ISSN 0972-8406
The NEHU Journal Vol. XXII, No. 1&2, 2024 (2025), pp. 31-43

Modulatory effect of vicenin-2 in mitigating biochemical and behavioural alteration in swiss albino mice subjected to sub-lethal dose of radiation

Larishisha Swer, Sansa Basaiawmoit, Casterland Marbaniang, and Lakhon Kma*
Cancer Biology & Radiation Countermeasure Unit, Department of Biochemistry
North-Eastern Hill University
Shillong-793022, Meghalaya, India
**Corresponding author: lakhonkma@gmail.com*

Abstract

The modulatory effect of vicenin-2 (Vcn-2) was studied in mice subjected to sub-lethal X-ray irradiation. The mice were randomly divided into Group I (Normal)- no treatment, Group II (Control)-Vcn-2 administration only (50mg/kg body weight), Group III (IR)- whole-body X-ray irradiation, Group IV (IR+Vcn-2)- administration of Vcn-2 intraperitoneally (50mg/kg b.w.) before and after whole-body irradiation. The survival rate and the body weight of the IR+Vcn-2 group were significantly higher compared to the IR group at 15-30 days following irradiation with statistical significance ($p<0.001$*). Treatments with Vcn-2 in the irradiated group significantly reduced DNA damage in bone marrow cells. Additionally, oxidative stress analysis indicated that Vcn-2 significantly improves the antioxidant capacity by increasing the level of oxidative enzymes and decreasing the level of malondialdehyde (MDA) in the IR+Vcn-2 group compared to the IR group. These findings suggest that Vcn-2 has a radiomodulatory effect in mice, primarily through the reduction of oxidative damage.*

Keywords: Glutathione (GSH), malondialdehyde (MDA), oxidative stress, vicenin-2 (Vcn-2), X-rays.

Introduction

Exposure to ionising radiation (IR) during radiotherapy or accidents can induce extensive cellular and molecular disruption which poses a significant health risk (Mu *et al.* 2018). Radiation exposure directly alters atomic structures, which trigger a series of events amplified by endogenous signals inducing a range of cellular damage leading to complex biological responses (Soriano *et al.* 2019). Radiation absorption by the tissue generates a considerable amount of highly reactive free radicals which include superoxide anion ($O_2^{\bullet}$),

hydroxyl radical ($OH^{\bullet}$), and hydrogen peroxide (H_2O_2) (Srinivasan *et al.* 2007). These reactive oxygen species (ROS) can interact with biomolecules like nucleic acid, proteins, and lipids, inducing damages that alter their structure and function (Reisz *et al.* 2014; Islam 2017). One of the major cellular damage caused by radiation is increased levels of lipid peroxidation (LPO) , a process that can severely compromise cellular membranes and functionality (Kamat *et al.* 2000).

Under physiological conditions, a homeostatic balance exists between the formation of ROS and their removal by endogenous antioxidant scavenging compounds (Victor *et al.* 2004). However, oxidative stress which occurs from an imbalance in ROS production and the cells neutralizing capacity, can lead to a significant change in the redox status. These changes can drive cells to transition from a quiescent to a proliferative state, trigger growth arrest or initiate cell death pathway (Obrador *et al*. 2022). When the harmful effects exceed those of homeostatic biochemical processes, the resulting biological changes can be long lasting and may be transmitted to subsequent generation of cells (Azzam *et al.* 2012; Buonanno *et al.* 2023). Depending on the extent of damage, the cells may initiate a damage repair mechanism or the changes could result in permanent physiological alteration, ultimately resulting in cell death (Szumiel 2015; Buonanno *et al.* 2023).

Studies on natural products especially plant extracts and phytochemicals as modulators of radiation effect are a new area of research. It is necessary to evaluate the modulatory activity of commonly used phytochemicals for exploring their possible application in radiotherapy as a radioprotective agent. Vicenin-2 (Vcn-2) is a bioactive flavonoid present in *Ocimum sanctum*, commonly known as tulsi or holy basil, a herb widely used for centuries in Ayurvedic medicine (Garima *et al.* 2019; Rasheed *et al.* 2022). Reports suggest that Vcn-2 have been shown to possess strong antioxidant properties through mechanisms such as free-radical scavenging, inhibition of inflammation, promotion of repair of damaged DNA and inhibition of cell death pathways (Venuprasad *et al.* 2013; Venuprasad *et al.* 2014; Makni *et al.* 2018; Almatroodi *et al.* 2020;Jit *et al.* 2022; Zhang *et al.* 2023). Previous studies have also shown that Vcn-2 exhibits a potential radiosensitizing activity in non-small cell lung cancer cells by regulating the components of the PI3K/ Akt pathway (Baruah *et al.* 2018; Baruah *et al.* 2019). Therefore, our study aims to investigate the effects of Vcn-2 in mitigating biochemical and behavioural changes in mice subjected to sub-lethal X-ray irradiation.

