Introduction

Detrimental effects of radiation have been surfaced time and again and at times turned out as major threat for life. Ionizing radiation is amply known to generate highly unstable free radicals in biological system which attack nearest available molecules to ensure their stability by obtaining electrons. Error prone DNA lesions, protein denaturation and peroxidation of lipids resulting in loss of cellular homeostasis and death, are some of the major consequences of radiation exposure [1]. Routinely generated free radicals, as byproducts of cellular metabolism, are constantly countered by endogenous defense system. However, high doses of ionizing radiation introduces biological imbalance which overpower the efficacy of existing endogenous antioxidants [2].

Hematopoietic and gastrointestinal (GI), the major governing organs for survival, are highly susceptible to radiation [3]. Intestine harbors stem cells at the base of crypts which maintains the population of intestinal cells, being regularly lost from the villi tip [4]. Although mechanism of radiation induced GI pathogenesis has not yet been clearly understood, however, as per the prevailing hypothesis, radiation attacks clonogenic cells of GI leading short supply of cells required to maintain mucosal lining. This causes shortening and rupturing of villi [5]. Thus formed mucosal lesions lead to fluid & electrolytes imbalance, impaired absorptive function, inflammation and septic shocks. These conditions collectively result into development of GI syndrome causing death of the individual within few days of whole body exposure to lethal doses of radiation [6].

Extensive work has been carried out on prevention and cure of radiation induced damage to...
GI, [7]. But till date, even after screening lots of chemicals and synthetic compounds for radio-protection/mitigation, desirable success has not yet been achieved [8]. Most of the potential agents are restricted from bedside use due to their inherent toxic nature. After enormous efforts, amifostine (WR-2721) is the only compound being recommended clinically as an adjuvant during radiotherapy [8]. In search of a safe and effective radioprotector many researchers are now extensively exploring natural resources, nutraceuticals, minerals etc. Several antioxidants and free radical scavengers like melatonin also reduces radiation toxicity [8]. Plants, being in vast use for health rejuvenation and treatment of various chronic illnesses under ancient medicinal system [9], are also exploited for minimizing radiation effect.

*Podophyllum hexandrum* (Himalayan mayapple) from family Berberidaceae has been reported to cure various bacterial and viral infections, metabolic disorders, monocytoid leukemia, lymphomas, veneral warts and rheumatoid arthralgia [10]. Studies on radioprotective ability of whole and semipurified extract of *P. hexandrum* have revealed >90% whole body protection with the ‘Dose Modifying Factor’ (DMF) of 1.5 in mice against whole body lethal irradiation [11]. Extracts of *P. hexandrum* (rhizomes) have also been reported for rich antioxidant properties and protective to DNA, lipids, bone marrow stem cells, immune system, hematopoietic system, etc [12, 13].

The objective of the current study was to investigate the role of *P. hexandrum* against whole body irradiation (WBI) induced intestinal injury in mice. The study has mainly focused on biochemical and histological changes in GI response towards radiation and G-001M pretreatment. Biochemical assays included measurement of lipid peroxidation, superoxide dismutase (SOD), reduced glutathione (GSH) & glutathione reductase (GR) in jejunum of various treatment groups. Histological observations have focused on apoptosis, mitosis, cell count in crypts/villi, crypt survival and other pathological features in jejunum of irradiated and G-001M treated animals.

**Materials and methods**

**Preparation of G-001M**

The semipurified extract of *Podophyllum hexandrum* was prepared from rhizomes of the plant growing at >3000 meter altitude of Himalayan region of India. Collected material was shade dried in dust free environment and crushed to obtain fine powder which was later extracted with petroleum ether (60-80°C) in soxhlet for 16 h. The material left behind after extraction with different solvents was dried to remove residual solvent. G-001M was prepared by the method reported earlier [14]. The preparation was analyzed analytically to confirm chemoprofiling details described in above mentioned manuscript. Voucher specimen was deposited in repository of IIIM, Srinagar (Voucher no. RRL/PH/Srinagar-2006).

