphabet {0,1}, so that chromosomes values are uniquely mapped onto the decision variable domain. Once the decision variable domain representation of the current population is calculated, individual performance is assumed according to the objective function which characterizes the problem to be solved. It is also possible to use the variable parameters directly to represent the chromosomes in the GA solution. At the reproduction stage, a fitness value is derived from the raw individual performance measure given by the objective function and used to bias the selection process. Highly fit individuals will have increasing opportunities to pass on genetically important material to successive generations. In this way, the genetic algorithms search from many points in the search space at once and yet continually narrow the focus of the search to the areas of the observed best performance. The selected individuals are then modified through the application of genetic operators. In order to obtain the next generation Genetic operators manipulate the characters (genes) that constitute the chromosomes directly, following the assumption that certain genes code, on average, for fitter individuals than other genes. Genetic operators can be divided into three main categories: Reproduction, crossover and mutation [14].

**6. Design methodology**

The proposed supplementary stabilizer is designed based on the SSSC in the given test system. The performance index is considered as (3). In fact, the performance index is the Integral of the Time multiplied Absolute value of the Error (*ITAE*).

$$ITAE = \int_0^t t|\Delta\omega|dt \quad (3)$$

It is clear to understand that the controller with lower performance index is better than the other controllers. To compute the optimum parameters, different faults are assumed and then the best responses are chosen. It should be noted that GA algorithm is run several times and then optimal set of parameters is selected. The optimum values of the stabilizer parameters are obtained by using GA and summarized in the Table 1

Table 1: Obtained parameters of stabilizer

parameter	K	T <sub>1n</sub>	T <sub>1d</sub>	T <sub>2n</sub>	T <sub>2d</sub>
value	12.0	0.39	0.01	0.30	0.01

**7. Simulation result**

The proposed stabilizer is evaluated based on the test system. Large disturbance is considered to show ability of the proposed stabilizer. The simulation results are depicted in figures 6-8. Each figure contains two plots as: **Solid**: with stabilizer and **dashed**: without stabilizer. It is seen that the system without stabilizer contains insufficient damping and the responses are pendulous. But the stabilizer can greatly enhance power system stability and damp out the oscillations and the advantages of the proposed stabilizer are visibly seen.

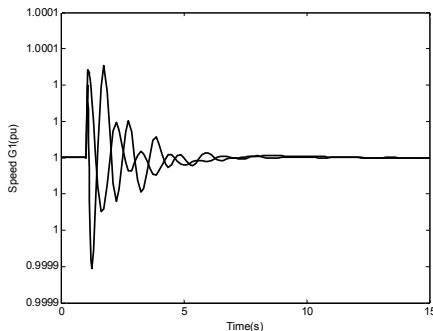


Figure 6: Speed G<sub>1</sub> following 10 cycle three phase short circuit in bus 1

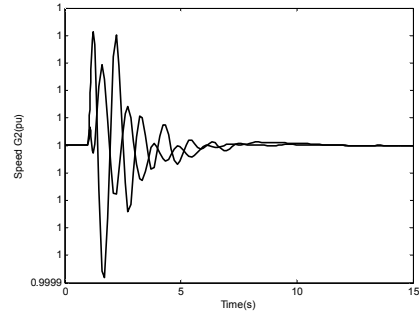


Figure 7: Speed G<sub>2</sub> following 10 cycle three phase short circuit in bus 1

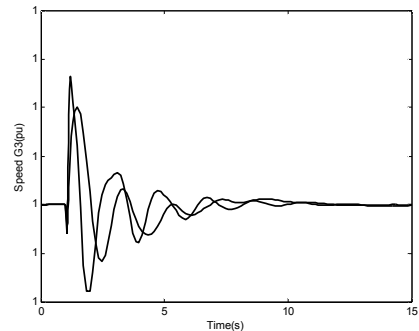


Figure 8: Speed G<sub>3</sub> following 10 cycle three phase short circuit in bus 1

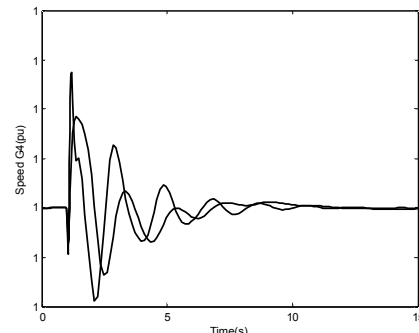


Figure 9: Speed G<sub>4</sub> following 10 cycle three phase short circuit in bus 1

**8. Conclusion**

A supplementary stabilizer based on SSSC presented here. A two area power system assumed to show the ability of the proposed method. Non linear simulation results demonstrated that the designed stabilizer capable to guarantee the robust stability and robust performance under disturbances. Also, simulation results show that the PSO is a suitable tool to design stabilizer parameters.

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9/20/2012

## **Biostratigraphy, Microfacies and sedimentary environment of of the Oligo-Miocene sequence (Asmari Formation) in Chidan area, Zagros Basin, southwest Iran**

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**Abstract:** The foraminifers biostratigraphic study in Chidan area led to recognition of 2 biozones, In this study, eight different microfacies types have been recognized. These carbonate microfacies belonging to: open marine (A), bar/shoal (B), lagoon (C) and tidal flat (D). The depositional environment of the Asmari Formation is interpreted as a shallow carbonate ramp.

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**Key words:** Asmari Formation; Zagros; Chidan; Gachsaran; Pabdeh; Zagros; Iran

### **Introduction**

The Oligocene-Miocene Asmari Formation is famous as the most prolific oil producing sequences in the Zagros basin in the southwest of Iran. It has been recognized that some of the richest oil fields in the Middle East occur in the younger Cenozoic rocks of Iran and Iraq (Ala et al., 1980; Beydoun et al., 1992). The carbonate rocks of the Asmari Formation have been well studied (Lacassagne, 1963; Seyrafian, 2000; Vaziri-Moghadam et al., 2006).

The Asmari Formation was deposited in the Oligocene-Miocene shallow marine environment of the Zagros forland basin (Alavi, 2004) and is best developed in the Dezful embayment zone (a part of Khuzestan Province). Lithologically, the Asmari Formation consists of 314 m of limestone beds (Motiei, 1993).

In the south of the Dezful embayment, its lithology changes to a mixed siliciclastic-carbonate deposit consisting of carbonate beds with several intervals of sandstone, sandy limestone and shale. This facies is attributed to the Ahwaz Sandstone Member (Motiei, 1993).

Most of the studies of the Asmari formation in this basin are related to subsurface data, while this study is focused on an outcrop.

The main objectives of this research were focused on biostratigraphy of the Asmari Formation in Chidan area (SW Iran).

### **Methods And Materials**

This paper is the first report on the biostratigraphy of the Asmari formation at the Chidan area. Two sections

of the Asmari Formation were measured bed by bed, and sedimentologically investigated. Fossils and facies characteristics were described in thin sections from 160 samples. Limestone classification followed the Dunham (1962) and Embry and Klovan (1972) nomenclature system.

Foraminifers named base on Adams and Burgeois (1967), Loeblich and Tappan (1988).

Samples were collected from an outcrop in the Khuzestan Province (Chidan area), which is representative of the entire thickness of the Asmari Formation. Thin sections were stained to distinguish calcite and dolomite.

The foraminiferal assemblages of the Asmari Formation consist of various imperforate and perforate forms. This fauna is a good tool for biofacies analysis, recognition of paleoecology and lithostratigraphy.

### **Previous Studied**

The Asmari Formation was named as a Cretaceous-Eocene interval by Busk and Mayo (1918); it was defined as an Oligocene Nummulitic limestone (Richardson, 1924). Lees (1933) considered the age of the Asmari Formation as Oligocene-Miocene. He chose the type section in Tange gole torsh, located in southeast Masjed soleiman (SW Iran), and based on lithology features divided it into the following three members from base to top: The lower Asmari, middle Asmari and upper Asmari. James and Wynd (1965) carried out the first study of the biostratigraphic properties of this formation. And reviewed by Adams



and Burgeois (1967) designed four assemblages of Asmari Formation indicating Oligo-Miocene age. Recently published research on the Asmari Formation are: Seyrafian, 2000; Seyrafian et al., 1996; Seyrafian et al., 2003 and Vaziri Moghaddam et al., 2006; Parvaneh Nejad et al., 2012.

### **Paleogeographic History**

The southwestern marginal active fold belt of Iran, the Zagros, is formed on the northeastern margin of the Arabian continental crust. The geological history of the Zagros belt is simply marked by relatively quiet sedimentation continuing from late Precambrian to Miocene time. The sedimentation was of platform-cover type in the Paleozoic, miogeosynclinal from the Motiei, 1993).

#### **Asmari Formation (Oligocene-Early Miocene)**

The formation in Khuzestan province (Iran) consist of 340 m of thick, well-bedded limestones with shelly horizons. In the Ahwaz and Mansuri fields the basal third consists of calcareous sandstone and sandy limestone with minor shales, corresponding to the Ahwaz Member reported by James and Wynd (1965). Although the base of the Asmari Formation seems to be conformably overlying the Pabdeh Formation in the Fars Province, it is diachronous in Lurestan and Khuzestan Provinces. The reverse is true of the top of the formation, with a conformable contact with the overlying Gachsaran Formation in the latter two regions but a diachronous relationship in the Fars province. In southeastern Iran the Asmari grades into the marls of the uppermost part of the Pabdeh Formation, as revealed by wells drilled on Qeshm Island(SE Iran).

The lower part of the formation has been dated as Chattian-Rupelian by Eames et al. (1962) and the middle and upper parts as early Miocene. The Oligocene to earliest Miocene Asmari limestones have

Middle Triassic to Miocene, and synorogenic with conglomerates in Late Miocene-Pleistocene times (James and Wynd, 1965; Stockline, 1968; Berberian, 1976).The belt was folded during Plio-pleistocene orogenic movements.

The Zagros Paleogene succession can be divided into two cycles (Seyrafian, 2000). The first is the Jahrum cycle, Dating from Paleocene to Oligocene times. This cycle comprises the deep Pabdeh Formation (containing of marl, shale and marly limestone) and shallow Jahrum Formation (dolomitic limestone and limestone). The second cycle is the Oligocene to early middle Miocene Asmari cycle.

Overall, the Asmari Formation can be considered as a late transgression in the Zagros basin (

also been encountered in the subsurface in the offshore northern Emirates and in an outcrop on Jabal Hafit (Abu Dhabi) close to the Oman Mountains (Alsharhan et al., 1995).

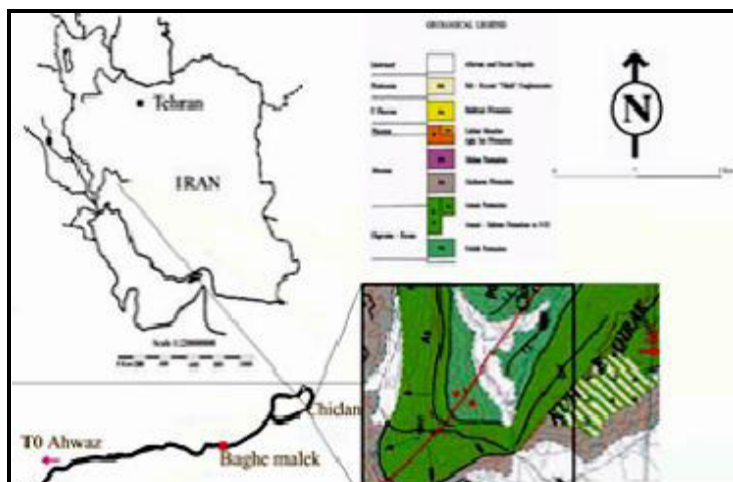
### **Geological Setting**

The Zagros Mountains are situated within the NE part of the southern neotethys ocean.

Geographically the Zagros Mountains belong to the Alpien-Himalayan chain, but clearly do not fit into models for the Alps or Himalayas (Takin, 1972). Some of these difficulties were discussed by Stocklin (1968), who concluded that Iran had a peculiar type of Alpien tectonics.

The Study area is located in Khuzestan province, 152 km from Ahwaz and east of Baghmalek (Figure 1). It is measured in detail at N 48° 33' 48" , E 49° 59' 50" at surface.

In this area, the Asmari Formation is consists of 340 m of thick and cream thin-medium-bedded limestones and calcareous marl that the upper part of Asmari Formation are divided into two parts by coral limestone.



**Figure 1.** Location and geological map of the study area.

## Discussion And Results

### Biostratigraphy

Biostratigraphic criteria of the Asmari Formation were established by Adams and Bourgeois (1967). Adams and Bourgeois (1967) designed four assemblage zones for the Asmari Formation (Table 1). Recently, Laursen et al (2009) have established a new biozonation for the Asmari Formation (Figure 2).

Based on this biozonation, the sediments ascribed to the Miocene (Aquitanian) are in fact late Oligocene, Chattian in age. This was proved by the application of strontium isotope stratigraphy.

From base to top, 2 foraminiferal assemblages were determined in study area (Figure 4).

(1) *Assemblage 1* consist of *Meandropsina iranica*, *Elphidium* sp. 1, *Elphidium* sp. 14, *Dendritina rangi*, *Miogypsina* sp., *Bigenerina* sp., *Schlumbergerina* sp., *Valvulinid* sp. 2, *Quinqueloculina* sp., *Miliolid*, *Peneroplis* sp., *Triloculina trigonula*, *Discorbis* sp., *Reusella* sp.,

*Rotalia* sp., *Ammonia* sp., *Asterigerina* sp., *Amphistegina* sp., *Acervulina* sp.,

This fauna corresponds to the *Miogypsina-Elphidium* sp. 14-*Peneroplis farsensis* Assemblage Zone of Laursen et al.(2009) and *Elphidium* sp.14 – *Miogypsina* Assemblage subzone of Adams and Bourgeois (1967) and indicate a Aquitanian age.

(2) foraminifera of assemblage 2 include *Borelis melo curdica*, *Borelis melo*, *Meandropsina iranica*, *Meandropsina anahensis*, *Miogypsina* sp., *Miogypsinoides* sp., *Dendritina rangi*, *Peneroplis* sp., *Peneroplis evolutus*, *Bigenerina* sp., *Schlumbergerina* sp., *Valvulinid* sp. 2, *Quinqueloculina* sp., *Miliolid*, *Pyrgo* sp., *Spirolina* sp., *Triloculina tricarinata*, *Triloculina trigonula*, *Discorbis* sp., *Reusella* sp., *Rotalia* sp., *Elphidium* sp. 1, *Ammonia* sp., *Amphistegina* sp., *Acervulina* sp.,. These foraminifera are correlated with *Borelis melo curdica*- *B. melo melo* and *Borelis melo* group-*Meandropsina iranica* Adams and Bourgeois (1967). Therefore, the assemblage is attributed to the Burdigalian based on the content of foraminifers.

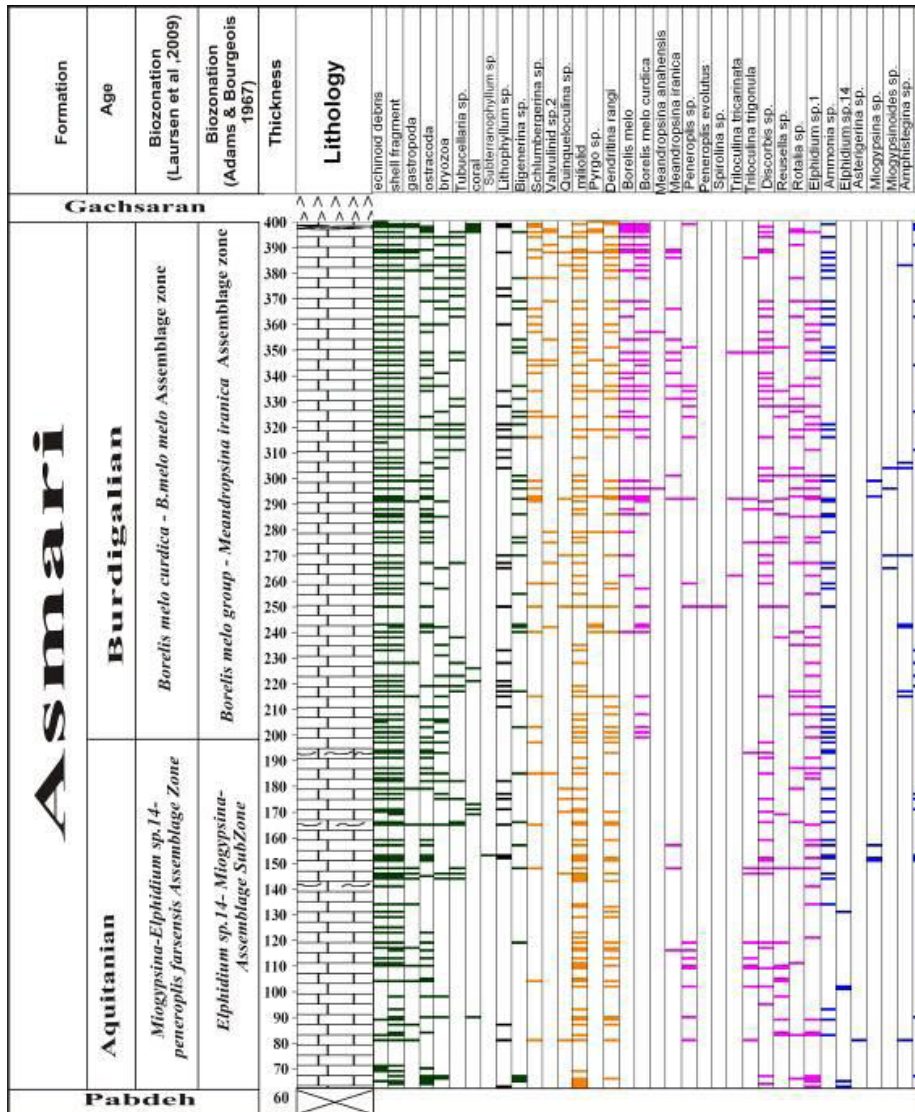


Figure 2. Biozonation of Asmari Formation in chidan area.

	Adams & Bourgeois(1967)	Laursen et al. (2009)	This study
Area	(Lorestan & Khuzestan)	(Izeh & dezful Embayment)	(Chidan section)
Age (Million year)			
16.4			
Burdigalian	<i>Borelis melo group - Meandropsina iranica</i> Assemblage Zone	<i>Borelis melo curdica- B. melo melo</i> Assemblage Zone	<i>Borelis melo curdica- B. melo melo</i> Assemblage Zone
20.5			
Aquitanian	<i>Elphidium sp. 14 - Miogypsin</i> Assemblage SubZone	<i>Miogypsina- Elphidium sp. 14- peneroptis fursensis</i> Assemblage Zone	<i>Miogypsina- Elphidium sp. 14- peneroptis fursensis</i> Assemblage Zone

**Table 1.** Comparison identified biozones of Asmari Formation in Chidan area with Adams & Bourgeois (1967), Laursen et al. (2009)

### Microfacies Types And Facies Interpretation

Eight microfacies were defined from the Asmari Formation (Chidan area at Baghemalek, SW Iran), which were grouped into four facies associations representing subenvironments.

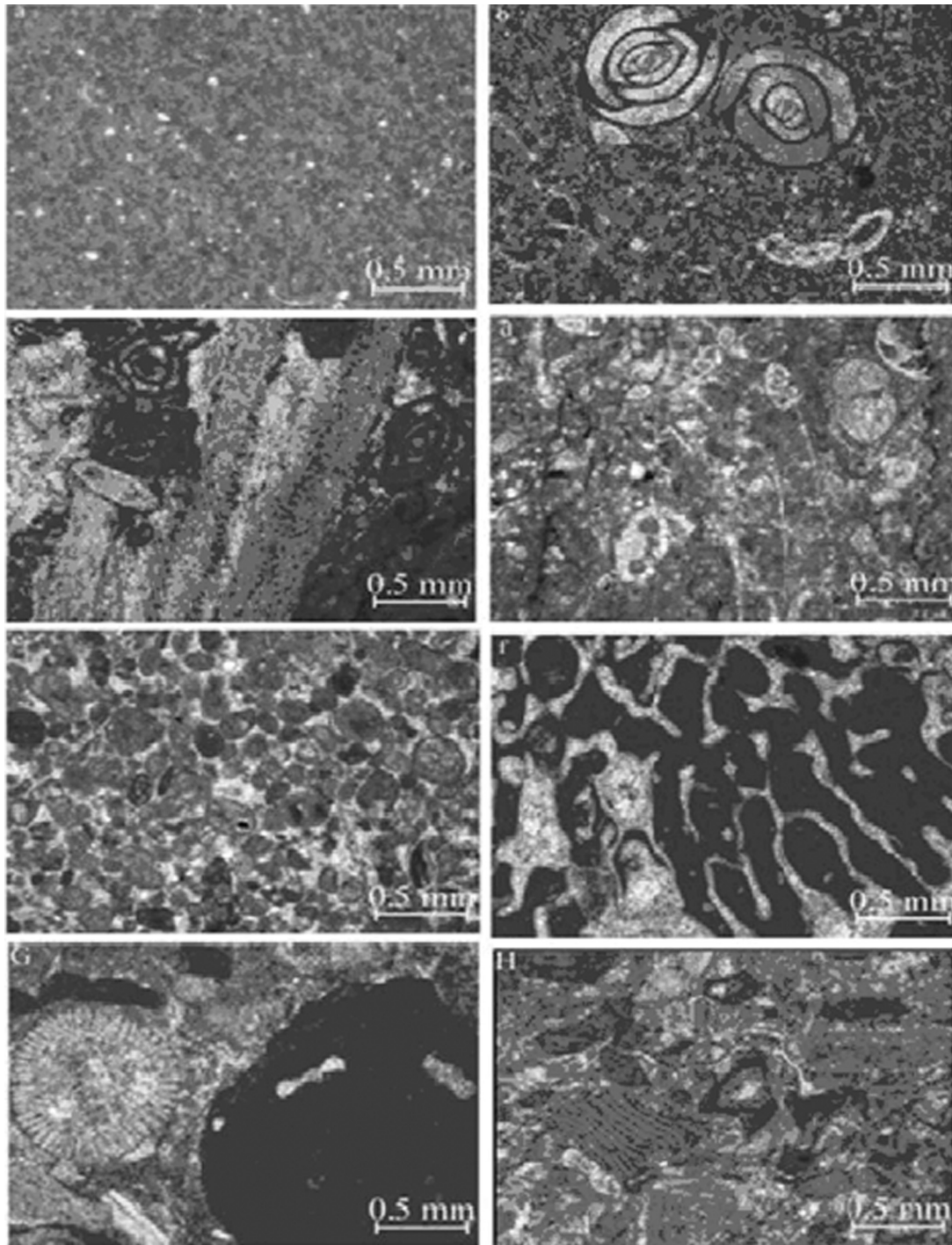
#### Tidal flat Facies

##### *D: Limemudstone*

The microfacies mainly consists of micrite, lacking lamination and with rare bioturbation. In some parts, moulds of evaporates are observed. In some thin sections quartz grains are visible (Figure 3a). Similar present-day conditions are seen in hot and dry carbonate platforms with high evaporation, such as the Persian Gulf (Tucker and Wright, 1990).

Observations indicate that this microfacies is deposited in an upper tidal flat to supratidal environment.





**Figure 3.** Microfacies types in the Chidan area. a: limemudstone, microfacies D. b: Miliolid/ Discorbis Wackestone, microfacies C1. c: Bioclast / Miliolid Packstone, microfacies C2. d: Bioclast/ Rotalia Wackestone, microfacies C3. e: Bioclast / Peloidal / Miliolid Grainstone, microfacies C4. f: Coral Boundstone, microfacies B2. g: Bioclast /Corallinacea Wackestone, microfacies B1. h: Intraclast / Miliolid / Bioclast Packstone – Wackestone, microfacies A.



## Lagoon Facies

### *C1: Miliolid/ Discorbis Wackestone*

The main feature of the microfacies is a relatively large amount of shell fragments in the matrix, mainly comprising *Discorbis* shells. Also, other shell fragments (bivalves, echinoderms) and miliolids can be seen (Figure 3b). This microfacies is associated with the lagoon of an internal ramp (Flügel, 2004).

### *C2: Bioclast / Miliolid Packstone*

Porcelaneous foraminifera (Figure 3c) are the main constituents of this microfacies. Echinoderms and bivalves debris are present in small quantities. The existence of porcelaneous foraminifera and microfacies type packstone is related to a low-energy lagoon environment (Flügel, 2004).

### *C3: Bioclast / Rotalia Wackestone*

The main constituent microfacies are *Rotalia*, echinoderms and bivalves debris (Figure 3d). Biodiversity is low. The microfacies has been associated with a lagoon of the internal ramp (Buxton and Pedley, 1989).

### *C4: Bioclast / Peloidal / Miliolid Grainstone*

Peloid and foraminifera such as miliolids (Figure 3e) are the main constituents. Echinoderms debris and intraclast contents are low. Miliolids live in shallow saline to hypersaline waters (Gell, 2000). Considering the available allochemes, grainstone texture, intraclasts and low foraminifera diversity, this microfacies is associated with an inner ramp and a relatively limited environment with high-energy.

## Barrier Facies

### *B2: Coral Boundstone*

This microfacies is formed by the growth of coral networks (Figure 3f). Echinoderms debris, miliolids and rarely *Miogypsinoides* can be seen. The skeleton space of coral is mainly filled by sparite and rarely micrite. This facies is formed in patch reefs and represents the mid - ramp environment (Buxton and Pedley, 1989).

### *B1: Bioclast / Corallinacea Wackestone*

The main components of this microfacies included fragments of corallinaceans, bryozoans, bivalves,

echinoderms and benthic foraminifera (*Miogypsinoides*, *Rotalia*, *Discorbis*). The matrix consists mainly of micrite. Red algae are discoidal. Patch reef corals are also observed (Figure 3g). The microfacies is equivalent to microfacies 5 reported by Buxton and Pedley (1989) and is associated with a mid - ramp environment.

## Open marine Facies

### *A: Intraclast / Miliolid / Bioclast Packstone – Wackestone*

The bioclastic content of this microfacies is mainly composed of algal crust debris (Figure 3h), echinoderms, bivalves and foraminifera (miliolids and lesser numbers of *Miogypsinoides*, *Rotalia*, *Discorbis*); intraclasts are also seen. The microfacies texture is grain supported. Considering the diversity of existing allochemes, evidence of bioclastic smashing and disturbance, and the presence of micrite, this microfacies is attributed to an environment that was sometimes high energy (causing smashing and disruption of allochem) and sometimes low energy (leading to the micrite carbonate between allochemes) (Flügel, 2004). These are typical conditions of the mid -ramp.

## Sedimentary Environment In The Studied Section

After studying the thin sections and identifying the microfacies, a facies profile was constructed (Figure 4). The lack of reworked sediment and lack of falling and sliding facies indicates a gentle slope depositional environment during deposition and shows that Asmari Formation was deposited in a shallow carbonate platform with a gentle slope. Deposition of the Asmari Formation in the study area started with microfacies related to the middle ramp environment and transgressed to beach facies as water depth decreased. Accordingly, the Asmari Formation in the Chidan area was mainly determined by the internal ramp characteristics. In other words, most of the Asmari Formation sedimentary rocks in the study area were deposited on the inner ramp. Considering the type of carbonate sediments produced and the main locations of sediment accumulation in the study section, a reconstructed sedimentary model is provided in Figure 5.

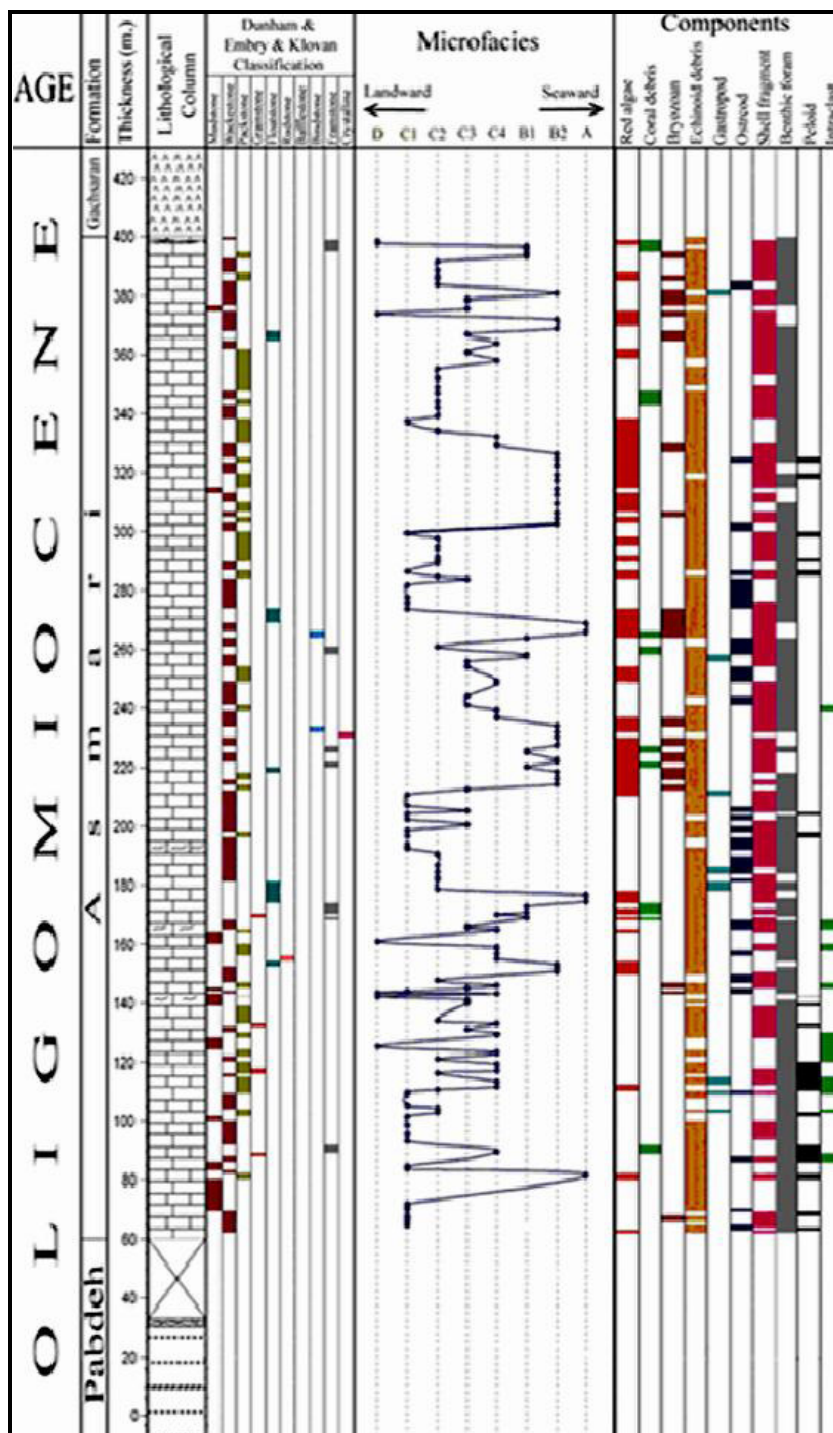


Figure 4. Facies variation and biodiversity in the Chidan area.



## Conclusions

The Asmari Formation in the study area is composed of limestone, and also the upper part of Asmari Formation is divided into two sections by limestone containing coral.

foraminifers biostratigraphic study of the Asmari Formation (Chidan section) led to recognition of 2 biozones, including:

1- *Miogyssina- Elphidium* sp. 14-*Peneroplis farsensis* Assemblage Zone (Aquitanian)

2- *Borelis melo curdica- B. melo melo* Assemblage Zone (Burdigalian)

The microfacie study based on foraminifers led to recognition of eight carbonate microfacies belong to four subenvironments.

The depositional environment of the Asmari Formation is interpreted as a shallow carbonate platform with a low slope. The most part of the Asmari Formation in the Chidan area was deposited in an inner ramp environment.

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## Investigation of the Parameters of EDM Process Performed on Smart NiTi Alloy Using Graphite Tools

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**Abstract:** Shape Memory Alloys (SMAs) are types of Smart Materials (SMs) which are used in many industries nowadays. The high hardness value and the intelligence of these alloys have made the traditional machining processes not cost effective or incapable of machining ability these metals. The NiTi alloy is one of the SMAs, which are used in aerospace and medical industries. Electrical Discharge Machining (EDM) is a known method for the machining of shape memory alloys. In this research, the effect of input parameters of electrical discharge machining including the voltage (V), discharge current (A), pulse-ON-duration ( $\mu$ s), pulse-OFF-duration ( $\mu$ s), tool material and the dielectric on the material removal rate (MRR), tool wear rate and surface roughness has been investigated for NiTi alloy. Graphite tools and de-ionized water have been used for the machining operation, and the Taguchi's method, L18 orthogonal array and the 'Minitab R.16.1.1' software have been employed for the design of experiment. The results indicate that with the increase of discharge current, the tool wear, material removal rate and surface roughness increase. The increase of voltage causes the reduction of tool wear and material removal rate, but it has little effect on surface roughness. With the increase of pulse-ON-duration, the surface roughness increases and the material removal rate diminishes. Also the increase of pulse-OFF-duration, up to a certain time, leads to the increase of material removal rate and tool wear rate (TWR) and the reduction of surface roughness.

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**Keywords:** Electrical discharge machining; Shape memory alloys; Smart material; Graphite tool; Material removal rate; Tool wear rate

### 1. Introduction

Smart materials are types of materials that can detect external stimuli and environmental changes. These alloys enjoy properties such as high corrosion resistance, high electrical resistivity, good mechanical properties, fatigue resistivity and compatibility with body tissue, which make them suitable to be used in aerospace and medical industries [1, 2]. Nickel–titanium (NiTi) alloys are commonly used in shape memory applications, although many other kinds of alloys also exhibit shape memory effects. These alloys can exist in final product form in two different temperature-dependent crystalline states or phases. The primary and higher temperature phase is called the austenite state. The lower temperature phase is called the martensite state. The physical properties of the material in the austenite and martensite phases are quite different. The material in the austenite state is strong and hard, while it is soft and ductile in the martensite phase. The austenite crystal structure is a simple body-centered cubic structure, while martensite has a more complex rhombic structure. With respect to its stress–strain curve, the higher temperature austenite behaves similarly to most metals. The stress– strain curve of the lower temperature martensitic structure, however, almost looks like that of an elastomer in that it has plateau stress-deformation characteristics where large

deformations can easily occur with little force. In this state, it behaves like pure tin, which can (within limits) be bent back and forth repeatedly without strain hardening that can lead to failure. The thermally induced shape memory effect is associated with these different phases. In the primary high temperature environment, the material is in the austenite phase. Upon cooling, the material becomes martensitic. No obvious shape change occurs upon cooling, but now the material can be mechanically deformed. It will remain deformed while it is cool. Upon heating, the austenitic structure again appears and the material returns to its initial shape. A related mechanically induced phenomenon called superelasticity can also take place. The application of a stress to a shape memory alloy being deformed induces a phase transformation from the austenite phase to the martensite phase (which is highly deformable). The stress causes martensite to form at temperatures higher than previously and there is high ductility associated with the martensite. The associated strains or deformations are reversible when the applied stress level is removed and the material reverts to austenite. High deformations, on the order of 5–8%, can be achieved. Changes in the external temperature environment are not necessary for the superelasticity phenomenon to occur [3].

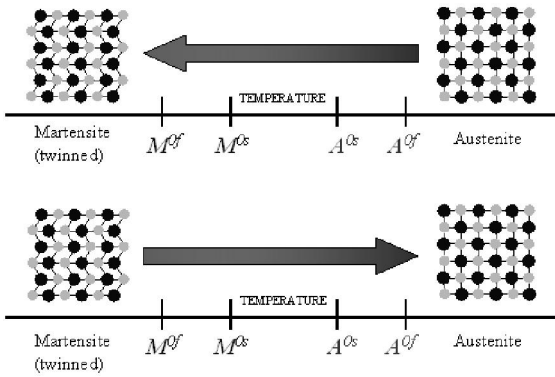


Figure 1. Phase transformation resulting from temperature in shape memory alloys without the application of force [4]

Considering the importance of temperature change in these types of alloys and their high strength and hardness, the use of traditional techniques for the machining of these alloys is not cost effective [5]. One of the methods which are appropriate for the machining of these alloys and which do not depend on the hardness and strength of the workpiece is electrical discharge machining (EDM) [6,7]. EDM is the process of machining electrically conductive materials by using precisely controlled sparks that occur between an electrode and a workpiece in the presence of a dielectric fluid. The electrode may be considered the cutting tool. EDM differs from most chip-making machining operations in that the electrode does not make physical contact with the workpiece for material removal. Since the electrode does not contact the workpiece, EDM has no tool force. The electrode must always be spaced away from the workpiece by the distance required for sparking, known as the sparking gap. Should the electrode contact the workpiece, sparking will cease and no material will be removed. Sparking occurs in a frequency range from 2,000 to 500,000 sparks per second causing it to appear that many sparks are occurring simultaneously. The spark removes material from both the electrode and workpiece, which increases the distance between the electrode and the workpiece at that point. EDM is a thermal process; material is removed by heat. Heat is introduced by the flow of electricity between the electrode and workpiece in the form of a spark. Material at the closest points between the electrode and workpiece, where the spark originates and terminates, are heated to the point where the material vaporizes. While the electrode and workpiece should never feel more than warm to the touch during EDM, the area where each spark occurs is very hot. The area heated by each spark is very small so the dielectric fluid quickly cools the vaporized material

and the electrode and workpiece surfaces. However, it is possible for metallurgical changes to occur from the spark heating the workpiece surface [8]. Using this method; conductor or semiconductor materials can be machined. The advantage of this technique is that it does not need to apply mechanical force and it is indifferent to material hardness. Material removal is mainly a thermal process, and heat treatment is not needed subsequent to the machining operation. EDM is a complex process that includes many input and output parameters [9]. In this research, the impact of input parameters on output parameters in the machining of NiTi shape memory alloy has been investigated. The discharge current, pulse-ON-duration, gap voltage, electrode polarity, electrode material, type of dielectric and the method of flushing are the input parameters that are adjusted prior to the machining operation. The output parameters include the material removal rate, surface roughness, tool wear rate and the machining precision. Selecting the optimum values for the off-line input parameters has a significant impact on the off-line output parameters, which is considered in the present investigation. So far, numerous research works have been carried out on the machining of NiTi SMAs by the EDM process. In 2004, Schvermann and Thisen conducted some research on the electrical discharge machining of nickel-titanium alloy using tungsten and copper tools and concluded that by changing the current and voltage, the depth of cracks and surface roughness can be affected [10]. In 2007, Chen et al. studied the effect of machining on Ni-Al-Fe alloy and found out that material removal rate is inversely related to the alloy's melting point and thermal conductivity. They also investigated the impact of MRR on surface roughness and recast layers [11]. In this research, the impacts of input parameters of the EDM process performed on NiTi alloy using graphite tools and de-ionized water as the dielectric on the output parameters are evaluated.

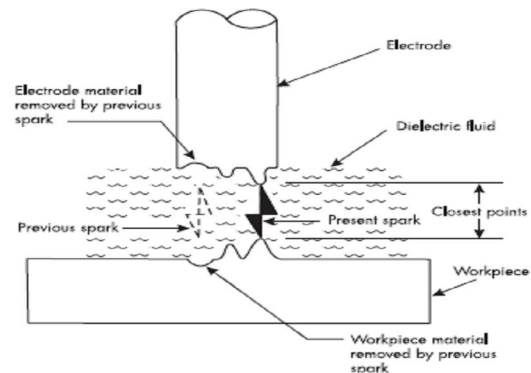


Figure 2. Principles of material removal by the EDM process [8]

## 2. Test Equipment and Method

The EDM specimens were performed on a die-sinking EDM machine model type 204-H, made by Tehran Ekram Co. in Iran. fig.3



Figure 3. EDM machine (model: 204H)

The workpiece material is NiTi60, with a density of  $6.45 \text{ gr/cm}^3$ . The samples have been wire cut as plates from raw materials with dimensions of  $40 \times 50 \text{ mm}$ , and then they have been grinded. Table 1 shows the mechanical and physical properties of NiTi60 material. The tools used in this research are made of graphite with dimensions of  $\phi = 8 \times 40 \text{ mm}$ . To avoid the problem of workpiece and tool surface not being parallel, and to consider the impact of surface roughness of tools on workpieces, the surfaces of all the tools were machined and grinded using abrasive grinding. To avoid the changes of test conditions, all the tests were performed in one day. To raise the accuracy of the tests and to prevent the effect of oil-based dielectrics in reacting with the workpiece surface, de-ionized water with an EC of less than  $1 \text{ ms}$  (micro-Siemens) has been used in this investigation. A constant spray type flushing system was used in all the experiments. To measure the volumes of material removed from the workpiece and tool, an 'AND' balance (model: GR-300) with a precision of  $\pm 0.0001 \text{ gr}$  was employed (Fig.4). The 'Mahr' roughness measuring instrument (model: M300-RDI8) was used to measure the surface roughness of the workpiece.



Figure 4. 'AND' balance (model: GR-300) used for weight measurements

Table 1. Mechanical and physical properties of Nitinol-60 [12]

Density	6.45 G/cc
Tensile strength, ultimate	754 - 960 Mpa
Tensile strength, yield	560 Mpa
Elongation at break	15.5 %
Modulus of elasticity	75.0 Gpa
Poissons ratio	0.300
Shear modulus	28.8 Gpa
Electrical resistivity	0.0000820 Ohm-cm
Magnetic susceptibility	0.00000380
Specific heat capacity	0.320 J/g-°c
Thermal conductivity	10.0 W/m-k
Melting point	1240 - 1310 °C
Solidus	1240 °C
Liquids	1310 °C
Nickel, Ni	55.0 %
Titanium, Ti	45.0 %

## 3. Design of Experiments

Among the effective factors of an experiment, some are very important and the rest have lesser effects. By using the design of experiment, we are able to obtain some information regarding the factors that have a significant impact on the response; and from a large number of parameters, those needing further research can be selected. The controllable input parameters can be systematically altered and their impacts on output parameters can be evaluated and discussed. In this investigation, the Taguchi's design of experiment method has been employed as one of the strongest techniques of design and analysis of experiments [13]. To optimize the number of experiments and to generalize the results to all the levels under investigation, the orthogonal array of LI8 ( $2^1 \times 3^3$ ) has been used. There are 18 experiments and 4 factors in this research. The factors or input parameters of this experiment include the current, voltage, pulse-ON-duration and pulse-OFF-duration. In this research, the voltage factor has two levels and the other factors have three levels. The lowest and highest values of discharge current were considered as 10A and 20A, respectively; because at discharge currents less than 10A, material removal rate is low, and at currents higher than 20A, surfaces with acceptable qualities are not obtained. With regards to equipment capacity, the voltages used in this research were 80V and 250V. Pulse-ON-durations of 35, 50 and 100  $\mu\text{s}$  were chosen. At durations longer than 100  $\mu\text{s}$ , flushing intensity diminishes and adversely affects the quality and rate of material removal. Pulse-OFF-durations of 30, 70 and 200  $\mu\text{s}$  have been chosen. The design factors and selected levels for each one of the test parameters have been listed in Table 2. The Minitab® 16.1.1 software program has been used for process

analysis. The machining operation has been carried out at constant times, and the material removal rate has been determined by measuring the difference between workpiece weights before and after the machining process. Material removal rate (mm<sup>3</sup>/min) is determined from Eq. 1.

$$MRR = \frac{(W_1 - W_2)}{\rho_w \times t} \times 10^3 \quad (1)$$

In this relation, MRR is the volumetric material removal rate (mm<sup>3</sup>/min), w<sub>1</sub> and w<sub>2</sub> are the workpiece weights before and after machining, ρ<sub>w</sub> is the density of NiTi60 shape memory alloy, and t is the machining time (min). The tool wear rate (mm<sup>3</sup>/min) is obtained from Eq. 2:

$$TWR = \frac{(T_1 - T_2)}{\rho_T \times t} \times 10^3 \quad (2)$$

In this relation, TWR is the tool wear rate (mm<sup>3</sup>/min), T<sub>1</sub> and T<sub>2</sub> are the tool weights before and after machining, ρ<sub>T</sub> is the density of graphite tools, and t is the machining time (min). The electrode wear rate (EWR) is obtained from Eq. 3.

$$EWR = \frac{TWR}{MRR} \times 100 \quad (3)$$

TWR: volume of material removed from the tool (mm<sup>3</sup>/min)

MRR: volume of material removal from the workpiece (mm<sup>3</sup>/min)

EWR: electrode wear rate (%)

Factors		Levels	
Gap voltage (V)	30	250	-
Discharge current (A)	10	15	20
Pulse duration (μs)	35	50	100
Pause duration (μs)	30	70	200
Electrode	Work piece (-)	Tool (+)	
Dielectric	De-ionized water		

#### 4. Output Parameters of the EDM Process

##### 4.1 Analysis of Material Removal Rate

Material removal rate is proportionate to the amount of consumed power. Research has shown that in iso-frequency circuits, power is obtained from Eq. 4 [14].

$$P = \frac{V_{sp} I_{sp} (T_i - T_d)}{T_i + T_o} \quad (4)$$

The performed tests have indicated that with regards to Eq. 4, for most alloys, the material removal rate increases with the increase of discharge current (I<sub>sp</sub>), reduction of pulse-OFF-duration (T<sub>o</sub>), reduction of discharge delay (T<sub>d</sub>) and the increase of pulse-ON-duration. The effects of discharge current, voltage, pulse-ON-duration and pulse-OFF-duration on material removal rate have been illustrated in Fig. 5 for the NiTi SMA.

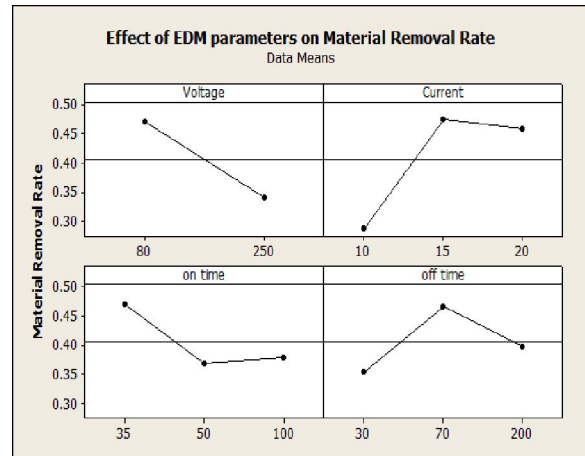


Figure 5. Impact of input parameters of the EDM process on the MRR of NiTi SMA

As is shown in Fig. 5, discharge current has the largest effect on material removal rate in NiTi SMAs. With the increase of discharge current, the amount of energy discharged with each pulse increases and a larger amount of workpiece material melts and evaporates. With the increase of discharge current up to 15 A, the rate of material removal for NiTi SMA using graphite tools has an ascending trend, and beyond 15A, it declines a little. The effect of voltage on MRR indicates that with the increase of voltage, material removal rate diminishes. With the increase of pulse-ON-duration from 35 to 50μs, MRR is reduced; and a further increase of pulse-ON-duration from 50 to 100μs, leaves little effect on the rate of material removal. In principle, with the increase of pulse-ON-duration, the amount of pulse energy (obtained from Eq. 5) increases, and consequently, the material removal rate should increase; but this didn't happen for NiTi SMA using graphite tools.

$$W = V_{sp} \cdot I_{sp} \cdot (T_i - T_d) \quad (5)$$

The increase of pulse-OFF-duration to 70μs leads to the increase of MRR; however, the material removal rate diminishes beyond the 70μs point. Fig. 5



shows that the minimum and maximum rates of material removal are obtained at pulse-OFF-durations of 30 and 70 $\mu$ s, respectively, which could be attributed to the eradication or the preservation of the plasma channel.

#### 4-2-Analysis of Tool Wear Rate

According to Fig. 6, the most influential parameter on graphite tool wear in the machining of NiTi alloys is the discharge current. The increase of discharge current leads to the increase of spark energy and causes the tool to melt more. There is a linear relationship between discharge current and tool wear. With the increase of pulse-ON-duration up to 50 $\mu$ s, graphite tool wear diminishes, and after 50 $\mu$ s, it increases with a mild slope.

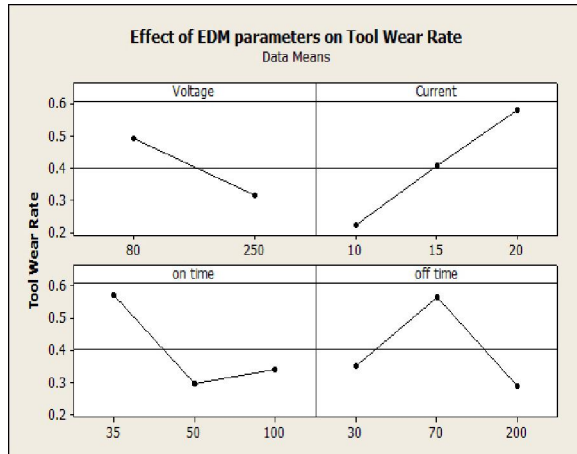


Figure 6. Impact of input parameters of the EDM process on graphite tool wear

With the workpiece and tool attached to the negative (cathode) and positive (anode) poles of the apparatus, respectively, when the pulse is initially turned on, the plasma channel diameter is small, and the flow of electrons from the negative to positive pole results in the tool wear. With the increase of pulse-ON-duration, the plasma channel diameter gradually increases, and the positive ions (with sizes 1847 times larger than electrons) become more active. This gradually reduces the movement of electrons towards the tool; and as a result of less energy and heat reaching the tool, the amount of tool wear diminishes. Therefore, with the increase of pulse-ON-duration in the machining of SMAs using graphite tools, tool wear rate diminishes. Another parameter that affects tool wear is voltage. The increase of voltage from 80 to 250V results in the reduction of tool wear rate. With the increase of pulse-OFF-duration from 30 to 70 $\mu$ s, the tool wear rate exhibits an ascending trend and increases, and as the pulse-

OFF-duration increases further from 70 to 200 $\mu$ s, the tool wear rate declines after reaching a maximum value. With the increase of pulse-OFF-duration, flushing improves and a new plasma channel forms, which at the onset of spark, has a strong material removal power on the tool.

#### 5. Analysis of Electrode Wear Rate

Fig. 7 demonstrates the effect of discharge current, voltage, pulse-ON-duration and pulse-OFF-duration on the electrode wear rate in the machining of NiTi SMA using graphite tools and de-ionized water as the dielectric. With the increase of pulse-ON-duration, tool wear rate decreases and the volume of material removed from the workpiece increases. In the EDM process with positive polarity, when the pulse-ON-duration is short, the material removal mechanism is the flow of electrons from cathode (workpiece) to anode (tool), which causes more wear on the positive end (the tool). But with the increase of pulse-ON-duration, as a result of plasma channel expansion, the flow of positive ions from tool (positive pole) to workpiece (negative pole) becomes easier and tool wear diminishes. The increase of discharge current up to 15A causes a reduction in the electrode wear rate, and then with the further increase of discharge current to 20A, the electrode wear rate increases as well. The increase of voltage also causes the electrode wear rate to increase. Pulse-OFF-duration is another parameter that affects the electrode wear rate. With the increase of pulse-OFF-duration, electrode wear rate decreases, which is due to the lack of electrical discharge.

