RESEARCH ARTICLE

Cytoprotective Potential of Rutin and Quercetin in Swiss Mice Exposed to Gamma Radiation

Shrikant L. Patil[1*], Tanhaji Ghodke[2], Shilpa M. Patil[3], Swaroop K[4], H. M. Somashekarappa[5]

[1]Assistant Professor, Department of Physiology, K. S. Hegde Medical Academy, Nitte University, Mangalore, India
[2]Junior Research Fellow, Department of Biophysics, Govt. Institute of Science, Aurangabad, India
[3]Assistant Professor, Department of Biophysics, University of Mumbai, Kalina Campus, Mumbai India
[4]Centre for Application of Radioisotopes and Radiation Technology, USIC, Mangalore University, Mangalore, India
[5]Centre for Application of Radioisotopes and Radiation Technology, USIC, Mangalore University, Mangalore, India

[*]**Address for Correspondence:** Dr. Shrikant L. Patil, Assistant Professor, Department of Physiology, K. S. Hegde Medical Academy, Nitte University, Mangalore, India

Received: 21 June 2017/Revised: 17 July 2017/Accepted: 24 August 2017

ABSTRACT- Radioprotective mechanisms of Rutin (RUT) and Quercetin (QRT) against gamma radiation was studied by investigating recovery of histopathology of intestinal mucosa and bone marrow in Swiss albino mice. These mice were treated with RUT (10mg/kg.b.wt.) and QRT (20 mg/kg.b.wt.) once daily for five consecutive days and exposed to 7.5 Gy of gamma radiation after the last administration. RUT and QRT treatment before exposure to 7.5 Gy of gamma radiation. To assess the intestine and bone marrow protective potential of RUT and QRT, histological analysis was carried out by observing the villus height, crypt survival, number of goblet cells/villus section and dead cells/villus section in the mouse jejunum and bone marrow cellularity at 24 hours post-irradiation. Mice exposed gamma radiation caused a significant decline in the villus height and crypt number with an increase in goblet and dead cell number with a significant decrease in bone marrow nucleated cells. The potent antioxidant nature of RUT and QRT mitigate the oxidative stress induced by gamma radiation and thus protect the mice from gastrointestinal damage.

Key-words- Cytoprotective, Irradiation, Rutin, RUT, Quercetin, QRT

INTRODUCTION

Radiation therapy has been successfully used to treat malignant tumours of different histological origin and stages, (individually or in combination with chemotherapy and surgery, or both) for several decades. The response of mammalian cells to ionizing radiations at the cellular and molecular level is complex and is an active irreversible process that is dependent on both the radiation dose and the tissue-weighting factor [1]. Most of the tissue damage caused by ionizing radiation is mediated by the reactive oxygen species (ROS) generated from the interaction between radiation and water molecules in cells [2]. These ROS react with biological molecules including proteins, lipids, lipoproteins and DNA [3].

Many synthetic compounds have been studied for their ability to protect against adverse effects of radiation ever since the original observation of radioprotection by Patt and co-workers [4].

Access this article online	
Quick Response Code	Website: www.ijlssr.com
	DOI: 10.21276/ijlssr.2017.3.5.10

However, the practical applicability of the majority of these synthetic compounds remains limited, owing to high toxicity at their optimum protective dose [5]. Due to lack of effective protective agents, new compounds are currently under investigation as a possible adjuvant in radiation treatment of cancer. Herbal medicines have only recently begun to receive some attention as possible modifiers of the radiation response [6-9]. Naturally occurring dietary components also offer opportunities for development as effective radioprotective agents because of their potential low toxicity [8-10]. Natural antioxidants can protect the human body from free radicals and retard the progress of many chronic diseases as well as radiation-induced oxidative damages [11]. Hence, the studies on natural antioxidants have gained increasing greater importance.

Rutin and Quercetin are common dietary flavonoid that is present in fruits, vegetables and plant-derived beverages such as tea and wine. Recently, flavonoids have attracted attention because of their beneficial biological activities to human health. Rutin's anti-inflammatory potential has been demonstrated in a number of animal studies [12-14]. Quercetin also has demonstrated significant anti-inflammatory activity because of direct inhibition of several initial processes of inflammation. The intestinal mucosa is extremely sensitive to ROS [13]. Since there is limited information on the importance of rutin and

quercetin as an antioxidant *in vivo*, we focused on the protective effect of rutin on intestinal oxidative injury.

A severe depression of gastrointestinal function often takes place in patients undergoing radiotherapy due to the high sensitivity of these organs. [15-18] Developing a strategy to protect and stimulate these cell pools is very important and desirable to counteract the adverse effects of radiation, and thus allow a more intensive and effective therapy [17-20]. Therefore, in the present study, we have attempted to evaluate the protective role of RUT and QRT against radiation-induced alterations in clonogenicity of bone marrow cells and intestinal mucosa of mice as experimental end points.

MATERIALS AND METHODS

Animals: Swiss albino mice strain of either sex weighing 25 to 30 g, four to six weeks old were selected, and kept in well ventilated polypropylene cages under standard conditions of temperature (23±2ºC), humidity (50±5%) and light (10 and 14 hours of light and dark, respectively). Animals were allowed food and water *ad libitum.* The guidelines issued by the World Health Organization, Geneva, Switzerland and the Indian National Science Academy, New Delhi, India were followed during animal care and handling. Institutional Animal Ethics Committee approval was obtained for this animal experiment.

