

# Protective effects of curcumin against gamma radiation-induced ileal mucosal damage

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**Abstract** The major objective of this study was to test curcumin as a potential radioprotectant for the ileum goblet cells of the rat. Wistar albino rats were used in the study. Group A was the control group and group B was the single dose radiation group. Group C was the two dose radiation group (4 days interval). The rats in groups D and E were given a daily dose of 100 mg/kg of curcumin for 14 and 18 days, respectively. During the curcumin administration period, the rats in group D were exposed to abdominal area gamma ( $\gamma$ )-ray dose of 5 Gy on the 10th day and group E was exposed to same dose radiation on the 10th and 14th day. Irradiation and treatment groups were decapitated on the 4th day after exposure to single or two-dose irradiation and ileum tissues were removed for light and electron microscopic investigation. Single or two dose 5 Gy  $\gamma$ -irradiation caused a marked intestinal mucosal injury in rats on the 4th day. Radiation produced increases in the number of goblet cells. Curcumin appears to have protective effects against radiation-induced damage, suggesting that clinical transfer is feasible.

**Keywords** Radioprotection · Curcumin · Ileum · Goblet cell · Morphometry · Rat

## Introduction

Radiation therapy is an essential therapeutic modality in the management of a wide variety of tumors, but its immediate and delayed side effects on the normal tissues limit the effectiveness of the therapy (Grdina et al. 2002). Cell damage may develop, depending on dose and exposure time (Weiss et al. 1990). Moreover, the increased focus on treatment-related side effects in cancer survivors and the need for medical countermeasures against radiologic or nuclear accidents or terrorism have resulted in a resurgence of interest in the mechanisms of, and ways to modify, radiation injury in normal tissues (Denham et al. 2001).

The gastrointestinal tract is, after the bone marrow, the most sensitive organ to the effects of radiation. As a result of ionizing radiation, acute morphological changes of the intestine are observed within 24–48 h (Dalla 1968). Early radiation enteropathy develops during radiation therapy as a result of intestinal crypt cell death, disruption of the epithelial barrier, and mucosal inflammation (Wang et al. 2006).

Goblet cells are quantitatively the most important population of the small intestine epithelium after the columnar cells, among which they are intercalated (Becciolini et al. 1997). The gastrointestinal tract is covered by a mucous layer secreted by goblet cell, which arise from pluripotent stem cells present at the base of crypt. During migration in the crypt towards the villus, the goblet cells mature and lose the capacity to divide (Cheng and Leblond 1974). Mucus constitutes a protective barrier against microorganisms, physical and chemical attacks, and has the role of lubrication of the digestive tract (Forstner and Forstner 1994). Previous acute radiation studies indicate that the goblet cell response is complex. Some reports describe decreases or no change in cell number, while others demonstrate increases,

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particularly after several weeks and months (Brennan et al. 1998).

Detrimental effect of ionizing radiation on the living systems occurs mainly due to its indirect effects. On exposure to radiation, free radicals are generated from the radiolysis of water molecules. These free radicals interact with various biomolecules and bring about the changes in their structure and function (Jagetia and Reddy 2005).

Biologic modifiers targeting oxidative damage for radioprotection have been studied for decades with limited success. Hence, there is a need for better and more potent compounds, especially on herbal origin to boost antioxidant defence.

Curcumin is a dietary antioxidant derived from turmeric (*Curcuma longa*, Zingiberaceae) and has been known since ancient times to possess therapeutic properties. It has been reported to scavenge oxygen free radicals and to inhibit lipid peroxidation and protect the cellular macromolecules, including DNA from oxidative damage (Kalpana and Menon 2004; Polasa et al. 2004).

Meanwhile, administration of curcumin in cancer patients is claimed to kill the tumor cells effectively by enhancing the effect of radiation and, at the same time, protect normal cells against the harmful effects of radiation. The available information on curcumin suggests that the radioprotective effect might be mainly due to its ability to reduce oxidative stress and inhibit transcription of genes related to oxidative stress and inflammatory responses, whereas the radiosensitive activity might be due the upregulation of genes responsible for cell death (Jagetia 2007).

Most of the reports on the radioprotective role of curcumin have been restricted to animal studies, yet no reports are available on its role as a radioprotector in ileum goblet cells. Thus the aim of the present study was to evaluate the radioprotective effect of curcumin on  $\gamma$ -radiation-induced ileum goblet cells damage.

