Curcumin Reduced Potato Chips and Roasted Bread Induced Chromosomal Aberrations and Micronuclei Formation in Albino Rats

Ramadan A.M. Ali, Nadia H.M. Sayed and Dalia D. Abd El-Monem

Zoology Dept, Girls Collage for Arts, Science and Education, Ain Shams Univ., Heliopolis, Egypt
ramadanali27@gmail.com

Abstract: Detection of high concentrations of acrylamide (AA) in heated starch rich foodstuffs raises health concerns, particularly for children, because AA is relatively high in child-favored foods such as potato chips, French fries, roasted bread and cereals. So, we investigated the genotoxic and cytotoxic potentials of potato chips (FP) and roasted bread (RB) and the possible protective effect of curcumin (Cur) in albino rat bone-marrow cells, using chromosomal aberrations (CAs) and micronucleus (Mn-PCEs) assays. 90 adult female rats were divided into15 groups 6 animals each. Rats feed on diet contained 15 % or 30 % of fried potato chips and/or fried bread and supplemented with/without 1%curcumin addition for 2 months. Results showed that, treatment with Cur alone did not induce significant increases in CAs and Mn-PCEs in comparison to the control level. Meanwhile, diet supplemented with 30 % of FP and/or RB induced highly significant increases in CAs and Mn-PCEs frequencies ($P<0.001$). Moreover, fried potato chips and/or fried bread caused cytotoxic action in the form of a significant reduction in the proportion between polychromatic erythrocytes to normochromatic erythrocytes. Meanwhile, addition of 1% Cur powder induced significant decrease in CAs and Mn-PCEs frequencies in comparison to those induced by FP and/or RB alone. Such increases were dose dependent. On conclusion, curcumin exhibited antimutagenic properties against the mutagenicity induced by potato chips and/or roasted bread which make it a promising chemopreventive agent.
[Ramadan A.M. Ali Nadia H.M. Sayed and Dalia D. Abd El-Monem. **Potato Chips and Roasted Bread Induced Chromosomal Aberrations and Micronuclei Formation in Albino Rats.** Life Science Journal. 2012; 9(1):330-336] (ISSN: 1097-8135). http://www.lifesciencesite.com. 47

Key wards: Acrylamide, Curcumin, Chromosomes, Micronucleus, Rat, Potatoes chips, Roaster bread.

Introduction:

Frying food in fats and oils is a popular food preparation method. A huge public concern was generated after detecting a considerable concentration of the genotoxic and carcinogenic acrylamide in starch-containing foods cooked at high temperatures as fried potatoes, potato chips and the brown roasted bread (**Taubert *et al*., 2004**).

Epidemiological studies gave an evidence for cancer risk factor in correlation with consumption of the fried potatoes and the acrylamide content in foods with the incidences of cancer in various body organs. For instance, analysis of epidemiological data showed a parallel link between high consumption of fried potatoes cooked at high temperatures and risk of bladder cancer in a case-control study in Uruguay (**De Stefani *et al*., 2008**), risk of lung cancer among Canadian women due to evaporated burned oils (**Hu *et al*., 2002**), risk of laryngeal cancer in a case-control study from Italy and Switzerland (**Bosetti *et al*., 2002**), cancer risk of oral cavity, pharynx, esophagus, larynx, breast, colon and rectum (**Pelucchi *et al*., 2004**) and risk of renal cell carcinoma from a population-based Swedish case-control study (**Mucci *et al*., 2004**), risk of pancreatic cancer in an Italian case-control study (**Pelucchi *et al*., 2011**).

Acrylamide induced single and double-strand DNA breaks and DNA adducts (**Koyama *et al*., 2011**). Moreover, acrylamide possessed mutagenic activity as revealed by chromosomal aberration, sister-chromatid exchange and micronucleus assays. Acrylamide induced chromosomal aberrations in mouse zygotes (**Marchetti *et al*., 1997**), in bone marrow and spleen cells of mice and rats (**Krishna and Theiss, 1995**), in spermatogenic cells (**Schmid *et al*., 1999**) and in Chinese hamster V79 cells (**Oliveira *et al*., 2009**). Acrylamide also decreased the mitotic activity of rat bone marrow cells (**Yener and Dikmenli, 2011).** Moreover, acrylamide induced sister-chromatid exchanges in spleen cells (**Backer *et al*., 1989**), in mice bone marrow cells (**Russo *et al*., 1994**) and in Chinese hamster V79 cells (**Oliveira *et al*., 2009**). In addition, acrylamide proved to be a potent micronuclei inducer in peripheral blood erythrocytes and spermatids of mice (**Russo *et al*., 1994**), in spleen cells of mice (**Krishna and Theiss, 1995**), in human lymphoblastoid TK6 cells (**Koyama *et al*., 2006**) and in bone marrow cells of mice and rats (**Koyama *et al*., 2011**)

