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Influence of turmeric on biochemical disorders induced by exposure to γ-rays or chlorpyrifos pesticide on rats.

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ABSTRACT

Toxicity of Chlorpyrifos and γ-radiation exposure on rats were examined in the presence or absence of Turmeric (200 mg/ kg/ b.wt.). Effects chlorpyrifos when administrated orally to rats at a dose 9 mg/ kg b .wt (1/ 4 LD_{50}) for 7 and 28 days showed increased level of malondialdehyde (MDA) concomitant with depletion in the levels of glutathion (GSH), superoxide dismutase (SOD) and catalase (CAT).γ-radiation exposure effect on rats was examined in the presence or absence of turmeric . Exposure of rats to γ-radiation (8 Gy) at a fractionated dose levels (2 Gy/ week for 4 weeks) exhibited an elevated level of MDA and decreased level of GSH, SOD and CAT. Administration of Turmeric to animals which were previously treated with Chlorpyrifose or γ-rays showed an amelioration response to the antioxidant regime. Treatment of rats with Chlorpyrifose for 7and 28 days or γ-radiation induced an elevated serum transaminases level(ALT&AST),Alkaline phosphatase (ALP) and Acid phosphatase activitey (ACP), creatinine concentration, blood urea and uric acid.Also treatment of rats with Chlorpyrifose for 7and 28 days or γ-radiation induced a decline in the testosterone level associated with alteration in the levels of follicular stimulating hormone (FSH),Iuetinizing hormone (LH) and prolactin (PRL).Results observed due to Chlorpyrifose pesticide or radiation-exposure have been ameliorated by turmeric administration. It could be concluded that turmeric might protect from oxidative stress.

Keywords: Pesticide/ gamma-radiation/ turmeric/ antioxidants/ hormones

INTRODUCTION

Organophosphate (OP) insecticides Which are used in the agricultural and domestic pest control[(1)],account for 50% of the global insecticidal use[(2)]**.** Their use is, however, accompanied by widespread toxicity in non-target organisms, including man. Chlorpyrifos (CPF) is one of the most widely used OP insecticides until 2006 when the United States Environmental Protection Agency restricted some of its domestic uses due to its toxicity. Despite this, CPF remains one of the most widely used OP insecticides. Anemia and alteration in other hematological parameters have been recorded following repeated CPF exposure [(3)].The mechanism of acute CPF toxicity involves generation of reactive oxygen species (ROS) and alteration of antioxidant enzymes activity in the intoxicated rats [(4)].Turmeric (Curcuma longa L. rhizomes) is considered a herb perennially cultivated in the Far East and other tropical areas. It belongs to the ginger famil,Zingiberaceae.Chemically, it contains 14% of volatile oil, which is mainly composed of atlantone,turmerone and zingiberrone.Also,this herb is composed of 0.3-5.4% curcumim,28% glucose,12% fructose,1% arabinose as well as resins,protein,vitamins and minerals.The volatile oil components and curcumin are considered the most active agents; turmeric has proved a great deal of pharmacological activity.It

has been found to exert an effective antioxidant, anticarcinogenic, antinflammatory and anti-microbial properties[5].Accordingly,Turmeric is widely used as food additive mostly all over the world.

Exposure to ionizing radiation causes injuries to the biological system and many defense mechanisms , as enzymes and antioxidant [6].One effect of ionizing radiation is to generate oxygen free radicals,causing cell damage by removing hydrogen atom from fatty acids,resulting in lipid peroxidation with subsequent change in membrane fluidity and permeability. Free radicals are also capable of causing protein oxidation [7].This investigation was designed to test the hypothesis that Turmeric can provide protection from CPF and radiation damage.

MATERIALS AND METHODS

A pilot test for detecting the LD_{50}:

LD_{50} was determined according to Litchfoeld and Wilcoxon[8] method. LD_{50} of Chlorpyrifos was found to be 36 mg/ kg b.wt. of rat. Chlorpyrifos stock formulation (48 % E.C) was obtained from Summitomo Company (Japan).It was determined by diluting 1 ml of stock formulation up to 13.3 ml with corn oil to give the desired LD_{50} obtained dose.

