



## Therapeutic Role of Curcumin Loaded Magnetic Nanoparticles Against Gamma-Irradiation Hazards in Rats

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The present study has been carried out to investigate the possible therapeutic effect of curcumin loaded iron oxide nanoparticles (MNP-CUR) administered through intraperitoneal (i.p) injection after whole body gamma irradiation of rats. Whole body gamma irradiation of rats at 6 Gy (single dose) caused significant reduction in red blood cells count, hemoglobin levels, lymphocytes, neutrophils, and monocytes associated with highly significant elevation in malondialdehyde (MDA). The reduction in catalase (CAT) activity and the reduced levels of glutathione GSH were observed after three weeks post-irradiation. Administration of MNP-CUR after irradiation resulted in a significant improvement of the hematological parameters and reduced changes in MDA, GSH and CAT levels were induced by gamma irradiation. The combination of MNP and CUR was found to be advantageous for the after-exposure treatment because the effect of radiation is stealth. An individual may spend days, weeks or even months exposed to radiation doses without becoming alarmed. Exposure to ionizing radiation is known to have an effect on the body cells, especially the blood cells and cause a marked decline in their viability and proliferation.

**Keywords:** Magnetic iron oxide nanoparticle, Gamma irradiation, Curcumin-loaded Magnetic nanoparticles, Herapeutic

### Introduction

Ionizing radiation (IR) causes damage in biological tissues by exciting or ionizing their atoms and molecules. Depending on the radiation exposure dose, and the biochemical processes, the biological response to radiation damage may be prompt (the expression time may be within minutes to weeks after exposure) or delayed (the expression time may extend to several months or even years after exposure) [1]. With sufficient amount of radiation deposited energy within biological tissue, IR may induce physical symptomatology within minutes of exposure; the prodromal phase includes nausea, vomiting, and fatigue. These prodromal symptoms can be followed by a dramatic decrease in peripheral blood cell counts, as the blood renewal system of highly proliferating hemopoietic cells are known to be sensitive to IR [2]. The white

blood cells show the most immediate response to IR by exhibiting a dramatic drop within 24h (one day) following radiation exposure. In contrast, RBCs and platelets decline more gradually, over a longer time period [3, 4]. Exposure to IR induces the production of reactive oxygen species (ROS), which include superoxide, hydroxyl radicals, singlet oxygen and hydrogen peroxide. These free radicals react with critical cellular components, such as DNA, RNA, proteins, and membranes, resulting in cell dysfunction and the initiation of apoptotic pathways leading to cell death [5, 6]. Magnetic iron oxide nanoparticles (MNPs) are one of the most extensively investigated compounds, due to their excellent biocompatibility and ease of synthesis for a wide variety of applications [7-12]. Curcumin (CUR), (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione), is a

linear diarylheptanoid natural pigment isolated from the rhizome of *Curcuma Longa* [13]. CUR possesses a wide range of pharmacological activities, such as anticancer, anti-inflammatory, anti-oxidant and antimicrobial activity [14, 15]. In addition, it has been also reported as a potential radio-protective agent [16, 17]. CUR exists in solution as a tautomeric mixture of keto and enol forms.

The keto-enol tautomerism is responsible for the free radical scavenging property of CUR [18, 19]. The clinical use of CUR is of significant challenge due to its poor solubility in aqueous solutions, relatively low bioavailability, intense staining color and rapid metabolism [20]. The aim of the present study is to investigate the therapeutic effect of curcumin-loaded magnetic nanoparticles (MNP-CUR) in the treatment of the harmful effects of IR in rats.

### Materials and Methods

Iron (II) chloride tetrahydrate ( $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ ), iron (III) chloride hexahydrate ( $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ ), polyethylene Glycol 600, and curcumin ( $\text{C}_{21}\text{H}_{20}\text{O}_6$ ), were purchased from Sigma-Aldrich (USA). Ammonium hydroxide solution ( $\text{NH}_4\text{OH}$ ) was obtained from Merck (Germany). Iron oxide nanoparticles were prepared according to the method in Ref [21]. Loading CUR into the MNPs, was conducted according to a previously reported protocol [22].

Produced MNP-CUR were characterized with transmission electron microscope (TEM), (EFI Netherland, Model Tecani G20), supertwin, double tilt, and Gun type LaB<sub>6</sub>. The applied voltage was 200 KV and magnification reached 1000,000 X. The particle size and distribution in aqueous medium of the MNP-CUR formulation (50  $\mu\text{L}$  of 500  $\mu\text{g}/\text{mL}$  dispersed in 3 mL of distilled water and using ultrasonic path for 30 minutes). Spectral properties of freeze-dried CUR and MNP-CUR were also characterized and compared using Fourier transform infrared (FTIR), as powder in KBr at scanning speed of 4  $\text{cm}^{-1}$  between 400-4000  $\text{cm}^{-1}$  (32 scans) on an illuminate IR TM FT-IR microscope (Smiths Detection, Danbury, CT).