Curcumin powder is a yellow pigment obtained from ground dried rood rhizomes of curcuma plant (*Curcuma longa*), commonly used as natural food additive as a spice and food coloring agent. Curcumin is able to inhibit the genotoxic and histochemical changes induced in the experimental animals by various chemical agents as it reduced the percentages of micronucleated polyc-

hromatic erythrocytes in bone marrow cells of mice (**Azuine *et al.*, 1992**) and inhibited chromosomal aberrations, micronuclei formation, and sister chromatid exchanges (SCEs) incidences in mouse bone marrow cells induced by benzo(a)pyrene (**Shukla *et al*., 2003**) and lead acetate (**El-Ashmawy *et al.*, 2006**). Moreover, curcumin reduced the levels of benzo[a]pyrene-DNA adducts in liver, lung, and forestomach (**Thapliyal *et al*., 2002**) and DNA damage induced by benzo[a]pyrene in human peripheral blood lymphocyte cells as revealed by single cell gel electrophoresis assay (**Polasa *et al*., 2004**). In addition, Curcumin has been shown to inhibit chemical carcinogenesis (**Garg *et al.*, 2008**) and chemical mutagenesis (**Peng *et al*., 2010**).

This investigation aimed to show the frequencies of damaged cells (DC) and micronuclei in polychromatic erythrocytes (Mn-PCEs) induced by feeding female rats with diets containing fried potato chips and roasted bread for a long time. As well as to reduce the induced chromosomal aberrations through feeding the animals with the same diets supplemented with 1 % curcumin powder.

Material and methods

A- Animals and treatments:

The experiments were carried out on 90 adult female albino rats 3-4 months age and 130-150 g in weight which were purchased from Helwan Farms of the Egyptian Organization for Vaccines and Biological Preparations, Cairo. Rats were accommodated according to the protocol of animal welfare of Ain Shams University in which the commercial food and tap water were supplemented ad libitum during the acclimatization and the experimental period. Animals were divided into 15 groups 6 animals each. Table (1) shows animal groups, treatment schedule and the composition of diet for each animal group. Animals feed on diet contained 15 % or 30 % of fried potato chips and/or fried bread and supplemented with/without 1% curcumin addition for 2 months.

B-Chemicals

AA with 99% purity was purchased from sigma chemical company. It is white powder, water-soluble vinyl monomer. With molecular formula: C_3H_5NO and chemical formula: CH_2=$CHCONH_2$. Curcumin powder was obtained from the local herbal shop.

C- Preparation of fried potatoes and roasted bread

The fried potatoes chips were prepared according to the protocol regularly applied in the home: potatoes were washed with the tap water and the covering skin removed with a sharp knife and the potatoes pulps trimmed into thin slices (chips) with a thickness about 1 to 2 mm approximately. Commercial frying oil currently consumed by the native Egyptians was chosen from the supermarket.

After oil boiling, the potatoes slices were dropped into the boiled oil till the surface of slices turned into golden brown in color. Similarly, the bread of whole wheat seed was fried by the same way. The fried potatoes slices and the roasted bread were fragmented into powder and added to the commercial diet in appropriate percentages.

2-D- Chromosomal aberrations assay:

Metaphase chromosomal spreads were prepared from bone marrow cells by air-drying technique previously postulated by **Hliscs *et al.* (1997)**. Animals were injected intraperitoneally with colchicine (1 cc/ 200g b.w. from 0.04 % colchicine powder in dH_2O) 2 h perior to chromosomal preparation. Animals were killed by cervical dislocation and bone marrow of femur was aspirated for chromosomal preparation. The prepared slides were stained with 5% Giemsa stain. Chromosomal aberrations were scored and recorded among 100 well-spread metaphase /animal. Moreover, mitotic index was calculated by counting the dividing cells among 2000 cells/ animal and expressed in percentage.

E- Micronucleus assay:

Micronucleus assay in polychromatic erythrocytes of bone marrow was carried out by the method of **Schmid (1976)** from bone marrow of the femur. The bone marrow was flushed in the form of a fine cell suspension into a centrifuge tube containing 1 ml of fetal calf serum. The cell suspension was centrifuged at 1000 r.p.m. for 5 min and the supernatant was discarded. The pellet was resuspended in a drop of serum for slides preparing. The air-dried slides were stained with Giemsa. A total of 2,500 polychromatic erythrocytes (PCEs) were scored per animal to determine the frequency of Mn-PCEs. In addition, the ratio of PCE to NCE was recorded.