## Experimental

### Materials and methods

#### Animals

A total of 30 12–14 weeks old Male Wistar albino rats weighing between 250 and 300 g (Trakya University Animal Care and Research Unit, Edirne, Turkey) were housed under constant temperature (21°C) and photoperiod (12 h light/dark cycle). They had free access to standard rat chow diet. All animals received human care according to the criteria outlined in the “Guide for the Care and Use of Laboratory Animals” prepared by the National Academy of Sciences and published by the National Institutes of Health.

The study was approved by the Institutional Animal Ethical Committee of the Trakya University, Edirne, Turkey.

#### Experimental design

The rats were randomly allotted into one of five experimental groups: A (control), B (single dose radiation treated), C (two dose radiation treated), D (single dose radiation treated with curcumin) and E (two dose radiation treated with curcumin); each group contain six animals (Table 1).

#### Irradiation

Irradiation was delivered by a  $^{60}\text{Co}$  teletherapy unit (Cirrus, *cis*-Bio Int., Gif Sur Yvette, France) at a source-skin distance of 100 cm. Five Gy radiation were given at a depth of 1.5 cm (half thickness) with a dose rate of 62.41 cGy/min to the whole abdominal area in supine position. Correct positioning of the fields was controlled for each individual rat using a therapy simulator (Mecaserto-Simics, Paris, France). The  $^{60}\text{Co}$  unit was calibrated with an Exradin Farmer type ionization chamber (Keithley 35040 radiation dosimeter, Cleveland, Ohio, USA). A  $\pm 3\%$  uncertainty in absorbed dose was estimated.

The rats were anesthetized by i.p. administration of 90 mg/kg ketamine and 10 mg/kg xylazine. Animals in single dose radiation treated groups B and D, and two dose radiation treated groups C and E (on the 4th day following the first dose) were exposed to 5 Gy  $\gamma$ -radiation. The control rats (group A) were treated similarly and taken to the theater, but they were not irradiated. The initial and final body weight changes of the various groups were recorded.

**Table 1** Experimental design

Day	
1	Randomization Administration of physiologic saline to the rats in groups A, B and C by gavage Administration of curcumin to the rats in groups D and E by gavage
10	First irradiation of the rats in groups B, C, D and E Administration of curcumin to the rats in groups D and E by gavage
14	Second irradiation of the rats in groups C and E Killing of the rats in groups A, B and D Administration of curcumin to the rats in group E by gavage
18	Killing of the rats in groups C and E

*Group A* control; *group B* single dose radiation treated; *group C* two dose radiation treated; *group D* single dose radiation treated with curcumin; *group E* two dose radiation treated with curcumin group

### Drug preparation and sample collection

Groups A, B and C received 1 ml serum physiologic, and group D for 14 days (10 days before and 4 days after irradiation) and group E for 18 days (14 days before and 4 days after the 2nd dose irradiation) were given curcumin (in a dose of 100 mg/kg body weight) once a day orally by using intra gastric intubation. Irradiation and curcumin-treated groups were decapitated on the 4th day exposure to single or two dose irradiation and ileum tissues were removed for light and electron microscopic investigation.

### Light and electron microscopic procedures

For light microscopic observation, ileum specimens were embedded in the paraffin blocks after they had been fixed in Bouin's solution. Five micrometer ( $\mu\text{m}$ ) sections were obtained and stained with hematoxylin + eosin (H + E) and periodic acid + Schiff + hemalen (PAS + HI).

For electron microscopy, ileum tissue specimens were fixed with 2.5% glutaraldehyde in 0.1 M sodium phosphate buffer (pH 7.2) for 1.5 h at 4°C, tissues were washed in same buffer overnight after primary fixation. The tissues were postfixed with 1% osmium tetroxide in sodium phosphate buffer for 1 h at 4°C. Then the postfixed tissues were washed in same buffer and dehydrated by graded series of ethanol starting at 50% each step for 10 min and finally with propyleneoxide. The tissue specimens were embedded in araldite. Ultrathin sections were obtained by ultramicrotome (RMC-MTX Ultramicrotome-USA) and collected on copper grids for double staining (uranyl acetate and Reynold's lead citrate). Stained sections were finally observed under a Jeol-JEM 1010 transmission electron microscope.

### Histopathologic analysis

Ileum sections were stained with H + E, and mucosal injury, inflammation and hyperemia/hemorrhage were assessed and graded in a blinded manner by a histologist using the histologic injury scale previously defined by Chiu et al. (1970). Briefly, mucosal damage was graded from 0 to 5 according to the following criteria: grade 0, normal mucosal villi; grade 1, development of subepithelial Gruenhagen's space at the apex of the villus, often with capillary congestion; grade 2, extension of the subepithelial space with moderate lifting of the epithelial layer from the lamina propria; grade 3, massive epithelial lifting down the sides of villi, possibly with a few denuded tips; grade 4, denuded villi with lamina propria and dilated capillaries exposed, possibly with increased cellularity of lamina propria; and grade 5, digestion and disintegration of the lamina propria, hemorrhage, and ulceration. The sum of the scores for the individual alterations constitutes the Radiation Injury Score (RIS).