Radiation facility:

The source was ^{137}Cesium, Gamma Cell-40 manufactured by the Atomic Energy of Canada (Ltd.) provided at NCRRT, Nasr City, Cairo , Egypt. Groups of 14 rats were placed in ventilated plastic cages and allowed for free movement. Animals were exposed to 8 Gy fractionated dose of irradiation given as 2 Gy weekly for 4 weeks at a dose rate of 1 Gy / 2.10 min.

Turmeric Treatment :

Turmeric was purchased from Plant Protection Research Institute,Agriculture Research Center , Egypt. Animal received turmeric orally for 7 consecutive days before CPF pesticide or radiation exposure and treatment was continued during the whole period of irradiation and CPF processing (4 weeks).The administered dose was 200 mg/kg b.wt/day suspended in 0.5 ml of distilled water based on protocol described by Rukkumani et al.,[9].

Animal groups under investigations:

Adult male rats (l10± 10g) were obtained from the Holding Company for Biological Products and Vaccines (VASERA), Cairo, Egypt, housed in specially designed cages and allowed to receive standard balanced diet and free water supply. The animals were divided into 6 groups (each of 14 rats):

(1): Control group. **(2)**: Rats orally intubated a single dose of 1/4 LD_{50} (9 mg/ kg rat) of Chlorpyrifos daily for 4 weeks. **(3)**: Rats subjected to 8Gy. fractionated doses of γ-rays (2 Gy) once a week for 4 weeks. 8 Gy exposure was started from the 3th day of treatment with CPF. **(4):** Rats received orally Turmeric for 4 weeks at daily dose of 200 mg/Kg b.wt., **(5):** Chlorpyrifos group was given Chlorpyrifos at a dose of 9 mg/kg b.wt. after which the turmeric has been orally administered. **(6):** Rats received orally Turmeric and in the same time the were exposed to the fractionated gamma-irradiation dose (2 Gy weekly).

14 animals from each group were sacrificed 24 hours post the end of the experiment. Blood (by cardiac puncture) was collected and prepared following normal laboratory procedures, for the measurement of the biochemical and hormonal parameters.

Biochemical Analysis:

Lipid peroxidation product was measured using the method of Yoshioka,et al.,[10] by the measurement of MDA as one of the main end products of LPO. GSH content and SOD activity were determined following the method reported by Beutler, et al., and Minami & Yoshikawa[11,12].CAT activity was determined according to the method described by Johansson and Borg[13]**.** AST and ALT activities were measured according to Reitman and Frankel[14]**.**ALP activity was performed according to method of Kind and King[15].ACP activity was measured according to method of Vanha and Nikkan[16]**.** Urea concentration was measured according to the procedure described by Hallett and Cook[17] and creatinine concentration according to the method **of** Faulkner and King[18]**.**Serum uric acid was determined following the method reported by Barham and Trinder[19]**.**

Hormonal assay:

Estimation of testosterone hormone was carried out using diagnostic kit purchased from DPC company as described by Yen and Jaffe[20], LH hormone was assayed with the use of diagnostic kit described by Santner, et al.,[21]. Plasma FSH concentration was measured using a double antibody radio-immuno-assay (RIA) according to the standard method of Snedecor, and Cochran[22]**.** PRL hormone was determined by specific double antibody radio-immuno-assay as described by Djursing[23]**.** The level of the hormones were calculated according to standard curves.

Statistical analysis:

Data are represented as mean± SE. Results obtained were statistically analyzed as described by Sendcor[24].