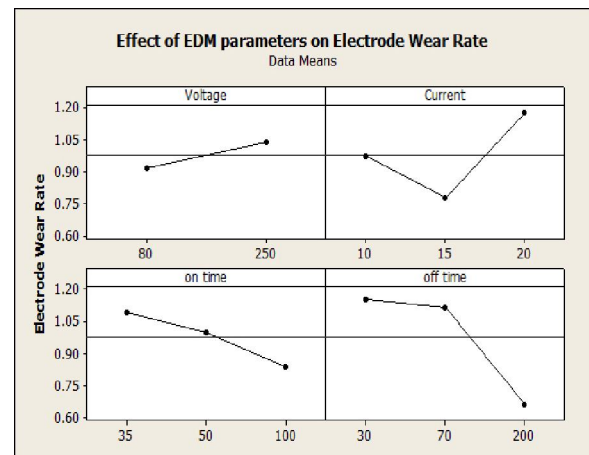


Figure 7. Impact of input parameters of the EDM process on electrode wear rate

#### 6. Analysis of Surface Roughness

Fig. 8 shows the effects of input parameters of the EDM process on the surface roughness of NiTi shape memory alloy. Discharge current, pulse-ON-



duration and pulse-OFF-duration greatly affect the surface roughness; while the impact of voltage changes on surface roughness is negligible. The increase of discharge current leads to the increase of spark energy and consequently, the reduction of surface roughness. In the iso-pulse circuit, the amount of spark energy is obtained from Eq. 5.

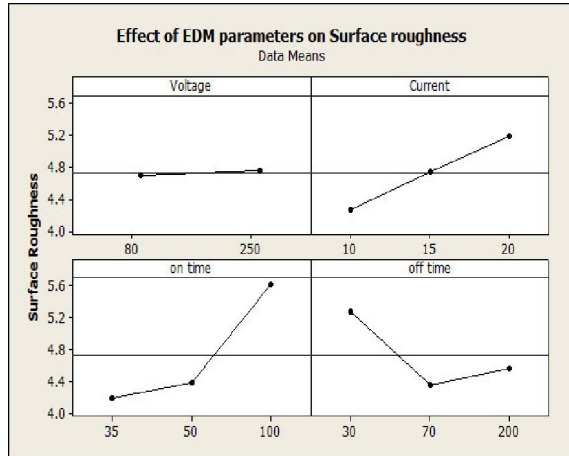


Figure 8. Impact of input parameters of the EDM process on surface roughness of NiTi SMA

In the machining of NiTi SMA using graphite tools and de-ionized water, the increase of voltage has little effect on surface roughness. The increase of pulse-ON-duration up to 50 $\mu$ s doesn't have much of an impact on the surface roughness of the workpiece; however, with further increase of pulse-ON-duration to 100 $\mu$ s, because the diameter of plasma channel increases and the protons, which are larger than electrons by 1837 times, hit the workpiece, the surface roughness of the workpiece diminishes. The increase of pulse-OFF-duration leads to the increase of surface roughness.



Figure 9. Surfaces of machined workpieces

### Conclusion

In this research, the effects of input parameters of electrical discharge machining including the discharge current, pulse-ON-duration, voltage, pulse-OFF-duration, de-ionized water and graphite tools on the output parameters of the process such as tool wear rate, material removal rate, surface roughness and electrode wear rate were analyzed and evaluated for NiTi shape memory alloy. The Taguchi's method and L18 orthogonal array were employed for the design of experiment. The obtained

results indicate that the most influential parameter on the increase of material removal rate is the discharge current. With the increase of discharge current, due to the increase of spark energy, both the MRR and TWR increase. Another effective factor is the pulse-OFF-duration, whose increase up to an optimal value, results in the increase of material removal rate and tool wear, and whose further increase past the optimal value leads to the reduction of the latter parameters. The maximum rate of material removal for NiTi SMA is achieved with a discharge current of 15A, voltage of 80V, pulse-ON-duration of 35 $\mu$ s and pulse-OFF-duration of 70 $\mu$ s. With the increase of pulse-ON-duration up to 50 $\mu$ s, the MRR and TWR both decrease, and as the pulse-ON-duration is increased from 50 to 100 $\mu$ s, the MRR and TWR also increase as a result of the expansion of plasma channel diameter. The minimum rate of graphite tool wear is achieved with a discharge current of 10A, voltage of 250V, pulse-ON-duration of 50 $\mu$ s and pulse-OFF-duration of 30 $\mu$ s. The increase of voltage results in the reduction of material removal rate and tool wear rate. The increase of voltage and discharge current up to 15 A leads to the reduction of electrode wear rate and consequently, the increase of material removal rate. The maximum value of electrode wear rate in the machining of NiTi SMA is achieved with a discharge current of 20A, voltage of 250V, pulse-ON-duration of 35 $\mu$ s and pulse-OFF-duration of 30 $\mu$ s. Surface roughness diminishes with the increase of discharge current and pulse-ON-duration, due to the intensification of spark energy. The maximum degree of surface roughness in the machining of NiTi SMA is achieved with a discharge current of 10A, voltage of 80V, pulse-ON-duration of 35 $\mu$ s and pulse-OFF-duration of 70 $\mu$ s.

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## Environmental management accounting with an emphasis on it cost

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**Abstract:** Although environmental costs are only one of the many costs incurred by businesses, they deserve management's attention. For companies in the service sector with office environments, better insight into environmental costs can lead to them being reduced while environmental performance is improved with costs being offset through the recycling or sale of waste and improved costing of services. It will also help with the justification of environmental improvement initiatives, and support of a company's environmental policy, management system or data collection for public reporting. Environmental management accounting can be used as a tool to reap these benefits, and refers to "the process of identifying, collecting and analyzing information about the environmental costs and performance to help an organization's decision making."

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KEY WORDS: environmental management, accounting management, cost management

### 1. INTRODUCTION

Environmental issues along with the related costs, revenues and benefits are of increasing concern to many countries around the world. But there is a growing consensus that conventional accounting practices simply do not provide adequate information for environmental management purposes. To fill in the gap, the emerging field of Environmental Management Accounting (EMA) has been receiving increasing attention. In recent years, environmental management accounting has been attracting increasing attention throughout the world. Environmental accounting is an inclusive field of accounting. It provides reports for both internal use, generating environmental information to help make management decisions on pricing, controlling overhead and capital budgeting, and external use, disclosing environmental information of interest to the public and to the financial community. Internal use is better termed environmental management accounting [1]. For the purpose of this research, both internal and external uses are considered. The contribution of multiple disciplines provides a base for determination of environmental impacts and related costs. Specific details of that determination serve one or both of the uses. Impact of business activity on the environment is found in several forms.

### 2. ENVIRONMENTAL MANAGEMENT ACCOUNTING

Environmental management accounting is viewed as an extension of conventional management accounting. Management accounting is defined as measuring and reporting 'financial and non-financial information that helps managers make decisions to fulfil the goals of an organization' [16]. Birkin indicates that 'EMA is a straightforward development

of management accountancy' [6]. Bennett and James (1997) explain that EMA can be seen as 'environment-related management accounting', but does not have a bias towards financial information [4]. According to the United Nations Division for Sustainable Development EMA is 'simply a better and more comprehensive approach to management accounting' [23]. The UNDSO states:

The general use of environmental management accounting information is for internal organizational calculations and decision making. EMA (environmental management accounting) procedures for internal decision making include both physical procedures for material and energy consumption, flows and final disposal, and monetarized procedures for costs, savings and revenues related to activities with potential environmental impact. The International Federation of Accountants (IFAC) defines EMA as [17]. The management of environmental and economic performance through the development and implementation of appropriate environment-related accounting systems and practices. While this may include reporting and auditing in some companies, environmental management accounting typically involves life-cycle costing, full-cost accounting, benefits assessment, and strategic planning for environmental management.

The two definitions reveal that the development of EMA is set within an environmental management context. Management accounting has an important role to play in managing environment related issues. For example, management accountants have the expertise and skills to improve the quality of environment-related information, which can be applied to assist in decision-making in relation to

investment appraisal, capital budgeting and strategic management [11][18]. As EMA is a flexible tool, there are many other definitions existing in the literature differing in the scope or boundary of application. An important feature of EMA as reflected in some definitions is the focus of EMA on both monetary and physical aspects of organizational environmental impacts [8][13]. Being the focus of this study, EMA will be revisited and discussed in

greater detail in this paper. However, some frequently used EMA definitions are summarized in Table 1 For the purpose of this study, EMA is defined as the generation, analysis and use of monetary and physical (or financial and non-financial) environment related information in order to improve organizational financial and environmental performance.

**Table 1 A summary of definitions of environmental management accounting**

Source	Definition
Birkin	EMA provides a service to management that is rooted in the internal functions of the firm but is outward-looking where appropriate.... EMA is a straightforward development of management accountancy.
Bennett and James	[EMA is] the generation, analysis and use of financial and non-financial information in order to improve corporate environmental and economic performance.
Graff et al.	In terms of management (or internal) accounting, EA (environmental accounting) is the way that business can account for the material use and environmental costs of their operations. Material accounting is a means of tracking material flows through a facility in order to characterize inputs and outputs for purposes of evaluating both resource efficiency and environmental improvement opportunities. Environmental cost accounting is how environmental costs – including those that are often hidden in general overhead accounts – are identified and allocated to the material flows or other physical aspects of a firm's operations (as might be identified via material accounting).
Bartolomeo et al.	EMA is the generation, analysis and use of financial and related non-financial information in order to integrate corporate environmental and economic policies, and build sustainable business.
UNSD	EMA thus represents a combined approach which provides for the transition of data from financial accounting and cost accounting to increase material efficiency, reduce environmental impact and risk and reduce costs of environmental protection.
Burritt, Hahn and Schaltegger	It is proposed that EMA be defined as a generic term that includes both Monetary Environmental Management Accounting (MEMA) and Physical Environmental Management Accounting (PEMA).
UNSD	EMA is simply a better and more comprehensive approach to management accounting, with a particular focus on costs related to wasted raw materials and other environmental issues. Key points are: <ul style="list-style-type: none"> <li>• y EMA focuses on costs internal to the company; EMA does not include costs to society or the environment for which a company is not held accountable.</li> <li>• EMA places particular emphasis on accounting for environment-related costs such as waste management costs and the lost value of wasted raw materials.</li> <li>• EMA encompasses not only cost information, but also information on quantities, flows and disposal of materials and energy.</li> <li>• EMA information is valuable for many types of management activities or decisions, but is particularly useful for environmental management.</li> <li>• EMA's main use is typically for internal management and decision-making, but EMA information is increasingly being used for external reporting purposes in financial reports or annual environmental reports.</li> </ul>
Bouma and Correlje	EMA can be regarded as a subset of environmental accounting which refers to accounting systems and techniques that provide decision-makers and management with financial and non-financial information about the firm or organisation and its environment.
Bennett, Rikhardsson and Schaltegger	EMA is understood here as environmental accounting which is specifically addressed to supporting the information needs of the organisation's own management.
Rikhardsson et al.	EMA is a form of technology. Not in the sense that a car or a computer is a technology, but in the sense of a managerial technology, which combines knowledge, methodology and practice and applies these to linking environmental management and economic results. Technology is often defined as putting knowledge to practical use, and EMA covers various tools and techniques of targeted information collection, analysis and communication and is thus a type of information management technology or managerial technology... it is important to emphasize that EMA covers a large set of different tools ranging from environmental cost accounting, to investment appraisal, budgeting, performance measurement and material flow accounting.

### 3. Environmental management accounting and the role of accountants

Most business activities have environmental impacts. Almost all environmental impacts also have business costs, such as consuming raw materials, using utilities such as water and energy, and generating waste[20]. Environmental management accounting uses standard accountancy methods to identify, analyze, manage and reduce these costs in a way that can benefit both the business and the environment. In addition to financial costs, you can use environmental management accounting to identify other issues such as non-compliance, negative public relations and health and safety problems. The process also enables you to identify which activities have the biggest environmental impacts and costs. This enables managers to set goals and priorities for managing these activities and reducing their impact.

### 4. The role of environmental management accounting in the development of management accounting for the environmental

In response to criticisms of management accounting in general, a number of innovative management accounting techniques have been developed. These techniques have shifted the focus and impacted on the whole process of management accounting, including planning, controlling, decision making and communication [19][21]. EMA is also subject to the same influence. In 1998, the International Federation of Accountants (IFAC) issued a statement on management accounting concepts outlining the development of management accounting through four distinguishable stages with a different focus in each stage. The four stages are:

- Stage 1 (pre 1950) – a focus on cost determination and financial control;
- Stage 2 (by 1965) – a focus on the provision of information for management planning and control;
- Stage 3 (by 1985) – a focus on the reduction of waste in resources used in business processes; and
- Stage 4 (by 1995) – a focus on generation or creation of value through the effective use of resources (IFAC 1998b).

The focus of management accounting has been extended from information provision

Stage 2) to the reduction of resource loss (Stage 3) and to the effective use of resources (Stage 4) [18]. The shift in focus has made management accounting an integral part of the environmental management process in contemporary organizations. In particular,

the focus in Stage 3 is central to physical EMA in terms of accounting for the flows of natural resources (i.e. energy, water and other materials), whereas the focus in Stage 4 is parallel to that of EMA that considers benefits and costs with regard to eco-efficiency. For most organizations having applied or implemented EMA, their main focus is on meeting the goals of Stages 1 and/or 2 with implemented practices ranging from simply adjusting existing accounting systems to adopting an integrated EMA system that links monetary and physical information. The International Federation of Accountants (2005) comments that the current EMA applications are continuing to move in the same direction as suggested in the development of management accounting. When inattention to environmental costs is justified to be ineffective, and the efficient use of resources proves to create value over the long run, EMA is part of the solution to problems with conventional management accounting, and fits in well with the trend of management accounting for the environment.

### 5. Types of information included under environmental management accounting

In practice, EMA adoption ranges from simple adjustments to existing accounting systems to implementation of a comprehensive EMA system that links conventional monetary and physical information systems. To implement EMA practices, both monetary and physical data on material uses, labor hours and other cost drivers are relevant and required. The two types of information monetary and physical – included under EMA are discussed below .

#### 5.1 Physical environmental information

According to the International Federation of Accountants (IFAC) (2005), EMA places particular emphasis on the physical information related to the flow of energy, water, materials and wastes. It is because material purchase costs can be a significant cost driver, and many of the organizational environmental impacts are directly associated with the use of these resources and the generation of wastes. The physical information collected under EMA is therefore essential to the identification of many environmental costs, and allows an organization to assess and report the physical aspects of its environmental performance. This is true not only for manufacturing industries but also for service organizations. Resources such as energy, water and other materials are essential to support organizational activities and operations. To set measurable environmental targets and effectively manage environmental impacts, tracking and reducing the amounts of resources used and wastes generated is



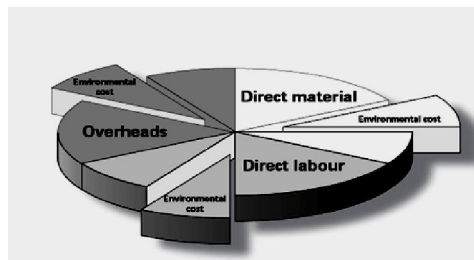
necessary. Physical EMA requires an organization to trace resources/materials inputs and outputs and to ensure that the resources/materials are not left unaccounted for. The physical information collected can then be used to create environmental performance indicators (EPIs), which in turn help an organization set environmental targets and report its environmental performance. The IFAC (2005) states that physical information does not provide all the required data to effectively manage organizational environmental impacts, but it is the information that management accounting can provide for the purpose of environmental management.

### 5.2. Monetary environmental information

How monetary environmental costs (or simply environmental costs) are measured mainly depends on the intended use of the information. Environmental costs typically refer to the types of costs that are clearly driven by efforts to control or prevent environmental damages (e.g. the costs associated with cleaning up sites after production or wastewater treatment costs). According to the IFAC (2005), environmental costs under EMA comprise other monetary information needed to cost-effectively manage organizational environmental performance. Examples include the purchase costs of natural resources (e.g. energy and water) and materials that are used or eventually become wasted. The IFAC (2005) explains that resource/material purchase costs are certainly considered in internal management decision-making, but they do not necessarily be considered as environmental costs. However, the costs are environment-related and this information is required to evaluate the financial aspects of organizational environmental management related to the use of the resources and materials. In this regard, physical EMA can be linked to monetary EMA by supplying the required information on the amounts of resources/materials used and wastes generated to assess the purchase costs. As mentioned, the intended use of information helps determine the environmental costs an organization would choose to trace. For organizations to determine relevant environmental costs that suit their operations and strategic planning, an introduction to environmental cost categorization is required.

### 6. Research objectives

The below diagram illustrates that the environmental cost is being hidden under direct labor, direct material and overheads.



To accrue greater benefits from the environmental management accounting system the company should also identify opportunities that may generate revenue by selling waste by-products and integrating the environment with various other aspects of business management that support and implement the system. The firm should also determine the costs and savings that the system might generate, and identify the precise method for pricing products as per industry standards. Last but not the least; companies should also focus on designing more environmental friendly products and attuning the processes that might provide a competitive edge to the company over its nearest rivals [15].

Most businesses have therefore become aware of the implication of environmental issues on its operations, services and products. The firms are aware that risks associated to environment cannot be ignored and form an integral part of running a business successfully by implementing innovative product designs, marketing concepts and managing the finances. On the other hand, ignoring environmental issues may result into adverse impact on the businesses. Oftentimes, government and other regulatory authorities impose fines and environmental taxes on companies that do not abide by the rules and damage the environment. Other punishments or losses include decrease of land value, devaluation of brands, loss of sales, boycotts by consumers, loss of insurance, legal notices and law suits, and damage of the company's image in the market. Most of the businesses are affected by pressures due to environmental issues, and therefore, from the accounting viewpoint, the pressure is felt on external reporting, which includes disclosing environmental issues in financial or annual reports under separate accounts. Although, experts have differing views about the quality and nature of such accounts, most environmental issues cannot just be dealt through external reporting. However, it is important to manage environmental issues even before reporting them for which a sound environmental management accounting system is required.

## 7. Environmental management accounting and cost factor

Some of the cost information that managers need to identify and project are environmental performance and the associated economic performance. EMA practitioners and researchers have developed various EMA methodologies and approaches that can be followed by various organizations. It has been seen and dealt with that not all emissions and waste can be reduced. Some of them are inevitable but it is financial best interest of the organizations to use the materials, water and energy in as much less quantity for achieving their goals. Proactive and preventive environmental management that can help reduce the amount of the waste generation, also treating the waste material for reuse can reduce purchase costs of the material not used or lost as wastes. Therefore, assessment of these costs allows the managers to better understand the potential monetary value of the environmental management for preventive measures. In operations related to manufacturing includes, the processing cost of raw material and other materials. This has been adjudged till the point that till the point it is converted into waste and emissions. The processing costs can also include the proportion of equipment depreciation also the labor costs that can be aided to generate the emission and waste rather than producing the final product. Waste and emission control cost covers the costs of handling, treating and disposing emissions and waste. It may also include compensation costs and remediation related to environmental damage. Also, any regulatory compliance costs related to waste and emission control. Environmental accounting system is often influenced by the end treatment of the data analysed, which might be used for reporting financial figures, evaluating the overall performance of the company or to analyze the role of the management in general. For instance, while using environmental accounting in terms of monetary analysis, it is important to take into account the environmental performance results. Thus, in the absence of an environmental accounting system, it would become difficult to collect the facts and information for making a corporate environmental report card. Such a reporting system would also rely heavily on the financial units of measurement. Additionally; the social costs are also taken into account. These costs are incurred by a company are those that represent the organization's expenditure towards environment and society. For these costs, the businesses can not be held legally accountable. These costs are met by public funding and are mostly labeled as externalities. Although, calculating social costs can be difficult and often controversial, it is nonetheless, important for an

organization to incur these costs, as these costs provide the precision to publish claims about environmental costs.

## 8. Identify opportunities to cut environmental costs

Once you have identified environmental costs, you should analyze them to see where they can be reduced or eliminated. The largest environmental costs are likely to include:

- waste and effluent disposal
- water consumption
- energy
- transport
- consumables and raw materials

### Waste

Waste production offers significant opportunities for savings because of its effect on:

- costs of unused raw materials and disposal
- costs of transport, storage and handling
- possible penalties for compliance failures such as pollution
- taxes for landfill

## 9. The challenge for accounting – accounting for the environment

Accounting is now facing the challenge to account for the environment through its traditional role of recording and reporting financial information and through its potential role to manage environmental performance. Long ago, Tinker and Niemark (1987) argued that society expects that organizations repair or prevent damage to the environment (i.e. manage and minimize their environmental impacts). Much of the challenge for accounting has now been reinforced further by the changing societal expectations and ever-growing pressure on improving organizational environmental performance. Due to the increasing community concerns over the environment, organizations have to face the fact that they do not have an inherent right to the environment (in particular the use of natural resources) and they have to fulfill a new 'social contract' that is emerging. Gray, Owen and Adams describe a society as essentially 'a series of individual "social contracts" between members of society and society itself'. These contracts define the rights and responsibilities of the parties in that relationship and change the challenge facing the business organizations. Donaldson and Dunfee indicate that the business game is now 'played by different rules and harbours different penalties and benefits than it did decades ago' [10]. Organizations today are held responsible and accountable for a

variety of issues, including environmental issues. Failure to meet the expectations will result in the revocation of an organization's 'license to operate' and affect its long-term survival [9][10]. The changing society expectations have brought about more and tighter environmental regulations. Gray and Bebbington argue that 'without a "greener accounting" many environmental initiatives will simply not get off the ground' [14]. To manage the environmental issues, pressures, associated costs and potential cost savings, various types of expertise from the accounting discipline are required. Research and studies regarding how accounting can contribute to the environment are well documented [3][5]. They also indicate problems with conventional accounting in addressing these issues. Conventional accounting, in an economic/business context, involves identifying, measuring, and communicating economic information to facilitate informed judgments and decisions by users of information [12]. It seems that annual reports prepared by companies that adopt this objective should be primarily economic in focus. A review of the International Accounting Standards Board Conceptual Framework (or IASB Framework) reveals that conventional accounting does not usually give explicit, separate recognition to organization-related environmental impacts and fails to provide a full account of the use of many resources, such as land, air and water. To manage the environmental issues, pressures, associated costs and potential cost savings, various types of expertise from the accounting discipline are required. Research and studies regarding how accounting can contribute to the environment are well documented. They also indicate problems with conventional accounting in addressing these issues. Conventional accounting, in an economic/business context, involves identifying, measuring, and communicating economic information to facilitate informed judgments and decisions by users of information

## 10. CONCLUSION

Accounting is now facing the challenge to account for the environment through its traditional role of recording and reporting financial information and through its potential role to manage environmental performance. The central theme of this paper is to illustrate the benefits of environmental management accounting system and find out how businesses can implement this system to garner better market value and position. Some of the major benefits of the environmental management accounting include aiding companies to take responsible decisions relating to issues such as allocating costs, capital budgeting or designing

processes. Experts believe that companies can use the following steps to implement the accounting system in an effective manner. The first and the foremost step are to identify the opportunities so that unnecessary costs are eliminated that does not give any value to a product or process.

Furthermore, companies need to find out the environmental costs from the account sheets which are often hidden under the overhead accounts, direct labor accounts or direct material accounts. It has been found that in most cases, environmental costs are hidden in different parts of the management accounting system. The largest environmental costs are likely to include:

- Waste and effluent disposal
- Water consumption
- Energy
- Transport
- Consumables and raw materials

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## Genotypic Detection of Polyhydroxyalkanoate-producing Bacilli and Characterization of *phaC* Synthase of *Bacillus* sp. SW1-2

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**Abstract:** A group of bacilli phenotypically screened for synthesis and intracellular accumulation of PHAs granules by the use of Sudan Black B stain, eight strains were detected. Pair of specific PCR primers was designed and applied for genotypic detection of *phaC* synthase gene. Approximately, 760 bp DNA fragment was successfully amplified in the eight strains. Among the positive strains, *Bacillus* sp SW1-2, produced 36 g/L of the biopolymer during growth on modified E2 medium supplemented with glucose. Spectroscopic analysis by <sup>13</sup>C-NMR and <sup>1</sup>H-NMR revealed four narrow peaks (lines) (CH<sub>3</sub>; 21.2 ppm, CH<sub>2</sub>; 42.7, CH; 68.5 and C=O; 169.7 ppm) and 3 groups of signals (2.45, 2.58 and 5.2 ppm) identical and characteristic to polyhydroxybutyrate (PHB); respectively. Furthermore, the amplified PCR fragment, from genomic DNA of *Bacillus* sp SW1-2, was cloned in pGEM-T-Easy vector and sequenced with universal T7 and SP6 primers. The sequence showed 99% identity to *phaC* gene for polyhydroxyalkanoate synthase of many *B. megaterium* strains deposited in Genbank. While, showed 73% and 72% identity to synthases of *Bacillus mycoides* and *Bacillus* sp. INT005, respectively.

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**Keywords:** Polyhydroxybutyrate, genotypic, *Bacillus megaterium*, *phaC* synthase, NMR

### 1. Introduction

Polyhydroxyalkanoates (PHAs) are group of polyesters synthesized and intracellular accumulated by several microorganisms, especially when the carbon substrate is in excess to other nutrients (Sanger et al., 1977; Madison and Huisman, 1999; Kimm and Lenz, 2001; Steinbuchel, 2001; Shamala et al., 2003; Reddy et al., 2003). PHAs can be classified into different types according to the number of repeating units in the polymers. These polyesters are biodegradable and biocompatible thermoplastics (Madison and Huisman, 1999; Ojumu et al., 2004). Among PHAs, polyhydroxybutyrate (PHB) is the best known polyester due to its similarity to synthetic petroleum-based plastics (Mokhtari-Hosseini et al., 2009). PHB has many applications in medicine, veterinary practice, tissue engineering materials, food packaging and agriculture (van der Walle et al., 2001; Zinn et al., 2001; Borah et al., 2002; Luengo et al., 2003; Chen and Wu, 2005).

Currently, there are variety of methods for selecting polyhydroxyalkanoate (PHA)-accumulating bacteria. These include both phenotypic and genotypic detection methods. The first apply stains; Sudan Black staining (Schlegel et al., 1970), Nile blue A staining and direct staining of bacterial colonies by fluorescence (Spiekermann et al., 1999). While, genotypic detection methods based on the use of various polymerase chain reaction (PCR) protocols

(Sheu et al., 2000; Solaiman et al., 2000; Shamala et al., 2003; Solaiman and Ashby, 2005). Indeed, genotypic methods have become a highly sensitive and precise tool for detecting and amplifying the gene encoding PHA synthase.

Among PHB producer, members belong to genus *Bacillus* have been reported and extensively studied (Chen et al., 1991; Caballero et al., 1995; Labuzek and Radecka, 2001; Wu et al., 2001; Belam et al., 2002; Borah et al., 2002; Satoh et al., 2002; Tajima et al., 2003; Valappil et al., 2007b; Valappil et al., 2008; Adwitiya et al., 2009; Reddy and mahmood, 2009; Gurunathan et al., 2010). Recently, molecular investigation on polymer production revealed that poly (3-hydroxybutyrate) biosynthesis genes are *phbA*, *phbB*, and *phbC* (PHB synthase); these genes have been cloned and expressed in *E. coli* and their genetic organization has been extensively reported (Madison and Huisman, 1999; Zhang et al., 2001; Enan and Bashandy, 2004). PHA synthases (*phaC*) are key enzymes in PHA producing polymer granules. These enzymes are classified into four classes according to genetic sequence- deduced primary structure, substrate specificity and subunit composition (Steinbuchel, 2001). Novel PHA synthase from *Bacillus megaterium* required PhaC and PhaR for activity in vivo and in vitro reported by (McCool and Cannon, 2001). PhaCBm showed greatest similarity to the PhaCs of class III in both size and sequence. Unlike those in class III, the 40-



kDa PhaE was not required and the 22-kDa PhaRBm protein had no obvious homology to PhaE.

The main objective of this study was the phenotypic as well as genotypic detection of PHAs production and intracellular accumulation by a group of bacilli isolated from soil and sewage samples. Production of PHB biopolymer from *B. megaterium* SW1-2 and chemical characterization of the produced polymer by  $C^{13}$ NMR and  $H^1$ NMR spectroscopy was closely investigated. Special emphasis was given to molecular characterization of *phaC* synthase of *B. megaterium* SW1-2 by use of specific primers. Degree of identity of the nucleotide sequence compared to corresponding sequences of *phaC* synthases of other bacilli was also reported.

## 2. Materials and Methods

### Microorganism; enrichment and isolation

Screening was carried out by enrichment and isolation of spore-forming bacilli from sewage and soil samples obtained from Dammam, Eastern province, Saudi Arabia. Samples were treated for 20 min at 90 °C and subsequently cultivated on nutrient agar medium. Purified strains were cultivated on modified E2 medium supplemented with glucose as carbon source. Screening for PHB accumulation was carried out by staining with Sudan Black (0.3% (w/v) in 70% ethanol). Bluish-black colonies indicating PHB production and thus used for further studies (Belma et al., 2002). Isolates were maintained on nutrient agar slant composed of (g/L): peptone; 5, beef extract; 3, NaCl; 2 and agar; 20. Stock cultures were subcultured at regular intervals of one month and stored under refrigeration. Potential PHB producing strain, *Bacillus* sp SW1-2, was molecularly identified by 16S rDNA analysis as previously described (Berekaa and Al Thawadi, 2012).

### Growth and biopolymer production

The bacterium was grown in 50ml aliquot of nutrient broth dispensed in 250ml Erlenmeyer flask and incubated at 37°C for 24h at 150 rpm. 1.5% inoculums of the overnight culture was used to inoculate modified E2 medium of the following composition (g/L): ammonium sulfate; 2.5, glucose; 20,  $KH_2PO_4$ ; 1.5,  $Na_2HPO_4$ ; 3.5,  $MgSO_4 \cdot 7H_2O$ ; 0.2, beef extract; 0.5 and trace element solution composed of (g/L);  $H_3BO_3$ , 0.3;  $NaMoO_4 \cdot 2H_2O$ , 0.03;  $CuSO_4 \cdot 5H_2O$ ; 0.01,  $CuSO_4 \cdot 5H_2O$ ; 0.01;  $NiCl_2 \cdot 6H_2O$ , 0.02;  $ZnSO_4 \cdot 7H_2O$ , 0.1 and traces of ammonium ferric citrate. 50 ml of the medium placed in 250 ml Erlenmeyer flasks were inoculated with 750  $\mu$ l of the pre-culture. At the end of incubation period, PHB was determined and the cell dry weight was estimated.

### Extraction of PHB from *B. megaterium* SW1-2

PHB was extracted from the cell masses by using modified Hypochlorite method (Rawte and mavinkurve, 2002). For this purpose, *B. megaterium* cells were grown in 250 ml Erlenmeyer flasks containing 50 ml of the modified E2 medium. At the end of incubation period, one ml of cell suspension was centrifuged at 6,000 rpm for 15 min. Cell pellet was washed once with 1 ml saline and was re-centrifuged. Subsequently suspended in equal volume of sodium hypochlorite (5.5% active chlorine) and incubated at 45°C for 60 min. This extract was centrifuged at 10,000 rpm for 20 min and the pellet of PHB was washed with water and twice with ethanol:acetone mixture (2:1). The pellet was again centrifuged at 10,000 rpm to get purified PHB. Determination of PHB yield was performed routinely by dry weight estimation. The ultraviolet (UV) absorption spectrum of the polymer was analyzed following its conversion to crotonic acid by treatment with concentrated  $H_2SO_4$ , and the absorbance was scanned between 200 and 350 nm with UV-1800 spectrophotometer (Shimadzu Scientific, USA). For dry weight estimation, the pellet after extraction was dried to constant weight.

### Analysis of biopolymer

#### Cell dry weight (CDW)

After centrifugation of the culture medium, the supernatant was discarded and the cell pellet was washed with distilled water. The washed pellet was resuspended in 1 ml distilled water, transferred to pre weighed boats and dried to constant weight at 60°C.

#### Characterization of extracted PHB by $C^{13}$ NMR and $H^1$ NMR analysis

Extracted PHB biopolymer of *B. megaterium* SW1-2 was characterized by spectroscopy analysis.  $H^1$  NMR spectrum was recorded on a JEOL JNM-LA 500 MHz spectrometer 30°C in  $CDCl_3$  as solvent. While,  $C^{13}$ NMR spectral experiments were performed at 125.65 MHz with the following acquisition parameters: 32 k data point, 0.967 s acquisition time, recycle delay 1 s and contact time 4.50 ms.

### Bacterial strains and plasmids

#### Nucleic acid techniques

Genomic DNA was isolated by the use of DNA isolation kit (QIAamp DNA Mini, QIAGEN) according to the manufacturer instructions, with some modification. Lysozyme (20mg/ml) in TE buffer was used for lysis of the cells by incubation at 37°C for 30 min. Recombinant *E. coli* DH5a cells harboring recombinant plasmids were screened separately by blue-white selection utilizing LB-agar plates supplemented with ampicillin and IPTG.

#### PCR Technique

PCR reaction was carried out in a final volume of 50  $\mu$ l using HotStar PCR Master Mix Kit,

according to the manufacturer instructions (QIAGEN). The PCR reaction contained 1 ul of each primer (10 pmol). The PCR condition was 1 cycle at 95°C for 15 min followed by 35 cycles at 95°C for 55 sec, 58 °C for 55 sec, and 70°C for 55 sec. The final extension step was carried out at 72°C for 10 min and PCR reaction was run in Eppendorf Mastercycler personal, Germany.

#### Designing specific primers

Pair of specific primer, corresponding to two conserved regions (Figure 1), was designed for amplifying Class IV *phaC1* gene by aligning and analyzing Class IV PHA biosynthesis operon sequences belonging to the following *Bacillus* species: *Bacillus megaterium*1 AB525783, *Bacillus* sp. INT005 AB077026, *Bacillus megaterium*2 AF109909, *Bacillus* sp. CFR13 HM370560, *Bacillus megaterium*3 strain BPK-3 GU190757, *Bacillus cereus* strain DC4 HM122247, *Bacillus cereus* strain DC3 HM122246, *Bacillus cereus* strain DC2 HM122248. The primers designs were; forward primer P1:5'-GAT GTG TAT TTG CTT GAC TGG GG-3', reverse primer P2: 5'-AGC CAA TCG CCG ATT GAA GGA TA-3'). Primers were synthesized by *metabion*, Martinsried, Germany.

#### Detecting PCR products

Electrophoresis on 1% (w/v) agarose gels (1X TAE) was used for detecting PCR amplification products.  $\Lambda$  DNA/*Hind* III (0.2  $\mu\text{g}/\mu\text{l}$ ) was used as DNA size marker. Run conditions were 6.5 volts/cm for 2 and half hrs. The gel was stained with a 0.5  $\mu\text{g}/\text{ml}$  ethidium bromide solution and amplified DNA fragments were visualized under UV light and recorded with a GelDoc image digitalizer (Bio-Rad).

#### DNA sequencing data analysis

Analysis of nucleotide sequences was performed using BioEdit computer based program. Alignments and comparison of sequences were carried out using Blast program. The nucleotide sequencing data reported in this work submitted to the GenBank nucleotide sequence database and is listed under the accession number JQ755810.

#### Cloning and Sequencing of the PCR Products

To ligate the generated PCR products onto pGEM-T-Easy vector (Promega Co.), 2 ul was taken in a clean 0.5 ml tube to which 1 ul pGEM-T-Easy vector (50 ng) and 1 ul ligase buffer were added, followed by the addition of 2 U ligase enzyme. Final volume of the ligation reaction was adjusted to 10 ul by the addition of nuclease-free distilled water. The tube was incubated at 16°C for 16 h. Transformation of *Escherichia coli* DH5a competent cells was carried out according to Sambrook et al. (1989). Recombinant *E. coli* DH5a harboring the pGEM-T-Easy vector was screened in selective LB/IPTG/X-gal/Ampicillin/agar plates. Plasmids were prepared

from some positive clones using the PureYield Plasmid Miniprep System (A1222, Promega, USA). Sequencing of the PCR products cloned onto pGEM-T-Easy vector (four different clones) was carried out according to Sanger et al. (1977), using the MegaBACE 1000 DNA Sequencing System (Pharmacia/Amersham Co.). The chain termination sequencing reaction was conducted utilizing the DYEnamic ET terminator kit as an integral part of the MegaBACE 1000 DNA sequencing system. Sequencing reaction products were purified using DyeEx 2.0 Spin Kit (63206 QIAGEN) and applied to MegaBace 1000 Sequencing machine.

### 3. Results and Discussion

#### Enrichment and isolation of PHAs accumulating bacilli

A group of endospore-formers bacilli was subjected to phenotypic and genotypic detection of PHAs synthesis. Bacilli were selectively enriched and isolated from sewage and soil samples from Dammam, Saudi Arabia, by heat treatment and subculture on nutrient agar medium. Purified strains were phenotypically screened for PHAs synthesis and intracellular accumulation by cultivation on modified E2 medium supplemented with glucose as a sole carbon source. Eight strains revealed purple-blue colored colonies after stain with Sudan Black B. In accordance, Sudan Black staining (Schlegel et al., 1970), Nile blue A staining and direct staining of bacterial colonies by fluorescence (Spiekermann et al., 1999) were used as phenotypic methods of detection. For genotypic detection of *phaC* synthase gene, pair of specific PCR primers was designed and applied. Approximately, 760 bp DNA fragment was amplified in the eight strains (Figure 2). Several genotypic methods applied various PCR protocols; using degenerate primers to detect and amplify the PHA synthase gene(s) have been reported (Solaiman et al., 2000; Sheu et al., 2001; Shamala et al., 2003; Solaiman and Ashby, 2005; Chien et al., 2007; Berekaa and Al Thawadi, 2012). Interestingly, successful application of polyphasic approach using combination of phenotypic and genotypic screening method was recorded by Chien et al. (2007). This polyphasic approach helps to overcome drawbacks of the individual detection method.

#### PHB accumulation by *Bacillus* sp. SW1-2

Among the positive strains a bacterium, previously isolated and identified as *B. megaterium* SW1-2 (Berekaa and Al Thawadi, 2012), was used for chemical and molecular analysis of PHB production. PHB was closely monitored during growth of *Bacillus megaterium* SW1-2 on modified E2 medium supplemented with glucose as a sole carbon source and in presence of beef extract. Results in figure 3 showed the growth and PHB accumulation

measured during a period of 96 hr. Obviously, maximum PHB production was attained (36% CDW) after 48 h. Amount of PHB was clearly decreased (15% CDW) at the end of incubation period. Similarly, *B. megaterium* OU303A, *B. cereus* SPV and other bacilli produces PHA co-polymer composed mainly of PHB during growth on modified E2 medium supplemented with glucose as a carbon source and in presence of traces of yeast extract instead of beef extract (Gouda et al., 2001; Law et al., 2001; Valappil et al., 2007b; Adwitiya et al., 2009; Reddy and Mahmood, 2009; Berekaa and Al Thawadi, 2012), support the results presented in this work. Interestingly, monitoring of PHB production in *B. megaterium* cells indicated that it is produced during logarithmic phase and maximally accumulated just prior to the formation of spores and was degraded during the process of sporulation (data not shown).

#### Chemical analysis of the polymer

Preliminary analysis of polymeric material digested with concentrated H<sub>2</sub>SO<sub>4</sub> and scanned with UV-Vis spectrophotometer revealed a sharp peak at 235 nm characteristic of crotonic acid indicating the presence of PHB biopolymer (data not shown).

#### Characterization of the extracted PHB

##### C<sup>13</sup> NMR analysis

Furthermore, C<sup>13</sup>NMR analysis was used to determine the structure of the isolated polymer from *B. megaterium* SW1-2 grown on the modified E2 medium (Figure 4a). Four narrow lines appeared which were identical to the C<sup>13</sup>NMR spectra of PHB, as reported previously (Doi and Abe, 1990). These four peaks were assignable to the methyl (CH<sub>3</sub>; 21.2 ppm), methylene (CH<sub>2</sub>; 42.7 ppm), methine (CH; 68.5 ppm) and carbonyl (C=O; 169.7 ppm) carbon resonance of PHB (Doi and Abe, 1990). This analysis thus confirmed the molecular composition of the polymer to be PHB.

##### H<sup>1</sup> NMR analysis

The extracted polymer was dissolved in 1 ml CDCl<sub>3</sub> followed by H<sup>1</sup>NMR analysis. Three groups of signals characteristic of polymer PHB were seen in the spectrum (Figure 4b). A doublet at 1.26 ppm represented the methyl group (CH<sub>3</sub>) coupled to one proton while a doublet of quadruplet at 2.45, 2.58 ppm resulted from methylene group (CH<sub>2</sub>) adjacent to an asymmetric carbon atom bearing a single proton. The third signal was a multiplet at 5.2 ppm, which was attributed to a methyne group (CH). From the contribution of various groups to the NMR spectra, it was concluded that the biodegradable polymer accumulated in the bacterial biomass is in the form of PHB.

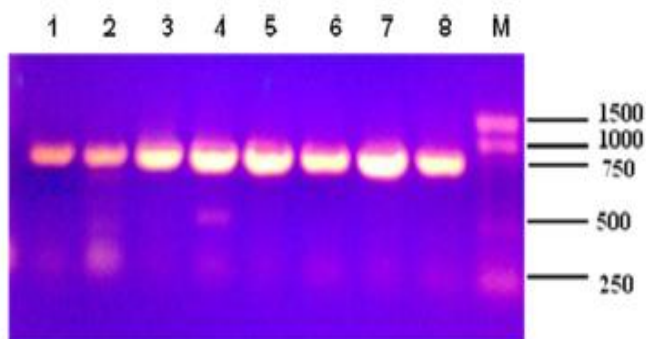
**Figure 1.** Alignment of nucleotide sequence of polyhydroxyalkanoate *phaC* gene from *B. megaterium* SW1-2 as compared to other sequences of *phaC* synthase gene from different bacilli.

<i>B. cereus</i> DC4	CGTGGTTTTGATGTATATAT	GCTTGATTGGGGCACATTTG	GTTTAGAAGATAGTCATTTG
<i>B. cereus</i> DC3	CGTGGTTTTGATGTATATAT	GCTTGATTGGGGCACATTTG	GTTTAGAAGATAGTCATTTG
<i>B. cereus</i> DC2	CGTGGTTTTGATGTATATAT	GCTTGATTGGGGCACATTTG	GTTTAGAAGATAGTCATTTG
<i>B. sp</i> INT005	CGTGGTTTTGATGTGTATAT	GCTTGATTGGGGCACATTTG	GTTTAGAAGATAGTCATTTG
<i>B. sp</i> CFR13	CGTGGTTTTGATGTGTATAT	GCTTGATTGGGGCACATTTG	GTTTAGAAGATAGTCATTTG
<i>B. mega</i> 1	CGTGGTTTTGACGTGTATTT	GCTTGACTGGGGAACCTCCAG	GGCTTGAAGACAGCAATATG
<i>B. mega</i> 2	CGCGGTTTTGACGTGTATTT	GCTTGACTGGGGAACCTCCAG	GGCTTGAAGACAGCAATATG
<i>B. mega</i> 3	CGCGGTTTTGACGTGTATTT	GCTTGACTGGGGAACCTCCAG	GGCTTGAAGACAGCAATATG
<i>B. meg</i> SW1-2	GATGTGTATTT	GCTTGACTGGGGAACCTCCAG	GGCTTGAAGACAGCAATATG
	** ***** **.*:**	***** *****.*:** :*	* *:***** ** .*:**
<b>Forward</b>			
<i>B. cereus</i> DC4	AAATTTGATGATTTTCGTGTT	TGATTATATTGCAAAAGCAG	TAAAAAAGTAATGCGAACT
<i>B. cereus</i> DC3	AAATTTGATGATTTTCGTGTT	TGATTATATTGCAAAAGCAG	TAAAAAAGTAATGCGAACT
<i>B. cereus</i> DC2	AAATTTGATGATTTTCGTGTT	TGATTATATTGCAAAAGCAG	TAAAAAAGTAATGCGAACT
<i>B. sp</i> INT005	AAATTTGATGATTTTGTGTT	TGATTATATTGCAAAAGCAG	TGAAAAAAGTAATGCGAACT
<i>B. sp</i> CFR13	AAATTTGATGATTTTGTGTT	TGATTATATTGCAAAAGCAG	TGAAAAAAGTAATGCGAACT
<i>B. mega</i> 1	AAGCTAGATGATTATATTGT	AGATTATATTCCAAAAGCGG	CGAAAAAGGTGCTGCGCACT
<i>B. mega</i> 2	AAGCTAGATGATTATATTGT	AGATTATATTCCAAAAGCGG	CGAAAAAGGTGCTGCGCACT
<i>B. mega</i> 3	AAGCTAGATGATTATATTGT	AGATTATATTCCAAAAGCGG	CGAAAAAGGTGCTGCGCACT
<i>B. meg</i> SW1-2	AAGCTAGATGATTATATTGT	AGATTATATTCCAAAAGCGG	CGAAAAAGGTGCTGCGCACT
	** .*:*****:.* *	:***** *****.*	.*****.*.*.*.*.*.*
<i>B. cereus</i> DC4	GCAAAATCGGACGAGATTTT	TTTACTTGGTTATTGCATGG	GTGGAACGCTAATTCTATT
<i>B. cereus</i> DC3	GCAAAATCGGACGAGATTTT	TTTACTTGGTTATTGCATGG	GTGGAACGCTAATTCTATT

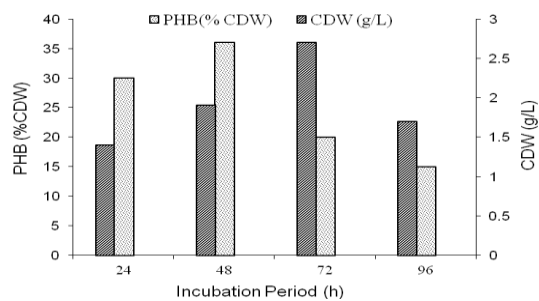
<i>B. cereus</i> DC2	GCAAAATCGGACGAGATTTTC	TTTACTTGGTTATTGTATGG	GTGGAACGCTAACTTCTATT
<i>B. sp</i> INT005	GCAAAATCGGACGAGATTTTC	TTTACTTGGTTATTGCATGG	GGGGAACGCTAACTTCTATT
<i>B. sp</i> CFR13	GCAAAATCGGACGAGATTTTC	TTTACTTGGTTATTGCATGG	GGGGAACGCTAACTTCTATT
<i>B. mega</i> 1	TCTAAATCTCCTGATTTGTC	TGTTCTTGGTTACTGCATGG	GCGGAACATGACATCTATT
<i>B. mega</i> 2	TCTAAATCTCCTGATTTGTC	TGTTCTTGGTTACTGCATGG	GCGGAACATGACATCTATT
<i>B. mega</i> 3	TCTAAATCTCCTGATTTGTC	TGTTCTTGGTTACTGCATGG	GCGGAACATGACATCTATT
<i>B. meg</i> SW1-2	TCTAAATCTCCTGATTTGTC	TGTTCTTGGTTACTGCATGG	GCGGAACATGACATCTATT
	*:***** . ** :* ** *	*:***** ** ***** *	***** .*:**:******
<i>B. cereus</i> DC4	TATGCAGCGCTTCATCCGCA	CATGCCAATTCGTAATTTAA	TTTTTCATGACAAGTCCTTTT
<i>B. cereus</i> DC3	TATGCAGCGCTTCATCCGCA	CATGCCAATTCGTAATTTAA	TTTTTCATGACAAGTCCTTTT
<i>B. cereus</i> DC2	TATGCAGCGCTTCATCCGCA	CATGCCAATTCGTAATTTAA	TTTTTCATGACAAGTCCTTTT
<i>B. sp</i> INT005	TATGCAGCGCTTCATCCGCA	CATGCCAATTCGTAACCTAA	TCTTTATGACAAGTCCTTTT
<i>B. sp</i> CFR13	TATGCAGCGCTTCATCCGCA	CATGCCAATTCGTAACCTAA	TCTTTATGACAAGTCCTTTT
<i>B. mega</i> 1	TTTGCTGCATTAATGAAGA	C TTGCCGATTA AAAA ACTTAA	TTTTTTATGACAAGTCCATTT
<i>B. mega</i> 2	TTTGCTGCATTAATGAAGA	C TTGCCGATTA AAAA ACTTAA	TTTTTTATGACAAGTCCATTT
<i>B. mega</i> 3	TTTGCTGCATTAATGAAGA	C TTGCCGATTA AAAA ACTTAA	TTTTTTATGACAAGTCCATTT
<i>B. meg</i> SW1-2	TTTGCTGCATTAATGAAGA	C TTGCCGATTA AAAA ACTTAA	TTTTTTATGACAAGTCCATTT
	*:*** ** .*:** .. *	:****.***.:** ** *	* ** *****:***
<i>B. cereus</i> DC4	GATTTCTCTGAAACAGGATT	GTATGGTCCTTTATTAGATG	AGAAATACTTCAATTTAGAT
<i>B. cereus</i> DC3	GATTTCTCTGAAACAGGATT	GTATGGTCCTTTATTAGATG	AGAAATACTTCAATTTAGAT
<i>B. cereus</i> DC2	GATTTCTCTGAAACAGGATT	GTATGGTCCTTTATTAGATG	AGAAATACTTCAATTTAGAT
<i>B. sp</i> INT005	GATTTCTCTGAAACAGGATT	ATATGGTCCTTTATTAGATG	AGAAATACTTCAATCTAGAT
<i>B. sp</i> CFR13	GATTTCTCTGAAACAGGATT	ATATGGTCCTTTATTAGATG	AGAAATACTTCAATCTAGAT
<i>B. mega</i> 1	GATTTTTTCGGATACAGGTTT	ATACGGAGCATTCCCTAGACG	ATCGCTACTTTAATTTAGAT
<i>B. mega</i> 2	GATTTTTTCGGATACAGGTTT	ATACGGAGCATTCCCTAGATG	ATCGCTACTTTAATTTAGAT
<i>B. mega</i> 3	GATTTTTTCGGATACAGGTTT	ATACGGAGCATTCCCTAGACG	ATCGCTACTTTAATTTAGAT
<i>B. meg</i> SW1-2	GATTTTTTCGGATACAGGTTT	ATACGGAGCATTCCCTAGACG	ATCGCTACTTTAATTTAGAT
	***** ** *:*****:**	.** ** *:**.* ** *	* ..***** ** *****
<i>B. cereus</i> DC4	AAAGCGGTTGATACATTTGG	AAATATTCCGCCAGAAATGA	TTGATTTTCGGAAACAAAGTG
<i>B. cereus</i> DC3	AAAGCGGTTGATACATTTGG	AAATATTCCGCCAGAAATGA	TTGATTTTCGGAAACAAAGTG
<i>B. cereus</i> DC2	AAAGCGGTTGATACATTTGG	AAATATTCCGCCAGAAATGA	TTGATTTTCGGAAACAAAGTG
<i>B. sp</i> INT005	AAAGCGGTTGATACATTTGG	AAATATTCCGCCAGAAATGA	TTGATTTTCGGAAACAAAGTG
<i>B. sp</i> CFR13	AAAGCGGTTGATACATTTGG	AAATATTCCGCCAGAAATGA	TTGATTTTCGGAAACAAAGTG
<i>B. mega</i> 1	AAAGCAGTAGATACATTCCG	AAACATCCCTCCAGAGATGA	TTGACTTTGGAAACAAGATG
<i>B. mega</i> 2	AAAGCAGTAGATACATTCCG	AAACATCCCTCCAGAGATGA	TTGACTTTGGAAACAAGATG
<i>B. mega</i> 3	AAAGCAGTAGATACATTCCG	AAACATCCCTCCAGAGATGA	TTGACTTTGGAAACAAGATG
<i>B. meg</i> SW1-2	AAAGCAGTAGATACATTCCG	AAACATCCCTCCAGAGATGA	TTGACTTTGGAAACAAGATG
	***** .**:****** **	*** ** ** ***** .****	***** ** ***** .**
<i>B. cereus</i> DC4	TTAAAGCCAATTACGAACTT	TGTTGGTCCATATGTTGCTC	TAGTAGATCGTTCAGAGAAT
<i>B. cereus</i> DC3	TTAAAGCCAATTACGAACTT	TGTTGGTCCATATGTTGCTC	TAGTAGATCGTTCAGAGAAT
<i>B. cereus</i> DC2	TTAAAGCCAATTACGAACTT	TGTTGGTCCATATGTTGCTC	TAGTAGATCGTTCAGAGAAT
<i>B. sp</i> INT005	TTAAAACCAATTACGAACTT	TGTTGGTCCATATGTTGCTT	TAGTAGATCGTTCAGAGAAT
<i>B. sp</i> CFR13	TTAAAACCAATTACGAACTT	TGTTGGTCCATATGTTGCTT	TAGTAGATCGTTCAGAGAAT
<i>B. mega</i> 1	TTAAAGCCAATCACGAATTT	CTATGGCCCATATGTAACGT	TGGTGGACCGTTCGGAAAAAT
<i>B. mega</i> 2	TTAAAGCCAATCACGAATTT	CTACGGCCCATATGTAACGT	TGGTGGACCGTTCGGAAAAAT
<i>B. mega</i> 3	TTAAAGCCAATCACGAATTT	CTATGGCCCATATGTAACGC	TAGTGGACCGTTCGGAAAAAT
<i>B. meg</i> SW1-2	TTAAAGCCAATCACGAATTT	CTATGGCCCATATGTAACGT	TGGTGGACCGTTCGGAAAAAT
	*****.***** ***** **	: ** **.******:.*	*.*** ** *****.***.***
<i>B. cereus</i> DC4	GAACGCTTCGCCGAAAGCTG	GAGATTGGTTCAAAGTGGG	TTGGTGATGGTATTCCGTTC
<i>B. cereus</i> DC3	GAACGCTTCGCCGAAAGCTG	GAGATTGGTTCAAAGTGGG	TTGGTGATGGTATTCCGTTC
<i>B. cereus</i> DC2	GAACGCTTCGCCGAAAGCTG	GAGATTGGTTCAAAGTGGG	TTGGTGATGGTATTCCGTTC
<i>B. sp</i> INT005	GAGCGCTTCGTTGAAAGCTG	GAGGTTAGTTCAAAGTGGG	TTGGCGATGGCATTCCGTTC
<i>B. sp</i> CFR13	GAGCGCTTCGTTGAAAGCTG	GAGGTTAGTTCAAAGTGGG	TTGGCGATGGCATTCCGTTC
<i>B. mega</i> 1	CAGCGGTTTGTGAAAGCTG	GAAGCTAATGCAAAGTGGG	TTGCTGACGGAATCCCATTT
<i>B. mega</i> 2	CAGCGGTTTGTGAAAGCTG	GAAGCTAATGCAAAGTGGG	TTGCTGACGGAATCCCATTT
<i>B. mega</i> 3	CAGCGGTTTGTGAAAGCTG	GAAGCTAATGCAAAGTGGG	TTGCTGACGGAATCCCATTT
<i>B. meg</i> SW1-2	CAGCGGTTTGTGAAAGCTG	GAAGCTAATGCAAAGTGGG	TTGCTGACGGAATCCCATTT



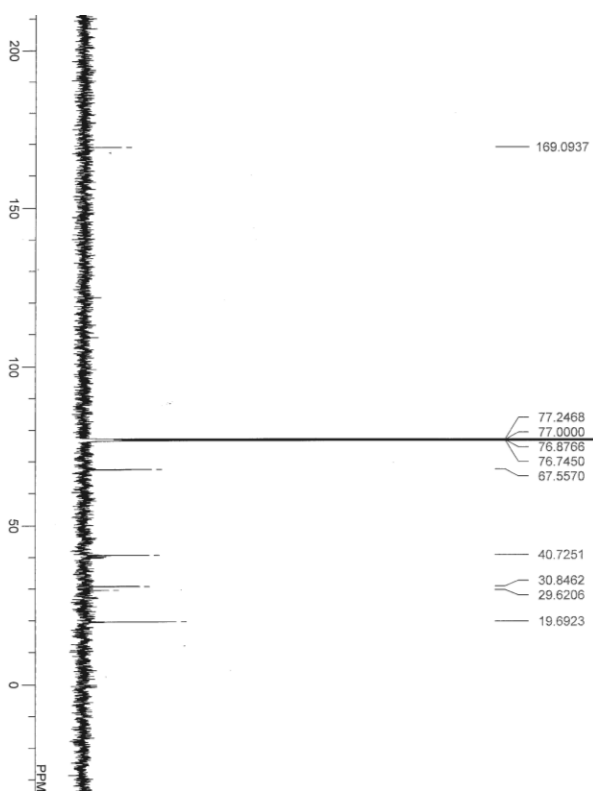




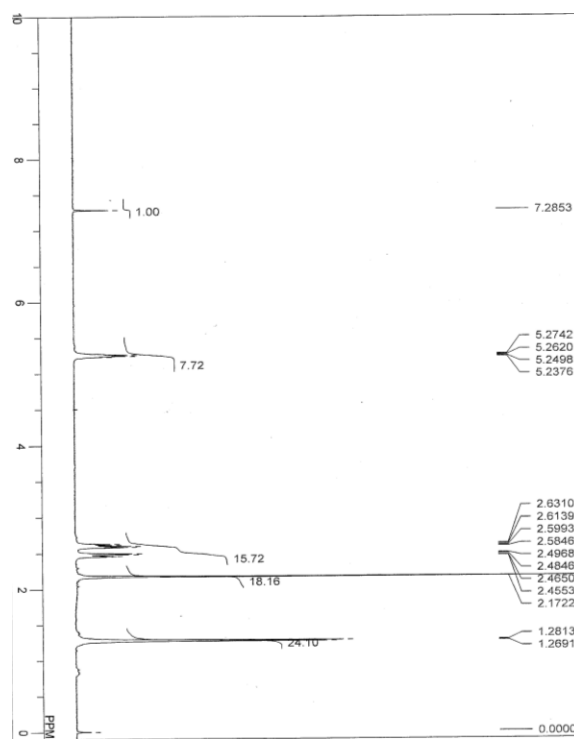
**Figure 2.** Agarose gel electrophoresis of PCR products from different bacilli (Lanes 1-6,8) and *B. megaterium* SW1-2 (Lane 7) with gene specific primer set and 1.0 kbp DNA ladder (lanes 9).



