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TURMERIC MAY PROTECT CELLS FROM OXIDATIVE STRESS BY ACRYLAMIDE *IN VIVO*

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ABSTRACT

Turmeric is a perennial herb; the rhizome is the portion of the plant that is used medicinally. It is the source of the spice turmeric with characteristic yellow color. Acrylamide is found in some foods that are cooked at high temperatures. It appears to be formed as a by product of the Maillard reaction. Maillard reaction is a type of non –enzymatic browning, which involves the reaction of simple sugars (carbonyl groups) and amino acids. Only the acrylamide monomer is toxic. Present work is focused on turmeric's antioxidant activity against acrylamide toxicity. Rats were divided into three groups (7 rats/ group). Group A served as negative control that was fed on standard diet (commercial diet) for 11days. Group B was fed for 11days on standard diet containing 0.34g acrylamide / kg diet as a positive control. Group C received standard diet with turmeric (0.5 %) and same concentration 0.34g acrylamide / kg diet for 11days as a protective group. Results revealed that kidney, brain and lung tissues were disturbed when rats were fed on acrylamide diet. Turmeric had ameliorated the antioxidant status in these organs. It is concluded that turmeric as a natural antioxidant has protected from acrylamide toxicity.

Key words: Turmeric, Acrylamide *in vivo*, Rats

INTRODUCTION

The therapeutic benefits of dietary constituents of plant origin have been the focus of many extensive studies (Stravic, 1994). Food plays a major role in the concepts of illness and curing (Stone, 1977). Turmeric (Curcuma Longa), a member of the ginger family, is used as a yellow food coloring agent and has been used in traditional medicine in India and Ancient Egypt for at least 6000 years (Majeed, *et al.*, 1995). Turmeric has traditionally been used as a treatment for inflammation, skin wounds and tumors (Rao, *et al.*, 1995). Turmeric offers protection by inhibiting lipid peroxidation and scavenging free radicals (Srinivas *et al.*, 1992). The numerous beneficial effects attributed to turmeric stem in large measure from the antioxidant properties of curcumin. Antioxidants neutralize free radicals, which are highly unstable molecules that can damage cellular structures through abnormal oxidative reactions (Rao, and Rao, 1996). From previous studies, turmeric fed at levels varying from 1-10 per cent did not exhibit any adverse effects on organs and tissues. Turmeric and curcumin fed at 0.5 per cent and 0.15 per cent, respectively, for 12 weeks did not produce any genetic damage (Vijayalaxmi, 1980). Alcoholic extracts of turmeric, fed at a level of 60 mg to rats, monkeys, guinea pigs and dogs for 12-13 weeks, were again negative for toxicity. Rats administered curcumin in doses of 400, 800 and 1,600 mg/kg/day for 90 days did not show any change. Growth, behavior, and biochemical and histological parameters failed to detect any possible toxicity (Deodhar, *et al.*, 1980).

Acrylamide is highly reactive and water-soluble polymer, which is commonly used in industry (Nordin, *et al.*, 2003). The exposure of acrylamide by "chips and comparable products" (approximately 20% of total acrylamide exposure) is attributed to most home cooking processes because acrylamide amounts of unfried frozen chips are relatively low (mean: 62 mg/kg, n=6) compared to the deep-fried product (mean: 436 mg/kg, n=6). Furthermore, acrylamide amount is affected by frying temperature and frying time, so cooking conditions might influence acrylamide formation (IPCS and WHO, 2002; NFCA, 2002 & Konings, *et al.*, 2003). Exposure to acrylamide can occur dermally, by inhalation and by ingestion (Tyl, *et al.*, 2000a). Acrylamide is a potent neurotoxin affecting both central and peripheral nervous systems. The magnitude of the toxic effect depends on the duration of exposure and the total dose (Tyl, *et al.*, 2000 b). Only the

acrylamide monomer is toxic, while acrylamide polymers are non-toxic (IPCs 1999). Acute oral exposure to acrylamide has resulted in neurotoxic effects in rats and affects the kidney in monkeys exposed by injection (HSDB, 1993). Tests involving acute exposure of animals, such as the LD_{50} test in rats, mice, rabbits, and guinea pigs, have demonstrated acrylamide to have high acute toxicity from oral or dermal exposure (RTECS,, 1993). The previous study for author (El-Sayed *et al.*, 2007) found that acrylamide had toxic effect on liver, kidney, heart, testes, brain, spleen and lung.