F- Statistical analysis:

All the data were analyzed with Student's *t*-test and a *P*- value ($P<0.05$) was considered statistically significant (**Fowler *et al.*, 1998**).

Results and Discussion

As shown in tables (2 and 3) and figures (1 and 2); diet supplemented with 30 % of FP and/or RB exhibited 13, 16 and 8.33 damaged cell / 100 metaphase spreads and 18.67, 21.16 and 12.83 Mn-PCEs / 2500 PCEs, respectively. Furthermore, animals feed on FP induced higher incidences of damaged cells and micronuclei in comparison to those feed on RB. This observation could be explained through the fact that, animals treated with

fried potatoes were subjected to the effect of both the oxidative compounds of boiled oil and the brown crust which containing acrylamide **(Becalski *et al*., 2003)**.

The fried potatoes and the roasted bread possibly induced the chromosome breaking activity through three mechanisms: 1- The natural antioxidants content present in oils and potatoes are declined through frying process at high temperatures. The process of food frying destruct the natural antioxidants present in oil and potatoes as (alpha-tocopherol and phenolic compounds) which led to the lipid peroxidation in liver microsomes of rats after feeding with the fried potatoes (**Quiles *et al*., 2002 and Yen *et al*., 2010**). This assumption was ascertained by **Andrikopoulos *et al.* (2002)** who observed that the fried oil content of antioxidants was deteriorated during eighth successive frying of virgin olive oil, sunflower oil and a vegetable shortening. Where, the retention of tochopherols ranged from 85-90% (first frying) to 15-40 (eighth frying) except for tocopherols of sunflower oil, which almost disappeared after the sixth frying and the retention of total phenolics ranged from 70-80% (first frying) to 20-30% (eighth frying). In addition, **Battino *et al.* (2002)** observed that, the intake of such altered oil by rats mainly affected the respiratory chain components (Coenzyme Q, cytochromes) of the mitochondrial membranes which are considered as another source for genotoxicity.

The boiling of oils at high temperatures induced the formation of genotoxic oxidative compounds (**Dung *et al.*, 2006**). Deep fat frying is a popular food preparation method because it produces desirable fried food flavor, golden brown color and crisp texture (**Warner, 1999**). Throughout, deep frying of oils, the oxidation process of oils is occurred and the genotoxic derivatives like linoleic acid hydroperoxides and squalene compounds are produced (**Chaiyasit *et al.*, 2007**). **Hageman *et al.* (1989 and 1990)** found that, linoleic acid hydroperoxides extracted from deep-frying fat samples induced mutagenicity to Salmonella tester strains TA97 and TA100, in presence of S9 mix. Moreover, consumption of heated oils by rats enhanced cell proliferation of the esophagus lining epithelium cells (**Hageman *et al*., 1991**). In addition, **Kalogeropoulos and Andrikopoulos (2004)** detected the genotoxic agents, squalene compounds that produced during deep-frying of potatoes.

The formation of the chemical compound known as acrylamide during heating of starch with the amino acid asparagine in the brown crust of fried potatoes and roasted bread (**Pedreschi and zuniga, 2009**). Asparagines, is the major amino acid in potatoes and cereals, which acts as a crucial participant in the production of acrylamide (**Mottram *et al*., 2002**). Moreover, **Tareke *et al*. (2002)** detected a moderate level of acrylamide (5-50 microg/kg) in heated protein-rich foods and higher contents (150-4000 microg/kg) in carbohydrate-rich foods, such as fried potatoes. Furthermore, the acrylamide content consistently increased with increasing temperature and processing times (**Majcher and Jeleń, 2007**).

Acrylamide acts as an indirect genotoxic agent and cannot induce chromosomal damage but it converted to the mutagenic metabolite glycidamide in the liver cells. Glycidamide is potent genotoxic agent (**Puppel *et al.*, 2005**). It induced DNA adducts in normal human bronchial epithelial cells and Big Blue mouse embryonic fibroblasts, (**Besaratinia and Pfeifer, 2004**), in V79 Chinese hamster cells (Matins *et al*., 2007) and in mouse lymphoma cells (**Mei *et al*., 2008**).

On the other hand, diet supplement contains several natural substances capable of inhibiting genotoxic chemicals either directly by scavenging the reactive substances or indirectly by promoting mechanisms, which enhance detoxification of mutagenic agents.