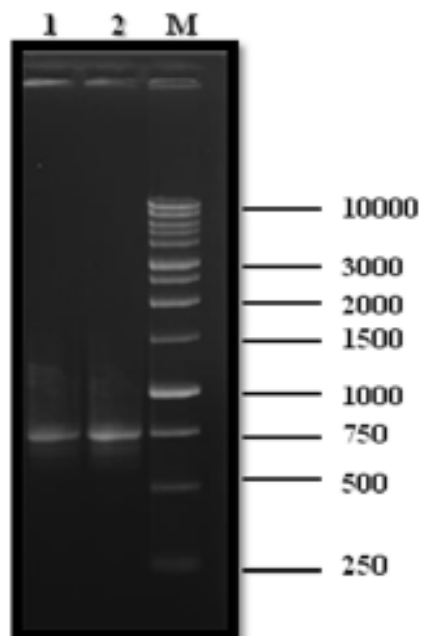
**Figure 3.** Growth and polyhydroxybutyrate (PHB) production by *B. megaterium* WS1-2 during different time intervals.



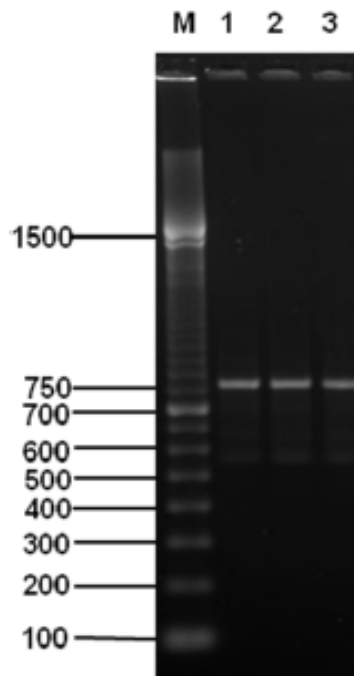
**Figure 4a.** <sup>13</sup>C-NMR Spectroscopy of PHB biopolymer produced from *B. megaterium* SW1-2.



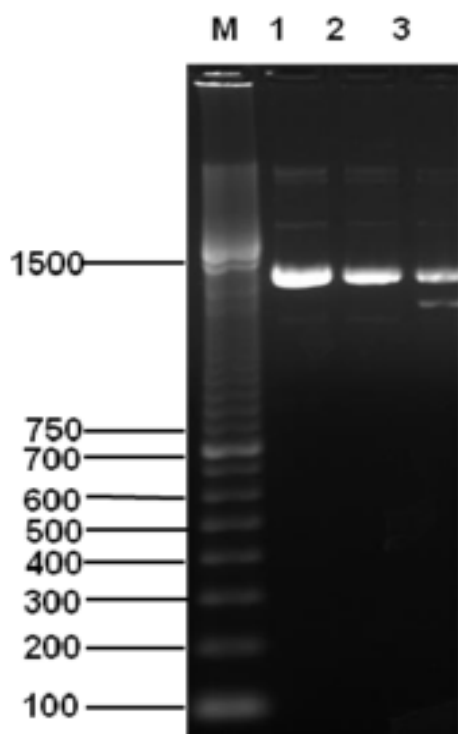
**Figure 4b.** <sup>1</sup>H-NMR Spectroscopy of PHB biopolymer produced from *B. megaterium* SW1-2.



**Figure 5.** Agarose gel electrophoresis (1%) of PCR products from *B. megaterium* SW1-2 (Lanes 1-2) with gene specific primers set and 1.0 kbp DNA ladder (Lane M).



**Figure 7.** Agarose gel electrophoresis (1%) of PCR fragment from *B. megaterium* SW1-2 (Lane 1-3) amplified with T7 and SP6 primer set and 100 bp DNA ladder (Lane M).



**Figure 6.** Agarose gel electrophoresis (1%) of plasmid minipreps from *B. megaterium* SW1-2 cloned PCR product onto pGEM-T-Easy vector (Lane 1-3) and 100 bp DNA ladder (Lane M).

#### Analysis of *B. megaterium* SW1-2 *phaC* synthase gene

The PCR fragment amplified from genomic DNA of *B. megaterium* SW1-2 was cloned in pGEM-T-Easy vector, transform into *Escherichia coli* DH5a competent cells. Recombinant *E. coli* DH5a harboring the pGEM-T-Easy vector was screened in selective LB/IPTG/X-gal/Ampicillin/agar plates. Plasmids prepared from some positive clones, isolated and purified (Figure 6). The presence of a cloned DNA insert was tested and verified by PCR amplification of the plasmid with T7/SP6 primers, which anneal to the vector region flanking the DNA insert (Figure 7). Several clones containing the DNA insert were then sequenced to ensure their uniqueness. Sequencing revealed that most of the amplified products were uniform and corresponded to *phaC* synthase of *Bacillus* sp. Nucleotide sequences corresponding to 761 bp compared with the nucleotide sequences deposited in the GenBank database using the Blast family program (Figure 1). The sequence was deposited in GenBank under accession number JQ755810. Indeed, the sequence of *phaC* synthase gene of *B. megaterium* revealed very close identity to other *phaC* gene sequences from other bacilli. It showed 99% identity to *phaC* gene for polyhydroxyalkanoate synthase of *Bacillus megaterium* DSM319, *Bacillus megaterium* QM

B1551, and 98% to synthase of *Bacillus megaterium* WSH-002 (Liu et al., 2011). However, the sequence showed 73% identity to synthase of *Bacillus mycoides* strain DFC1 and the *Bacillus thuringiensis* serovar finitimus YBT-020 (Zhu et al., 2011) and 72% to synthase of *Bacillus* sp. INT005 (Satoh et al., 2002). In concurrence, successful application of different molecular approaches for detection of PHAs accumulation by a variety of bacteria was reported by many scientists (Sheu et al., 2000; Castano et al., 2007; Chien et al., 2007).

### Conclusion

PHAs are synthesized and intracellular accumulated as granules in many bacteria. Results revealed that phenotypic detection of PHAs accumulating bacteria can be supported by genotypic detection method. This polyphasic approach satisfies the minimal industrial standards for screening potentially useful organisms for PHA production. Pair of specific conserved primers ( P1 and P2) can be used as universal primers to amplify partial segment from *phaC* gene of several bacilli among of them *B. megaterium* SW1-2. Indeed, the ability to produce PHB was confirmed by  $C^{13}$  and  $H^1$ NMR spectroscopy. Furthermore, *phaC* synthase gene of *B. megaterium* SW1-2 showed 98%-99% identity to *phaC* gene for polyhydroxyalkanoate synthase of many *Bacillus megaterium* strains. However, the sequence showed 73% identity to synthase of *Bacillus mycoides* strain DFC1 and the *Bacillus thuringiensis* serovar finitimus YBT-020 and 72% to synthase of *Bacillus* sp. INT005. Consequently, cloning of the whole synthase gene might allow for recombinant production of the biodegradable biopolymer to be used in the field of medical and environmental biotechnology.

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## Evaluation of the efficiency of Restaurants using DEA Method (the case of Iran)

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**Abstract:** The purpose of this study is to evaluate the efficiency and ranking of 15 Restaurants in Iran, paying attention to efficiency improvement using a data envelopment analysis (DEA) model. The model considers three inputs (monthly working hours, branch area (square meters), and years of experience as manager) and two outputs (monthly number of customers who bought something from the branch, and monthly sales in USD). The results indicate that data envelopment analysis is a Useful tool to evaluate the efficiency of Restaurants. Moreover, the results show that Noor restaurant and Nemoone restaurant is the most efficient restaurants Compared to other restaurants. Restaurants or other service providers should find this alternative DEA model helpful and more flexible in re-examining their resource utilization and possibly reshuffling their resource pool.

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**Keywords:** Efficiency, Evaluation, Restaurant, Data Envelopment Analysis (DEA)

### 1. Background

The DEA Model measures the relative efficiency of public and nonprofit organizations having no market value. One of the main advantages in using the DEA Model is that it can measure the efficiency of a group without adopting predetermined fractional linear programming while evaluating the input and output factors. Many services such as banks, hotels, and food chains like Pizza Hut and McDonald's and retail stores like Wal-Mart are composed of multi-branch firms. Numerous papers have explored the efficiency and relative efficiency of branches. Typically, these papers used the data envelopment analysis (DEA) methodology, its variants, various ranking methods, regression analysis and other indicators. Past literature on DEA has shown that DEA has been widely applied in measuring efficiency particularly in external benchmarking issues. DEA has been utilized for selection of partners for benchmarking in telecommunications industry (Collier and Storbeck, 1993) and in travel management (Bell and Morey, 1995). Collier and Storbeck (1993) used standard DEA approach, which calculate "technical" efficiencies for determining benchmarking partners. Bell and Morey (1995) used DEA to identify appropriate benchmarking partners that use a different mix of resources that are more cost efficient compared to that used by the firm. Other areas on external benchmarking using DEA are the banking and finance industry (Barr and Seiford, 1994) and grocery industry (Athanasopoulos and Ballantine, 1995). Wang et al. (2005) use a fixed and unified production frontier (i.e.

the same constraint set) to measure the interval efficiencies. Jahanshahloo et al. (2004) solve interval efficiencies by analysis of sensitivity and stability in DEA with interval data. Post and Spronk (1999) present a performance measurement technique that combines DEA and interactive multiple goal programming and call it "a decision support tool to select performance benchmarks that are both feasible and desirable." Donthu et al. (2004) while using DEA for benchmarking "marketing productivity" state, "We use DEA to identify benchmarks (role models) and set goals for improvement. These represent two very important steps of benchmarking." Soteriou and Stavrinides (1997) and Soteriou and Zenios (1999) have proposed DEA as a technique for benchmarking of "service delivery system characteristics of bank branches." Manandhar and Tang (2002) present a framework for simultaneous benchmarking of "performance of bank branches" using a modified DEA formulation DEA has been successfully used to provide bank branch benchmarks in line with three approaches (Paradi et al., 2004; Giokas, 2008): production, intermediation and profitability or profit.

The remainder of this paper is organized as follows: Section 2 presents the DEA Method. Section 3 presents a real-life case study of 15 restaurants that their efficiency is evaluated. Section 4 presents the Efficiency analysis. Section 5 gives a summary and suggestions.



**2. Data envelopment analysis (DEA)**

The methodology of data envelopment analysis, initially introduced by Charnes *et al.* (1978), is a mathematical programming technique used to evaluate the relative efficiency of homogeneous units. This efficiency evaluation derives from analysing empirical observations obtained from decision-making units (DMUs), a term coined by Charnes *et al.* (1978) to define productive units which are characterized by common multiple outputs and common designated inputs. DEA can be used to measure the efficiency of each similar firm or decision-making unit (DMU), and it is a powerful tool to determine whether DMUs perform efficiently or inefficiently on the efficiency performance (Zhang *et al.*, 2006). The objective of the DEA exercise is to identify the DMUs that produce the greatest amount of outputs by consuming the least amount of inputs. A DMU is deemed to be efficient if the ratio of weighted sum of outputs to the weighted sum of inputs is the highest. Hence, the DEA program maximizes the ratio of weighted outputs to weighted inputs for the DMU under consideration subject to the condition that similar ratios for all DMUs be less than or equal to one.

Every decision-making unit (DMU) is measured relative to all other DMUs. A composite unit (hypothetical best practice unit) is composed of a subset of efficient DMUs. The efficient DMUs define a production frontier that envelops the observed data of inefficient DMU's. The DMU being measured will be judged inefficient if the hypothetical composite unit requires fewer inputs to obtain the same output. A unit will be judged efficient if it requires the same amount of inputs to produce an output as the composite unit. Distance from the frontier determines how inefficient an individual DMU is. Inefficient DMUs can become efficient by increasing outputs or decreasing inputs in a fashion that causes them to resemble their efficient reference set. Golany and Roll (1989) generalize the main process of employing DEA to assess the performance of a group of organizations including decision-making unit decisions; input and output selection; data collection; assessment model choice; model administration; assumptions and the explanation of outcome. Oral and Yolalan (1990) proposed the reference aggregate of the inefficiency unit and the relative dual weight of the reference aggregate, which is helpful in identifying the local leader and analyzing local economies of scale.

The relative efficiency of the multiple input and multiple output in DMU is typically defined as an engineering like ratio( weighted sum of the DMU 's outputs divided by weighted sum of the DMU ' s input),i.e. for the generic *j*th DMU:

$$E_j = \frac{\text{weighted sum of outputs}}{\text{weighted sum of inputs}}$$

DEA model computes weights that give the highest possible relative efficiency score to a DMU while keeping the efficiency scores of all DMUs less than or equal to 1 under the same set of weights. The fractional form of a DEA mathematical programming model is given as follows:

$$\text{Maximize } Z = \frac{\sum_{r=1}^t U_r Y_{rj_0}}{\sum_{r=1}^m V_r X_{ij_0}}$$

Subject to:

$$\frac{\sum_{r=1}^t U_r Y_{rj}}{\sum_{r=1}^m V_r X_{ij}} \leq 1 \quad j = 1, 2, \dots, n \quad i = 1, \dots, m \quad U_r, V_i \geq 0 \quad (1)$$

Where  $U_r$ , the weight for output  $r$ ;  $v_i$ , the weight for input  $i$ ;  $y_{rj}$ , the amount of output  $r$  of DMU  $j$ ;  $x_{ij}$ , the amount of input  $i$  of DMU  $j$ ;  $t$ , the number of outputs;  $m$ , the number of inputs;  $n$ , the number of DMUs. The objective function of equation (1) seeks to maximize the efficiency score of a DMU<sub>*j*0</sub> by choosing a set of weights for all inputs and outputs. The first constraint set of equation (1) ensures that, under the set of chosen weights, the efficiency scores of all DMUs are not more than 1. The second and third constraint sets of equation (1) ensure that no weights are set to 0 in order to consider all inputs and outputs in the model. A DMU<sub>*j*0</sub> is considered efficient if the objective function of the associated (equation (1)) results in efficiency score of 1, otherwise it is considered inefficient. By moving the denominator in the first constraint set in equation (1) to the right-hand side and setting the denominator in the objective function to 1, (equation (1)) can be converted into a LP problem as follows:

$$\text{Maximize } Z = \sum_{r=1}^t U_r Y_{rj_0}$$

Subject to:

$$\sum_{i=1}^m V_i X_{ij_0} = 1$$

$$\sum_{r=1}^t U_r Y_{rj} - \sum_{i=1}^m V_i X_{ij} \leq 0 \quad j = 1, \dots, n$$

$$r = 1, \dots, t \quad i = 1, \dots, m \quad U_r, V_i \geq 0 \quad (2)$$

$U_r$ : the weight given to output  $r$ .

$V_i$ : the weight given to input  $i$ .

$Y_{rj}$ : the amount of output  $r$  ( $r = 1, \dots, t$ ) from DMU " $j$ "

$Y_{rj_0}$ : the amount of output  $r$  ( $r = 1, \dots, t$ ) from DMU " $j_0$ "

$X_{ij}$ : the amount of input  $i$  ( $i = 1, \dots, m$ ) from DMU $^j$ .  
 $X_{ij0}$ : the amount of input  $i$  ( $i = 1, \dots, m$ ) from DMU $^j0$ .  
 $n$ : the number of DMU.  
 $t$ : the number of outputs.  
 $m$ : the number of inputs.

The above constraints restrict the efficiencies of all of the DMUs ( $j = 1, \dots, N$ ) to have an upper bound of 1. The variables  $U_r$  ( $r = 1, \dots, n$ ) and  $V_i$  ( $i = 1, \dots, m$ ) are the weights to be derived for the corresponding output and input factors while maximizing the efficiency of the  $k$ th DMU. That is, DEA allows that individual DMUs may have their own preference structures and value systems, and thus, can determine their own weights.

**3. The case study**

Restaurants are characterized as a day-to-day high-risk business (Muller, 1999). Demand is highly randomized, and the arrival of customers is highly unpredictable. Moreover, other external factors have to be taken into account, such as seasonal fluctuations. The data set of our case study includes 15 restaurants in Iran. Iran has thousands of fast-food businesses and sales points selling hamburgers, pizzas, falafel, kebab, etc.

In order to demonstrate the applicability of the proposed method, we performed a case study involving 15 restaurants belonging to one of Iran's cities. The outputs, the inputs for our restaurant case study include the following:

(1) Inputs:

- V1- monthly working hours.
- V2-branch area (square meters).
- V3-years of experience as manager.

(2) Outputs:

- U1-monthly number of customers who bought something from the branch.
- U2-monthly sales in USD.

An important issue in employing DEA is the appropriate selection of inputs and outputs. In this case study, the inputs and outputs were chosen by consulting experts. Table 1 includes the data (three inputs and two outputs) for 15 restaurants in Iran. For the data given in Table 1, we set bounds for various weights according to the DEA method. Then we ran the A&P super-efficiency model that ranks all the branches from 1 (the most efficient branch) to 15 (the most inefficient one).

**Table 1. Inputs and outputs for 15 restaurants**

Branch	DMU	Inputs			Outputs	
		V <sub>1</sub>	V <sub>2</sub>	V <sub>3</sub>	U <sub>1</sub>	U <sub>2</sub>
Tajmahal	1	900	60	2	3600	4100
Noor	2	800	130	5	7600	7450
Eghbali	3	1200	90	8	5400	6250
Yas	4	1050	35	6	3855	4220
Nemoone	5	950	55	4	8560	8500
Khatam	6	750	40	1	4000	4000
Bahar	7	1100	70	6	3500	3950
Tiktak	8	950	25	8	2400	2800
Good boy	9	825	30	1	1855	2450
Khansalar	10	925	35	3	2650	2700
Deshlame	11	1075	38	5	2750	2900
Ponak	12	950	40	1	1500	2100
Ghasr	13	1300	100	9	4700	4900
Ghods	14	850	110	10	5200	5150
Baghgherdoo	15	1000	170	2	2600	2830

For example linear programming form for DMU 10 as follows:

$$\text{Max } z = 2650u_1 + 2700u_2$$

Subject to

- $925v_1 + 35v_2 + 5v_3 = 1$
- $3600u_1 + 4100u_2 - 900v_1 - 60v_2 - 2v_3 \leq 0$
- $7600u_1 + 7450u_2 - 800v_1 - 130v_2 - 5v_3 \leq 0$
- $5400u_1 + 6250u_2 - 1200v_1 - 90v_2 - 8v_3 \leq 0$
- $3855u_1 + 4220u_2 - 1050v_1 - 35v_2 - 6v_3 \leq 0$
- $8560u_1 + 8500u_2 - 950v_1 - 55v_2 - 4v_3 \leq 0$
- $4000u_1 + 4550u_2 - 750v_1 - 40v_2 - 1v_3 \leq 0$
- $3500u_1 + 3950u_2 - 1100v_1 - 70v_2 - 6v_3 \leq 0$
- $2400u_1 + 2800u_2 - 950v_1 - 25v_2 - 8v_3 \leq 0$
- $1855u_1 + 2450u_2 - 825v_1 - 30v_2 - 1v_3 \leq 0$
- $2650u_1 + 2700u_2 - 925v_1 - 35v_2 - 5v_3 \leq 0$
- $2750u_1 + 2900u_2 - 1075v_1 - 38v_2 - 5v_3 \leq 0$
- $1500u_1 + 2100u_2 - 950v_1 - 40v_2 - 1v_3 \leq 0$
- $4700u_1 + 4900u_2 - 1300v_1 - 100v_2 - 9v_3 \leq 0$
- $5200u_1 + 5150u_2 - 850v_1 - 110v_2 - 10v_3 \leq 0$
- $2600u_1 + 2830u_2 - 1000v_1 - 170v_2 - 2v_3 \leq 0$

$$u_1 \geq 0 \quad u_2 \geq 0 \quad v_1 \geq 0 \quad v_2 \geq 0 \quad v_3 \geq 0$$

**4. Efficiency analysis**

In evaluating restaurant efficiency, we calculated the efficiency scores for all 15 restaurants using DEA model. In this paper for calculate the efficiency scores used LINDO software. The scores of all the branches were computed. The results are presented in Table 2. According to the results, DEA model indicate that almost one- Seventh of the restaurants (2 of 15) were efficient, having an efficiency score one. In this case study, it was found that only Noor restaurant and Nemoone restaurant are efficient. All the other DMUs are inefficient. Inefficient restaurants are: Tajmahal (0.5289), Eghbali (0.5812), Yas (0.7807), Khatam (0.7189), Bahar

(0.3989), Tiktak (0.7252), Good boy (0.3528), Khansalar (0.4995), Deshlame (0.4930), Ponak (0.2646), Ghasr (0.4165), Ghods (0.6592), and Baghgherdoo (0.3311). These DMUs should improve their efficiency by increasing the values of their outputs given the existing levels of the inputs. Those with an efficiency score of one do not need to make such changes (Noor and Nemoone).

This section highlights the managerial implications which can be inferred from the solutions obtained from the DEA model. Noor restaurant and Nemoone restaurant is the most efficient restaurant, with efficiency score of one. Ponak restaurant is the most inefficient restaurant, with an efficiency score only 0.2646 (from Table 2). It is also the last ranked observation (ranking 15 from Table 2). Next, managers need to identify the sources of inefficiencies for ponak restaurant and all the other DMUs that are inefficient.

**Table2: The scores and the ranking of the branches**

Branch	DMU	Score	Rank
Tajmahal	1	0.5289	8
Noor	2	1	1
Eghbali	3	0.5812	7
Yas	4	0.7807	3
Nemoone	5	1	1
Khatam	6	0.7189	5
Bahar	7	0.3989	12
Tiktak	8	0.7252	4
Good boy	9	0.3528	13
Khansalar	10	0.4995	9
Deshlame	11	0.4930	10
Ponak	12	0.2646	15
Ghasr	13	0.4165	11
Ghods	14	0.6592	6
Baghgherdoo	15	0.3311	14

## 5. Summary

This study is initiated by the authors because there is a lack of tools to measure restaurant efficiency. DEA has been proven to be a reliable, flexible and efficient tool in measuring restaurant performance. In summary, this paper presents a standard methodology for assessment and ranking of restaurants efficiency. The results indicate that data envelopment analysis is a Useful tool to evaluate the efficiency of Restaurants. Moreover, the results show that Noor, Nemoone and Yas are respectively the best restaurants Compared to other restaurants. All the other DMUs are inefficient. The structure and approach of this paper could be applied for other sectors in particular and other countries in general. The results of such studies would help policy makers and top managers to have better understanding of their sectors. The framework presented in this paper may be used by top managers to compare the performance of various units within an organization. The contribution

of this study provides useful insights into the use of DEA as a modeling tool to aid managerial decision making in measuring restaurant efficiency. Reynolds and Thompson (2007) made a multiunit restaurant productivity assessment using three-phase DEA. Hadad et al. (2007) used DEA and some ranking methods to measure efficiency of restaurants and to rank them. Barros and Alves (2004) estimated total productivity changes and decomposed them into technically efficient changes and technological changes for a Portuguese retail store chain by implementing the efficient frontier approach and using the Malmquist productivity index (Caves et al., 1982). Their aim was to discover what practices best lead to improved performance throughout the whole chain. They ranked the stores according to their total productivity changes for the period 1999-2000. There are other multiple attribute decision-making methods such as ELECTRE, TOPSIS and VIKOUR, which could be applied for ranking the assessment and ranking of restaurants efficiency. Further research may be the application of these methods to the ranking of restaurants efficiency and the comparison of the results.

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## Phenomenology of Scientific Board's Views about Electronic Learning

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**Abstract:** Increased availability of appropriate software and hardware has built a new horizon in educational institutions in order to facilitate electronic learning, especially the development of global web net. Importance of this problem in medical sciences which is associated with human life is twice. Hence the aim of this study was phenomenology of scientific board's views about electronic learning in Mazandaran University of Medical Sciences. In this descriptive study 40 scientific board members of Mazandaran University of Medical Sciences were enrolled. The method was based on goal and information was collected on basis of deep and semi-structured personal interview, and encoded and analyzed with Smith method. The results were grouped in 5 clusters and 15 groups. The main extracted cluster included: information, public facilities, availability, organization, language and comment evaluation. According to some advantages of electronic learning, there is no doubt about necessity of electronic learning. But the most concern in using electronic learning is expressed in aspect of information and public facilities, availability and comment evaluation that prompt lack of tendency and affinity of scientific boards in using this method, mentioning that adaption of some existing processes in world and using other countries experiences in achieving the most comprehensive model in university from Educational Development Center is unavailable. (*Abstract truncated at 212 words*).

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**Keywords:** phenomenology, view, scientific boards, electronic learning

### Introduction:

Electronic learning (e-learning) adoption of information technology tools in human education and training has created the possibility of learning anything in each field, for anyone, anywhere (Taran, 2006). E-learning is presentation of education and educational program by electronic equipment. E-learning implements computer or other electronic devices in several methods for providing education or educational material that is mandatory for important evolutions in continual medical education. Continuing medical education is an important part of education, has global availability and opportunity to perform flexible educational designs (Duplaga, Zielinski, Ingram, 2004). Physical educational and learning areas designed as university and class walls will no longer be necessary and it will be possible to access the science learning and teaching in anywhere in this world. Those universities which are not planning a prospective vision will be deferred in this way. It seems that medical universities have no

choice except to pay importance to electronic learning in order to accomplish success in comparison with other universities in the world, to educate a wide range of students and also fulfill new needs (Ghanbari, Askari, Taheri, 2010).

Today's world is a world of information and knowledge; and information is based on the development and progress of any society. Since the nature of higher education is the exchange of information and knowledge, it's reasonable to assume that changes in information technology, colleges and universities will change, and this seems to be unavoidable that these changes will lead to a re-definition of the roles, needs and expectations of students and changes in performance and structure of the universities (DellaCorte, La Mura, Petrino, 2005). The first and essential goal of electronic learning especially in Iran could be expressed like, "extension and creation in capability of education in our country with aid of information technology and communication and response to comprehensive need



for more quality and flexibility, leading to a better education with less cost" (Safavi, Bavaghar, Ghafari, 2006). In Iran learning experience is limited. The first conventional virtual electronic university in Iran is opened by Shiraz University and it began to accept students practically in 2003. And now about 800 students are studying in four fields consisting of Masters of Science in electronic commerce, Bachelors of Science in controlling and correction of utilities, functional electronics and law. The first electronic students in country were graduated from Shiraz University in winter of 2009 (Safavi, bavaghar, Ghafari, 2005).

Presently, also other universities practice in this field in Iran. Then, many problems and questions may arise this field in worldwide are also highlighted in Iran and it is needed to explore these fields more deeply. On the other hand, because this issue is novel in the world and especially in Iran, there is need for re-assessment of the science from a perspective that is especially provided by e-learning services in medical sciences in concepts of recognizing fields, substructures and properties (Daraghi, ghazi, 2007). Functional experience in research field confirmed that there are still many refined obstacles for qualitative studies. Expression of the view from people applying this method could be effective in recognition of this issue and its understanding. In this situation, using descriptive methods in study would be more useful. Nowadays using descriptive method for assigning and assessment of the subjects which have not been recognized and present obstacles could provide valuable information in association with preferences and concepts of person about desired papers. Phenomenology is a descriptive method that studies or discusses people's experiences, concepts and feelings. Research on the numbers of scientific boards can detect from perspective or aspects of this group about the experiences in using electronic methods and show that how could creating a bridge to fill the existing space between their experiences and their needs. Keeping this view and behaviors in mind provides a possibility to address the actual issue. It should be a searched concept and factors effecting use of in vivo e-learning in this group should be sought. In Iran behavioral perceptions and viewpoints of scientific board members also could be a base for researchers and politics for effective designing of programs to utilize the electronic learning in enormous community.

Keeping that background in mind, these experiences are important for medical education; aim of this research in specialized e-learning in Mazandaran University of Medical Sciences is to evaluate the phenomenology of scientific board members' view. It is hoped that results of this

research obtained from using this e-learning method would be effective as well as efficient for a detailed careful planning to keep responsible managers aware.

#### **Methods:**

This descriptive study has been performed by modern descriptive phenomenology method. Descriptive phenomenology consists of a phenomenon that possibly defines a free pro-hypothesis that has not been confirmed, includes its assessment, analyzing and description. Phenomenology emphasizes on depth of experiences and increases our understanding about experiences consisting of three phases including direct understanding, analysis and description (VanMannen, 2006). Select value in statistical community has selected 30 males and 10 females based on aims and numbers of scientific boards in different colleges. In this descriptive study, required data was collected in one phase (40 interviews during 30 minutes individually). The main method for collecting data began by open semi-structured interview with a general question about the study for example, "*What do you general information do you think is necessary for e-learning and also as a professor how do you define the education?*". All or recoded interviews plus non verbal message of participant noted by researcher during the interview such as tune, silence, laugh,... was noted immediately after finishing every session. From first to last interview participants were assured that all information will be confidential under any circumstances. Data were analyzed by using Smith method described as below:

- 1- The first encounter to text: reading and review a case.
- 2- Recognizing and marking the themes.
- 3- Listing and categorizing the items
- 4- Creating a table to summarize and finally
- 5- Combining the cases to obtain the final result.

To assure the accuracy of summarizing data, ideas from professors who had several descriptive researches, were used.

#### **Results:**

It is apparent from this research that five significant categories obtained from analyzing the information from scientific board members interview about e-learning were general information, availability, organization, language, evaluation of the content. Secondary issues were classified in sub-set of main issues and some of the participants' point of views which resulted defining the clusters and themes extracted clusters and themes are noted as following:

##### **1. Information and general facilities**

Themes of scientific board member's statement in this category, consists of: the aim and importance of the lesson and its comments requiring hardware

and software, internet speed and contacts and necessary guide for discussion and questions. These themes have been shown in many cases of interviews that we review some of the participants' view points on this topic:

*“Educational Development Center (EDC) in university has not introduced this course so that we could know what is the aim of this method, what should be educated with this method, what should be commented, and finally how should be this lesson intellectually interact with other lessons.”*

*“As I know, hardware facilities and especially software are not provided enough that this educational method could be implemented. Overall it has been studied that whether all of students use these enough facilities in this field or not? We have no high speed internet connection in college. We usually cannot open an email and respond it. How we can perform this educational method in presence of these problems? It's necessary that this situation should be studied carefully and all of existing problems which may be an obstacle defined, then perhaps we could succeed.”*

*“It is ensured that nowadays this method has developed in the world and maybe many countries have been using it, but in my opinion, a student is deprived from discussion in class and learning is just a theory more than being practical, especially for lessons in which we need to discuss and discussion involves the student to perform his role. Maybe this problem could be solved, but I have no information.”*

## 2. Availability

Another research's question is *“What is your opinion on availability of details in education with electronic methods?”* Statements such as: availability of related lesson by user or the rate of student's skill to utilize this way can be concluded from extracted themes, student's access to professor and dictionary for technical and hard terms are included in this category.

The most statements are quoted below:

*“In my idea, student should be educated enough even in a lesson frame and the availability of texts and rate of necessary skill in this field should be evaluated. I don't know how student can communicate with his professor; whether the possibility has been provided for a particular time other than working hours for both the professor and the student? Who should perform this coordination? If student is confronted with a problem and technical terms in text, how does he solve his problem? In general, when the perception of the subject is different in students, then how can they standardize it?”*

As about the possible obstacles, it has been considered that scientific board members were

extremely stressed or concerned about the rate of students concept, availability of the text as the same and even better, proper and prompt response to unpredictable questions and this issue requires special notation and attention of managers in designing these courses.

## 3. Organization

This theme consists of two subsets: **a)** syllabus organization **b)**referring discipline and dissociations in syllabus and content

**Syllabus organization:** this category showed that there is extreme concern in scientific boards member for achievement of electronic learning about organizing the syllabus and content.

Professor Number 16 said about this.... *“Who can recognize that if the syllabus is organized correctly or not? Can the student recognize the correlation among different parts of a comment? If it creates a problem, how could it be understood? Is the main outline detectable with a sub-set and is it separable? When we explain and analyze clearly the syllabus and contents in the class, and the student again has a major problem in understanding the topic then imagine what about he would feel about the e-learning method”*

Professor Number 23 declared: *“In my opinion use of e-learning method is creating dissociation in contents and syllabus and learning is interrupted. In my opinion, for us who are practicing in medical education section, using possibility of this method it is limited, because teaching is medicine is not confined and limited to a set of formulas like engineering and context cannot be justified. In medical fields expressing the cause and effect between phenomenons is very important such as disease diagnosis, and this kind of expressing and discussion is limited in e-learning.*

## 4. Language

In face to face education, language has an important and identifiable role in maintaining effective communication. Whereas coordination of context and contents of topic being taught with expression of gestures and other body movements in students is required in face to face learning.

### This theme is categorized as:

a) The type and method of speech b) structured speech with appropriate grammar

Professor Number 36 said in the interview *“I don't know how to communicate with the student using this method and encourage him/her to make enough effort in learning the topic. Because the e-learning is associated with speech text, in my opinion it is really hard to motivate and encourage the student to promote his educational skills in this method”.*

According to Professor Number 7, *“Scientific language concept is very important. The tone of teacher voice is also important that wouldn’t bore the students and encourage them”*.

Professor Number 24 says, *“In my opinion, in a classroom the communication with the student is continuous, there is no need to state or express the contents and context regarding or observing the structural rules; but in this type of education method in my idea, it is necessary to observe and regard structural rules carefully because I think it is more formal. I don’t think that all of colleagues have these necessary skills. I think that someone else should be used for speech and whether this person has scientific qualifications? And also convincing this person for the speech section of e-learning is also a bit difficult.”*

### 5. Concept evaluation

Identifying category in this theme consists of

a) Concept evaluation b) Evaluation method

Method of testing and evaluation of the students effects on learning and their inspiration, enthusiasm and motivation on learning. In fact, not only the students would like to know why and to what extent they have learned but also the professor would like to be aware of their students’ skills development, quality and quantity. On the other hand, evaluation is one of the most important educational management that content of evaluation and correct evaluating process provides a very useful information about designing and educational program performing.

Most professors have some ideas addressing this important issue. Some of the interviews on this topic are presented below:

Professor number 31 *“In my idea, examination and evaluation methods are not performed in this method as they should be. I have a question and answer (Q&A) session in class. It seems that in this method it is impossible to have a Q&A. We should evaluate the students classically which seems to be unattractive”*.

Professor number 38 *“Online examinations are my favorite and in my opinion, if the professors are trained about online examination and obtained the necessary skills, this would be very good and it is welcomed”*.

### Conclusion:

This research showed that the most people in board have no positive viewpoints on e-learning and this could have an important aspect in volunteering the e-learning by scientific board members. Vajargah and Azadmanesh also believed that one of effective factors on lesson planning in scientific board is their belief and view about e-learning (Vajargah, Azzadmanesh, 2007). Then to assign the view of students and professors on e-learning could be

associated with proper designing and basic technology which could prevent the failure of e-learning design in performance of electronic functional learning (Moniee, 2004). An organization should be enable to ease and create positive view regarding information technology (IT) in order to create positive view on e-learning (Ho li, KhuoTsung Hseien, 2010). Findings showed that professors have been expressing their concern about having no necessary skills in using appropriate softwares, as both students and professors have some lack of IT skills. Tucker and et al., believed that educational staff of an organization should be educated completely on designing and implementing IT skills which is beneficial for successful performance in e-learning in that organization. Educational staff should have necessary experience and capability in creating e-learning program and use of multimedia programs (Tucker, Zaugg, Tom, 2002). In this way Muirhead believes that most of teachers who had no skill and enough awareness of computer would have been confronted by several problems (Muirhead, 2000). On one hand, this research showed that most of professors have not been assured of software and hardware facilities and have considered this deficit as a large barrier to follow and developing an e-learning course in the university. Another studies have showed that identifying strengths and weaknesses, threats and existing opportunities in that environment which is considered to perform e-learning, such as identifying lecturer’s requirements, designing and efficacy of presented educational material, would be a guarantee for successful e-learning (Eslaminejad, Masood, Norzilah, 2010). In this research, most of the professors have declared the inability of board’s designing, syllabus organization, and even educational and content of e-learning. Research units need e-learning education and obtaining necessary abilities in order to increase awareness about e-learning. Glava believes that university needs to increase work and functionality of teacher’s education with different educational history in field of use of educational technologies, increase skill in teachers and availability of IT facilities for teaching staff. Using of e-learning by teachers, is creating this concept that novel technologies are enable to develop the whole learning and education practices (Glava, Glava, 2010). Finally, following steps are suggested in performance of e-learning; proper infrastructure for the use of new educational technology, performing educational workshops in order to increase the ability of using the novel and up to date technologies, continuing to create sustained learning in teacher, creation of appropriate infrastructure in universities and colleges, elimination of structural and administrative barriers, inspire and motivate the

students and teachers in using e-learning and ultimately encouraging designers to optimize e-learning based courses,

Finally, other studies designed to focus on other aspects of e-learning in universities and design appropriate models and the role of other variables affecting on operational process, which was also performed in this research, and helped to evaluate and understand the role of the present situation in education. Undoubtedly, understanding the facts, circumstances and existing prerequisites require the use of additional tools that could be found in other studies.

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## Ratings of Iranian Cement Companies Based on Financial Ratio Analysis

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**Abstract:** This research discusses Ratings of Iranian cement companies according to the analysis of their financial information. In this grading, it was determined how successful is the management of companies. In fact, Ratings companies is classifying them based on the ability of managers to maintain profitability of companies. In today's competitive world in which the most important issue is survival of organizations, managers are required to adopt appropriate strategies through studying market and competitors accurately. This way, they would be helpful for the organization like an accurate and planned program. The grade, which is allocated to a company, may be related to different factors; however, In this research, we have analyzed financial ratios and determined the grade and position of every 23 cement companies of Islamic Republic of Iran on profitability and determined their management level. [Issa Heidari. **Ratings of Iranian Cement Companies Based on Financial Ratio Analysis.** *Life Sci J* 2012;9(4):540-544] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 81

**Keywords:** Ratings, profitability, competitive, management level, financial ratios,

### 1. Introduction

The present research has used financial ratios to determine the grade and management level of each company. While most business owners focus on providing exceptional products and services to their customers, they must also pay attention to the performance and health of their company. Financial ratios provide insight into the strengths and weaknesses of a business and give the managers indications of areas that need improvement. A thorough knowledge of which ratios to use and how to use them is a critical management skill.

The primary focus of every business is to make a profit, have enough liquidity to pay its bills and maintain control of borrowed funds. Several ratios give managers the tools to evaluate these areas and measure their performance. Businesses should constantly monitor these ratios to detect negative trends and identify areas that need improvement. However, it also helps for a manager to rank the performance of his company against major competitors and other businesses in the same industry. Two sources to find the average financial ratios for a wide range of industries are the Robert Morris and Associates Annual Statement Review, Almanac of Business and Industrial Financial Ratios, and the key business ratios published by Dun & Bradstreet. Managers should use the financial ratios that analyze profitability, liquidity and debt leverage to make the comparison and determine the ranking of their company relative to the industry averages [7].

A financial ratio (or accounting ratio) is a relative magnitude of two selected numerical values taken from an enterprise's financial statements. Often used in accounting, there are many standard ratios used to try to evaluate the overall financial condition of a

corporation or other organization. Financial ratios may be used by managers within a firm, by current and potential shareholders (owners) of a firm, and by a firm's creditors. Financial analysts use financial ratios to compare the strengths and weaknesses in various companies.[4] If shares in a company are traded in a financial market, the market price of the shares is used in certain financial ratios.

### 2. Purpose and types of ratios

Financial ratios quantify many aspects of a business and are an integral part of the financial statement analysis. Financial ratios are categorized according to the financial aspect of the business which the ratio measures. *Liquidity ratios* measure the availability of cash to pay debt. *Activity ratios* measure how quickly a firm converts non-cash assets to cash assets. *Debt ratios* measure the firm's ability to repay long-term debt [8]. *Profitability ratios* measure the firm's use of its assets and control of its expenses to generate an acceptable rate of return. *Market ratios* measure investor response to owning a company's stock and also the cost of issuing stock. These are concerned with the return on investment for shareholders, and with the relationship between return and the value of an investment in company's shares[2].

Financial ratios allow for comparisons

- between companies
- between industries
- between different time periods for one company
- between a single company and its industry average

Ratios generally are not useful unless they are benchmarked against something else, like past



performance or another company. Thus, the ratios of firms in different industries, which face different risks, capital requirements, and competition, are usually hard to compare.

### 3. Accounting methods and principles

Financial ratios may not be directly comparable between companies that use different accounting methods or follow various standard accounting practices. Most public companies are required by law to use generally accepted accounting principles for their home countries, but private companies, partnerships and sole proprietorships may not use accrual basis accounting[8]. Large multinational corporations may use International Financial Reporting Standards to produce their financial statements, or they may use the generally accepted accounting principles of their home country. There is no international standard for calculating the summary data presented in all financial statements, and the terminology is not always consistent between companies, industries, countries and time periods.

### 4. Literature

There are different grading systems in various branches of economy in the western countries and Russia, one of which is the American System of CAML, which is used by supervisors in banks.

The CAMEL ratings system is a method of evaluating the health of credit unions by the National Credit Union Administration (NCUA). The rating, adopted by the NCUA in 1987, is based upon five critical elements of a credit union's operations:[6]

- (C) Capital
- (A) Asset quality
- (M) Management
- (E) Earnings
- (L) asset Liability management

This rating system is designed to take into account and reflect all significant financial and operational factors examiners assess in their evaluation of a credit union's performance. Credit unions are rated using a combination of financial ratios and examiner judgment.

### 5. CAMELS rating

The CAMELS ratings or Camels rating is a United States supervisory rating of the bank's overall condition used to classify the nation's fewer than 8,000 banks. This rating is based on financial statements of the bank and on-site examination by regulators like the Federal Reserve, the Office of the Comptroller of the Currency and Federal Deposit Insurance Corporation. The scale is from 1 to 5 with 1 being strongest and 5 being weakest. These ratings are not released to the public but only to the top management of the banking company to prevent a bank run on a bank which has a bad CAMELS rating [1].

It is a tool being used by the United States government in response to the global financial crisis of 2008 to help it decide which banks to provide special help for and which to not as part of its capitalization program authorized by the Emergency Economic Stabilization Act of 2008 .

### 6. Components

The components of a bank's condition that are assessed:

- (C) Capital adequacy,
- (A) Asset quality,
- (M) Management,
- (E) Earnings,
- (L) Liquidity and
- (S) Sensitivity to Market Risk

Based these features Credit rating agencies rate instruments proposed to issue by the respective company [3].

Another system was used by Smatov .A. K (1996), a researcher from Republic of Tajikistan, which determines the position of each company in an industry. The researcher divides grading into 5 groups:

- Liquidity Ratios
- Leverage Ratios
- Profitability Ratios
- Activity Ratios
- Quality Management

Mr. Smatov carried out grading of companies based on these Financial ratios [5].

### 7. Methodology

The statistical population of this research includes 23 companies listed in Iran Stock Exchange. The present research was carried out based on the grading criteria of Mr. Smatov in the Iranian cement companies and it was prepared according to the characteristics of Iranian cement industry. Using such grading in the other branch of industry is limited; however, it does not mean that it is impossible to use it for the other industry.