Limited information was found on the acrylamide toxicity with diet especially on kidney, brain and lung, ditto the improvement of this toxicity by turmeric as a natural antioxidant. Therefore, the present study investigated the efficacy of dietary turmeric to alleviate the adverse effect of acrylamide diet on rats' organs (kidney, lung and brain).

MATERIALS AND METHODS

Chemicals:

Turmeric root was obtained from local market. Acrylamide pure chemical with molecular formula NH_2-C=O-CH-CH_2 and purity of > 99% was purchased from Sigma Chemical Company, U.S.A. All other chemicals were of analytical grade.

Animals:

Twenty one adult male albino rats Sprague-Dawley strain (weighing 160-180g) were obtained from Vaccine and Immunity Organization, Hellwan farm, Cairo, Egypt. Rats were housed individually in mesh bottomed metallic cages under healthy environmental conditions. Water and diet were provided *ad-libitum.* Acrylamide application was (0.34g/kg diet) for 11days as described by (Lehning *et al.*, 2003). Turmeric was added (0.5 %) on diet according to Suryanarayana *et al.*, (2005).

Experimental diet:

Commercial diet as a standard diet was obtained from Alexandria Company for feeding. The diet had the following composition: protein 16%, fat 10%, fiber 2%, ash 5%; moisture 7% and total digestion ingredients 60%.

Experimental design:

Rats were divided into three groups (7 rats/ group). Group A was fed on standard diet for 11days as negative control. Group B was fed on standard diet to which acrylamide is added (0.34g / kg diet) for 11days as a positive control. Group C received the standard diet with turmeric 0.5 % and same concentration 0.34g acrylamide / kg diet for 11days as a protective group.

The consumed feed intake and body weight of rats were recorded twice a week to monitor feed intake, body weight gain and feed efficiency.

-Feed intake was calculated as g /day/rat.

$$\text{- \% Body weight Change} = \frac{\text{Final body weight} - \text{Initial body weight}}{\text{Initial body weight}} \times 100$$

$$\text{- Feed efficiency} = \frac{\text{Body weight gain (g)}}{\text{Feed intake (g)}}$$

At the end of the experimental period (11 days), all rats were anesthetized with diethyl ether after overnight fasting and sacrificed. Blood samples were taken from hepatic portal vein, blood were left in centrifuge tube at room temperature for 15min and then centrifuged at 4000 r.p.m for 10 min. Serum was separated in plastic vials at -20^{o}C until analysis. Kidneys, brain and lungs were isolated immediately, plotted free from adhering blood, washed with cold saline and dried between filter paper. All organs were frozen at -20^{o}C till further analysis.

Biochemical analysis:

Glutathione (GSH) was determined as described by Beutler *et al.*, (1963) and Superoxide dismutase (SOD) was determined according to Beauchamp and Fridovich (1971). Malondialdehyde (MDA) was assayed as described by Uchiyama and Mihara (1978). Nucleic acid was extracted from brain homogenate as specified by Shibko *et al.*, (1967). Lactate dehydrogenase (LDH) activity in brain homogenate was determined according to Kachmar and Moss (1976). Determination of total protein in serum was determined as reported of Weissman *et al.*, (1950). Quantitative enzymatic determination of blood urea nitrogen in serum was determined using stanbio laboratory Kit according to Tabacco *et al.*, (1979). Enzymatic method for determination of uric acid was determined using Sentinel kit according to Fossati *et al.*, (1980). Kinetic determination of creatinine was determined using BioMerieux kit according to Houot, (1985).

Statistical analysis:

The data were subjected to statistical analysis using computer program SPSS (1996). Independent F-test and one-way analysis of variance (ANOVA) were used, the difference was considered significant at P-value < 0.05 (Zar, 1984).

RESULTS

The present study was carried out to evaluate the interaction between acrylamide and turmeric in rats against the disorders of acrylamide. No animal mortality occurred in all groups. Overt signs (i.e

weakness and loss weight) observed in rats fed acrylamide (positive control) in the end of experiment.

1- Nutritional status of rats groups:

The present data in Table (1) showed the feed intake, body weight changes and feed efficiency of rats fed turmeric and acrylamide. The rats received acrylamide decreased significantly in feed intake, body weight change and feed efficiency as compared with negative control (A). Rats treated with turmeric showed attenuate effect of acrylamide toxicity.