This investigation revealed also that, curcumin significantly reduced the percentages of damaged cells from 3.67±0.8 to 2.33±0.8 damaged cells/100 metaphase and from 13±1.34 to 8±1.03 damaged cells/100 metaphase induced by 15% and 30% FP, respectively. Similarly, curcumin significantly reduced the percentages of damaged cells from 3.67±0.8 to 2.33±0.8 damaged cells/100 metaphase and from 13±1.34 to 8±1.03 damaged cells/100 metaphase induced by 15% and 30% FP, respectively. Furthermore, it inhibited the mean frequencies of micronuclei induced by 30% FP from 18.67±1.02 to 11.17±0.98 Mn-PCEs / 2500 PCEs and 30% RB from 12.83±0.79 to 9.17 ±1.25 Mn-PCEs / 2500 PCEs (as presented in tables 2&3.)

Curcumin may be induced its antigenotoxicity via liver antioxidant enzymes superoxide dismutase, catalase and glutathione peroxidase (**Reddy and Lokesh, 1994**) which lowered lipid peroxidation and protected rats from iron-induced lipid peroxidation. Curcumin pretreatment protect mice from DNA damage and carcinogenicity induced by benzo(a)pyrene and isothiocyanate via superoxide dismutase, catalase and glutathione peroxidase production **(Polasa *et al*., 2004)**. Another possible mechanism for antigeneotoxicity of curcumin via reducing the activity of cytochrome P450 (CYP450) isozymes CYP 1A1, 1A2 and 2B1 in liver, lung, and forestomach and elevating the activity of hepatic glutathione S-transferase (**Singh and Sharma, 2011**).

On conclusion, curcumin the yellow pigment commonly used as a spice and food coloring agent obtained from rhizomes of *Curcuma longa* exhibited antimutagenic properties on the genotoxicity induced by fried potatoes and roasted bread.

Table (1): Categorization of the animal groups according to the percentage of diet content of fried potato chips, roasted bread, Curcumin and commercial diet.

	Treatment (Group / 6 animals)	Diet Composition (%)				
		Fried Potato Chips	Roasted bread	Curcumin	Acrylamide	Commercial Diet
	Control 1	-	-	-	-	100
	Control 2	-	-	1	-	99
	Positive Control	-	-	-	1	99
Without Curcumin	FP 15%	15	-	-	-	85
	RB 15%	-	15	-	-	85
	FP+RB 15%	15	15	-	-	70
	FP 30 %	30	-	-	-	70
	RB 30 %	-	30	-	-	70
	FP + RB 30 %	30	30	-	-	40
With Curcumin	FP 15%	15	-	1	-	84
	RB 15%	-	15	1	-	84
	FP+RB 15%	15	15	1	-	69
	FP 30 %	30	-	1	-	69
	RB 30 %	-	30	1	-	69
	FP + RB 30 %	30	30	1	-	39

Control 1 = Includes animals feed only on the commercial diet
Control 2 = Included animals feed on commercial diet and supplemented with 1 g turmeric
RB = Roasted bread
FP = Fried potatoes chips

Table (2): Average of damaged metaphases induced in bone marrow cells of animals feed on diet contained 15 % or 30 % of fried potatoes chips and/or fried bread and supplemented with/without curcumin addition for 2 months.

	Treatment	Number of damaged cells			Mitotic index	
		Total	Mean %	SE ±	Mean%	SE ±
	Control	10	1.67	0.61	3.83	0.30
	1% Curcumin	4	0.67	0.21*	4.33	0.33*
	1%AA	133	22.16	0.91*****	1.16	0.16
Without Curcumin	FP 15%	22	3.67	0.80*	3.00	0.25*
	RB 15%	16	2.67	0.66*	3.50	0.42*
	FP + RB 15%	30	5.00	0.85***	2.83	0.30**
	FP 30%	78	13.0	1.34*****	2.00	0.25****
	RB 30%	50	8.33	0.95*****	2.50	0.34**
	FP + RB 30%	96	16.0	1.46*****	1.33	0.21*****
With Curcumin	FP 15%	14	2.33	0.80[a]	3.50	0.34[a]
	RB 15%	12	2.00	0.51[b]	4.00	0.36[b]
	FP + RB 15%	24	4.00	0.89[c]	3.00	0.36[c]
	FP 30%	48	8.00	1.03[g]	2.50	0.22[e]
	RB 30%	30	5.00	1.12[f]	3.00	0.45[g]
	FP + RB 30%	71	11.83	1.1[h]	1.50	0.22[i]

AA = Acrylamide FP = fried potatoes chips RB= fried breadSE=Standard error
*P>0.05 compared with control **P<0.05 compared with control ***P<0.01 compared with control ****P<0.001 compared with control *****P<0.0001 compared with control [a]P>0.05 compared with 15% FP [b]P>0.05 compared with 15%RB [c]P>0.05 compared with 15% FP +RB[d]P<0.001 compared with 30%FP [e]P>0.05 compared with 30% FP [f]P<0.05 compared with 30%RB[g]P>0.05 compared with 30%RB [h]P<0.05 compared with 30% FP +RB[i]P<0.05 compared with 30% FP +RB

Table (3): Frequency of micronucleated erythrocytes and PCE/NCE ratioinduced in bone marrow cells of rats feed on diet contained fried potatoes chips and/or fried bread and supplemented with/without curcumin addition.