Chemicals

Drug preparation and mode of administration Various doses of RUT and QRT 10–100 mg/kg body weight orally once a day for five consecutive days was given. Rutin (RUT) and Quercetin (QRT) powder was, suspended in water using 0.5% w/v Carboxy Methyl Cellulose (CMC) and was given once daily (5 ml/kg body weight), Rutin and Quercetin was purchased from Himedia Laboratories Pvt. Ltd., Mumbai, India. Radiation exposure was performed 1 hour after the last dose of RUT and QRT administration.

Other chemicals: Acridine orange (AO) was purchased from BDH Chemicals Ltd, Poole, England. The other chemicals such as absolute alcohol, dimethyl sulphoxide (DMSO), ethylene diamine tetraacetic acid (EDTA), sodium bicarbonate, sodium chloride, potassium hydrogen phosphate and hydrochloric acid were purchased from Qualigens Fine Chemicals (A Division of GlaxoSmithKline Pharmaceuticals), Mumbai, India. RUT and QRT, glutathione, chloro-2,4-dinitrobenzene (CDNB), 5,5-dithiobis-2- nitrobenzoic acid (DTNB), trichloroacetic acid (TCA), thiobarbituric acid (TBA), ethidium bromide, normal melting agarose (NMA), low melting agarose (LMA) and fetal bovine serum (FBS) were purchased from Sigma Chemical Co. (St. Louis, MO, USA).

Radiation exposure: ^{60}Co Tele-therapy facility (Theratron Atomic Energy Agency, Canada) at the Shirdi Sai Baba Cancer Hospital, Manipal was used for whole body irradiation. Unanesthetized mice were restrained in a specially designed, well-ventilated acrylic box and exposed to gamma radiation, at a dose rate of 1.33 Gy/minute & source to surface distance (SSD) of 61 cm**.**

Histopathological studies

Effect of RUT and QRT on radiation induced changes in intestinal mucosa- In this study, we have examined histopathologically the anatomy of the small intestine of mice after irradiation and the protective role of RUT and QRT; animals were divided into following groups with six animals per group.

1. **Untreated Control group-** These groups of animals were given 0.1 ml/kg.b.wt. of CMC orally for five consecutive days.
2. **RUT and QRT alone-** These groups of animals were given an optimum dose of 10 mg/kg.b.wt. RUT and 20 mg/kg.b.wt. QRT orally for five consecutive days.
3. **Radiation alone group:** These groups of animals were given 0.1 ml /kg.b.wt. of CMC orally for five consecutive days. One hour after the last administration on the third day, animals were exposed to 12 Gy gamma radiation.
4. **RUT and QRT + Radiation group-** These groups of animals were given an optimum dose of 10 mg/kg.b.wt. RUT and 20 mg/kg.b.wt. QRT orally for five consecutive days. One hour after the last administration, animals were exposed to 12 Gy gamma radiation.

Animals from above groups were euthanized 72 hours after irradiation. Paraffin sections of the small intestine (jejunum) fixed in Bouin's fixative for 24 hours and were stained with hematoxylin and eosin (H&E). Histological alterations produced in the jejunum such as changes in villus height, the population of crypts/jejunal circumference; goblet and dead cells/villus section in response to different treatments were analysed (Fig. 1 B and 1 C).

Effect of RUT and QRT on radiation induced changes in bone marrow nucleated cells: To study the effect of RUT and QRT on radiation induced changes in bone marrow nucleated cells, animals were divided into following groups with six animals per group.

1. **Untreated Control group:** These groups of animals were given 0.1 ml/kg.b.wt. of CMC orally for five consecutive days.
2. **RUT and QRT alone:** These groups of animals were given an optimum dose of 10 mg/kg.b.wt. RUT and 20 mg/kg.b.wt. QRT orally for five consecutive days.
3. **Radiation alone group:** These groups of animals were given 0.1 ml/kg.b.wt. of CMC orally for five consecutive days. One hour after the last administration on the third day animals were exposed to 6 Gy gamma radiation.
4. **RUT and QRT + Radiation group:** These groups of animals were given an optimum dose of 10 mg/kg.b.wt. RUT and 20 mg/kg.b.wt. QRT orally for five consecutive days. One hour after the last administration on the fifth day animals were exposed

to 6 Gy gamma radiation.

Animals from above groups were euthanized nine days after irradiation; femurs were removed and fixed in 10% formaldehyde solution for 5 hours. The samples were decalcified in 12–18% sodium EDTA (pH 7.4–7.5) for 10 days. Bone specimens were then dehydrated through graded ethanol concentrations. Paraffin embedding was carried out and bone tissues were cut into 5µm sections using microtome and then stained with H&E. In decalcified, H&E stained paraffin sections an estimate of general hematopoietic activity (cellularity) was observed and compared (Fig. 1 C and 1 D).

RESULTS

RUT and QRT protect radiation induced changes in intestinal mucosa

RUT and QRT alone treatment did not alter the histology of jejunum when compared to the sham-irradiation group (Fig. 1 and 2). Whole body irradiation of mice showed distorted villus morphology, with depopulated and degenerating crypts with a reduction in the villus height and reduction in crypt cell number.