Sixty adult male albino rats of pure strain ranging from 130-150g body weight were obtained from the animal house of the Animal Nutrition Research Unit in the National Center for Radiation Research and technology, Egyptian Atomic Energy Authority. Animals were housed in especially

designed cages (5 rats/ cage). All rats were kept under good conditions, allowed free access to tap water and pellet diet *Ad libitum*. The animals were divided into six groups (10 rats each): control group (Control), magnetic nanoparticles group (MNPs) which was injected i.p. with 1.5mg/ kg magnetite twice for three weeks, curcumin loaded magnetite group (CUR-MNPs) which was injected i.p. with 1.5mg /kg curcumin loaded magnetite twice a week for three weeks, irradiated group (gamma radiation) exposed to sub-lethal (6Gy) whole body  $\gamma$ - irradiation, Irradiated magnetic nanoparticles group (R+MNPs) which was exposed to sublethal dose (6Gy) gamma irradiation and then injected i.p. with magnetite NPs twice a week for three weeks and irradiated CUR-MNP Group (R+CUR-MNPs) which was exposed to sublethal dose (6 Gy) gamma irradiation and then injected i.p. with curcumin loaded magnetite NPs twice a week for three weeks. Whole body gamma irradiation was performed by Gamma- cell 40 (with cesium-137 gamma source) belonging to the National Center for Radiation Research Technology (NCRRT), Cairo, Egypt. Animals were exposed to irradiation 6 Gy as a single dose, at a dose rate of 0.957 Rad/s. Blood samples were taken weekly from the retro-orbital venous plexus. Each blood sample was collected into tubes containing heparin for complete blood picture. At the end of the experiment after three weeks animals in all groups were sacrificed by decapitation and their livers were excised, then perfused with cold saline to exclude the blood cells and then blotted on filter paper, and stored at -20°C for subsequent biochemical analysis (MDA, CAT and GSH). Complete blood counting (CBC) was determined by cell counter fully automated (Sysmex, Japan) [23]. Liver glutathione concentration was determined according to the method described by [24]. Catalase activity was determined according to the method described by [25]. MDA concentration was determined according to the method described by [26]. All results were expressed in mean  $\pm$  SE. Statistical analysis was performed using statistical package for the social science for windows (SPSS, version 11.0, Chicago, IL, USA). The data were analyzed by one-way analysis of variance (ANOVA).

## Results

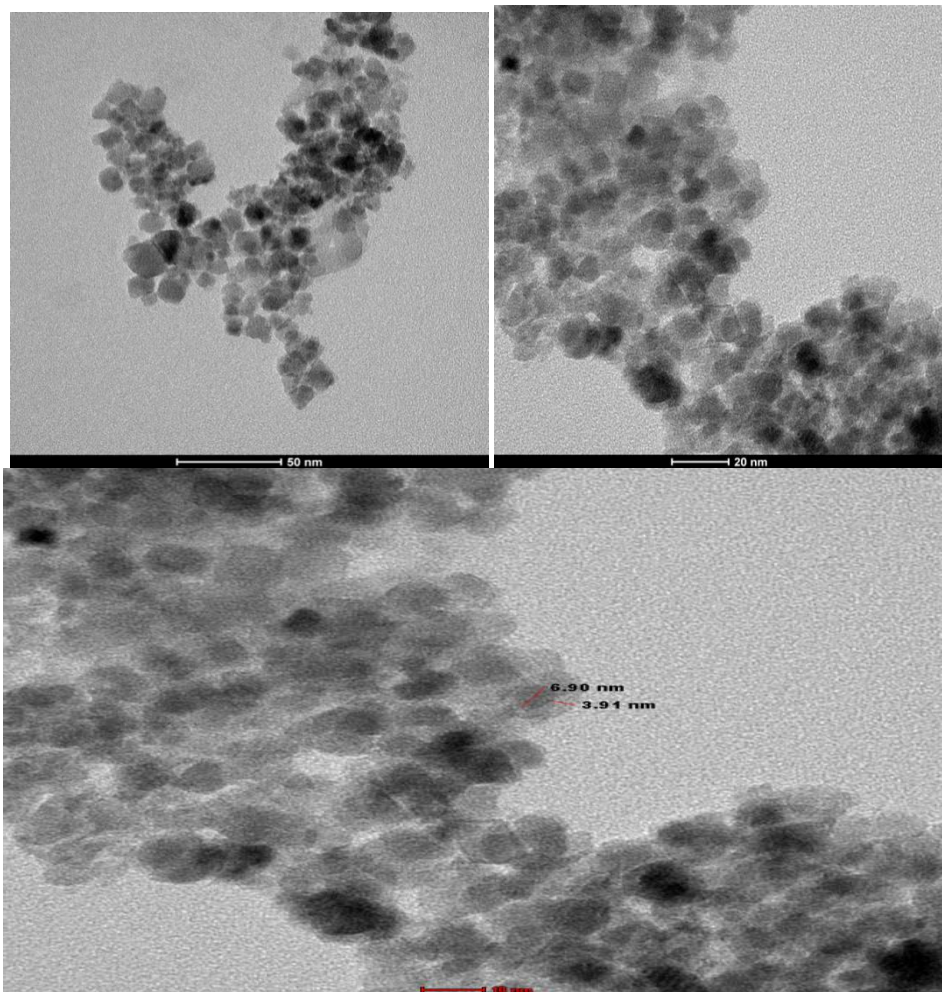
The TEM image in Fig.(1) revealed an average size of 10-20 nm for CUR-MNPs. The TEM image of specific areas showed particles with spherical-like shapes, although for a few particles with the largest diameters observed faceted particles. The latter shape is probably related to the high crystallinity of the particles reflecting the cubic crystal habit of the  $\text{Fe}_3\text{O}_4$  phase.