2- Biochemical Results:

The effect of feeding Acrylamide and Turmeric on some kidney oxidative stress and kidney function parameters was shown in Table 2. Feeding rats with acrylamide for 11 days had increased tissue MDA, serum Urea and Uric acid level compared with the normal control rats; although there was an increase in creatinine but this increase was not significant in comparison with other groups. There was a significant decrease in GSH, SOD and total protein compared with negative control rats. On the other hand, rats fed acrylamide with turmeric, the acrylamide toxicity effect was ameliorated.

Data in Table 3, clarified the effect of receiving acrylamide and turmeric on the brain. Tissues MDA and LDH increased significantly in the group fed acrylamide compared with the normal group but tissue GSH, SOD, DNA and RNA declined significantly. There was a significant in decrement acrylamide toxicity effect in the group of rats treated with turmeric and acrylamide versus the other groups.

As illustrated in Table 4, a marked reduction in GSH, SOD content of lung tissue for rats fed acrylamide versus normal control rats but for MDA a significant increase was found. Treatment of rats by turmeric had attenuated the acrylamide toxicity effect.

Table (1): Feed Intake, Body Weight Changes and Feed Efficiency of Rats Fed Turmeric and Acrylamide.

Groups / Parameter	Group (A) Negative control	Group (B) Positive control	Group (C) Turmeric +acrylamide
Feed intake (g/ day/rat)	30.7± 0.93	25.2± 2.8*	29.3±0.7
% Body weight change	22.7± 1.7	5.8± 0.3*	18.8±0.8
Feed efficiency	0.1	0.03*	0.09

* Difference is significant P< 0.05

Table (2): The Effect of Feeding Acrylamide and Turmeric on Kidneys Function Parameters (mean ±SD).

Groups / Parameter	Group (A) Negative control	Group (B) Positive control	Group (C) Turmeric +acrylamide
GSH mg/g	31.3±0.6 [a]	17.8±0.7 [c]	29.0±1.3 [b]
SOD U/g	431.4±1.0[a]	221.0±1.9 [c]	376.0±1.6 [b]
MDA n mol/g	186.4±2.1[c]	316.0±1.5 [a]	233.9±2.2 [b]
Creatinine mg/dl	1.1±0.2 [a]	1.6±0.4 [a]	1.12±0.2 [a]
Urea mg/dl	29.5±1.5 [b]	43.6±0.9 [a]	30.1±1.4 [b]
Uric acid mg/dl	1.12±0.08 [b]	2.5±0.16[a]	1.24±0.05[b]
T. protein mg/dl	6.84±0.3 [a]	4.94±0.4 [b]	7.14±0.5 [a]

Means with the same letter in the same row are not significantly difference at 0.05 level of significance.

Table (3): The Effect of Feeding Acrylamide and Turmeric on Brain Parameters (Mean ±SD).

Parameters \ Groups	Group (A) Negative control	Group (B) Positive control	Group (C) Turmeric +acrylamide
GSH mg/g	28.1±0.7 [b]	14.3±0.4 [c]	30.3±1.0 [a]
SOD U/g	267.2±2.7 [b]	160.5±2.4 [c]	281.0±2.3 [a]
MDA n mol/g	201.2±3.2 [c]	431.2±2.0 [a]	294.6±3.7 [b]
DNA mg/g	28.3±0.8 [b]	21.9±1.2 [c]	35.0±0.9 [a]
RNA mg/g	50.7±0.8 [b]	27.2±1.6 [c]	64.3±2.3 [a]
LDH U/g	1.026±0.8 [c]	2.257±1.6 [a]	1.149±0.8 [b]

Means with the same letter in the same row are not significantly difference at 0.05 level of significance.

Table (4): The Effect of Feeding Acrylamide and Turmeric on Lungs Parameters (Mean ± SD).

Parameters \ Groups	Group (A) Negative control	Group (B) Positive control	Group (C) Turmeric +acrylamide
GSH mg/g	22.6± 1.04 [a]	16.9±1.3 [b]	22.3±1.6 [a]
SOD U/g	371.5±6.7 [b]	180.4±4.8 [a]	271.4±5.5 [b]
MDA nmol/g	48.9±1.7 [a]	78.2±2.5 [c]	50.8±1.1 [b]

Means with the same letter in the same row are not significantly difference at 0.05 level of significance.