Materials and methods

Experimental animal

The study protocol was approved by the Institutional Animal Ethics Committee (animal model), North-Eastern Hill University, Shillong. Male BALB/c (age, 8 weeks; weight, 20-23 g) procured from an inbred colony Pasteur's Institute, Shillong, Meghalaya. The animals were grouped and housed in polypropylene cages and maintained under standard laboratory conditions (temp 25°-28°C) with a 12 h light and 12h dark cycle. They were allowed free access to a standard dry pellet diet and water *ad libitum*.

Experimental Designs

Mice selected from an inbred colony were divided into 4 groups (n=20 per group)

Group I (Normal): the mice of this group received no treatment

Group II (Control): the mice of this group received only Vcn-2 (50mg/kg body weight)

Group III (IR): the mice of this group are whole-body exposed to X-ray

Group IV (IR+Vcn-2): in this group, intraperitoneal administrations of Vcn-2 (50mg/ kg body weight) were made before and after the mice were whole-body exposed to X-ray.

The mice in the irradiated groups were exposed to a sub-lethal radiation dose (6.5 Gy). The control mice were sham irradiated. The mice were fed and observed for 30 days following irradiation.

Irradiation

The CP160 X-ray irradiation system, Faxitron, USA in the Biochemistry Department, North-Eastern Hill University, Shillong, was used for irradiation. Unanesthetized mice were restrained in a well-ventilated acrylic box and whole-body exposure to ionizing radiation (IR) at a distance of 15 inches approx. delivering a dose rate of 0.42 Gy/min.

Biochemical analysis

Lipid peroxidation (LPO) assay

Lipid peroxidation was estimated calorimetrically using thiobarbituric acid reactive substances (TBARS) and was measured using the method described by Silva *et al.* (2011). In brief, 0.5mL of tissue homogenate was treated with 1.5 mL of TBA-TCA-HCI (1:1:1) reagent. The mixture was incubated in a 95°C water bath for 30 min and then cooled. The absorbance was measured spectrophotometrically at 532 nm. The lipid peroxidation was expressed as Malondialdehyde (MDA) in nM MDA/gm tissue.

Protein assay

The total protein concentration was determined by Bradford's method (1976) using bovine serum albumin (BSA) as the standard. The absorbance of standard, as well as test solutions, was read at 595 nm. A standard calibration curve was obtained by plotting the concentration of standard solutions. This curve was used to determine the concentration of protein in test samples.

Reduced glutathione (GSH) assay

GSH content of the tissue sample was performed using the method described by Ellman (1959). Briefly, 1.0 ml of tissue homogenate and 1.0 mL phosphate buffer were added followed by 2.0 ml of freshly prepared DTNB (2,2'-dinitro-5,5'-dithiobenzoic acid or Ellman's reagent) solution. The intensity of the yellow colour formed was read at 412 nm in a spectrophotometer after 10 min. The values are expressed as μmoles of GSH/mg protein.

Superoxide dismutase Enzyme activity **(SOD)**

The activity of SOD was assayed according to the method described by Marklund and Marklund (1974) with some modifications. The reaction mixture of autooxidation consists of 2 ml of Tris HCL buffer (0.1M, pH 8.2), 0.5 ml of 2 mM pyrogallol, and 1.5 ml of water. Initially, the autooxidation rate was noted at an interval of 60 seconds for 3 min at 470 nm. The assay mixture for the enzyme consists of 2 ml of Tris HCL. Buffer (0.05M), 0.5 ml pyrogallol, 0.5 ml of the homogenate, and water to give a final volume of 4 ml. The rate of inhibition of pyrogallol autooxidation after the addition of the enzyme was noted at the same time interval. Iron accelerates pyrogallol oxidation even in trace amounts. DETAPAC acts as a chelator and prevents Fe, Cu^{2}, and Mn^{2} interference. Enzyme activity is defined as the amount of enzyme required to inhibit 50% pyrogallol auto-oxidation/min (U/mg protein).

