Hypoglycemic Efficacy of Date Kernels Coffee on Diabetic and Nephrodiabetic Patients

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Abstract: Recently, date seeds powders are marketed and are a source of choice to people preferring a non-caffeinated coffee with coffee-related flavor. In addition, insulin-date seed extract combination minimizes the toxic effects of diabetes. Hence, the study aimed to find out the efficacy of the date kernels drink in ameliorate serum glucose and insulin resistance. Fifty five patients, ten of them were classified as **negative control group (NCG)**, and forty five patients received their standard medical treatment (tablets or insulin). The date kernel coffee (DKC) supplementation is given to every patient in the experimental groups twice daily in cups. Each cup contains 10g of DK in 200 ml. this was given for three consecutive months. Patients were divided into subgroups as follows: **Diabetic control group 1 (DCG1)** receiving their medical tablets only along the experimental period; **Diabetic group 1 (DG1)**treated with the same tablets plus DKC supplement; **Diabetic control group 2 (DCG2)** received their medical insulin only along the experimental period; **Diabetic group 2 (DG2)**treated with the same dose of insulin plus DKC supplement; **Nephro-diabetic control group (NDCG)** received their medical treatment only along the experimental period; **Nephro-diabetic group (NDG)** received their medical treatment plus DKC supplement. The results indicated that fasting glucose to insulin ratio (FG/I ratio) was significantly diminished ($p \leq 0.001$) after administrating DKC. Significant amelioration on markers of insulin resistance (HOMA-IR) was induced in diabetic and nephrodiabetic patients treated with insulin as compared to baseline (by means of 2.61±0.30 versus 2.09±0.38 at ($p\leq$ 0.001) and 6.10±1.03 versus 3.82±0.39 at ($p\leq0.05$)). β-cell function index had significantly increased at ($p\leq0.001$) and NDG had the best effect by mean of 1.07±0.05 versus 0.49±0.03 at baseline. We concluded that serum glycemic profiles had significantly improved after treatment.
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Key words: date kernels coffee, insulin resistance and diabetes.

1. Introduction

Date palm is one of the oldest trees cultivated by man **(Vayalil, 2012).** Dates are mentioned in several verses in the Holy Quran. Muslims everywhere used to break fasting at the end of each day during the holy month of Ramadan **(Al-Shahib and Marshall, 2003)**. The date palm (*Phoenix dactylifera L.*) has been an important crop in Egypt and Middle Eastern countries. Date production of Egypt alone represented about 20% of the total world production for 2008 **(Arab Organization for Agricultural Development (AOAD), 2008; and El-Juhany, 2010)**.

Diabetes mellitus is increasingly becoming a major chronic disease health burden all over the world. In 2011, about 14 million individuals were estimated to have diabetes in Africa, and this is expected to rise to 28 million by 2030 **(International Diabetes Federation, 2011)**.In traditional Egyptian medicine, *Phoenix dactylifera L.*, (date palm) seeds are listed in folk remedies for the management of diabetes, liver diseases and gastrointestinal disorders **(Abdelaziz and Ali, 2014)**. The glycemic index (GI) of different varieties of dates ranged between 47.6 and 57.7 (**Ali *et al.*, 2009**). Moreover, date seeds contain higher protein (5.1 g/100 g) and fat (9.0 g/100 g) as compared to the flesh. It is also high in dietary fiber (73.1 g/100 g), phenolics (3942 mg/100 g) and antioxidants (80400 micromol/100 g).

Recently, date seeds powders are marketed and are a source of choice to people preferring a non-caffeinated coffee with coffee-related flavor **(Baliga *et al.*, 2011)**. Administration of date seeds extract is safe on the liver and kidney. In addition, date seed extract in combination with insulin minimizes the toxic effects of diabetes as mentioned by **El-Fouhil *et al.* (2011)**.

There are few published data on antidiabetic effect of date palm seeds in diabetic patients. Accordingly, the present study aimed to find out the efficacy of the date kernels drinktoameliorate serum glucose and insulin resistance.

2. Patients and Methods

1. Date kernels

The study was conducted on date kernels of "Sukkary "date (*Phoenix dactylifera L.*) that purchased from the sale and distribution outlet of the Center for Public Service at the Faculty of Agriculture, Menufiya University, Egypt. Total amount of kernels were directly isolated from 5kg of date fruit and represent about 11-18% of the date fruit flesh as the same findings of **Amira *et al.* (2011)**. The mean weight of each kernel is11.69±0.70 g.

2. Preparation of date kernels powder

The kernels were manually separated from the flesh fruit and washed clear of any adhering date flesh by water, repeatedly for several times. Then soaked in water more than once, then washed in hot water more than once, too, and then scrubs by the hand to coarsely pounded date impurities, and then dried in the sun for a period ranging from 7 to10 days. The dried date kernels were oven dried for seven days at 50°C and then finely ground into powder using a stainless-steel blender. After that, the date kernels powder becomes ready to use and then preserved at -20^{o} C till used for chemical analysis and for drink.