In addition, we divided the following grading into 4 groups to determine the grade and position of the companies based on Smatov's grading system:

1. Companies with excellent management and high profitability ( 4.5 to 5)
2. Companies with average management and average profitability (4 to 4.49)
3. Companies with inefficient management and without profitability (3.5 to 3.99)
4. Companies with poor/bankrupt and loss-making management; with a grade lower than(3.49)

Profitability of companies determines management level. In the present research, management level refers to liquidity profitability and appropriate use of assets and investment. Consequently, economic profitability

of companies was evaluated by the following criteria based on the grading system:

**Table 1. Grading criteria for cement production companies**

Indicators	limitation	Higher ratings	Criterion corrected
<u>Shareholders Equitys</u> Assets	> 0.5	5,0	-0,05=-1,0
<u>Current Assets</u> <u>Current Liabilities</u>	>1,5	5,0	-0,2=-1,0
Inventory turnover ratio	To 60 п̄з	5,0	+30=-1,0
<u>Net Income</u> Sales	>25%	5,0	-6%=-1
<u>Growth in Income</u> <u>Growth in Sales</u>	>1.0	5,0	-0,1=-1,0
ROA	> 15%	5,0	-3,0%=-1,0
ROE	>40%	5,0	-8=-1,0
Cost one dollar sold	To 0,75	5,0	+0,05=-1,0
Percent Direct cost of sales	To 0,5	5,0	+0,04=-0,1
Percent Direct costs to total costs	To 0,7	5,0	+0,05=-0,1
Quality Management (1*2*3*4)	>5	5,0	-1=-1.0

Choosing these criteria shows management quality. It can be stated that each of these criteria, by itself, indicates management level. An informed manager does not allow level of debits increases and profitability and sales of company products decrease. As, in the economic literature, such criterion indicates management level. Following formula is used to calculate the real grade of a company:

$$A = Mb \pm \frac{b - c}{Ki}$$

A=the grade was calculated

Mb= Highest grade (maximum grade)

b = Size of indicator

C= Real size of indicator

Ki= Correction criterion of indicator

In addition, we used the following formula to calculate management level:

$$R = \frac{\sum Ki}{N}$$

R = Factory grade

$\sum Ki$  = Calculated grade for each criterion

N = Number of criteria

## 8. Research Result

To show the grade of each ratio of the ratios used in this research, for instance in 2010, the ratio of the salary of stockholders to the assets of cement companies was 0.49, which is 0.01 less than 0.5:

$$A = \frac{b - c}{Ki} = 5 - \frac{0,5 - 0,49}{0,05} = 5 - 0,3 = 4,7$$

The results showed that the ratio of the stockholders' salaries to the assets of the factory in 2010 was 4.7. The following result was obtained to show the management level of companies:

$$R = \frac{\sum Ki}{N}$$

$$\text{Management level} = \frac{4,7+2,9+3,8+5}{4} = 4,1 \text{ Ratings}$$

The result shows that the grade is 4.1, which indicates the position and grade of Iranian cement companies in 2010. The grades of the companies during 2008 - 2010 were as follows:

**Table 2- The grades of companies obtained during 2008 – 2010**

Group of Companies	Range	2010		2009		2008	
		Number of Companies	Percent	Number of Companies	Percent	Number of Companies	Percent
Companies with top management and high profitability	4,5-5,0	4	17,4%	7	30,4%	0	0,0%
Companies with middle management and above average profitability	4,0-4,49	7	30,4%	5	21,7%	4	17,4%
Companies Patient management and No profitable	3,5-3,99	3	8,7%	5	21,7%	9	39,1%
Companies With poor management or Bankruptcy and the loss	to 3,49	9	43,5%	6	26,1%	10	43,5%
<b>Total</b>	<b>X</b>	<b>23</b>	<b>100%</b>	<b>23</b>	<b>100%</b>	<b>23</b>	<b>100%</b>

The results extracted from this table shows that companies management was at a lower level in 2008, as 19 out of 23 companies were placed in Group 3 and 4; in other words, 82.6 percent of the companies had a poor management.

However, the managers of companies had a good performance in 2009, as 7 companies were placed in Group 1. It can be stated that 12 out of 23 companies were placed in Groups 1 and 2. It shows that the companies had successful managers and

number of successful companies exceeds half of the sample companies. Nevertheless, in 2010, the managers could not continue and the number of 7 companies, which used to be in Group 1 in 2009, descended to 4 companies. In 2010, totally, half of the companies, i.e. 11 companies were placed in Groups 1 and 2. Nine companies, 43.5% of them, were in Group 4. It shows that the companies are in an unpleasant situation.

The following table shows the grades obtained from analyzing financial information of the sample companies and the grade of each company, which were determined during 2008 - 2010.

**Table 3 - The grade of each company during 2008 – 2010**

Company Name	Rank		
	2010	2009	2008
Tehran	4,0	4,4	3,9
Bojnourd	2,9	2,1	2,4
Dapab	4,4	4,5	3,6
Dshststan	4,4	3,9	3,8
Doroud	3,1	3,7	3,8
Elam	2,8	3,7	2,6
Fares	3,8	4,3	3,9
Gharb	3,5	2,8	1,5
Hormozgan	4,5	4,8	3,6
Kerman	4,0	4,4	3,9
Khzar	1,7	2,1	2,5
Mazandaran	4,3	2,3	2,8
Arrowmyh	3,4	3,9	3,3
Sfyda Neiriz	4,5	4,6	4,3
Sepahan	3,1	3,2	3,3
Shmal	2,5	2,8	2,4
Svfyan	2,5	3,9	3,5
Gain	4,4	4,8	4,3
Kurdistan	4,7	4,5	4,0
Kash	3,8	4,7	3,8
Caron	3,2	4,0	3,2
Asfhan	4,4	4,5	4,2
Hegmatan	4,5	4,1	2,1
<b>Iran</b>	<b>4,1</b>	<b>4,2</b>	<b>3,7</b>

## 9. Summary

In the present research, we studied Ratings of 23 Iranian cement companies. The results obtained based on the analysis of their financial ratios during 2008 - 2010 showed that management of cement companies in Iran was in a favorable condition and their grades in 2008 - 2010 were 3.7, 4.2 and 4.1, respectively. However, the obtained results do not mean that all the companies enjoyed an excellent level of management. It can be stated that the Iranian.

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## Management Accounting and its Role in Organizations

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**Abstract:** In this study, the role and importance of management accounting in organizations in achieving the organizational goals has been discussed. Management accounting in the world has enjoyed a rapid growth and dynamics and has regularly presented new intellectual products to the managers and leaders of the organizations. In addition, management accounting, as new business knowledge, can help the managers in successful interactions with one another with a variable environment through providing information. Managers in both profit and nonprofit organizations have an interaction with their own management accounting system. Sometimes, a manager uses the management accounting system for planning and decision making and in some other times, this system measures the performance and affects the managers' behavior. Management accounting system is considered as a source of information for making planning decisions and at the same time it is considered as a part of control system of an organization. Management accounting helps to create value in an organization through improving decision making process and control of organizational members.

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**Key words:** management accounting, cost management, Development, Organization

### 1. Introduction

Nowadays, the organizations are faced with severe complexities and changes due to the technological development in the industries and changes in production systems. These changes are to the extent that the management alone could not fully understand its environment in the organization. Therefore, it has become necessary to provide a system to help the management in specifying the problems, setting goals, precisely identifying the issue, defining possible solutions, evaluating solutions, and selecting, implementing, monitoring and evaluating the optimum solution. Management information system and decision support systems have been created and developed for this purpose. Management accounting information system has been also developed in the same field, so that it provides an important part of the information required by management. For these reasons, the manager cannot perform its duties efficiently, even by relying on personal information and experiences and the information reflected in the financial statements. Management accounting information system has been emerged, grown and developed with development and complication of the production system in order to help the management in decision making. The role of management accounting "is to prepare and provide relevant and useful information to help management in planning the activities, applying management control and rational decision making in achieving the organization's goals". Management accounting should not be considered as a set of fixed rules, because it tries to help the intra-organizational

individuals in making decisions and is a reliable guide in determining future policies and planning of the organization.

### 2. What is Management accounting?

Management accounting is a system of measuring and providing operational and financial information that guides managerial action, motivates behaviors, and supports and creates the cultural values necessary to achieve an organization's strategic objectives. There are four key ideas contained in this definition of management accounting. These ideas capture the nature, scope, purpose, and attributes of management accounting.

1. By nature management accounting is a measurement process.
2. The scope of management accounting includes financial information, such as cost, and operational information, such as percentage of defective units produced.
3. The purpose of management accounting is to help an organization reach its key strategic objectives. It is not meant for mandated financial and tax reporting purposes.
4. Good management accounting information has three attributes:
  - Technical—it enhances the understanding of the phenomena measured and provides relevant information for strategic decisions.
  - Behavioral—it encourages actions that are consistent with an organization's strategic objectives.
  - Cultural—it supports and/or creates a set of shared cultural values, beliefs, and mindsets in an organization and society.



### 3. Definitions of management accounting:

Managerial accounting is concerned with providing information to managers- that is, to those who are inside an organization and who direct and control its operations. Managerial accounting can be contrasted with financial accounting, which is concerned with providing information to stockholders, creditors and others who are outside an organization [4]

International Federation of Accountants (IFAC), has defined management accounting as follows: "Management accounting is the process of recognition, measurement, accumulation, analysis, planning, interpretation and relation of (financial and operational) information which is used by the managers to plan, evaluate and control the organization and to ensure accounting and how to use the respective sources".

Institute of Management Accountants (IMA) defines management accounting as follows: "Management accounting is the process of identification, measurement, collection, analysis, preparation, interpretation, evaluation and internal control of the organization's activities to ensure the appropriate use of capital."

According to the definition of Chartered Institute of Management Accountants (CIMA), The world's largest international source of management accounting, management accounting is defined as follows:

Management accounting is to apply the principles of accounting and financial management in order to create, preserve, store and increase value from the view point of public or private profit or nonprofit organizations [10]. Management accounting is the part of management which identifies, produces, provides and interprets the information associated with the following objectives[14]:

- Helping to make strategic decisions and design organizational strategies
- Long-term, medium-term and short-term planning of activities
- Determining the capital structure and financing this structure
- Designing motivational strategies for senior managers and stakeholders
- Contribution to making the operational decisions
- Control of operations and ensure of efficient use of resources
- Measuring and reporting financial and non-financial performance to the managers and the other stakeholders
- Safeguarding tangible and intangible assets

- Implementing processes of administration of organization, risk management and internal controls

### 4. The importance of management accounting

Management accounting is one of the most important management tools in designing the required guidelines and planning to achieve the organizational goals. According to the type of activity, the organizations have different goals but at the same time they have also common goals in some cases, such as resource management and cost reduction of activities and services [12]. In today's world, technological changes and changes of customer tastes and the international market competition have made the organizations the dynamic units whose prerequisite for survival and excellence in this field have been made by them. Inevitably, these organizations choose systems through which they can provide their required information along with these changes. Since the management accounting does not follow a closed framework and accepted rules and principles, it has the required flexibility. Management accounting is responsible for providing the information required by managers in decision-making process, planning, leadership and control of normal activities as well as the possibility of measurement and evaluation of performance of sub-units, managers and other employees and ultimately helps in achieving the organizational goals, including profitability, cost price reduction, product diversification, risk mitigation, preeminence in the competition market, product quality, increase of productivity and efficiency.

Naturally, management accounting is a process and a system used to collect information and measure whose performance is represented as operational and financial information and its purpose, as an effective tool for managers, is to help the organization to achieve its great goals [8]. The role of management accounting can analytically be considered as creation of solutions to get the information in the past and present and future programs, derived from extra-organizational and intra organizational factors which provides appropriate information and make it available to the management using tools as understandable models and interprets this information in a way that it would allow the assessment of the internal units and products and facilitates decision making by providing effective information in contrast to the problems beyond the enterprise and makes it possible to focus on future events through preparing the ground for strategic planning. Accounting management can play a highly valuable role in identifying and revising work procedures to control and review the activities and identifies the deviations

occurred by comparing the predicted goals with actual performance, and analyzing and interpreting them, presents appropriate strategies to the management to improve the structure and activities.

It can be generally noted that management accounting is a system to measure and collect financial and operational information which leads management activities and motivational behaviors and creates and supports the cultural values needed to achieve strategic goals of the organization [2].

### 5. Key processes of management accounting

Key processes of management accounting include the following items:

**Analysis:** Endogenous and exogenous complications from past and present information and future plans are resulted from the internal and external environment of the company [7]. The role of management accounting is to design mechanisms to obtain financial information with a cost effective (cost - benefit) method and then to make the information available to the management at the right time [3].

**Decision making:** management accounting, in fact, plays an important role in providing effective information for the managers' decision making on solving the existing problems [11].

**Planning:** One of the key and major tasks of management accounting is to focus on future events. In many companies, the historical data can be used to evaluate the changes in major operations and a guide for the strategic operations. Management accounting has an important role in providing the ground for planning of providing trivial activities in quantitative goals.

**Control:** Although management accounting normally has no updated control on the operations of the organization, it can play an important role in determining and improving the mechanisms for reviewing and controlling the organization's activity [9]. Comparing goals of planned and actual activities (what has happened), management accounting can detect the differences, investigate further commitments and then, present practical and useful suggestions to the managers.

#### Main topics of management accounting

All aspects of management accounting are practically influenced by several major topics, which include:

**a. Information:** The need for information is usually considered as a driving force to the management accounting [6]. Management accounting information often satisfies two main purposes:

- Facilitating decision making
- Affecting decision making

Decision makers will be provided with information to help them choose the best solution. This information often affects the decision of managers. For example, imagine the annual budget of a profit organization. Although the budget is provided by management accounting, it must be finally approved by senior management of the profit organization. In addition, budget information affects the managers' decision making. Because, at the end of the year, actual expenditure will be compared with budgeted amounts and any significant deviation will be analyzed.

**b. Behavioral effects:** reaction of managers and staff to management accounting information often has important effects on the events of profit units. For example, what is the reaction of production manager to the approved budget? Or how does the information of the cost price goods affect the pricing of goods and services? Or ... All these questions are related to behavioral tendencies of people and their limitations in the related information. The more understanding of the management accountants of the employees' behaviors; the more effective will be the provision of required information for them.

**c. Costs and benefits:** Information can be considered as goods. Information can be obtained or purchased and used as other goods. Information can be of high or low quality, can be presented timely or delayed, and finally can be relevant or irrelevant. Like other goods and services, providing information is costly and is expected to have benefits. Cost of providing accounting information in profit organizations usually includes salaries and benefits of management accounting staff, purchasing and computer operation costs and expenses spent by the data users for studying, and comprehension and using information. Benefits of information also include more effective planning, improvement of decision-making, higher efficiency of operations and leadership and better control of operations.

### 6. The purpose of management accounting in achieving organizational goals

Today, organizations have different goals and may be even qualified to a combination of goals. Thus, no comprehensive and uniform rule can be developed for all organizations [14]. The goals which are frequently emphasized by the organizations include:

1. An acceptable level of profit (profitability)
2. Growth
3. Financial self-sufficiency
4. Market Diversity
5. Social Services
6. Observation of social responsibilities

Regardless of which one of the above points are considered by the organizational objectives, the

management's duty has been to ensure of achieving goals.

Today, unstructured and unconsidered achievement of the goals involving changes in structural and technological elements and functional goals and patterns, makes the organization undergo crisis and stagnation for various reasons. Following factors have made it difficult for today's management to develop the organizational goals:

- As an open system, the organizations are exposed to serious effectiveness from the surrounding and internal environment. Factors and elements such as the increasing technological progress, economic developments, intertwined and complex commercial networks, difficulties in meeting the market needs and passing through winding path of competitions, have made the rules and regulations overseeing the function of the organization's goals achievement more difficult.

- Today's organizations are faced with the phenomenon of conflict between the various components forming the whole system i.e. their subsets and subsystems. This conflict which occurs as a results of factors such as difference in perception and cognition, ideas and norms, goals and values and attitudes of managers, the interdependence of various sectors of the organization's activity, confusion in roles and responsibilities and so, is an inevitable trait which must be controlled or resolved through management's strategy.

- As a dynamic phenomenon, the organizations are always subjected to changes. Mystery and key to escape from the problems and achieve goals of the organization in complex and difficult conditions is the rational management plan which will be possible by relying on reassuring data. Meanwhile, the management accounting system is one of the methods of providing information. Management accounting is a branch of accounting planned to meet the needs of the intra-organizational managers and administrators which will provide a variety of information regarding different financial and operational issues. This information which is prepared in the form of detailed reports, is interpreted, translated and used by managers and other users. Actually, it is worth mentioning that the success of management accounting depends on how much managers' decision making improves by presenting accounting information. Thus, providing information cannot merely help management in performing its duties, but the presented information must have the following features (e.g., relevance, timeliness, validity, importance, and comparability) to be used in decision making by the management. If management accounting fails to provide the information required

by the management with the required quality to be effective in management decision making, the mentioned system will have no effect but imposing costs to the organization. Thus, the quality of the provided information is of high importance and should be particularly considered.

Generally, the fundamental purpose of management accounting is to help the organization achieve strategic objectives. Realization of these goals meets needs of customers and the other shareholders. As a result, achieving these goals, the organization can preserve its position and distinguish itself from the other competitors.

Today most organizations face stiff global competition. To kee customers satisfied and meet the demands of other resource providers, contemporary firms must compete simultaneously on three dimensions: quality, cost, and time. These three elements form a strategic triangle. Each one is quite broad [13].

And it varies from one organization to another organization or from one product to another product (see figure 1).

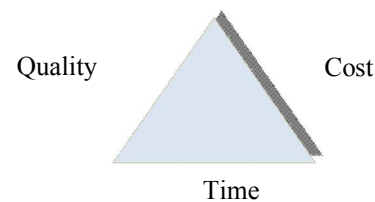


Figure 1: Elements of Strategy

- Quality is the total experience of a customer with a product. It includes the Physical characteristics of a product, such as its features, and the reliability of performance of these features. Quality also includes service features such as after-Sale support and service, and the performance level at which these services are Performed by an organization [1].

- Cost includes the resources expended by producers and their support organizations such as suppliers and dealers. Production costs encompass the entire "value Chain," that is, all parties from suppliers to after-sales service and disposers or Recyclers that create value for customers. Cost also includes resources expended by customers. Customer's cost includes the cost of maintaining and disposing of a product. This is often called their "cost of ownership".

- Time means that existing products must be available when a customer needs

them. Time also means that a firm develops products with new features or innovative technologies rapidly and takes these products to the market quickly. It also encompasses the time it takes to complete a cycle of activities such as start to end of production.

It should be noted that management accounting is not the goal, but it is important to achieve the goals of the organization. Management accounting helps the managers to assist the organizations in achieving the objectives and competitive advantage through collecting and disseminating information about the strategic elements.

Figure 2 captures this interactive relationship between organizational strategies, management accounting, and the daily activities of individuals in the organization. The information flows in both directions.



Figure 2: Role of Management Accounting in Strategy Deployment

In fact, providing the appropriate information, management accounting system helps the organization on quality, cost and time in order to achieve the organizational goals[2].

### 7. Accounting management and helping the managers

- Perception of cause and effect relationships: Management accounting can help the management in what has caused the cost or why there is an empty or useless capacity for production.
- Identifying activities that do not develop value added or are not efficient: Identifying inconsistent or repetitive activities or tasks that are not related to the customer needs, management accounting helps to redesign business processes.
- Understanding the relationship between different components of a value chain: management accounting information can show the impact of intermediate or supplier's activities on what the customer finally pays for a product.

- Identifying the process bottlenecks inside or outside the company: management accounting can show what components of the business process (machine or human) limits the efficiency of system and can cause customer dissatisfaction.
- Clarification of issues and changing the individuals' understanding
- Motivating managers and employees: Measurement of the components specifies the desirable behavior. People usually respond to these measurements
- Change of trends and directions: criteria which are surely of evaluation type will cause changes in levels of trends and efforts. For example, time standard for performing an activity specifies a goal that is expected to be achieved by reasonable efforts of the employees. In case of success, they will revise their effort level and, consequently, they will have a better performance next time.
- Change of relations: people tend to attribute success to their activities, but they attribute failures to the environmental factors. Research has shown that this attribution can change through management accounting criteria and finally can alter the behaviors.



### 8. Conclusion

Since management accounting has no similarity with financial accounting, a manager can select the tools and techniques that likes. Sometimes, this selection is successful and in other cases, it depends on the strategy of the organization. However, selection of the accurate strategy for the organization is a major factor. In addition, through the development of technology in the industries and the changes in production systems, the organizations have been faced with so severe complexities and changes that the management could not alone have enough knowledge about its environment in the organization. Therefore, it is essential that a system should be created in which it helps the management in identifying problems, setting goals, determining the issue precisely, defining possible solutions and evaluating these solutions and selecting, implementing, monitoring and evaluating an optimum solution. Management accounting information system has been developed in the same field; so that it provides an important part of the

information needed by management. Thus, the role of management accounting includes preparation, measurement and collection of financial and operational information which leads management activities and motivational behaviors and creates and supports the cultural values needed to achieve strategic goals of the organization.

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## Stochastic Frontier Approach (SFA) to Measure Inefficiency in Food Industries of Iran

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**Abstract:** The food industries in Iran is widely recognized as a 'sunrise industry', with a huge potential for uplifting the agricultural economy, creating large scale processed food manufacturing and food chain facilities and resulting in the generation of employment and export earnings. Due to the importance of Food Industries in Iran this paper estimated and investigated the efficiency in this industry. The stochastic frontier approach is applied. The result showed that the measure of the average technical inefficiency of the Iranian food industries was 26%. In other words, the food industries of Iran are only 74% technically efficient. The important factors that affect on efficiency in food industries of Iran are Education (ED), skilled (SK), specialization (SP) and workers insurance (IN). All the factors have the expected significance values and are consistent with theory.

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**Keywords:** Technical Efficiency (TEF); Technical Inefficiency (TINEF); Stochastic Frontier Approach (SFA); Food Industries (FI).

### 1. Introduction

Food processing plays an important role in economic development. It can provide new outlets for agricultural output, raising the income of farmers, who tend to be poorer than non-farmers. The sector is sometimes involved in providing credit, seed, and technical assistance to producers in order to obtain higher-value crops. Furthermore, food processing generates employment, more so than many other manufacturing sectors because it is relatively labor-intensive. Since food processing plants are often located in rural areas, they create jobs for rural households, where poverty is often concentrated. Finally, the food processing sector can play a role in improving nutrition through fortification and the supply of foods with longer shelf-life. As a result, this industry is one of the largest industries in Iran. Based on the 2010 reports by the Statistical Centre of Iran (SCI), the sector is ranked first in terms of employment (18.9 percent). Moreover, in terms of value-added, it is ranked third (19 percent). In addition, the development of these industries would increase the demand for agricultural products in food processing and reduce the level of waste. The importance equally lies in identifying the strength and the weakness of the food industry in presenting scientific solutions to researchers. It will also assist economic policymakers to reach their program goals quickly. Briefly, the importance of food industries is due to three important factors; 1) Priority of the Non-oil Exports in Foreign Trade, 2) Respond to Nutrition of population, 3) Prevention of Wastage. Over the last two decades the government has encouraged the expansion of agro-industries and food industries. The increment of productivity and efficiency are the best

ways that can increase the firms' profit in this sector. However the author have been studied related to determinants of productivity (Afrooz, et al. 2011) but unfortunately, there weren't a robust research regarding to efficiency and it's determinant in this sector. Therefore this paper estimated the technical efficiency by using the stochastic frontier approach (SFA).

### 2. Literature review

There are two approaches that can be used to estimate efficiency, i.e. parametric and nonparametric. The parametric approach involves estimation of a SFA models, whereas the non-parametric approach uses a linear programming method i.e. DAE approach. Parametric approach is preferred over the non-parametric approach because of its ability to relax the constant returns to scale assumption imposed under the latter approach, and application of mathematical forms as opposed to the linear programming of the nonparametric approach. In the usual stochastic frontier model it is acknowledged that the estimation of production or cost functions must respect the fact that actual production cannot exceed maximum possible production given input quantities, (Aigner, Lovell and Schmidt 1977, and Meeusen and Broeck 1977). Kumbhakar, Ghosh and McGuckin (1991) and Battese and Coelli (1995) were the first to suggest that determining the factors responsible for inefficiency is an essential component of efficiency analysis. The important task is to relate inefficiency to a number of factors that are likely to be determinants, and measure the extent to which they contribute to the presence of inefficiency. Kumbhakar, Ghosh and McGuckin (1991) and Battese

and Coelli (1995) suggested that under the assumption of truncated normal one-sided error term, the mean of the truncated normal distribution could be expressed as a function of certain covariates, a closed form likelihood function can be derived, and the method of maximum likelihood may be used to obtain parameter estimates, and provide inefficiency measures. Stochastic frontier approach has found wide acceptance within the agricultural economics literature and industrial settings (Battese and Coelli, 1992; Coelli and Battese, 1996), because of their consistency with theory, versatility and relative ease of estimation. A number of studies examined the technical efficiency of manufacturing industries in developing countries (Nishimizu and Page, 1982; Abdulkhadiri and Pickles, 1990; and Chuang, 1996; Harris, 1993; Sheehan, 1997) and steel production (Wu, 1996). Some literature focused on stochastic frontier model with distributional assumptions by which efficiency effects can be separated from stochastic element in the model and for this reason a distributional assumption has to be made (Bauer, 1990). Among others, an exponential distribution (Meeusen and Broeck, 1977); a normal distribution truncated at zero (Aigner, Lovell and Schmidt 1977); a half-normal distribution truncated at zero (Jondrow, *et al.* 1982) and a two-parameter Gamma or Normal distribution (Greene, 1990). However, these are computationally more complex, there are no priori reasons for choosing one distributional form over the other, and all have advantages and disadvantages (Coelli, Rao and Battese 1998). Ritter and Simar (1997) found that the requirement for the estimation of two parameters in the distribution may result in identification problems and several hundreds of observations would be required before such parameters could be determined. Further a maximum of the log-likelihood function may not exist under some circumstances. In general there are two types of panel data that can be adopted in measuring efficiency: time-invariant and time-variant. The former type of panel data model is specified in a way that the TE does not change over time (i.e. constant) but varies across firms, while the latter type of models allow the TE to vary across firms and through time for each firm. A number of studies have also attempted to estimate time-varying inefficiency. Cornwell, Schmidt and Sickles (1990) replaced the firm effect by a squared function of time with parameters that vary over time. Kumbhakar (1990) allowed a time-varying inefficiency measure assuming that it was the product of the specific firm inefficiency effect and an exponential function of time. This allows flexibility in inefficiency changes over time, although no empirical applications have been developed using this approach (Coelli, Rao and

Battese, 1998). ML estimates of stochastic frontier functions for panel data with time varying efficiencies was estimated by Battese and Coelli (1995). More specifically, Battese and Coelli (1995) propose a stochastic frontier function for panel data in which inefficiencies are expressed as specific functions of explanatory variables. The model assumes firm effects to be distributed as truncated normal random variables, which are also permitted. In this analysis we use parametric approach, specifically SFA model to estimate the TE associated with the FI in Iran.

### 3. Methodology

We used a time-varying inefficiency effects measure assuming truncated at zero of normal distribution by Battese and Coelli (1995) in this paper. Stochastic estimations impose

$$y_{it} = f(x_{it}, \beta) e^{v_{it} - u_{it}} \quad (1)$$

For time  $t = 1, 2, \dots, T$ ,  $y_{it}$  output,  $x_{it}$  is a  $(1 \times k)$  vector of inputs and  $\beta$  is a  $(k \times 1)$  vector of parameters to be estimated. The error term  $v_{it}$  is assumed to be independently and identically distributed as  $N(0, \sigma_v^2)$  and captures random variation in outputs due to factors beyond the control of firms. The error term  $u_{it}$  captures INEF in production. Coelli *et al.* (2005), assumed that: The error term  $\varepsilon = (v_i - u_i)$  and  $u_i$  is a non-negative random error which is assumed to account for errors and other factors under the control of a firm.  $v_i$  is the asymmetric random error which is assumed to be normally distributed as  $N(0, \sigma_v^2)$  and accounts for measurement of errors and other factors beyond the control of the firm and also  $v_i$  is a two-sided random errors while  $u_i$  is a one-sided EF component. The parameters of  $v_i$  and the parameters of  $u_i$  are assumed to be independent of each other. The error term  $u_{it}$  captures INEF in production, specified by:

$$u_{it} = z_{it} \delta + w_{it} \quad (2)$$

Where  $z_{it}$  a  $(1 \times m)$  is the vector of explanatory variables,  $\delta$  a  $(m \times 1)$  is the vector of unknown coefficients and  $w_{it}$  a random variable such that  $u_{it}$  is obtained by a non-negative truncation of the parent distribution  $N(z_{it} \delta, \sigma_u^2)$ . The condition  $u_{it}$  in the equation (2) guarantees that all observations lie on or beneath the stochastic production frontier. Following Battese and Coelli (1995; 2005), the variance terms are parameterized by replacing  $\sigma_v^2$  and  $\sigma_u^2$  with  $\sigma^2 = \sigma_v^2 + \sigma_u^2$  and  $\lambda = \sigma_u^2 / (\sigma_v^2 + \sigma_u^2)$ . The value of  $\lambda = 0$  when there are no deviations in output due to INEF and  $\lambda = 1$  implies that there is no deviations in output result from stochastic variations in the production possibility frontier. The firm or sub-sector

EF of the *i*-th firm or sub-sector in the *t*-th period for the basic case can be defined as:

$$TE_{it} = \frac{E(y_{it} | u_{it}, x_{it})}{E(y_{it} | u_{it} = 0, x_{it})} = e^{-u_{it}} = \exp(-\delta z_{it} - w_{it}) \quad (3)$$

The EF measured must have a value between 0 and 1. The empirical stochastic frontier model is usually specified in (natural) logs, so in INEF term,  $u_{it}$  can be interpreted as the percentage deviation of observed performance,  $y_{it}$  from the firm's own frontier. This model is estimated using Maximum Likelihood Estimation (MLE).

**4. Data sources**

Annual data on output, value added, capital a, labor and factors that affect efficiency such as education of workers(ED), skilled of workers(SK) and specialty of workers (SP)for the food industries were compiled in the periods 1995–2006 from the *Annual Survey of Manufacturing Industries* published by the Statistical Centre of Iran. The variables were deflated by using price index of each group on the base year 1997 that was published by the Central Bank of Iran.

**Table 1.** Tests of hypothesis for coefficient of the TEF

Null hypothesis	Log-likelihood value	Test Statistic $\lambda$	Critical Value $\chi^2_{0.95}$	Decision
$H_0: \gamma = \delta_0 = \dots = \delta_8 = 0$ (No technical INEF exists)	68.5	82.8	18.3	reject $H_0$

**5. Empirical results**

In this study, the equation (1&2) is utilized simultaneously in the program FRONTIER4.1 (Coeli, 1966) to measure INEF and determinants of INEF in total FI of Iran. The empirical equation can be defined as:

$$\ln Y_{it} = \beta_0 + \beta_1 \ln K_{it} + \beta_2 \ln L_{it} + v_{it} - u_{it} \quad (4)$$

$i = (1, 2, 3, \dots, 22)$  sub-sector  $t = (1995, \dots, 2006)$   
Where;  $Y$ ,  $K$  and  $L$  are output, capital stock and labour respectively.  $v_{it}$  is error term and  $u_{it}$  is measure of inefficiency that for the 22 sub-sector of food industries of Iran over 12 years (panel data sets) are defined by equation (5):

$$u_{it} = \delta_0 + \delta_1 SK_{it} + \delta_2 SP_{it} + \delta_3 ED_{it} + \delta_4 CN_{it} + \delta_5 PW_{it} + \delta_6 FS_{it} + \delta_7 NC_{it} + \delta_8 IN_{it} + w_{it} \quad (5)$$

$i = (1, 2, 3, \dots, 22)$  sub-sector,  $t = (1995, \dots, 2006)$   
Where:  $SK$  is ratio of skilled workers to total workers,  $SP$  is specialization or ratio of engineers to

total workers,  $ED$  is ratio of educated workers to total workers,  $PW$  is ratio of product workers to non-product workers,  $IN$  is insurances per worker in each sub-sector,  $NC$  is nutrition cost per worker and  $FS$  is firm size. A formal hypothesis test was conducted in order to determine the random variables associated with the TINEF and the residual error term of the data sets. Table 1 shows the value of the test statistic  $\lambda$  over the critical value, meaning that the null hypothesis ( $H_0$ ) indicates that TINEF does not exist in the FI ( $\gamma = \delta_0 = \dots = \delta_8 = 0$ ) is strongly rejected, indicating that TINEF effects are present.

**Table 2.** MLE of the production frontier and determinants of TINEF of FI

Variable	Expected sign	Coefficient
Stochastic Frontier Model		
Constant	n	1.53***
Log-labor	+	0.73***
Log-capital	+	0.24***
INEF effects		
Constant	n	1.005***
<i>ED</i>	-	-0.57***
<i>SP</i>	-	-1.13***
<i>SK</i>	-	-0.51***
<i>PW</i>	-	0.0003
<i>IN</i>	-	-0.18**
<i>NC</i>	-	-0.089***
<i>FS</i>	-	-0.055***
Variance parameters		
$\sigma_u^2$		0.13***
$\gamma$		0.78***
Mean Technical EF		0.74

\*, \*\*, \*\*\* denote statistical significance at the 10%, 5% and 1%, respectively

The estimation of TINEF for 22 sub-sector of FI is presented in Table (2) The results of the stochastic frontier model are presented in the first section of the table which shows the correlation between the total FI production value and the factors of production (i.e. labor and capital). Meanwhile, the results of the INEF effects model are presented in the second section of the tables showing the impact of  $Z_i$  variables on the TINEF.

The estimated value of the variance  $\lambda$  (0.78) indicates that the INEF effects are likely to be highly significant in the analysis. The estimated average

TINEF is 26%. In other words, the Iranian FI of is only 74% technically efficient. The estimated coefficients in the TINEF model for the Education (ED), skill (SK), specialization (SP), workers insurance (IN), worker nutrition (NC) and firm size (FS), have the expected values and significance, meaning that an increase in ED, SK, SP, IN, NC and FS lead to increased production EF. The most striking result to emerge from the data is that fact that the values of all parameters were as expected. Specialization (SP), Education (ED) and skills (SK) were important determinants of the EF in the FI of Iran. In the other word, increasing human capital cusses decreasing inefficiency in FI of Iran. The specialization coefficient is -1.13 this means if the specialist worker increase one percent inefficiency in FI will be decrease 1.13 percent. After specialization the educations level of workers and skilled of workers have more effect on efficiency than other factors. The educated workers (ED) coefficient and SK coefficient are -0.57 and -0.51 respectively that they are close together. The results, as shown in Table 2 indicate that the other factors that affect TINEF are IN, NC, FS and PW. The results show that there are significant relationships between TINEF and them except PW. The coefficients of the factors are -0.18, -0.089 and -0.055 for IN, NC and FS respectively. Among these factors IN has more effect on TINEF. That means increase in social insurance and health insurance increases the efficiency of the workers. The NC coefficient indicates that a weakly significant relationship was found between the nutrition of workers and TINEF. The average EF of the 22 sub-sectors of FI illustrated that the highest average of EF among all sub-sectors is related to sub-sector 1514 (Vegetable and animal oils and fats), while the lowest average of EF is for subsector 1517 (Cleansing, sorting and packaging of dates), i.e. 0.94 and 0.53 respectively. One of the main reasons for the high INEF in sub-sector 1517 is that the "Cleansing, sorting and packaging of dates" was a seasonal industry and manufacturers could not use production factors to their full capacity.

## 6. Conclusion

As aforementioned, TINEF was estimated and the average TINEF of the Iranian FI measured was 26%. In simpler words, the FI of Iran was technically and only 74% efficient. The important factors affecting the efficiency of FI are the estimated coefficients in the TINEF model for the Education (ED), skilled (SK), specialization (SP), workers' insurance (IN), workers' nutrition (NC) and firm size (FS). All the factors have the expected significance values and are consistent with the theory. Specialization (SP), Education (ED) and skills (SK)

were shown to be the important determinants of the EF in the FI of Iran. They particularly illustrate that increasing human capital will cause inefficiency in FI of Iran to decrease. The highest average of EF among all the sub-sectors was indicated for sub-sector 1514 (namely, vegetables and animal oils and fat), while the lowest average of EF was for sub-sector 1517 (namely, cleaning, sorting and packing of dates), with 0.94 and 0.53, respectively.

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## Approach Based on Motivation Theories

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**Abstract:** Motivation theories and their application constitute one of the broadest issues among researchers of organizational behaviour of which motivation is the most fundamental issue. Therefore, in this paper, four new theories of motivation are studied to explain the effects of these theories in organizations. The results show that applying these theories in the organization improves employee performance and job satisfaction, and that using these theories, can be justified, the rate of productivity, absenteeism and staff mobility, in the use and application of these theories needs to be carefully because the only motivating factor in the break back, will not be enough to boost performance. These theories are three needs theory, equity theory, expectancy theory and attribution theory.

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<http://www.lifesciencesite.com>.

**Keywords:** Three needs theory, equity theory, expectancy theory, attribution theory, productivity, satisfaction.

### 1. Introduction

Motivation is the desire to strengthen the effort to achieve a goal or objective. The overall motivation for all categories, including stimulant, desires, needs, and forces are similar, and attaining a goal can be achieved without enthusiasm. In order to encourage people to do the best with excellent results requires identifying the motivational force, and understanding how the motivational forces behave with such concepts, goals, and needs and their relationship with the concept of motivation.

Motivation is the force that causes people to behave in a certain way. Motivating employees so that it leads to the highest level of organizational performance is an important management task, thereby enabling someone to reach a high level of motivation to decide to take action (Moorhead & Griffin, 2003). Subject motivation is the most basic issue of organizational behaviour issues under study and implementation is a means of motivation to respond to confusing questions about humans and human behaviour, such as why some employees in organizations have more than others and have better performance and why an organization's employees do not have equal performance under the same conditions. Actually, motivation causes behaviour and direction is determined by their behaviour. Motivation for the consensus of the employees of the organization in respect of the organizational goals and the staff's ability to facilitate the maximum output of employees in organizations is important in organization and management theories (Jahromi, 2005).

For many people, motivation is not a personality trait that they possess. Motivation is the interaction with the situation and the individual. Thus, individuals differ in terms of motivational dynamics,

and the amount and level of motivation, varies not only between individuals, but also at different times (Robbins, 2004).

Motivation is of importance not only for economic organizations, but many psychologists (Glover & Bruning, 2008; Greenberg, 1989). Consider motivation as a factor for increasing the capacity of individuals.

### 2. New theories of motivation

The 1950s was very rich in terms of presenting the concepts of motivation. During this decade, three major theories – Maslow's hierarchy of needs (1954), MacGregor's motivation theory (1960), and Herzberg's hygiene theory (1966), were formulated. Although they constituted the cornerstone of theories that were presented later and practiced by managers, critics have attacked their credibility and trust (Frederick, 1966; Maslow, 1954; McGregor, 1960). Criticisms against the early theories of motivation will lead to changes in the concept of motivation. Many researchers (Adams, 1965; McClelland, 1976; Vroom, 1964) have found that previous models fail to easily explain the motivation of staff. In fact the difference between the content and the process of the separation of the two theories is that early theories of content tend to suggest reasons to describe the behaviour, whereas the new theories tend to have processes that describe the behaviour. Previous theories received wide recognition but could not gain enough credibility and trust. However, this does not mean that they will be forgotten when the new theories are introduced. This is because the new theories owe their existence to the documentation of the previous theories. Modern theories of motivation in the status quo are used by organizations and managers to raise staff motivation or to explain the staff's motivation.

**3. Three Needs Theory**

David McClelland’s theory (1976) has three motivation factors (three needs):

**A.** Need to achieve success (trying to shine)

McClelland thinks that successful people have distinguished themselves, and have always wished to do things to the best of their ability. These people choose challenging targets for themselves. They are personally responsible for their failure and success, and are not willing to accept and engage in work that has a high probability of failure.

**B.** The need for power. (Tendency to manipulate and control others) These people are always trying to influence others. They prefer to work in competitive conditions and are always seeking to gain reputation.

**C.** The need to belong (tendency to interact with others)

Groups	Characteristics
Need to achieve Success. (McClelland1961)	High personal responsibility, challenge, attracted to moderate risk, high creativity
Need for power	Due to the high position and reputation, attracted to competitive work, authoritarian, high self-control
Need to belong	Due to feeling for others, attracted to cooperation work, establish relationships based on mutual understanding.

The shared friendship with others is the third need that researchers have considered and to which McClelland gave special attention. They always try to get others to accept and they like to work in collaboration and in activities that are not competitive. The aforementioned characteristics are listed in the table below for convenience (McClelland, 1976). This theory in the organizational environment is extremely important. Especially the need to achieve success, which is also a personality trait. Those who feel the need to assume personal responsibility want to see results quickly, and tend to do commercial and entrepreneurial activities and manage business units; however, business success does not necessarily mean that a person is a good manager. Nevertheless, to develop friendship and gain power through a close relationship can result in successful management. In fact, the best managers are those who need to gain power and have little sense of belonging?

**4. Equality theory**

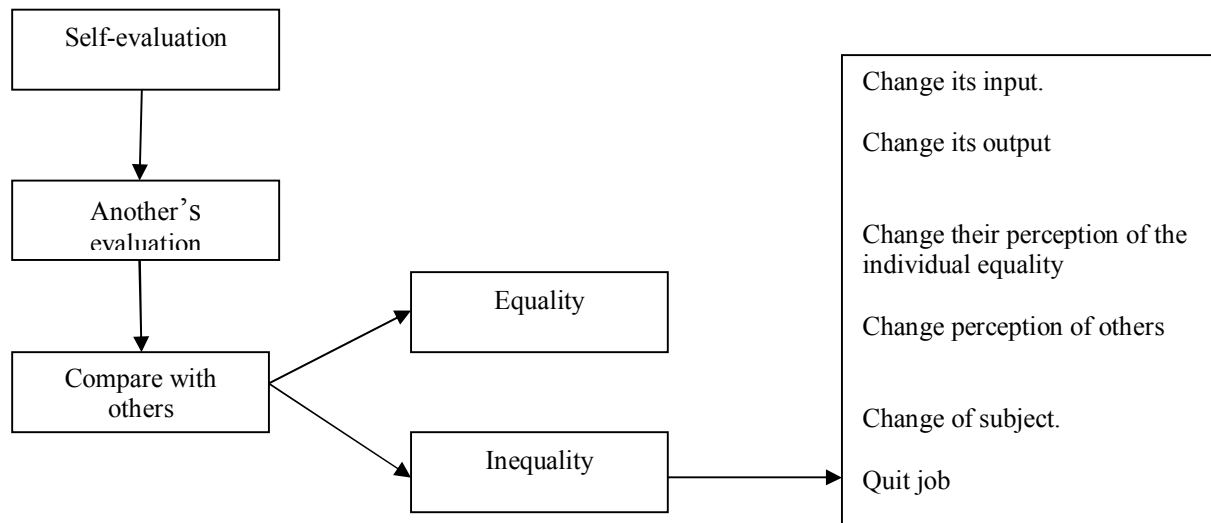
This theory was first proposed in 1965 by Stacy Adams. The main point of this theory is equivalent (fair treatment of individuals in the organization) to the inequality of the four sub-processes obtained.

-How individuals evaluate their organizational behaviour with themselves.

-How individuals evaluate their organizational behaviour with others.

-How individuals compare the organization behaviour of another person and themselves.

-The outcome is compared to the feeling of equality and inequality (Adams, 1965).



**Figure 1.** Equality theory

If someone offers a different reaction to inequality when a person makes sense of inequality,

they have a different reaction, and may adopt one of the following six behaviours.

1. Reduce the amount of activity.
2. Change production rate.
3. Revise their perception.
4. Change the perception of others about themselves
5. Change their comparison of reference
6. Leave office.

In the equality theory, a member compares the level of their own activity, experience, education and competency with their rights and the reputation of the organization, even if this comparison can be generalized to others. Therefore, if the person observes oppression, inequality and injustice between their input and the output of others, they may suffer from stress.

This tension is caused and motivates people to look for something that they assume is inequality. Generally, the equality theory contains three important messages for managers:

- \_ All members should be aware of the basis of payment
- \_ All members have two views (tangible and intangible) of their rewards
- \_ Members activities are based on their perception of reality (Adams, 1965).

**5. Expectancy theory**

The expectancy theory is a complex motivational model. This theory is a very complete than theory of equality. The original theoretical model belongs to Kurt Lewin (1930). However, Victor Vroom (1964) used this theory in the workplace for the first time. He thinks that the expectancy theory is: How the work is done by others

This theory has the following three variables:

1. Effort and performance (the expected performance of individual effort)
2. Performance and reward (expect to achieve results through individual performance)
3. Outcome (the relationship between personal goals and rewards)

In this theory, the motivation for work is related to the topic that people believe in doing the work and success, if the person is to reach an acceptable practice and whether they will receive an appropriate reward, and whether this reward meets their personal goals.

Thus, the four major steps in the expectancy theory include:

1. What is the result of the work and reward for the individual? The result can be both positive (salary, security, marginal benefits) or negative (anxiety and stress, fear of dismissal and expulsion), however, what is important is that as a result the work is done.
2. Do employees know the importance of work outcomes and results? If the work is important for a person, this gives a positive charge and they try to meet it. Conversely, if the work is not deemed important the individual thinks negatively, and does not do it. People sometimes think that this is natural.
3. What kind of behaviour should people display to achieve important results?
4. What kind of luck is important for a person at work? And, what is the role of competence and qualification?

Therefore, the idea of competence in the expectancy theory understands the relationship between effort and performance, performance and rewards, and, ultimately, the rewards and personal goals it provides. Victor Vroom's (1964), motivational model was revised several times. One idea and a new issue – satisfaction – were presented by Porter and Lawler (1968). They claimed that a high level of performance in organizations leads to satisfaction, and that individual performance depends on both internal and intangible rewards (feelings about work, feeling successful) and on external or tangible rewards (salary and promotion) (Porter & Lawler, 1968; Vroom, 1964).

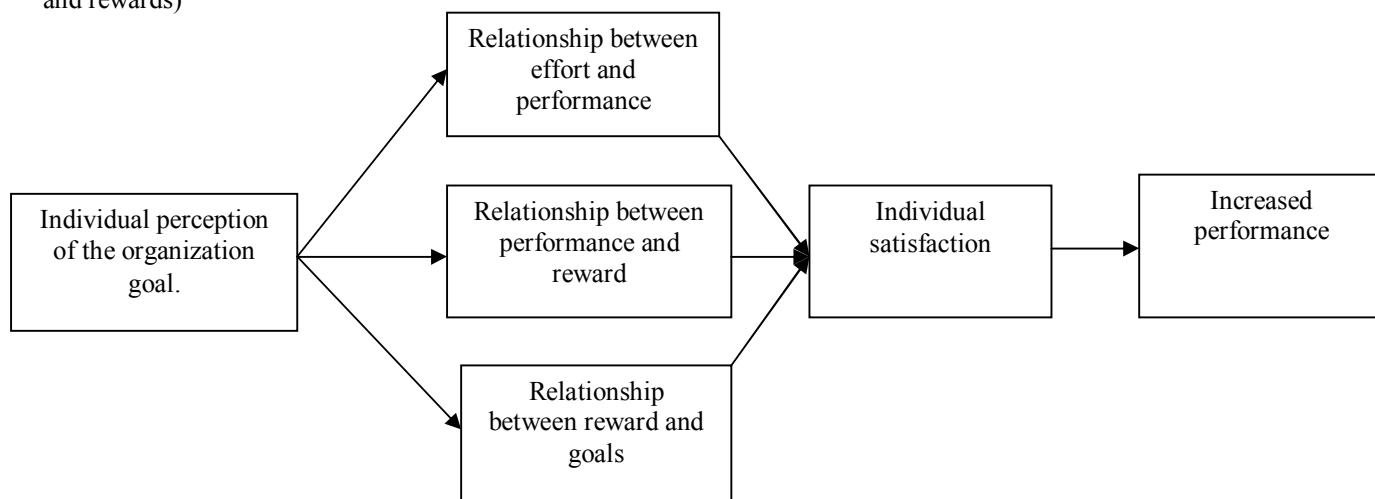
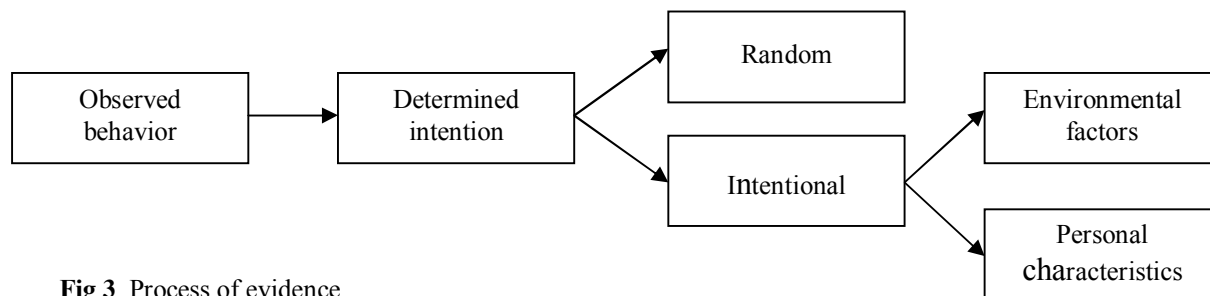


Fig 2. Expectancy theory



**Fig 3.** Process of evidence

## 6. Theory

Theory is an important factor in understanding social events and determining responsibility for human behaviour. In fact, this theory examines the cognitive processes that humans have interpreted the reason for their behaviour and others, and whether humans are responsible for the behaviour is related to personal characteristics or the surrounding circumstances.

The evidence theory is based on Kurt Lewins (1930) work. In 1951, he claimed that human behaviour is formed from a combination of a series of external (fortune, environment) and internal (ability, effort and knowledge) forces. Shaver (1975) believes that the process of evidence occurs in three stages:

1. When individual behaviour is observed in position (by him or others).
2. When individuals determine that behaviour is random or premeditated and the intent. In this stage, the first phase of the behaviour reasons begins if the behaviour is happening for no particular reason. However, if the behaviour is premeditated (intention) then it is guided to the next stage.
3. When a person gives reasons for the behaviour, the effect of environmental factors or personal characteristics of each will be determined at this stage (Shaver, 1975)

## 7. Conclusion

Organizations can run multiple programmes and the aim is to increase staff motivation, increase productivity, efficiency, productivity and job satisfaction, and, the most important point is that these programmes are based on the theories of motivation. Motivational theories are criticized for simply being theoretical. Although management and daily operations are available, they are less practical. There should be no gap between the principles of motivational theories and the methods of their use of the board of directors, which is possible through the application of the concepts of motivation in an organization. All motivation theories have potential applications in the workplace.

According to McClelland's theory there is a high correlation between a need for success and good performance (Winter, 1992). A successful manager is one who possesses the following three conditions:

- Power exercised in the interest of the organization
- Paid relatively low and does not form friendships
- Relatively little attention is paid to the spill and the need for strict control

The equality theory is an appropriate guide for management reward systems. These systems are a tool that managers can use to direct their employee's motivation. In this regard they use a series of programmes such as variable pay (skill-based, salary-based). Under these programmes the amount received depends on the person to change his performance. This means that poor performance is equal to less wages and salary; however, strong performance is equal to the increase in wages and salary. Furthermore, this factor has a positive impact on the outcome of motivation in an organization. Another project that has an effect on employee motivation is flexible benefit plans. In conclusion, the application of the equality theory, for most employees, is that their motivation is influenced by the relative salary (the absolute salary). According to this theory, equal salary can have an important role in the motivation of employees. This plan is consistent with expected theory, which requires that organizational rewards are associated with individual goals. Therefore, each member of the organization selects a set of objectives that can provide its current needs. This project was implemented in the early 1990s in American companies and more than 80 per cent of its members use it. The expected theory has limited application because of its complexity (Muchinsky, 1977). This theory is ideal (House, Shapiro, & Wahba, 1974). According to Steers and Porter (1983) the research expectancy theory is a promising approach to understanding work motivation. They stated that this theory provides a suitable framework to deal with the complex behaviour of employees (Scott H.) in studying the relationship between structure and motivation (Steers & Porter, 1979). In a study by Scott Herrick (1973) the relationship between organizational structure and motivation was

examined. He found a strong negative correlation between power motivation and concentration. Therefore, organizations that are very concentrated have staffs who are less motivated. The whole expectancy theory is a good predictor of job satisfaction (Herrick, 1973).

Most of the research results supported this theory because when people think that working in an organization is good it is likely to lead to a desired reward and they work very well. There is no doubt that the documents theory has promise for understanding organizational behaviour, because knowledge of attribution errors leads to better judgement.