Catalase activity **(CAT)**

CAT activity was determined from the rate of decomposition of H_2O_2. Catalase was assayed colorimetrically at 620 nm and expressed as μmoles of H_2O_2 consumed/min/mg protein as described by Sinha *et al.* (2016). The reaction mixture (1.5 ml) contained 1.0 ml of (0.01 M pH 7.0) phosphate buffer, 0.1 ml of tissue homogenate (supernatant), and 0.4 ml of 2 M hydrogen peroxide. The reaction was stopped by adding 2.0 ml of dichromate-acetic acid

reagent (5% potassium dichromate and glacial acetic acid were mixed in a 1:3 ratio and then the absorbance was measured.

Bone marrow DNA content

The bone marrow of the mice was collected immediately after the mice were sacrificed by flushing it out with Phosphate Buffer Saline. The flushed bone marrow was used to extract DNA to assess any damage. The concentration of DNA obtained from the sample was evaluated using a spectrophotometric measurement of absorbance at 260 nm.

Statistical Analysis

All the data were expressed as mean ± standard error mean (SEM). Data were analyzed by the one-way analysis of variance (ANOVA) method followed by Tukey's test (multiple comparison tests). All statistical analyses were performed using the GRAPH PAD Prism software, Version 8.0 with a significance value of $P< 0.05$.

Results

General behavioural observation

In the present investigation, the mice in the irradiated groups were exposed to 6.5 Gy X-ray radiations. The irradiated mice exhibit signs of radiation sickness within two to three days after irradiation as shown in **Table 1**. The physical observation includes signs of agitation, weight loss, reduction in food and water intake, diarrhoea, profuse perspiration, shivering and extensive grooming or ruffling of hair leading to hair loss, with some mice showing signs of paralysis and curved posture with difficulty in locomotion were also observed.

Vcn-2 increases the survival rate of mice subjected to ionizing radiation

Following exposure it was observed that the irradiated mice gradually died the next day, the survival rate was monitored from 0-30 days as shown in **Fig. 1**. However, treatment of Vcn-2 in the irradiated group prolongs the survival time, compared with the IR control group ($p<0.05$). Maximum mortality was observed in the irradiated group at 10-15 days, on the 30^{th} day the survival of IR+Vcn-2 was 78% and that of the IR group was 50%. Compared with the control group, the survival time of the mice in the IR+Vcn-2 was also significantly prolonged ($p<0.05$).

Table 1. General appearance and behavioural observation of mice in the control, IR and IR+Vcn-2 groups following irradiation.

Parameters	Control	IR	IR+Vcn-2
Urination	Normal	Increased	Decreased
Food intake	Normal	Increased	Moderate
Water intake	Increase	Increased	Moderate
Fur condition	Normal	Wet	Wet
Posture	Normal	Curved	Normal
Movement	Active	Weak/Not active	Not active
Body temperature	Normal	High	Moderate
Behavior	Normal	Extensive grooming/ruffling of hair	Ruffling of hair observed
Clinical sign	Normal	Diarrhea/shivering	Diarrhea