	Treatment	The frequency of MN			PCE/NCE	
		Total Mn/15000 PCEs	Mean Mn/2500 PCEs	SE ±	Mean%	SE ±
	Control	20	3.33	0.56	53.50	0.84
	1% Curcumin	15	2.5	0.65*	56.00	0.77*
	1%AA	238	39.66	1.14****	30.83	1.08****
Without Curcumin	FP 15%	35	5.83	0.98*	46.83	1.08***
Without Curcumin	RB 15%	50	8.33	1.17**	49.67	0.56**
Without Curcumin	FP + RB 15%	70	11.67	1.30***	44.50	1.23****
Without Curcumin	FP 30%	112	18.67	1.02****	35.50	1.38****
Without Curcumin	RB 30%	77	12.83	0.79****	43.17	0.60****
Without Curcumin	FP + RB 30%	130	21.16	1.62****	29.83	0.87****
With Curcumin	FP 15%	30	5.00	1.81^{a}	51.67	0.66^{b}
With Curcumin	RB 15%	17	2.83	0.79^{c}	52.33	0.42^{c}
With Curcumin	FP + RB 15%	46	7.67	1.17^{d}	50.50	0.84^{e}
With Curcumin	FP 30%	67	11.17	0.98^{f}	38.17	1.25^{g}
With Curcumin	RB 30%	55	9.17	1.25^{h}	44.67	0.76^{i}
With Curcumin	FP + RB 30%	105	17.5	0.92^{j}	31.50	1.17^{k}

AA = Acrylamide; FP = fried potatoes chips; RB= fried bread; SE=Standard error

*P>0.05 compared with control; **P<0.01 compared with control; ***P<0.001 compared with control ****P<0.0001 compared with control; ^{a}P>0.05 compared with 15% FP; ^{b}P<0.01 compared with 15%FP^{c}P<0.01 compared with 15%RB ^{d}P<0.05 compared with 15% FP +RB^{e}P<0.01 compared with 15% FP +RB^{f}P<0.001 compared with 30%FP^{g}P>0.05 compared with 30%FP^{h}P<0.05 compared with 30%R; ^{i}P>0.05 compared with 30%FP^{j}P<0.05 compared with 30% FP +RB^{k}P>0.05 compared with 30% FP +RB.

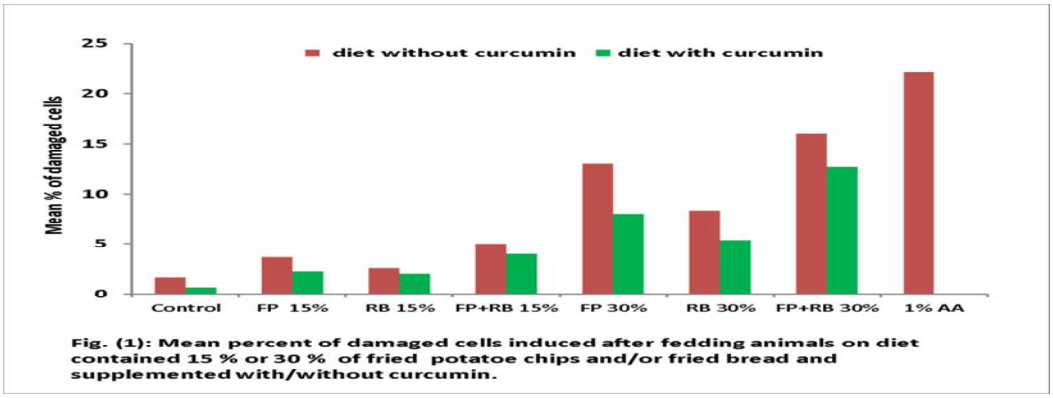

Fig. (1): Mean percent of damaged cells induced after fedding animals on diet contained 15 % or 30 % of fried potatoe chips and/or fried bread and supplemented with/without curcumin.