Statistical analysis

All the values are expressed as mean±SEM and the statistical analyses were performed using one-way analysis of variance (ANOVA) followed by Bonferroni's Post-hoc test to determine the significance between the various groups. The differences between the groups were compared and $p<0.05$ was considered significant.

Histological demonstrations in Fig. 1 were shown the representative images showing the villi height (cross section of jejunum) and crypt survival in the hematoxylin and eosin-stained sections of the untreated control. A: Untreated control-arrow indicates normal jejunal crypts, B: RUT alone, C: Irradiation alone-single arrow indicates degenerating crypts and D: Rutin + Irradiation- normal jejunal crypts.

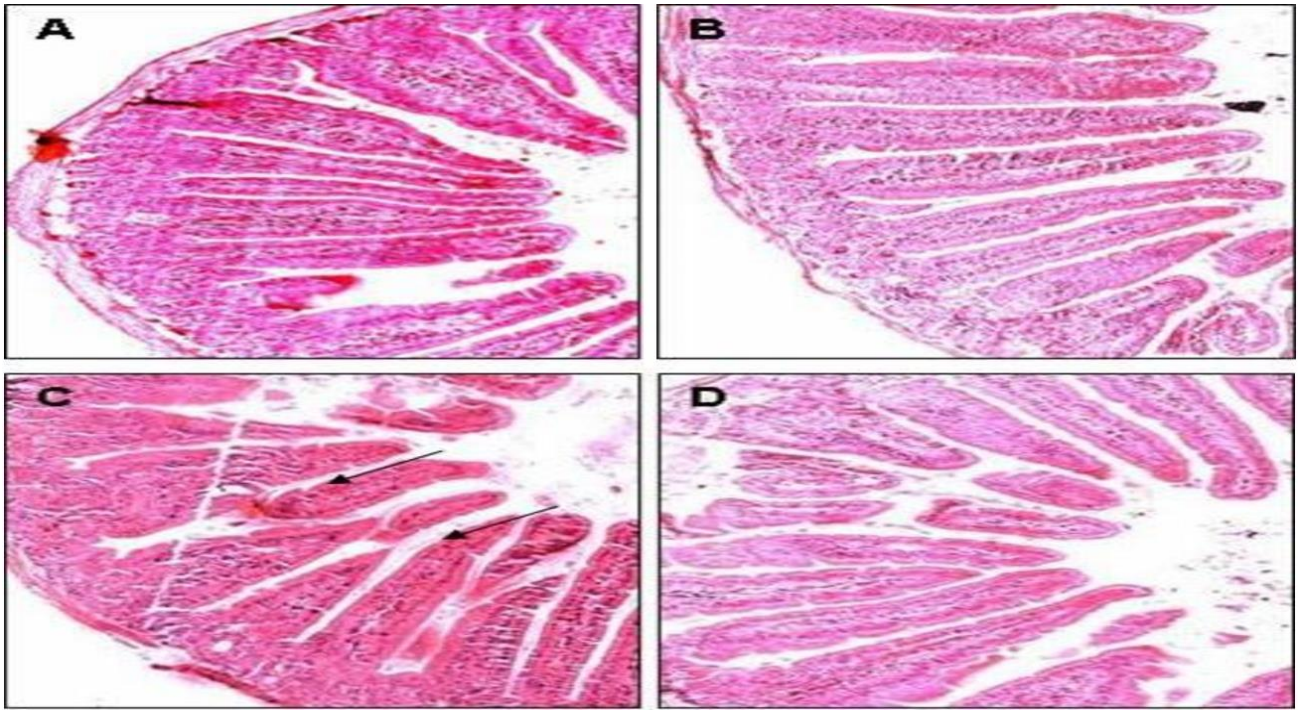

Fig. 1: Histopathological representation of protective effect of RUT (10 mg/kg.b.wt.) in the small intestine of irradiated mice

A) Untreated control; B) RUT (10 mg/kg.b.wt.) alone; C) Radiation alone (6 Gy); D) RUT (10 mg/kg.b.wt.) + 6 Gy Radiation

Above Fig. 2 shown the Histopathological presentation of protective effect of Quercetin (20 mg/kg.b. wt) in the small intestine of irradiated mice. Photomicrographs of jejunum sections, A: Control showing normal morphology; B: (20 mg/kg.b.wt. QRT alone) showing normal morphology; C: Radiation treated (12 Gy) showing shortened, irregular and thickened villi with increased number of goblet cells; D: QRT + Irradiation indiciates-normal villi, occasional occurrence of thickened villi, restoration of crypt cells and normal distribution of goblet cells.

RUT and QRT protects radiation induced changes in bone marrow nucleated cells

RUT treatment did not affect the bone cellularity, which was similar to that of untreated control group (Fig. 3B). Significant decrease in the nucleated cells in mouse bone marrow cellularity was observed in radiation group which was normalized in the group of mice receiving RUT (10 mg/kg.b.wt.) before irradiation (Fig. 3D).