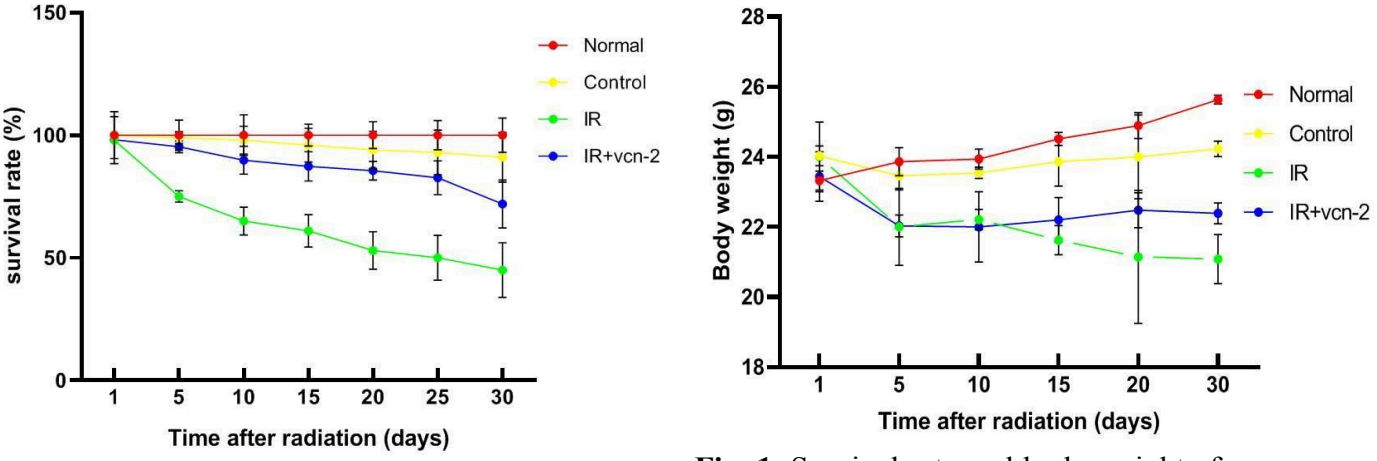

Fig. 1. Survival rate and body weight of mice following irradiation. Each vertical bar indicates the standard deviation. Data are represented as the mean ± standard deviation (n=6). IR, irradiated mice; IR+Vcn-2, irradiated mice+ Vcn-2. ($p<0.05$)

Vcn-2 reduced the IR-induced body weight changes

The body weight of the mice was measured at various intervals following irradiation, the mean weight was calculated among surviving mice as shown in (**Fig. 1**). Maximum increase in body weight was observed in the normal and control group at 30 days compared to all other groups which showed decreased body weight after exposure to whole-body irradiation. Statistical analysis showed that the body weight was significantly higher in the IR+Vcn-2 group compared to the IR group ($p<0.05$). However, the body weights of the IR+Vcn-2 group on the 20-30 days remained constant with no significant changes compared to the normal and control groups.

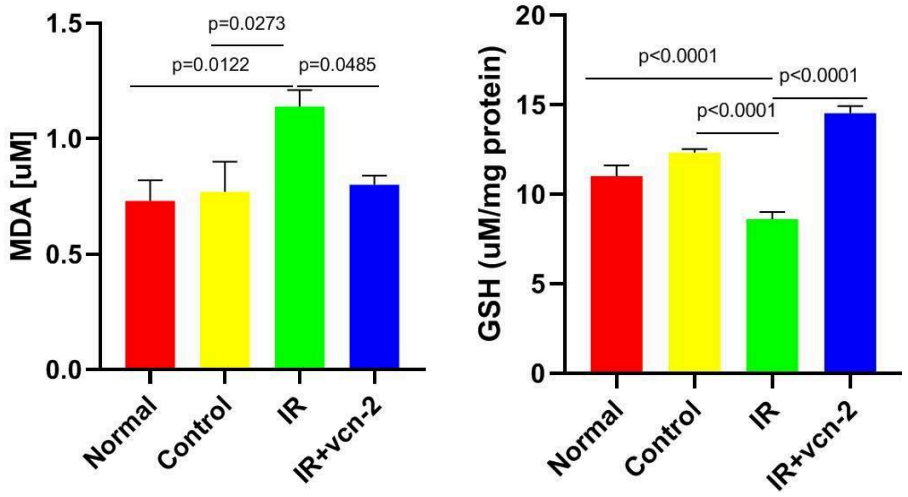

Fig. 2. MDA and GSH levels in hepatic tissue following irradiation. Each vertical bar indicates the standard deviation. Data are represented as the mean ± standard deviation (n=6). IR, irradiated mice; IR+Vcn-2, irradiated mice+ Vcn-2. ($p<0.05$).

Vcn-2 increases antioxidant capacity

The MDA content, associated with lipid peroxidation (**Fig. 2**), was significantly reduced in the IR+Vcn-2 group compared to the IR group ($p < 0.05$), indicating that Vcn-2 administration helps prevent lipid peroxidation in tissues. The GSH level (**Fig. 2**) significantly decreased in the IR group, whereas it significantly increased in the IR+Vcn2 group ($p < 0.0001$). The activity of SOD and CAT (**Fig. 3**) also significantly decreased in the IR group, while it significantly increased in the IR+Vcn2 group ($p < 0.05$). The increase in activity of SOD, CAT, and GSH indicates the generation of oxidative stress which is prevented by the administration of Vcn-2 in the IR+Vcn-2 group, significantly reducing the oxidative damage caused by radiation.

Protein estimated also showed a statistically significant decrease in the IR group and such a decrease in protein content was noted 30 days post-radiation (**Fig. 4**). However, in the IR+Vcn-2 group, a significant increase in protein content was observed 30 days following radiation compared to the normal and irradiated mice ($p<0.05$).