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## The Survey Relationship between Service Quality, Customer Satisfaction, and Behavioral Intentions from Viewpoint of Customers in Arak Private Bank Branches

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**Abstract:** One of the biggest contemporary challenges of management in service industries is providing and maintaining customer satisfaction. Service quality and customer satisfaction have increasingly been identified as key factors in the battle for competitive differentiation and customer retention. Service quality brings many advantages to the company. It allows the company to differentiate itself from its competitors by increasing sales and market shares, providing opportunities for cross-selling, improving customer relations and thus, enhancing the corporate image. It results in the satisfaction and retention of customers and employees, thus reducing turnover rates. The purpose of this research is to survey relationship between service quality, customer satisfaction and behavioral intention in the private banks, to measure service quality we used an adaptation of the SERVQUAL scale. To test hypothesis used structural equation models and LISREL Software. Finally second and third hypothesis are accepted also research results suggest that dominant dimensions of Service Quality in the Private Bank Are: 1) Responsiveness, 2) Knowledge, 3) Tangibles and 4) Recovery.

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**Keywords:** Service Quality, Customer Satisfaction, Behavioral Intentions

### 1. Introduction

In marketing contexts and activities, the concept of service quality and service satisfaction has been paid a lot of attention during the last decades. Marketing researchers have praised the advantages of satisfaction and quality and have named them as two criteria for competitive advantages of an organization, although the accurate nature of judgment of customers and the relationship between these two criteria are under a shadow of ambiguity. Tendency to offer high quality services has an important role in service industries such as insurance, banking, etc, because service quality is essential for existence and profitability of organizations. Nowadays, in fact, customer satisfaction and service quality are crucial affairs in most of service industries (1). Service quality may help an organization make it distinct among other organizations and achieve a stable competitive advantage. High service quality is a key factor for long-term profitability not only for service companies, but also for productive companies (2).

### 2. A definition of the subject

Service sector plays a very important role in modern economy. Recent news show that although productive sector in the USA lost its more than 40 job positions for 40 continuous months during the last three months of 2003, but service sector achieved a remarkable profit during the same period. Whereas, service sector has allocated 80 percent of national gross production in 2002 and has attracted about 80 percent of working power in the USA; so, the sector

has been paid a great attention. Consequently, service managers and academic researchers have focused their efforts to understand the perception of customers about service quality and to know more about the way through which, these perceptions change to customer satisfaction and behavioral intentions. According to this orientation, a great interest is expressed to comprehend such these important structures such as service quality, customer satisfaction and behavioral intentions.

Mirral and Kamakura have indicated that behavioral intentions may be accurate forecasting factors for behavior, or may not be such forecasters. But if they are supposed so, the structure and concept of behavioral intentions will be important for service providers. Specifically, whether customer saves its repetitive commercial relation and whether stays with company for a long time or not? (3).

Offering better services to customers repeats purchases and develops positive verbal advertisements toward potential customers. Another direct effect of service quality is to increase the capability of organization to offer services more efficiently and effectively, because the organization has understood requirements and demands of customers, so it has reduced or eliminated unnecessary services. More the efficiency and effectiveness of services, the higher profitability of organization (1). Customer satisfaction is another important aspect of service organizations and enjoys higher relationship with service quality. Improving the quality of services will increase

probability of customer satisfaction. Participating, saving customers, creating bilateral rewarding relationship (link) between service provider and user, increasing customer tolerance toward service problems and positive verbal advertisement to advertize the organization are behavioral results of increasing customer satisfaction. In banking industry, there is also a relationship between service quality and customer satisfaction. Now, bank managers know that providing high quality services for customers is essential for success and existence of banks in competitive environment of today. Increasing the number of private banks and ever-changing and high-competitive environment in which the banks provide their services, are the reasons for bank managers to change their conception about customer satisfaction and optimization of service quality. So, the researcher plans to consider the relationship between service quality, customer satisfaction and behavioral intentions in private banks in Arak.

### 3. Importance and necessity of research

Customer satisfaction is an explicit factor for a successful marketing, and includes suitability of customer intentions about a service or article and real function of that service or article which includes customer services too. The companies which are able to make their customers satisfied, will be able to change them to loyal customers and will provide the possibility for those customers to buy their requirements from them for a long term (4). It is approved according to studies about behavior of customers that providing customer satisfaction will gradually create a feeling of loyalty and reliance in customers toward the organization. A loyal customer not only refers to his/her favorable organization to enjoy services or to buy requirements more and more, but also acts as a double factor to advertize products and services, and plays an important role to promote the level of profitability and to improve the image of organization in opinion of potential customers by recommending relatives, friends and others. According to studies of a research center, it is defined that 90% of dissatisfied customers will never return to use products and services of that organization. Furthermore, any dissatisfied customer explains his/her problems with that organization for at least 9 other people and 13% of these people continue to tell the subject to more than 20 other ones. Thus, during a very short time, the number of dissatisfied customers increases; some of whom maybe have not even heard the name of unlucky organization. It is obvious that these people will not like to use products and services of mentioned organization (5). In a study about giving-up behavior of customers in service industries, it is

concluded that near 60 percent of interviewees who had stated that they would restrain themselves to refer to an organization due to bad imagination, have not referred really. Among whom, 25% pointed at imperfect basic preference, 19% pointed at not pleasant confrontation of workers, 10% pointed at lack of favorable reaction of organization to remove imperfection of previous services and 4% pointed at immoral behavior of service providers. The companies which have attracted a great share of loyal customers, have increased the level of profitability by various measures such as rate of repurchases, advertisement and oral recommendation for products and less intention to change provider of products. Based on this direct relationship between customer loyalty and profitability of organization, the main attention of many organizations is focused on provision of circumstances to increase loyalty and reliability of customers. Promotion of service quality is an intelligent effort in this direction.

### 4. A Review on Study Literature:

- Fornell and Wernerfelt have performed a study about the relationship between market share, service costs and customer satisfaction. They understood that investigating critique of customers and effective management of their complaints has an enormous impression to improve customer satisfaction (6). Expanded studies of Buzzell and Gale about the effect of marketing strategies on the profit have provided undeniable evidences about bilateral relationship between service quality and profitability of organization. The studies showed that organizations which enjoy the greatest level in return of equity (ROE), are those organizations which offer services in higher quality.
- Richheld and Sasser assessed the effect of withstanding against losing customers on profitability and defined the value to save more customers for different industries. The researchers showed that saving only 5% of customers will increase annual income of provider company as 25 to 85% (7).
- According to the model of Zeithaml & et al (1996) behavioral intentions can be defined by means of some criteria such as repurchase intention, oral advertisement, loyalty, plaintive behavior and prices. High service quality (in viewpoint of customer) will mostly result in desirable behavioral intentions, but low service quality will result in unpleasant behavioral intentions.

Table 1. According to performed studies, the effect of independent variable of service quality on dependent variable of customer satisfaction is classified as following:

Independent variable	Dependent variable	Relationship	Researchers	Year
Service quality	Customer satisfaction	Positive	Parasuraman & et al	1985
Service quality	Customer satisfaction	Positive	Parasuraman & et al	1988
Service quality	Customer satisfaction	Positive	Cronin & Taylor	1992
Service quality	Customer satisfaction	Positive	Peter & et al	1993
Service quality	Customer satisfaction	Positive	Rust & Oliver	1994
Service quality	Customer satisfaction	Positive	Lee & et al	2000
Service quality	Customer satisfaction	Positive	Sivadas & Baker-Prewitt	2000
Service quality	Customer satisfaction	Positive	Cronin & Taylor	2000
Service quality	Customer satisfaction	Positive	Brady & Robertson	2001
Service quality	Customer satisfaction	Positive	Caruana & Malta	2002
Service quality	Customer satisfaction	Positive	Arasli & et al	2005
Service quality	Customer satisfaction	Positive	Olorunniwo & et al	2006
Service quality	Customer satisfaction	Positive	Gonzalez & et al	2007
Service quality	Customer satisfaction	Positive	Lin & et al	2007

Table 2. The effect of independent variable of customer satisfaction on dependent variable of behavioral intentions is classified as following:

Independent variable	Dependent variable	Relationship	Researchers	Year
Customer satisfaction	Behavioral intentions	Positive	Zeithamel & et al	1996
Customer satisfaction	Behavioral intentions	Positive	Cronin & et al	2000
Customer satisfaction	Behavioral intentions	Positive	Guenzi & Pelloni	2004
Customer satisfaction	Behavioral intentions	Positive	Olorunniwo & et al	2006
Customer satisfaction	Behavioral intentions	Positive	Gonzalez & et al	2007

Zeithaml & et al (1996) emphasized that behavioral intentions will be observable when the customer decides to accompany the organization or leave it (8). Burton & et al (2003) concluded that the experience of customer is related to behavioral intentions. The more positive experience of customer, the higher probability of customer intention to reuse services (9)

### 5. Theoretical Framework of Research Model

Theoretical framework of this study is derived from the result of studies, some of which have been pointed in study literature.

### 6. Analytical Model of Research

Analytical model of research is a structural model including some latent variables and causal relationship between them. Each of these latent variables is described by indicators measured by auditing and asking customers. Required data to assess the model is collected by means of a questionnaire and the answers of customers who have been recently users of the bank services. The model, at last, is assessed by structural equations method in

which contemporary relationships between variables are considered in a causal framework.

### 7. Study Theories

Theory 1- Service quality has a direct effect on behavioral intentions.

Theory 2- Service quality has a direct effect on satisfaction.

Theory 3- Satisfaction has an indirect effect on behavioral intentions.

### 8. Study Method

Whereas, the goal of this study is to achieve the relationship between variables in a multi-variable model and their effect on customer satisfaction; so, the study is a correlation study, and is also a measuring study because data is collected by sampling among society to consider distribution of qualifications of statistical society. The goal of study is research-application. Statistical Society, Sample and Sampling Method: Statistical society in this study includes all customers of private banks in Arak. But because data collecting among the entire statistical society is actually impossible, a sample of statistical society was selected (even if possible, it was not

economical because of spent time, cost and other feasibilities). In this study, proportional classification sampling was the method to take sample. In this method, a random sample is selected in any sampling unit, proportional with the volume of unit. Indication guarantee according to qualifications as the base of classification of units is an advantage of this sampling method (10). Whereas, modeling methodology for structural equations is similar to some aspects of multi-variable regression to a great extent, it is possible to use definition principles of sample volume in multi-variable regression analysis to define sample volume in structural equation modeling (11). In multi-variable regression analysis the ratio of the number of samples (observations) to independent variables should not be less than 5. Otherwise, the results of regression equation will not be extendable. Proposed by Halinski & Feldt (1970) and Miller & Kunce (1973), the more conservative ratio is 10 observations for each independent variable and is (12).

In viewpoint of James Stevens, 15 observations for each forecasting variable in multi-regression analysis by ordinary the least standard squares method will be a good tiptoe principle (11). So, generally sample volume in modeling methodology of structural equations can be defined between 5 and 15 observations for each measured variable. In which:  $5q \leq n \leq 15q$ . Where, q is the number of observed variables (indicators of questionnaire) and n is sample volume.

The questionnaire includes 19 indicators. So, if we consider even 10 observations for each indicator, at most 190 required samples will be calculated.

### 9.Data Collection Tool

A nameless questionnaire has been used to collect data for the goals of this study. The questionnaire is completed by customers of private banks in Arak. Study questions are set as the questions of questionnaire. Based on the main goal and designed questions and also replies to questions, each indicator of questionnaire is a step to provide main goal of study. The questionnaire includes 19 questions in this study.

### 10.Validity and Reliability of Measuring Tool

Regarding that international questionnaires – approved and used by well-known experts and researchers of marketing and management – are used to prepare the questionnaire of this study; so, the used questionnaire as the tool to collect information has enough validity and is valid. To be assured of validity of questionnaire, it was offered to some experts such

as management and commercial professors and also supreme managers and experts in banks, whose opinion confirmed the validity of questionnaire.

The “reliability index” indicator was used to assess reliability of questionnaire, which amplitude was between zero and one. Reliability index equal with zero refers to unreliability and reliability index equal with one refers to complete reliability. Reliability is the rate of capability of a measuring tool to save stability during the time. The most important method for status scales (systematic) is Cronbach method or observation-meter method which is studied and offered by three researchers: Cronbach, Rajaratnam and Glazer, but it is known only in the name of Cronbach, and not only reveals an indicator to confirm measurement of groups and people, but also defines extendibility of these measures to other sizes (13). With initial distribution of 20 questionnaires, reliability index for questionnaire with 19 questions was calculated as 0.96. Regarding that the least reliability index for research questionnaires is 0.70, it is considered that the obtained Cronbach’s Alpha is higher.

### 11.Data Analysis Method:

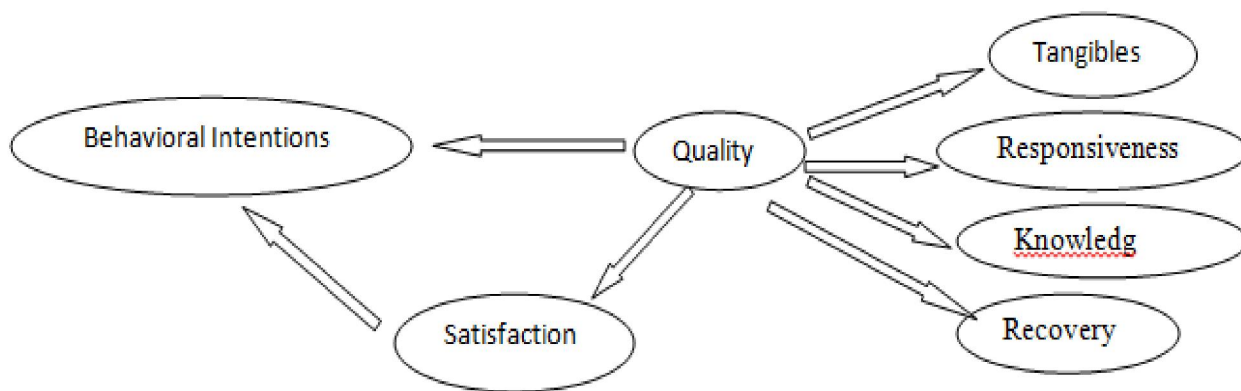
Current research model is represented in figure 1. The model is a structural model including some latent variables and causal relationship among them. Any of these latent variables are described by indicators, measured through auditing and asking customers. At last, two groups of index are assessed between latent variables in methodology of structural equations:

First: Gamma ( $\gamma$ ) which refers to correlation coefficient between an exogenous latent variable and an endogenous latent variable.

Second: Beta ( $\beta$ ) which refers to correlation coefficient between an endogenous latent variable and another endogenous latent variable. Moreover, T-Statistics which refers to significance of relationship between latent variables, will be calculated and achieved during analysis of structural equations.

If T-Statistics between two variables is greater than 1.96 in 95% reliability level, zero hypothesis is rejected which refers to no relationship between two latent variables, and substitute hypothesis is accepted which refers to significant relationship between two latent variables.

On the other hand, the measuring model describes the relationships between measured variables and latent variables used for approximate assessments. There are some indicators in measuring model for each latent variable.



**Figure 1. Analytical Model of Study**

In methodology of structural equations, coefficient  $\lambda$  is evaluated for each indicator. The coefficient is  $\lambda_x$  for exogenous latent variables and is  $\lambda_y$  for endogenous latent variables and introduces effective load between indicator  $x$  and related exogenous latent variable. Effective load shows a ratio of variance of indicator  $x$ , described by related exogenous latent variable. On the other hand,  $\lambda_y$  introduces an effective load between indicator  $y$  and related endogenous latent variable. In addition, T-Statistics shows the significance of  $\lambda_x$  and  $\lambda_y$ . Figure 2 illustrates the measuring model and an assessment of study models.

**12. Suitability of Study Model:**

“Suitability” is fitness and efficiency of data for under examination model, namely if indicators of

suitability show that the model is befitting, the data will be sufficient and enough to analyze and assess the relations in the model. During previous decade, various suitability tests are presented for structural equation models. Although different kinds of test, generally called suitability indicators, are being compared, developed and completed continually, but there is not yet any total agreement for even one optimum test and these indicators are classified by various methods (11). Table 1 shows suitability indicators for this study model.

**13. Test of Study Theories:**

As it was mentioned in analysis method of data, the theories of study are tested in methodology of structural equations and by means of Gamma.

**Table 1. Suitability Indicators**

Chi-Square	241.97
Root Mean Square Error of Approximation (RMSEA)	0.067
Normed Fit Index (NFI)	0.94
Non-Normed Fit Index (NNFI)	0.95
Comparative Fit Index (CFI)	0.96
Goodness of Fit Index (GFI)	0.86
Adjusted Goodness of Fit Index (AGFI)	0.83
P < 0.05	

Theory	T-Statistics	Result
Service quality has direct effects on behavioral intentions	1.85	Rejected
Service quality has direct effects on satisfaction	2.09	Approved
Satisfaction has indirect effects on behavioral intentions	6.95	Approved



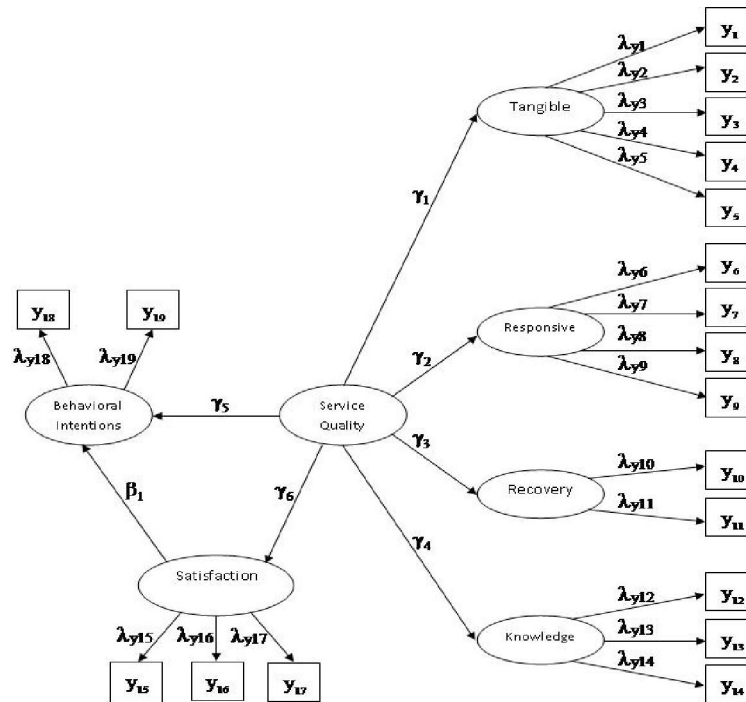


Figure 2. Structural and Measuring Model of Study

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**Synthesis of some medicinal and biological active (E)-2-arylidene-4-oxo-4-(4-(N-arylsulfamoyl)phenylamino)butanoic acids and (E)-4-(3-arylidene)-2,5-dioxopyrrolidin-1-yl)-N-arylbenzenesulfonamides**

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**Abstract:** Microwave irradiation of anhydride (E)-3-(3,4-dimethoxybenzylidene)dihydrofuran-2,5-dione **1** gives with N-aryl-4-aminobenzenesulfonamides (a and d) separable mixtures of (E)-2-(3,4-dimethoxybenzylidene)-4-oxo-4-(4-(N-arylsulfamoyl)phenylamino)butanoic acids **3** and **6**, and (E)-4-(3-(3,4-dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-arylbenzenesulfonamides **10** and **13**, respectively. Also anhydride (E)-3-(benzo[d][1,3]dioxol-5-ylmethylene)dihydrofuran-2,5-dione **2** gives with amines (a, b, d, and g), separable mixtures of (E)-2-(benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-arylsulfamoyl)phenylamino)butanoic acids **16**, **17**, **19** and **22**, and (E)-4-(3-(benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-arylbenzenesulfonamides **23**, **24**, **26**, and **28**, respectively. On the other hand, reaction of **1** with amines (b, c, e, and g) gives benzenesulfonamides **11**, **12**, **14**, and **15**, whereas compound **2** gives with amines (c and e) the corresponding benzenesulfonamides **25** and **27**, as only products. Compounds **1** and **2** give, either in presence or absence of solvent DMF, with amine (f) the corresponding butanoic acids **8** and **21**, respectively. Microwave irradiation of (g) with **1** gives benzenesulfonamide **15** as an only product, whereas with **2**, it gives a separable mixture of **22** and **28**, whereas in DMF, it gives compound **28** as an only product. Reaction of **1** and **2** with (a-g) using the conventional thermal heating technique, gives the corresponding butanoic acid derivatives **3-7**, **9** and **16-20**, **22**, respectively. Trials to react **1** and **2** with (f) were unsuccessful. The structural formulas of the products obtained **3-28** were assigned by their spectral analysis. Cytotoxic and antimicrobial activities of some prepared compounds have been studied and reported.

[Boshra M. Awad, Shadia M. Abdallah, Halima A. Hefny, Mervat H. Abdou, Fatehia I. Abd-Elmonem and Noura A. Abd-Elmonem. **Synthesis of some medicinal and biological active (E)-2-arylidene-4-oxo-4-(4-(N-arylsulfamoyl)phenylamino)butanoic acids and (E)-4-(3-arylidene)-2,5-dioxopyrrolidin-1-yl)-N-arylbenzenesulfonamides.** *Life Sci J* 2012;9(4):567-577] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 86

**Keywords:** Microwave irradiation, butanoic acids, arylbenzenesulfonamides, antimicrobial and cytotoxic activities

## 1. Introduction

Microwave technology has become very important in many areas of preparative science and particularly in the area of synthetic chemistry. Microwave methods have become reliable, safe and relatively inexpensive<sup>1,2</sup>. It proved to accomplish the reactions with excellent yields, high purity, assist cyclization, regioselectivity, and convenient working out<sup>3-12</sup> than the conventional thermal heating technique. Moreover it proves to be more economically and environmentally safe (green chemistry) than thermal heating technique. Sulfonamides represent an important class of medicinally important compounds which are extensively used as antibacterial agents<sup>10-14</sup>. The synthesis of 1-aryl-6,7-dimethoxy-3,4-dihydroisoquinoline-2(1H)-sulfonamides under microwave irradiation showed that the presence of sulfonamide group deepens the structure activity, where it is capable to inhibit the enzymes<sup>13</sup>.

The aim of the present work is to synthesize some new 2-substituted methylene-4-oxo-4-arylamino-butanoic acid and pyrrolidine-2,5-dione derivatives as antimicrobial and cytotoxic compounds in an efficient procedure, offered by microwave technique; short time with high yield and purity, and also to study the factors affecting the reactions such as structure of reactants, basicity of amines, and effect of solvent.

## 2. Experimental

(E)-3-(3,4-dimethoxybenzylidene)dihydrofuran-2,5-dione **1** and (E)-3-(benzo[d][1,3]dioxol-5-ylmethylene)dihydrofuran-2,5-dione **2** were prepared<sup>15</sup> and reacted with different sulfonamides (a-g); N-phenyl-, N-(4-methylphenyl)-, N-(4-methoxyphenyl)-, N-(4-chlorophenyl)-, N-(4-nitrophenyl)-, N-(1-naphthyl)-, and N-benzyl-4-aminobenzenesulfonamides (1:1) using microwave irradiation and conventional thermal heating

techniques. The factors affecting the reaction such as structure of reactants, basicity of amines, effect of solvent, and technique, were also studied. The results obtained are given in Table 1.

#### General remarks

Microwave irradiation was carried out in a Galanz Microwave Oven, WP1000AP30-2, Chemistry Department, College of Women for Arts, Science and Education, Ain Shams University.

Spectral measurements were carried out at Micro Analytical Centre, Faculty of Science, Cairo University, using:

- (a) FTIR: PERKIN-ELMER-1430, Infrared Spectrophotometer.
- (b) GCMS QP 1000 EX Shimaedzy; MS spectra.
- (c) Varian Gemmi (300 MHz); <sup>1</sup>H-NMR spectra.

Biological activity: Antimicrobial screenings were measured in the Botany Department, College of Women for Arts, Science, and Education, Ain Shams University, Cairo, Egypt.

Cytotoxic measurements were carried out in the National Institute of Cancer, Cairo University, Cairo, Egypt.

#### Solvent-free microwave irradiation technique

##### General procedure

In a microwave oven (1000 watt, 30-80% of its total power) a grind equimolecular mixture of (E)-3-(3,4-dimethoxybenzylidene)dihydrofuran-2,5-dione **1** or (E)-3-(benzo[d][1,3]dioxol-5-ylmethylene)dihydrofuran-2,5-dione **2** and sulfonamide (a-g) was dry-irradiated in an open vessel for 2-20 minutes. The reaction progress was monitored by thin layer chromatography (TLC) until no more unreacting starting materials were observed. The reaction mixture was then cooled down to the room temperature and the product obtained was dissolved in chloroform followed by washing the organic layer several times with ice-cold dilute hydrochloric acid to remove the unreacted amine. Treatment of the organic layer with 10% ice-cold sodium carbonate solution followed by acidification of the aqueous layer with ice-cold concentrated hydrochloric acid precipitated the produced (E)-2-(3,4-dimethoxybenzylidene)-4-oxo-4-(4-(N-arylsulfamoyl)phenylamino)butanoic acids **3,6**, and **8** or (E)-2-(benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-arylsulfamoyl)phenylamino)butanoic acids **16,17,19**, **21**, and **22**. Thoroughly washing of the organic layer with water followed by its dryness over anhydrous sodium sulfate and evaporation, gave (E)-4-(3-(3,4-dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-(4-aryl)benzenesulfonamides **10-15** or (E)-4-(benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-(4-

aryl)benzenesulfonamides **23-28**, respectively. The products obtained were crystallized from the appropriate solvent and their structures were confirmed by their spectral data; IR, <sup>1</sup>H-NMR and MS. Yields of products are given in Table 1.

#### Conventional thermal heating technique

##### General procedure

A homogenous equimolecular mixture of **1** or **2**, and different sulfonamides (a-g) in ethanol was refluxed for 4-10 hrs. The reaction progress was monitored by TLC. The reaction mixture was then concentrated and the precipitate formed was filtered off to give the corresponding butanoic acid derivatives **3-7** and **9**, or **16-20** and **22**, respectively. The products were dissolved in chloroform then worked out in the same way as that given in the solvent-free microwave irradiation technique. Yields of products are given in Table 1.

#### Biological activity: Antimicrobial screening

The antimicrobial screening of compounds; **4**, **5**, **7**, **14**, **17**, **18**, **20**, **25**, and **27**, was carried out using the disk diffusion method, inhibition zone diameter (mm/mg sample) in DMSO as solvent. It showed that all derivatives examined have antimicrobial activity ranging from high to moderate values against; *Bacillus subtilis* (G<sup>+</sup>), *Staphylococcus aureus* (G<sup>+</sup>), *Escherichia coli* (G<sup>-</sup>), and *Pseudomonas aeruginosa* (G<sup>-</sup>). The results obtained are given in Table 2.

#### Medicinal application: Cytotoxic activity

Cytotoxic activity of compounds **8**, **10**, **12**, **21**, and **25** was tested by using Flouraciele as a reference drug, against human breast carcinoma cell line using the method reported by Skehan *et al.*<sup>16</sup>. The results obtained are given in Table 2.

**(E)-2-(3,4-Dimethoxybenzylidene)-4-oxo-4-(4-(N-phenylsulfamoyl)phenylamino)butanoic acid (3);** White crystals from ethanol, mp 142-143 °C, 10% yield in microwave and 65% yield in thermal. FTIR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3460-3300 (2NH), 3500-2500 (OH, acid), 1728 (CO, acid) and 1669 (CO, amide), 1267 (SO<sub>2</sub>, asy.), and 1187 (SO<sub>2</sub>, sym.). MS: m/z = 497 (M<sup>+</sup>, 1%, C<sub>25</sub>H<sub>24</sub>N<sub>2</sub>O<sub>7</sub>S), 294 (5, C<sub>18</sub>H<sub>16</sub>NO<sub>3</sub>), 248 (3, C<sub>13</sub>H<sub>12</sub>O<sub>5</sub> or C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>S), 233 (0.65, C<sub>12</sub>H<sub>11</sub>NO<sub>2</sub>S), 176 (25, C<sub>11</sub>H<sub>12</sub>O<sub>2</sub>), 161 (15, C<sub>10</sub>H<sub>9</sub>O<sub>2</sub>), 139 (1, C<sub>6</sub>H<sub>5</sub>NOS), 133 (29, C<sub>8</sub>H<sub>5</sub>O<sub>2</sub>), 131 (32, C<sub>9</sub>H<sub>7</sub>O<sub>2</sub>), 119 (12, C<sub>7</sub>H<sub>5</sub>NO), 115 (47, C<sub>4</sub>H<sub>5</sub>NO<sub>3</sub>), 102 (61, C<sub>8</sub>H<sub>6</sub>) and 62 (100, NOS). <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>):  $\delta$  (ppm) = 3.7879 (3H, s, H-1), 3.8048 (3H, s, H-2), 3.8307 (2H, s, H-7), 6.99 (1H, d, H-5), 7.0053-7.0466 (1H, q, H-4), 7.0894-7.1047 (1H, d, H-3), 7.202-7.262 (5H, m, H-12), 7.3309 (1H, s, H-6), 7.499 (1H, s, H-8), 7.5326-7.551 (2H, d, H-9), 7.8567-7.8735 (2H, d, H-10), and 10.3985 (1H, s, H-11).

**Table 1:** Comparison between yields of products resulted from the microwave irradiation and conventional thermal heating techniques

	Anhydride 1				Anhydride 2			
	Microwave irradiation		Conventional thermal heating		Microwave irradiation		Conventional thermal heating	
	Butanoic acid	Benzene sulfonamide	Butanoic acid	Benzene sulfonamide	Butanoic acid	Benzene sulfonamide	Butanoic acid	Benzene sulfonamide
N-phenyl-4-aminobenzenesulfonamide (a)	3, 10%	10, 83%	3, 65%	-	16, 33%	23, 50%	16, 55%	-
N-(4-methylphenyl)-4-aminobenzenesulfonamide (b)	-	11, 92%	4, 75%	-	17, 30%	24, 60%	17, 67%	-
N-(4-methoxyphenyl)-4-aminobenzenesulfonamide (c)	-	12, 93%	5, 82%	-	-	25, 89%	18, 74%	-
N-(4-chlorophenyl)-4-aminobenzenesulfonamide (d)	6, 13%	13, 65%	6, 45%	-	19, 37%	26, 40%	19, 45%	-
N-(4-nitrophenyl)-4-aminobenzenesulfonamide (e)	-	14, 93%	7, 40%	-	-	27, 92%	20, 36%	-
N-(1-naphthyl)-4-aminobenzenesulfonamide (f)	8, 75% 8, 83%*	-	-	-	21, 69% 21, 85%*	-	-	-
N-benzyl-4-aminobenzenesulfonamide (g)	-	15, 82%	9, 55%	-	22, 35%	28, 52% 28, 90%*	22, 50%	-

\* (in presence of DMF)

**(E)-2-(3,4-Dimethoxybenzylidene)-4-oxo-4-(4-(N-(4-methylphenyl)sulfamoyl)-phenylamino)butanoic acid (4);** White crystals from ethanol, mp 105-107 °C, 0% yield in microwave and 75% yield in thermal. FTIR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3500-3200 (2NH), 3500-2800 (OH, acid), 1700 (CO, acid) and 1687 (CO, amide), 1263(SO<sub>2</sub>, asy.), and 1156 (SO<sub>2</sub>, sym.). MS: m/z = 510 (M<sup>+</sup>, 2%, C<sub>26</sub>H<sub>26</sub>N<sub>2</sub>O<sub>7</sub>S), 492 (2, C<sub>26</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub>S), 464 (1, C<sub>25</sub>H<sub>24</sub>N<sub>2</sub>O<sub>5</sub>S), 403 (2, C<sub>19</sub>H<sub>17</sub>NO<sub>7</sub>S), 288 (2, C<sub>14</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>S), 262 (46.5, C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>S), 107 (100, C<sub>7</sub>H<sub>9</sub>N), 106 (74, C<sub>7</sub>H<sub>8</sub>N), and 92 (61, C<sub>7</sub>H<sub>8</sub>).

**(E)-2-(3,4-Dimethoxybenzylidene)-4-oxo-4-(4-(N-(4-methoxyphenyl)sulfamoyl)-phenylamino)butanoic acid (5);** White crystals from ethanol, mp 212-214 °C, 0% yield in microwave and 82% yield in thermal. FTIR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3444-3263 (2NH), 3600-2800 (OH, acid), 1727 (CO, acid) and 1646 (CO, amide), 1233 (SO<sub>2</sub>, asy.), and 1155 (SO<sub>2</sub>, sym.). MS: m/z = 526 (M<sup>+</sup>, 0.04%, C<sub>26</sub>H<sub>26</sub>N<sub>2</sub>O<sub>8</sub>S), 508 (0.03, C<sub>26</sub>H<sub>24</sub>N<sub>2</sub>O<sub>7</sub>S), 480 (1, C<sub>25</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub>S), 323 (1, C<sub>19</sub>H<sub>17</sub>NO<sub>4</sub>), 319 (0.05, C<sub>15</sub>H<sub>15</sub>N<sub>2</sub>O<sub>4</sub>S), 278 (17.5, C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub>S), 249 (8.5, C<sub>13</sub>H<sub>13</sub>O<sub>5</sub>), 248 (60, C<sub>13</sub>H<sub>12</sub>O<sub>5</sub> or C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>S), 247 (2, C<sub>13</sub>H<sub>13</sub>NO<sub>4</sub>), 122 (100, C<sub>7</sub>H<sub>8</sub>NO), 115 (11, C<sub>4</sub>H<sub>5</sub>NO<sub>3</sub>), 92 (13, C<sub>6</sub>H<sub>6</sub>N), and 63 (22.5, HNOS).

**(E)-2-(3,4-Dimethoxybenzylidene)-4-oxo-4-(4-(N-(4-chlorophenyl)sulfamoyl)-phenylamino)butanoic acid (6);** Yellow crystals from ethanol, mp 144-146 °C, 13% yield in microwave and 45% yield in thermal. FTIR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3446 and 3373 (2NH), 3200-2500 (OH, acid), 1729 (CO, acid) and 1669 (CO, amide), 1268 (SO<sub>2</sub>, asy.), and 1187 (SO<sub>2</sub>, sym.). MS: m/z = 530.9 (M<sup>+</sup>, 0.12%, C<sub>25</sub>H<sub>23</sub>ClN<sub>2</sub>O<sub>7</sub>S), 294 (2.3, C<sub>18</sub>H<sub>16</sub>NO<sub>3</sub>), 282 (0.14, C<sub>12</sub>H<sub>11</sub>ClN<sub>2</sub>O<sub>2</sub>S), 248 (3, C<sub>13</sub>H<sub>12</sub>O<sub>5</sub>), 247 (0.5, C<sub>13</sub>H<sub>13</sub>NO<sub>4</sub>), 176 (5.5, C<sub>11</sub>H<sub>12</sub>O<sub>2</sub>), 161 (2.5, C<sub>10</sub>H<sub>9</sub>O<sub>2</sub> or C<sub>9</sub>H<sub>7</sub>NO<sub>2</sub>), 126 (35, C<sub>6</sub>H<sub>5</sub>NCl), 115 (12, C<sub>4</sub>H<sub>5</sub>NO<sub>3</sub>), 101 (38, C<sub>8</sub>H<sub>5</sub>), and 62 (100, NOS).

**(E)-2-(3,4-Dimethoxybenzylidene)-4-oxo-4-(4-(N-(4-nitrophenyl)sulfamoyl)phenylamino)-butanoic acid (7);** Brown crystals from ethanol, mp 188-190 °C, 0% yield in microwave and 40% yield in thermal. FTIR (KBr):  $\nu$  (cm<sup>-1</sup>) = 3441 and 3300 (2NH), 3500-2400 (OH, acid), 1732 (CO, acid) and 1660 (CO, amide), 1267 (SO<sub>2</sub>, asy.), and 1156 (SO<sub>2</sub>, sym.). MS: m/z = 541 (M<sup>+</sup>, 1%, C<sub>25</sub>H<sub>23</sub>N<sub>3</sub>O<sub>9</sub>S), 294 (2.5, C<sub>18</sub>H<sub>16</sub>NO<sub>3</sub>), 293 (0.5, C<sub>12</sub>H<sub>11</sub>N<sub>3</sub>O<sub>4</sub>S), 248 (2, C<sub>13</sub>H<sub>12</sub>O<sub>5</sub>), 176 (4, C<sub>11</sub>H<sub>12</sub>O<sub>2</sub>), 175 (2, C<sub>11</sub>H<sub>11</sub>O<sub>2</sub>), 161 (1.5, C<sub>10</sub>H<sub>9</sub>O<sub>2</sub>), 138 (1, C<sub>6</sub>H<sub>6</sub>N<sub>2</sub>O<sub>2</sub>), 115 (7, C<sub>4</sub>H<sub>5</sub>NO<sub>3</sub>), 102 (29, C<sub>8</sub>H<sub>6</sub>), and 62 (100, NSO).

**(E)-2-(3,4-Dimethoxybenzylidene)-4-oxo-4-(4-(N-(1-naphthyl)sulfamoyl)phenylamino)-butanoic acid (8)**; Pale violet crystals from ethanol, mp 130-132 °C, 75% yield in microwave, 83% in microwave with DMF, and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) = 3475-3250 (2NH), 3500-2800 (OH, acid), 1674 (CO, acid) and 1627 (CO, amide), 1261 ( $\text{SO}_2$ , asy.), and 1154 ( $\text{SO}_2$ , sym.). MS:  $m/z$  = 546 ( $\text{M}^+$ , 0.37%,  $\text{C}_{29}\text{H}_{26}\text{N}_2\text{O}_7\text{S}$ ), 248 (0.48,  $\text{C}_{13}\text{H}_{12}\text{O}_5$  or  $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_2\text{S}$ ), 161 (2,  $\text{C}_{10}\text{H}_9\text{O}_2$  or  $\text{C}_7\text{H}_6\text{N}_2\text{O}_2\text{S}$  or  $\text{C}_9\text{H}_7\text{NO}_2$ ), 156 (2,  $\text{C}_6\text{H}_6\text{NO}_2\text{S}$ ), 142 (4,  $\text{C}_{10}\text{H}_8\text{N}$ ), 128 (0.54,  $\text{C}_{10}\text{H}_8$ ), 115 (100,  $\text{C}_4\text{H}_5\text{NO}_3$ ), 102 (2,  $\text{C}_8\text{H}_6$ ), 65 (47,  $\text{HSO}_2$ ), and 62 (72, NOS).

**(E)-2-(3,4-Dimethoxybenzylidene)-4-oxo-4-(4-(N-benzylsulfamoyl)phenylamino)-butanoic acid (9)**; White crystals from ethanol, mp 219-222 °C, 0% yield in microwave and 55% yield in thermal. FTIR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) = 3443 and 3300 (2NH), 3500-2800 (OH, acid), 1731 (CO, acid) and 1660 (CO, amide), 1264 ( $\text{SO}_2$ , asy.), and 1160 ( $\text{SO}_2$ , sym.). MS:  $m/z$  = 510 ( $\text{M}^+$ , 0%,  $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_7\text{S}$ ), 466 (0.01,  $\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_5\text{S}$ ), 464 (0.01,  $\text{C}_{25}\text{H}_{24}\text{N}_2\text{O}_5\text{S}$ ), 356 (0.12,  $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_4\text{S}$ ), 295 (100,  $\text{C}_{18}\text{H}_{17}\text{NO}_3$ ), 294 (99.5,  $\text{C}_{18}\text{H}_{16}\text{NO}_3$ ), 290 (1,  $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_3\text{S}$ ), 250 (27,  $\text{C}_{10}\text{H}_6\text{N}_2\text{O}_4\text{S}$ ), 249 (87,  $\text{C}_{10}\text{H}_5\text{N}_2\text{O}_2$ ), 247 (80,  $\text{C}_{13}\text{H}_{13}\text{NO}_4$ ), and 176 (100,  $\text{C}_{11}\text{H}_{12}\text{O}_2$ ).  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ):  $\delta$  (ppm) = 3.831 (3H, s, H-1), 3.85 (3H, s, H-2), 3.901 (2H, s, H-7), 4.035-4.056 (2H, d, H-12), 7.070-7.098 (1H, d, H-5), 7.277 (5H, s, H-13), 7.566 [(1H, d, H-3) & (1H, q, H-4)], 7.592-7.620 [(2H, d, H-9) & (1H, imp, H-6)], 7.932-7.960 [(2H, d, H-10) & (1H, imp, H-8)], and 8.246 (1H, t, H-12).

**(E)-4-(3-(3,4-Dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-(4-phenyl)benzenesulfonamides (10)**; Yellow crystals from benzene, mp 138-140 °C, 83% yield in microwave and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) = 3248 (NH), 1766 and 1710 (2CO, imide), 1266 ( $\text{SO}_2$ , asy.), and 1160 ( $\text{SO}_2$ , sym.). MS:  $m/z$  = 478 ( $\text{M}^+$ , 18%,  $\text{C}_{25}\text{H}_{22}\text{N}_2\text{O}_6\text{S}$ ), 463 (6,  $\text{C}_{25}\text{H}_{22}\text{N}_2\text{O}_5\text{S}$ ), 401 (8,  $\text{C}_{19}\text{H}_{17}\text{N}_2\text{O}_6\text{S}$ ), 400 (6,  $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_6\text{S}$ ), 328 (8,  $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_4\text{S}$ ), 294 (16,  $\text{C}_{18}\text{H}_{16}\text{NO}_3$ ), 247 (28,  $\text{C}_{13}\text{H}_{12}\text{NO}_4$ ), 176 (19,  $\text{C}_{11}\text{H}_{12}\text{O}_2$ ), 161 (8,  $\text{C}_{10}\text{H}_9\text{O}_2$  or  $\text{C}_9\text{H}_7\text{NO}_2$ ), and 149 (100,  $\text{C}_9\text{H}_9\text{O}_2$ ).

**(E)-4-(3-(3,4-Dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-(4-methylphenyl)benzenesulfonamide (11)**; Brown crystals from benzene, mp over 300 °C, 92% yield in microwave and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) = 3247 (NH), 1765 and 1707 (2CO, imide), 1277 ( $\text{SO}_2$ , asy.), and 1158 ( $\text{SO}_2$ , sym.). MS:  $m/z$  = 492 ( $\text{M}^+$ , 32%,  $\text{C}_{26}\text{H}_{24}\text{N}_2\text{O}_6\text{S}$ ), 491 (46,  $\text{C}_{26}\text{H}_{25}\text{N}_2\text{O}_6\text{S}$ ), 322 (41,  $\text{C}_{19}\text{H}_{16}\text{NO}_4$ ), 288 (42,  $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_3\text{S}$ ), 176 (39,  $\text{C}_{11}\text{H}_{12}\text{O}_2$ ), 156 (44,  $\text{C}_7\text{H}_7\text{NOS}$ ), and 107 (100,  $\text{C}_7\text{H}_9\text{N}$ ).  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ):  $\delta$  (ppm) = 2.203 (3H, s; H-13), 3.8 (2H, s., H-7), 3.852 [6H, s, (H-1) & (H-

2)], 6.48-6.52 (1H, d, H-5), 6.9-7.2 (2H, d, H-12), 7.564-7.9 [(2H, d, H-9), (2H, d, H-8), (1H, q, H-4), (1H, d, H-3), and (1H, d, H-11)], and 10.3 (1H, s, H-10).

**(E)-4-(3-(3,4-Dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-(4-methoxyphenyl)benzenesulfonamide (12)**; Grey crystals from ethanol, mp 193-195 °C, 93% yield in microwave and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) = 3244 (NH), 1750 and 1707 (2CO, imide), 1388 ( $\text{SO}_2$ , asy.), and 1161 ( $\text{SO}_2$ , sym.). MS:  $m/z$  = 508 ( $\text{M}^+$ , 13%,  $\text{C}_{26}\text{H}_{24}\text{N}_2\text{O}_7\text{S}$ ), 480 (4,  $\text{C}_{25}\text{H}_{24}\text{N}_2\text{O}_6\text{S}$ ), 479 (5,  $\text{C}_{25}\text{H}_{23}\text{N}_2\text{O}_6\text{S}$ ), 322 (9.5,  $\text{C}_{19}\text{H}_{16}\text{NO}_4$ ), 306 (3,  $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_4$ ), 252 (4,  $\text{C}_{10}\text{H}_8\text{N}_2\text{O}_4\text{S}$ ), 176 (8,  $\text{C}_{11}\text{H}_{12}\text{O}_2$ ), 122 (100,  $\text{C}_7\text{H}_8\text{NO}$ ), 108 (13,  $\text{C}_7\text{H}_8\text{O}$ ), and 97 (10.5,  $\text{C}_4\text{H}_3\text{NO}_2$ ).  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ):  $\delta$  (ppm) = 3.671 (2H, s, H-7), 3.776-3.886 [9H, s, (H-1), (H-2), and (H-13)], 6.917-6.961 [(2H, d, H-12) and (1H, d, H-5)] 7.046-7.141 [(1H, q, H-4), (1H, d, H-3), and (1H, imp, H-6)], 7.549-7.593 [(2H, d, H-8) and (2H, d, H-11)], 7.875-7.897 (2H, d, H-9), and 10.044 (1H, s, H-10).

**(E)-4-(3-(3,4-Dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-(4-chlorophenyl)benzenesulfonamide (13)**; Yellow crystals from benzene, mp 115-118 °C, 65% yield in microwave and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) = 3241 (NH), 1766 and 1707 (2CO, imide), 1270 ( $\text{SO}_2$ , asy.), and 1157 ( $\text{SO}_2$ , sym.). MS:  $m/z$  = 512 ( $\text{M}^+$ , 20%,  $\text{C}_{25}\text{H}_{21}\text{ClN}_2\text{O}_6\text{S}$ ), 484 (11.6,  $\text{C}_{24}\text{H}_{21}\text{ClN}_2\text{O}_5\text{S}$ ), 478 (11,  $\text{C}_{25}\text{H}_{22}\text{N}_2\text{O}_6\text{S}$ ), 360 (14,  $\text{C}_{16}\text{H}_{19}\text{ClN}_2\text{O}_4\text{S}$ ), 360 (14,  $\text{C}_{16}\text{H}_9\text{ClN}_2\text{O}_4\text{S}$ ), 322 (60,  $\text{C}_{19}\text{H}_{16}\text{NO}_4$ ), 176 (83,  $\text{C}_{11}\text{H}_{12}\text{O}_2$ ), 175 (20,  $\text{C}_{11}\text{H}_{11}\text{O}_2$ ), 161 (68,  $\text{C}_{10}\text{H}_9\text{O}_2$ ), 156 (80,  $\text{C}_6\text{H}_6\text{NO}_2\text{S}$ ), 126 (46,  $\text{C}_6\text{H}_5\text{NCl}$ ), 111 (21,  $\text{C}_6\text{H}_5\text{NCl}$ ), 102 (24,  $\text{C}_8\text{H}_6$ ), 92 (100,  $\text{C}_6\text{H}_6\text{N}$ ), and 63 (54, HNOS).

**(E)-4-(3-(3,4-Dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-(4-nitrophenyl)benzenesulfonamide (14)**; Brown crystals from ethanol, mp 178-180 °C, 93% yield in microwave and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) = 3240 (NH), 1764 and 1711 (2CO, imide), 1277 ( $\text{SO}_2$ , asy.), and 1159 ( $\text{SO}_2$ , sym.). MS:  $m/z$  = 523 ( $\text{M}^+$ , 0%,  $\text{C}_{25}\text{H}_{21}\text{N}_3\text{O}_8\text{S}$ ), 477 (5,  $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_6\text{S}$ ), 361 (5,  $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_6\text{S}$ ), 320 (5,  $\text{C}_{13}\text{H}_{10}\text{N}_3\text{O}_5\text{S}$ ), 175 (7,  $\text{C}_{11}\text{H}_{11}\text{O}_2$ ), 149 (100,  $\text{C}_9\text{H}_9\text{O}_2$ ), 138 (14,  $\text{C}_6\text{H}_6\text{N}_2\text{O}_2$ ), and 63 (21, HNOS).

**(E)-4-(3-(3,4-Dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-benzylbenzenesulfonamide (15)**; White crystals from benzene, mp 212-214 °C, 82% yield in microwave and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) = 3280 (NH), 1761 and 1709 (2CO, imide), 1330 ( $\text{SO}_2$ , asy.), and 1155 ( $\text{SO}_2$ , sym.). MS:  $m/z$  = 492 ( $\text{M}^+$ , 61%,  $\text{C}_{26}\text{H}_{24}\text{N}_2\text{O}_6\text{S}$ ), 461 (2,  $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_5\text{S}$ ), 356 (3,  $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_4\text{S}$ ), 322 (8,  $\text{C}_{19}\text{H}_{16}\text{NO}_4$ ), 290 (2,  $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_3\text{S}$ ), 251 (4,



C<sub>10</sub>H<sub>7</sub>N<sub>2</sub>O<sub>4</sub>S), 176 (44, C<sub>11</sub>H<sub>12</sub>O<sub>2</sub>), and 106 (100, C<sub>7</sub>H<sub>8</sub>N). <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>): δ (ppm) = 3.518 (2H, s, H-7), 3.771 (3H, s, H-1), 3.801 (3H, s, H-2), 4.092-4.126 (2H, d, H-11), 7.48-6.52 (1H, d, H-5), 7.001-7.182 (5H, s, H-12), 7.04-7.059 (1H, q, H-4), 7.059-7.088 [(1H, d, H-3) and 1H, imp, H-6)], 7.252 (2H, d, H-8), 7.874 (2H, d, H-9), and 8.516-8.545 (1H, t, H-10).

**(E)-2-(Benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-phenylsulfamoyl)phenylamino)butanoic acids (16)**; White crystals from ethanol, mp 196-198 °C, 33% yield in microwave and 55% yield in thermal. FTIR (KBr): ν (cm<sup>-1</sup>) = 3282 (2NH), 3600-2500 (OH, acid), 1663 (2CO, acid and amide), 1243 (SO<sub>2</sub>, asy.), and 1161 (SO<sub>2</sub>, sym.). MS: m/z = 480.5 (M<sup>+</sup>, 0%, C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O<sub>7</sub>S), 462 (2, C<sub>24</sub>H<sub>18</sub>N<sub>2</sub>O<sub>6</sub>S), 248 (32, C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>S), 232 (37, C<sub>12</sub>H<sub>8</sub>O<sub>5</sub>), 160 (41, C<sub>10</sub>H<sub>8</sub>O<sub>2</sub>), 159 (14, C<sub>10</sub>H<sub>7</sub>O<sub>2</sub>), 156 (60, C<sub>6</sub>H<sub>6</sub>NO<sub>2</sub>S), 130 (14, C<sub>9</sub>H<sub>6</sub>O), 115 (2, C<sub>4</sub>H<sub>5</sub>NO<sub>3</sub>), 102 (52, C<sub>8</sub>H<sub>6</sub>), 92 (94, C<sub>6</sub>H<sub>6</sub>N), 65 (100, HSO<sub>2</sub>), and 62 (100, NOS).