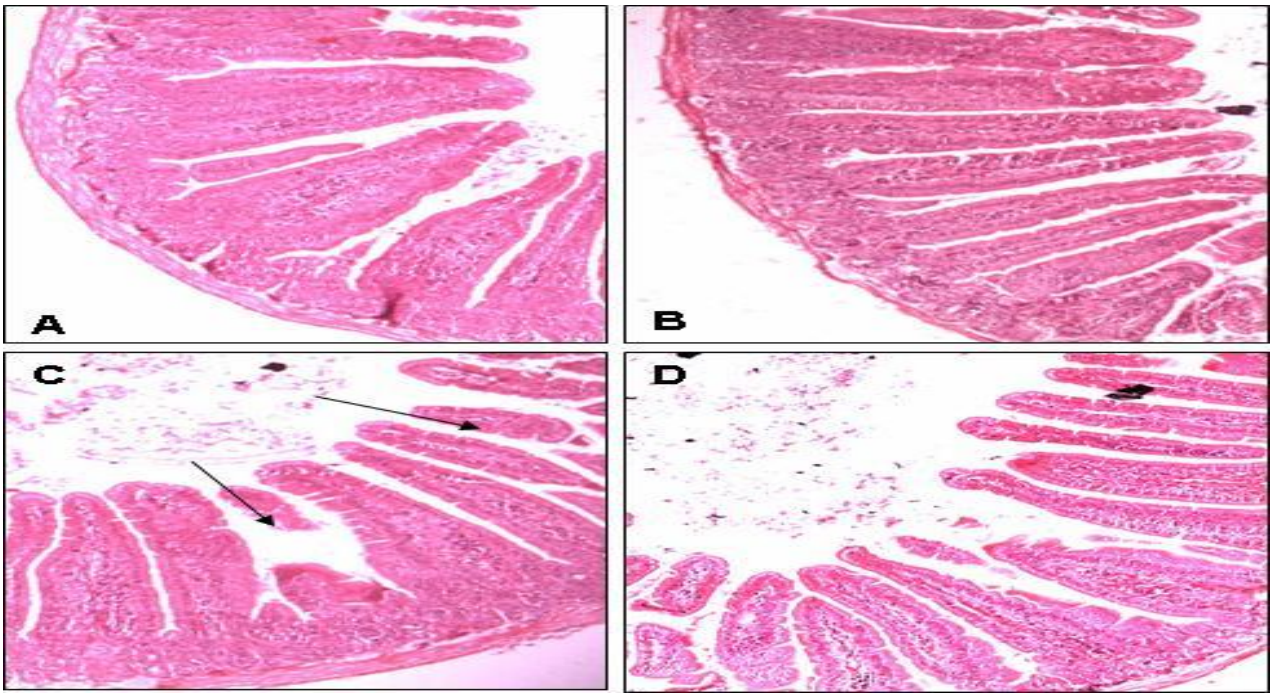

Fig. 2: Histopathological representation of protective effect of QRT (20 mg/kg.b.wt.) in the small intestine of irradiated mice

A) Untreated control; B) QRT (20 mg/kg.b.wt.) alone; C) Radiation alone (6 Gy); D) QRT (20 mg/kg.b.wt.) + 6 Gy radiation