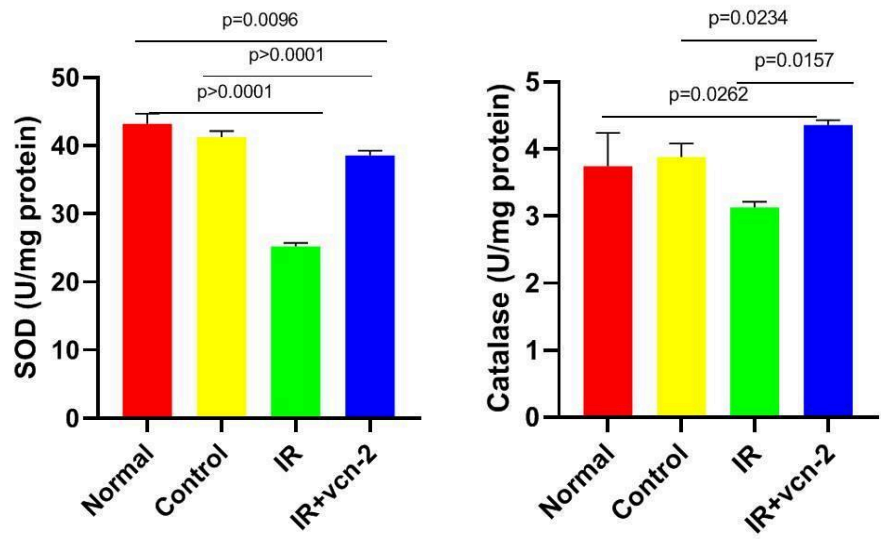

Fig. 3. SOD and CAT activity in hepatic tissue following irradiation**.** Each vertical bar indicates the standard deviation. Data are represented as the mean ± standard deviation (n=6). IR, irradiated mice; IR+Vcn-2, irradiated mice+ Vcn-2. ($p<0.05$).

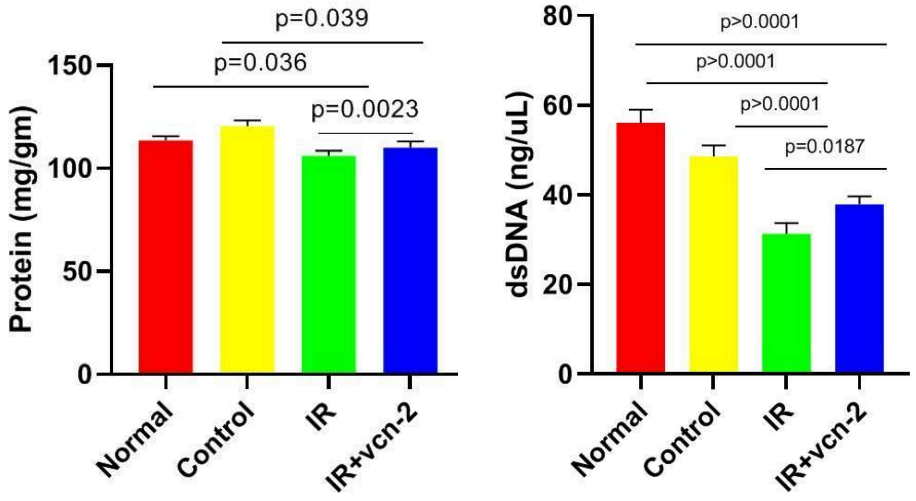

Fig. 4. Protein level and bone marrow DNA content following irradiation. Each vertical bar indicates the standard deviation. Data are represented as the mean ± standard deviation (n=6). IR, irradiated mice; IR+Vcn-2, irradiated mice+ Vcn-2. ($p<0.05$)

Vcn-2 accelerates the recovery of bone marrow DNA damage in irradiated mice

DNA content in the bone marrow of mice in the IR+Vcn-2 and control group 30 days post-irradiation (**Fig. 4**) was significantly increased as compared to the IR group ($p<0.0001$). Compared with the vicenin-2 treated group the bone marrow DNA content of mice in the irradiated group was significantly decreased ($p<0.05$).