RESULTS AND DISCUSSION

Oxidant and antioxidant levels:

Data shown in table (1) demonstrate that the treatment of animals with Chlorpyrifos alone after 1 week and 4 weeks revealed a significant increase of MDA by 111.8%, 108.3% compared to the control group. Whereas, in the same group there was a significant decrease in the GSH by 92.4% , 93.6 % , significant decrease occurred in the SOD activity by 90.3% , 87.9% and CAT by 82.3% , 91% compared to the corresponding control values. Exposure of rats to γ-radiation exhibited a significant increase in MDA (120.4%, 117.9%) compared to the control group. The other biochemical parameters showed a significant decrease (88.9%, 88.2%) for GSH content, (88.3%, 90.2%) for SOD activity and 75.8%, 77.4% for CAT compared to the control ones.

Treatment of animals with Turmeric and in the same time with Chlorpyrifos pesticide (at 1 week , 4 weeks) , showed an ameliorative to effect on the levels of the tested MDA, GSH , SOD and CAT levels in comparison with those of the Chlorpyrifos group No. 3 reaching (101% ,99.3%) , (96.4% ,98.1%) , (95.3% ,97.5%) , (90.3 ,%,94 %),respectively. Finally, the treatment of animals with Turmeric as well as exposure to γ-rays through the period of experimentation showed an improvement in the level of MDA, GSH, SOD and CAT, respectively in comparison with the values of the radiation group No. 4 reaching (104% ,104%) , (93.6% ,95.9%), (95.9% , 95.9%) , (83%, 90.2),respectively.

Table (1): **Influence of turmeric supplementation to rats on the hazardous effect of chloropyrifose and gamma- irradiation on MDA, GSH, SOD and CAT levels.**

Group		MDA (n mol./ml.)		GSH (mg/dl)		SOD (U/ml.)		CAT (U/g)	
Time		**1 week**	**4 week**	**1 week**	**4 week**	**1 week**	**4 week**	**1 week**	**4 week**
control	Mean	28.8±0.13	28.96±0.16	53.2±0.03	53.7±0.08	44.4±0.12	44.7±0.18	24.8±0.64	23.5±0.53
turmeric	Mean	28.7±0.11	28.9±0.13	53.5±0.07	53.8±1.2	44.7±0.14	44.9±0.16	23.2±0.67	23.7±0.33
	% of change	99.6%	100%	100.5%	100.3%	100.6%	100.8%	93.55%	108%
	Significance								
chloropyrifos	Mean	32.2±0.18	31.3±0.17	49.2±0.12	50.3±1.4	40.11±0.13	39.3±0.18	20.4±0.42	21.4±0.51
	% of change	111.8%	108.3%	92.4%	93.6%	90.3%	87.9%	82.3%	91%
	Significance	a	a	a	a	a	a	a	a
Radiation	Mean	34.7±0.16	34.1±0.15	47.6±0.18	47.4±0.16	39.2±0.11	40.03±0.14	18.8±0.62	18.2±0.60
	% of change	120.4%	117.9%	88.9%	88.2%	88.3% a	90.2%	75.8%	77.4%
	Significance	a	a	a	a		a	a	a
Turm.+Chlor.	Mean	29. 1±0.14	28.7±0.19	51.3±0.21	52.7±0.13	42.3±0.15	43.6±0.17	22.4±0.41	22.1±0.51
	% of change	101%	99.3%	96.4%	98.1%	95.3%	97.5%	90.3%	94%
	Significance	b	b	ab	b	ab	b	ab	b
Turm+Rad.	Mean	30.01±0.13	30.3±0.16	49.8±0.11	51.5±0.16	42.6±0.13	42.9±0.14	20.6±0.43	21.2±0.39
	% of change	104%	104.1%	93.6%	95.9%	95.9%	95.9%	83%	90.2%
	Significance	c	c	ac	ac	ac	ac	ac	ac

The values are the mean of 14 rats± SE.

a = Significant when compared with the control group.
b = Significant when compared with the group treated with pesticide.
c = Significant when compared with the group treated with gamma rays.