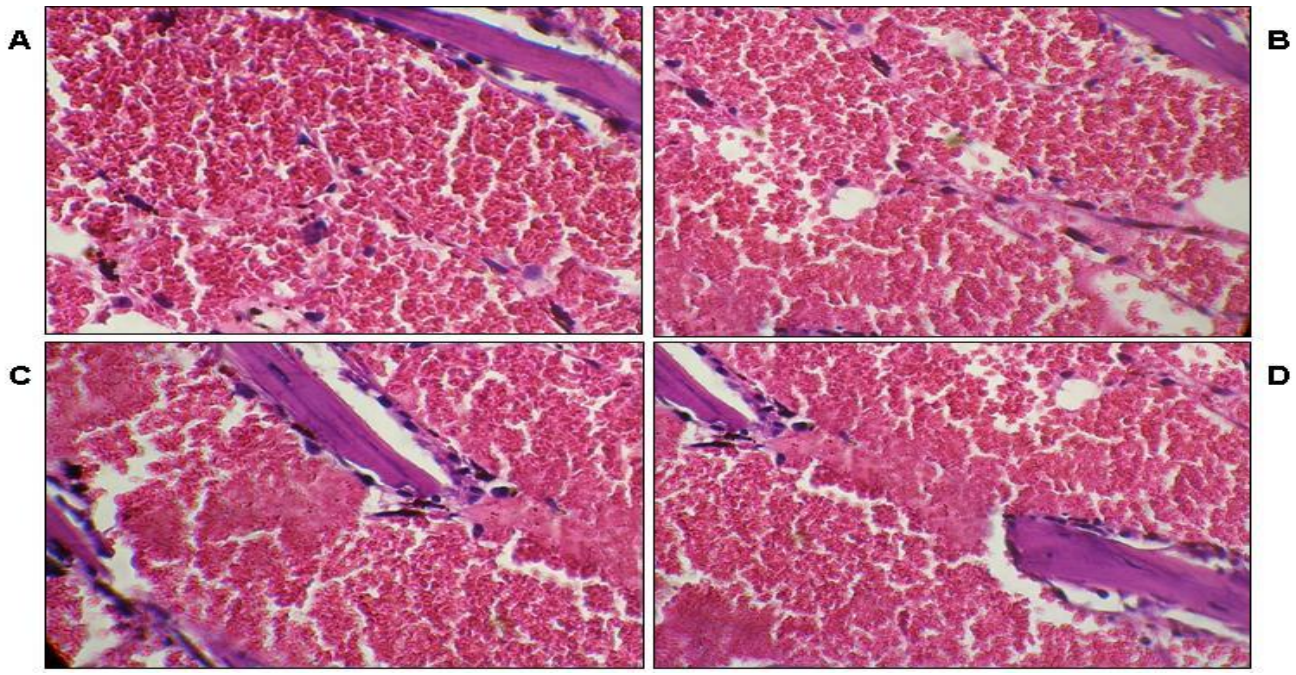

Fig. 3: Histological representation of bone marrow of mice with H&E stained, untreated or treated with RUT (10 mg/kg.b.wt.) before exposure to 6 Gy gamma radiation

A) Untreated control; B) RUT (10 mg/kg.b.wt.) alone; C) Radiation alone (6 Gy); D) RUT (10 mg/kg.b.wt.) + 6 Gy Radiation

Histological examination of mouse bone marrow cellularity from QRT alone treated group was similar to that of the sham-irradiated group (Fig. 4 A and B). As obvious, radiation exposure resulted in a significant decline of nucleated cells, which was normalized in the group of mice receiving QRT (20 mg/kg.b.wt.) before irradiation (Fig. 4 C and D).

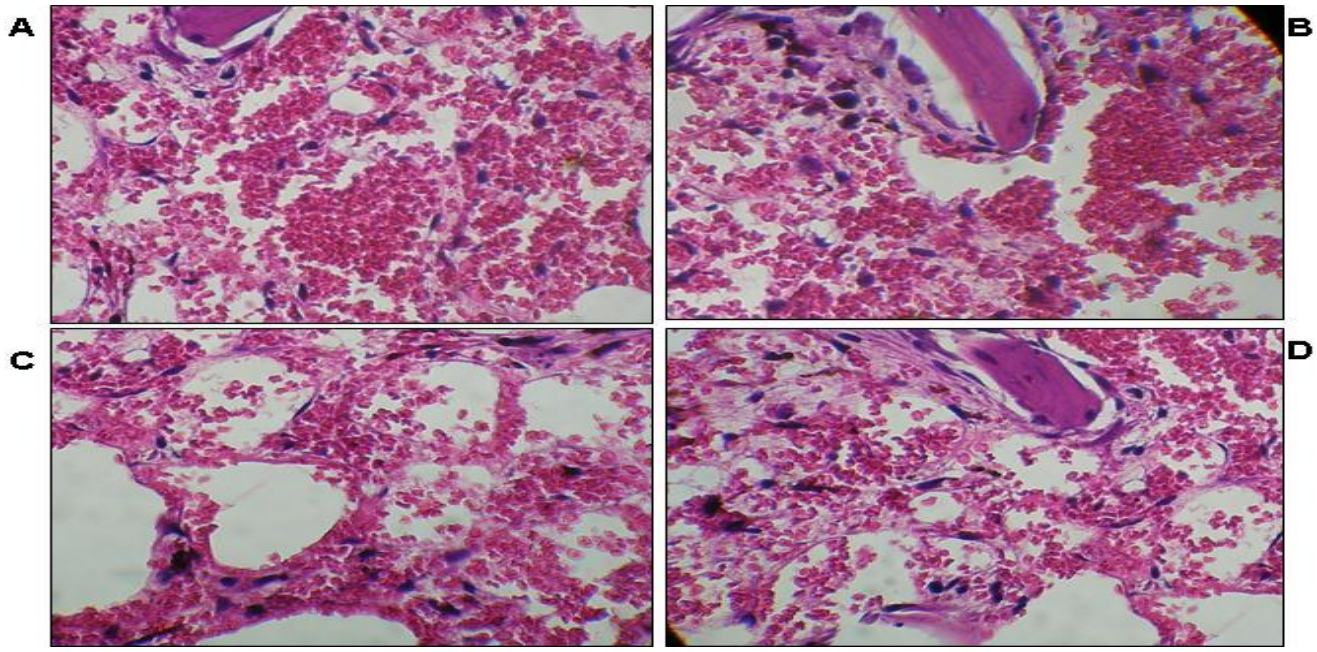

Fig. 4: Histological representation of bone marrow of mice with H&E stained, untreated or treated with QRT (20 mg/kg.b.wt.) before exposure to 6 Gy gamma radiation
A) Untreated control; **B)** QRT (20 mg/kg.b.wt.) alone; **C)** Radiation alone (6 Gy);
D) QRT (20 mg/kg.b.wt.) + 6 Gy radiation

DISCUSSION

Toxicity to normal organs not only limits the use and achievement of the complete therapeutic potential of radiotherapy but also cost in terms of patient morbidity and mortality. In clinics, the current therapeutic approaches favour treatment intensification, with the supposition that higher radiation therapy doses or novel fractionation schemes will result in increased patient survival [21]. However, the major challenge is to optimize the therapeutic ratio by minimizing treatment-related morbidity, while maintaining or improving local control and survival by selectively protecting the normal cells from the radiation effects [22-24]. One of the approaches to minimize the damaging effect of radiotherapy is the use of radioprotective agents.

