

USE OF CURCUMA AS A RADIOPROTECTOR

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ABSTRACT

Curcuma longa is the scientific name of Turmeric, which can be found on spice racks worldwide. This herb is responsible for the yellow coloring of many Currie dishes.

Female albino rats were treated with oral administration of curcumin for 14 days before γ -irradiation.

γ Radiation was applied in 0.1, 0.75 and 2 Gy, 1 hour after the last dose of curcuma administration. Animals were divided into control and 6 treated groups, all were irradiated with γ -rays, only three were injected with curcumin. Blood collected 1 and 48 hours after irradiation. Serum total protein, albumin, globulins, cholesterol, triglycerides, SGOT and SGPT were determined.

Curcuma was found to elevate the protein profile (total protein, albumin and globulin) and ameliorates the hyperlipidemic effects of γ -radiation. Curcuma also improved the liver functions affected by γ -irradiation.

The experiment concluded that curcuma can be used as a radioprotector for occupationally exposed individuals to low doses and low dose rates.

Key words: Curcuma, Proteins, Cholesterol, triglycerides, Liver function

INTRODUCTION

Curcuma longa is the scientific name of **Turmeric**, which can now be found on spice racks worldwide. This herb is responsible for the yellow coloring of many currie dishes. Not only does this herb enhance flavor, it also has a variety of physiologic effects including inhibiting platelet aggregation (**Lee, 2006**), anti-cholesterol activity, and fibrinolytic action (**Zoltan P. Rona, 2004**). The active ingredient is Curcumin, essential oil (p-tolymethylcarbinol), present in Rhizome of the plant (Encyclopedia of Natural Medicine, 1998). This spice is consumed in the diet in quantities up to 49 gm/adult/day in some countries (**Sambaiah et al., 1982**)

Curcumin is a good antioxidant and inhibits lipid peroxidation in rat liver microsomes, erythrocyte membranes and brain **homogenates** (**Pulla Reddy and Lokesh, 1994**)

Curcumin is also a good scavenger of reactive oxygen species and lowers its formation as well as the formation of inflammatory compounds such as prostaglandins and leukotrienes (**Unnikrishnan and Rao, 1992**).

Leela Srinivas et al., (1992) reported that curcumin like turmerin, (is a component of turmeric) in vitro studies protects erythrocyte membranes and phospholipid fatty acids from oxidation. Recently, **Park-Banjeon et al., (2002)**

reported that curcumin lowered the serum levels of ALT, AST, bilirubin and cholesterol in rats induced liver injury.

The hypolipidemic effect of curcumin was studied in rats that were fed a high-cholesterol diet (HCD). Lipid profile and aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were assessed in serum, and anti-oxidant parameters were assessed in liver tissues (**Arafa, 2005**).

Reduction in the body weight occurs in curcumin-fed rats having a decreased concentration of serum triglycerides (Inano et al., 1999)

When the rats were given curcumin for 14 days, their livers' production of GST increased by 16%, and a marker of free radical damage called malondialdehyde decreased by 36% when compared with controls (Asai et al., 1999).

In a recent rat study that was conducted to evaluate the effects of turmeric on the liver's ability to detoxify xenobiotic (toxic) chemicals, levels of two very important liver detoxification enzymes (UDP glucuronyl transferase and glutathione-S-transferase) were significantly elevated in rats fed turmeric as compared to controls. The researchers commented, "The results suggest that turmeric may increase detoxification systems in addition to its anti-oxidant properties. Turmeric used widely as a spice would probably mitigate the effects of several dietary carcinogens (Asai et al., 1999).

MATERIALS AND METHODS

Animals

Forty-two female albino rats weighting 140-150 g were used. Animals were kept under good ventilation and illumination conditions and allowed balanced diet and tap water was offered liberally. γ irradiation was performed by using C^{60} source, installed in Middle Eastern Regional Radioisotope Center for the Arab Countries. Animals were exposed to whole body γ -rays with dosage level of 0.1, 0.75 and 2 Gy as a single dose. The dose rate was 1.4 Gy/minute at the time of the experiment.

Treatment:

curcuma (Curcuma longa, Turmeric) was purchased from El-Gomhoria Pharm. Indust. and Med. Suppl. Co., and diluted with distilled water. Oral administration to rats at a concentration of 100 mg/Kg body weight daily for 14 days before irradiation. Radiation processing was performed 1 hour after the last dose of curcuma administration.