3. Chemical Analysis of date kernels powder:

3.1. Methods of measuring macronutrients

Moisture, crude protein, lipids, fiber and ash were determined by the standard procedures of the **AOAC (2000)**. All analytical determinations were carried out in triplicate and the final data were expressed on a dry weight basis. Carbohydrates were estimated by difference as dry matter basis as follows: %Carbohydrates=100-(%protein+%fat+%fiber+ %Ash). Total phenols content also were determined in addition to the identification of phenolic compounds by HPLC according to the folinciocalteu method as mentioned by **Meda *et al.* (2005)**.

3.2. Methods of measuring micro minerals

Accurately weighed sample (3g) of date kernels powder in a crucible was subjected for as hing in furnace for 4 hours at 550 ºC. After cooling in desiccators, 2.5 mL of 6N HNO3 was added to the crucible. The solution was filtered and diluted up to 100 mL with distilled water. The solution was analyzed for K, Mg, Ca, P, Zn and Fe by using Atomic Absorption Spectrophotometer (AAS-Perkin Elmer, Model analyst 800). (Khan *et al*., 2008; Hussain *et al*., 2009; Hussain *et al*., 2010).

4. Preparation of date kernel coffee (DKC) as a drink for diabetics:

An equivalent amount of twice tea spoon of the powder (10g) was added to a cup of water and prepared like Arabic coffee without sugar, the mixture was boiled until it becomes brownish in color then filtered to be ready for drinking a non-caffeinated coffee with coffee-related flavor twice a day, once in the morning and once in the evening by a cup of tea for three consecutive months (**Abdelaziz and Ali, 2014**).

5. Experimental design

Fifty five (55) volunteers (60% females (33 case) and 40% males (22 case), aged 36 to 87 by mean 52.65±10.78 years old agreed to participate in the study during the period between March to September 2013.

The subjects were selected from outpatient clinics in Cairo University Hospitals under Medical supervision of the staff member. Metformin at a dose of 1000 mg was given orally twice a day with meals. Insulin injection was given to the patients according to the level of blood sugar.

Ten volunteers were normal and healthy, they didn't receive any supplements along the experimental period, were recruited as **negative control group (NCG)**, the other forty five volunteers with inclusion criteria over 18 years of age, and were diabetic for a period less than one year, and not suffering from other diseases and agreed to sign the consent form, and received their standard medical treatment (tablets or insulin). They accepted to drink a cup of date kernels coffee (DKC) twice a day (each cup contain 10 g of DK per cup 200 ml) for three consecutive months, they were divided into subgroups as follows: **Diabetic control group 1 (DCG1)** included ten diabetic patients that received their medical treatment (tablets twice a day) only along the experimental period. **Diabetic group 1 (DG1)** included ten diabetic patients treated with the same tablets plus DKC supplement. **Diabetic control group 2 (DCG2)** included five diabetic patients receiving their medical treatment (insulin twice a day) only along the experimental period. **Diabetic group 2 (DG2)** included ten diabetic patients treated with the same dose of insulin plus DKC supplement. **Nephro-diabetic control group (NDCG)** included five nephro-diabetic patients receiving their medical treatment only along the experimental period (insulin twice a day). **Nephro-diabetic group (NDG)** included five nephro-diabetic patients receiving their medical treatment (insulin twice a day) plus DKC supplement.

6. Anthropometric measurements:

Anthropometric measurements included body weight and body height were determined according to (**Jellife, 1966).**Body mass index (BMI) was calculated as body weight in kg divided by the square of the height in meters (kg/m2) according to **Geoffrey (1995).**

6. Biochemical Analysis:

Venous blood samples from fasting volunteers were obtained. Blood samples were obtained by venipuncture at two time points: the initial Week

(*baseline, immediately before the trial began*) and at the end of three consecutive months (*after cases stopped consuming the supplementation*).The following blood parameters were determined; Enzymatic colorimetric method used to determined blood glucose according to **Trinder (1969).** Insulin was estimated according to **Wilson and Miles (1977)**. Serum alanine aminotransferase (ALT) was determined according to the method of **Satoh and Clinica Chemica Acta (1978)**.Serum asparatate aminotransferase (AST) was determined according to the method of **Hafkenscheid, (1979)**. Serum alkaline phosphatase (ALP) was determined according to the method of **Moss (1982)**.Serum urea was determinate by enzymatic method according to **Patton and Crouch (1977)**.Serum creatinine was determined according to the method described by **Henry (1974)**. Uric acid determination was according to **Carawy, (1955)**. HbA1c levels were determined using the Immunoturbidimetric method by using Roche Cobas Integra 400 plus autoanalyzer (Roche, Mannheim, Germany).