Fourier transform infrared (FTIR) spectra of CUR, CUR-MNP, and MNPs are illustrated in Fig.(2a). The transmittance of FTIR results is converted to absorption coefficient in the unit of  $\text{g}^{-1}$  was obtained from the relation

$$\alpha = \frac{1}{m} \ln \frac{100}{T}$$

Where  $m$  is the absolute mass of the curcumin in the KBr pellet and  $T$  is the infrared transmittance (%). Using this technique, the normalized infrared absorption was calculated and presented in Fig.(2b); the comparison between the absorption curves showed the following:

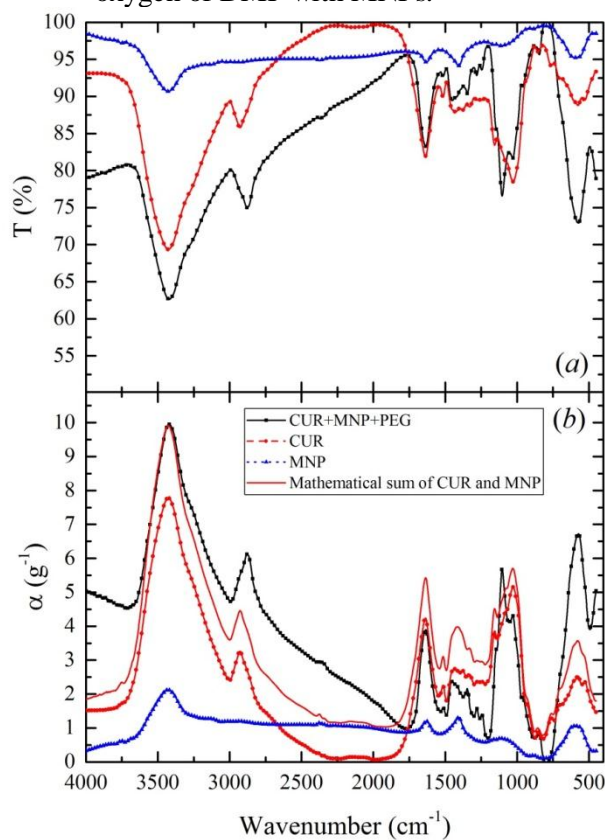
1. A characteristic band at around  $3443 \text{ cm}^{-1}$  which is attributed to the O-H stretching vibration of curcumin while, in the loaded system, in the presence of PEG assisted nanoparticles, the O-H stretching vibration shifted to  $3423.4 \text{ cm}^{-1}$ . The O-H absorption around  $3443 \text{ cm}^{-1}$ , nearly, did not change on loading the CUR on MNPs. Similarly, the absorptions at  $2880 \text{ cm}^{-1}$ ,  $1616 \text{ cm}^{-1}$ , and around  $1100 \text{ cm}^{-1}$ . This observation indicates that the antioxidant property of CUR did not change by legation to MNPs.



**Figure (1):**TEM image of curcumin loaded  $\text{Fe}_3\text{O}_4$  magnetic nanostructurestransmission electron microscopy. The micro-structural features of the MNP-CUR were studied using TEM



2. The apparent increase in the peak intensity is associated with increasing the wide bands at  $1360\text{ cm}^{-1}$  and  $990\text{ cm}^{-1}$ . These bands may be associated with Mono-Alkyl (vinyl group of reduced PEG at the magnetite surface, i.e.  $\text{R-CH=CH}_2$ ). Furthermore, shifting of the strong band at  $1655\text{ cm}^{-1}$  of CUR to  $1649\text{ cm}^{-1}$  in conjugated system indicated the participation of the dione moiety in conjugation. Moreover, the shifting of the stretching vibrational band from  $1027.8\text{ cm}^{-1}$  to  $1030.7\text{ cm}^{-1}$  in the loaded system is an indication of interaction of oxygen of DMF with MNPs.



**Figure (2):**FTIR of dried curcumin (CUR), magnetite (MNP), and CUR-MNP. Part a) transmission mode, Part b) mass absorption coefficient in the units of  $\text{g}^{-1}$

As shown in Table (1) and Figs. (3,4,5 and 6), there was a significant decline, where the decision p value where  $P < 0.05$ , in WBCs count, lymphocyte, Neutrophil and Monocyte in all irradiated groups in the first week (T1) post 6Gy  $\gamma$  irradiation. In the later samples of the second week (T2) and the third week (T3), unlike radiation group, there was gradual recovery in the levels of all WBCs types of R+MNP and R+CURMNP groups which became in the range of the levels of the control group. The best improvement was in R+CURMNP group which recorded  $6.7 \pm 0.46 \times 10^3$ ,  $5.2 \pm 0.03 \times 10^3$ ,  $0.4 \pm 0.005 \times 10^3$ ,  $0.5 \pm 0.05 \times 10^3$  for the values of WBCs count, lymphocyte, Neutrophil and Monocyte, respectively, with no significant difference compared to the control group after three weeks of irradiation.