**(E)-2-(Benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-(4-methylphenyl)sulfamoyl)phenylamino)butanoic acid (17)**; White crystals from ethanol, mp 192 °C, 30% yield in microwave and 67% yield in thermal. FTIR (KBr): ν (cm<sup>-1</sup>) = 3266 and 3110 (2NH), 3600-2200 (OH, acid), 1690 (CO, acid) 1666 (CO, amide), 1242 (SO<sub>2</sub>, asy.), and 1155 (SO<sub>2</sub>, sym.). MS: m/z = 494.5 (M<sup>+</sup>, 0.2%, C<sub>25</sub>H<sub>22</sub>N<sub>2</sub>O<sub>7</sub>S), 248 (0.2, C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>S), 247 (0.2, C<sub>13</sub>H<sub>13</sub>NO<sub>5</sub>S), 160 (0.54, C<sub>10</sub>H<sub>8</sub>O<sub>2</sub>), 106 (45, C<sub>7</sub>H<sub>8</sub>N), 102 (32, C<sub>8</sub>H<sub>6</sub>), 91 (16, C<sub>7</sub>H<sub>7</sub>), 77 (63, C<sub>6</sub>H<sub>5</sub>), 65 (27.5, HSO<sub>2</sub>), and 62 (100, NOS). <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>): δ (ppm) = 2.174 (3H, s, H-13), 3.65 (2H, s, H-6), 6.048 (2H, s, H-1), 6.405-6.45 (1H, d, H-2), 6.998 (1H, d, H-12), 7.389-7.399 (2H, d, H-8), 7.405-7.602 [3H, m, (H-3), (H-4) & (H-5)], 8.010-8.048 (2H, d, H-11), 8.389-8.402 (2H, d, H-9), 10.01 (1H, s, H-7), 10.6 (1H, s, H-10), and 12.4 (1H, broad, H-14).

**(E)-2-(Benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-(4-methoxyphenyl)sulfamoyl)phenylamino)butanoic acid (18)**; Pale grey crystals from ethanol, mp over 300 °C, 0% yield in microwave and 74% yield in thermal. FTIR (KBr): ν (cm<sup>-1</sup>) = 3436 (2NH), 3400-2600 (OH, acid), 1711 (CO, acid), 1636 (CO, amide), 1248 (SO<sub>2</sub>, asy.), and 1138 (SO<sub>2</sub>, sym.). MS: m/z = 510 (M<sup>+</sup>, 0%, C<sub>25</sub>H<sub>22</sub>N<sub>2</sub>O<sub>8</sub>S), 278 (23, C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub>S), 232 (4, C<sub>12</sub>H<sub>8</sub>O<sub>5</sub> or C<sub>12</sub>H<sub>10</sub>NO<sub>2</sub>S), 175 (18, C<sub>10</sub>H<sub>7</sub>O<sub>3</sub>), 160 (9, C<sub>10</sub>H<sub>8</sub>O<sub>2</sub>), 122 (2, C<sub>7</sub>H<sub>8</sub>NO), and 93 (2, C<sub>6</sub>H<sub>5</sub>O).

**(E)-2-(Benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-(4-chlorophenyl)sulfamoyl)phenylamino)butanoic acid (19)**; White crystals from ethanol, mp 134-136 °C, 37% yield in microwave and 45% yield in thermal. FTIR (KBr): ν (cm<sup>-1</sup>) = 3450 (2NH), 3600-2500 (OH, acid), 1731 (CO, acid), 1662 (CO, amide), 1251 (SO<sub>2</sub>, asy.), and

1167 (SO<sub>2</sub>, sym.). MS: 514 (M<sup>+</sup>, 1%, C<sub>24</sub>H<sub>19</sub>ClN<sub>2</sub>O<sub>7</sub>S), 232 (5, C<sub>12</sub>H<sub>8</sub>O<sub>5</sub> or C<sub>12</sub>H<sub>10</sub>NO<sub>2</sub>S), 175 (2, C<sub>10</sub>H<sub>7</sub>O<sub>3</sub>), 160 (1, C<sub>10</sub>H<sub>8</sub>O<sub>2</sub>), 157 (0.82, C<sub>6</sub>H<sub>7</sub>NO<sub>2</sub>S), 127 (1, C<sub>6</sub>H<sub>6</sub>NCl), 92 (2, C<sub>6</sub>H<sub>6</sub>N), 65 (6, HSO<sub>2</sub>), and 62 (100, NOS).

**(E)-2-(Benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-(4-nitrophenyl)sulfamoyl)phenylamino)butanoic acid (20)**; Brown crystals from ethanol, mp 140-141 °C, 0% yield in microwave and 36% yield in thermal. FTIR (KBr): ν (cm<sup>-1</sup>) = 3386 (2NH), 3400-2500 (OH, acid), 1731 (CO, acid), 1662 (CO, amide), 1252 (SO<sub>2</sub>, asy.), and 1166 (SO<sub>2</sub>, sym.). MS: m/z = 525.5 (M<sup>+</sup>, 0%, C<sub>24</sub>H<sub>19</sub>N<sub>3</sub>O<sub>9</sub>S), 293 (3, C<sub>12</sub>H<sub>11</sub>N<sub>3</sub>O<sub>4</sub>S), 278 (70, C<sub>12</sub>H<sub>10</sub>N<sub>2</sub>O<sub>4</sub>S), 277 (100, C<sub>12</sub>H<sub>9</sub>N<sub>2</sub>O<sub>4</sub>S), 232 (95.5, C<sub>12</sub>H<sub>8</sub>O<sub>5</sub> or C<sub>12</sub>H<sub>10</sub>NO<sub>2</sub>S), 175 (67, C<sub>10</sub>H<sub>7</sub>O<sub>3</sub>), 160 (40, C<sub>10</sub>H<sub>8</sub>O<sub>2</sub>), and 93 (0.2, C<sub>6</sub>H<sub>5</sub>O).

**(E)-2-(Benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-(1-naphthyl)sulfamoyl)phenylamino)butanoic acid (21)**; Pale violet crystals from ethanol, mp 130-121 °C, 69% yield in microwave, 75% yield in microwave with DMF, and 0% yield in thermal. FTIR (KBr): ν (cm<sup>-1</sup>) = 3302 and 3227 (2NH), 3300-2800 (OH, acid), 1715 (CO, acid), 1666 (CO, amide), 1256 (SO<sub>2</sub>, asy.), and 1150 (SO<sub>2</sub>, sym.). MS: m/z = 530.5 (M<sup>+</sup>, 0%, C<sub>28</sub>H<sub>22</sub>N<sub>2</sub>O<sub>7</sub>S), 159 (0.37, C<sub>10</sub>H<sub>7</sub>O<sub>2</sub>), 156(2, C<sub>6</sub>H<sub>6</sub>NO<sub>2</sub>S) 142 (5.4, C<sub>10</sub>H<sub>8</sub>N), 128 (0.32, C<sub>10</sub>H<sub>8</sub>), 115 (100, C<sub>4</sub>H<sub>5</sub>NO<sub>3</sub> or C<sub>9</sub>H<sub>7</sub>), 102 (0.85, C<sub>8</sub>H<sub>6</sub>), 65 (42, HSO<sub>2</sub>), and 63 (29, HNOS).

**(E)-2-(Benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-(4-benzylsulfamoyl)phenylamino)butanoic acid (22)**; White crystals from ethanol, mp 222-223 °C, 35% yield in microwave and 50% yield in thermal. FTIR (KBr): ν (cm<sup>-1</sup>) = 3297 and 3200 (2NH), 3500-2200 (OH, acid), 1695 (CO, acid), 1664 (CO, amide), 1243 (SO<sub>2</sub>, asy.), and 1161 (SO<sub>2</sub>, sym.). MS: m/z = 494.5 (M<sup>+</sup>, 0.54%, C<sub>25</sub>H<sub>22</sub>N<sub>2</sub>O<sub>7</sub>S), 262 (31, C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>S), 232 (94, C<sub>12</sub>H<sub>8</sub>O<sub>5</sub>), 160 (87, C<sub>10</sub>H<sub>8</sub>O<sub>2</sub>), 159 (24, C<sub>10</sub>H<sub>7</sub>O<sub>2</sub>), 106 (67, C<sub>7</sub>H<sub>8</sub>N), 102 (77, C<sub>8</sub>H<sub>6</sub>), 91 (53, C<sub>7</sub>H<sub>7</sub>), 65 (69, HSO<sub>2</sub>), and 63 (33, HNOS). <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>): δ (ppm) = 3.856 (2H, s, H-6), 4.041-4.062 (2H, d, H-11), 6.126 (2H, s, H-1), 7.042-7.069 (1H, d, H-2), 7.235-7.290 [8H, m, (H-3), (H-4), (H-5) & (H-12)], 7.541 (1H, s, H-7), 7.585-7.614 (2H, d, H-8), 7.930-7.959 (2H, d, H-9), and 8.224-8.265 (1H, t, H-10).

**(E)-4-(3-(Benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-(4-phenyl)benzenesulfonamides (23)**; Yellow crystals from benzene, mp 226-227 °C, 50% yield in microwave and 0% yield in thermal. FTIR (KBr): ν (cm<sup>-1</sup>) = 3255 (NH), 1762 and 1704 (2CO, imide), 1246 (SO<sub>2</sub>, asy.), and 1163 (SO<sub>2</sub>, sym.). MS: m/z = 462 (M<sup>+</sup>, 70%, C<sub>24</sub>H<sub>18</sub>N<sub>2</sub>O<sub>6</sub>S), 370 (5, C<sub>18</sub>H<sub>12</sub>NO<sub>6</sub>S), 306 (90, C<sub>18</sub>H<sub>12</sub>NO<sub>4</sub>), 232 (69, C<sub>12</sub>H<sub>8</sub>O<sub>5</sub>), 231 (7,

$C_{12}H_9NO_4$ ), 160 (100,  $C_{10}H_8O_2$ ), 159 (47,  $C_{10}H_7O_2$ ), 102 (98,  $C_8H_6$ ), 92 (71,  $C_6H_6N$ ), 65 (67,  $HSO_2$ ), and 63 (40,  $HNOS$ ).

**(E)-4-(3-(Benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-(4-methylphenyl)benzenesulfonamide (24)**; Yellow crystals from benzene, mp 190-194 °C, 60% yield in microwave and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $cm^{-1}$ ) = 3267 (NH), 1770 and 1706 (2CO, imide), 1245 ( $SO_2$ , asy.), and 1163 ( $SO_2$ , sym.). MS:  $m/z$  = 476 ( $M^+$ , 20%,  $C_{25}H_{20}N_2O_6S$ ), 160 (22,  $C_{10}H_8O_2$ ), 134 (25,  $C_8H_6O_2$ ), 122 (36,  $C_6H_4NS$ ), 106 (23,  $C_7H_8N$ ), 102 (33,  $C_8H_6$ ), 97 (37,  $C_4H_3NO_2$ ), 91 (21.5,  $C_7H_7$ ), 62 (32,  $NOS$ ), and 57 (100,  $C_2H_5NO$ ).

**(E)-4-(3-(Benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-(4-methoxyphenyl)benzenesulfonamide (25)**; Grey crystals from ethanol, mp 210-211 °C, 89% yield in microwave and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $cm^{-1}$ ) = 3261 (NH), 1769 and 1704 (2CO, imide), 1250 ( $SO_2$ , asy.), and 1166 ( $SO_2$ , sym.). MS:  $m/z$  = 492 ( $M^+$ , 10%,  $C_{25}H_{20}N_2O_7S$ ), 463 (3,  $C_{24}H_{19}N_2O_6S$ ), 232 (2,  $C_{12}H_{10}NO_2S$ ), 231 (1.5,  $C_{12}H_9O_4$ ), 175 (2,  $C_{10}H_7O_3$ ), 160 (13,  $C_{10}H_8O_2$ ), 122 (100,  $C_7H_8NO$ ), 102 (8,  $C_8H_6$ ), 92 (9.5,  $C_6H_6N$ ), and 65 (14,  $HSO_2$ ).  $^1H$ -NMR (DMSO- $d_6$ ):  $\delta$  (ppm) = 3.67 (2H, s, H-6), 3.834 (3H, s, H-12), 6.123 (2H, s, H-1), 6.791-6.801 (1H, d, H-2), 7.031-7.194 [4H, m, (H-3), (H-4) & (H-11)], 7.238-7.355 (2H, d, H-7), 7.645 (1H, imp, H-5), 7.765 (2H, d, H-10), 7.875-7.897 (2H, d, H-8), and 10.094 (1H, s, H-9).

**(E)-4-(3-(Benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-(4-chlorophenyl)benzenesulfonamide (26)**; Yellow crystals from benzene, mp 122-124 °C, 40% yield in microwave and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $cm^{-1}$ ) = 3244 (NH), 1760 and 1711 (2CO, imide), 1257 ( $SO_2$ , asy.), and 1167 ( $SO_2$ , sym.). MS:  $m/z$  = 498 ( $M+1$ , 7%,  $C_{24}H_{18}ClN_2O_6S$ ), 306 (7,  $C_{18}H_{12}NO_4$ ), 232 (100,  $C_{12}H_8O_5$  or  $C_{12}H_{10}NO_2S$ ), 175 (20,  $C_{10}H_7O_3$ ), 160 (37,  $C_{10}H_8O_2$ ), 159 (37,  $C_{10}H_7O_2$ ), 127 (14,  $C_6H_6NCl$ ), 102 (85,  $C_8H_6$ ), 92 (24,  $C_6H_6N$ ), 65 (31.5,  $HSO_2$ ), and 63 (64,  $HNOS$ ).

**(E)-4-(3-(Benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-(4-nitrophenyl)benzenesulfonamide (27)**; Brown crystals from benzene, mp 178-180 °C, 92% yield in microwave and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $cm^{-1}$ ) = 3251 (2NH), 1768 and 1711 (2CO, imide), 1244 ( $SO_2$ , asy.), and 1164 ( $SO_2$ , sym.). MS:  $m/z$  = 507.5 ( $M^+$ , 3%,  $C_{24}H_{17}N_3O_8S$ ), 370 (3,  $C_{18}H_{12}NO_6S$ ), 278 (3,  $C_{12}H_{10}N_2O_4S$ ), 232 (17,  $C_{12}H_{10}NO_2S$ ), 175 (3,  $C_{10}H_7O_3$ ), 160 (100,  $C_{10}H_8O_2$ ), 102 (72.5,  $C_8H_6$ ), 92 (15,  $C_6H_6N$ ), 65 (20,  $C_5H_5$ ), and 63 (32.5,  $HNOS$ ).

**(E)-4-(3-(Benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-**

**benzylbenzenesulfonamide (28)**; Yellow crystals from benzene, mp 212-214 °C, 52% yield in microwave, 90% yield in microwave with DMF, and 0% yield in thermal. FTIR (KBr):  $\nu$  ( $cm^{-1}$ ) = 3219 (NH), 1757 and 1697 (2CO, imide), 1261 ( $SO_2$ , asy.), and 1170 ( $SO_2$ , sym.). MS:  $m/z$  = 476.5 ( $M^+$ , 4%,  $C_{25}H_{20}N_2O_6S$ ), 371 (2.5,  $C_{18}H_{13}NO_6S$ ), 307 (4,  $C_{18}H_{12}NO_4$ ), 289 (2.5,  $C_{14}H_{12}N_2O_3S$ ), 231 (3,  $C_{12}H_9N$ ), 160 (19.5,  $C_{10}H_8O_2$ ), 106 (100,  $C_7H_8N$ ), 102 (16,  $C_8H_6$ ), 91 (45,  $C_7H_7$ ), 65 (36.5,  $HSO_2$ ), and 63 (14,  $HNOS$ ).  $^1H$ -NMR (DMSO- $d_6$ ):  $\delta$  (ppm) = 3.65 (2H, imp, H-6), 4.048-4.104 (2H, d, H-10), 6.134 (2H, s, H-1), 7.077-7.099 (1H, d, H-2), 7.283-7.295 (5H, s, H-11), 7.593-7.601 [5H, m, (H-3), (H-4), (H-5) & (H-7)], 7.895-7.947 (2H, d, H-8), and 8.314 (1H, t, H-9).

### 3. Results and Discussion

Microwave irradiation of anhydride (E)-3-(3,4-dimethoxybenzylidene)dihydrofuran-2,5-dione **1** or (E)-3-(benzo[d][1,3]dioxol-5-ylmethylene)dihydrofuran-2,5-dione **2** with N-phenyl-4-aminobenzenesulfonamide (a) as an unsubstituted amine gave separable mixtures, **3** (10%), **10** (83%), and **16** (33%), **23** (50%), respectively. This can be attributed to the low basicity of the reacted amine. Also with N-(4-chlorophenyl)-4-aminobenzenesulfonamide (d) that containing the electron attracting chlorine atom, both anhydrides **1** and **2** formed separable mixtures from **6** (13%), **13** (65%) and **19** (37%), **26** (40%), respectively. These results can be ascribed to the low nucleophilicity of the nitrogen atom in the amido group, due to the presence of the electron withdrawing chlorine atom, which causes incomplete transformation of the resulted butenamide to the cyclic compound.

However, microwave irradiation of anhydride **1** or **2**, with N-(4-methoxyphenyl)-4-aminobenzenesulfonamide (c) gave the corresponding (E)-4-(3-(3,4-dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-(4-methoxyphenyl)benzenesulfonamide **12** (93%) or (E)-4-(3-(benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-(4-methoxyphenyl)benzenesulfonamide **25** (89%) as only products. This can be attributed to the high basicity of the electron releasing methoxyl group in amine (c) which facilitates the intramolecular nucleophilic attack of the amido nitrogen on the carbonyl carbon.

On the other hand in spite of the low basicity of N-(4-nitrophenyl)-4-aminobenzenesulfonamide (e) due to the presence of the electron attracting nitro group, both of anhydrides **1** and **2** gave the corresponding (E)-4-(3-(3,4-dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-(4-nitrophenyl)benzenesulfonamide **14** (93%) and (E)-4-

(3-(benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-(4-nitrophenyl) benzenesulfonamide **27** (92%), as only products. This could be ascribed to the microwave effects on the dipolar nitro group in amine (e) where microwave thermal and specific non-purely thermal effects, resulted from material-wave interactions<sup>17</sup> led to further intramolecular nucleophilic attack by the amido nitrogen on the carbonyl carbon. The greater the polarity of a molecule, the more pronounced microwave effects to enhance the formation of the cyclic product. The combination of these two contributions can be responsible for regiospecific selectivity and the formation of the cyclic compounds.

Reaction of N-(4-methylphenyl)-4-aminobenzenesulfonamide (b) with anhydride **1** gave (E)-4-(3-(3,4-dimethoxybenzylidene)-2,5-dioxopyrrolidin-1-yl)-N-(4-methylphenyl)benzenesulfonamide **11** (92%) as an only product, whereas with anhydride **2** it gave a separable mixture from (E)-2-(benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-(4-methylphenyl)sulfamoyl)phenylamino)butanoic acid **17** (30%), and (E)-4-(3-(benzo[d][1,3]dioxol-5-ylmethylene)-2,5-dioxopyrrolidin-1-yl)-N-(4-methylphenyl)benzenesulfonamide **24** (60%). These results can be explained on the basis of the anhydrides structure where in anhydride **2** the distortion exerted by the 2-benzo[d][1,3]dioxol moiety, could decrease the complete coplanarity, that is necessary for ring closure, to form the corresponding pyrrolidine-2,5-dione, to be an only product.

On the other hand with N-(1-naphthyl)-4-aminobenzenesulfonamide (f), anhydrides **1** and **2**, produced (E)-2-(3,4-dimethoxybenzylidene)-4-oxo-4-(4-(N-(1-naphthyl)sulfamoyl)phenylamino)butanoic acid **8** (75%) and (E)-2-(benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-(1-naphthyl)sulfamoyl)phenylamino)butanoic acid **21** (69%), respectively, as only products. This result can be ascribed to the low nucleophilicity of the amido nitrogen towards further attack on the carbonyl carbon.

However, microwave irradiation of N-benzyl-4-aminobenzenesulfonamide (g), as a relatively high basic aliphatic amine, with compound **1** gave benzenesulfonamide derivative **15** (82%) as an only

product, whereas with compound **2**, it gave a separable mixture from **22** (35%) and **28** (52%). In presence of the aprotic solvent DMF, compound **2** gave with amine (g), **28** (90%) as an only product. The presence of the aprotic solvent (DMF), caused the super heating effect in the microwave irradiation, where the energy transferred from large excess solvent molecules to the reaction mixture. The presence of solvent also slightly enhanced the yield of the products where microwave irradiation reactions of compound **1** or **2** with amine (f), in DMF gave the corresponding butanoic acids in slightly better yields **8** (83%), **21** (75%) instead of (75%) and (69%), respectively. This result indicated that in such a case, no more agitation or molecules reorientation could take place by microwave irradiation, to allow further intramolecular nucleophilic attack by the nitrogen atom of amido group on the carbonyl carbon to form the cyclic compound (Schemes 1 and 2).

#### Thermal conventional heating technique

Conventional thermal condensation of anhydrides **1** or **2** with N-substituted aryl-4-aminobenzenesulfonamides (a-e, and g) gave the corresponding (E)-2-(3,4-dimethoxybenzylidene)-4-oxo-4-(4-(N-arylsulfamoyl)phenylamino)butanoic acids **3-7** and **9**, and (E)-2-(benzo[d][1,3]dioxol-5-ylmethylene)-4-oxo-4-(4-(N-arylsulfamoyl)phenylamino)butanoic acids **16-20**, and **22**, respectively.

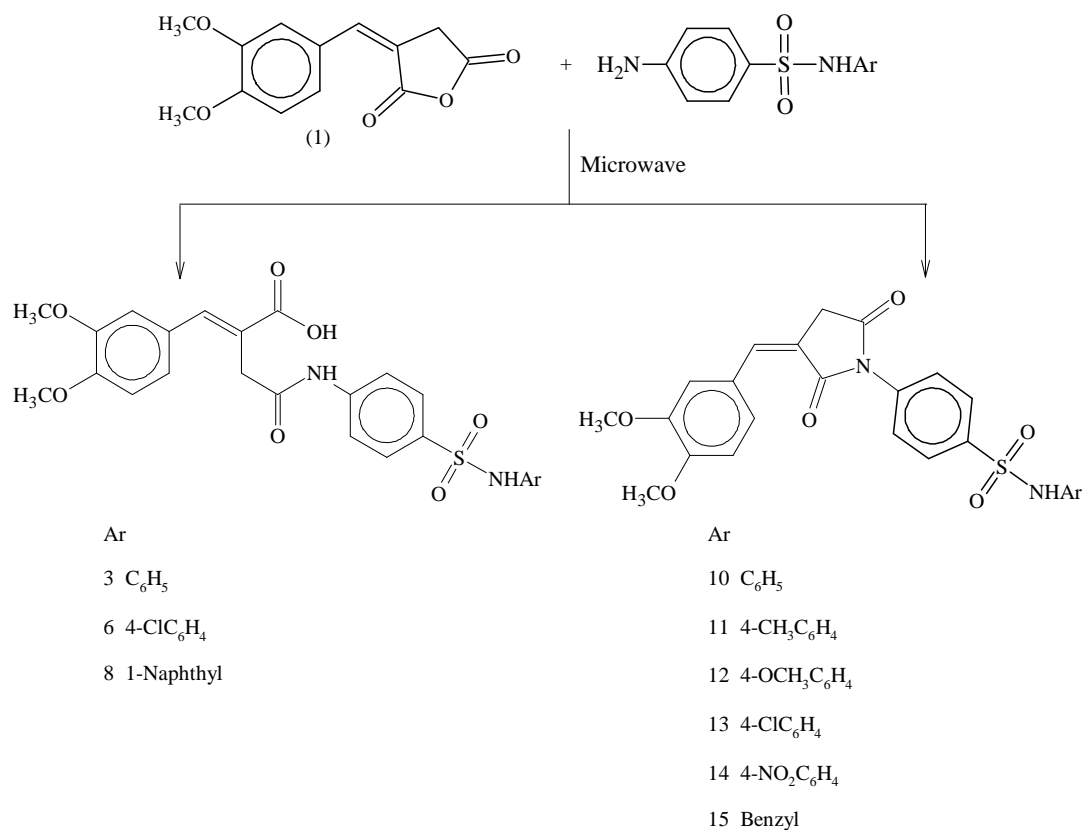
However, with amine (f), all trials carried out for its reaction with **1** or **2**, under reflux or fusion, were unsuccessful. These results were attributed to the low basicity of amine (f).

In general, the results indicated that microwave irradiation effects enhance the susceptibility of amido nitrogen towards further intramolecular nucleophilic attack to form the cyclic product, more than the conventional thermal heat technique (Scheme 3).

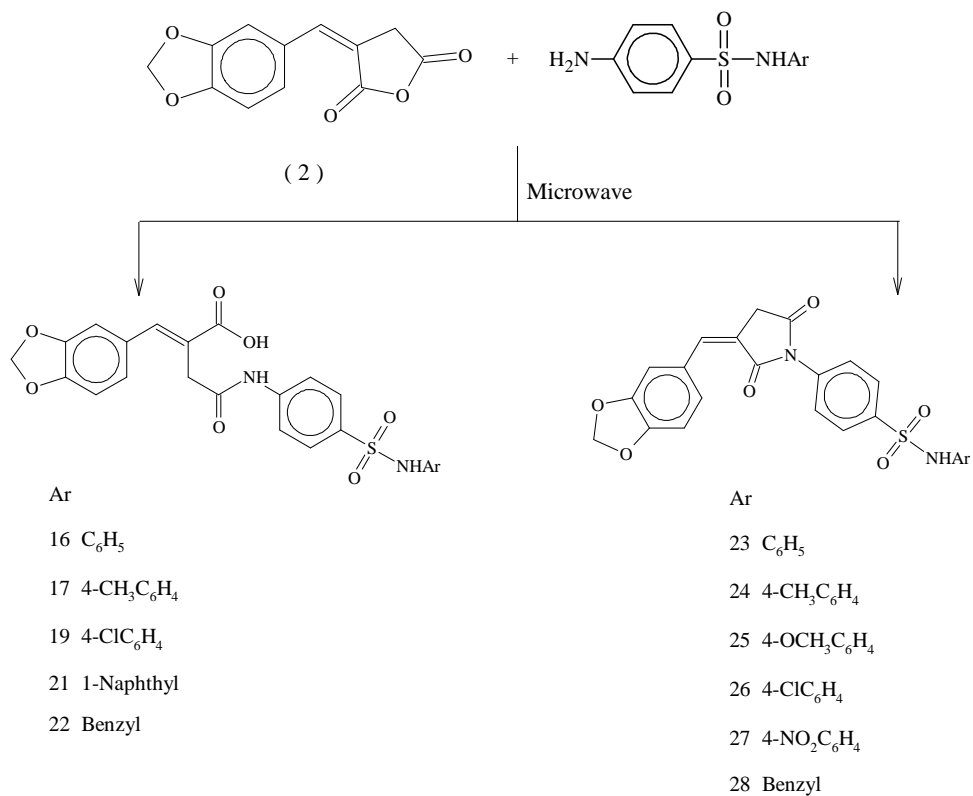
Molecular structures of compounds **3-28** were assigned by their spectral analyses; IR, MS, and <sup>1</sup>H-NMR. Protons numbering of <sup>1</sup>H-NMR spectra of some compounds are given in Figure 1.

The most pronounced antibacterial activities with compounds **5**, **14**, **17**, **20** and **27** could be attributed to the presence of carboxyl (COOH), methoxyl (OCH<sub>3</sub>), and nitro (NO<sub>2</sub>) groups.

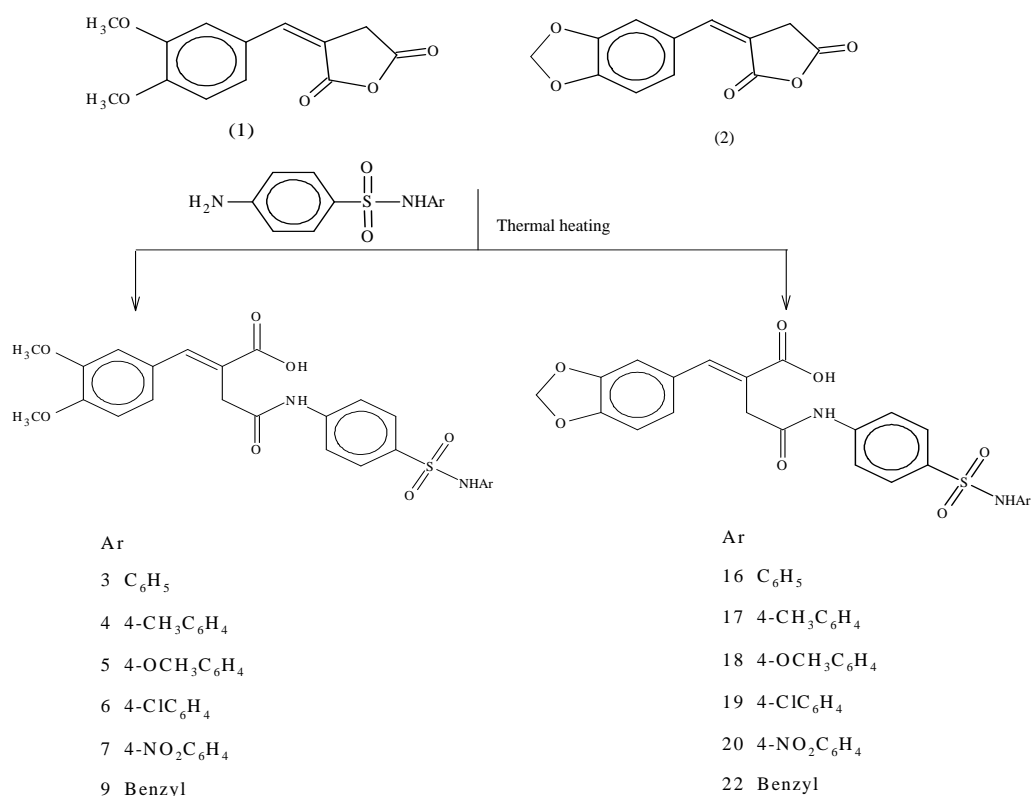
The results of cytotoxic activity of screened compounds showed low activity (Table 2).



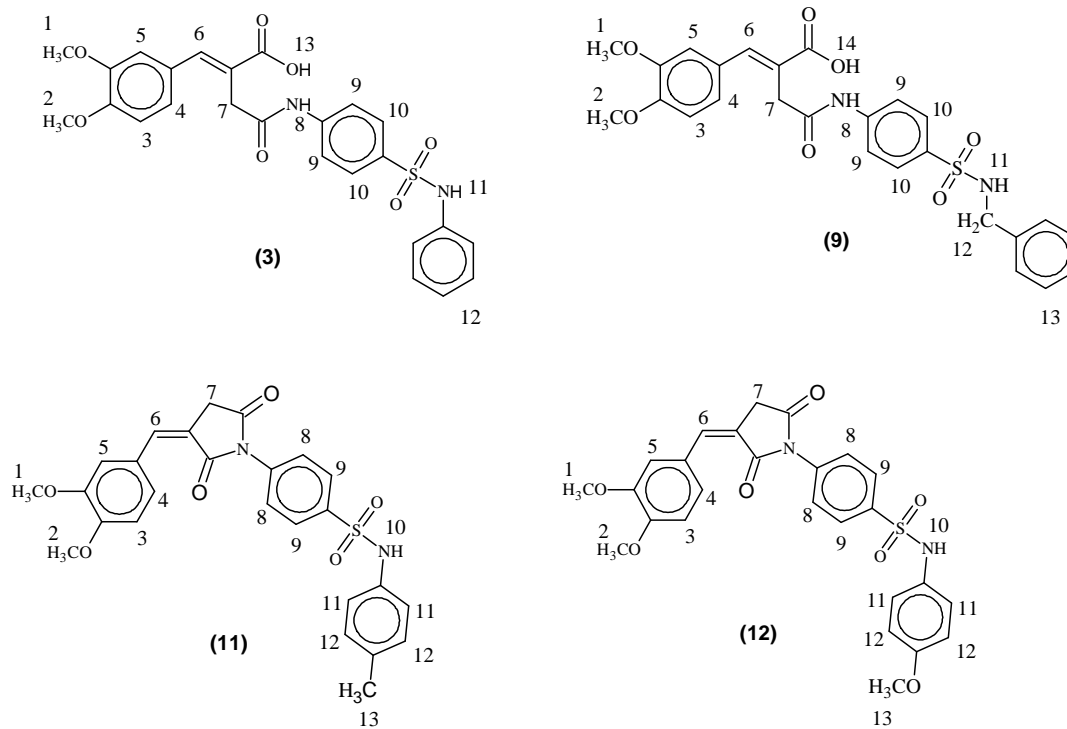
Scheme 1



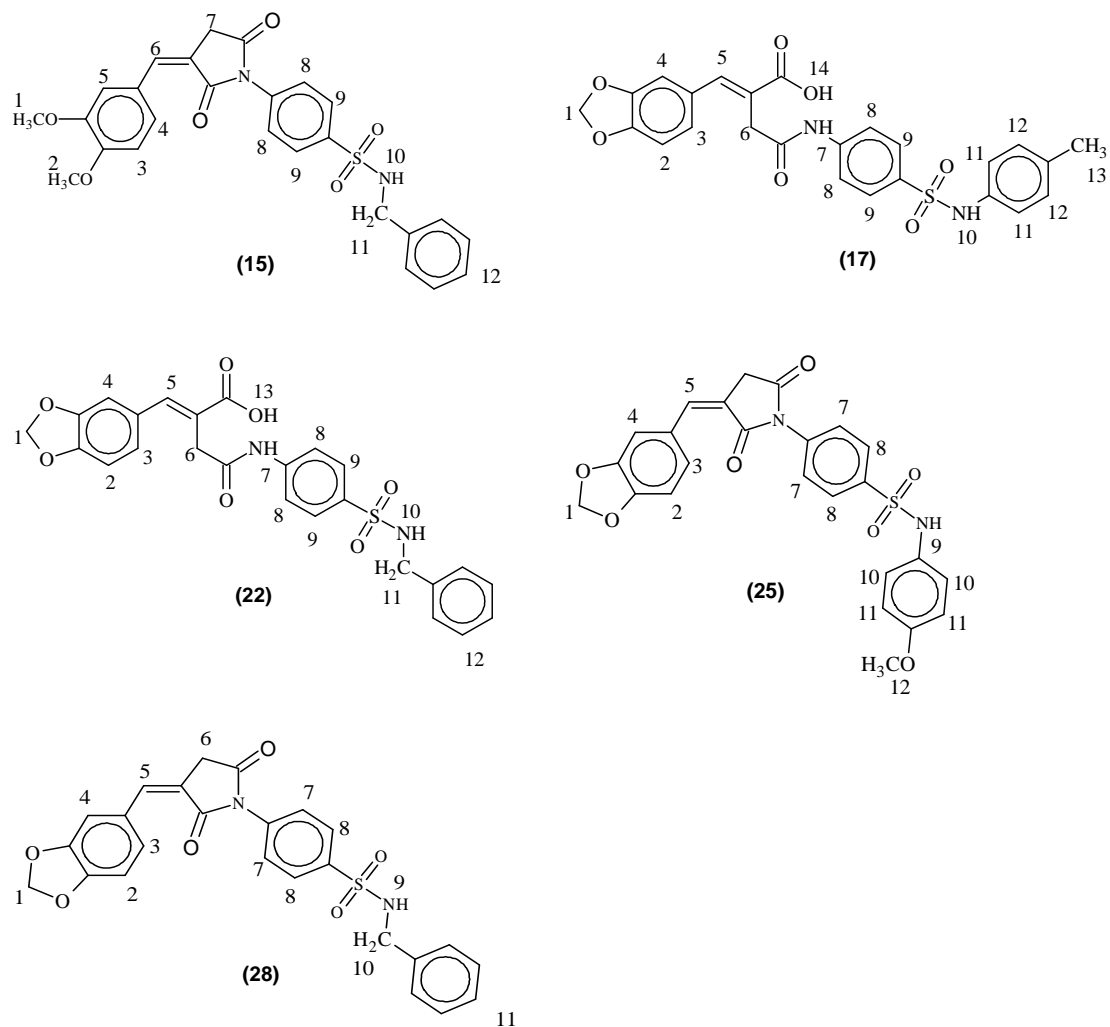
Scheme 2



Scheme 3





Figure 1: Protons Numbering of <sup>1</sup>H-NMR Spectra**Table 2:** Biological activities of some compounds

Compound	Antimicrobial Activity Inhibition zone (mm/mg sample)				Cytotoxic activity IC <sub>50</sub> µg/ml
	<i>Bacillus subtilis</i> (G <sup>+</sup> )	<i>E. Coli</i> (G <sup>-</sup> )	<i>Pseudomonas aeruginosa</i> (G <sup>-</sup> )	<i>Staphylococcus Aureus</i> (G <sup>+</sup> )	
4	13	---	---	13	
5	14	15	15	16	
7	13	13	---	---	
8					20.7
10					20.7
12					16.7
14	13	13	14	13	
17	16	12	---	20	
18	18	13	---	15	
20	16	14	---	14	
21					18.9
25	12	---	---	---	19.7
27	15	15	15	14	
Flouraciele					2.97

## Conclusion

Microwave irradiation effects enhance the yield, purity, regioselectivity, and cyclization, more than the conventional thermal heat effect. The distortion exerted by the 2-benzo[d][1,3]dioxol moiety, could decrease the probability of molecular coplanarity that is necessary for ring closure to form the corresponding cyclic products. Aprotic solvent (DMF), assists the super heating effect in the microwave irradiation where the energy transfers from large excess solvent molecules to the reaction mixture so that it facilitates the formation of the cyclic products and enhances the yields. Compounds containing carboxyl (COOH), methoxyl (OCH<sub>3</sub>), and nitro (NO<sub>2</sub>) groups showed high activity towards antimicrobial activities. Compounds that screened for cytotoxic activity IC<sub>50</sub>µg/ml showed low reactivity towards it.

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## Length of trauma patients' stay in imam Reza hospital as a tertiary center of Trauma and effective factor such as Routine Trauma X-rays

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**Abstract:** Emergency department is the first place that medical team gets contact with the patient. In order to have higher standards in traumatic patient care, continuous quality control is an essence and time is an important factor for this perspective in emergency department. Current study evaluates management of traumatic patients visiting emergency department (ED) in Imam Reza hospital by assessing length of stay and its effective factors such as Routine Trauma X-rays. Between April and December 2011, 300 traumatic patients visiting emergency department, Imam Reza hospital were randomly studied. Time needed to perform the routine trauma x-rays (lateral cervical vertebra, AP chest and AP pelvis radiographies), and the length of stay (LOS) in the ED were recorded. Mean physician and nurse first visit was  $7.93 \pm 0.47$  and  $11.91 \pm 9.38$  minutes, respectively. X-rays in was performed within  $70.30 \pm 53.08$  minutes. Mean surgery and neurosurgery visits were obtained within  $37.40 \pm 3.16$  minutes and  $33.48 \pm 2.10$  minutes, respectively. The average LOS in the ED was  $404 \pm 238.51$  minutes. There was no significant difference in LOS in the ED according to age, gender and trauma severity. Total ED stay of trauma patients in our ED was found to be significantly longer than other advanced centers. Structural improvement of emergency department and diagnostic modalities availability could reduce LOS in ED.

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**Keywords:** Emergency department; Trauma; Trauma management

### 1. Introduction

Emergency Department (ED) of a hospital is the initial entrance for the majority of patients with emergency and non-emergency medical problems to the healthcare system. ED care is a proper opportunity to study the problems and differences due to the pervasive health problem of accumulation of patients in ED, where patients wait often for a long time to be examined by a physician for the initial evaluations, treatment and hospitalization (Andrulis, 1991; Derlet and Richard, 2001). The crowding in the ED is accompanied by delayed antibiotic treatment of pneumonia, delayed thrombolysis in acute myocardial infarction and delayed prescribing of analgesic drugs for patients with severe pain (Pines, 2006; Schull, 2004; Pines and Hollander, 2008; Pines, 2007; Fee, 2007).

Lack of sufficient attention to trauma and traumatic patients leads to death or disability and composes destructive effects on the social economic structure of countries and is becoming an epidemic across the world (Aksoy, 2001). In order to have high standards in providing medical care to traumatic patients, continuous quality control is a necessity. Within the framework of quality control, traumatic

patients should be determined and proper medical care algorithms be provided for these patients (Walters and McNeill, 1990). In recent years, an algorithm called "advanced trauma Support, ATLS" has been applied by the American College of Surgeons. Reduction in preventable mortality and shorter hospitalization duration can only be achieved through improved quality of trauma care. "Time" is an important factor in managing multi-traumatic patients in the ED.

Due to either insufficient medical knowledge or lack of the necessary facilities, services by emergency physicians for traumatic patients may often cause chronic or fatal and severe injuries for young patients or patients with relatively good health condition at the time of the incident, or when taking a proper action could have given them the best quality of life. Use of Radiology, guidelines and the patterns of traumatic patients increase the chance of diagnosis. Modern facilities gradually phased in EDs will lead to improved procedure of timely diagnosis (Oyar and Aktuglu, 2000). Given that traumatic patients, especially those in shock, will have 1 percent increased mortality for every three minutes delay in the emergency intervention, in this study, we

intended to evaluate the quality of service to traumatic patients admitted to ED of Imam Reza hospital of Tabriz assessing the duration of patient's stay and determining the factors effective on it.

## 2. Material and Methods

In a descriptive-analytical study in the ED of Imam Reza hospital of Tabriz in 2011, the relationship between staying duration of traumatic patients in Imam Reza ED as a third-level trauma center, and the factors involved in it was studied.

In this study, 300 traumatic patients were randomly selected and included in the study from among traumatic patients admitted to ED of Imam Reza hospital.

In all cases, the start time of the Primary Survey and requesting other routine graphs of trauma (radiographs of lateral spinal column, anterior-posterior chest and pelvis) was recorded and the interval was calculated. The time of requesting surgical and neurosurgical consultation and its conduction time were also recorded and the time interval calculated. Finally, the time of patient's discharge or un-discharge due to either decease, operating room, admission in intensive care unit (ICU), ward, or dispatched to another hospital were recorded. Selected patients were included in one of the following three groups:

Group 1: Multiple traumatic patients with life-threatening problems (respiratory airway, blood circulation), unstable Hemodynamic, and patients not responding to resuscitation in the Primary Survey.

Group 2: Patients who have no life-threatening problems, but they need emergency surgery or ICU admission.

Group 3: Patients with stable Hemodynamic who eventually need hospitalization (such as admission to operating room, ICU and ward).

### Ethical Considerations

This study was in perfect compliance with privacy protection, and all patients' information is completely confidential and their name and specifications have never been revealed.

The study data was collected through questionnaires and entered into SPSS software and assessed by t-test and chi square tests and the power of the test was calculated at the end.

Table 1. Evaluation of findings between two genders

	Gender		P
	Male	Female	
Age	35.76±18.77	37.07±19.46	0.65
First Visit	7.86±0.5	8.28±1.27	0.73
Nursing Visit	11.64±9.05	13.19±10.81	0.28
Routine Trauma X-rays	70.53±47.50	70.25±54.27	0.97
Suture and Dressing	51.97±5.65	45±9.70	0.58
Splints	53.92±10.67	61.87±38.35	0.78
Surgery Visits	40.76±3.73	21.55±3.43	0.02
Neurosurgery Visits	34.09±2.33	30.67±4.83	0.53
Final Decision	397.18±242.54	442.07±216.61	0.21

Table 2. Evaluation of findings based on Trauma or CPR ward

	Emergency ward		P
	Trauma	CPR	
Age	35.26 ± 18.98	37.84 ± 18.62	0.28
First Visit	8.62 ± 0.57	6.18 ± 0.78	0.02
Nursing Visit	13.53 ± 0.65	7.82 ± 0.79	<0.001
Routine Trauma X-rays	66.32 ± 2.71	80.36 ± 8.29	0.03
Suture and Dressing	45.03 ± 4.27	63.51 ± 12.72	0.08
Splints	43.18 ± 9.89	81.06 ± 25.08	0.10
Surgery Visits	40.43 ± 4.19	29.83 ± 3.49	0.13
Neurosurgery Visits	33.66 ± 2.27	33.04 ± 4.68	0.89
Final Decision	410.67 ± 250.61	390.52 ± 250.40	0.51

Table 3. Evaluation of findings based on the patients' age groups

	Age Group			P
	<14	14-55	>55	
First Visit	6.19 ± 1.17	7.73 ± 0.52	10.30 ± 1.57	0.07
Nursing Visit	9.58 ± 6.90	12.10 ± 9.60	12.61 ± 9.71	0.32
Routine Trauma X-rays	67.90 ± 52.58	72.90 ± 56.79	58.00 ± 23.37	0.23
Suture and Dressing	30.00 ± 20.00	48.88 ± 4.55	85.00 ± 39.93	0.13
Splints	34.16 ± 7.23	55.27 ± 12.40	71.12 ± 38.46	0.66
Surgery Visits	28.68 ± 6.44	37.04 ± 3.36	45.35 ± 12.41	0.44
Neurosurgery Visits	25.48 ± 4.32	32.93 ± 2.49	41.97 ± 5.58	0.15
Final Decision	427.22 ± 252.58	399.97 ± 234.50	415.52 ± 253.63	0.79

## 3. Results

In the present study, 300 traumatic patients, including 248 men (82.7%) and 52 women (17.3%) were studied.

The mean age was 35.76±18.77 years (Chart 1) in the male cases and 37.07±19.46 years in the female cases (P= 0.650). In terms of age, patients were divided into three groups of under 14 years (31 cases, 10.3%), 14 to 55 years (227 cases, 75.7%), and over 55 years (42 cases, 14%).

As seen, most of the patients were dispatched from the hospital by an ambulance.

At the time of reference, 215 cases (71.7%) were admitted in trauma section, and 85 cases (28.3%) in Cardiopulmonary resuscitation (CPR) section of ED due to their deteriorated condition.

The mean duration of the first visit by emergency attendant or Resident was 7.93±0.47 minutes. The mean duration of the first action by the nurse was 11.91±9.38 minutes. The mean duration from the time of request to the conduction of simple graphs was 70.30±53.08 minutes. The mean duration from the time of request to the surgical visit was 37.40±3.16 minutes. The mean duration from the time of request to the neurosurgical visit was 33.48±2.10 minutes.

Suture and dressing was requested in 88 cases (29.3%) where the mean duration from the time of request to application of suture and dressing was 50.70±4.94 minutes respectively. Splinting was necessary in 47 cases (15.7%) where the mean duration from the time of request to application of splint was 55.27±10.78 minutes.

Finally, out of the 300 patients, 34 (11.3%) were sent to the orthopedic hospital, 47 (15.7%)

hospitalized in the Surgery ward, and 139 (46.3%) in neurosurgery ward. 80 cases (26.7%) were also discharged after completing the assessments.

The mean duration of request for transferring to orthopedic hospital was  $475.05 \pm 223.75$  minutes. The mean duration of transferring to orthopedic hospital was  $487.05 \pm 22.81$  minutes. The mean duration from the time of request to transferring to orthopedic hospital was  $30.44 \pm 21.00$  minutes. The mean duration of making the final decision in all patients was  $404.97 \pm 238.51$  minutes.

Table 1 shows the different findings between the two genders. As seen, there is a statistically significant difference between the two genders in

terms of neurosurgical visits and hospitalization in Neurosurgical ward.

Table 2 shows the different findings among the admission areas. As seen in the table, the patients admitted in the CPR have had significantly shorter durations of visit by nurse, graphing and surgery visit.

Table 3 shows the different findings based on different age classes. As seen in the table, there is no significant statistical difference in the variables under study among the different age classes.

Table 4 shows the different findings based on the outcome of patients. As observed, there is a statistically significant difference in age and the time of the final decision among the four groups.

Table 4. Evaluation of findings based on the Patient's Outcome

	Patient's Outcome				P
	Orthopedy Ward	Surgery Ward	Neurosurgery Ward	Discharge	
Age	$31.14 \pm 19.21$	$33.34 \pm 16.57$	$39.18 \pm 18.69$	$34.06 \pm 19.66$	0.045
First Visit	$10.26 \pm 1.84$	$7.38 \pm 0.91$	$7.39 \pm 0.69$	$7.27 \pm 0.86$	0.32
Nursing Visit	$14.05 \pm 10.89$	$10.78 \pm 9.39$	$12.10 \pm 9.55$	$11.27 \pm 8.34$	0.42
Routine Trauma X-rays	$72.08 \pm 28.49$	$81.14 \pm 52.20$	$72.74 \pm 66.49$	$58.92 \pm 28.30$	0.11
Suture and Dressing	$37.11 \pm 11.37$	$65.90 \pm 22.77$	$55.34 \pm 7.48$	$42.00 \pm 5.54$	0.34
Splints	$52.82 \pm 17.76$	$75.09 \pm 32.47$	$45.76 \pm 15.41$	$46.50 \pm 14.76$	0.78
Surgery Visits	$47.85 \pm 15.04$	$31.89 \pm 3.97$	$34.76 \pm 3.55$	$40.92 \pm 7.64$	0.50
Neurosurgery Visits	$40.18 \pm 8.47$	$35.72 \pm 4.27$	$34.19 \pm 3.48$	$28.00 \pm 2.45$	0.37
Final Decision	$487.50 \pm 224.81$	$563.08 \pm 273.00$	$381.51 \pm 195.13$	$317.75 \pm 240.43$	<0.001

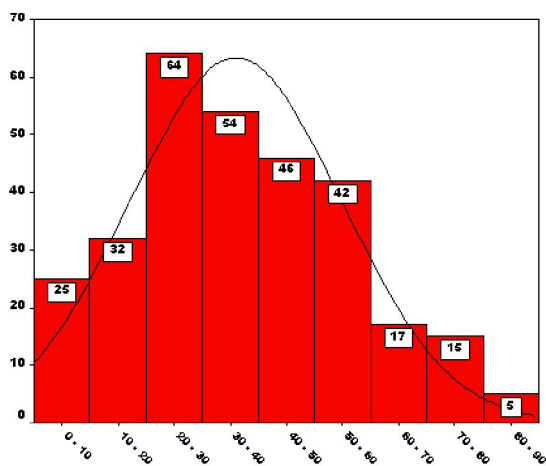


Chart 1. Age distribution of patients

#### 4. Discussions

Patients often wait for a long time at the ED of hospital to get examined by a physician for the initial evaluations, treatment and hospitalization. "Time" is an important factor in managing multi-traumatic patients in the ED. Since multi-traumatic patients require a systematic, standard and regular approach in a short timeframe, healthcare quality control, especially in such patients, is a necessity in order to offer an adequate and appropriate care to these patients (Waydhas, 2001).

In the present study, assessing 300 traumatic patients admitted to ED of Imam Reza hospital, the quality of healthcare was studied regarding the elapsed time. In the current study, the mean durations to the first visit by physician and nurse were  $7.93 \pm 0.47$  and  $11.91 \pm 9.38$  minutes respectively; where the time of the first visit by physician and nurse to the patients in the CPR were  $6.18 \pm 0.78$  and  $7.82 \pm 0.79$  minutes, respectively that is significantly shorter than to the cases admitted to the trauma section of ED. This may be due to the badly dangerous condition of the CPR patients who are more in need of quicker attention. Some other factors such as less number of nurses in the trauma section, visits by first-year residents in ED who have less experience and lower agility in the evaluation of patients are also involved.