DISCUSSION

The toxic effect of acrylamide on human and experimental animals was well documented in a series of reports since the Swedish Food Administration alarm in 2002 (Van Landingham *et al.*, 2004 & LoPachin, 2004). Acrylamide has been shown to be carcinogenic in animals and has been classified by the WHO among others as probably carcinogenic for human. Previous studies of acrylamide toxicity in rats following feeding the acrylamide diet (El Sayed *et al.*, 2007) or its oral administration (Doerge *et al.*, 2005a) showed that acrylamide is rapidly and extensively absorbed and widely distributed throughout the body. The metabolism of acrylamide in the body may result in the generation of reactive oxygen species which play a role in the oxidative stress of acrylamide and cause oxidative DNA damage, which may play a role in its carcinogenicity (Bergmark *et al.*, 1991 & Patel *et al.*, 2003). Moreover, lipid peroxidation is one of the main manifestations of oxidative damage and has been found to play an important role in the toxicity and carcinogenesis of many carcinogens.

Turmeric is capable of suppressing the activity of several common mutagens and carcinogens in a variety of cell types in both *in vitro* and *in vivo* studies (Boone *et al.*, 1992). The anti-carcinogenic effects of turmeric is due, in part, to its direct antioxidant and free radical scavenging effect; but , it also enhance the body's natural antioxidant system, increasing glutathione level(Pizorrno and Murray 1999).

The decline in body weight gain obtained in the present research (Table, 1) is in agreement with the observation of Yang *et al.* (2005), who found that the body weight was significantly lower in acrylamide treated rats than in the normal control animals. This decrease may be related to the accompanied significant decrease in reduced GSH levels in different organ tissues of rats. Martensson *et al.* (1990) reported that GSH is essential for the function and structural integrity of the gut, and those GSH deficient mice showed severe degradation of jejunum and colonic mucosa and were found to have weight loss. Acrylamide is oxidized to glycidamide, a reactive epoxide, and undergoes conjugation with glutathione (Dybing and Sanner, 2003). The increase in GSH level of the group treated with turmeric may be the reason of improving the body weight gain.

As shown in (Tables 2, 3 & 4) the levels of lipid peroxidation in (kidney, brain and lung) organs were significantly increased while the SOD activity antioxidant with acrylamide treated group was significantly decreased compared with their levels in the control group. These results clearly indicated that SOD plays a role in the suppression of oxygen free radical formation in the organs tissue. In previous work, Abdel-Wahab and Ahmad (2004) reported that lipid peroxidation is directly related to free radical mediated toxicity. Free radicals are known to attack the highly unsaturated fatty acid of cell membrane to induce lipid peroxidation which is considered a key process in many pathological events and is one of the

reactions induced by oxidative stress (Schinella *et al.*, 2002). Turmeric, as an antioxidant and anti-carcinogenic substance, was reported to have a protective effect against lipid peroxidation. The decrease in SOD activity in organs of acrylamide treated rats might indirectly led to an increase in oxidative DNA damage (Abdel-Wahab and Ahmad, 2004). Turmeric may function as an effective antioxidant as a protective agent against organs cells injuries. Receiving antioxidants may exhibit pro-oxidants properties (Tylicki *et al.*, 2003) or this may be due to natural antioxidant which causes a significant increase in renal activates of total superoxide scavenger activity and decrease in renal MDA, blood urea and creatinine (Durak *et al.*, 2002).

The decrease in nucleic acid synthesis might be due to the fact that acrylamide, which binds with protein endoplasmic reticulum, could inhibit the nucleus activity leading to the decrease in DNA, RNA and protein content. On the other hand, during absorption and metabolism acrylamide produce free radical, which may has an effect via per-oxidative change in membranes and other cellular component including oxidative DNA damage (Ramotar et al., 1999).

The increase in LDH activity in brain of acrylamide intoxicated rats indicated that acrylamide may induce neuromuscular effect. These results may suggest the presence of a hidden embolus (Schwartz, 1982). Chatterly *et al.* (1991) reported that increased LDH activity in the brain may be complicated by the possibility of contamination by hemorrhage or the disruption of the blood –brain barrier by disease which resulted from brain infarction. On the other hand, animals fed on a diet containing turmeric and acrylamide showed a significant lower in LDH activity in brain than the rats fed on acrylamide alone, these results are in agreement with those reported by Kwon and Jang, (2004).

Conclusion:

Turmeric was found to have a protective effect against acrylamide toxicity. One can then conclude that turmeric may be useful when added to certain food that are processed at a very high temperature and to people who may be exposed to acrylamide.

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