Changes in serum ALT, AST, ALP and ACP:

As shown in Table (2) the treatment of animals with Chlorpyrifos pesticide alone for 1 week and 4 weeks revealed a significant increase in the serum AST , ALT,ALP and ACP by (171.7 % ,171 %) , (132.3%,135.8 %),(125.2 % 123.4%) and(111.4% ,113.1%) respectively, in comparison with those of the control ones. Whereas, exposure of rats to γ-radiation alone, exhibited a significant increase in AST by(186.8% ,180%) , ALT by (137.5% ,136.1%) ,ALP by (129.9% ,133.4%) and ACP by (115.4% ,117.4%) respectively, after 1 week and 4 weeks compared to the control ones. Treatment of animals with Chlorpyrifos pesticide for 1 week, 4 weeks, and in the same time received Turmeric, exhibited an ameliorative effect on the levels of the tested AST, ALT, ALP and ACP levels in comparison with the Chlorpyrifos group No. 3. Finally the treatment of animals with γ- radiation and in the same time injected with Turmeric, through the experimental period showed a marked restoration in the level of AST,ALT, ALP and ACP by (163.9%, 162%) , (113.8 %,104.7 %) ,(117.8 ,117.8%), (107.8%,111.5%) respectively in comparison with those of the radiation group No.4 .

Table (2): Influence of turmeric supplementation to rats on the hazardous effect of chloropyrifose and gamma- irradiation on AST, ALT, ALP and ACP levels.

Group		AST (U/L.)		ALT (U/L.)		ALP (U/L.)		ACP (U/L.)	
Time		**1 week**	**4 week**	**1 week**	**4 week**	**1 week**	**4 week**	**1 week**	**4 week**
control	Mean	25.8±2.04	25.6±2.01	29.7±1.6	29.9±1.4	36.5±0.49	35.9±0.38	109.8±0.82	109.2±0.80
turmeric	Mean % of change Significance	26.4±2.01 102.3%	26.6±1.9 103.9%	30.1±1.4 101.3%	30.6±1.9 102.3%	37.01±0.37 101.3%	37.1±0.29 103.3%	112.3±0.62 102.2%	110.3±0.41 101%
chloropyrifos	Mean % of change Significance	44.3±1.6 171.7% a	43.8±1.7 171% a	39.3±1.8 132.3% a	40.6±1.3 135.8% a	45.7±0.72 125.2% a	44.3±0.69 123.4% a	122.3±0.57 111.4% a	123.6±0.71 113.1 a
Radiation	Mean % of change Significance	48.2±2.02 186.8% a	46.1±2.06 180% a	41.4±2.01 137.5% a	40.7±1.8 136.1% a	47.4±0.65 129.9% a	47.3±0.55 133.4% a	126.8±0.67 115.4% a	128.2±0.53 117.4% a
Turm.+Chlor.	Mean % of change Significance	37.8±1.08 146.5% ab	38.1±2.01 148.8% ab	30.6±1.9 103% b	30.4±1.2 101.7% b	40.7±0.65 111.5% ab	41.1±0.61 114.4% ab	115.3±0.61 105% ab	116.1±0.58 106.3% ab
Turm+Rad.	Mean % of change Significance	42.3±1.05 163.9% ac	41.5±1.07 162% ac	33.8±1.9 113.8% ac	31.3±2.03 104.7% c	42.8±0.51 117.3% ac	42.3±0.46 117.8% ac	118.3±0.49 107.8% ac	121.8±0.60 111.5% ac

The values are the mean of 14 rats± SE.

a = Significant when compared with the control group.
b = Significant when compared with the group treated with pesticide.
c = Significant when compared with the group treated with gamma rays.

Changes in Serum level of Creatinine , Urea and Uric Acid :

As shown in Table (3), treatment of rats with Chlorpyrifos pesticide for 1 week & 4 weeks revealed a significant elevated levels of renal function parameters by (138.7%,154%), (122.9%,128.6%) and (135.3%,161.6%) respectively for creatinine, urea and uric acid cpompared to the control levels. Exposure of anima1s to γ-radiation doses induced also a highly significant increase in renal function parameters by 161.2%,166%for creatinine , 131%,135.3% for urea and 150%,181.6% for uric acid compared to the control levels.Treatment of rats with Chlorpyrifos pesticide for 1 week &4 weeks, and in the same time administered turmeric, renal function parameters become better in comparison with the levls the Chlorpyrifos group No 3. Treatment of animals with γ-radiation through the experimentation period and in the same time ingested with Turmeri,showed an improvement action on the renal function parameters in comparison with the radiation group No. 4 , reaching 108.1%, 128% for creatinine, 109% ,115% for urea and 102.9%,108.3% for uric acid respectively.