In a study of healthcare quality management by Nast-Kolb et al, the duration of trauma team's arrival at trauma CPR room had reduced from 10 minutes to 3. The goal of this action is for the leader in charge of the trauma team to arrive at CPR room before or at the time of the traumatic patient's arrival (Nast-Kolb and Ruchholtz, 1999). In order to achieve this objective, informing the ED about the patient before their arrival is a prerequisite and a necessary condition.

The most effective factor on hospitalization duration of multi-traumatic patients in the ED is clearly the time spent for radiological studies. The ideal condition includes these routine radiological



studies in restoration room in the ED (Oktay, 2000; Eray, 2002; Oyar and Aktuglu, 2000) (13-15).

In this study, the mean duration of performing routine radiographies of trauma was  $70.30 \pm 53.08$  minutes. In studies by Cebicci et al, radiographies were performed in the range of  $47 \pm 20$  minutes (Çebicci, 2008). The results of the above mentioned study are much lower than those of the current study. Similarly, Waydhas et al with the help of their quality improvement studies, reduced the duration of performing routine trauma radiographies from 24 minutes to 14. In this study too, the mean duration of conducting laboratory tests was reduced from 50 minutes to 24 (Waydhas, 2001).

The main reason for such delays in various studies is that there has been no automation system, nor personnel in charge of transferring the samples required for testing to the lab, conveying the patient to the radiology room and fetching the results of lab and radiology to the physician, and all of these are done by the patient's companions. Only in cases of patients in the restoration room of ED, a patient-carrier is in charge of these tasks which, in case ED is crowded, are done only for some patients.

Patient's staying in ED decelerates the course of action on ED patients, and leads to crowding due to the occupation of emergency beds by these people for a long time that reduces the capacity of admission, examination and attending the new patients (Rathlev, 2007; Zintl, 1997).

Other researchers have expressed this duration as short as between 31-75 minutes. However, such results are corresponding to the initial evaluations in the CPR and recovery stage, and do not include the time spent for additional evaluations, assessments and interventions (such as radiographies and CT scan) performed in the ED (Zintl, 1997).

Unlike the above mentioned findings in this study, the mean duration of making the final decision in all patients was  $404.97 \pm 238.51$  minutes. There was no significant statistical difference in duration of staying in ED in terms of age, sex and severity of trauma based on the place of admission. One of the reasons for prolonged duration of making the final decision for the patients is the multitude crowding in this center as the main trauma referral center in Eastern Azerbaijan province, which makes it impossible to offer quick services to all patients. However, in this study, the amount of crowding in ED is not mentioned, because it may have a significant effect on the conduction of diagnostic evaluations.

In the present study, duration of patients' hospitalization in the surgical ward, transferring to orthopedic hospital admission in Neurosurgical ward, and discharge time was significantly prolonged.

Quick discharge of the patients with non-severe trauma is justifiable. One of the reasons of prolonged hospital stay of patients in the surgical ward is the lack of adequate number of visiting resident surgical freshmen. Besides, considering the fact that the majority of hospitalized patients have been admitted from Trauma section and not from CPR, the bustle in trauma section during most hours of the day can be one of the other causes to this issue.

Due to the need for quicker hospitalization and treatment follow-up, Neurosurgical patients were hospitalized earlier than the other cases. However, due to presence of only one Neurosurgical resident in ED, delay in performing the CT scan and other assessments, and delay in getting the approval for surgery make it impossible to reduce this duration.

In the case of transferring to Orthopedic hospital, insufficient number of staff to accompany the patient, lack of well-equipped vehicles to transport patients, and delay in getting the approval for the surgical and Neurosurgical issues can be mentioned as the causes of delay.

### Conclusion

In this study, staying duration of traumatic patients is much higher than previous studies. Development and improvement of infrastructures of ED and diagnostic modalities can be helpful in improving the issue.

### Suggestions

According to the results of this study and other studies, it is recommended to provide the possibility of fulfilling various modalities for trauma section of ED dedicating the ultrasound, CT scan and radiology sections to it to reduce the duration of traumatic patients' staying and making the final decision for them.

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## Study on uterine artery blood flow in myomatous uterus

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**Abstract:** Leiomyomas constitute the most common female pelvic tumor, becoming increasingly prevalent with age. Although transabdominal ultrasound is usually used for observation of the large uterine tumors outside the focal zone of the transvaginal transducer, but transvaginal ultrasound is the standard imaging modality for this purpose. Recently with introduction of transvaginal color Doppler ultrasonography some studies have been performed on uterine artery blood flow in myomatous uterins, however these studies are scanty. Our object in this study is the determination of probable particular effects of leiomyoma on blood flow in uterine arteries. In this cross sectional study 50 women with myomatous uterine and 50 healthy volunteer woman were enrolled in the study. Transvaginal color Doppler was used for observation of uterine arteries and vascularity of myomas. The mean uterine volume was significantly lower in control group ( $97.00 \pm 37.71$  cm<sup>3</sup>) than in cases ( $351.16 \pm 222.94$  cm<sup>3</sup>). The mean peak systolic velocity (PSV) was significantly lower in control group ( $36.42 \pm 9.28$  cm/s) than in case group ( $49.34 \pm 16.37$ cm/s). Significant correlation between uterus volume and PSV was not seen in control group but medium positive correlation between mean uterus and mean PSV was seen in case group. Mean pulsatility index (PI) was  $1.59 \pm 0.36$  in case group and  $2.40 \pm 0.46$  in control group. Significant correlation between mean uterus volume and mean pulsatility index (PI) in study group was seen. Mean resistance index (RI) was  $0.74 \pm 0.19$  in case group and  $0.85 \pm 0.23$  in control group. No correlation was found between uterine volume and number of myomas. Only in %34 cases myomas artery was detectable and mean myomas artery RI was  $0.57 \pm 0.18$ . We observed significant differences between uterine arterial Doppler indices in patients with myomatous uterins and control group. The presence of myomas result in uterine volume increasing and uterus Volume has significant correlation with PI decreasing. Also PSV has significant correlation with uterine Volume. This significant difference suggests that, we can use serial measurements in duration of treatment in monitoring response to medical treatment.

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**Keywords:** Myomas; Peak Systolic Velocity; Vascular Impedance; Transvaginal Color Doppler Sonography

### 1. Introduction

Myomas are the most common pelvic tumor in women and its prevalence increases with increase of age. 25% of white women and 50% of black women over 30 years old have at least one myoma. Cause of myoma is not completely identified yet, but it is undoubtedly estrogen dependent (Callen, 2000). Most of myomas are symptomless and maybe indicated as various complaints such as bleeding, lower abdominal pain or sensitivity, urinary symptoms or constipation (Alcazar, 1997).

With transvaginal color Doppler ultrasound method developed, evaluation of blood flow in pelvic organs has become possible. Many investigations have been carried out on cases of normal, infertile, and ovarian masses and endometrial abnormalities which have mostly been limited to benign lesions such as myoma (Alcazar, 1997).

Studies have shown that vascular impedance decreases in myomatous uterine, and the flow rate

increases. This is clinically determinant. Hysterectomy is the classic and selective treatment of symptomatic uterine myomas. Showing increased blood flow in uterine arteries of the myomatous uteruses, other therapies for myoma can be also considered, including GnRH and angiographic embolization.

If peak systolic velocities (PSV), resistance index (RI) and pulsatility index (PI) of myomatous uterine have significant difference with healthy individuals, uterine artery embolization can be used as a method for treatment of uterine myoma and assist the surgical treatment (McLucas, 2002).

If studies show that blood flow characteristics of myomatous uterins are different from the normal uterus can be PSV and RI and PI monitoring can be used for monitoring response to GnRH treatment.

Previously, some studies have been performed on blood flow in the uterine arteries of myomatous uterine, but these studies are limited and further

studies in this area seem necessary. The aim of this study is to determine the rate of blood flow in uterine arteries of myomatous uterus.

**2. Material and Methods**

A case-control study was performed on patients with uterine myoma and normal women, and uterine artery flow in the myomatous uterus was reviewed. 50 patients with uterine myoma and 50 healthy subjects were randomly selected. Patients with a history of HTN, diabetes, thyroid disorders, hormone therapy, pregnancy, smoking, and menstrual disorders and also, patients with sub mucous myoma, sub serous, corneal and degenerated myoma were excluded.

Uterine size and Number of myomas were determined by transabdominal sonography.

Transvaginal sonography and evaluation color Doppler was performed in lytotomic position with empty bladder by a Hitachi model EUB-52S vaginal with prub 7.5 MHZ device.

Uterine morphology was reviewed by B-Mode and uterine volume was calculated with prolate ellipsoid method.

Transvaginal color Doppler was used to observe the uterine arteries and vascularity of myomas.

With color signals detected, spectral signals were measured using 1mm Sample Volume. PI, RI, PSV were drawn from FVU and calculated by computer.

Uterine artery on its main body was evaluated near the outside edge of cervix on the surface of its inner hole. In the largest myoma, myoma indices were obtained from myoma vessels which had created color image on the edges or center of the myoma.

Doppler wave forms were obtained during four consecutive cardiac cycles. In case of several different RI obtained in a myoma, the lowest RI was recorded.

**3. Results**

Color Doppler finding were shown in the table 1. There is a very weak relationship between PSV and uterine volume in the control group that was not significant ( $p < 0.5$ ) (Figure 1). There is a moderate relationship between PSV and uterine volume in the case group ( $R = 0.362$  and  $P = 0.01$ ) (Figure 1). There is a very weak relationship between PI and uterine volume in the control group that was not significant ( $P > 0.05$  and  $R > 0.033$ ) (Figure 2). There is a moderate inverse relationship between PI and uterine volume in the case group ( $P = 0.01$  and  $R = -0.461$ ) (Figure 2). There is a weak correlation between uterine volume and number of myomas in the control group that is not significant ( $P > 0.05$  and  $R = 0.106$ ). Evaluating color Doppler of myomas, only 14 cases

(32%) had visible arteries of myoma and mean RI in myoma artery was  $0.57 \pm 0.18$ .

Table 1. Color Doppler finding of patients in two groups

	Group		P
	Control	Case	
Uterine Volume( $\text{cm}^3$ )	$381.16 \pm 222.93$	$97.00 \pm 37.71$	$< 0.001$
peak systolic velocity( $\text{cm/s}$ )	$49.33 \pm 16.37$	$36.42 \pm 9.28$	$< 0.001$
pulsatility index	$2.4 \pm 0.46$	$1.59 \pm 0.36$	$< 0.001$
resistance index	$0.85 \pm 0.23$	$0.74 \pm 0.19$	$< 0.001$

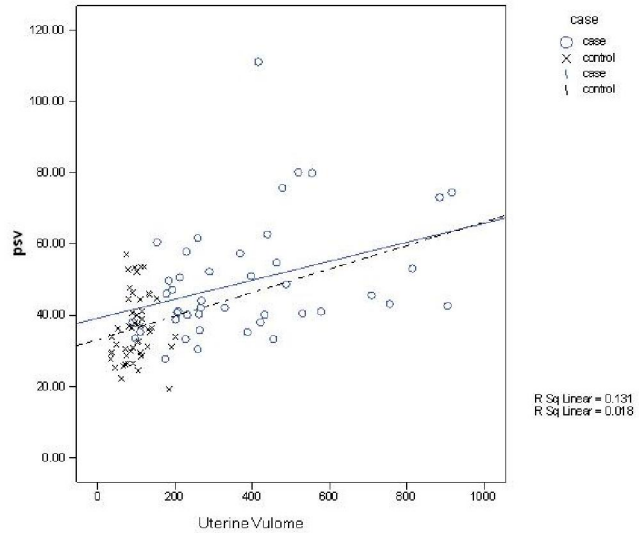


Figure 1. Correlation between PSV and uterine volume in two groups

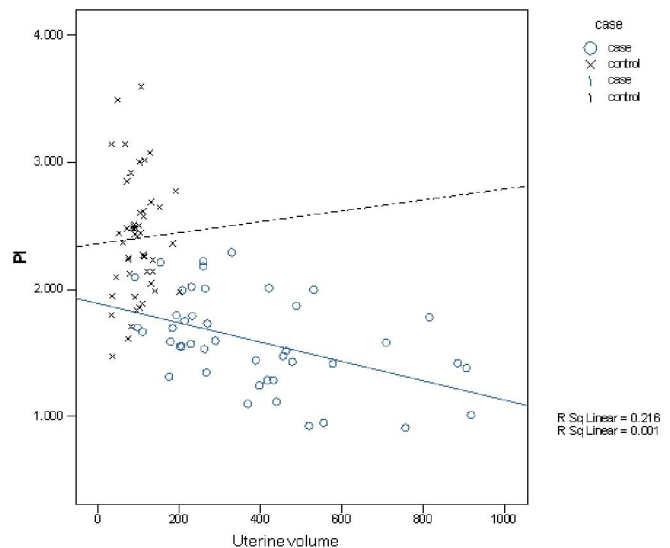


Figure 2. Correlation between PI and uterine volume in two groups

#### 4. Discussions

Transvaginal color Doppler sonography is an established technique in the study of vascular impedance which enables evaluation of uterine perfusion in physiological and pathological conditions (Kurjak, 1992).

Tsuda et al expressed that uterine volume in women with uterine myoma was  $276.2 \pm 163.4$  which significantly higher than that of control group (Tsuda, 1998).

Also in the study by Danisman et al, mean uterine volume in patients with myoma was 312 cc (Danisman, 1998).

In our study, the average volume in patients with and without uterine myoma was  $381.16 \pm 222.9$  cc and  $97 \pm 37.71$  cc respectively which was significantly higher in the patients with myoma ( $p < 0.001$ ).

In the study by Alcazar et al, the average number of myomas was 1.8 which had a significant relationship with patients' uterine volume (Alcazar, 1997).

In this study, the mean number of myomas was 5.28 and had no correlation with uterine volume of patients. What distinguishes this study from the above mentioned one is the presence of small myomas in a large number of patients.

In a study by Mclucas et al, mean PSV in patients with myoma was  $47.4$  cm/s (McLucas, 2002) and in a study by Alcazar et al, mean PSV in patients with and without myoma was  $83.5 \pm 22.3$  cm/s and  $70.2 \pm 15.4$  cm/s respectively which is significantly higher in the patients with myoma (Alcazar, 1997).

In our study, mean PSV in patients with and without myoma was  $49.3 \pm 16.3$  cm/s and  $36.4 \pm 9.28$  cm/s respectively ( $P < 0.001$ ) which is similar to Mclucas's study; and in comparison to Alcazar's study, PSV difference in both case and control groups was identical.

Alatas et al expressed that uterine volume plays a greater role in uterine blood flow compared with the presence or status of vascularity of myoma (Alataş, 1997) and also, Mclucas found a significant relationship between uterine volume and PSV. (McLucas, 2002)

In our study, there was a significant moderate relationship between PSV and uterine volume.

In the study by Alcazar et al, the mean PI for patients with and without myoma was  $2.5 \pm 0.7$  and  $3.4 \pm 1.3$  respectively ( $P = 0.007$ ) (Alcazar, 1997). In a study by Kurjuh et al, mean PI in patients with myoma was  $2.52 \pm 0.87$  (Kurjak, 1992); and in the study by Alatas, it was significantly higher in the patients with myoma (Alataş, 1997).

In our study, the mean PI in patients with and without myoma was  $1.59 \pm 9.36$  and  $2.4 \pm 0.46$

respectively, which indicates the effect of presence of myoma on increasing of uterine blood flow.

Sladkeuicius et al suggested that any increase or change in Doppler indices depends on increasing of uterine volume but not myoma size (Sladkeuicius, 1996). Tsuda suggested that there was a significant relationship between reduction of PI and uterine volume in myomatous uteruses (Tsuda, 1998).

In our study, there was a moderate inverse relationship between PI and uterine volume in patients with uterine myoma.

Sosić et al suggested that myoma size is the most important single factor affecting the visibility of myoma blood flow and RI (Sosić, 1996).

In a study by Alatus et al, mean RI in patients with and without uterine myoma was  $0.77 \pm 0.08$  and  $0.82 \pm 0.06$  respectively that was significantly lower in the case group (Alataş, 1997).

In the studies by Kuvjah and Danisman, mean RI in patients with myoma was significantly lower than that in patients without myoma (Danisman, 1998).

In our study, similar to the results by Kurjau and Alatas, the mean RI in patients with myoma was significantly lower.

Regarding the relationship between uterine volume and uterine artery Doppler indices, any action leading to reduction of the uterine volume is expected to cause change in Doppler indices as the reduction of systolic flow velocity and increase of vascular impedance.

Methods which can be taken to reduce uterine volume include non-surgical treatment methods and surgical methods (myomectomy).

Nonsurgical procedures include uterine artery embolization and treatment with GnRH agonists which can be applied as the selective or auxiliary treatment.

With Color Doppler transvaginal sonography before treatment and then repeated assessment during therapy, response to treatment can be evaluated.

#### Conclusion

According to our results, presence of myoma leads to increased uterine volume and reduction of vascular resistance and increased uterine artery blood flow velocity. Reduction of vascular resistance and increased blood flow are in significant relationship with increased uterine volume.

Increased blood flow in myomatous uterine raises the choice of nonsurgical treatment. Uterine artery embolization or treatment with GnRH agonists can be applied for a certain or pre-surgical treatment. With color Doppler sonography, response to treatment can be monitored as serial measurements of uterine volume and Doppler indices.



It should be noticed that interpretation of the color Doppler results in myomatous uteruses is different from healthy individuals.

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## Investigating The Effect of Number of Steps on Energy Dissipation of Stepped Spillways Based on the New Design Approach

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**Abstract:** Stepped spillways are hydraulic structures that, because of their significant capacity in energy dissipation, have been widely used by designers. Flow mechanism over them is complex and many investigations have been performed to study that mechanism. The effect of some parameters such as the number of steps in energy dissipation has not been fully investigated. In this study the latest design criteria have been reviewed and then an algorithm has been developed to design the stepped spillways which are based on the effect of number of steps. Results show that the number of steps affects the energy dissipation. With increasing the number of steps energy dissipation increases and then decreases. Thus for specific discharge and spillway slope, the number of steps can be optimized for maximum energy dissipation. By reducing design discharge the optimum number of steps increases. Research work on this subject can be continued in the future and various aspects of the design parameters may be investigated [Mohammad Karami . **Investigating The Effect of Number of Steps on Energy Dissipation of Stepped Spillways Based on the New Design Approach.** *Life Sci J* 2012;9(4):587-592] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 89

**Keywords:** Design discharge, Energy dissipation, Number of steps, Spillway slope.

### 1. Introduction

The main objective of application of stepped spillways in structure of a reservoir dam is the high impact it has on the rate of energy flow. The height of a reservoir dam and its spillway during the flood makes the water flow over the spillway toward the downstream. At this time, high kinetic energy of water can cause severe erosion of the river bottom, scour or erosion under the floor slab concrete foundation and flat or pond overflow and eventually cause phenomenon of cavitation.

High construction costs overruns smooth (or overflow of water slides Oji standard) due to the high volume of excavation is usually in place in the coastal basins of peace and tranquility of the pond for proper hydraulic jump, high jump and the depth of resistance to the wall with height, including technical reasons, instead choosing to use an overflow spillway steps are smooth. In this option, a flat section of the spillway will be replaced with steps. Steps as large roughness and the flow resistance and thus increase the energy flow are beneficial. Another reason to use the stair concrete spillway dam has been a roller or the RCC. This is why the attention of researchers and designers now overflow with stairs too much. The mechanism of such structures on complex and much research is being done in recognition of its world-wide. New findings and changes in the previous design criteria, which sometimes are also associated with violations of the older theory faced with the problem and confusion and the different methods used to close in design. Also, recent studies showed that some overflow geometric profile of the stairs in

the reports have remained unexplained or has not been provided a full report on them. From among these studies we can name Ohotsu et al. (2004) and Gonzalez et al. (2008). The aim of this study is the examination of a new method to design stepped spillways and the impact of number of the stairs on the energy wastage based on the design of the weir.

Most researchers consider three different flow regimes based on the rate of energy dissipation mechanisms, namely a falling, non-falling as well as being second conversion (Chanson 1994, Chamani and Rajaratnam 1999). The falling type occurs in low-flow discharge and the large step height. Each step acts as a separate vertical drop waterfall and the stream moves on overflow as downstream collision jets sequence at the bottom of the stairs. Non-falling type occurs in larger overflows with and lower step height. Due to the high discharge current, the stairs are completely submerged below the water level. In this regime, a false bottom is formed which connects successive steps of the trailing edge. The eddy currents are formed in this false bottom. Major part of this energy dissipate in this regime is created of spin currents under false bottoms. There are three distinct regions in this regime:

Area with smooth flow and without air, the spreading area with quasi-uniform current and, the fully developed area or uniform flow.

The flow is without air and smooth over the spillway. With the growth of turbulent boundary layer and reaching the water level, air enters downstream steps and the turbulence hits its peak. In case of the spillway being lengthy, the

current becomes foamy and will appear as white water.

Note that uniform flow, in the real sense of the word, does not form on the spillway, because the rotating three-dimensional vortex formed below the triangular false floor space between the stairs creates a non-uniform flow rate. For this reason, some researchers use the term quasi-uniform in case there is a long length overflow (Ohotso et al., 2004).

Since the aim of constructing spillways on the dam is to safely convey flood discharge to downstream, the stepped spillway design criteria with the maximum flood discharge, is a non-falling flow regime. Obviously, if the flood of overflow is relatively lower than the overflow design, there is possibility of creating falling regimes over the spillway. Conversion regime is a moderate situation which is accompanied with high dispersion of water droplets. Accordingly, many dynamic forces are exerted into the spillway structure, therefore, it is not recommended on its basis.

Little research has been done on this type of flow regime in the world (Chanson and Gonzalez, 2006).

**Materials and Methods**

The first criterion for starting the non-falling regime was presented by Rajaratnam (1990). He presented starting the non-falling flow regime for  $h/d_c < 8/0$ . DC is the critical depth and H is the height of each step. These criteria are based on information from tests in the range of slopes  $9/0$  to  $4/0 = h/1$ . 1 is the horizontal length of each step. The next relationship was presented by Chanson (1994b). This relationship was based on available data from tests for slopes of  $1/2$  to  $2/0 = h/1$  (11 to 51 degrees). His studies showed that for the non-falling flow regime to occur, the discharge amount must become higher than flow from a more critical characteristic value. This characteristic discharge for the onset of non-falling regime was presented as equation 1:

In overflows with mild to moderate slopes, Chanson and Gonzalez (2006) divided the non-falling regime into the following two sub-parts: sk1 and sk2. Sk2 is for gentle slopes less than 19 degrees and sk2 is for average slope more than 19 degrees. The segmentation method is presented in Figure 1. Note that spillovers commonly called steep slopes greater than 25 degrees, average slopes with 15 to 25 degrees, and less than 15 degrees slopes are called soft.

Ohotso et al. (2004) marked the occurrence limit of non-falling regime with functions 2:

$$\left(\frac{h}{d_c}\right)_s = \frac{7}{6} (\tan \alpha) c x^{1.6} \text{ for } 5.7^\circ < \alpha \leq 55^\circ$$

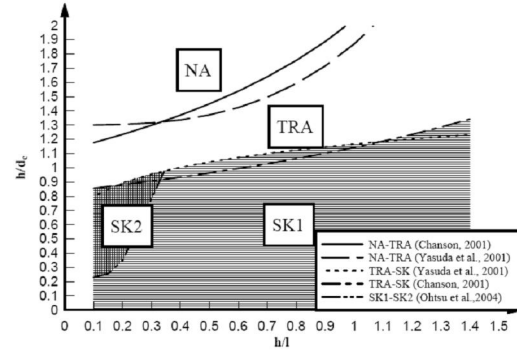


Figure 1 - Determination of flow regimes on a stepped spillway. Note: NA-TRA is the boundary between falling regime and conversion regime; TRA-SK, conversion toward non-falling (Gonzalez and Chanson 2006)

For the spillway of bridges with equal fixed slope having large number of steps with a fixed height (h) and horizontal length of the stairs (l), we can assume that the flow after crossing the first few primary steps will be fully developed or uniform. In such a flow with constant average velocity (v) and normal depth (d) and assuming the uniform length for the overflow, we can write (Rajaratnam, 1990):

$$\tau = d \cdot \gamma \cdot \sin \alpha$$

where  $\gamma$  is the specific gravity of water,  $\tau$  is Reynolds' shear stress between the non-falling flow and the rotating flow below it. If we have:

$$\tau = \frac{f}{4} \left( \frac{\rho \cdot v^2}{2} \right)$$

where f is Darcy-Visbach friction factor and  $\rho$  is the fluid special mass, by combining equations 3 and 4 we can have the following:

$$f = \frac{8 g d \cdot \sin \alpha}{v^2} = \frac{8 g \cdot d^3 \cdot \sin \alpha}{q^2}$$

Where g is the acceleration of gravity and q is discharge per width of the spillway unit. For gradual changing S

$$q = \int_{y=0}^{y=90} (1 - C) dy = (1 - C_{mean}) y_{90}$$

the energy equation as follows:

The friction slope is  $s_{fin}$  in the above relationship. Note that in the above relations, the flow depth (d) is the net water depth without air. Previously, Chanson (1994a), by analysis of experiments conducted on the stepped spillway with steep slopes of 50 to 55 degrees, showed that the friction coefficient between ranges between 0.17 to 5 and the average number was announced 1. Recently Chanson and Gonzalez (2006) showed that the

coefficient of friction is changing between 0.1 and 0.25, and its average is 0.2. As noted, this is because the flow is highly aerated over the spillway and energy dissipation occurs because of water flow and therefore depth of the air should be deducted from total depth. It should be reminded that the air density is eight hundred times the less than that of water and its shear stress impact will be far lesser. Thus we have:

$$C = 1 - \tanh^2 \left( k - \frac{y \cdot y_{90}}{2D_0} + \frac{(y \cdot y_{90} - 1.3)^3}{3D_0} \right)$$

where C is the concentration of air bubbles and y<sub>90</sub> corresponds to the depth in which the air comprises 90 percent.

It is noted that the concentration of air bubbles at a certain point vary in different ways with different values of c. Test results of Gonzalez et al (2008) show that the hyperbolic tangent function of the concentration distribution of air bubbles can be used here:

In the above equation, k and D<sub>0</sub> are obtained from the following relations:

$$K = 0.327 + \frac{1}{2D_0} - \frac{8}{81D_0}$$

$$C_{mean} = 0.762(1.043 - \exp(-3.61D_0))$$

$$C_{mean} = \frac{1}{y_{90}} \int_{y=0}^{y_{90}} C \cdot dy$$

D<sub>0</sub> is a parameter dependent upon the average concentration of air bubbles (C<sub>mean</sub>). The spillway designers do not have the concentration distribution of air bubbles, so the researchers have tried to simplify the regression relationships provide for designers. From these relationships one can refer to Ohotsu et al. (2004) as follows:

$$C_{mean} = D - 0.3 \exp \left( -5 \left( \frac{h}{d_c} \right)^2 - 4 \left( \frac{h}{d_c} \right) \right)$$

$$D = 0.3 \text{ for } 5.70 < a < 190$$

$$D = -0.00024a^2 + 0.0214a - 0.0357$$

$$\text{for } 190 \leq a \leq 550$$

Friction factor is presented by the following equation Ohotsu et al. (2004):

$$f = f_{max} - A \left( 0.5 - \frac{h}{d_c} \right)^2$$

$$\text{for } 0.1 \leq \frac{h}{d_c} \leq 0.5$$

$$f = f_{max} \text{ for } 0.5 \leq \frac{h}{d_c} \leq \left( \frac{h}{d_c} \right)$$

$$A = -1.7 \cdot 10^{-3} a^2 + 6.4 \cdot 10^{-2} a - 1.5 \cdot 10^{-1}$$

$$f_{max} = -4.2 \cdot 10^{-4} a^2 + 1.6 \cdot 10^{-2} a + 3.2 \cdot 10^{-2}$$

$$\text{for } 5.70 \leq a \leq 190$$

$$A = 0.452$$

$$f_{max} = 2.32 \cdot 10^{-5} a^2 - 2.75 \cdot 10^{-3} a + 2.31 \cdot 10^{-1}$$

$$\text{for } 190 \leq a \leq 550$$

The aeration locations (aeration start) from the spillway crest and the water depth at that point are obtained by the following relations (Chanson, 19):

$$\left( \frac{q}{g \cdot \sin a (h \cos a)^3} \right)^{0.713}$$

$$\frac{L_1}{h \cdot \cos a} = 9.719 a^{0.0796}$$

$$\frac{d_1}{h \cdot \cos a} = \frac{0.4034}{(\sin a)^{0.04}}$$

$$\left( \frac{q}{\sqrt{g \cdot \sin a (h \cos a)^3}} \right)^{0.592}$$

Designer should check that the spillway length be larger than L<sub>1</sub>. In this case, the quasi-uniform flow will occur over the spillway. Ohotsu et al. (2004) proposed the following relationship for the quasi-uniform flow:

$$\frac{H_e}{d_c} = \left( \frac{-1.21 \cdot 10^{-5} a^3 + 1.60 \cdot 10^{-3} a^2 - 7.13 \cdot 10^{-2} a + 1.30}{10^{-3} a^2 - 7.13 \cdot 10^{-2} a + 1.30} \right)^{-1}$$

$$\left( 5.7 + 6.7 \exp \left( -6.5 \frac{h}{d_c} \right) \right)$$

$$\text{for } 5.70 \leq a \leq 550$$

that is:

$$\frac{H_{dam}}{d_c} \approx \frac{H_e}{d_c}$$

The remaining energy in quasi-uniform flow on the spillway is calculated as follows:

$$E_{res} = d \cdot \cos \alpha + \frac{V^2}{2g} =$$

$$d \cdot \cos \alpha + \frac{d_c^3}{2d^2} \Rightarrow$$

$$\left( \frac{E_{res}}{d_c} \right)_U = \frac{d}{d_c} \cos \alpha + \frac{1}{2} \left( \frac{d_c}{d} \right)^2 = \quad [ ]$$

$$\left( \frac{f}{8 \sin \alpha} \right)^{1/3} \cos \alpha + \frac{1}{2} \left( \frac{f}{8 \sin \alpha} \right)^{-2/3}$$

The remaining energy in spillovers on non-uniform flow is calculated as follow:

$$\frac{E_{res}}{d_c} = 1.5 + \left( \left( \frac{E_{res}}{d_c} \right)_U - 1.5 \right) * \left( 1 - \left( 1 - \frac{H_{dam}}{H_e} \right)^m \right)$$

$$m = -\frac{\alpha}{25} + 4$$

Relative energy dissipate is determined as follows:

$$\frac{\Delta E}{E_{max}} = \frac{E_{max} - E_{res}}{E_{max}} = 1 - \frac{E_{res}}{H_{dam} + 1.5 d_c}$$

In this study, first, an algorithm for the design of spillway hydraulic regime of quasi-uniform is presented which is usable for related operators. The proposed method is based on the results of tests conducted worldwide on a large-scale physical models and can be safely used for the prototype design (Ohotsu et al, 2004). Then, based on the developed algorithm, examination of the effect of number of steps on energy dissipate will be conducted; because as previously mentioned, in the available literature, choosing the appropriate number of steps for the better design of the spillway has gone untapped.

Below, the step by step spillway design method is explained:

1 - Height ( $H_{dam}$ ) and the spillway slope ( $\alpha$ ) are obtained from topographic and locational map; the discharge amount ( $Q$ ) is estimated based on the flood with a given return period. An initial assumed width ( $W$ ) of overflow is chosen.

2 - The critical depth is calculated from this relationship:

3 - The next parameter  $H_{dam} / d_c$  is determined.

4 - Height of stairs is chosen for the non-falling regime to occur such that  $0.25 \leq h / d_c \leq (h / d_c)_s$  where  $(h / d_c)_s$  is obtained from equation 2. According to Chanson and Gonzalez (2006), in most stepped spillways in the building of Gabion dams and roller concrete dams, step heights in the executive area ranges from 0.2 to 0.9 meters that can be used as a criterion in selecting the proper height of stair design.

5 - The amount  $h / d_c$  is determined.

6 - The amount of  $\alpha$  is calculated from the relationship 12. If the condition was established, the

quasi-uniform flow has been produced and the friction factor is calculated from equation 10.

7 - Flow depth is calculated using relationship 5. Flow rate as is obtained as such:....

8 - The average concentration of air bubbles is calculated from equation 9 and  $y_{90}$  is obtained from equation 7.

9 - Protective side walls heights determined from  $h_w = 1.4 y_{90}$ . The remaining energy of quasi-uniform or non-uniform flow regime is calculated by relationship 13 or 14.

10 - Residual energy with quasi-uniform or non-uniform flow regime is determined with relationship 13 or 14.

11 - Relative energy dissipate is determined using equation 15.

The proposed algorithm for the step by step design of overflow was formulated in the Excel spreadsheet. The purpose is to examine the effect of the number of steps on the energy wastage. The more energy is dissipated, the more will be reduced the amount of administrative costs for constructing energy depreciating facilities like peace pond.

## Discussion and Results

Figure 2 presents changes in the energy dissipation curve on the vertical axis proportioned to the number of steps in the horizontal axis. From other influential parameters, one can mention the total spillway height, slope and discharge amount. In this figure, the spillway slope is assumed to have a constant 22 degrees, and discharge in the height and width unit has been taken as changing. That is, the ratio of  $H_{dam} / d_c$  changes from 59.71 to 124.2. Figure 2 has been plotted based on the proposed algorithm for designing the stepped spillway.

According to figure 2, corresponding to a constant rate of  $H_{dam} / d_c$ , increasing number of steps causes the increase in energy dissipation to a certain extent, and then makes the relative energy dissipation reduce. The slope of the ascending part, however, is greater than that of the descending one.

It can be seen that, corresponding to any  $H_{dam} / d_c$ , of an optimized number of steps to maximize energy dissipation can be determined. Also, per a fixed number of steps with  $H_{dam} / d_c$  reached from 59.71 to 124.2, the relative energy dissipation rises.

According to figure 2, with reduction of the dam discharge or augmentation of the height of the spillway, the optimal number of steps also shows increases.

This shows that although the current regime is assumed as non-falling, but with reduced flow and a tendency toward the falling regime, the optimal



number of steps increases. On the contrary, in higher discharge amounts with falling flow regime and all steps are submerged below water level, the optimal number of steps shows reduction.

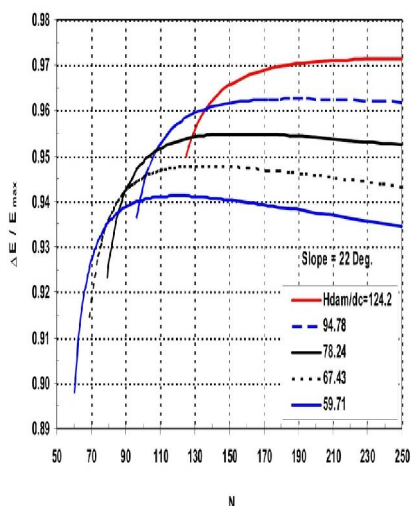


Figure 2 - Effect of number of steps in increasing energy dissipation

According to Figure 2, the exact number of optimal steps per different flows is presented in Table 1. In this table, discharge amount has been assumed as changing for 0.8 to 3.2 meters per second and it can be more easily expanded in an Excel spreadsheet for higher values; also, its corresponding energy dissipation and other parameters can be calculated based on this table. The spillway slope is assumed to be 22 degrees which can be modified to any desired changes in any given conditions and data in the project.

Table 1 - Number of optimal steps per different flows over the spillway and the its energy dissipation amount

دبی در واحد عرض بر حسب متر مربع بر ثانیه (q)	نسبت ارتفاع سرریز به عمق بحرانی (H <sub>dam</sub> / d <sub>c</sub> )	تعداد پله‌های بهینه (N)	استهلاک انرژی نسبی (ΔE / E <sub>max</sub> )
۰/۸	۱۲۴/۲	۲۰۰	۰/۹۷۱
۱/۲	۹۴/۷۸	۱۷۹	۰/۹۶۳
۱/۶	۷۸/۲۴	۱۳۹	۰/۹۵۵
۲	۶۷/۴۳	۱۲۲	۰/۹۴۸
۲/۴	۵۹/۷۱	۱۰۲	۰/۹۴۱
۲/۸	۵۳/۸۸	۹۶	۰/۹۳۵
۳/۲	۴۹/۱۹	۸۶	۰/۹۲۹

Figure 3 variously displays the effect of number of steps in the relative amount of energy dissipation. In the horizontal axis, BI BAAD parameter has been used; that is, the ratio of the spillway height to critical depth. Each curve in Figure 3 is related to a number of steps. It can be noted that the relative energy dissipation in a certain amount of H<sub>dam</sub> / d<sub>c</sub> reaches its maximum. That is, the ascending curves, energy dissipation correlates directly with the spillway height and inversely with the discharge amount. These relationships are reversed in the descending curves. Also, the maximum point of energy dissipation is seen in lesser than 40 steps; and in more than 40 the maximum point on the curves get paler. Such charts can help in better understanding these complex relationships and play an important role in designingsuch structures. Without drawing the graphs, one cannot make presumptions about the effectiveness of the steps.

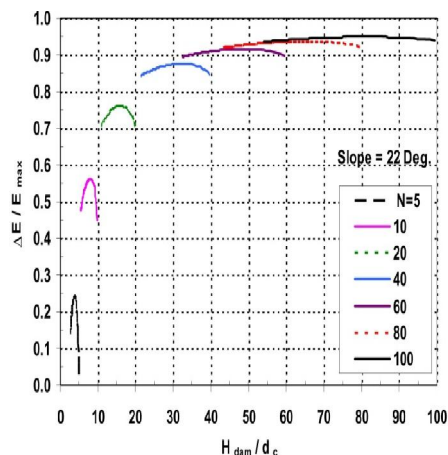


Figure 3 - Effect of the parameter H<sub>dam</sub> / d<sub>c</sub> on the energy dissipation per different number of steps

In Table 2, for example, 10 overflow bridges are designed with different hydraulic conditions. Parameters involved in the design and other BI BAA Dparameters have been provided in 21 columns. Also, according to figure 2 and 3, we can determine optimal number of steps based on maximum energy dissipation given different geometric and hydraulic conditions in the stepped spillway design which have not been discussed in previous studies of the subject.

**Conclusion**

Per a fixed ratio of H<sub>dam</sub> /d<sub>c</sub>, increase in the number of steps in the stepped spillway will increase the relative energy dissipation to a certain extent and then decreases the relative energy dissipation; the slope of ascending part is higher than that of the



## The Role of Beta Catenin and Platelet Derived Growth Factor Antibodies in Head and Neck Intermediate Grade Soft Tissue Tumors

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**Abstract: Background:** Intermediate soft tissue tumors were included in the new WHO classification of soft tissue tumors. They were addressed as locally aggressive tumors with reports of their recurrence or even malignant transformation. This study was conducted to detect the immunoeexpression of Beta Catenin and Platelet Derived Growth Factor in order to predict their potential for malignant transformation. Methods: Twenty three different intermediate soft tissue tumors were included as well as three recurrent cases diagnosed as fibrosarcoma. All lesions were prepared and were subjected to Beta Catenin and Platelet Derived Growth Factor antibodies. **Results:** From the 26 selected cases, 9 were Juvenile fibromatosis, 5 were haemangiopericytoma. 9 were desmoplastic fibroma 3 of which showed recurrence and were diagnosed as Fibrosarcoma. All cases of juvenile fibromatosis, desmoplastic fibroma and fibrosarcoma, showed positive nuclear reaction to **Beta Catenin antibody**. Cytoplasmic reaction of Platelet Derived Growth Factor antibody were observed in 6 cases of juvenile fibromatosis and 5 cases of desmoplastic fibroma as well as the 3 cases that showed recurrence in the form of fibrosarcoma .Conclusion: Intermediate tumors have a benign clinical course, but their clinical behavior is unpredictable.

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**Keyword:** Intermediate soft tissue tumors, Beta Catenin, Platelet Derived Growth Factor

### 1. Introduction

The WHO has a new classification of soft tissue tumors that was introduced in late 2002. As part of this new WHO classification, the Working Group has focused on the definition and the biological potential of lesions, that were addressed as 'intermediate malignancy' or 'borderline malignant potential.' With this goal in mind, they recommended to divide soft tissue tumors into the following four categories: benign, intermediate (locally aggressive), intermediate (rarely metastasizing) and malignant [1]. The Intermediate (locally aggressive) and Intermediate (rarely metastasizing) tumors often recur locally and are associated with an infiltrative and locally destructive growth pattern [2].

$\beta$ -Catenin is a multifunctional protein, which plays a very important role in cell adhesion and it is localized to the adherence junction on the cell membrane and free cytoplasmic . Mutation of the  $\beta$ -catenin gene results in its stabilization and a significant increase in this protein within the cell. Mutations of  $\beta$ -catenin have been identified in various cancers such as colon cancer and more recently, in soft-tissue tumors [3]. The expression of PDGF and their receptors was demonstrated in a broad spectrum of human cancers [4].

Recent studies have mentioned that PDGF is also expressed in gliomas and sarcomas, which derive from cell types that are normally responsive to PDGF.

Furthermore, it was mentioned that the increased expression of PDGF correlates with the degree of malignancy [4, 5].

The aim of this research is to study the clinical and pathological features of intermediate soft tissue tumors and to investigate whether  $\beta$ -Catenin and Platelet derived growth factor antibodies have a role in finding the liability of malignant transformation of these intermediate tumors.

### 2. Materials and Methods

Materials were obtained from patients who had undergone surgical excision of their tumors at Maxillofacial Department, Faculty of Dentistry, Alexandria University, Egypt, during the years 2010 through 2012.

A portion of the tumor was used for research after informed consent was obtained .All specimens were fixed in 10% formalin, embedded in paraffin, stained with haematoxylin and eosin for diagnosis.

For immunohistochemical analysis, all sections were cut 5 $\mu$ m, embedded in superfrost plus slides. All sections undergo deparaffinization. Antigen retrieval was performed in a microwave oven using 10mM citrate buffer. Endogenous peroxidase activity was blocked with 0.03% hydrogen peroxide containing sodium azide. Slides were incubated with non-immune serum for 30 minutes and were then incubated with the primary antibody for overnight in a moist chamber,



The following antibodies, manufactured by Neo Markers for Lab Vision Corporation (Fermont.CA94538, USA) were used according to manufacturers' recommendations:

- i- Catenin Beta Ab-1 (cat #RB-090-R7)
- ii- Platelet Derived Growth Factor PDGFR (cat#RB-090-R7)

Positive and negative controls as well as oral fibroma that served as an endogenous control group were used. Biotinylated Rabbit anti-Mouse (1:200 w/ 10% NRS) were incubated for 30 min. Slides were rinsed in PBS 3 X 5 min. each. Followed by the application of conjugated HRP Streptavidin (1:1000) incubate to 30 min. Brown color was developed using DAP working solution for 5 min, counter stained with haematoxylin for 15min, washed, dehydrated and mounted.

Cellular localization for Catenin Beta was nuclear and cytoplasmic, while for PDGF was cytoplasmic only.

Nuclear and cytoplasmic immunostaining was determined semi quantitatively.

### 3. Results

Twenty six selected cases of soft tissue intermediate tumors were collected from head and neck region. Female to male ratio was 1:1.625 with average age 16.5.

The selected cases were diagnosed as follow: nine were Juvenile fibromatosis, five haemangiopericytoma, nine desmoplastic fibroma , three of which showed recurrence and were diagnosed as Fibrosarcoma (3 cases).

Nuclear localization of Beta Catenin antibody was found in almost all the cases with different intensity; All cases of juvenile fibromatosis, desmoplastic fibroma and fibrosarcoma (Figs. 1-3 )

Cases of haemangiopericytoma and the endogenous control (intraoral fibroma) showed no reaction.

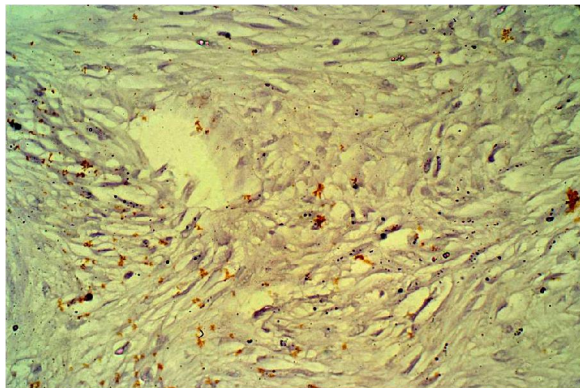


Figure 1: Desmoplastic fibroma with +ve nuclear [beta]-Catenin antibody (X400)

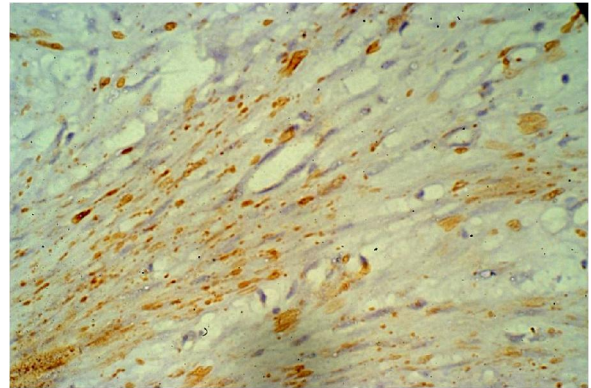


Figure 2: Photo microgram of desmoplastic fibroma with +ve immunohistochemical nuclear stain ( $\beta$ -Catenin x400)

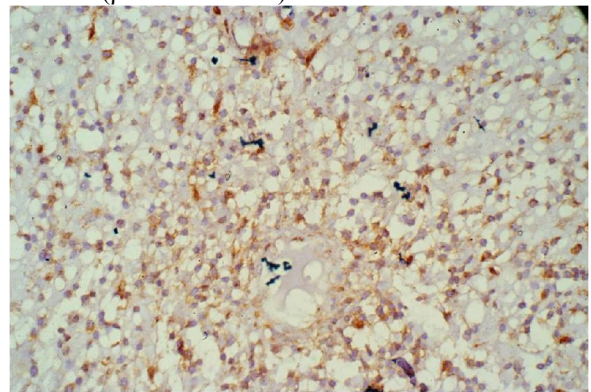


Figure 3: Photo microgram of desmoplastic fibroma with +ve nuclear immunohistochemical stain ( $\beta$ -Catenin x200)

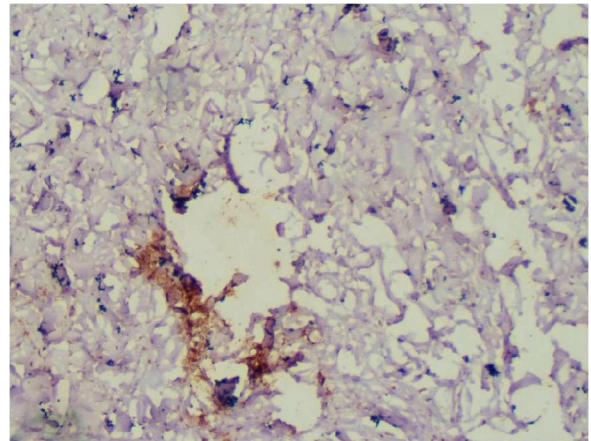


Figure 4: Photo microgram of desmoplastic fibroma with +ve immunohistochemical cytoplasmic & cell membrane stain (PDGFx400)

Cytoplasmic reaction of PDGF were observed in 5 desmoplastic fibroma (Fig 4) including the 3 cases that showed recurrence, cases of fibrosarcoma, and 6 cases of juvenile fibromatosis. (Fig 5)

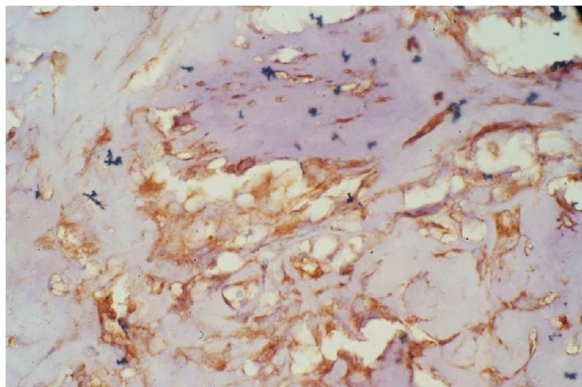


Figure 5: Photo microgram of desmoplastic fibroma with +ve immunohistochemical cytoplasmic & cell membrane stain (PDGFx400)

#### 4. Discussion

On the basis of the microscopic findings it is not always easy to draw a presumptive line dividing what we call intermediate tumors from what we call Grade I fibrosarcoma. This distinction can, in theory be reasonably precise, but considerable possibilities of error must be taken into consideration.

Immunohistochemistry (IHC) is presently the most important adjunct tool in the evaluation of soft tissue tumors because of its practicability and relatively low cost [6]. Furthermore, a small group of soft tissue tumors remains unclassified despite extensive ancillary studies except with IHC [4].

This survey was performed on soft-tissue tumors to find out whether nuclear expression of  $\beta$ -Catenin, as determined by immunohistochemical staining would be relatively specific to and sensitive for tumors in this class.

Our results showed the absence of nuclear localization of  $\beta$ -Catenin in normal fibroblast. This was in accordance with Kim *et al.* [7] who reported a cytoplasmic distribution of  $\beta$ -catenin in fibroblasts without significant amounts at the cell surface, and no nuclear accumulation of  $\beta$ -catenin in regular fibroblasts.

The five cases of haemangiopericytoma showed no immunohistochemical reaction to  $\beta$ -Catenin. Studies conducted by other authors [8] recommend the use of other antibodies panel to distinguish endometrial stromal sarcomas from tumors with a predominant hemangiopericytomatous growth pattern.

On the other hand, high-level nuclear expression of  $\beta$ -Catenin was seen desmoid-type fibromatosis, Juvenile fibromatosis and fibrosarcoma. The findings presented in this study substantiate the significance of  $\beta$ -catenin for soft tissue intermediate tumors and sarcomas as shown by the large nuclear accumulation

which accentuate its role as an oncoprotein. This was in accordance with Kuhnen *et al.* [9] and Al-Daraji *et al.* [6]. In the contrary, other studies have mentioned that nuclear expression of  $\beta$ -Catenin was seen in a very restricted subset of mesenchymal tumors [10, 11].

The role of  $\beta$ -Catenin as an oncoprotein has been analyzed so far in a number of epithelial tumors; an increased expression was also shown in aggressive fibromatosis as a representative of mesenchymal tumors [12, 13].

The present study demonstrate the cytoplasmic accumulation of PDGF antibody in 5 cases of desmoplastic fibroma including the 3 cases that showed recurrence, cases of fibrosarcoma, and 6 cases of juvenile fibromatosis.

It is well known that tumor cells assign neighboring blood vessels to support their own blood supply for oxygen and nutrients and finally for intravasation (to enter into the blood vessels) and extravasation (metastatic spread) through promoting pathologic neovascularization/angiogenesis [14]. This event is potentiated by tumor cells through the production of diffusible angiogenic factors [15].

The expression of PDGF and their receptors was demonstrated in a broad spectrum of human cancers [16]. Furthermore, studies have mentioned that PDGF is also expressed in gliomas and sarcomas, Moreover it was suggested that the increased expression of PDGF correlates with the degree of malignancy [3,4].

#### Conclusion

On the whole, intermediate tumors have a benign clinical course, but the clinical behavior is unpredictable and the relationship between morphology and clinical behavior is poor.