Experimental design:

- The animals were divided into 7 groups,
- Group 1: Comprised 6 animals considered as control animals (not injected or irradiated).
 - Group 2: Comprised 6 animals were exposed to whole body γ irradiation at a dose of 0.1 Gy.
 - Group3: Comprised 6 animals administered orally curcuma 14 days before whole body irradiation with 0.1 Gy.
 - Group 4: Comprised 6 animals were exposed to whole body γ irradiation at a dose of 0.75 Gy.
 - Group5: Comprised 6 animals administered orally curcuma 14 days before whole body irradiation with 0.75 Gy.
 - Group 6: Comprised 6 animals were exposed to whole body γ irradiation at a dose of 2 Gy.
 - Group7: Comprised 6 animals administered orally curcuma 14 days before whole body irradiation with 2 Gy.

Experimental Methods:

Blood samples were collected from orbital venous plexus after 1 and 48 hours after irradiation exposure. Serum samples were separated by centrifugation at 3000 rpm for 15 minutes and stored frozen until the biochemical analysis.

Serum total proteins were determined by kinetic procedures using STANBIO kits according to methods of Cannon DC (1974). Albumin, (Dumas and Biggs, 1972). Cholesterol, (Flegg, 1973). Triglycerides, (Scheletter and Nussel, 1975). Glutamic oxalacetic transaminase (GOT), (Bergmeyer 1978). Glutamic pyrovic transaminase (GPT) was determined by colourimetric method using Quimica Clinica Aplicada S.A. procedures (Reitman, and Frankel, 1957). Serum globulin was calculated.

Computer program "Excel 2000" under windows XP was used for the calculations (Mean \pm Standard Error and Student T-test). T-test was calculated for control group with all groups, and between irradiated groups to its identical (same dose of radiation and same time of blood collection, differ only in injection of curcuma or not) injected irradiated ones.

RESULTS

The results of the effect of oral curcuma administration (100 mg/Kg) for 14 successive days pre-irradiation (with doses 0.1, 0.75 and 2 Gy) for each group on serum total proteins, serum albumin and serum globulins are shown in table (1).

There was a significant decrease in serum total proteins in irradiated groups with 2 Gy and sacrificed after 1 and 48 hours in comparison with control group. There was also a significant increase in serum total proteins in groups injected with curcuma pre-irradiation in comparison with its identical irradiated group.

There was a significant decrease in serum albumin of irradiated groups with 0.75 and 2 Gy compared to control group. There was also a significant increase in serum albumin in all groups that injected with curcuma pre-irradiation in comparison with its identical irradiated group.

Table (1) Effect of γ -irradiation on serum Total Protein, Albumin and Globulins with and without curcuma administration (mean \pm S.E. and T-test)

Group Parameter	Control	Irr. 0.1 Gy		Inj. irr. 0.1 Gy		Irr. 0.75 Gy		Inj. irr. 0.75 Gy		Irr. 2 Gy		Inj. irr. 2 Gy	
		1 h	48 h	1 h	48 h	1 h	48 h			1 h	48 h	1 h	48 h
T.P. gm/dl	9.58 \pm 0.04 a	9.30 \pm 0.11 b	9.57 \pm 0.39 c	10.55 \pm 0.33 a,b	10.73 \pm 0.23 a,c	9.33 \pm 0.21 d	9.50 \pm 0.37 e	10.40 \pm 0.26 a,d	10.57 \pm 0.10 a,e	9.27 \pm 0.10 a,f	8.80 \pm 0.15 a,g	10.10 \pm 0.13 a,f	9.48 \pm 0.20 g
Albumin gm/dl	5.00 \pm 0.20 a	4.87 \pm 0.20 b	4.52 \pm 0.13 c	6.12 \pm 0.11 a,b	5.95 \pm 0.17 a,c	4.40 \pm 0.11 a,d	4.08 \pm 0.23 a,e	5.07 \pm 0.06 d	4.85 \pm 0.05 e	4.25 \pm 0.05 a,f	3.42 \pm 0.31 a,g	4.97 \pm 0.09 f	4.35 \pm 0.07 a,g
Globulin gm/dl	4.58 \pm 0.16 a	4.43 \pm 0.13	5.05 \pm 0.26	4.43 \pm 0.23	4.78 \pm 0.08	4.93 \pm 0.10	5.42 \pm 0.17 a	5.33 \pm 0.21 a	5.72 \pm 0.05 a	5.02 \pm 0.05	5.38 \pm 0.17 a	5.13 \pm 0.05 a	5.13 \pm 0.13 a

Inj. Irr. = Injected irradiated

Irr. = Irradiated only

Similar subscript litters mean significant change.