Discussion

Flavonoids of *Osmium sanctum* such as orientin and vicenin demonstrate protective effects against radiation by neutralizing free radicals produced by radiation exposure (Uma *et al.* 2000). Additionally, studies have shown that tulsi extract can significantly reduce the production of MMP-9, an enzyme associated with lipid peroxidation that contributes to tissue damages (Ghosh *et al*. 2016; Prasad *et al*. 2021). Tulsi extract has also been found to enhance the levels of antioxidant molecules, including GSH, as well as antioxidant enzymes like SOD, CAT, GPx and GST, which safeguard cell organelles and membranes by eliminating harmful free radicals (Sumran and Aggarwal 2019). The present study was to demonstrate the modulatory effects of Vcn-2 in mitigating biochemical and behavioural alteration in mice subjected to sub-lethal X-ray irradiation. The results demonstrated that the mice in the irradiated group showed signs of radiation sickness within two to three days following irradiation such as agitation, weight loss, decreased intake of food and water, profuse perspiration, shivering and extensive grooming and ruffling of hair leading to hair loss. The time period selected for the study is because the 30-day survival study following whole-body irradiation is the most widely used test (Koch *et al.* 2016). The result of this study showed that the survival rate of the mice in the IR+Vcn-2 group is noticeably higher than that of the IR group, indicating that pre-treatment of Vcn-2 enhances the survival rates of mice exposed to radiation. Radiation exposure can damage the gastrointestinal mucosa leading to an abnormality in absorption (Hauer-Jensen *et al*. 2007); which significantly reduced the body weight of the IR group, whereas, the weight of the mice in the IR+Vcn-2 showed significant recovery. In addition to the behavioural observation the biochemical analysis suggested alteration to a great extent. Free radicals generated from water radiolysis, triggered by ionizing radiation, play a major role in damaging biological molecules (Ahaskar *et al.* 2007). Normally, the natural defence mechanism of the body activates and protects against oxidative damage after exposure to radiation. Oxidative stress is a state of imbalance between the generation of ROS and the levels of the antioxidant defence system (Srinivasan et *al.* 2007). This imbalance leads to lipid peroxidation, protein fragmentation, DNA damage, modulation of genomic expression, calcium influx, inactivation of many metabolic enzymes, mitochondrial swelling and lyses, age-related diseases, genomic instability cell death (Sumran and Aggarwal 2019). Superoxide dismutase (SOD), glutathione reductase (GSH), and catalase (CAT) are key antioxidant enzymes that help mitigate ROS damage (Nuszkiewicz *et al.* 2020; Li *et al.* 2021). In this study, Vcn-2 treatment increased SOD, CAT activity and GSH levels in the liver while significantly reducing the MDA level. MDA is

lipid peroxide formed when free radicals interact with polyunsaturated fatty acids in cell membranes, indicating the level of lipid peroxidation (Jadoon and Malik 2017). Exposure to radiation can also cause significant damage to bone marrow, leading to a reduction in bone marrow cells and diminished DNA content (Green and Rubin 2014; Obrador *et al*. 2022). Prolonged resting phase or a delay in DNA synthesis following radiation exposure may be another reason for decreased DNA content (Sisodia and Singh 2009). The results may not be accurate due to contamination from the presence of a small amount of single-stranded DNA. However, studies have shown that Vcn-2, curcumin and related compounds have the potential to protect DNA against oxidative damage induced by free radicals (Srinivasan et *al.* 2007; Sumran and Aggarwal 2019). Vcn-2 treatment provides a significant protection which is indicated by increased DNA concentration together with increased protein concentration. In conclusion, the above result suggests that administration of Vcn-2 prolong the survival time, helps in restoring body weight, improves antioxidant capacity and accelerates bone marrow DNA damage recovery. These synergistic effects lead to better behavioural responses noted in the mice, underscoring the potential advantages of Vcn-2 in alleviating radiation-induced alteration.

References

Ahaskar, M., Sharma, K. V., Singh, S. and Sisodia, R. 2007. 'Radioprotective effect of fruit extract of Grewia asiatica in Swiss albino mice against a lethal dose of γ-irradiation', *Asian Journal Experimental Sciences*, 21(2), 00-00.

Almatroodi, S. A., Alsahli, M. A., Almatroudi, A. and Rahmani, A. H. 2020. '*Ocimum sanctum*: role in disease management through modulating various biological activity', *Pharmacognosy Journal*, 12(5).

Baruah, T. J. and Kma, L. 2019. 'Vicenin-2 acts as a radiosensitizer of non-small cell lung cancer by lowering Akt expression', *Biofactors*, 45(2): 200-210.