Hormonal levels assay:

Results presented in table (4), display that the treatment of rats with Chlorpyrifos pesticide for 1 week &4 weeks induced a significant decrease in the testosterone level (75.5 % , 67%), compared with the corresponding control level. Also, the treatment caused a significant increase in the FSH level by 171.9%, 172.5%, LH level by 110.6%, 122.4% and PRL hormone level by106.8% , 117.6% , compared with control group. Exposure of animals to γ-radiation showed a highly significant decline in the content of testosterone (69.6%, 58.6%) compared to the control level. Meanwhile, the levels of FSH, LH and PRL in the same group revealed a significant augmentation in their levels (183.1%,

178.5%), (139.5%, 142.5%), (106.4%, 114.9%) respectively compared to the control values. Treatment of animals with Chlorpyrifos.

Table (3): Influence of turmeric supplementation to rats on the hazardous effects of chloropyrifos and gamma- irradiation Creatinine, Urea and Uric acid levels.

Group		Creatinin (mg/dl)		Urea (mg/dl)		Uric acid (mg/dl)	
Time		**1week**	**4 weeks**	**1week**	**4 weeks**	**1week**	**4 weeks**
Control	Mean	0.49±0.04	0.50±0.03	29.32±0.81	28.6±0.03	6.8±0.22	6.01±0.35
Turmeric	Mean % of change Significance	0.47±0.04 95.9%	0.45±0.05 90%	28.8±0.41 93.3%	27.5±0.43 96.2%	5.9±0.27 86.7% a	5.8±0.23 95%
Chloropyrifos	Mean % of change Significance	0.68±0.04 138.7% a	0.77±0.06 154% a	36.01±0.02 122.9% a	36.8±1.2 128.6% a	9.2±0.05 135.3% a	9.7±0.04 161.6% a
Radiation	Mean % of change Significance	0.79±0.03 %161.2 a	0.83±0.06 %166 a	38.5±0.46 %131 a	38.7±1.4 135.3% a	10.2±0.06 150% a	10.9±0.08 181.6% a
Turme+Chlorp	Mean % of change Significance	0.58±0.37 118.3% ab	0.51±0.04 102% b	31.3±0.03 106.4% ab	32.3±0.14 112.9% ab	8.4±0.18 123.5% ab	7.8±0.21 130% ab
Turme.+Rad	Mean % of change Significance	0.53±0.22 108.1% ac	0.64±0.03 128% ac	32.9±0.41 109.5% ac	32.9±0.43 115% ac	7.01±0.22 102.9% c	6.5±0.23 108.3% c

The values are the mean of 14 rats± SE.

a = Significant when compared with the control group.
b = Significant when compared with the Chloropyrifose group.
c = Significant when compared with the Radiation group.

Pesticide and in the same time delivered Turmeric, revealed amilioration in the levels of the tested hormones (testosterone, FSH ,LH and PRL) by 91.7%, 96.2 % , 137.6% , 124.1% , 107.1% , 111.7% and 101% , 101.8% respectively in comparison with the Chlorpyrifos group No.3 levels. The exposure of animals to γ-radiation and the same time treated with turmeric improved the levels of the tested parameters compared with those of the radiation group No.4

Table (4): Influence of turmeric supplementation to rats on the hazardous effects of chloropyrifose and gamma-irradiation on Testosterone, FSH, LH, and PRL.