The CBC parameters levels in the CUR-MNP group showed a significant ( $P < 0.05$ ) improvement in the values of RBCs and Hb levels compared to control and MNP groups, as demonstrated in Table (2) and Figs. (7,8,9, and 10). For this reason, the CBC values of the CUR-MNP group was used as reference values for changes in CBC of irradiated groups. There was a significant decline in the RBC, Hb level, HCT% and platelet of the irradiated groups compared to CUR-MNP ( $P < 0.05$ ) in samples of the first week post 6Gy  $\gamma$ -irradiation. This decline continued in the radiation group in the later samples obtained at the second- and third-weeks post irradiation. On the other hand, recovery in CBC parameters levels was recorded in the T2 and T3 samples obtained from R+MNP and R+CURMNP groups. As in WBCs results, the improvements were highest in R+CUR-MNP which reached near the CBC values of CUR-MNP group ( $P < 0.05$ ). The recorded data in Table (3) and Figs. (11 and 12) showed that at the first week (T1), second week (T2) and third week (T3) post 6Gy  $\gamma$ -irradiation, the activity of the antioxidant enzymes; CAT, GSH in the liver tissue in irradiated group was significantly decreased ( $P < 0.05$ ), as compared the control group, However, the liver tissue MDA, in the irradiated group, was significantly increased ( $P < 0.05$ ) when compared to the control group. Conversely, the irradiated rats treated with MNPs and CUR-MNP showed a significant improvement in the antioxidant status via enhancement of the antioxidant enzymes activities (GSH, CAT).

Table (1): the effect of MNP and MNP-CUR on the recovery of different types of white blood cells in in samples obtained from animals exposed to 6 Gy whole body  $\gamma$ -Irradiation at three weeks of study

Groups	Post irradiation (Therapeutic experiment)											
	WBCs ( $\times 10^3$ )			Lymphocyte ( $\times 10^3$ )			Neutrophil ( $\times 10^3$ )			Monocyte ( $\times 10^3$ )		
	T1	T2	T3	T1	T2	T3	T1	T2	T3	T1	T2	T3
Control	7.2 <sup>a</sup> ± 0.13	7.1 <sup>a</sup> ±0.13	7.8 <sup>a</sup> ± 0.37	5.8 <sup>a</sup> ±0.03	5.9 <sup>a</sup> ± 0.358	6.4 <sup>a</sup> ±0.202	0.3 <sup>abc</sup> ±0.14	0.3 <sup>ab</sup> ± 0.016	0.5 <sup>ab</sup> ±0.050	0.4 <sup>bc</sup> ±0.070	0.5 <sup>ab</sup> ± 0.016	0.7 <sup>a</sup> ±0.01
MNPs	7.6 <sup>a</sup> ± 0.23	7.5 <sup>a</sup> ± 0.2	7.7 <sup>a</sup> ± 0.21	5.8 <sup>a</sup> ±0.032	5.7 <sup>a</sup> ±0. 031	6 <sup>ab</sup> ± 0.033	0.5 <sup>a</sup> ±0.064	0.4 <sup>ab</sup> ±0.040	0.5 <sup>abc</sup> ±0.062	0.4 <sup>dc</sup> ±0.011	0.5 <sup>ab</sup> ± 0.015	0.6 <sup>a</sup> ±0.01
CURMNPs	7.6 <sup>a</sup> ± 0.34	7.3 <sup>a</sup> ± 0.34	6.8 <sup>a</sup> ±0.60	6.5 <sup>a</sup> ±0.0 2	6.3 <sup>a</sup> ±0.010	5.8 <sup>a</sup> ±0.020	0.4 <sup>ab</sup> ±0.062	0.5 <sup>a</sup> ±0.028	0.2 <sup>d</sup> ±0.037	0.7 <sup>a</sup> ± 0.085	0.6 <sup>a</sup> ± 0.033	0.6 <sup>a</sup> ± 0.09
Radiation	1.2 <sup>d</sup> ± 0.20	1.3 <sup>d</sup> ±0.20	2.4 <sup>b</sup> ±0.10	0.5 <sup>c</sup> ± 0.71	0.7 <sup>c</sup> ±0.72	1.4 <sup>c</sup> ±0.12	0.02 <sup>d</sup> ±0.33	0.03 <sup>c</sup> ±0.033	0.02 <sup>d</sup> ± 0.037	0.03 <sup>e</sup> ±0.01	0.02 <sup>c</sup> ±0.054	0.1 <sup>b</sup> ± 0.04
R+MNPs	2.2 <sup>c</sup> ± 0.08	3.5 <sup>c</sup> ± 0.08	5.9 <sup>a</sup> ± 0.67	1.2 <sup>b</sup> ±0.32	2.1 <sup>b</sup> ±0. 42	4.1 <sup>abc</sup> ±4.3	0.05 <sup>dc</sup> ± 0.33	0.13 <sup>bc</sup> ±0.033	0.3 <sup>dc</sup> ±0.040	0.07 <sup>de</sup> ±0.033	0.2 <sup>b</sup> ±0.0251	0.4 <sup>a</sup> ± 0.05
R+ CURMNPs	3.6 <sup>b</sup> ± 0.08	5.0 <sup>b</sup> ± 0.08	6.7 <sup>a</sup> ± 0.46	2 <sup>b</sup> ± 0.33	3.1 <sup>b</sup> ±0.04	5.2 <sup>ab</sup> ±0.03	2.7 <sup>bdc</sup> ± 0.033	0.2 <sup>ab</sup> ±0.051	0.4 <sup>bdc</sup> ±0.005	0.1 <sup>dce</sup> ±0.005	0.4 <sup>ab</sup> ±0.05	0.5 <sup>a</sup> ± 0.05