Baruah, T. J., Sharan, R. N. and Kma, L. 2018. 'Vicenin-2: a potential radiosensitizer of non-small cell lung cancer cells', *Molecular Biology Reports,* 45: 1219-1225.

Bradford, M. M. 1976. 'A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding', *Analytical Biochemistry*, 72(1-2): 248-254.

Buonanno, M., Gonon, G., Pandey, B. N. and Azzam, E. I. 2023. 'The intercellular communications mediating radiation-induced bystander effects and their relevance

to environmental, occupational, and therapeutic exposures', *International Journal of Radiation Biology*, 99(6): 964-982.

Dainiak, N., Gent, R. N., Carr, Z., Schneider, R., Bader, J., Buglova, E. and Meineke, V. 2011. 'Literature review and global consensus on management of acute radiation syndrome affecting nonhematopoietic organ systems', *Disaster Medicine And Public Health Preparedness*, 5(3), 183-201.

Ellman, G. L. 1959. 'Tissue sulfhydryl groups. Archives of Biochemistry and Biophysics', 82(1): 70-77.

Ghosh, N., Ali, A., Ghosh, R., Das, S., C Mandal, S. and Pal, M. 2016. 'Chronic inflammatory diseases: progress and prospect with herbal medicine', *Current Pharmaceutical Design,* 22(2): 247-264.

Gulawani, S., Pandey, S.K. and Srivastava, P. 2024. 'Reactive oxygen species in cancer management: understanding the transformation of antagonists turning allies', *Health Science Journal*, 18(1): 1-16.

Green, D. E. and Rubin, C. T. 2014. 'Consequences of irradiation on bone and marrow phenotypes, and its relation to disruption of hematopoietic precursors', *Bone*, 63: 87-94.

Hauer-Jensen, M., Wang, J., Boerma, M., Fu, Q. and Denham, J. W. 2007. 'Radiation damage to the gastrointestinal tract: mechanisms, diagnosis, and management', *Current Opinion In Supportive And Palliative Care*, 1(1): 23-29.

He, L., He, T., Farrar, S., Ji, L., Liu, T. and Ma, X. 2017. 'Antioxidants maintain cellular redox homeostasis by the elimination of reactive oxygen species', *Cellular Physiology and Biochemistry*, 44(2): 532-553.

Islam, M. T. 2017. 'Radiation interactions with biological systems', *International Journal of Radiation Biology*, 93(5): 487-493.

Jadoon, S. and Malik, A. 2017. 'A review article on the formation, mechanism and biochemistry of MDA and MDA as a biomarker of oxidative stress', *International Journal Advance Research*, 5: 811-818.

Jit, B. P., Pattnaik, S., Arya, R., Dash, R., Sahoo, S. S., Pradhan, B. and Behera, R. K. 2022. 'Phytochemicals: A potential next-generation agent for radioprotection', *Phytomedicine*, 106: 154188.

Koch, A., Gulani, J., King, G., Hieber, K., Chappell, M. and Ossetrova, N. 2016. 'Establishment of early endpoints in mouse total-body irradiation model', *PLoS One*, 11(8): e0161079.

Li, T., Cao, Y., Li, B. and Dai, R. 2021. The biological effects of radiation-induced liver damage and its natural protective medicine. Progress In Biophysics And Molecular Biology, 167, 87-95.

Makni, M., Jemai, R., Kriaa, W., Chtourou, Y. and Fetoui, H. 2018. '*Citrus limon* from Tunisia: Phytochemical and physicochemical properties and biological activities', *BioMed Research International*, 2018(1): 6251546.

Marklund, S. and Marklund, G. 1974. 'Involvement of the superoxide anion radical in the autoxidation of pyrogallol and a convenient assay for superoxide dismutase', *European Journal of Biochemistry*, 47(3): 469-474.

Mu, H., Sun, J., Li, L., Yin, J., Hu, N., Zhao, W. and Yi, L. 2018. 'Ionizing radiation exposure: hazards, prevention, and biomarker screening', *Environmental Science and Pollution Research*, 25: 15294-15306.

Nuszkiewicz, J., Woźniak, A. and Szewczyk-Golec, K. 2020. 'Ionizing radiation as a source of oxidative stress—the protective role of melatonin and vitamin D', *International Journal Of Molecular Sciences*, 21(16), 5804.