Groups		Testosterone (ng/ ml)		FSH (ng/ml		LH (mIu/ml		PRL (mIu)	
Time		**1week**	**4 week**	**1week**	**4week**	**1week**	**4week**	**1week**	**4week**
Control	Mean	2.54±0.06	2.61±0.06	3.21±0.04	3.31±0.06	2.81±0.02	2.63±0.05	4.66±0.04	4.42±0.05
Turmeric	Mean % of change Significance	2.57±0.04 101.2%	2.51±0.08 96.2%	3.27±0.07 101.8%	3.35±0.04 101.2%	2.77±0.08 98.6%	2.74±0.09 104.1%	4.70±0.03 100.8%	4.48±0.03 101.3%
Chloropyrifos	Mean % of change Significance	1.92±0.03 75.5% a	1.75±0.05 67% a	5.52±0.08 171.9% A	5.71±0.06 172.5% a	3.11±0.02 110.6% a	3.22±0.06 122.4% a	4.98±0.04 106.8%	5.20±0.05 117.6% a
Radiation	Mean % of change Significance	1.77±0.04 69.6% a	1.53±0.06 58.6% a	5.88±0.07 183.1% A	5.91±0.05 178.5% a	3.92±0.06 139.5% a	3.75±0.08 142.5% a	4.96±0.02 106.4%	5.8±0.06 114.9% a
Turme+Chlorp	Mean % of change Significance	2.33±0.07 91.7% b	2.61±0.05 96.2% b	4.42±0.09 137.6% Ab	4.11±0.05 124.1% ab	3.01±0.08 107.1% a	2.94±0.07 111.7% ab	4.71±0.03 101%	4.50±0.06 101.8%
Turme.+Rad	Mean % of change Significance	2.17±0.03 85.4% c	2.49±0.07 95.4% c	4.91±0.06 152.9% ac	4.55±0.04 137.4% ac	3.31±0.07 117.9% ac	3.46±0.03 131.5% a	4.46±0.05 95.7%	4.63±0.07 104.7%

The values are the mean of 14 rats± SE.

a = Significant when compared with the control group.
b = Significant when compared with the Chloropyrifose group.
c = Significant when compared with the Radiation group.

Oxidative stress is known to be a disparity between the rates of free radical production and rate of elimination [(25)]. Exposure to ionising radiation eventually results in injuries to the biological systems depending on the dose, duration and type of radiation exposure and radio-sensitivity of various tissues. It has been conformed that 6 Gy γ-rays alter chemical aspects in rats[(26)].Bashir et al.,[(27)] reported that propagation of LPO in biological membranes, accompanied by the dysfunction of the antioxidant system and depletion of GSH, were attributed to pesticide toxicity that may cause excessive production of free radicals.

In the present study, administration of Chlorpyrifos pesticide to male rats day/ for 1 week, and 4 weeks could enhance the oxidative stress that was accompanied by augmentation of LPO and depletion of GSH content, SOD and CAT activity. The antioxidant defensive mechanism in rats is characterized by chronic inflammatory syndrome associated with severe oxidative damage of lipid molecules and depleted antioxidant capacity [(28)]. Consequently, dramatic fall has occurred in GSH leading to membrane LPO in Chlorpyrifos pesticide and γ-irradiated groups. The above mentioned results are in harmony with present findings in which Chlorpyrifos pesticide and γ-rays could cause elevation in MDA level and reduction in GSH content, SOD and ACT activity. The vital importance of Turmeric for health and as reducing agent of oxidative stress is now fully recognized and it has been tested for their radioprotective effects on different animals [(29)].

In the present study, Turmeric intake modulated the dangers of Chlorpyrifos pesticide and γ-rays and resulted in superior therapeutic effect and give rise to non-significant differences in MDA, GSH, SOD and CAT levels in comparison with control groups. In the present study, the exposure of

rats to the applied dose level of Chlorpyrifos pesticide for 1 week, 4 weeks induced a significant elevation in serum transaminases level. This increase could be attributed to hepatocellular impairment which subsequently caused the release of greater levels of intracellular enzymes into the blood as a result of massive damage of liver and other organs. The elevation in the liver enzymes activity may be due to insufficiency of ATP which is necessary as an energy source for building protein and amino acids.Chlorpyrifose is well absorbed by ingestion, inhalation and skin contact and metabolized in liver by microsomal xenobiotic metabolizing enzymes..Hence both chlorpyrifose and chlorpyrifose oxon (organophosphours compounds) are toxic compounds and have harmful effect on liver [30] .The toxicity of organophosphorus insecticides varies depending on the route of administration,vehicle.species and sex [31] .