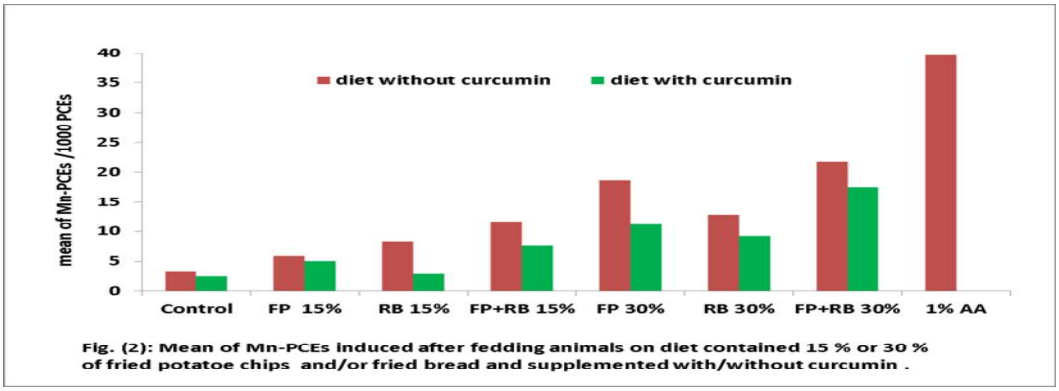

Fig. (2): Mean of Mn-PCEs induced after fedding animals on diet contained 15 % or 30 % of fried potatoe chips and/or fried bread and supplemented with/without curcumin .

Corresponding author
Ramadan A.M. Ali
Zoology Dept, Girls Collage for Arts, Science and Education, Ain Shams Univ.
ramadanali27@gmail.com

References

1. **Andrikopoulos, N.; Dedoussis, G.; Falirea, A.; Kalogeropoulos, N. and Hatzinikola, S. (2002):** Deterioration of natural antioxidant species of vegetable edible oils during the domestic deep-frying and pan-frying of potatoes. Int. J. Food Sci. Nutr., 53(4): 351-363.
2. **Azuine, M.; Kayal, J. and Bhide, V. (1992):** Protective role of aqueous turmeric extract against mutagenicity of direct-acting carcinogens as well as benzo [alpha] pyrene-induced genotoxicity and carcinogenicity. J. Cancer Res. Clin. Oncol., 118(6): 447-452.
3. **Backer, C.; Dearfield, L.; Erexson, L.; Campbell, A.; Westbrook-Collins, B. and Allen, W. (1989):** The effects of acrylamide on mouse germ-line and somatic cell chromosomes. Environ. Mol. Mutagen., 13(3): 218-226.
4. **Battino, M.; Quiles, J.; Huertas, R.; Ramirez-Tortosa, C.; Cassinello, M.; Manas, M.; Lopez-Frias, M. and Mataix, J. (2002):** Feeding fried oil changes antioxidant and fatty acid pattern of rat and affects rat liver mitochondrial respiratory chain components. J. Bioenerg. Biomembr., 34(2):127-134.
5. **Becalski, A.; Laup, Lewis, D. and Seaman, W. (2003):** Acrylamide in foods: occurrence, sources, and modeling. J. Agric. Food Chem., 51(3):802-808.
6. **Besaratinia, A. and Pfeifer, P. (2004):** Genotoxicity of acrylamide and glycidamide. J. Natl. Cancer Inst., 96(13): 1023-1029.
7. **Bosetti, C.; Talamini, R.; Levi, F.; Negri, E.; Franceschi, S.; Airoldi, L. and La Vecchia, C. (2002):** Fried foods: a risk factor for laryngeal cancer. Br. J. Cancer, 87(11): 1230-1233.
8. **Chaiyasit, W.; Elias, R.J.; McClements, D.J. and Decker, E.A. (2007):** Role of physicalstructures in bulk oils on lipid oxidation. Crit. Rev. Food Sci. Nutr., 47(3): 299-317.
9. **De Stefani, E.; Boffetta, P.; Ronco, A.L.; Deneo-Pellegrini, H.; Acosta, G. and Mendilaharsu, M. (2008):** Dietary patterns and risk of bladder cancer: a factor analysis in Uruguay. Cancer Causes Control, 19(10): 1243-1249.
10. **Dung, C.H.; Wu, S.C. and Yen, G. C. (2006):** Genotoxicity and oxidative stress of the mutagenic compounds formed in fumes of heated soybean oil, sunflower oil and lard. Toxicology *in Vitro*, 20 (4): 439-447.
11. **El-Ashmawy, I. M.; Ashry, K. M.; El-Nahasa, F. and Salama, O. M. (2006):** Protection by turmeric and myrrh against liver oxidative damage and genotoxicity induced by lead acetate in mice. Basic Clin. Pharmacol. Toxicol., 98(1):32-7.