***7.* Homeostatic model assessment**

Using the serum glucose and insulin concentrations during fasting, we calculated the following parameters:

A. FG/I ratio, fasting serum glucose (mg/dL) to fasting serum insulin concentration (micro-international units per mL) (**Galluzzo *et al.*, 2008**).

B. HOMA-IR (homeostasis model assessment for insulin resistance) = fasting serum insulin (microinternational units per mL) × fasting serum glucose (mmole/L) / 22.5 (**Radziuk, 2000**and**Quon, 2001**).

C. β cell function index = 20 × fasting serum insulin (microinternational units per mL) concentration/fasting serum glucose concentration (mmole/L) - 3.5 (**Lord*et al.*, 2003**).

***8.* Statistical analysis**

The results were expressed as Means ± Standard Deviation. All data were computerized using the Statistical Package for Social Sciences (SPSS, version 22) (**SPSS, 2015**). The results were statistically analyzed by using one-way analysis of variance (ANOVA) followed by Duncan's multiple range test (DMRT) for comparison between different treatment groups. Statistical significance was set at $P< 0.05$, $P< 0.01$ and $P< 0.001$.

***9.* Ethical Consideration**

Each one of subjects were informed about the protocol, objectives, and duration of the study then persons who met the inclusion criteria and agreed to participate were enrolled in the study and received suggested supplementation (DKC) for three consecutive months.

3. Results and discussion

***1.* Chemical composition of date kernels**

Table (1) shows the main chemical composition (%) of date kernels powder on dry matter basis.

Table(1): The main chemical composition (%) of date kernels powder on dry matter basis.

	Moisture	Protein	Fat	Fiber	Ash	CHO	K.cals
Mean±SD (g/100g)	10.22±0.57	5.41±0.28	9.92±0.79	25.66±3.51	1.16±0.06	47.61±3.72	301.40±14.63

The mean weight of each kernel removed from date fruit flesh sample was 11.69±0.70 gas the same findings of **Al-Shahiband Marshall, (2003)** and **Amira *et al.* (2011)** who obtained that about 11-18% of the seeds comes from date fruit. Normally, seeds are composed of macronutrients as proteins, carbohydrates and lipids, the average contents were 5.41±0.28, 47.61±3.72and 9.92±0.79 respectively. Furthermore, **Al-Shahib and Marshall (2003)** mentioned that date kernels contain 5.1%protein and 9% fat when compared to the flesh. Also, the results found a higher amount of dietary fiber as 25.66±3.51g per100g as evaluated by **Ishrud *et al.*, (2001)** who isolated a water-soluble polysaccharide from the seeds of dates. Moreover, **Al-Faris and Lee (2008)** showed that more than half of insoluble dietary fiber namely as hemicelluloses, cellulose and lignin beside resistant starch. Energy value of dried date kernels was 301.40±14.63 kcals per100g as mentioned by **Juhaimi *et al.* (2012)**. This information on nutritional aspects enhance the appreciation for the use of dates in the daily diet and their seeds as a functional food ingredient.

***2.* Main minerals in studied sample of date kernels**

Macro and micro minerals content as mg per 100g of date kernels powder on dry matter basis are listed in table (2).

Table (2): Macro and micro minerals content as (mg/100g) of date kernels powder on dry matter basis.

	K	Mg	Ca	P	Zn	Fe
Mean±SD (mg/100g)	361±3.61	89.66±2.08	62.33±2.08	44.66±2.51	4.93±0.27	3.98±0.21

For the macro-elements, potassium concentration was the highest (361±3.61mg %), followed in descending order by magnesium (89.66±2.08mg%), calcium (62.33±2.08mg %) and phosphorus (44.66±2.51mg%). Regarding to micro-elements, zinc showed the highest concentration (4.93±0.27mg %), followed in descending order by iron (3.98±0.21mg %), these results were in agreement of that reported by **Omri *et al.* (2010)** and **Juhaimi *et al.* (2012)**.

***3.* Phenolic compounds of date kernels**

Table(3) show the differential phenolic compounds of date kernels on dry matter basis.