### Morphometric analysis

For morphometric analysis four whole circumference sections, 5- $\mu\text{m}$  thick and 20  $\mu\text{m}$  apart were cut per animal and stained with PAS + HI. Tissue sections were examined and the number of the villus goblet cells counted within random high-power fields using a Olympus Bx 51 light microscope incorporating a square graticule in the eyepiece (eyepiece  $\times 10$ , objective  $\times 40$ , a total side length of 25  $\mu\text{m}$ ). Villus goblet cell density in each site was calculated and recorded as the number of goblet cells/ $\mu\text{m}^2$ .

### Statistical analysis

All statistical analyses were carried out using SPSS statistical software (SPSS for windows, version 11.0). All data were presented in mean ( $\pm$ ) standard deviations (SD). Differences in measured parameters among the five groups were analyzed with a nonparametric test (Kruskal–Wallis). Dual comparisons between groups exhibiting significant values were evaluated with a Mann–Whitney *U* test. These differences were considered significant when probability was less than 0.05.

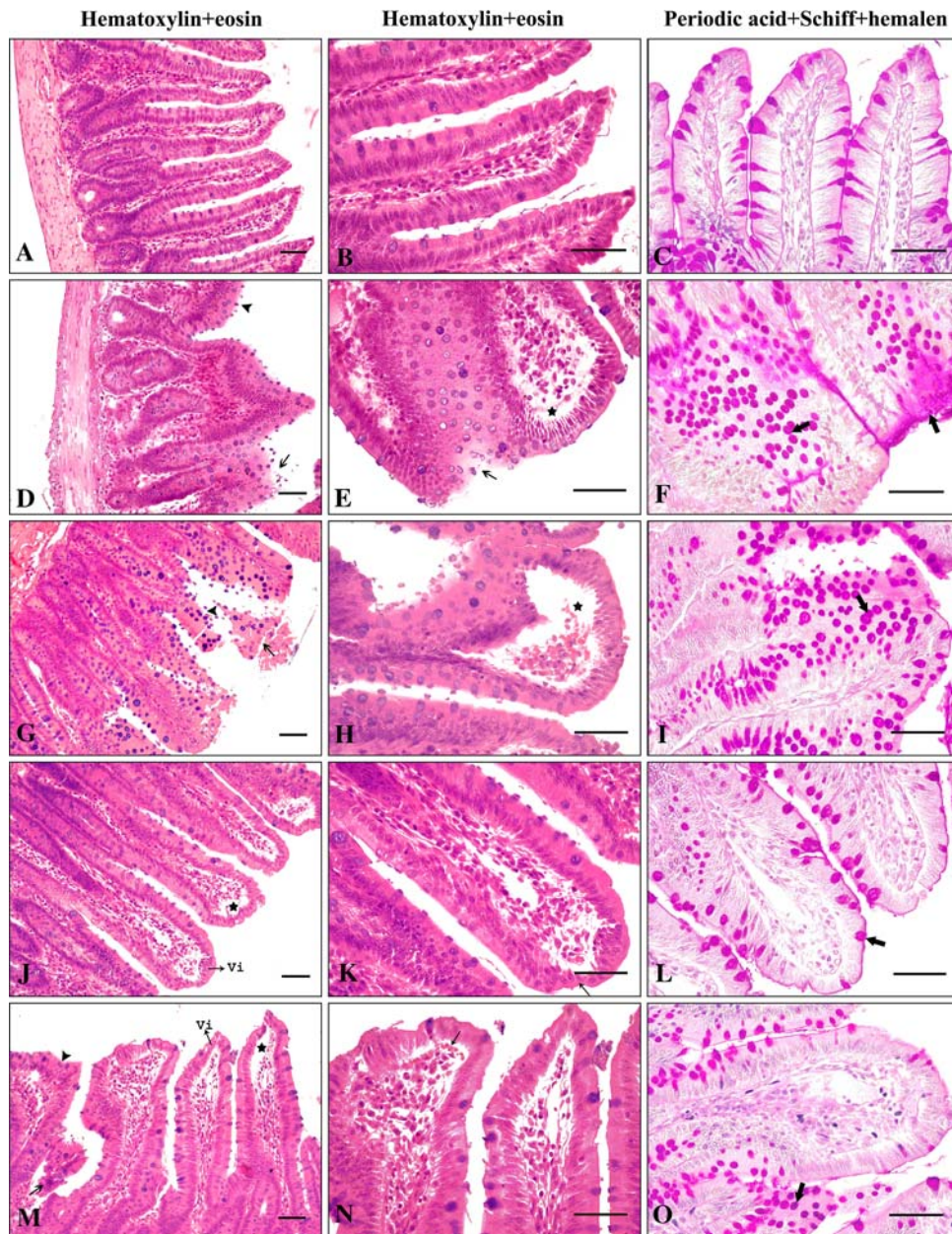
## Results

### Histopathologic findings

When the ileum specimens obtained from the control group were examined as light and electron microscopic, normal histologic structure of the villi intestinalis and Lieberkühn crypts were observed (Fig. 1a–c). In the single and two dose radiation treated groups, the most consistent findings occurring in the histologic tissue sections stained with H + E and PAS + HI were those indicating severe degenerative changes. Four days after irradiation, the morphological structure of the ileum changed. Concomitantly with cell depletion, additional alterations in cell morphology were observed in the epithelium. The atrophic mucosa was lined with a continuous layer of grossly abnormal epithelial cells, racket-shaped cells at the luminal side of the ileum. Ionizing radiation-induced cell loss led to reduced circumference of the crypts and shortened the length of villi. In addition to the decrease of the villus height, light microscopic investigations revealed further alterations in shape and surface of the villus (Fig. 1d–i).

The epithelial cell damage in the single dose radiation treated group was not widespread as compared to two dose radiation treated group (Fig. 1d–i). In the single dose radiation with curcumin (Fig. 1j–l) and two dose radiation with curcumin-treated (Fig. 1m–o) rat ileum, the intensity of epithelial cell damages were less than in the only radiation