Data in table (2) showed the effect of curcuma oral administration (100

mg/Kg) for 14 successive days pre-irradiation with doses 0.1, 0.75 and 2 Gy for each group on serum cholesterol and serum triglycerides.

On comparison with control group cholesterol showed a significant increase in all irradiated groups, except that group irradiated with 0.1 Gy and sacrificed after 1 hour (non-significant increase). Also, there was a significant decrease in serum cholesterol in all injected irradiated groups compared to those irradiated.

Serum triglyceride showed a significant increase in all irradiated groups in comparison to control group except that group irradiated with 0.1 Gy and sacrificed after 1 hour (non-significant increase). Also, there were a significant decrease in serum triglycerides between all injected irradiated groups in comparison with its identical irradiated group.

Table (2) Effect of irradiation on serum Cholesterol and Triglycerides with and without curcuma administration (mean \pm S.E. and T-test)

Group Parameter	Control	Irr. 0.1 Gy		Inj. irr. 0.1 Gy		Irr. 0.75 Gy		Inj. irr. 0.75 Gy		Irr. 2 Gy		Inj. irr. 2 Gy	
		1 h	48 h	1 h	48 h	1 h	48 h	1 h	48 h	1 h	48 h	1 h	48 h
Chole	188.0 \pm 3.61 a	194.0 \pm 4.39 b	201.8 \pm 3.75 a,c	177.2 \pm 1.14 a,b	182.2 \pm 0.72 c	205.3 \pm 4.54 a,d	211.3 \pm 3.78 a,e	187.2 \pm 2.11 d	194.0 \pm 1.05 e	219.3 \pm 4.20 a,f	228.3 \pm 3.52 a,g	201.2 \pm 2.83 a,f	207.7 \pm 2.43 a,g
	Trigly	121.7 \pm 1.19 a	122.5 \pm 1.59 b	129.2 \pm 1.56 a,c	117.2 \pm 1.06 a,b	120.8 \pm 1.54 c	134.0 \pm 0.82 a,d	140.3 \pm 0.97 a,e	124.2 \pm 0.96 d	130.7 \pm 2.15 a,e	145.2 \pm 0.65 a,f	155.1 \pm 2.62 a,g	134.5 \pm 1.75 a,f

Inj. Irr. = Injected irradiated

Irr. = Irradiated only

Similar subscript litters mean significant change.

Table (3) showed the effect of γ irradiation on SGOT/(AST) and SGPT/(ALT) in rats with and without oral curcuma administration (100 mg/Kg) daily for 14 successive days then exposed to γ radiation with doses 0.1, 0.75 and 2 Gy for each group.

In comparison to control group, all irradiated groups showed a significant increase in SGOT, with the use of 0.75 and 2 Gy γ -irradiation dose levels while the change was insignificant with the use of 0.1 Gy. Comparison between irradiated groups at the same dose, sacrificed in the same day showed significant increase in SGOT with the injected irradiated groups.

In comparison to control group, all irradiated groups showed a significant increase in SGPT, with 2 Gy γ -irradiation and non-significant change with 0.75 and 0.1 Gy. Comparison between irradiated and injected irradiated groups showed significant decrease in the last ones.

Table (3) Effect of irradiation on SGOT and SGPT with and without curcuma administration (mean \pm S.E. and T-test)

Group Parameter	Control	Irr. 0.1 Gy		Inj. irr. 0.1 Gy		Irr. 0.75 Gy		Inj. irr. 0.75 Gy		Irr. 2 Gy		Inj. irr. 2 Gy	
		1 h	48 h	1 h	48 h	1 h	48 h	1 h	48 h	1 h	48 h	1 h	48 h
SGOT (AST)	177.0 \pm 1.75 a	183.0 \pm 2.05 b	188.3 \pm 4.91 c	133.7 \pm 3.60 a,b	166.7 \pm 2.88 a,c	190.3 \pm 2.40 a,d	195.7 \pm 3.78 a,e	168.0 \pm 6.82 d	169.7 \pm 3.49 e	200.7 \pm 1.35 a,f	210.3 \pm 5.47 a,g	176.7 \pm 4.89 f	177.8 \pm 2.13 g
	SGPT (ALT)	8.98 \pm 0.35 a	9.00 \pm 0.20 b	9.13 \pm 0.14 c	6.77 \pm 0.13 a,b	7.00 \pm 0.09 a,c	9.33 \pm 0.17 d	9.53 \pm 0.10 e	7.27 \pm 0.22 a,d	7.42 \pm 0.21 a,e	10.02 \pm 0.20 a,f	10.13 \pm 0.05 a,g	7.92 \pm 0.34 f