Table (3): Different phenolic compounds of date kernels powder

Items	ppm	Items	ppm
Syringic	0.20	Epicatechen	557.08
Pyrogallol	376.02	Caffeic	43.12
Gallic	7.93	Vanillic	83.60
Protocatechuic	44.35	Caffein	17.63
Catechol	15.48	Ferulic	27.77
4-Aminobenzoic	83.39	Benzoic	31.59
Catechein	71.22	Ellagic	10341.63
Chlorogenic	249.61	Coumarin	10.57
P.OH.Benzoic	202.82	Cinnamic	66.65

* ppm = part per million

The polyphenol contents of date seeds were shown to be safe and supplya good source of natural antioxidants, hypoglycemic, hypolipidimic effect, and could potentially be considered as a functional food as reported by **Al-Farsi *et al.* (2005)**. The higher aspects of total phenolic acid contents of seeds were found as ellagic acid which was 10341.63 ppm, then chlorogenic which was 249.61 ppm and epicatechen which was 557.08ppm. In addition, free phenolic acids including protocatechuic acid which was44.35 ppm, vanillic acid was 83.60 ppm, syringic acid0.20 was ppm and ferulic acid was27.77 ppm. Moreover, bound phenolic acids including gallic acid which was7.93 ppm, p-hydroxybenzoic acid was202.82, caffeic acid was43.12 ppm andcoumarin acid was10.57 ppm, were tentatively identified, these results are in parallel with those obtained by **Juhaimi*et al.* (2012)**. Other phenolics including caffeine, pyrogallol, catechol, 4-Aminobenzoic and cinnamic acids were similar to that reported by **Hammouda *et al.* 2013**).

***4.* Anthropometric measurements**

Anthropometric measurements of diabetic and nephrodiabetic patients are listed in table (4).

Table (4): Anthropometric measurements of diabetic and nephrodiabetic patients

		NCG	Diabetic patients treated with tablets.			Diabetic patients treated with insulin.			Nephro-diabetic patients treated with insulin.		
			DCG1	DG1	Mean Differ.	DCG2	DG2	Mean Differ.	NDCG	NDG	Mean Differ
Type	Male	4	3	3	--	2	5	--	2	3	--
	Female	6	7	7	--	3	5	--	3	2	--
Age (year)		58.00±17.60	43.90±4.93	52.60±7.60	--	57.20±6.18	51.20±9.14	--	55.80±10.89	54.80±5.40	--
Height (cm)		1.62±0.04	1.65±0.04	1.63±0.06	--	1.65±0.06	1.64±0.05	--	1.64±0.07	1.59±0.06	--
Weight (Kg)	Before	90.40±16.11	93.60±17.03	84.80±16.78	8.80 NS	81.80±11.32	97.30±16.66	-15.50 NS	79.20±19.85	73.40±7.02	5.80 NS
	After	88.15±12.20	94.90±18.79	85.20±14.52	9.70 NS	80.20±10.71	98.05±14.77	-17.85*	77.20±19.12	71.20±6.42	6.00 NS
% of change		-2.49	1.39	0.47	--	-1.96	0.77	--	-2.53	-2.99	--
T. value		1.274 NS	-1.165 NS	-0.343 NS	--	1.042 NS	-0.929 NS	--	2.390 NS	2.557 NS	--
BMI (Kg/m^2)	Before	34.17±4.52	34.32±5.12	31.88±4.59	2.44 NS	29.84±3.09	36.44±7.02	-6.60 NS	29.20±6.07	29.18±3.32	0.02 NS
	After	33.38±3.29	34.79±5.81	32.11±4.15	2.69 NS	29.25±2.68	36.71±6.37	-7.46*	28.48±5.89	28.32±3.22	0.16 NS
% of change		-2.31	1.37	0.72	--	-1.98	0.74	--	-2.47 NS	-2.95	--
T. value		1.220 NS	-1.163 NS	-0.522 NS	--	1.059 NS	-0.891 NS	--	2.408 NS	2.540 NS	--

NCG: Negative Control group; DCG1:Diabetic control group1; DG1:Diabetic group1;DCG2: Diabetic control group2; DG2:Diabetic group2; NDCG: Nephro-diabetic control group; NDG: Nephro-diabetic group; BMI: Body mass index. Mean differ: Mean difference statistics between values at baseline and after supplementation. Significant difference between values at baseline and after month statistics by paired sample t-test. NS: Not significant, * significant in: $p<0.05$, ** significant in: $p<0.01$,***significant in: $p<0.001$.

Table (4) shows the characteristics of the studied patients. Most diabetic patients were females while men were higher than women with nephron diabetes in our sample. The age ranged from 43.90±4.93 to 58.00±17.60 years. For BMI, there was non-significant changes among studied groups, except between DCG2 and DG2 at p<0.05 after administration of DKC.

***5.* Renal functions of diabetic and nephrodiabetic patients**

Renal functions of diabetic and nephrodiabetic patients before and after oral administration of DKC are listed in table (5).