Recent reports have shown that dietary phytochemicals act as excellent free radical scavengers in different experimental systems [25]. The use of polyphenols as potential radioprotectors is of increasing interest because of their adaptogenic ability and abundance in the diet. The present study demonstrated the potential of RUT and QRT, dietary polyphenols in ameliorating radiation induced toxicity under *in vivo* condition. Various tissues and organ systems of an individual differ in their response to radiation and as a rule the systems with proliferating cells are most sensitive.

In clinical studies, the acute and chronic bone marrow toxicities are the major limiting factors in the treatment of cancer as sub-lethal doses of radiations are used [26,27]. The bone marrow progenitor cells and the gastrointestinal epithelium are crucial for the maintenance of life and any damage to these cells will impair the normal physiological processes drastically, causing an undesirable impact on survival. It is generally agreed that radiation death in the sub-lethal dose range is due to impairment of bone marrow haemopoietic function and that the leucopenia, erythropenia and thrombocytopenia, which ultimately predisposes to infection, haemorrhage and death [10]. In the present study, it is important to note that RUT and QRT could check the bone marrow histological observations of irradiated animals indicated a significant hypocellularity, especially in the nucleated cells and which was normalised by RUT and QRT.

The whole-body high dose gamma ray irradiation of mice is known to result in the depletion of bone marrow owing to the intensive destruction of irradiated cells and the violation of their reproduction due to decreased ability to proliferate [28-30]. The so called hematopoietic syndrome death is often sufficient for the organism lethality as a result of infection due to the impairment of the immune system. The whole-body irradiation of mice was found to produce DNA damage and a marked decrease in antioxidants in the bone marrow. Various mechanisms such as prevention of damage through inhibition of free radical generation or their intensified scavenging, enhancement of DNA and membrane repair, replenishment of dead hematopoietic and other cells and stimulation of immune cell activity are considered important for radioprotection [27-36].

Radiation causes destruction of the marrow and haematopoietic cells, but may not cause their complete disintegration. Such treatments destroy dividing cells within the tumour, but also devastate other highly proliferative cell populations such as the bone marrow and gut epithelial cells. The gastrointestinal epithelium is less sensitive to radiation than the bone marrow (BM) progenitor cells, as the gastrointestinal epithelial cell transit time is quick. The damage will be expressed earlier than that of haemopoietic syndrome. Radiation induced mortality within 10 days of post-irradiation is

generally considered to be the outcome of gastrointestinal damage, while death between 11 days and 30 days of post-irradiation is attributed to haemopoietic damage which is characterized by symptoms such as weight loss, irritability, lethargy, ruffling of hair, emaciation and epilation [37-40]. The pattern of increased survival after RUT and QRT at various irradiation doses indicates the effectiveness in arresting GI damage as well as bone marrow damage and the resultant deaths in comparison to that of irradiated animals. It is known that, villi architecture and crypts of Lieberkuhn continuously engender cells in a regulated manner and hence are highly sensitive to radiation injury. Crypt stem cells also play a central role in mucosal regeneration following injury, whereas, the intestinal stem cell has the role of maintaining the epithelial cell population of the crypts. Crypts contain a few stem cells which continue to proliferate in a regulated way and the transit time of cells from proliferative compartment in the crypts in the extrusion zone at the tip of the villus is between 3–5 days in the mouse. This rapid turnover makes crypts as one of the most radio sensitive tissues of the body. Stem cells of the crypts get sterilized by lethal irradiation, subsequently the crypts shrink and disappear within 2–3 days; transit cells, however continue to divide for a few divisions and migrate to the villus, which itself is lost within 3–5 days leading to the manifestation of gastrointestinal syndrome [38,39]. In our study, a dose of 12 Gy caused damage to GI system and especially to the stem cells in the crypts, which is in agreement with earlier studies [38-42]. It was clearly observed from the gross histopthalogical section of jejunum in the present study that pre-treatment with RUT and QRT restored the crypt architecture with an elevation in crypt and goblet cell number in 24 hours of post incubation. These results are in good agreement with earlier reports, where WR-2721, MPG, vitamin E, and *Mentha piperita* has been reported to protect against the radiation-induced goblet cell changes in the intestinal mucosa of irradiated mice [40-46].

The GI protection rendered by RUT and QRT may be either directly or indirectly by decreasing the damage to crypt cells through the protection against vascular endothelial injury in the GI tract, thereby retaining the intestinal function by facilitating proper absorption of the nutrients contributing to increased animal survival.

CONCLUSIONS

The present study indicated that Rutin (RUT), and Quercetin (QRT) pre-treatment with radiation normalized the bone-marrow cells, protected the radiation- induced gastrointestinal stem cells and intestinal mucosa of Swiss albino mice. To conclude, the protective effects rendered by the RUT and QRT to mitigate the radiation induced damage in bone-marrow and intestinal cells of mice may be partly attributed by the inhibition of radiation induced oxidative stress and also to scavenging of radiation induced reactive oxygen species.