Inj. Irr. = Injected irradiated

Irr. = Irradiated only

Similar subscript litters mean significant change.

DISCUSSION

Curcumin administrated to irradiated rats improved the tested biochemical parameters assayed. This reflects its possible action as an antioxidant. Curcumin induces its activity through free radicals quenching mechanism and electron hydrogen donation (Chaudhary et al., 1999). The bioavailability of curcumin is reported to be at least in part due to the presence of tetrahydrocurcumin, which is a major metabolite of curcumin in the body. Both functional groups phenolic hydroxyl and diketo contribute to tetrahydrocurcumin antioxidant action where phenolic hydroxyl is a better scavenger of free radicals. The phenolic groups in curcumin showed hydrogen bond acceptor properties, while those in bisdemethoxycurcumin acted as hydrogen bond donor and that explaining the differential polarity of these compounds when mixed with various alcohol and variation in antioxidant potency (Okada et al., 2001).

Total proteins, albumin and globulins decrease with irradiation of rats. Administration of curcumin possibly tolerated this hypoproteinemic effect of γ radiation as shown in table 1. Roushdy et al. (1989) suggested that the decrease in total protein of irradiated rats might be referred to either damage of vital biological processes or to changes in permeability of liver, kidney and other tissue cells leading to leakage of proteins via the kidney.

The present results revealed a significant decrease in serum total protein and albumin accompanied by marked alterations in serum protein fractions following exposure of rats to 2 Gy whole body gamma irradiation. Keren (1994) stated that the decrease in concentration of serum albumin might result from excessive loss through injury to the kidneys or gastrointestinal tract or from thermal injury to the skin. It also occurs in hypercatabolic states (Lessard et al., 1985). In addition, this decrease could be related in part to hepatic dysfunction and decreased protein synthesis (Choldhari and Chakrabati, 1983). These phenomena might be, at least partially responsible for protein loss after irradiation.

Fat is more easily digested with the use of Curcuma herb because it stimulates the flow of bile. The liver is highly susceptible to damage when using alcohol or pharmaceutical drugs, especially acetaminophen in high doses. Turmeric may be used to prevent this damage. Curcuma, exhibits anti-inflammatory, antitumor and antioxidative properties (Balch and Balch 1997).

Ten healthy volunteers consumed 500 mg of curcumin per day for 7 days, not only did their blood levels of oxidized cholesterol drop by 33%, but their total

cholesterol dropped 11.63%, and their HDL "good" cholesterol increased by 29% (Soni and Kuttan, 1992). Our results reveal that all groups irradiated with γ radiation showed an increase in cholesterol and triglycerides significantly in relation to control group, which justify the hyperlipidemic effect of γ radiation. This hyperlipidemic effect of γ radiation was ameliorated with the treatment of rats with curcuma, which reflected on the significant decrease in the level of cholesterol and triglycerides in all groups irradiated in comparison with the corresponding ones, which irradiated and injected with curcumin.