Table (5): changes in urea, creatinine and uric acid in blood ofdiabetic and nephrodiabetic patients before and after oral administration of DKC

		NCG	Diabetic patients treated with tablets.			Diabetic patients treated with insulin.			Nephro-diabetic patients treated with insulin.		
			DCG1	DG1	Mean Differ.	DCG2	DG2	Mean Differ.	NDCG	NDG	Mean Differ.
Urea (mg/dl)	Baseline	34.87±9.79	58.80±12.25	49.20±6.23	9.60*	52.60±6.69	54.30±8.34	-1.70 NS	77.20±6.02	61.80±8.96	15.40*
	After	36.50±8.07	57.40±11.95	41.90±5.49	15.50**	50.00±6.12	48.90±8.24	1.10 NS	72.20±5.17	49.80±7.22	22.40***
% of change		4.67 NS	-2.38NS	-14.84**	--	-4.94 NS	-9.94***	--	-6.48NS	-19.42*	--
T. value		-1.412	0.464	5.104		2.152	5.713		1.876	4.022	
Sig.		0.192	0.654	0.001		0.098	0.000		0.134	0.016	
Creatinine (mg/dl)	Baseline	0.79±0.12	1.05±0.37	0.95±0.29	0.11 NS	0.61±0.11	0.90±0.24	-0.30*	1.07±0.17	1.81±0.79	-0.74 NS
	After	0.74±0.11	0.98±0.38	0.83±0.23	0.15 NS	0.55±0.09	0.74±0.16	-0.19*	1.02±0.18	1.21±0.37	-0.20 NS
% of change		-6.33NS	-6.67NS	-12.63NS	--	-9.84NS	-17.78 **	--	-4.67NS	-33.15*	--
T. value		1.539	1.679	2.178		2.401	3.897		2.620	3.131	
Sig.		0.158	0.128	0.057		0.074	0.004		0.059	0.035	
Uric acid (mg/dl)	Baseline	5.26±1.07	6.02±1.18	5.07±1.70	0.95 NS	4.35±0.59	4.83±1.30	-0.47 NS	5.78±0.38	4.67±1.08	1.11 NS
	After	4.70±0.71	6.14±1.26	4.60±1.01	1.54*	4.17±0.33	4.29±0.92	-0.12 NS	5.58±0.54	3.99±0.`17	1.58*
% of change		-10.65*	1.99NS	-9.27NS	--	-4.14NS	-11.18 *	--	-3.46NS	-14.56NS	--
T. value		2.453	-0.578	1.453		0.692	2.583		1.877	2.222	
Sig.		0.037	0.577	0.180		0.527	0.030		0.134	0.090	

NCG: Negative Control group; DCG1:Diabetic control group1; DG1:Diabetic group1;DCG2: Diabetic control group2; DG2:Diabetic group2; NDCG: Nephro-diabetic control group; NDG: Nephro-diabetic group. Mean differ: Mean difference statistics between values at baseline and after supplementation. Significant difference between values at baseline and after month statistics by paired sample t-test. NS: Not significant, * significant in: p<0.05, ** significant in: *p*<0.01,***significant in: *p*<0.001. Reference values obtained from: Fischbach and Dunning, (1996).

As shown in Table 5, oral administration of DKC to diabetic decreased renal profiles significantly. DG2 showed a drop in serum urea, creatinine and uric acid by -9.94 (*p*≤0.001), -17.78 (*p*≤0.01) and -11.18% (p≤0.05), respectively. Whilst, NDG had significant difference in urea and creatinine at p<0.05.Whereas for DG1 had significant decrease in serum urea 41.90±5.49at p≤0.01 by-14.84%while no significant difference in serum creatinine and uric acid.

***6.* Hepatic enzymes in diabetic and nephrodiabetic patients**

Table (6) shows hepatic enzymes in diabetic and nephrodiabetic patients before and after oral administration of DKC.

Table (6): Hepatic enzymes in diabetic and nephrodiabetic patients before and after oral administration of DKC