**Fig. 1** Histological examination of rat small intestine taken from the segments of ileum. Photomicrographs of ileum sections stained with H + E (a, b, d, e, g, h, j, k, m, n), and PAS + HI (c, f, i, l, o). **a–c** Control rats ileum; showing normal morphology. **d–f** Single dose radiation-treated rats; shortened and thickened villi (arrowhead) and degenerative changes in the epithelial cells (arrow), lifting of epithelial layer from the lamina propria (asterisks), and increase in the goblet cells and mucins showing strongly positive to PAS staining (thick arrows). **g–i** Two dose radiation-treated rats; shortened and irregular villi (arrowhead) and breaking in the epithelial cells (arrow), massive subepithelial lifting and capillary congestion in the villus (asterisks), and

increase in the goblet cells and mucins showing strongly positive to PAS staining (thick arrows). **j–l** Single dose radiation-treated with curcumin rats; villi were generally normal (Vi) although apical regions of some villi were lightly subepithelial lifting (asterisks) and thinning (arrow), normal scattered goblet cells (thick arrows). **m–o** Two dose radiation-treated with curcumin rats; development of subepithelial space (asterisks) and lightly capillary congestion (thick arrows) usually at the apex of the villus, occasional occurrence of thickened villi (arrowhead) along with normal villi (Vi) and breaking in the epithelial cells (arrow), goblet cells showing strongly positive to PAS staining (thick arrows) (scale bar: 50  $\mu$ m)

treated groups. In the curcumin-treated groups, villi were generally normal although apical regions of some villi were thinner. On the other hand, the number of goblet cell profiles were increased significantly in both only radiation treated and radiation with curcumin-treated rats when

compared to villus intestinalis areas of the control rats (Table 2). Both the decrease in enterocytes and the increase in the percentage of goblet cells led to an increase of mucin exposed to the villous surface. A few apoptotic bodies (not quantified) were seen following both irradiation regimes.

**Table 2** The numbers (number/ $\mu\text{m}^2$ ) of goblet cells in the villi intestinalis of A (control), B (single dose radiation treated), C (two dose radiation treated), D (single dose radiation treated with curcumin) and E (two dose radiation treated with curcumin) groups

Groups	Goblet cell number/ $0.625 \mu\text{m}^2$ Mean $\pm$ SD
A	62.75 $\pm$ 8.83
B	120.45 $\pm$ 12.66 <sup>a</sup>
C	154.38 $\pm$ 17.91 <sup>b</sup>
D	94.98 $\pm$ 9.87 <sup>c</sup>
E	109.20 $\pm$ 11.12 <sup>a</sup>

<sup>a</sup>  $P < 0.01$  compared to control group<sup>b</sup>  $P < 0.001$  compared to control group,  $P < 0.01$  compared to group E<sup>c</sup>  $P < 0.05$  compared to control group,  $P < 0.05$  compared to group B,  $P < 0.01$  compared to group C

Table 3 shows mucosal histopathologic changes. The radiation injury score was significantly higher in the all irradiated rats when compared to the control animals. The radiation injury score reflects the global level of injury.