**Experimental animals**

Strain ‘A’ 7-8 weeks old female mice, weighing 27±2 g were used in this study. Mice were fed standard laboratory pellets and filtered water *ad libitum*. All the experiments were done strictly under Institutional Animal Ethical Committee (IAEC) approved guidelines. Permission for use of animals was obtained from Institutional Animal Ethical Committee held on 19th February 2009. For each experimental point 3 mice were taken. Experiment was repeated thrice (3x3=9). For whole study total 279 mice were used divided into following groups:

- **Group-I** (control); received no treatment and served as normal control group.
- **Group-II** (G-001M); administered intra-muscularly with single dose of G-001M (6 mg/kg b.w) alone.
- **Group-III** (10Gy); exposed to 10 Gy whole body radiation alone.
- **Group-IV** (G-001M + 10Gy); administered intra-muscularly with G-001M (6 mg/kg b.w) 1h prior to 10 Gy whole body irradiation.

**Irradiation**

The animals were irradiated in 60Co gamma chamber (Gamma Cell-220, Atomic Energy of Canada Ltd.) at the dose rate of 0.37-0.3 cGy/sec and were exposed individually under continuous air supply. Dosimetry was carried out using Baldwin Farmer’s secondary dosimeter and Fricke’s chemical dosimetry.

**Isolation of tissue for biochemical assays**

Jejunum was dissected out from mice (n=3x3) of different treatment groups sacrificed at various time intervals. To estimate lipid peroxidation, 10% (w/v) tissue homogenate was prepared in chilled phosphate buffer saline (PBS). Aliquots of homogenates were spun in cold centrifuge at 2000 rpm for 10 min and the supernatant was assayed for SOD, GSH & GR.

**Histology**

Jejunum (1-2 cm) was fixed in 10% neutral buffered formaldehyde. Tissue was gradually dehydrated in graded ethanol and embedded in
paraffin wax. Transverse sections (2-5 µm thick) were cut using microtome and mounted on glass slide. Sections were stained with hematoxylin & eosin as per the standard protocol. Mounted slides were studied under compound microscope using various magnifications (20x, 40x &100x).

**Crypt survival assay**

Crypt survival assay or microcolony assay was performed by following the method of Withers and Elkind [15]. On 3rd day of treatment, total number of viable crypts per circumference in jejunum region was scored. Crypts consisting of 10 or more clustered cells, appearing crowded with little cytoplasm and prominent nucleus, were considered as viable crypts. Crypts containing sparsely populated enlarged cells with prominent eosinophilic cytoplasm were identified as non viable crypts. In each mouse 8-10 circumferences were scored and results are expressed as the average number of surviving crypts per circumference. Average from each mouse was considered as a single value for statistical purpose.

**Mitotic index**

Mitotic cells in the crypts were observed as darkly stained bodies showing chromatin condensation without any sign of cytoplasmic and nuclear shrinkage. Additionally, mitotic nucleus also appears horizontally displaced towards lumen in comparison to nuclei of other cells in epithelial lining [16]. Minimum twelve different crypts per transverse section and 3-4 separate sections of jejunum per mouse were scored. Results are expressed as average percent mitosis per crypt.

**Crypt cell apoptosis**

Apoptotic cells in the crypts of jejunal transverse section were scored for morphological changes viz cell shrinkage, chromatin condensation, pycnotic nuclei and cellular fragmentation [17]. Apoptosis was confirmed by ‘Terminal deoxy transferase-mediated deoxy-Uri dine triphosphate Nick End Labeling’ (TUNEL) assay in paraffin wax sections using ApopTag Fluorescein in situ apoptosis detection kit (Millipore). TUNEL assay was performed to stain oligofragmented DNA which is the characteristic of apoptotic nuclei. Total number of apoptotic cells per crypt was scored. Data are expressed as mean number of apoptotic cells per crypt obtained from minimum four cross sections per mouse.

**Total number of cells per crypt per villous**

In jejunum region of small intestine, cells were counted in complete crypt including its opening. In villous, total cell counting was done from base to tip [18]. In each transverse section of jejunum 8-12 different crypts and villi were scored. Data from three to four separate transverse sections per mice were pooled. Results are expressed as total number of cells per crypt/villous.

**Lipid peroxidation**

Lipid peroxidation was measured as earlier described technique [19] at 2 h, 6 h and 24 h post treatment. To 200 µl of the tissue homogenate, 400 µl of Beuge Aust reagent (0.37% thiobarbituric acid and 15% tri-chloro acetic acid) was added. Reaction mixture was incubated at 95°C for 15 min. Samples were then centrifuged at 2000 rpm for 10 min and absorbance of the supernatants was recorded at 535 nm. The lipid peroxidation level was measured in µM of malondialdehyde (MDA) per mg protein.