12. **Fowler J., Cohen L. and Jarvis P. (1998)**. Practical statistics for field biology. 2nd ed. John Wiley & Sons, Chichester, New York
13. **Garg, R.; Ingle, A. and Maru, G. (2008):** Dietary turmeric modulates DMBA-induced p21ras, MAP kinases and AP-1/NF-kappa B pathway to alter cellular responses during hamster buccal pouch carcinogenesis.Toxicol. Appl. Pharmacol., 232(3): 428-439.
14. **Hageman, G; Hermans, R.; Ten Hoor, F. and Kleinjans, J. (1990):** Mutagenicity of deep-frying fat, and evaluation of urine mutagenicity after consumption of fried potatoes. Food Chem. Toxicol., 28(2): 75-80.
15. **Hageman, G.; Verhagen, H.; Schutte, B. and Kleinjans, J. (1991):** Biological effects of short-term feeding to rats of repeatedly used deep-fryingfats in relation to fat mutagen content. Food Chem. Toxicol., 29(10): 689-698.
16. **Hageman, G.; Kikken, R.; Ten Hoor, F. and Kleinjans, J. (1989):** Linoleic acid hydroperoxide concentration in relation to mutagenicity of repeatedly used deep-frying fats. Lipids, 24(10): 899-902.
17. **Hliscs, R.; Muhlig, P. and Claussen, U. (1997):** The spreading of metaphases in a slow process which leads to stretching of chromosomes. Cytogenet. Cell Genet., 76: 167-171.
18. **Hu, J.; Mao, Y.; Dryer, D. and White, K. (2002):** Risk factors for lung cancer among Canadian women who have never smoked. Cancer Detect. Prev., 26(2): 129-138.
19. **Kalogeropoulos, N. and Andrikopoulos, K. (2004):** Squalene in oils and fats from domestic and commercial fryings of potatoes. Int. J. Food Sci. Nutr., 55(2): 125-129.
20. **Koyama, N.; Sakamoto, H.; Sakuraba, M.; Koizumi, T.; Takashima, Y.; Hayashi, M.; Matsufuji, H.; Yamagata, K.; Masuda, S.; Kinae, N. and Honma, M. (2006):** Genotoxicity of acrylamide and glycidamide in human lymphoblastoid TK6 cells. Mutat. Res., 28 603(2): 151-158.
21. **Koyama, N.; Yasui, M.; Kimura, A.; Takami, S.; Suzuki, T.; Masumura, K.; Nohmi,T.; Masuda, S. Kinae, N. Matsuda, T. Imai T. and Honma M. (2011):** Acrylamide genotoxicity in young versus adult gpt delta male rats. Mutagenesis., 26(4): 545-549.
22. **Krishna, G. and Theiss, C. (1995):** Concurrent analysis of cytogenetic damage *in vivo*: a multiple endpoint –multiple tissue approach. Environ. Mol. Mutagen., 25(4): 314-320.
23. **Majcher, M. A. and Jeleń, H. H. (2007):** Acrylamide formation in low-fat potato snacks and its correlation with colour development . Food Additives and Contaminants, 24 (4): 337-342
24. **Martins, C.; Oliveira, G.; Pingarilho, M.; Gamboa, Da Costa, G.; Martins, V.; Marques, M. M.; Bel-**