Exposure of adult rats to gamma-radiation dose exhibited a significant increase in the level of serum ALT,AST,ALP and ACP which could be considered an indication to the toxicity induced by radiation exposure.These results are in agreement with those previously reported Kaplan **[32].** The increase in serum level of these enzymes may be due to alteration in the dynamic permeability of membranes by ionizing radiation, allowing leakage of biological active material out of the injured cell,which may be associated with cell death or injuries.Also, ALP is considered as an enzyme of the hepatocytes plasma membrane,thus an increase in serum ALP activity has been related to damage of liver cell membranes **[33]**. Exposure of rats to ionizing radiation eventually results in injuries to the biological systems depending on the dose, duration and type of radiation exposure, the radio-sensitivity of different tissue besides several other important factors **[34].**

In the present study, the treatment of rats with Chlorpyrifos pesticide doses for 1 week and 4 weeks and exposed to γ- radiation doses displayed a significant elevation in the serum renal function parameters (creatinine, urea and uric acid). These results are in accordance with the results of Robbins, et al., **[35]**. Who reported an increase in the blood creatinine level in the irradiated rats.They reported also that irradiation of rats at dose level from 6-13 Gy induced extensive retention in daily excreted urine which result in creatinuria that lead to increase in its level in the blood. They attributed this action to the interaction of creatinine with their sites of biosynthesis. The exposureof animals to ionizing radiation induce protein breakdown manifested by an increase in the protein end-products. Urea being the major end-product of protein catabolism.The degradation of protein by ionizing radiation exposure is accompanied by an increase in the serum urea in animals exposed to γ- radiation and therefore increase in the free ammonia in different tissues **[36].** Also, sustaining that result of the increased rate of protein catabolism in animals exposed to γ-radiation, that lead to increased urea level.

In the present investigation increased serum uric acid could be an indication of renal disease and elevated serum uric acid may also reflect a metabolic defect in purine metabolism that caused increased production of uric acid. The increase in blood urea level could be at attributed, in part, to an impairment of kidney function. The present data are in harmony with earlier reports documenting elevated serum urea after treatment with different pesticides. Acute doses of 2, 4- dichlorophenoxuacetic acid at levels of 100, 300 and 600 mg/kg body weight increased serum urea in rats**[37]** and daily oral exposure of the synthetic pyrethroid cypermethrin produced a significant increase in serum urea and creatinine in rats**[38].** The pesticides caused a significant increase in both creatinine and urea levels. These results concord those of Aly et al.,**[39]** who stated that oral administration of the insecticide deltamethrin at 13 mg/kg or 26 mg/kg to male rats for 28 consecutive days caused a significant increase in creatinine and urea levels.

In the present study, the exposure of animals to Chlorpyrifos pesticide as well as γ-radiation exhibited a marked decrease in the testosterone level and significant increase in the level of FSH and LH due to the effect of the used pollutant [40]. The secretion of testosterone is under the control of LH and the mechanism by which LH stimulates the leyding cells involves increase formation of cyclic AMP. Testosterone is also formed in the adrenal cortex. Ninety-seven percent of the testosterone plasma is bound to protein: 40%is bound to B-globulin and called gonadal steroid binding and 40% to albumin and 17% is bound to other proteins [41]. The decrease in the level of testosterone accompanied with an atrophy in sex gonads was revealed by the destruction that occurred in the germinal cells of testis after exposure to pesticides or gamma rays .Similarly, a significant decrease in the testosterone level after treatment of rats with quinalphos or melathion.This decline coud be due to the inhibition of formation of 5-alpha-DHT which led to a decrease in the level of androstanedione. Recently, some authors attributed this decrease to the toxic effect of pesticides directly and/or indirectly via hypothalamic pituitary testis axis and the decrease in the testosterone concentration which was dependent on both dose and time of exposure [42].