**Superoxide dismutase**

Superoxide dismutase was determined by the method of Kakkar *et al* [20]. To the desired volume of enzyme preparation, 1.2 ml sodium pyrophosphate buffer (pH 8.3, 0.025 mol/L), 0.1 ml phenazine methosulphate (186 mM/L), 0.3 ml nitroblue tetrazolium (300 mM/L), 0.2 ml nicotinamide adenine dinucleotide (NADH) (780 mM/L) and distilled water was added to make total volume of 3 ml. The reaction mixture was incubated at 30°C for 90 sec. To stop the reaction 1 ml of glacial acetic acid was used. To this mixture, 4 ml of n-butanol was added followed by vigorous shaking. Color intensity of the chromogen in the butanol layer was measured at 560 nm against n-butanol. SOD activity was expressed as units/mg protein.

**Reduced glutathione**

The amount of GSH was assessed by using the method of Ellman *et al* [21]. Assay mixture consisted of 0.2 ml of tissue preparation, 1.8 ml of (0.5M) EDTA solution and 3 ml precipitating reagent (In 1 L-1.67 g of meta-phosphoric acid, 0.2 g of EDTA disodium salt and 30 g sodium chloride) was thoroughly mixed, kept for 5 min and then centrifuged for 15 min at 1500 rpm. To 2 ml of the supernatant, 4 ml disodium hydrogen phosphate solution (0.3 M) and 1 ml of 5,5-dithio-bis-2-nitrobenzoic acid (DTNB) was added. Absorbance was taken at 412 nm. GSH was measured in µg/mg protein.

**Glutathione reductase**

The activity of GR was measured using earlier described method [22]. The reaction mixture containing 0.2 M potassium phosphate buffer (pH 7.0), 2 mM nicotinamide adenine dinucleotide phosphate (NADPH) and 20 mM oxidized glutathione was mixed with distilled water to make
up the final volume to 3 ml. Enzyme preparation (0.1 ml) was added to initiate the reaction, absorbance was measured at 340 nm for one minute at 15 sec interval. Control inclusive of all components except enzyme was run simultaneously. GR activity was expressed as pM NADPH consumed/min/mg protein.

**Statistical analysis**

The Student’s t-test was used to make a statistical comparison between different treatment groups. Significance level was set at p<0.05. All the results obtained from various biochemical and histological parameters were expressed as mean±SD.

**Results**

**Crypt survival assay**

On 3rd day of lethal whole body radiation exposure (10Gy) there was significant reduction in the number of viable crypts (42±4.1) per transverse section (T.S.) of mice jejunum in comparison to the control group (128±5.2 crypts/T.S, p<0.001). In G-001M pretreated irradiated group total number of viable crypts (76±4.4) per transverse section was significantly higher (p<0.001) than radiation alone group. G-001M extract administration alone did not show any significant change in number of crypts per transverse section (125±3.8, p>0.05 vs. control).

**Mitotic index**

In radiation alone group, cryptal mitotic flux in jejunum was significantly lower on 1st and 2nd day post irradiation (10Gy) than untreated control group (6.17±1.2 per crypt, p<0.001). Mitotic index in this group increased by 3rd and 4th day but regressed again on 10th day (Fig.1). None of the mice survived beyond 11th day in this group. On 1st day of experimentation in G-001M pretreated irradiated group also there was a fall in mitotic activity, but significantly less than radiation alone group (p<0.001 vs. radiation alone). After this short fall till 48 h, mitotic recovery increased sharply at 72 h of study and upsurge continued till 15th day. Since, the crypts were holding more number of cells in treated irradiated group than normal they appeared very elongated. After 5th day budding in the crypts was also observed. G-001M alone did not disturb mitotic activity at any time interval of treatment.

**Crypt cell apoptosis**

Jejunum from mice of radiation alone group showed prominent increase in apoptotic content (4.45±0.48 cells/crypt, p<0.001 vs. control) on 1st day of experiment (Fig.2). On 5th day, apoptotic cell count in this group declined but was still higher than untreated control group. In G-001M pretreated irradiated group apoptotic number on first day of treatment was significantly lower than radiation alone group (0.61±0.1 cells/crypt, p<0.001) and similar status continued at other time points of study (2nd, 3rd, 4th, 5th and 10th). However, apoptotic activity in this group was relatively higher than untreated control group at most of the time intervals except on 30th day where values (p>0.05 vs. control) in both the groups were parallel. G-001M alone in single dose administration did not induce any significant variation in apoptotic cell count when compared with control.