Turmeric may lower lipid peroxidation by maintaining the activity of antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase). These enzymes play an important role in the regulation of lipid peroxidation (Harries, 1992). Curcumin can scavenge oxygen free radicals such as superoxide anions and hydroxyl radicals, which play an important role in the initiation of lipid peroxidation. Therefore, curcumin can lower lipid peroxidation by influencing a number of important factors that regulate lipid oxidation (Pulla Reddy and Lokesh, 1994). The data of serum triacylglycerol and cholesterol in rats affected by exposure to 0.1, 0.75 and 2 Gy of γ -irradiation reflected a significant increase in their levels. These data are in harmony with those reported by Abu-Ghadeer et al., (1996), who attributed the increase of total lipids in blood to the stimulation of the liver enzyme responsible for the biosynthesis of fatty acids due to γ -irradiated animals and to the mobilization of fat adipose tissue to the blood stream leading to hyperlipidemic state. Other study by Dousset et al., (1984) attributed such increase to inactivation of lipoprotein lipase enzyme as a result of whole body irradiation. Feurgard et al., (1998) reported that the increase of cholesterol level after irradiation may be due to decrease in lecithine cholesterol acetyl transferase, leading to decrease in cholesterol esterification of rats plasma. On the other hand, cholesterol efflux from peripheral tissues may be increased as a consequence of plasma membrane damage due to radiation and this cholesterol efflux should result in an increase in the formation of HDL-C. The newly synthesized cholesterol would participate in the formation of HDL-C. Part of constitutive material of HDL-C also comes from unesterified cholesterol, phospholipid and apolipoproteins, which are released during lipolysis of triglyceride-rich lipoproteins (Mathe et al., 1991). The data testify that the acute irradiation even at rather low doses (2 Gy) causes, in early terms after irradiation (2 days) the primary biological effects. The data obtained revealed a significant increase in plasma triglycerides and cholesterol due to exposure of rats to 2 Gy of whole body γ -irradiation. The results came correlating and consolidating to other findings of Nehru et al., (1991) using low (2.5 Gy) and high (10 Gy) levels of γ irradiation and Abou-safi et al., (2004) at 6 Gy γ irradiation. The elevation in plasma lipid fractions might result from: a- ionizing radiation ability to accelerate other pathways of cholesterol formation like increasing its rate of biosynthesis in the liver and other tissues (Feurgard et al., 1999). b- destruction of cell membranes by irradiation and enhancement of cholesterol release into the serum and/or disturbance of LDL-cholesterol receptors leading to hypercholesterolemia (Kolomijitseva, 1986). c- the free radicals generated by ionizing radiation affect particularly polyunsaturated fatty acids (Karbownik and Reiter, 2000) and increase in lipid peroxidation and specific products accompanying ionizing radiation. The ionizing radiation (4 Gy) caused a pronounced increase in serum total lipids, triglycerides and cholesterol concentrations. These findings confirm previous reports that ionizing radiation induces hyperlipidemia particularly at the 24 hrs postirradiation (Mathew and Daniel, 1996). The blood levels of lipids are controlled primarily by their production and

utilization by liver (Augusti and Mathew, 1974). However, irradiation of animals results in triglycerides build up which increase hepatic lipid accumulation (Gupta, 1996).

The groups of rats that irradiated at all doses of γ radiation induced an increase in the level of SGOT and SGPT but the groups that injected with curcuma showed decrease in those levels. This means that curcuma ameliorated the oxidative hazardous effect of γ radiation. Kalpana and his colleagues (2005) decided that curcumin and curcumin analog administration significantly reduced marker enzyme activity in the nicotine-treated rats (Fan et al., 2005). It was found that curcumin at a dose of 100 mg/kg partially prevented fibrotic processes and liver damage induced by 4 weeks of carbon tetrachloride administration (Eun-Jeon Park et al., 2000). This was in part by its ability to promote the hepatocyte membrane integrity as marked by the reduction in ALT (Magda M. Amer (2003). The data revealed a significant increase in transaminases activity (AST & ALT) in irradiated animals at 1 and 48 hours post irradiation periods. These increased levels could be referred to the destruction of the radiosensitive tissues of the hepatocytes.

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were assessed in serum and anti-oxidant parameters were assessed in liver tissues. Curcumin mixed with high cholesterol diet decreased serum total cholesterol. Curcumin decreased enzyme activities of serum AST and ALT (Arafa, 2005). On other hand, the data revealed significant increase in serum aminotransaminases activity (AST& ALT) in irradiated animals all over the experimental period (Fatome et al., 1976). Moreover, the drastic dysfunction of the liver cells induced by irradiation may lead to the elevation of transaminases level (Margison et al., 1985).

It is possible to conclude that:

Curcuma elevates the protein profile (total protein, albumin and globulins) of the body that caused by whole body γ -irradiation of rats. Curcuma ameliorates the hyperlipidemic effects of γ radiation effects. Curcuma improves the liver functions that had been affected by γ irradiation of animals. Curcuma can be used as a radioprotector in professional radiation workers who may be expose to low level of ionizing radiation.

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