Data are presented as means ± S.E

S.E.: Standard Error

Means values within the same column carrying different superscript letters are significantly different (P < 0.05)

Table(2): the effect of MNP and MNP-CUR on the recovery of different types of white blood cells in in samples obtained from animals exposed to 6 Gy whole body  $\gamma$ -Irradiation at three weeks of study

Parameter	Post irradiation (Therapeutic experiment)											
	RBCs			Hb			HCT			Platelet		
	T1	T2	T3	T1	T2	T3	T1	T2	T3	T1	T2	T3
Control	5.9 <sup>d</sup> ±0.2	5.80 <sup>b</sup> ±0.11	5.8 <sup>b</sup> ±0.1 1	12.72 <sup>c</sup> ±0.34	12.1b <sup>c</sup> ±0.23	12.2a b <sup>c</sup> ±0.31	37.1 <sup>a</sup> ±1.8 1	37.9 <sup>a</sup> ±1.2 2	37.8 <sup>a</sup> ± 0.05	711.2 <sup>a</sup> ±25.1	710 <sup>a</sup> ±25.4	729.8 <sup>a</sup> ±18.8
MNPs	6.45 <sup>b</sup> ± 0.22	6.33 <sup>ab</sup> ±0.11	6.33 <sup>a</sup> b ±0.1 1	12.72 <sup>b</sup> c ±0.32	12.6 <sup>ab</sup> ±0.39	12.0 <sup>bc</sup> ±0.25	37.2 <sup>a</sup> ± 0.58	38.1 <sup>a</sup> ±0.9 6	37.5 <sup>a</sup> ±1.13	659.2 <sup>a</sup> ±19.4	676.5 <sup>a</sup> ±27.5	674.2 <sup>a</sup> ±120. 9
CURMNP s	7.3 <sup>a</sup> ±0.09	6.80 <sup>a</sup> ±0.05 7	6.80 <sup>a</sup> ±0.0 5	13.85 <sup>a</sup> ±0.06	13.9 <sup>a</sup> ±0.14 9	13.6 <sup>a</sup> ±0.30	39.7 <sup>a</sup> ±1.1 5	39.4 <sup>a</sup> ±0.4 1	39.2 <sup>a</sup> ±0.63	716.7 <sup>a</sup> ±14.4	716.7 <sup>a</sup> ±14.4	761.4 <sup>a</sup> ±63.7
Radiation	4.6 <sup>e</sup> ±0.38	3.92 <sup>c</sup> ±0.39	3.92 <sup>c</sup> ±0.3 9	12.36 <sup>c</sup> ±0.44	5.98 <sup>e</sup> ±0.10	6.68 <sup>d</sup> ±0.47	36.9 <sup>a</sup> ±0.4 8	18.06 c ±0.8 2	28.5 <sup>b</sup> ±3.72	46.8 <sup>b</sup> ±20.1	139.2 <sup>e</sup> ±18.2	385.6 <sup>b</sup> ±33.4
R+MNPs	4.9 <sup>e</sup> ±0.28	6.93 <sup>ab</sup> ±0.06	6.98 <sup>a</sup> b ±0.0 6	12.83 <sup>b</sup> c ±0.08	10.94 <sup>b</sup> ± 0.88	11.15 <sup>c</sup> ±0.76	37.9 <sup>a</sup> ±0.4 8	25.6 <sup>b</sup> ±0.8 2	33.5 <sup>ab</sup> ±1	69.4 <sup>b</sup> ±13.7 2	501.4 <sup>d</sup> ±24.0	642.8 <sup>a</sup> ±162. 0
R+ CURMNP s	5.26 <sup>de</sup> ±0.33	7.06 <sup>a</sup> ±0.31	7.06 <sup>a</sup> ±0.3 1	13.3 <sup>ab</sup> ±0.11	12.5 <sup>ab</sup> ±0.31	13.22 <sup>a</sup> b ±0.13	39.1 <sup>a</sup> ±0.2 5	27.6 <sup>b</sup> ±2.5 2	37.6 <sup>a</sup> ±1.55	92.6 <sup>b</sup> ±20.8	606.8 <sup>c</sup> ±4.4	668.8 <sup>a</sup> ±81.4