**Figure 1.** Mitotic index per crypt of mice jejunum in various treatment groups: 1) G-001M alone, 2) 10Gy whole body irradiated and 3) G-001M Pretreated irradiated. Mitotic activity reduced in mice jejunum after irradiation. In G-001M pretreated irradiated group, after initial arrest, mitosis recovered significantly and reached to normal by 30th day. G-001M alone did not alter mitotic index. Results are expressed as Mean±SD.

**Figure 2.** Apoptotic cell count per crypt in mice jejunum of various treatment groups. Increase in apoptotic cells in crypts, after irradiation was significantly reduced by G-001M pretreatment. G-001M treatment alone did not lead to any significant apoptosis. Results are expressed as Mean ±SD. 2a*** p<0.001 (10Gy 1st day vs. control); 2b*** p<0.001 (G-001M+10Gy, 1st day vs. 10Gy, 1st day); 2c* p>0.05 (G-001M+10Gy, 30th day vs. control).
**Total number of cells per crypt per villous**

Whole body lethal irradiation (10Gy) significantly reduced total number of cells in crypt and villi of mice jejunum (Figs.3&4). In comparison to the normal control, cell number in the crypts was found depleted in radiation alone group on 1st and 2nd day (p<0.001 vs. control) of exposure. On 4th day increase in cell number was noticed though temporarily, as depletion was observed again on 10th day. At this time interval most of the crypts harbored only voids and enlarged cells. Cell count in the villi of this group depleted gradually from 1st to 5th day of irradiation. Morphologically also villi of this group appeared more congested, short in length, ruptured at terminus, denuded and showed frequent lesions making cell count absolutely difficult (Fig.5). In G-001M pretreated irradiated group there was a fall in crypt cell count on 2nd day (p<0.001 vs. control). On 3rd day the count increased sharply even higher than untreated group and same status continued up to 15th day of study. On 30th day difference in crypt cell count between treated irradiated group and normal control was non-significant (p>0.05). In this group, fall in villous cell count also followed the same pattern as in crypt i.e. decline up to 3rd day (91±9.9 cells/villous) and gradual increase afterwards reaching to normalcy by 30th day (165±14.7 cells/villous, p>0.05 vs. control) of experimentation. G-001M alone, on single dose administration, did not affect cell count either in crypt or villous at any time point of study.

**Lipid peroxidation**

Lipid peroxidation in jejunum of radiation alone group was observed to be significantly high as compared to the untreated control group (Fig.6). At 2h post irradiation MDA level increased exorbitantly (p<0.001 vs. control). However, the values declined within 24h of exposure. G-001M treatment prior to irradiation resulted into reduced MDA levels at 2h and decreased further at 24h (p>0.05 vs. control). In G-001M alone also MDA level increased at 2h and 6h though marginally only. At 24h (p>0.05 vs. control) this increase in MDA reverted to normal.

**Superoxide dismutase**

As depicted in Fig.7, radiation alone significantly reduced levels of SOD in mice jejunum. Decline in SOD as compared to untreated control was observed from 24h to 72h (p<0.001) however, at 96h of study SOD level got enhanced though marginally. G-001M pre-administration could significantly increase SOD from 24h to 72h (p<0.001) when compared with radiation alone group but values were still less in comparison to normal control group. At 96h, level of this enzyme in the same group was parallel to normal control. No marked difference was observed in SOD of jejunum from G-001M alone group at all the time intervals studied.

**Reduced glutathione**

G-001M pretreated irradiated group showed significantly enhanced levels of GSH in jejunum at various time intervals of study from 24h (Fig.8, p<0.001) to 96h (p<0.001) in comparison to
Figure 5. Histological studies in mice jejunum on 3rd and 10th day post-treatment. (a) Untreated control group; (b) 10Gy alone on 3rd day showing lacteal contraction, lesions & shrinkage of villi and loss of cells from epithelial lining; (c) G-001M+10Gy on 3rd day exhibiting elongated crypts with crowding of cells due to increased mitotic activity; (d) 10Gy whole body irradiation on 10th day projecting altered mucosal organization, reduced crypt number, disruption of villi and denudation; (e) G-001M+10Gy on 10th day showing, elongation of villi, lactal support and overall preservation of mucosal integrity. Hematoxylin and eosin staining, 100x magnification.