Obrador, E., Salvador, R., Villaescusa, J. I., Soriano, J. M., Estrela, J. M. and Montoro, A. 2020. 'Radioprotection and radiomitigation: from the bench to clinical practice', *Biomedicines*, 8(11): 461.

Obrador, E., Salvador-Palmer, R., Villaescusa, J. I., Gallego, E., Pellicer, B., Estrela, J. M. and Montoro, A. 2022. 'Nuclear and radiological emergencies: biological effects, countermeasures and biodosimetry', *Antioxidants*, 11(6): 1098.

Prasad, S. and Srivastava, S. K. 2021. 'Oxidative stress and cancer: Antioxidative role of Ayurvedic plants', *Cancer*, Academic Press: 301-310.

Preedy, V.R. and Patel, V.B. (Eds.). 2021. "Cancer: oxidative stress and dietary antioxidants", Academic Press.

Rasheed, H., Ahmed, S., Singh, H. and Sharma, A. 2022. 'Scientific evaluation of the role of *Ocimum sanctum* in ayurvedic formulations and its phytochemistry and pharmacological activities. in chemistry, in A. Amalraj, S. Kuttappan, and K. Varma (ed.), *Ch. 6 biological activities and therapeutic applications of medicinal plants in Ayurveda*, The Royal Society of Chemistry: 108-147.

Reisz, J.A., Bansal, N., Qian, J., Zhao, W. and Furdui, C.M. 2014. 'Effects of ionizing radiation on biological molecules—mechanisms of damage and emerging methods of detection', *Antioxidants and Redox Signaling*, 21(2): 260-292.

Silva, A.C.D.O., Mársico, E.T., Jesus, E.F.O.D., Guimarães, C.F. and Cortez, M.A.S. 2011. 'Effect of gamma radiation on lipids by the TBARS and NMR', *Brazilian Archives of Biology and Technology*, 54: 1343-1348.

Sisodia, R. and Singh, S. (2009). 'Biochemical, behavioural and quantitative alterations in cerebellum of Swiss albino mice following irradiation and its modulation by *Grewia asiatica', International Journal of Radiation Biology*, 85(9): 787-795.

Soriano, J.L., Calpena, A.C., Souto, E.B. and Clares, B. 2019. 'Therapy for prevention and treatment of skin ionizing radiation damage: a review', *International Journal of Radiation Biology,* 95(5): 537-553.

Srinivasan, M., Sudheer, A.R., Pillai, K.R., Kumar, P.R., Sudhakaran, P.R. and Menon, V.P. 2007. 'Modulatory effects of curcumin on γ-radiation-induced cellular damage in primary culture of isolated rat hepatocytes', *Environmental Toxicology and Pharmacology*, 24(2): 98-105.

Sumran, G. and Aggarwal, A. 2019. 'The prospect of Indian herbs as sources of antioxidants in combating oxidative stress', *Chemistry & Biology Interface,* 9(1).

Szumiel, I. 2015. 'Ionizing radiation-induced oxidative stress, epigenetic changes and genomic instability: the pivotal role of mitochondria', *International Journal of Radiation Biology*, 91(1): 1-12.

Uma Devi, P., Ganasoundari, A., Vrinda, B., Srinivasan, K. K. and Unnikrishnan, M. K. 2000. '*Radiation protection by the Ocimum flavonoids orientin and vicenin: mechanisms of action', Radiation research*, 154(4), 455-460.

Venuprasad, M.P., Hemanth Kumar, K. and Khanum, F. 2013. 'Neuroprotective effects of hydroalcoholic extract of *Ocimum sanctum* against H_2O_2 induced neuronal cell damage in SH-SY5Y cells via its antioxidative defence mechanism', *Neurochemical Research*, 38: 2190-2200.

Venuprasad, M.P., Kandikattu, H.K., Razack, S. and Khanum, F. 2014. 'Phytochemical analysis of *Ocimum gratissimum* by LC-ESI–MS/MS and its antioxidant and anxiolytic effects', *South African Journal of Botany*, 92: 151-158.

Victor, V.M., Rocha, M. and De la Fuente, M. 2004. 'Immune cells: free radicals and antioxidants in sepsis', *International Immunopharmacology*, 4(3): 327-347.

Zhang, Y., Huang, Y., Li, Z., Wu, H., Zou, B. and Xu, Y. 2023. 'Exploring natural products as radioprotective agents for cancer therapy: mechanisms, challenges and opportunities', *Cancers,* 15(14): 3585.