		Control negative group (ve-)	Diabetic patients treated with tablets.			Diabetic patients treated with insulin.			Nephro-diabetic patients treated with insulin.		
			DCG1	DG1	Mean Differ.	DCG2	DG2	Mean Differ.	NDCG	NDG	Mean Differ.
ALT (U/L)	Before	26.20±3.45	63.70±4.27	60.60±5.06	3.10NS	63.20±5.81	52.00±3.86	11.20NS	72.40±4.62	68.20±3.70	4.20NS
	After	26.50±4.74	63.20±4.52	55.70±3.80	7.50NS	62.60±5.77	48.20±3z.05	14.40NS	72.40±7.92	61.80±3.11	10.60NS
% of change		NS	NS	NS		NS	***		NS	***	
T. value		-0.452	0.400	3.280		0.248	7.125		0.000	16.000	
Sig.		0.662	0.698	0.10		0.816	0.000		1.000	0.000	
AST (U/L)	Before	24.70±2.79	58.15±4.87	52.40±4.53	5.75***	58.40±3.91	55.80±5.47	2.60NS	74.80±7.79	70.20±4.38	4.60NS
	After	23.40±2.76	56.80±5.20	47.60±4.38	9.20NS	56.80±6.38	51.40±5.36	5.40NS	66.40±4.16	64.20±2.28	2.20NS
% of change				*			**			*	
T. value		1.073	1.613	3.651		0.726	4.342		2.298	4.243	
Sig.		0.311	0.141	0.005		0.508	0.002		0.083	0.013	
ALP	Before	99.80±7.55	183.70±4.22	182.70±4.32	1.00*	178.20±3.77	179.60±3.10	-1.40**	187.00±7.00	188.60±4.83	-1.60NS
	After	98.20±6.68	184.80±4.47	177.10±3.96	7.70NS	180.00±1.87	174.10±2.47	5.90NS	183.80±7.26	182.40±6.35	1.40NS
% of change				***			**			*	
T. value		0.709	-0.767	6.952		-1.327	4.919		1.502	3.499	
Sig.		0.496	0.462	0.000		0.255	0.001		0.208	0.025	

NCG: Negative Control group; DCG1:Diabetic control group1; DG1:Diabetic group1;DCG2: Diabetic control group2; DG2:Diabetic group2; NDCG: Nephro-diabetic control group; NDG: Nephro-diabetic group. Mean differ: Mean difference statistics between values at baseline and after supplementation. Significant difference between values at baseline and after month statistics by paired sample t-test. NS: Not significant, * significant in: p<0.05, ** significant in: p<0.01,***significant in: p<0.001. Reference values obtained from: Fischbach and Dunning, (1996).

According to hepatic enzymes activity, there was ameliorated impact in diabetic groups after DKC administration in particular DG2 at $P \leq 0.001$ for ALT by mean value of48.20±3.05 U/L. Regarding to DG1, the mean value of AST and ALP was changed significantly, which were 47.60±4.38 ($P \leq 0.05$) and 177.10±3.96 U/L ($P \leq 0.001$), respectively, Whilst NDG had conservative change by mean of64.20±2.28 and 182.40±6.35 at $P \leq 0.05$ respectively. Generally, it could be observed that non significant difference between both control and its corresponding diabetic groups that administered with DKC.

7. Glycemic profiles in diabetic and nephrodiabetic patients

Table(7) showsthe glycemic profiles in diabetic and nephrodiabetic patients before and after oral administration of DKC.

Table (7): Glycemic profiles in diabetic and nephrodiabetic patients before and after oral administration of DKC

		NCG	Diabetic patients treated with tablets.			Diabetic patients treated with insulin.			Nephro-diabetic patients treated with insulin.		
			DCG1	DG1	Mean Differ.	DCG2	DG2	Mean Differ.	NDCG	NDG	Mean Differ.
FBG (mg/dl)	Before	80.40±10.82	233.20±21.77	167.00±45.01	66.20**	156.60±6.35	91.20±11.62	65.40***	198.20±10.83	251.80±13.27	-53.60***
	After	81.90±10.64	239.50±20.87	124.30±36.48	115.20***	136.20±8.58	71.50±6.33	64.70***	194.20±16.27	215.40±18.02	-21.20 NS
% of change		1.87	2.70	-25.57	--	-13.02	-21.60	--	-2.02	-14.46	--
T. value		-0.378	-1.252	3.368		4.230	8.117		0.925	3.380	
Sig.		0.714	0.242	0.008		0.013	0.000		0.407	0.028	
HB A1c (%)	Before	5.67±0.74	11.20±1.27	8.06±0.73	3.14***	7.36±1.07	7.03±1.05	0.33 NS	10.40±0.68	8.76±0.46	1.64**
	After	5.48±0.80	9.61±1.21	6.68±0.96	2.93***	6.52±0.84	5.35±0.42	1.17**	9.62±0.58	7.74±0.59	1.88**
% of change		-3.35	-14.20	-17.12		-11.41	-23.90		-7.5	-11.64	
T. value		0.676	3.341	5.637		3.200	5.154		2.014	4.083	
Sig.		0.516	0.009	0.000		0.033	0.001		0.114	0.015	
IH-free (µlU/mL)	Before	14.45±4.84	5.12±0.78	5.62±0.73	-0.50 NS	7.97±0.54	9.30±1.33	-1.32 NS	6.24±0.75	6.15±0.41	0.09 NS
	After	15.02±4.31	6.74±0.81	8.64±1.07	-1.90***	8.09±0.93	14.85±1.66	-6.76***	7.13±0.49	11.41±1.07	-4.29***
% of change		3.94	31.64	53.74		1.51	59.68		14.26	85.53	
T. value		-0.889	-5.862	-7.887		-0.454	-14.736		-6.875	-12.433	
Sig.		0.397	0.000	0.000		0.673	0.000		0.002	0.000	