ACKNOWLEDGMENT

We are thankful to Dr. B. Nagesh Rao, Dr. Archana P. R. and Prof. Sathish Rao, Head, Radiobiology Division, Manipal Life Sciences Centre, Manipal and Dr. J.G.R. Soloman of the Department of Radiotherapy and Oncology, Kasturba Medical College, Manipal, India for providing the necessary laboratory and irradiation facilities. We appreciate technical support received through Centre for Application of Radioisotopes and Radiation Technology (CARRT), Mangalore University. We also acknowledge the financial support by Board of Research in Nuclear Sciences (BRNS), Mumbai, India.

REFERENCES

[1] Hall EJ. Acute effects of total-body irradiation, Radiobiology for the Radiologist. Philadelphia, PA: Lippincott Williams Wilkins, 2000.
[2] Quintiliani M. The oxygen effect in radiation inactivation of DNA and enzymes. Int. J. Radiat Biol. Relat. Study Phys. Chem. Med., 1986; 50(4):573-94.
[3] Ross GM. Induction of cell death by radiotherapy. Endocr. Relat Cancer, 1999; 6(1):41-44.
[4] Patt HM, Tyree EB, Straube RL, et al. Cysteine Protection against X Irradiation. Sci., 1949; 110: 213-14.
[5] Sweeney TR. A survey of compounds from the antiradiation drug development program of the U.S. Army Medical Research Command. In: Institute WRA, editor. Washington D.C. 1979; 15-650.
[6] Arora R, Goel H. Herbal Radioprotectors; Proceedings of Indian Society for Radiation Biology by Regional Cancer Centre (RCC) Thiruvananthapuram, India, 2000; 17-19.
[7] Nair CKK, Parida DK, Nomura T. Radioprotectors in radiotherapy. J. Radiat Res. (Tokyo), 2001; 42(1): 21-37.
[8] Weiss JF, Landauer MR. Protection against ionizing radiation by antioxidant nutrients and phytochemicals. Toxicol., 2003; 189(1-2): 1-20.
[9] Maurya DK, Devasagayam TP, Nair CKK. Some novel approaches for radioprotection and the beneficial effect of natural products. Indian J. Exp. Biol., 2006; 44: 93-114.
[10] Coleman CN, Blakely WF, Fike JR, MacVittie TJ, Metting NF, Mitchell JB. Molecular and cellular biology of moderate-dose (1-10 Gy) radiation and potential mechanisms of radiation protection: report of a workshop at Bethesda, Maryland 2001. Radiat Res., 2003; 159(6): 812-34.
[11] Gulcin I, Mshvildadze V, Gepdiremen A, Elias R. Antioxidant activity of saponins isolated from ivy: alpha-hederin, hederasaponin-C, hederacolchiside-E hederacolchiside-F. Planta Med., 2004; 70(6): 561-63.
[12] Kostyuk VA, Potapovich AI. Antiradical and chelating effects in flavonoid protection against silica-induced cell injury. Arch. Biochem. Biophys., 1998; 355: 43-48.
[13] Kong SE, Blennerhassett LR, Heel KA, Mc-Cauley RD, Hall JC. Ischaemia-reperfusion injury to the intestine. Australian New Zealand J. Surg., 1998; 68: 554-61.
[14] Guardia T, Rotelli AE, Juarez AO, Pelzer LE. Anti-inflammatory properties of plant flavonoids. Effects of rutin, quercetin, and hesperidin on adjuvant arthritis in rat. Farmaco, 2001; 56(9): 683-87.
[15] Bond VP, Fliedner TM, Archambeau JO. Mammalian Radiation Lethality, A Disturbance in Cell Kinetics. Academic Press, New York, 1965; pp. 340.