In our opinion, it would therefore be more honest and practical for therapeutic purposes to consider desmoplastic fibroma and Grade I fibrosarcoma under the same heading, that is as well-differentiated fibrous tumors having very slow but progressive growth and recurring locally when incompletely removed.

Complete surgical resection is commonly accepted as a treatment of choice. Optimal adjuvant treatment for patient at high risk of recurrence or metastases is not known. Therefore, a close long-term follow-up has to be recommended even after radical excision.

#### Competing Interests

There is no competing interests'.



**Author(s) Contribution:****Am. N.:**

Participated in the study design, collection of the background references. Photomicrography of the immunohistochemical results, interpreting and displaying the results of the study, writing the discussion of the results and alignment of the references.

**Ib.M.:**

Participated in selecting study cases, follow up of these cases, interpreting and displaying the results of the study, writing the discussion of the results.

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## Management of metastatic breast cancer (MBC)

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**Abstract:** Chemotherapy, so far, of metastatic breast carcinoma is not curative using the currently available chemotherapeutic, hormonal or biologic agents. The treatment of metastatic breast cancer is aimed mainly at alleviation of symptoms rather than cure. The first choice of therapy is dependent on patient age, performance status, hormone receptor status, human epidermal growth factor receptor-2 (HER-2), involvement of the viscera, or enrollment of patients in investigational trials. Combination of chemotherapeutic drugs showed an advantage for survival, tumor response and time to progression, with adverse effects of these agents. It is very important, therefore, to balance between the benefits of treatment and the adverse effects and complication of therapy.

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**Keywords:** chemotherapy, metastatic, HER-2, breast, combination

### Introduction

Metastatic breast cancer is not curable by current treatment modalities, although temporary regression of the disease is attainable in about 65% of the patients. Clinical complete remission is observed in less than 20% of the patients but rarely of long duration. Median survival is of about 2 years. The goals of the treatment, therefore, is to palliate the symptoms of the patients and if possible prolongation of useful high quality life. Surgery and radiation therapy play a limited role in patients with metastatic breast cancer as to make a histological diagnosis or mastectomy to prevent local complications. Hormonal therapy, chemotherapy, monoclonal antibody therapy and combination of these agents have proved useful in the management of metastatic breast cancer. Since metastatic breast cancer is incurable and at present time there is no gold standard chemotherapy, we must emphasize early detection of breast cancer and to continue clinical researches to improve the outcome of metastatic breast cancer.

### Definition of MBC

The staging of breast cancer changes with time to reflect the extent of the disease and the prognosis as well as to incorporate the increasing use of novel imaging and pathology techniques employed at diagnosis. The number of lymph nodes involved as strong prognostic factor contributed to these changes. Haggensen and Stout in 1943 said supra-clavicular lymph nodes make patients inoperable. In 1987 The American joint committee on cancer (AJCC) considered supra-clavicular lymph nodes as M1 to reflect poor prognosis.<sup>1</sup> The American joint committee

on cancer (AJCC) implemented a revision of the cancer staging containing important changes and additions in the TNM staging system for breast cancer. The rationale for changes and additions stemmed from continuing development in the field of breast cancer diagnosis and management. This revision defined metastatic breast cancer (stage IV) as any T, any N but M1. Metastasis to ipsilateral supraclavicular lymph nodes is no longer considered M1 metastasis.<sup>2</sup>

### Clinical trials and end points definition:

Overall survival (OS) is defined as the time from randomization to death from any cause and has been regarded as the gold standard measure of clinical benefit. Progression-free survival (PFS) is defined as the time from randomization to tumor progression or death from any cause. Time to progression (TTP) is defined as the time from randomization to cancer progression.<sup>3,4,5</sup> The outcomes from meta-analysis of phase III trials, total of 73 trials, only 12% demonstrated an OS and 52% reported significant outcome in the form of PFS or TTP. Similar outcome from another meta-analysis, total of 76 trials, reported only 19.7% of trials demonstrated OS gain. The third meta-analysis, total of 63 trials, only 13% demonstrated OS benefit. These findings indicate that, so far, lack of cytotoxic, biological, and endocrine therapy to clearly prolong overall survival.<sup>3,4,6,7</sup>

Preferred chemotherapy regimens

Metastatic breast carcinoma can be categorized from management point of view to 2 main subtypes: (1) Human epidermal growth factor receptor type2 negative {HER2-} and estrogen receptor

negative {ER} disease. There is no randomized phase III trials showing a survival benefit of combinations compared to sequential chemotherapy of the same drugs for this subtype of malignant disease. (2) HER2 positive disease, data support the use of trastuzumab as a single agent or in combination with chemotherapeutic agents.

Chemotherapy is indicated for patient's refractory to hormonal manipulation, as an investigational studies, hormone-receptor negative and for those with an aggressive disease.<sup>8</sup> Several chemotherapy regimens have been used (Table 1). Since their introduction in the 1980s, the anthracyclines, doxorubicin and epirubicin, have been considered to be among the most active agents for the treatment of MBC. Meta-analysis demonstrated that first-line treatment with anthracycline-containing regimens confer a marginal survival benefits compared with non-anthracycline-containing regimens.<sup>9</sup> The taxanes, paclitaxel and docetaxel, have been developed in the 1990s and evaluated in the treatment of anthracyclines-pretreated MBC. Docetaxel significantly improved over all survival ( $p=0.0097$ ), time to disease progression ( $p=0.001$ ), and response rate ( $p<0.0001$ ) compared with mitomycin c plus vinblastine.<sup>10</sup> Docetaxel is the only single agent for which a survival benefit has been demonstrated in anthracycline-pretreated MBC.<sup>10</sup>

Recently, 2004, Gemcitabine in combination with paclitaxel demonstrated time to progression benefit in patients with MBC and approved by FDA as first line therapy after adjuvant anthracycline chemotherapy or contraindication to anthracycline treatment.<sup>4,11</sup>

### Combination therapy

There are ideal criteria which should be met when combination chemotherapy chosen for treatment of metastatic breast cancer. These criteria include:

1. Single agent activity
2. Distinct mechanism of action
3. Preclinical evidence of synergy
4. No cross resistance
5. No overlapping toxicity

However, all these criteria are rarely met and consequently many combination chemotherapies have failed to yield better result compared with sequential treatment and combination chemotherapy did not improve over all survival or quality of life compared to sequential therapy.<sup>12,13,14</sup> A major reason for combination chemotherapy failure is related to dose intensity ( $\text{mg}/\text{m}^2/\text{week}$ ). The dose intensity should be reduced in combination treatment to avoid drug overlapping related toxicity and absence of synergistic activity.

The treatment of metastatic breast cancer with combination chemotherapy prolong survival and

improve quality of life but not curative. In addition to that, they are toxic, rarely compared in randomized trial and ranked by single parameter [response rate (RR), PFS and TTP] which unlikely to affect over all survival.<sup>4</sup> Therefore, treatments associated with minimal toxicity may be preferred.

Therapeutic advances

Monoclonal antibody therapy

New developments in the treatment of MBC do, however, mean that MBC is increasingly being managed as a chronic disease. Therefore quality of life and the convenient of treatment become important factors in the management of patient with MBC. Trastuzumab is a humanized anti-HER2 monoclonal antibody. HER2, a transmembrane glycoprotein, is over expressed in 20%-30% of human breast cancer.<sup>15</sup> Trastuzumab is effective and safe as a single agent first-line treatment of patient with HER2 positive MBC.<sup>16</sup> When combined with taxane, they represent a rational designed combination treatment. Each component has single agent activity, distinct mechanism of action, evidence of synergy<sup>17</sup>, nonoverlapping toxicities and without cross-resistance. The result of this combination offers a survival advantage in patients with positive HER2 MBC.<sup>18</sup>

Combining anti-HER2 therapy with cytotoxic agents as taxane improve the response of patients to treatment with minimal toxicity and improved survival and quality of life. Trastuzumab has been approved by the FDA as a single agent for the treatment of patients with HER2 positive metastatic breast cancer and who have received one or more chemotherapy regimens or in combination with paclitaxel as first line treatment.<sup>19</sup> Trastuzumab then has been approved by the FDA as a first-line treatment for MBC in 1998 in combination with paclitaxel. Nowadays, Trastuzumab-based therapy is the standard of care for HER2 positive MBC.<sup>4,20</sup>

### Oral chemotherapy

Capecitabine has a unique enzymatic activation pathway. The drug is preferentially activated to its cytotoxic metabolite, 5FU, within the tumor site. The drug level is at a median level of 3.2 fold higher in the tumor tissues than in surrounding normal tissues.<sup>21</sup> This difference is due to higher activity of thymidine phosphorylase in tumor cells than in non-malignant cells. Capecitabine as monotherapy, an intermittent regimen of 1,250 mg/m<sup>2</sup> twice daily, day 1-14 of 21-day cycle is the standard approved regimen. It is approved in USA, Canada and the entire European Union for taxane-pretreated metastatic breast cancer. It is an oral convenient drug used as 2<sup>nd</sup> line treatment for MBC. The patient should be able to report any side effects, expectations of survival more than 3 months and performance status 0-2.

### Hormonal therapy or Chemotherapy or both

Endocrine therapy and chemotherapy are the two major classes of systemic therapy used in the treatment of MBC. Combination of these majors type of therapy is not preferred due to many factors as illustrated in Table 2.<sup>21-25</sup> Choosing therapy for patient with MBC requires an understanding of the natural history of the disease and careful evaluation of the patient. Multiple factors affect the choice of therapy as illustrated in Table 3. Premenopausal patients with MBC can be treated with tamoxifen or with ovarian ablation if tamoxifen used as first line therapy. Goserelin and tamoxifen has been used and reported as effective. However, postmenopausal patients, the options of hormonal therapy include aromatase inhibitors (anastrozole or letrozole), tamoxifen or exemestane.

Bone metastasis secondary to breast carcinoma are important complications and a common causes of morbidity of these patients. These complications include bone pain, bone fractures and spinal cord compressions which can complicate the clinical course of metastatic breast carcinoma. These complications need adequate prevention and intervention to improve the quality of life of these patients. Bisphosphonate by inhibiting the osteolytic activity are effective treatment in preventing complications of metastatic bones diseases and need to be part of the treatment of metastatic breast carcinoma.<sup>26-29</sup> A meta-analysis that included randomized trials of 12 studies of bisphosphonate treatment of patients with metastatic cancer of various malignancies demonstrated decreased the risk of skeletal related events (SRE) compared to placebo. There was no difference between pamidronate and zoledronate regarding SRE, pain reduction or survival in patients with MBC. However, zoledronate may be superior to pamidronate for reducing bony fracture, hypercalcemia of malignancy and reducing the need for palliative radiation treatment. In addition, zoledronate require shorter infusion time.<sup>30, 31</sup>

The benefits of high dose chemotherapy and bone marrow transplantation as well as immunotherapy were not proved. Alternative therapy in the form of Arabic medicine (quetry, black seed, special food or water) delay treatment and no single study proved its benefit. Surgical intervention and radiotherapy have a limited role in the management of MBC as shown in Table 4.

### Conclusion

Even though breast cancer is increasingly recognized as heterogeneous disease and of several important tumor subtypes with different natural clinical courses requiring different type of treatment, metastatic breast cancer is not curable by current

treatment modalities, although temporary regression of disease is attainable in the majority of patients. Clinical complete remission is observed in less than 20% of patients but rarely of long duration and still the median survival of about 3 years. The goals of the treatment, therefore is to palliate the symptoms of the patients and if possible prolongation of useful high quality life. Surgery and radiation therapy play a limited role in the treatment of MBC as to make histological diagnosis or to prevent complication. Hormonal therapy, chemotherapy, monoclonal antibody therapy or combinations of these treatments have proved useful in the management of MBC. Increased effort at early detection and continuing of clinical researches are most likely to result in improvement of the outcome of MBC.

Table 1. Preferred chemotherapy regimens for MBC

Preferred agents	Preferred combinations	Other active agents
Anthracyclines: Doxorubicin, Epirubicin.	CAF FEC AC	Gemcitabine Cis- Platinum
Taxanes: Paclitaxel, Docetaxel	AT CMF	Etoposide Vinblastine
Capcitabine	TC	
Vinorelbine	TAC	

C= cyclophosphamide; A= doxorubicin; F= 5FU; E= Epirubicin; T= docetaxel; M= methotrexate

Table 2. Reasons why endocrine and chemotherapy combination not preferred<sup>32</sup>

1. Hormone slows the growth of tumors and the tumors become less responsive to chemotherapy.
2. Thrombosis like DVT doubled when both combined.
3. Difficult to differentiate which one has conferred the benefit.
4. Little known about the cytokinetic interaction of chemotherapy and hormonal therapy.

Table 3. Factors affecting the choice of endocrine and chemotherapy<sup>32</sup>

Chemotherapy	Endocrine therapy
Young < 35 years	Old > 35 years
Poor performance status	Good performance status
DFI < 1 year	DFI > 1 year
ER/PR negative	ER/PR positive
Visceral metastases	Non-visceral metastases
Grade 3	Grade 1
HER2 positive	

DFI: Disease free interval; ER: Estrogen receptors; PR: Progesterone receptors



Table 4. Indications for surgical and radiotherapy

Surgery	Radiation ± steroids
Investigation of a lesion	Bony metastasis with complications
Intervention of complication:	Local recurrence
Hemorrhage/Abscess	Orbital Metastasis
Treatment of fracture	SVC obstruction
Surgical decompression of spinal cord	Brain metastasis
Solitary lesion	Symptomatic endobronchial tumor

SVC: superior vena cava.

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## Study on infectious causes of hospitalization in intravenous drug users

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**Abstract:** To evaluation of common infections in Intravenous drug users (IVDU). In a descriptive-analytical study that performed in Infection Diseases and Tropical Medicine Research Center of Tabriz form 2001-2011, 64 patients (63 male & one female) with IVDUs and had infectious signs were enrolled in to the study. The mean age of studied patients was 37.05±9.35 years. Heroin was the principle drug consumed by 78.125% of IVDUs. The most common chief complaints of patients were referring to liver biopsy, cough and pain with 21.87%, 20.31% and 20.31%, respectively. The most involved organs were liver (31.25%), lung (25%) and lower extremities (18.75%). Hepatitis 29.68%, skin infections 23.43%, pulmonary infections 21.87%, peripheral vascular infections 15.62%, AIDS 4.68%, endocarditic 1.56%, epididimorchitis 1.56% and drug toxicity 1.56% were the infectious etiologies of hospitalization in IVDUs. The most infections cause of IVDU hospitalization was hepatitis, skin infection and pulmonary infections.

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<http://www.lifesciencesite.com>.

**Keywords:** Intravenous drug users; Drug; Infections

### 1. Introduction

Addiction is one of the important problems in today's world. Annually, about 5 percent of the world's population, Equivalent to 200 million people, uses narcotics (White and Comiskey, 2007). Annual statistics by World Health Organization show an increase of injecting addicts worldwide especially in developed countries (Hosseini, 2011). There were approximately 13 million injecting addicts in the world about 78 percent of which are in developed countries (Hughes and Rieche, 1995). There are different ways of using narcotics that injecting is one of the most dangerous ways; because this way of using narcotics leads to increased susceptibility to, and metastasis of infectious diseases including AIDS, hepatitis and other bacterial infections (Palepu, 2001). Due to certain behaviors in the patient group, there is a possibility of simultaneous existence of several diseases in individuals, which leads to variation in their clinical symptoms (Mandel, 2010). Diagnosis and treatment of patients with injecting addiction is also very difficult due to various reasons including existence of non-infectious causes of fever such as toxins and impurities in the narcotics, self-treatment before referring to a doctor, having HIV infection and related diseases, inappropriate use and arbitrary cut off of medications (Samet, 1990). Due

to low acceptance of patients for treatment, mortality and morbidity in these patients are high. Infectious complications in injecting addicts are related to their environment and lifestyle (Mandel, 2010). Powder narcotics are dissolved in saliva or some water from any source, and injected by any available syringe into the vein or under the skin. Skin is not disinfected either, and is cleaned just by rubbing some saliva. In case of using a common syringe, some blood remains in the syringe and needle which is just diluted but not completely removed by rinsing with water; and in frequent use, this offers the best medium for transmission of infectious pathogens (Mandel, 2010). Given the importance of infections, especially metastatic ones in injecting addicts, and annual increase of the number of injecting addicts, this research has been conducted to determine the most common infections in this group of patients, in order to prevent the rate of infection and transmission of various diseases in the people at risk and also reduce disease mortality by the knowledge of the prevalence of infections and their complications, and with the diagnosis and treatment in one hand and changing patients' habits and behaviors through counseling on the other hand.

## 2. Material and Methods

In a cross - sectional descriptive-analytic study on injecting addicts admitted in infectious centers of Tabriz in 9 years during 2001-10, 64 out of 80 injecting addict cases, suitable for the purpose of the study were selected and evaluated. Reviewing of clinical records of the patients, Necessary information was extracted. Variables under study has included: gender and age, type of injecting addiction, period of injecting addiction, the main complaints of patients, the status of acute phase responses, precise anatomic localization of lesion, criteria and evidences leading to the diagnosis, hospitalization period, and anti-biogram culturing results, status of screening for HBV, HCV, HIV infections, number of previous hospitalization, hospitalization costs, and procedure of discharge.

Table 1. Infections cause to hospitalization of patients.

Causes of hospitalization		Percent of frequency	Cumulative Percent
Skin and soft tissue infections	Cellulitis	17.18	23.43
	Abscess	4.68	
	Necrotizing fasciitis	1.56	
Pulmonary infections	Pneumonia	17.18	21.87
	Tuberculosis	1.56	
	Lung abscess	1.56	
	Empyema	1.56	
Peripheral vascular infections	Septic thrombophlebitis	1.56	15.62
	Hematoma	1.56	
	Thrombosis (DVT)	12.5	
Hepatitis	Viral hepatitis C (HCV)	21.87	29.68
	Viral hepatitis B (HBV)	7.81	
Endocarditic		1.56	1.56
Epididimorchitis		1.56	1.56
AIDS		4.68	4.68
Drug Fever		1.56	1.56

## 3. Results

In this study, 63 male patients and one female patient with injecting addiction were studied. Mean age of patients was  $37.05 \pm 9.35$  in the range of 31-40 years. Addiction to heroin with 78.125% was the most common injecting drug in the addicts under study, and morphine with 9.37% was the next. Duration of addiction was 3 to 9 years with morphine and up to 12 years with heroin. During hospitalization, 40.62% of addicts were febrile, 29.68% were leukocytosis and 35.93% had increased

ESR. The main complaints of addicts under study are shown in Figure 1. Precise anatomic localization of lesions in the studied addicts is shown in Figure 2.

3.125% of studied addicts were HIV-positive, 6.25% HBV-positive and 37.5% HCV-positive; the screening status of HIV, HCV and HBV is shown in Figure 3. Mortality rate of the addicts under study was 10.93%; 18.75 % were discharged with complete remission and 70.31% with partial recovery, and mean admission fee was \$121 per person.

Six of the patients studied had a history of hospitalization in the infection center. Most common infections among the addicts under study was hepatitis in 19 and dermal infections in 15 patients; detailed infections of the addicts under study are shown in Table 1.

## 4. Discussions

Due to certain behaviors, injecting addicts are susceptible to various infections. Among the underlying causes of infection in injecting addicts, the increase of *Staphylococcus aureus* as the normal skin flora, mucosa and nasopharynx, non-sterile injection techniques, use of contaminated equipment or injection drugs such as infected syringes or solvents, suppression of immunity due to HIV infection or use of narcotics, poor oral hygiene or impaired gag reflexes and cough caused by drug use, low socio economic condition, and sometimes, homelessness which exposes the addict to certain pathogens such as TB bacilli can be mentioned (Mandel, 2010).

Among the most common infections in patients with injecting addiction, hepatitis with frequency of 32.7% was on top of the list in the current study, and among the types of hepatitis; hepatitis C with the prevalence of 23.1% was higher than all the other cases. In other studies, the prevalence of hepatitis C in injecting addicts reported high too (Young and Cheong, 1997; Devi, 2005).

Hepatitis is considered as a common complication of drug injection, and viruses are known as the only factor of hepatitis in addicts. Studies by Lee & Lemon indicate that simultaneous infection of Hepatitis B and D was more common in addicts often demonstrating as Fulminant form of hepatitis that leads to complete recovery for either viruses or death.

Vaccination against hepatitis B in addicts protects them from both viruses (Lemon and Thomas, 1997; Lee, 1997). A study by Novick et al also showed that injecting addicts make about 42 percent of patients with hepatitis C and often they proceed towards the chronic hepatitis (Novick and Reagan, 1997).

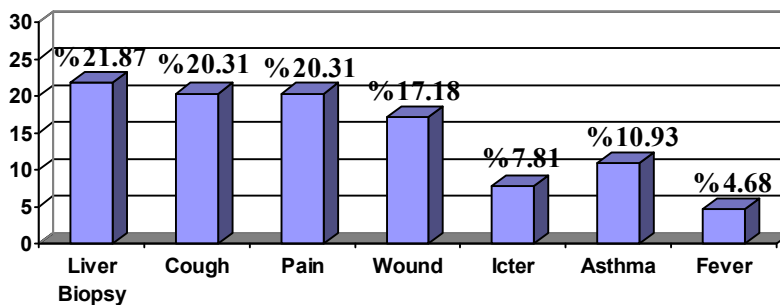


Figure 1. The most common chief complaints of patients

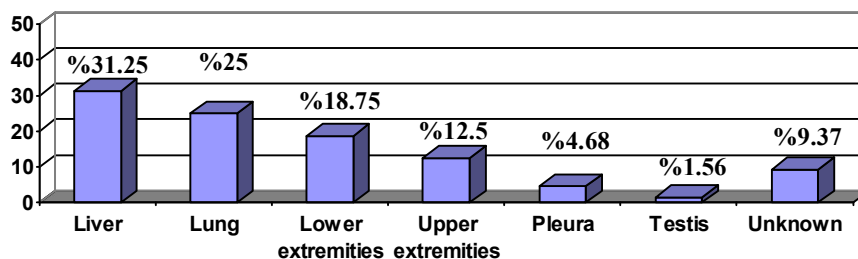


Figure 2. The most involved organs in the studied patients

As observed, the results by our study are in agreement with most other studies that seem to be due to use of contaminated shared syringes and the same risky behaviors among injecting addicts in different countries. Skin and soft tissue infection with 22.3% was the second most common cause of hospitalization of addicts.

In many other studies, this factor was the most frequent cause of reference of admitted addicted patients, and if outpatient centers were included in the study, it seems that most of the cases were related to skin and soft tissue infections, where, due to the superficiality of cases and outpatient treatment, or no consent of patients to get admitted, the admitted cases only include cases with deep infection and extensive gangrene or with poor general condition of the patient. From among skin and soft tissue infections, cellulitis with 66.7%, abscess with 25.1%, and necrotizing Faceit with 8.2% were of the important infections. In a study by Takahashi et al. patients with cellulitis were in a higher need for admission in comparison those with abscess(Takahashi, 2003), the fact which is in agreement with our study. Susceptibility to skin and soft tissue infections was due to repeated injections in the same area without disinfection, which leads to local ischemia and necrosis in the area. On the other hand, use of some substances as a solvent also increases the risk of infection, this substances cause the release of

norepinephrine and vascular spasms which lead to damage to entimaic vascular parts followed by vascular thrombosis and tissue infection. Skin and soft tissue infections vary from a simple abscess or cellulitis to life-threatening infections such as septic thrombophlebitis and fascia infection (Mandel, 2010).

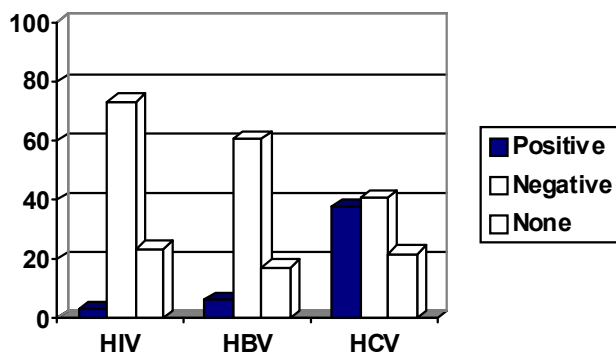


Figure 3. Screening of HIV, HBV and HCV between patients

The pulmonary infections with incidence of 19.3% were the third cause of reference of addicts, the most common of which were pneumonia and then, tuberculosis, lung abscess, and empyema with lower percentages. In similar studies, the most common pulmonary infections have been due to common pulmonary pathogens causing pneumonia (Fauci, 2008). Next to cellulitis, pneumonia has been the most common infection in injecting addicts which should be diagnosed by pulmonary emboli septic from right heart or peripheral vascular origin (Fauci, 2008). The most common pathogens of Pneumonia were *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aerogenosia* respectively, which cause disease by hematogen. Lung abscess and necrotizing pneumonia are their other pulmonary demonstrations (Mandel, 2010). Pulmonary infections in injecting addicts are due to reduced clearance of secretions, aspiration, and reduced immunity, particularly along with HIV infection (Mandel, 2010). Pulmonary Tuberculosis is a major problem in injection addicts with and without HIV infection. Homelessness, poverty and bad conditions and unwillingness are some factors predisposing the disease (Mandel, 2010).

Peripheral vascular infections with 13.4% the fourth cause of reference of addicts and DVT with 71.6%, septic thrombophlebitis and hematoma, each with 14.2% were of the important factors. Due to the injection, Peripheral and central vessels suffer multiple damages as hematoma, thrombosis, septic thrombophlebitis, mycotic aneurysms and arteriovenous- intravenous traumatic fistula. In another study on young patients with DVT, it was found that they had a background of drug injection, and concluded that drug injection is an important cause of DVT in young patients (Syed and Beeching, 2005). In our study, DVT is involved with most cases and the results are similar to other studies. AIDS, with 5.8%, is another one of the infections in addicts that the potential cause of acquisition of HIV infection in injecting addicts is due to the use of shared syringe and unsafe sexual contacts is in this group (Mandel, 2010). Similar studies on HIV and its relation to drug injection have been conducted, that provided statistics indicates an increase in AIDS patients due to drug injection in recent years. Endocarditis with 1.9% is one another infection diagnosed in these patients; in the studies conducted in Isfahan, 0.5% of the addicts suffered endocarditis (Abdali and Faiiaz, 2005). Statistics obtained in studies of other countries have indicated endocarditis as one of the common infections in addicts (Young and Cheong, 1997) and the most common cause of drug injection addicts has been attributed to infective endocarditis and the most common organism was

related to *Staphylococcus aureus* (Mandel, 2010; Young and Cheong, 1997). The difference of prevalence in our study with other studies is due to the admission and treatment of patients with endocarditis in the heart wards. 1.9% of infection cases were due to epididymo-orchitis that its lower percentage in this study and no report of it in other studies suggests that this infection is probably not related to drug injection.

#### Conclusion:

All patients were male with mean age of 37 years. The most common drug injected was heroin with 92.3% and the commonest infections leading to admission were hepatitis, skin and soft tissue and pulmonary infections. Since most people are in sexually active age groups, there is a probability of transmission of sexually transmitted infections (STI) and particularly HIV also in the patients' partners and diagnosis and treatment of patients not only reduces morbidity and mortality, but also may help promotion of the community health.

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9/26/2012

**Evaluation cervical cord changes in the patients with MS and their comparison with vasculitis patients**

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**Abstract:** Multiple sclerosis disease (MS) is a chronic inflammatory demyelinating disease. The aim of this study was to evaluate cervical cord changes and to determine abnormal cervical cord prevalence in the patients with MS and their comparison with vasculitis patients. In a descriptive-analytic study carried out on 50 patients with MS, 40 patients with vasculitis and 50 people as control group in Tabriz Razi hospital, we studied cervical cord changes and the prevalence of cervical cord abnormalities in the patients with MS and vasculitis. From 50 MS patients, only four people had diffused lesions in spine that were all related to Primary Progressive (P-P) type. From the 22 patients with MS, having spinal symptoms during the study, focal lesions were revealed in the cervical cord Magnetic Resonance Imaging (MRI) of eight people (36.4%) whereas the lesions were found in 28 patients with MS who had no spinal symptoms. Diffused lesions were also found in the cervical cord MRI of four patients (18.2%) who had spinal symptoms whereas the lesions were found in the 28 patients with MS who had no spinal symptoms. There was a meaningful and the reverse relations between EDSS mean and transverse cross-section of cervical cord. In every five patients with MS one patient had demyelinated lesions in cervical spine which was more obvious in progressive types and atrophy degree of cervical spine was more in the patients with P-P and Secondary progressive types compared to the patients with relapsing remitting.

[Nikanfar M, Charsouei S, Miabi Z, Sha'afi SH, Hashemilar M, Farhodi M, Ebrahimi A, Khabbazi A, Rikhtegar Ghiasi R. **Evaluation cervical cord changes in the patients with MS and their comparison with vasculitis patients.** *Life Sci J* 2012;9(4):607-613] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 93

**Keywords:** Multiple Sclerosis; Cervical Cord Changes; Vasculitis; MRI

## 1. Introduction

Multiple sclerosis disease (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS) which usually affects optic nerve, brain, spinal cord, brain stem and cerebellum (Rovira and León, 2008 ; Valsasina, 2005).

Spinal cord is commonly involved in MS and its disorders contribute to a part of disabilities of the disease (Rovira and León, 2008 ; Valsasina, 2005). Recently spinal cord has been comprehensively studied and some studies show that patients with MS have a smaller cervical cord cross-section compared to the control group which is in relation with disability. Furthermore several spines Magnetic Resonance Imaging (MRIs) may provide information on the disease progression which is not available through brain MRI. There are reports on cervical cord atrophy in the beginning of the disease as it is detectable in the patients with clinically isolated syndrome (C. I. S) and these findings show the importance of early diagnosis in MS patients as atrophy is equal to irreversible destructive pathology (Tench, 2005; Lin, 2004).

In cases with dubious or negative brain results or in MS onset associated with spinal symptoms, cervical cord MRI can play an important role in early diagnosis of MS (Simon, 2000; Lycklama, 2003; Grossman, 2000).

The validity of cervical spine studies have been emphasized on in the studies carried out in different countries in spite of limitations and controversial reports. As there is no integrated information regarding the prevalence of cervical spine changes and the importance of this region to be studied in MS patients, we decided to study this subject in patients with MS, however in a small population. The aim of this study was to evaluate cervical cord changes and to determine abnormal cervical cord prevalence in the patients with MS and their comparison with vasculitis patients.

## 2. Material and Methods

In a descriptive-analytic study carried out on 50 patients with MS, 40 patients with vasculitis and 50 people as control group in Tabriz Razi hospital from 2007-2008, we studied cervical cord changes

and the prevalence of cervical cord abnormalities in the patients with MS and vasculitis.

All the studied patients underwent cervical cord MRI with deep T1 and T2 weighted sequences and sagittal and axial sections were obtained using (1.5 Tesla, Signa, the US) unit. The diagnosis of MS was made using Mac Donald criteria and all the selected patients with vasculitis showed brain involvement in MRI.

All MRI images were reported by a neuro-radiologist regarding having any parenchymal lesions or plaques in cervical cord, the number, size, position, being focal or diffused of the lesions specially in T2 view. Other lesions were studied based on the number of the vertebral segments involved. Transverse cross-sections of cervical cord in C4-C5 level were measured by the software of the MRI unit. Diffused lesion is defined as hyper signal areas with indefinite margins which are clearly distinctable from CSF.

MS patients were selected using Mac Donald criteria. Patients with a history of neck trauma, degenerates and diseases of cervical cord and neck surgery were excluded from the study.

#### **Ethical considerations:**

No specific therapeutic intervention was done in this study. MRI was performed free of charge. Cervical cord MRI was performed for the patients with vasculitis and brain involvement without spinal symptoms. To avoid the probable complications of IV contrast, MRI was carried out without injection.

#### **Statistical analysis:**

All data were analyzed using descriptive and deductive statistics methods by SPSS Ver 11.5. The relation between qualitative data was evaluated using Chi-square test. And the relation between quality and quantity data were evaluated using T-test, Mann Whitney U-test, ANOVA and Kurksal Wallis tests and the relation between the variables were evaluated using Pearson and Spearman correlation coefficient.  $P < 0.05$  was considered meaningful.

### **3. Results**

From the 50 patients with MS, 30% were males and 70 % females. From the 40 patients with vasculitis, 22.5% were males and 77.5% female and there were 11 males (22%) and 39 females (78%) in control group. There was no meaningful difference regarding gender distribution between the three groups of patients with MS, vasculitis and the people of control group and all three groups were homogeneous regarding gender ( $P = 0.424$ ). Gender distribution in different types of MS in patients is

brought in table I. The mean age of the patients with MS was  $33.86 \pm 9.04$  years in the range of 18-54 years. The mean age of the patients with vasculitis was  $35.10 \pm 9.80$  years and  $34.23 \pm 8.45$  years for the people of control group. There was no meaningful difference regarding age between the three groups and all three groups were homogeneous regarding age ( $P = 0.535$ ). The mean age of symptoms onset was  $25.62 \pm 5.55$  years for patients with MS and  $29.65 \pm 8.25$  years in the patients with vasculitis which revealed a meaningful lower age for symptoms onset in patients with MS ( $P = 0.007$ ). There was no meaningful difference between the different types of MS regarding symptoms onset age ( $P = 0.482$ ). The mean time between symptoms onset and definite diagnosis in patients with MS was  $13.06 \pm 8.03$  months and  $8.17 \pm 4.96$  months in patients with vasculitis which was meaningfully less ( $P = 0.001$ ).

The most common onset symptoms in patients with MS were optic neuritis (42%), paresthesia (22%) and paraparesia (16%). 11 people (22%) of patients with MS had spinal symptoms (including paraparesia, urinary incontinence and Lehermit sensory level) in the beginning of the disease and 22 people (44%) within study period. The frequency of spinal cord MRI changes in patients with MS is brought in chart I (abnormal MRI means existence of focal or diffused demyelinated lesions.)

The frequency of spinal cord MRI changes has been summarized in table I according to the MS type.

From the 10 patients with demyelinated lesions in cervical cord, only six people had focal demyelinated lesions, 6 had diffused lesions and two people had focal and diffused demyelinated lesions. The maximum number of focal lesions was three and the maximum number of the involved spinal segments was two, mostly in C4 and C3 levels. Three segments were the most involved segments with diffused demyelinated lesions (mainly in C5 and C3). The frequency of focal lesions in cervical cord MRI is brought in table I according to MS types.

From the total 50 the patients with MS, only four people had diffused lesions in spine that were all related to Primary Progressive (P-P) type. From the 22 patients with MS, having spinal symptoms during the study, focal lesions were revealed in the cervical cord MRI of eight people (36.4%) whereas the lesions were found in 28 patients with MS who had no spinal symptoms. Diffused lesions were also found in the cervical cord MRI of four patients (18.2%) who had spinal symptoms whereas the lesions were found in the 28 patients with MS who had no spinal symptoms.

The mean expanded disability status scale (EDSS) was  $3.08 \pm 2.15$  in all patients with the maximum EDSS of 7.5 and the minimum of 1. There

was a meaningful statistical difference between EDSS and MS types ( $P < 0.0001$ ) and this meaningful difference is seen in chart II. There was no meaningful difference between the time of being affected by MS and transverse cross-section of cervical cord ( $P = 0.45$ ,  $r = -0.109$ ).

There were 40 patients with vasculitis including 19 patients with systemic lupus erythematosus, 12 patients with Behcet syndrome, seven patients with antiphospholipid syndrome and two patients with temporal arthritis in whose cervical cord MRI no parenchymal lesions were found. Cerebral symptoms in patients with vasculitis included seizure, blurred vision and stroke. The youngest patient with vasculitis was 20 years old and the oldest was 64. The youngest age for vasculitis symptoms onset was 18 and oldest was 60.

The mean transverse cross section of spinal cord in C4 and C5 was meaningfully less in patients with MS compared to the patients with vasculitis and the control group ( $P = 0.006$ ) (Chart III) but there was no meaningful difference between the patients with vasculitis and the control group ( $P = 0.999$ ). But most and least transverse cross-section of spinal cord were 84 mm<sup>2</sup> and 66.40 mm<sup>2</sup> for the patients with MS, 81.24 mm<sup>2</sup> and 77.47 mm<sup>2</sup> for the patients with vasculitis and 80.42 mm<sup>2</sup> and 77.69 mm<sup>2</sup> for the control group. The mean transverse cross section of cervical cord was meaningfully less in patients with P-P type MS compared to the other types ( $P < 0.0001$ ) which is brought in chart IV. The most and least transverse cross-sections of the cervical cord in P-P type were 77.60 and 66.44 accordingly, in Secondary progressive(S-P) type 80.20 and 70.30, in Relapsing Remitting(R-R) type 84 and 73.60 mm<sup>2</sup>.

The mean EDSS for the patients with MS having abnormal MRI was meaningfully more than patients with normal MRI ( $P = 0.004$ ) which is shown in chart V. There was a meaningful and the reverse relations between EDSS mean and transverse cross-section of cervical cord ( $P < 0.001$  and  $r = -0.623$ ) as disability degree increased when transverse cross-section of cervical cord decreased. This relation is shown in table II by MS types.

The mean transverse cross section of cervical cord was  $73.40 \pm 4.38$ mm<sup>2</sup> in nine patients with MS having abnormal MRI and  $77.23 \pm 3.48$ mm<sup>2</sup> for the patients with normal MRI. The mean transverse cross-section of cervical cord was meaningfully less in the patients with abnormal MRI compared to the patients with normal MRI ( $P = 0.006$ ). The mean transverse section of the cervical cord was  $76.70 \pm 5.49$ mm<sup>2</sup> in males and  $76.74 \pm 3.70$  mm<sup>2</sup> in the females having MS.

Table 1. Gender distribution, Frequency of MRI changes of cervical spinal cord and focal lesions in the spinal cord of MS patients by different types of disease

MS type	Gender		MRI		Local Lesions	
	Male	Female	Normal	Abnormal	Positive	Negative
Relapsing Remitting(R-R)	23	8	28	3	3	6
Secondary progressive(S-P)	1	9	8	2	2	8
Primary Progressive(P-P)	6	3	4	5	3	28

Table 2. Correlation of EDSS with cross-section of cervical cord by different MS types

MS type	R	P_ Value
Relapsing Remitting(R-R)	-0.191	0.304
Secondary progressive(S-P)	0.086	0.812
Primary Progressive(P-P)	-0.881	0.002
Total Ms Patients	-0.623	<0.0001

#### 4. Discussions

The frequency of demyelinated lesions in the cervical cord of the patients with MS was 20% which was significantly more in the patients with progressive type compared to the relapsing-remitting type ( $P = 0.036$ ). This 20% would definitely increase if spinal atrophy is also included. In the study of Filippi et al, from 96 patients with MS only 81 people had abnormal cervical cord images (Filippi, 2000).

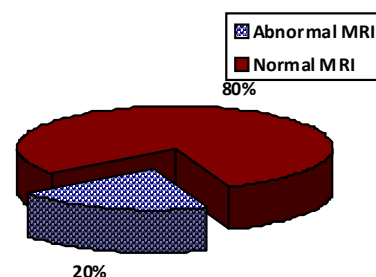


Chart 1. Frequency of MRI changes of cervical spinal cord in MS patients

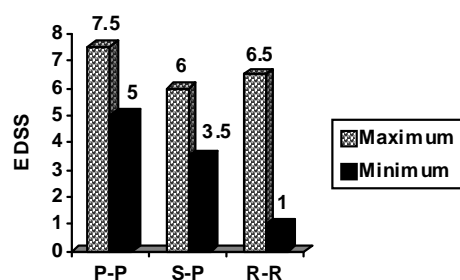


Chart 2. The mean, minimum and maximum of EDSS in MS patients by different MS types

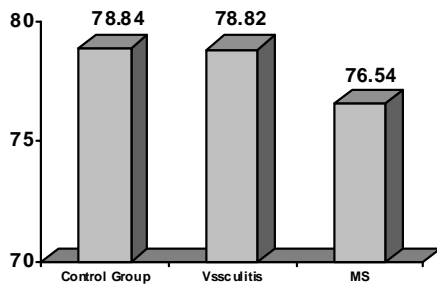


Chart 3. Mean cross-section of cervical cord (mm<sup>2</sup>) in the three groups under study

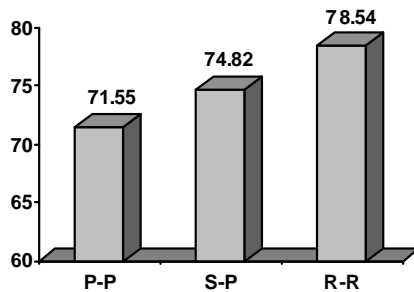


Chart 4. Mean cervical spinal cord profile area (mm<sup>2</sup>) by different MS types

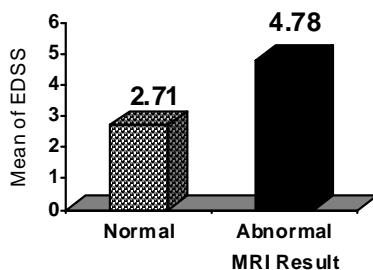


Chart V. Mean EDSS and MRI result of cervical spinal cord in MS patients

In two studies carried out in India and Thailand the frequency of abnormal MRI was accordingly reported as 93.75% and 86.66% and in the study carried out in Thailand the frequency of abnormal cervical cord MRI was 40% (Mani, 1999; Chawalparit, 2006). In the study of BOT, the frequency of focal lesions in entire spine was 70.02%, for the diffused lesions 2.9% and combination of both lesions 9.6%. (Bot, 2004).

In the study of Bonek, demyelinated lesions on the entire spine of the patients with MS were reported as 47-90% (Bonek, 2007). In the study of Chong et

al, 29% of the spinal lesions in the patients with MS were in cervical and thoracic regions (Chong, 2006). The time of being affected by MS, the percentage of the MS types being studied, receiving medication or not, MRI unit power and evaluation degree of spine can affect prevalence rate. On the other hand according to the study of Bot et al, almost 50% of spinal lesions are missed when only cervical spine is studied (Bot, 2004).

In our study 11 people had spinal symptoms in the beginning of their diseases which increased to 22 people (two times more) during the study from which 12 people (54.6%) had focal or diffused lesions in their spines. In the study of Bot et al 52% of the patients also had spinal symptoms during this study (Bot, 2004).

The mean duration between the first symptoms of the disease and the definite diagnosis in this study was  $13.06 \pm 8.03$  months for the patients with MS and  $8.17 \pm 4.96$  months for the patients with vasculitis which was a meaningful difference. The early diagnosis of vasculitis compared to MS is due to different reasons such as vasculitis having broader systemic signs, being considered by physicians, MS having more subtle clinical signs and .... In the study of Bot et al the study duration was 18.4 months (Bot, 2004).

As mentioned before, in our study demyelinated lesions in the cervical spine of the patients with progressive type MS are meaningfully more than R-R type.

In the study of Bonek et al, demyelinated lesions were found in cervical spine 62%, i.e 50% for R-R, 60 % for P-P and 75% for S-P types (Bonek, 2007). These differences are due to MRI power in diagnosing plaques, time duration between symptoms onset and definite diagnosis and other reasons. For instance, our patients being referred earlier, treated or our samples being few might have affected the current study. In Vaithianathar et al study, cervical spine MRI is mentioned to be able to differentiate between different types of MS as in progressive type vertical spine lesion are more frequent than R-R type (Vaithianathar, 2003).

The mean EDSS of the patients in our study in P-P, S-P, R-R types were accordingly 1.61, 4.90, 6.11 which had meaningful relation ( $P < 0.0001$ ) which were in accordance with studies of Bonek, Vaithianathar, Benedetti and Zivadinov (Bonek, 2007; Vaithianathar, 2003; Benedetti, 2006; Zivadinov, 2008).

The mean EDSS had a meaningful relation with MRI results in our study ( $P = 0.004$ ) as EDSS was much higher in the patients with abnormal cervical spine compared to the ones with normal cervical spine. These results are also in accordance with the



studies of Benedetti and Vaithianathar (Vaithianathar, 2003; Benedetti, 2006) which indicates that the result of cervical MRI could be helpful in predicting prognosis of the disease.

The study of the mean and transverse cross-section of cervical spine between different types of MS revealed that the patients with progressive, especially P-P, type MS have considerably lower cervical spine cross section compared to the R-R type patients which suggests that cervical spine atrophy is related to the progression of the disease. In the study of Bonek, total spine atrophy was reported in 13-41% of the patients (Bonek, 2007). But the most spinal atrophy was reported in S-P patients, which patient follow-up period would have caused this paradox.

In the present study, R-R type MS patients show no significant difference regarding cervical spine cross-section with the control group. Bot, in his studies, found out that spinal disorders are more frequent in patients with early stage MS (Bot, 2004). Rashid, in his study, showed that R-R type MS has no meaningful impact on cervical spine cross-section (Rashid, 2006). In Agosta study, the grey matter of vertical spine showed atrophy in the patients with R-R type MS compared to the control group (Agosta, 2007). But in the study of Rovaris patients with R-R type MS had no diffused injuries in the cervical spine (Rovaris, 2008). But in the study of Uros Rot this was not confirmed (Rot, 2008). Therefore most of the previous studies confirm the results obtained from our study regarding the cross-section of cervical spine in the patients with R-R type MS. At the mean time it can be said that degenerative changes start from the beginning of the disease and the study of the spine using accurate methods such as MRS can reveal these changes sooner than conventional MRI. Therefore Blamire in his studies suggested that a combination of MRI and MRS could provide a more complete picture of neuro-degeneration in the spine (Blamire, 2007).

In the present study, 40 patients with vasculitis were also studied regarding cervical spine in whom no parenchymal lesions or obvious atrophy were found which is in accordance with the studies of Flippi, Mani and Rovaris (Filippi, 2000; Mani, 1999; Rovaris, 2002; Rovaris, 2000).

It was concluded in Bot's study that unlike MS, cord lesions are uncommon in inflammatory diseases and these findings can assist with differential diagnosis (Bot, 2002). Studies with paradoxical results also exist showing cervical spine changes in patients with vasculitis (Yesilot, 2007; Ilniczky, 2007; Cakirer, 2003).

In a study Mentzel showed that in some German patients suffering Wager disease, there were posterior epidural masses in cervical spine (Mentzel,

2003). In a report presented by Mimenza –Alvarado, it has been mentioned that that disorders of brain stem in the patients with lupus are one of the rare CNS involvements (Mimenza-Alvarado, 2002). And in another report presented by Campi on two patients having primary CNS angiitis, it was reported that most of these lesions were small, enhancing and mainly located in the posterior parts of the spine (Campi, 2001).

Lin, in his study, suggested that the beginning of the disease (R-R MS) atrophy is limited to supratentorial area and in S-P stage there are some visible atrophies in the brain and cervical cord and the volume of brain and cervical cord is a valuable index of irreversible pathologic process in MS and considering the volume of supratentorial and lateral ventricles, cerebellum and brain stem is of great importance in evaluating the volume of all cervical cord in patients (Lin, 2003). Rashid suggested in his studies that there is a powerful relation between cervical spine cross-section and the total intracranial volume and that cervical spine cross section is smaller in females (Rashid, 2006). We studied the spinal cord separately from the other variables in our study and cervical spinal section had no meaningful difference in female patients compared to the males.

Other issue is the existence of OSMS, optical spinal MS, in Asians. In a study carried out in Japan, one fourth of the patients with conventional MS had wide longitudinal lesions and it was shown in the study that wide longitudinal cord lesions were meaningfully more common in OSMS patients compared to conventional MS patients and wide longitudinal cord lesions were commonly located in upper and middle parts of the thoracic spine in OS MS patients (Lin, 2003). Chong in a study suggested that the Asian patients have bigger spinal lesions (Chong, 2006). In a study carried out in Japan by Jun-Ichi Kira, it was reported that MS in Asian population is defined by severe and selected involvement of optic nerve and spine and almost 15-40% of MS types are optic spinal types in Japan which are associated with less brain lesions in MRI and longitudinal lesions in several vertebral segments (Kira, 2003). In the present study, also patients with MS had findings in their brains confirming MS. Only 22% of the patients had spinal symptoms in the beginning of their diseases. At the mean time the maximum number of the spinal segments showing demyelinated lesions was three segments. It should be considered that the patients with MS may refer to us only having spinal symptoms and cervical involvements in MRI.

On the other hand the characteristic appearance of spinal lesions in the patients with MS can be helpful in differentiating MS from other diseases

when the lesions are atypical. For instance contrast agent absorption by leptomeninges, lesions occupying more than half of the cord width, and hypo-intense lesions in spine T1 have been rarely reported, but the physician should be suspicious about vasculitis diseases (Bot, 2004). No pathologic findings were found in the patient with vasculitis in our study in cervical spine so that we can compare their characteristics with the patients with MS, contrast agent was not used on the other hand.

As for patients had been diagnosed by MS using McDonald's criteria, clinical findings and brain MRI, we were not able to evaluate the role of cervical spine MRI changes in approving or disapproving definite MS diagnosis but it is suggested in the study that when the spinal lesion, based on McDonald's criteria, is used, the number of patients not having MS criteria decreased from 35 cases to 16 (Bot, 2004). On the other hand in the mentioned study it was suggested that spinal lesions are independent of brain lesions and there is no powerful relation between brain and spine abnormalities.

In the MS patients of our study, EDSS had a meaningful relation with the cervical spine cross-section and in the patients with smaller cervical spine, disability degree was higher. Brain and spine tissue damage is one of the major causes of disability in MS patients and it has been shown in a study that the most brain and spine atrophy happens in the patients needing walking aid (Blamire, 2007) and in the study carried out by Blamire, using MRS, patients with EDSS= 2.5-7 had spinal atrophy (Blamire, 2007). It can be concluded that neuronal injury in cervical spine is related to the functional disability degree in the patients with MS. The study of cervical spine cross section and the result of cervical MRI in MS patients also revealed meaningful relation between these two variables meaning that cervical spine cross-section of the patients with demyelinated lesions in cervical spine was smaller in the patients without these lesions which may be indicating that patients with cervical spine demyelinated lesions in their spine are more probable to have atrophy in cervical spine followed by disability regression in the future.

### Conclusion

In this study, from every five patients with MS one patient had demyelinated lesions in cervical spine which was more obvious in progressive types and atrophy degree of cervical spine was more in the patients with P-P and S-P types compared to the patients with R-R. We found no pathologic finding in cervical spine parenchyma of the patients with vasculitis. It shows that using cervical spine MRI can be helpful in differentiating MS from the inflammatory diseases especially in uncertain

conditions. On the other hand existence of demyelinated lesions and atrophy in the cervical spine of the MS patients can also be helpful in differentiating MS types, choosing medication type and predicting clinical status of the patient in the future. Administrating early treatment can also prevent demyelinated lesions and spine atrophy and EDSS increase rate. Although MS patients in our study were definitely diagnosed in advance, it can be said that cervical spine study especially in uncertain MS cases can help clinical findings and brain MRI and reduce the time needed for definite diagnosis and early treatment, disability degree and the speed of disease progression. It is accepted that an increase in the power of MRI unit, diverse and accurate imaging techniques such as MRS, total spine study and increasing the volume of study can affect the obtained results from this study.

### Suggestions:

Based on the results obtained from this study, it is suggested that in evaluating imaging results of the patients with suspected MS, spine MRI specially cervical spine should be carried out. Also in uncertain cases which MS disease cannot be differentiated from other diseases such as vasculitis, spinal MRI should be used. It is also suggested that further studies with higher sample volume and total spine studies be carried out.

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