NCG: Negative Control group; DCG1: Diabetic control group1; DG1:Diabetic group1;DCG2: Diabetic control group2; DG2:Diabetic group2; NDCG: Nephro-diabetic control group; NDG: Nephro-diabetic group. FBG: Fasting blood glucose; **HB A1c: Glycosylated Hemoglobin; IH-free: Insulin hormone free.** Mean differ.: Mean difference statistics between values at baseline and after supplementation. Significant difference between values at baseline and after month statistics by paired sample t-test. NS: Not significant, * significant in: $p<0.05$, ** significant in: $p<0.01$,***significant in: $p<0.001$. Reference values obtained from: Fischbach and Dunning, (1996).

It could be observed from table (7) that serum glycemic profiles had significantly curable after treatment. Patients after oral administration of DKC showed significant reduction in serum FBG and HB A1c to almost normal levels, the percentage of decrease compared to diabetic control groups were-25.57% and -21.60% at $p \leq 0.001$in DG1 and were -17.12% and -23.90% at $p \leq 0.01$ in DG2, respectively. Non-significant differences was observed in serum FBG between NDG and NDCG, while HBA1c declined significantly ($p \leq 0.01$) by -11.64%. Accordingly, there was a significant improvement at $p \leq 0.001$ in serum IH concentrations for diabetic patients, and administration of DKC attained to increase insulin levels by 53.74%, 59.68% and 85.53% for DG1, DG2 and NDG, respectively as compared to each corresponding diabetic group.

8. Metabolic parameters in diabetic and nephrodiabetic patients

Metabolic parameters in diabetic and nephrodiabetic patients before and after oral administration of DKC are listed in table (8).

As shown in table (8), insulin metabolic parameters were similar to NCG at baseline. FG/I ratio was significantly diminished ($p< 0.001$) in treated groups after administration of DKC by mean value of14.71±5.17, 4.88±0.76 and 18.89±0.91 for DG1, DG2 and NDG, respectively. Significant riseofmarkers of insulin resistance (HOMA-IR) was induced indiabetic and nephrodiabetic patients treated with insulinas compared to baseline by mean of 2.61±0.30 versus 2.09±0.38 at ($p<0.001$) and 6.10±1.03 versus3.82±0.39 at ($p<0.05$).β-cell function index had significantly increased at ($p<0.001$).NDG had the best effect by mean of1.07±0.05 versus 0.49±0.03 at baseline.

Table (8): Metabolic parameters in diabetic and nephrodiabetic patients before and after oral administration of DKC

		NCG	Diabetic patients treated with tablets.			Diabetic patients treated with insulin.			Nephro-diabetic patients treated with insulin.		
			DCG1	DG1	Mean Differ.	DCG2	DG2	Mean Differ.	NDCG	NDG	Mean Differ.
FG/I ratio	Before	5.99±1.67	44.34±6.23	30.80±10.97	13.53NS	19.74±1.92	9.97±1.75	9.77NS	32.13±4.07	41.06±2.51	-8.93NS
	After	5.78±1.42	34.63±4.46	14.71±5.17	19.91NS	17.01±2.33	4.88±0.76	12.13**	27.41±3.60	18.89±0.91	8.51NS
% of change											
T. value		0.539NS	5.626***	5.418***		3.495*	13.512***		8.256**	20.184***	
HOMA-IR	Before	2.89±1.12	2.81±0.46	2.26±0.48	0.55NS	3.07±0.10	2.09±0.38	0.98*	3.05±0.39	3.82±0.39	-0.77NS
	After	3.00±0.72	3.83±0.47	2.62±0.72	1.20NS	2.71±0.32	2.61±0.30	0.10NS	3.40±0.25	6.10±1.03	-2.69*
% of change											
T. value		-0.492NS	-5.713***	-1.575 NS		2.587 NS	-5.722***		-2.831*	-4.971*	
B- cell function index	Before	3.77±1.14	0.46±0.07	0.76±0.31	-0.29***	1.04±0.11	2.15±0.41	-1.11*	0.64±0.08	0.49±0.03	0.14NS
	After	3.94±1.57	0.59±0.07	1.56±0.53	-0.96***	1.22±0.16	4.41±0.77	-3.19NS	0.75±0.09	1.07±0.05	-0.32NS
% of change											
T. value		-0.566NS	-5.692***	-5.575***		-3.483*	-14.274***		-6.972**	-24.040***	

NCG: Negative Control group; DCG1:Diabetic control group1; DG1:Diabetic group1;DCG2: Diabetic control group2; DG2: Diabetic group2; NDCG: Nephro-diabetic control group; NDG: Nephro-diabetic group. FG/I ratio: Fasting glucose to insulin ratio; HOMA-IR: Homeostasis model assessment for insulin resistance. Mean differ.:Mean difference statistics between values at baseline and after supplementation. Significant difference between values at baseline and after month statistics by paired sample t-test. NS:Not significant, * significant in: $p<0.05$, ** significant in: $p<0.01$,***significant in: $p<0.001$. Reference values obtained from Matthews *et al.,* (1985).