Table 4 shows body weight changes on the day 0 before irradiation, and on the killed day. Groups B and C rats developed diarrhea, characterized by loss of pellet formation and fecal adherence to the perianal region between day 3 and 4 after radiation. The body weight of the irradiated rats was significantly decreased on the 4th day after irradiation, and curcumin treatment normalized the body weight of groups D and E, assuring the safety of 100 mg/kg curcumin dose.

#### Electron microscopic findings

In the control group, the ultrastructure of epithelial cells in the ileum was normal (Fig. 2a, b). In ileal mucosa, there were ultrastructural changes in enterocytes and goblet cells following both irradiation regimes. Radiation had led to the dilatation of endoplasmic reticulum (ER) cisternae and

**Table 3** Mucosal histopathologic change scores of A (control), B (single dose radiation treated), C (two dose radiation treated), D (single dose radiation treated with curcumin) and E (two dose radiation treated with curcumin) groups

Groups	Minimum	Maximum	Mean $\pm$ SD
A	0.00	0.00	0.00 $\pm$ 0.00
B	2.00	4.00	3.00 $\pm$ 0.43 <sup>a</sup>
C	3.00	4.00	3.50 $\pm$ 0.47 <sup>b</sup>
D	1.00	1.00	1.00 $\pm$ 0.00 <sup>c</sup>
E	1.00	2.00	1.50 $\pm$ 0.24 <sup>d</sup>

<sup>a</sup>  $P < 0.001$  compared to control group<sup>b</sup>  $P < 0.0001$  compared to control group<sup>c</sup>  $P < 0.05$  compared to control group<sup>d</sup>  $P < 0.01$  compared to control group**Table 4** Body weight changes on the day 0 before irradiation, and on the killed day of A (control), B (single dose radiation treated), C (two dose radiation treated), D (single dose radiation treated with curcumin) and E (two dose radiation treated with curcumin) groups

Groups	0th day (g)	Killed day (g)
A	257.86 $\pm$ 2.72	260.12 $\pm$ 3.14
B	305.50 $\pm$ 2.34	284.50 $\pm$ 1.22 <sup>a</sup>
C	317.16 $\pm$ 2.04	296.33 $\pm$ 1.86 <sup>b</sup>
D	230.16 $\pm$ 2.48	228.50 $\pm$ 2.42
E	206.00 $\pm$ 1.78	205.16 $\pm$ 1.88

<sup>a</sup>  $P < 0.05$  compared to group B<sup>b</sup>  $P < 0.05$  compared to group C

degranulation of rough endoplasmic reticulum (RER) membranes (Figs. 3b, 4b). Radiation-induced loss of mitochondrial matrix and vacuolization–disruption of outer and inner membranes of mitochondria were frequently observed in the goblet cells. Irradiation caused marginal condensation of chromatin onto the nuclear lamina, and formation of large dense chromatin clumps in the nuclear matrix (Figs. 3a, b; 4a). Enterocyte profiles in the both regimes of irradiation showed signs of greater functional capacity as indicated by increases of mitochondria and decreased in the microvillous. Microvilli of epithelial cells also showed changes in length and frequency and gradually became shorter, thus alterations were observed in bordering membrane. Decreased length and surface of villi, as well as the microvillar changes, caused a reduction of surface area of the altered ileum (Fig. 3a).

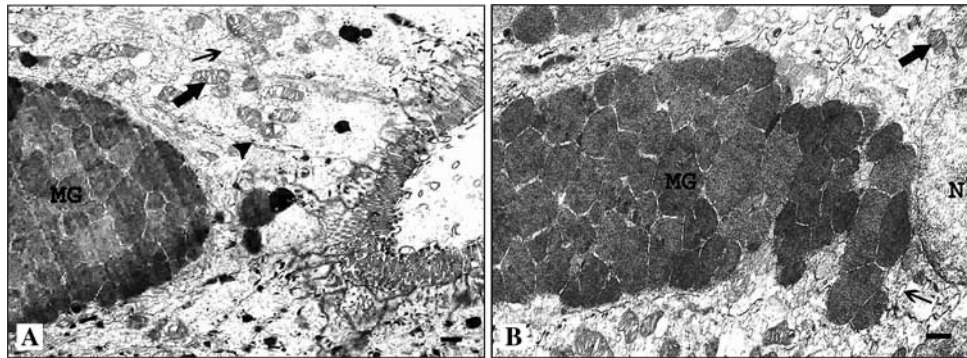
Mitotic figures were observed in the Lieberkühn crypts for both regimes of irradiation. Widening of intercellular spaces following irradiation was observed in intestinal epithelium (Fig. 4a).