Data are presented as means ± S.E

S.E.: Standard Error

Means values within the same column carrying different superscript letters are significantly different (P < 0.05)

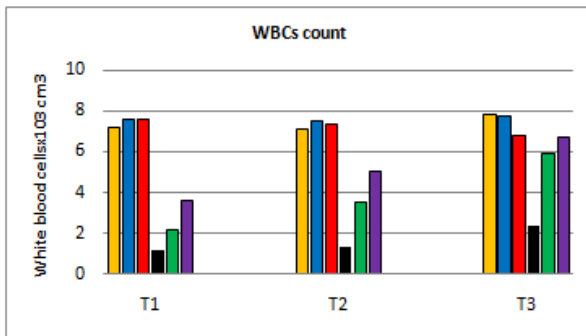


Figure (3): The effect of  $\gamma$ -irradiation and MNP-CUR on WBCs count

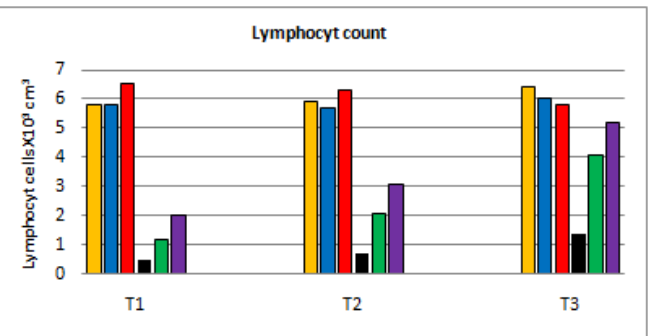


Figure (4): The effect of  $\gamma$ -irradiation and MNP-CUR on lymphocytes

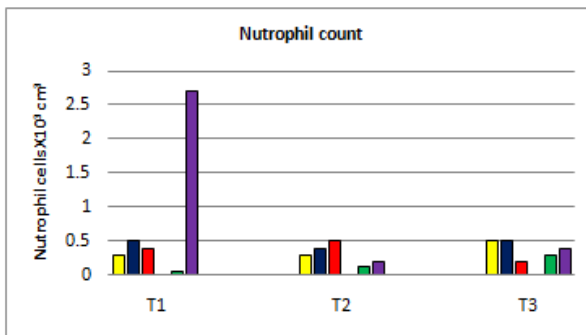


Figure (5): The effect of  $\gamma$ -irradiation and MNP-CUR on neutrophils count

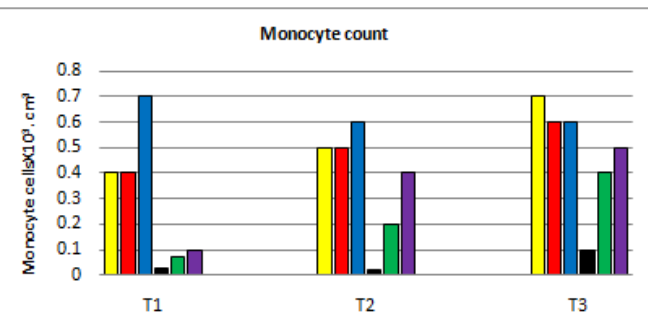


Figure (6): The effect of  $\gamma$ -irradiation and MNP-CUR on Monocytes

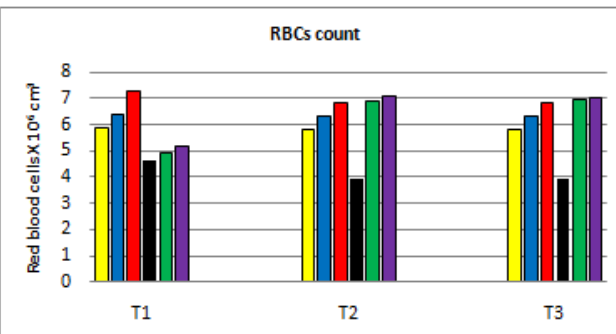
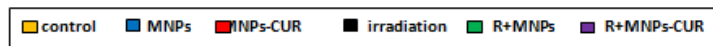