[16] Milas L, Hunter N, Ito H, Peters LJ. *In vivo* radioprotective activities of diethyldithiocarbamate (DDC). Int. J. Radiat. Oncol. Biol. Phys., 1984; 10(12): 2335-43.
[17] Ijiri K, Potten CS. Radiation-hypersensitive cells in small intestinal crypts; their relationships to clonogenic cells. British J. Cancer. Suppl., 1986; 7: 20-22.
[18] Hall EJ. Acute effects of total-body irradiation, Radiobiology for the Radiologist. Philadelphia, PA: Lippincott Williams Wilkins, 2000.
[19] Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics CA. Cancer J. Clin., 2002; 55(2): 74-108.
[20] Little MP. Cancer after exposure to radiation in the course of treatment for benign and malignant disease. Lancet Oncol., 2001; 2(4): 212-20.
[21] Coleman CN. Radiation oncology--linking technology and biology in the treatment of cancer. Acta Oncol., 2002; 41(1): 6-13.
[22] Grant S, Dent P. Overview: rational integration of agents directed at novel therapeutic targets into combination chemotherapeutic regimens Curr. Opin. Investig. Drugs, 2001; 2(11): 1600-05.
[23] Soobrattee MA, Neergheen VS, Luximon-Ramma A, Aruoma OI, Bahorun T. Phenolics as potential antioxidant therapeutic agents: mechanism and actions. Mutat Res., 2005; 579(1-2): 200-13.
[24] Tubiana M, Carde P, Frindel E. Ways of minimising hematopoietic damage induced by radiation and cytostatic drugs--the possible role of inhibitors. Radiother Oncol., 1993; 29: 1-17.
[25] Dainiak N, Waselenko JK, Armitage JO, MacVittie TJ, Farese AM. The hematologist and radiation casualties. Hematol., 2003; 473-96.
[26] Maezawa H, Ohizumi Y, Tamai Y, Fukuhara N, Ando F, et al. Survival of mice and hematopoietic stem cells in bone marrow after intermittent total body irradiation. Radiat. Med., 1987; 5(6): 215-19.
[27] Roots R, Okada S, Protection of DNA molecules of cultured mammalian cells from radiation induced single-strand scissions by various alcohols and SH- compounds Int. J. Radiat. Biol., 1972; 21: 329-42.
[28] Hoat J, Barkina NF. Quantitative study of haemopoietic recovery after a sublethal X-irradiation in the mouse. Acta Haematol., 1969; 42: 347.
[29] Goldin EM, Neff RD. Lymphocyte depletion in peripheral blood of acutely gamma-irradiated rats. Int J Radiat Biol. Relat Study Phys. Chem. Med., 1975; 27(4): 337-42.
[30] Daga SS, Jain VK, Goyal PK. Radioresponse of Leucocytes in Peripheral Blood of Mice against Gamma Irradiation and their Protection by Liv. 52. Probe 3, 1995; 222.
[31] Shrikant L. Patil, B. Nageshwar Rao H. Somashekarappa M. Rajashekhar KP. Antigenotoxic potential of rutin and quercetin in swiss mice exposed to gamma radiation. Biomed. J., 2014; 37(5): 305-13.
[32] Shrikant L. Patil H. Somashekarappa M, Rajashekar Patil H. Antioxidative and radioprotective potential of rutin and quercetin in Swiss albino mice exposed to gamma radiation. J. Med. Phys., 2013; 38(2): 87-92.
[33] Shrikant L. Patil H, Somashekarappa M, Rajashekar Patil H. Radiomodulatory role of Rutin and Quercetin in Swiss Albino mice exposed to the whole-body gamma radiation. Indian J. Nucl. Med., 2012; 27: 237-42.
[34] Shrikant L. Patil H, Somashekarappa M, Rajashekar Patil H. Evaluation of the radioprotective action of rutin in mice exposed to gamma-radiation. Int. J. Biol. Pharm. Res., 2012; 3 (1): 12-18.
[35] Shrikant L. Patil H. Somashekarappa M, Rajashekar Patil H. Ameliorative Effect of Rutin against Oxidative Stress in Mice Induced by Gamma-Irradiation. Res. J. Pharm. Biol. Chem. Sci., 2011; 2 (4): 694-701.
[36] Uma Devi P. Normal tissue protection in cancer therapy progress and prospects. Acta. Oncol., 1998; 37: 247-52.
[37] Potten CS, Morris RJ. Epithelial stem cells *in vivo*. J. Cell Sci. Suppl., 1988; 10: 45-62.
[38] Potten CS. A comprehensive study of the radiobiological response of the murine (BDF1) small intestine. Int. J. Radiat Biol., 1990; 58(6): 925-73.
[39] Indran M, Carr KE, Gilmore RS, Boyle FC. Mucosal changes in mouse duodenum after gamma-irradiation or reserpine treatment. J. Submicrosc. Cytol. Pathol., 1991; 23(2): 267-78.
[40] Samarth RM, Saini MR, Maharwal J, Dhaka A, Kumar A. *Mentha piperita* Linn leaf extract provides protection against radiation induced alterations in intestinal mucosa of Swiss albino mice. Indian J. Exp. Biol., 2002; 40(11): 1245-49.
[41] Veena K, Uma Devi P. Modification of radioresponse of sublethally irradiated mouse jejunum by misonidazole. Acta. Oncol., 1992; 31(5): 585-89.
[42] Saharan BR, Saini MR, Devi PU. MPG protection and goblet cell kinetics in mouse jejunum. Strahlentherapie. 1978; 154(1): 60-62.
[43] Felemovicius I, Bonsack ME, Baptista ML, Delaney JP. Intestinal radioprotection by vitamin E (alpha-tocopherol) Ann. Surg., 1995; 222(4): 504-08.
[44] Bisht KS, Prabhu S, Devi PU. Modification of radiation induced damage in mouse intestine by WR-2721. Indian J. Exp. Biol., 2000; 38(7): 669-74.
[45] Boudry G, Perrier C. Thyme and cinnamon extracts induce anion secretion in piglet small intestine via cholinergic pathways. J. Physiol. Pharmacol., 2008; 59(3): 543-52.
[46] Rosoff CB. The Role of Intestinal Bacteria in the Recovery from whole body radiation J. Exp. Med., 1963; 118: 935-43.

How to cite this article:
Patil SL, Ghodke T, Patil SM, Swaroop K, Somashekarappa HM: Cytoprotective Potential of Rutin and Quercetin in Swiss Mice Exposed to Gamma Radiation. Int. J. Life Sci. Scienti. Res., 2017; 3(5):1322-1328. DOI:10.21276/ijlssr.2017.3.5.10
Source of Financial Support: Nil, **Conflict of interest:** Nil