Curcumin treatment was effective in preventing the dilatation of ER, mitochondrial degeneration and irregularly shaped nuclei; the irregularly shaped chromatin clumps were observed in goblet cells especially in single dose radiation treated with curcumin group (Fig. 5a, b). In the curcumin-treated groups, the severity of degenerative changes in the cytoplasm and especially in the nuclei of cells were less than that observed in the only radiation treated groups (Figs. 5, 6).

#### Discussion

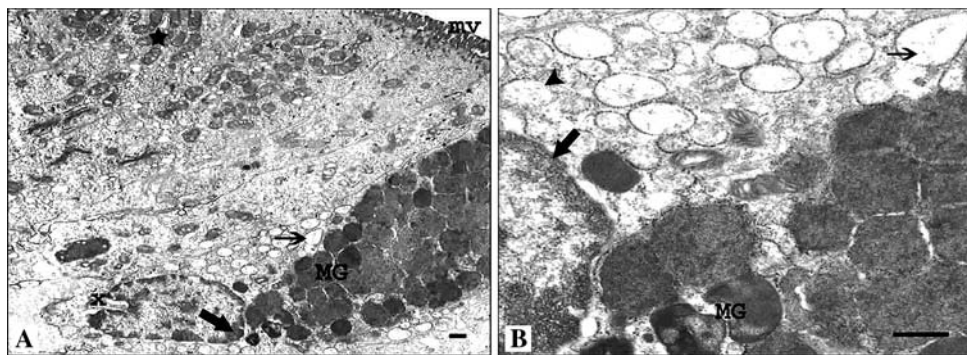
This study aims to evaluate the radioprotective effect of curcumin on  $\gamma$ -radiation-induced small intestinal damage. The efficacy of anticancer treatment increases the number of long-term survivors and thus the probability of late severe side effects. Therefore, a new challenge for physicians is to ensure patient quality of life by protecting normal tissue from radiation injury while enhancing anticancer





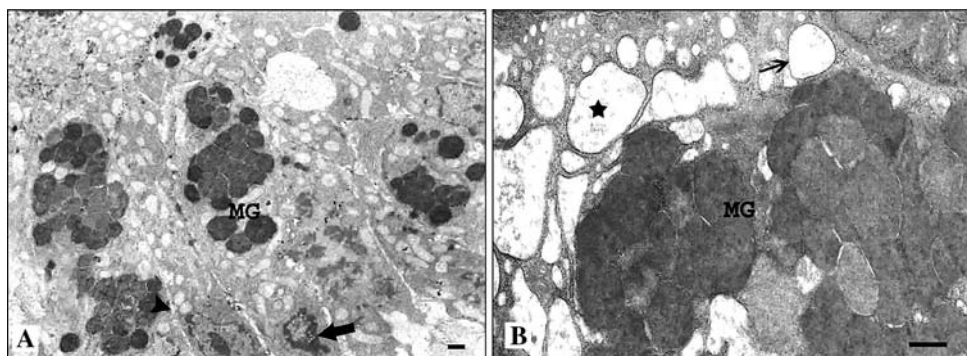
**Fig. 2** Electron micrographs of goblet cells in the Liberkühn cryptal and villus region of control rat ileum (**a, b**). The mucus granules (*MG*) have a typical honeycomb shape with well-packed in goblet cell. The cytoplasm of epithelial cells has cisternae of ER (*arrow*). Mitochondria

(*thick arrows*) have a typical cylindrical shape with organized cristae. Cell contact region (*arrowhead*) and oval shape nucleus (*N*) (uranyl acetate and lead citrate, scale bar 0.5  $\mu\text{m}$ )



**Fig. 3** Electron micrographs of single dose radiation-treated rat ileum (**a, b**). The dilatation of ER cisternae (*arrow*) and degranulation of RER membranes (*arrowhead*). Marginal condensation of chromatin onto the nuclear lamina (*thick arrows*) and invagination of the nuclear

envelope (*x*). Condensed mucus granules (*MG*). Increase in mitochondria (*asteriks*) and shortening in the microvillous of enterocytes (*mv*) (uranyl acetate and lead citrate, scale bar 0.5  $\mu\text{m}$ )