Figure (7): The effect of  $\gamma$ -irradiation and MNP-CUR on RBCs count

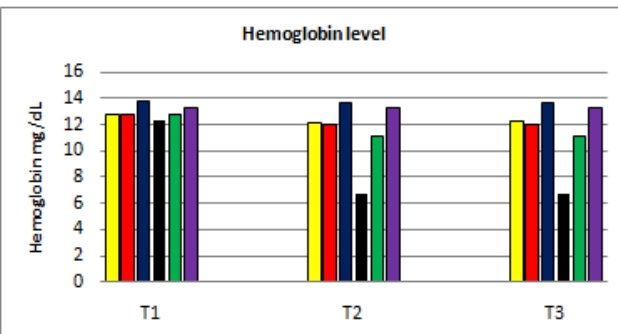


Figure (8): The effect of  $\gamma$ -irradiation and MNP-CUR on Hb level

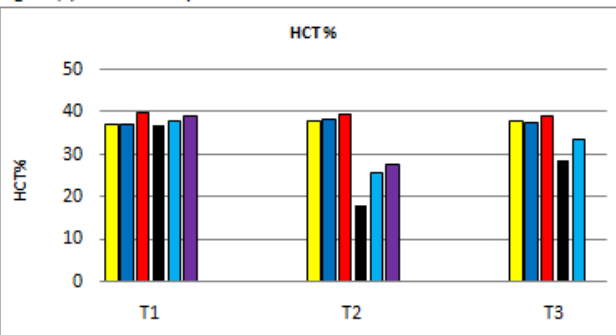


Figure (9): The effect of  $\gamma$ -irradiation and MNP-CUR on HCT%

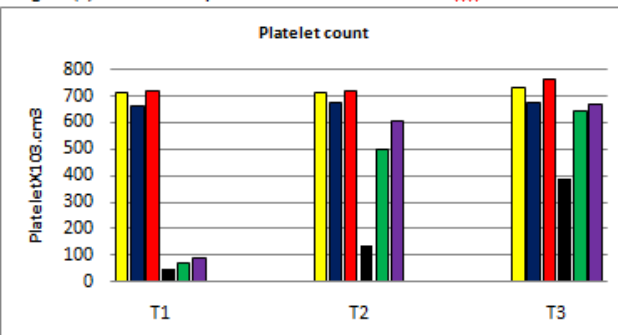


Figure (10): The effect of  $\gamma$ -irradiation and MNP-CUR on platelet count

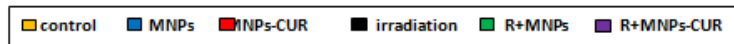
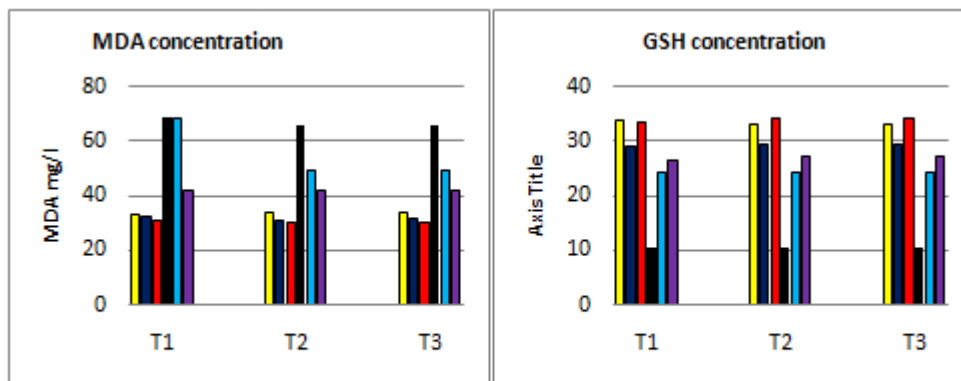
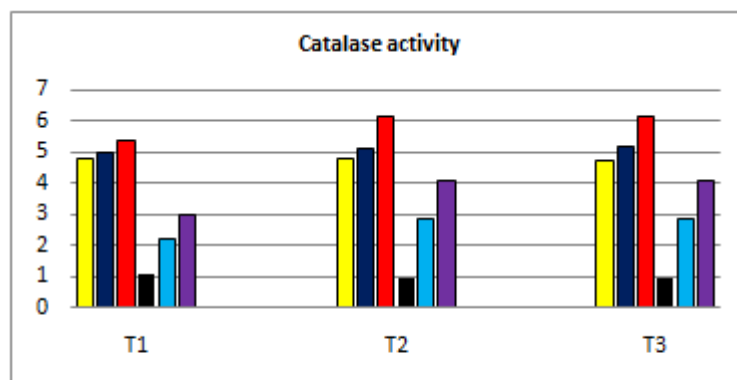
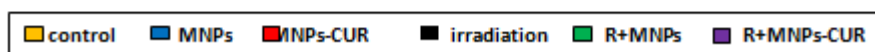


Table (3):the effect of  $\gamma$ - irradiation and MNPs-CUR on L-Malnodialdehyde, Glutathione and catalase