Figure 6. Lipid peroxidation in jejunum of differentially treated mice. Lipid peroxidation increased after whole body 10Gy irradiation. G-001M pretreatment significantly inhibited lipid peroxidation at all time intervals and by 24 h it was down to control level. Results are expressed as Mean±SD. 5a*** p<0.001 (10Gy, 2 h vs. control); 5b* p<0.05 (G-001M+10Gy, 2 h vs. 10Gy, 2 h); 5c** p>0.05 (G-001M+10Gy, 24 h vs. control).

Figure 7. Superoxide dismutase (SOD) level measured in jejunum of mice after various treatments. Reduction in enzyme level was recorded after irradiation. G-001M pretreatment significantly enhanced the level of SOD as compared to radiation alone at all time intervals. Results are expressed as Mean±SD. 6a*** p<0.001 (10Gy, 24 h day vs. control); 6b** p<0.05 (G-001M+10Gy, 24 h day vs. 10Gy, 24 h day).

DOI:10.5455/jeim.021211.or.019
radiation alone group. At 96 h, GSH level increased significantly in G-001M pretreated irradiated group. Jejunum GSH level in mice treated with G-001M extract alone remained close to normal (p>0.05) from 24 h to 96 h post treatment time of study.

**Glutathione reductase**

In radiation alone group, GR activity in jejunum declined drastically at 24 h post irradiation in comparison to untreated control group (p<0.001). Fall in GR activity continued till 72 h. Recovery, though marginal, was recorded at 96 h (p<0.01 vs. control) post irradiation (Fig 9). In G-001M pretreated irradiated group also GR activity decreased at 24 h but the fall was significantly (p<0.001 vs. radiation alone) less than radiation alone group. Study conducted at 96 h post treatment demonstrated appreciable increase (9.6±0.88 pM NADPH/min/mg protein, p<0.01 vs. control) in GR activity of this group. Administration of G-001M extract only did not alter GR status at any time interval of study.

**Discussion**

Cellular derangement as a consequence of ionizing radiation occurs mainly due to free radicals mediated single and double strand breaks in DNA which proves to be fatal if remain unrepaired/misrepaired [23]. The gastrointestinal tract has been invariably shown as one of the most radiosensitive organs of living system [5]. Gastrointestinal radiosensitivity has been reported due to more sensitive clonogenic cells residing in stem cell region of crypt of Lieberkuhn [24]. High radiosensitive nature of these clonogenic cells has been primarily because of their large proliferation rate and then their preference for suicide instead of attempting DNA repair [25]. In consonance, our study has shown steep rise in apoptotic content of crypts in mice jejunum after whole body irradiation to 10 Gy. Administration of G-001M before irradiation has been able to substantially counter radiation mediated yield of apoptotic population possibly due to DNA protective ability of *P. hexandrum* [14]. *P. hexandrum* has been amply reported to arrest cell cycle progression and rendering a fair chance to DNA to have better repair being in non proliferating phase.

Depending upon the cell cycle stage (G1, S, G2, M) some of the clonogenic cells are killed after irradiation while others undergo cell cycle arrest [26] which tends to increase with radiation dose. During the period of arrest, cells are accumulated in G1/S and S/G2 margins and are ready to divide in synchronization as soon as the arrest is resumed [26]. Most of these cells contain damaged DNA and face difficulty while dividing therefore they are eliminated in subsequent divisions [27]. This fact justifies our study wherein increased mitotic activity in jejunal crypts peaking on 4th day in
radiation alone group and deterioration thereafter has been observed (Fig.1). G-001M pretreatment also resulted into sudden jump in mitotic activity shortly after recommencing from temporary mitotic arrest (Fig.1). To explain further, release of cells from cell cycle block resumes proliferation rates faster than unirradiated controls [18, 28]. In addition, study conducted by Hagemann and Concannon [29] has demonstrated that negative feedback rising from depleted cell number accelerates proliferation rate by shortening of cell cycle (G1 phase) and expansion of proliferative compartment resulting in temporary hyperplasia of crypts. Timely increased proliferation in clonogenic compartment has been postulated to be essential for animal to prevent succumbing to death [28].