4. Discussion

The present study aimed to find out the efficacy of the date kernels drink to improve levels of serum glucose and insulin resistance. As mentioned by **Al-Shahib and Marshall (2003)** who reported that date kernels contain higher protein and fat. Also, it have higher amount of dietary fiber as evaluated by **Ishrud *et al.* (2001)** who isolated water-soluble polysaccharides from the seeds of dates. As, **Al-Faris and Lee (2008)** showed that more than half of it was insoluble dietary fiber namely as hemicelluloses, cellulose and lignin beside resistant starch. Energy value of dried date kernels was 301.40±14.63 kcals per 100g as detected by **Juhaimi *et al.* (2012)**. This information on nutritional aspects will enhance the appreciation for the use of dates in the daily diet and their seeds as a functional food ingredient. For the macro-elements, potassium concentration was the highest followed in descending value by magnesium. The micro-elements, zinc was present in the highest concentration, followed in descending order by iron these analysis of seeds were in agreement of **Juhaimi*et al.*, (2012)**.

The polyphenol contents of date seeds were shown to be safe and offered a good source of natural antioxidants, hypoglycemic, hypolipidimic effect, and could potentially be considered as a functional food as reported by **Al-Farsi *et al.* (2005)**. These results are in parallel with those obtained by **Juhaimi *et al.*, (2012)**, and obtained as the same findings of **Hammouda *et al.* (2013)**.

The date consumption did not significantly affect the subjects' BMI according to **Rock *et al.* (2009).** On the other hand, **Chao *et al.*, (2010)** showed that the compounds in date kernels as caffeic acid (CA) and ellagic acid (EA) alleviated body weight loss.

The anti-inflammatory effects of the soluble phenolics in date seeds consisted of mainly ferulic acid and ellagic acid and caffeic acid derivatives as detected by **Rock *et al.* (2009),** might be helpful for the prevention or attenuation of diabetic kidney diseases **Chao *et al.* (2010)**; that reduced plasma blood urea nitrogen and elevated creatinine clearance as evidenced by **Liu *et al.* (2013).**The protection afforded by caffeic acid is mediated through inhibiting renal lipid peroxidation **(Gökçe*et al.*, 2009).** These results supported by the findings of **Abdelaziz and Ali (2014)** who reported that the date seeds could be protect against the liver intoxication, and hepatoprotective effect might be attributed to the antioxidant and free radical scavenging activities. Also, **Yeh and Yen (2006)** confirmed that phenolic acids asprocyanidins, CA and FA could led to a significant reduction of indicators of hepatic toxicity, such as in serum alanine, aspartate aminotransferase, alkaline phosphatase activities and hepatic lipid peroxidation formation**(Yang *et al.*, 2013)**.

Moreover, the results indicated that the hypoglycemic effect of DKC combined with insulin was ameliorated the blood glucose level toward normal levels when compared to the effect of insulin as a single therapy for treatment of diabetes as the same findings obtained by **El-Fouhil*et al.* (2010)**.

The polyphenol derivatives of date interestingly procyanidins that concentrated in the stones was characterized by **Hammouda *et al.*, (2013**), causing a lack of triglyceride accumulation in β-cells allowing for healthy levels of insulin production under hyperlipidemic conditions **Castell-Auví *et al.*, (2013),** which may attributed to stimulating glucose transporter-4 translocation to the plasma membrane as mentioned by **Pinent *et al., (*2004)**. Also, **Chao *et al.*,**

(2010) stated that an insulin-independent action of caffeic acid (CA) decreased significant levels of plasma HbA1c, the anti-diabetic effect may be related to its anti-inflammatory and angiostatic effects (**Abduljawad *et al.*, 2013)**. Meanwhile, chlorogenic acid, as an inhibitor of glucose 6-phosphatase, is able to decrease glucose output from hepatocytes **(Azay-Milhau *et al.*, 2013)**. Furthermore, **Son *et al.*, (2010)** illustrated that ferulic acid may be beneficial for treatment of type 2 diabetes via regulation of insulin secretion **(Roy *et al.*, 2013)** and hepatic glucose-regulating enzyme activities. **Fujita *et al.*, (2008)** demonstrated the preventative effects of ferulic acid on diabetic nephropathy via suppression of transforming growth factor-beta1(TGF-β1) upregulation caused by diabetes.

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