Parameter	Post irradiation								
	MAD			GSH			CAT		
	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>
Control	33.3 <sup>e</sup> ±0.73	33.8 <sup>c</sup> ±0.55	33.73 <sup>e</sup> ±0.53	33.73 <sup>a</sup> ±0.91	33.03 <sup>ab</sup> ±0.37	33.23 <sup>ab</sup> ±0.41	4.75 <sup>b</sup> ±0.15	4.75 <sup>b</sup> ±0.38	4.74 <sup>b</sup> ±0.31
MNPs	32.0 <sup>ef</sup> ±0.58	31.1 <sup>f</sup> ±0.38	31.2 <sup>f</sup> ±0.37	29.07 <sup>b</sup> ±0.52	29.56 <sup>c</sup> ±0.54	29.58 <sup>c</sup> ±0.53	4.98 <sup>ab</sup> ±0.08	5.12 <sup>b</sup> ±0.18	5.14 <sup>b</sup> ±0.17
CURMNPs	30.8 <sup>f</sup> ±0.73	30.13 <sup>f</sup> ±0.44	30.15 <sup>f</sup> ±0.45	33.67 <sup>a</sup> ±0.88	34.24 <sup>a</sup> ±0.33	34.28 <sup>a</sup> ±0.38	5.33 <sup>a</sup> ±0.37	6.15 <sup>a</sup> ±0.08	6.16 <sup>a</sup> ±0.08
Radiation	68.4 <sup>a</sup> ±0.72	65.47 <sup>a</sup> ±0.88	65.46 <sup>a</sup> ±0.86	10.41 <sup>e</sup> ±0.30	10.41 <sup>e</sup> ±0.30	10.33 <sup>e</sup> ±0.32	1.07 <sup>e</sup> ±0.06	0.98 <sup>e</sup> ±0.02	0.97 <sup>e</sup> ±0.03
R+MNPs	68.4 <sup>a</sup> ±0.72	49.30 <sup>b</sup> ±0.35	49.28 <sup>b</sup> ±0.34	24.10 <sup>d</sup> ±0.55	24.10 <sup>d</sup> ±0.55	24.28 <sup>d</sup> ±0.54	2.23 <sup>d</sup> ±0.12	2.83 <sup>d</sup> ±0.12	2.84 <sup>d</sup> ±0.12
R+ CURMNPs	41.6 <sup>d</sup> ±0.68	41.6 <sup>d</sup> ±0.68	41.55 <sup>d</sup> ±0.68	26.40 <sup>c</sup> ±0.83	27.30 <sup>d</sup> ±0.51	27.32 <sup>d</sup> ±0.5	2.97 <sup>e</sup> ±0.15	4.06 <sup>c</sup> ±0.10	4.06 <sup>c</sup> ±0.09

Figure (11):The effect of  $\gamma$ -irradiation and MNPs-CUR on MDAFigure (12):The effect of  $\gamma$ - irradiation and MNPs-CUR on GSHFigure (13):The effect of  $\gamma$ -irradiation and MNPs-CUR on CAT

## Discussion

Bioactive substances are found to improve in efficacy when loaded in nanoparticles such as MNPs. This improvement is directly influenced by the efficiency of loading of the bioactive substance in nanoparticles [27]. Although CUR is known to have antioxidant and anti-inflammatory activity, its use is limited because of its low bioavailability and poor pharmacokinetics [28]. Therefore, a CUR-MNP nanosystem was developed to increase the bioavailability, pharmacokinetics and subsequently improve the therapeutic efficacy of CUR. Total body exposure to IR, as a cytotoxic agent, is generally assumed to cause damage to the hematopoietic cell system resulting in effects that contribute to the hematopoietic syndrome [29]. The results in the present study showed that WBCs were found to be most sensitive to  $\gamma$ -ray irradiation which is in agreement with the results of Sanzari, et al. (2013) [2]. The present results are also comparable with those of Thrall et al., (2013)[30], who detected a statistically significant reduction in WBC counts at 24h (one day) post-irradiation for animals at 6Gy gamma irradiation, and Seed et al., (2002), who reported that the lymphocytes, Neutrophils, Monocytes showed decrease within the first days after irradiation while platelet count declined 5-10 days post irradiation[31]. The continuous radiation induced excess cell losses in the stem and precursor cell pools, proposed by Graessle (2002), may explain the slow recovery in WBCs counts throughout time of the study [32].

A dramatic elevation of the ROS was proposed by Davis, et al., (2001) to induce apoptotic pathways in the cells as a result of the severe imbalance in the redox potential between ROS and endogenous thiol buffers[33].

Glutathione acts synergistically with other endogenous antioxidants and also acts as a co-factor with the enzyme glutathione peroxidase to scavenge free radicals, and detoxify xenobiotics [34]. Thus, the depletion of GSH contents after exposure to  $\gamma$ -radiation may be due to reaction of reduced form of Glutathione GSH with free radicals resulting in the formation of thiol radicals that react to produce oxidized form of Glutathione GSSG as reported earlier by Navarro, et al. in 1997 [35].

The intraperitoneal administration of MNP-CUR significantly enhanced the endogenous GSH and

reduced the MDA levels in the liver of the irradiated rats which may be attributed to increased bioavailability of CUR. This may be due to administration as CUR-MNP resulting in more efficient anti-oxidant action of CUR that subsequently reduced the overwhelming load of ROS, caused by  $\gamma$ -irradiation, on the endogenous antioxidant systems including the glutathione peroxidase and CAT systems.

## Conclusions

The efficacy of CUR-MNP to reduce the cellular damage induced by ionizing radiation was studied. MNP-CUR ameliorates the oxidative damage of  $\gamma$ -radiation. CUR-MNP provides a radio-resistance effect to bone marrow cells in animals that received  $\gamma$ -radiation. The use of commercial CUR may be limited due to its poor oral bioavailability and solubility in plasma. The present study, with these naturally antioxidant loaded nanoparticles, provides an extended window for protection against sublethal-dose irradiation. It could be concluded that CUR-MNPs can be used as a radio-protective agent to the professional radiation and remediation workers who may be exposed to low levels of ionizing radiation, and especially if it is administered after irradiation for therapeutic purposes.

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