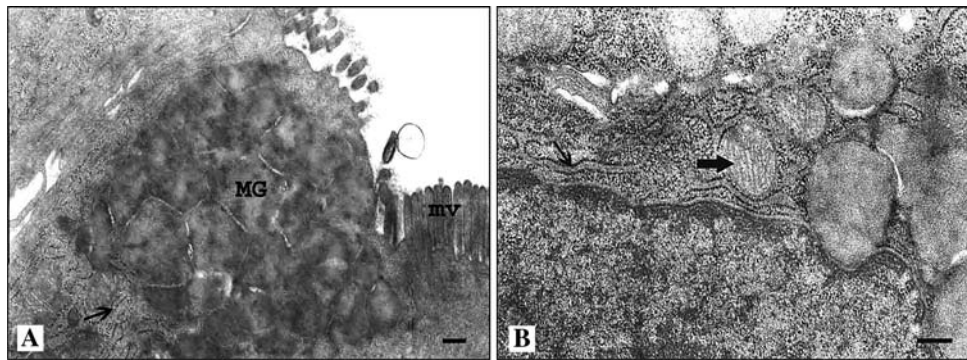
**Fig. 4** Electron micrographs of two dose radiation-treated rat ileum (**a, b**). The massive dilatation of ER cisternae (*asteriks*) and degranulation of RER membranes (*arrow*). Marginal condensation of chromatin onto the nuclear lamina (*thick arrows*). Abnormal spread and

condensation of mucus granules (*MG*) in goblet cell. Separation cell contact region (*arrowhead*) (uranyl acetate and lead citrate, scale bar 0.5  $\mu\text{m}$ )

efficacy (Weichselbaum 2005). Small intestine is one of the most radiosensitive organs (Smith and De Cosse 1986). Intestinal toxicity is a major type of complication. Whole abdominal irradiation causes inflammation in small intestine with submucosal edema, hyperemia and infiltration of

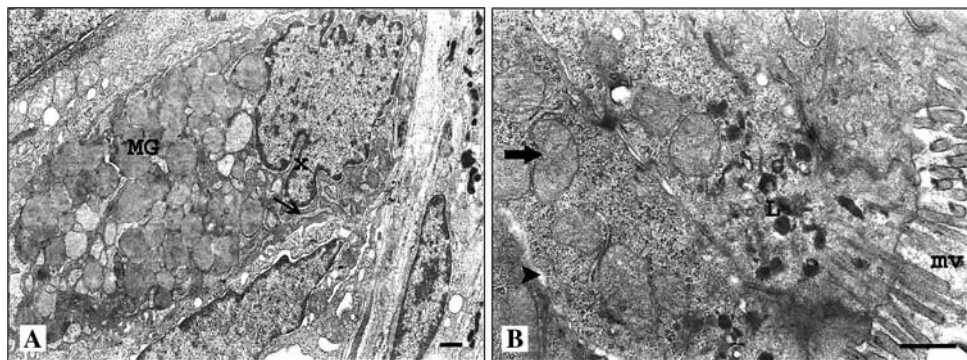
lamina propria with activated inflammatory cells, such as macrophages and neutrophils (Guzman-Stein et al. 1989; Klimberg et al. 1990).

Recently, curcumin has been evaluated for its radioprotective and radiosensitizing activities. Curcumin, a



**Fig. 5** Electron micrographs of single dose radiation-treated with curcumin rat ileum show little evidence of damaged cellular structure (**a, b**). The mucus granules (*MG*) have a typical honeycomb shape with well-packed in goblet cell. The goblet cell has regular cisternae of RER

(*arrow*). Mitochondria (*thick arrows*) have a typical cylindrical shape with organized cristae. Microvilli have uniform shape (*Mv*) (uranyl acetate and lead citrate, scale bar 0.2  $\mu\text{m}$ )