FSH may also augment testosterone secretion possibly by inducing maturation of the leyding cells. Testosterone also regulates the sensitivity of the pituitary to the hypothalamic-releasing factor luteinizing hormone-releasing hormone (LHRH). Although the pituitary can convert testosterone to dihydro testosterone and/or to estrogens, testosterone itself is the primary regulation of gonadotrophin secretion [43]. Testosterone reduces plasma LH but expect in large doses, it has no effect on the plasma FSH. Thus, it appears that testosterone feeds back to inhibit LH secretion, whereas FSH secretion is independently controlled by inhibin a protein secreted by sertoli cells and acts on the pituitary gland directly [44]. In response to LH, some of the testosterone secreted from the leyding cells bathes through the seminiferous epithelium layer and provides the high local concentration of androgen systemically [41]. The present observations match those found by [44]**.** Who reported that hazards induction by irradiation and of chemotherapy on the activity of sertoli cells lead to the destruction of germinal epithelium**.** They further stated that gonadal damage appear after fractionated irradiation doses. The implication of gonadal dysfunction induced by chemotherapy or irradiation go beyond the diagnosis of amenorrhea and altered gonadotrophin parameters. The naturally occurring polyphenolic antioxidant have received increased attention in the maintenance of health and in disease prevention [45]**.**

Recently, there has been an increasing interest in the protective function of dietary antioxidants, which are candidates for the treatment of atherosclerosis, cancer chemoprevention and extending lifespan [46]**.**Several antioxidants, such as vitamin E ,vitamin C, B-carotene, uric acid and flavonoids, have been found to to play important rols in the non-enzymatic protection against oxidative stress. Turmeric has been reported to posses a broad spectrum of chemopreventive activity in preclinical models and appears to be safe in animal and human studies [47]**.** In the present study, experimental animals receiving 200 mg/hg body wt. Turmeric, for 4 weeks induced ameliorative action on the redox system (Tables 1, 2, 3, 4). Turmeric undergoes extensive metabolic conjugation and reduction in the gastrointestinal tract in humans and rats. Turmeric exerted through free radicals scavenging property and electron hydrogen donation mechanism [48].Moreover, the antioxidant mechanism of turmeric is attributed to its unique conjugated structure, which includes two methoxylated phenols and an enol form of B-diketone; the structure shows typical radical-trapping ability as a chain- breaking antioxidant [49]**.** In the present study, administration of turmeric to irradiated rats has significantly ameliorated the changes induced by irradiation and pesticide exposure supporting the hypothesis that plant products are effective antioxidative agents, by scavenging or neutralizing free radicals interacting with oxidative cascade and preventing its outcome quenching singlet oxygen making it less available for oxidative reaction[50] ; inhibiting oxidative enzymes lik cytochrome P450 and by chelating metal ions like Fe ,inhibits peroxidation of membrane lipids and maintains cell membrane integrity and their function [51]**.** Furthermore, [52] found that, conversion of XD to XO is reduced by turmeric to the basal level *in vitro* study. It is suggested that, the major inhibitory mechanism of turmeric on increases in XO enzyme activities is through direct inactivation at the protein

level.Therefore, turmeric may stabilize the cell membrane and significantly reduce the extent of lipid peroxidation in the blood and liver induced by oxidative stress-released under influences of gamma radiation and Chlorpyrifose pesticide.

CONCLUSION

The development of procedures to ameliorate undesirable ROS production may be one of the central issues in research on aging and oxidative stress-related diseases in the near future. Dietary antioxidant are widely used to ameliorate excessive oxidative stress; despite scientific proof of their efficacy is scarce[53] .However, the antioxidant and cytoprtective activites induced by turmeric offers a great advantage for therapeutic purposes, and could become a part of daily diet as herbal supplement.

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