and, F.A.; Churchwell, M. I.; Doerge, D. R.; Rueff, J. and Gaspar, J. F. (2007): Cytogenetic damage induced by acrylamide and glycidamide in mammalian cells: correlation with specific glycidamide-DNA adducts. Toxicol. Sci., 95(2): 383-390.

25. **Mei, N.; Hu, J.; Churchwell, M.I.; Guo, L.; Moore, M.M.; Doerge, D.R. and Chen, T.(2008):** Genotoxic effects of acrylamide and glycidamide in mouse lymphoma cells. Food Chem. Toxicol., 46(2): 628-636.
26. **Marchetti, F.; Lowe, X.; Bishop, J. and Wyrobek, A. J. (1997):** Induction of chromosomal aberrations in mouse zygotes by acrylamide treatment of male germ cells and their correlation with dominant lethality and heritable translocations. Environ. Mol. Mutagen., 30(4): 410-417.
27. **Mottram, S.; Wedzicha, L. and Dodson, T. (2002):** Acrylamide is formed in the Maillard reaction. Nature, 419: 448-449.
28. **Mucci, L.A. ; Lindblad, P. ; Steineck, G. and Adami, O. (2004):** Dietary acrylamide and risk of renal cell cancer. Int. J. Cancer, 109(5): 774-776.
29. **Oliveira, N.G.; Pingarilho, M.; Martins, C.; Fernandes, A.; S. Vaz, S.; Martins, V.; Rueff, J. and Gaspar, J. F. (2009):** Cytotoxicity and chromosomal aberrations induced by acrylamide in V79 cells: role of glutathione modulators. Mutat. Res., 676(1-2): 87-92.
30. **Pedreschi, F.; and Zuniga, R. N. (2009):** Acrylamide and Oil Reduction in Fried Potatoes: A Review. Food, 3(2): 82-92.
31. **Pelucchi, C.; Franceschi, S.; Levi, F.; Trichopoulos, D. ; Bosetti, C.; Negri, E. and La Vecchia, C. (2004):** Fried potatoes and human cancer. Int. J. Cancer, 108(4): 634-635.
32. **Pelucchi, C.; Galeone, C.; Talamini, R.; Negri, E.; Polesel, J.; Serraino, D. and La Vecchia, C. (2011):** Dietary acrylamide and pancreatic cancer risk in an Italian case--control study. Ann. Oncol., 22(8): 1910-1915.
33. **Peng , C.H.; Chiu, W.T. ; Juan, C.W.; Mau, J.L.; Chen ,C.C.; Peng, C.C.; Lai, E.Y. and Chyau, C.C. (2010):** Pivotal role of curcuminoids on the antimutagenic activity of Curcuma zedoaria extracts. Drug Chem. Toxicol., 33(1): 64-76.
34. **Polasa, K. ; Naidu, N. ; Ravindranath, I. and Krishnaswamy, K. (2004):** Inhibition of B(a)P induced strand breaks in presence of curcumin. Mutat. Res., 557(2): 203-213.
35. **Puppel, N.; Tjaden, Z.; Fueller, F. and Marko, D. (2005):** DNAstrandbreakingcapacity of acrylamide and glycidamide in mammaliancells. Mutat. Res., 580(1-2): 71-80.
36. **Quiles, L. ; Huertas, R. ; Battino, M. ; Ramirez-Tortosa, C. ; Cassinello, M. ; Mataix, J. ; Lopez-Frias, M. and Manas, M. (2002):** The intake of fried virgin olive or sunflower oils differentially induces oxidative stress in rat liver microsomes. Br. J. Nutr., 88(1): 57-65.
37. **Reddy, C. and Lokesh, R. (1994):** Effect of dietary turmeric (Curcuma longa) on iron-induced lipid peroxidation in the rat liver. Food Chem. Toxicol., 32(3): 279-283.
38. **Russo, A.; Gabbani, G. and Simoncini, B. (1994):** Weak genotoxicity of acrylamide on premeiotic and somatic cells of the mouse. Mutat. Res., 309(2): 263-272.
39. **Schmid, E.; Xu, W. and Adler, D. (1999):** Detection of aneuploidy by multicolor FISH in mouse sperm after in vivo treatment with acrylamide, colchicine, diazepam or thiabendazole. Mutagenesis, 14(2): 173-179.
41. **Schmid, W. (1976):** The micronucleus test for cytogenetic analysis. In Hollaender,A. (ed.), Chemical Mutagens, Principles and Methods for their detection, Vol. 4. Plenum Press, New York, pp. 31—53.
41. **Shukla, Y. ; Arora, A. and Taneja, P. (2003):** Antigenotoxic potential of certain dietary constituents. Teratog. Carcinog. Mutagen., Suppl 1: 323-335.
42. **Singh, R. and Sharma, P. (2011):** Hepatoprotective Effect of Curcumin on Lindane-induced Oxidative Stress in Male Wistar Rats. Toxicol. Int., 18(2): 124-129.
43. **Tareke, E.; Rydberg, P. and Karlsson, P. (2002):** Analysis of ACR, a carcinogen formed in heated foodstuffs. J. Agric. Food Chem., 50 (17): 4998–5006.
44. **Taubert, D.; Harlfinger, S.; Henkes, L.; Berkels, R. and Schomig, E. (2004):** Influence of processing parameters on acrylamide formation during frying of potatoes. J. Agric. Food Chem., 52(9): 2735-2739.
45. **Thapliyal, R. ;Deshpande, S. and Maru, B. (2002**): Mechanism(s) of turmeric-mediated protective effects against benzo(a)pyrene-derived DNA adducts. Cancer Lett., 175(1): 79-88.
46. **Warner, K. (1999):** Impact of high-temperature food processing on fats and oils. Adv. Exp. Med. Biol., 459: 67-77
47. **Yen, P. L.; Chen, B.H.; Yang, F.L. and Lu, Y.F. (2010):** Effects of deep-frying oil on blood pressure and oxidative stress in spontaneously hypertensive and normotensive rats. Nutrition, 26(3): 331-336.
48. **Yener, Y. and Dikmenli, M. (2011):** The effects of acrylamide on the frequency of megakaryocytic emperipolesis and the mitotic activity of rat bone marrow cells. J. Sci. Food Agric., 15 91(10):1810-1813.

1/25/2012