**Fig. 6** Electron micrographs of two dose radiation-treated with curcumin rat ileum (**a, b**). The goblet cell has regular cisternae of RER (*arrow*). Invagination of the nuclear envelope (*x*) and slightly spread of mucus granules (*MG*) in goblet cell. Mitochondria (*thick arrows*) have

a typical cylindrical shape with organized cristae. Microvilli have a lightly irregular shape (*Mv*). Cell contact regions have a lightly disintegration (*arrowhead*). Lysosome (*L*) (uranyl acetate and lead citrate, scale bar 0.5  $\mu\text{m}$ )

polyphenol confers radiosensitizing effects in prostate cancer cell line by inhibiting the growth of human prostate PC-3 cancer cells and down regulating radiation-induced pro-survival factors (Chendil et al. 2004). Moreover, curcumin has also been shown to inhibit growth of myeloid leukemia cells, epidermoid carcinoma cells, HT29 colon cancer cells and human colon epithelial cells. It was suggested that arrest at the S/G2M phases of the cell cycle may have had a radioprotection action (Khafif et al. 2005; Shimizu and Weinstein 2005). This indicates that curcumin is probably a potent antitumor agent for some cancer cells. Pretreatment of mice with a single curcumin dose of 100 mg/kg body weight before exposure to different doses (2, 4, 6 or 8 Gy) of whole body irradiation resulted in an enhancement of wound healing, as evidenced by increased wound contraction and reduced wound healing time (Jagetia and Rajanikant 2004).

Several investigators have demonstrated natural antioxidants scavenge the free radicals and protect the cellular DNA against indirect effects of ionizing radiation (Sasaki

and Matsubara 1977). Importantly, Zhao et al. (1989) have shown removal of free radicals by curcumin using spin traps. Being a known antioxidant, it was quite possible that curcumin might have intercepted these various free radicals and inactivated them by electron donation/hydrogen transfer. On scavenging by curcumin, the availability of free radicals would decrease considerably resulting into lowering of damage and in turn the extent of regeneration in the liver and spleen. The health benefits of curcumin include many pharmacological activities such as cholesterol-reducing, antiinflammatory, antiplatelet, anticancer, antimutagenic, antiHIV, etc. (Sharma et al. 2005).

After ionizing irradiation, epithelial cells frequently lose their contact to each other and possess many lateral and basal projections (Carr 1981; Fatemi et al. 1985; Wartiovaara and Terpila 1977). The altered interactions between epithelial cells and their micro-environment may be critical for the maintenance of normal, balanced homeostasis. Experimental evidence shows that disrupting this balance can induce aberrant cell proliferation, adhesion, function



and migration reviewed by Barcellos-Hoff (1998). In Porvaznik's (1979) early freeze-fracture studies, a significant shift was mentioned in the mean depth of the tight junction zonule on the 3rd day after 3 and 5 Gy  $\gamma$ -irradiation in ileal epithelium. Our results indicate  $\gamma$ -irradiation-induced disorganization of the adherent junctions.

In the present study, radiation exposure caused severe degenerative changes, such as dilation of ER cisternae and degranulation of RER membranes, degeneration cristae of mitochondria, marginal condensation of chromatin onto the nuclear lamina and formation of large dense chromatin clumps in the nuclear matrix of epithelial cells. Microvilli of epithelial cells also showed changes in length and frequency and alteration of bordering membrane. These data are corroborated by previous studies reported by other investigators on radiation-induced intestinal injury in animals (Carr 1981; Carr et al. 1992a; Fatemi et al. 1985; Somosy 2000). Given the documented pharmacological safety of curcumin and scarcity of adverse side effects that typically accompany traditional chemotherapy, curcumin may represent an alternative therapeutic with potent and selective induction of tumor regression, while providing cytoprotection in normal cells. In our study, in the curcumin-treated rat ileum, the severity of degenerative changes in the cell organelles, especially in the ER cisternae and in nucleus of cells was less than that observed in the only radiation treated groups. The dilated ER cisternae and the distorted goblet cells were mainly absent in the curcumin-treated rats.

Our results indicate that also abdominal exposure of rats to a single or two doses of 5 Gy  $\gamma$  irradiation results in a disruption in the ileum mucosa, on the 4th day following irradiation. Both radiation regimes produced an increase in the number of goblet cell profiles, resulting in increase of the total production of mucin. In the curcumin-treated groups, number of goblet cells was less than in the only radiation treated groups. Mucin is known to contain secretory immunoglobulin A and could assist in preventing the colonization of the epithelium by opportunistic pathogens, known complications of post-irradiation injury (Walker and Conklin 1987). Previous acute radiation studies indicate that the goblet cell response is complex. Some reports describe decreases or no change in cell number at 72 h after irradiation (Becciolini et al. 1985; Carr et al. 1991; Carr et al. 1992a, b; Cooper 1974), while others demonstrate increases, particularly after several weeks and months (Lewicki et al. 1975; Van Dongen et al. 1976).

In conclusion, antioxidant treatment with curcumin prior to irradiation, provides effective protection against intestinal damage, suggesting that clinical transfer is feasible. Therefore, curcumin can be very useful in cancer patients receiving radiotherapy.

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