Current findings showing severe decline in crypts survival after acute irradiation is in accordance with Withers and Elkind [15] who developed the microcolony assay to study regeneration. Majority of crypts not having clonogenic cells and apical exclusion of remaining cells migrating in villi are the key cause for inability of GI to recover in animals exposed to large radiation doses [30]. Single surviving clonogenic stem cell in crypt is known to be capable of regenerating the entire crypt, which later supports repopulation of intestinal epithelium [31]. Existence of more number of surviving crypts in G-001M pretreated and irradiated mice, reported in our study, indicates the clonogenic cells protective ability of Podophyllum hexandrum. These results are in agreement with earlier reports showing GI protection mediated by Podophyllum hexandrum and other agents [17, 32].

Radiation mediated fall in crypt cellularity can be correlated with high apoptotic rate and suspended/reduced mitosis [33, 34]. Decline in viable crypts and mitotic yield leads to gradual decrease in villous cell count. During current study the onset of rapid repopulation in crypts was seen between 2 to 4 days in G-001M pretreated irradiated mice. This response owes to G-001M which was capable of reducing apoptotic yield and enhance mitotic index resulting into high crypt viability. The crypt cellularity in radiation alone group of our study was much lower due to higher apoptotic rate and significantly reduced mitotic index.

Reactive oxygen species (ROS) originating after ionizing radiation are the chief source of maximum damage in biological system. Excessive ROS produced reacts with unsaturated lipids that cause lipid peroxidation leading to altered membrane permeability [35]. Our study has shown increased lipid peroxidation in jejunum of radiation alone group. The G-001M treatment prior to irradiation could significantly reduce the MDA formation in mice suggesting effect of G-001M in preventing lipid peroxidation by donating hydrogen atoms required by secondary chain of fatty acids to fight radiation induced damage to lipids. Reduction in levels of MDA (major end product of lipid peroxidation) formation is of additional benefit as MDA also damages DNA by cross linking DNA-protein and nucleotides on the same and opposite strands [36].

Reactive oxygen species are detoxified by a variety of antioxidants present endogenously in biological system. Superoxide dismutase reduces superoxide radical to hydrogen peroxide (H2O2) and GSH helps in further metabolism of H2O2. Glutathione reductase on the other hand regenerates reduced form of GSH from its oxidized form and is essential for cell to combat oxidative stress [37]. In current study depletion of cellular antioxidants like SOD, GSH and GR after 10 Gy WBI in jejunum of mice is in line with reports demonstrating radiation mediated reduction in antioxidants of intestine and other organs [38]. A relatively enhanced level of these antioxidants was observed in jejunum of G-001M pretreated and irradiation mice. The antioxidant activity of G-001M has been primarily due to the presence of high polyphenolic content [14]. Flavonoids in specific are known to quench free radicals by virtue of their hydrogen donation ability [39]. Timely scavenging of free radicals prevents their amplification which otherwise could lead to their interaction with other cellular molecules like lipid, protein and DNA.

Ionizing radiation induced intestinal injury is multifactorial and one of the major limiting factor for whole body survival against lethal doses. Denudation and abrasion of the mucosal lining invite infective microorganism and loss of essential body fluids. Inflammation and electrolyte imbalance further intensifies the pathology leading to organ dysfunction [7]. Death due to GI syndrome is much faster and rescue from it even more difficult. Podophyllum hexandrum extract (G-001M) used in this study has been under continuous exploration for its radioprotective abilities against whole body lethal irradiation in mice. Single dose intramuscular administration of 6 mg/kg b.w of the extract rescued more than 90% of mice from death [14]. At functional level this plant has been reported for scavenging of ROS and reactive nitrogen species (RNS), transition metal chelation, protection and facilitating DNA to repair,
up-regulation of anti-apoptotic factors (PCNA, Bcl2) and down regulation of pro-apoptotic factors (p53, Bax). Support to hematopoietic and immune system by this plant formulation against radiation associated suppression also has documentary support [12, 13, 40, 41].

Our findings very strongly support the ability of G-001M, a subfraction prepared from Podophyllum hexandrum, in altering intestinal damage caused by whole body lethal irradiation in mice. This biological function is accomplished by improved crypt survival, reduced apoptosis in crypts and enhanced mitosis assisting repopulation of crypt-villus organization. Elevation in antioxidant status and reduction in lipid peroxidation also appear to have played important role in reducing radiation impact. Healthy intestine undoubtedly extends immense support for survival in lethally irradiated animal combating for life.

Acknowledgements

The authors gratefully acknowledge Defence Research & Development Organization (DRDO), Ministry of Defence for providing grants and Junior Research Fellowship to S.S. from Council for Scientific & Industrial Research (CSIR), India. Authors do not have any conflict of interest.

References


