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Revisión / Review

Radioprotective natural products as alternative complements in oncological radiotherapy

[Productos naturales radioprotectores como complementos alternativos en la radioterapia oncológica]

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Abstract: Humans when exposed to harmful ionising radiations suffer from various pathophysiological disorders including cancer. Radiotherapy is a treatment where these cancerous cells within a tumor are targeted and killed by means of high energy waves. This therapy is very expensive and involves highly sophisticated instruments. In addition to this, most synthetic radioprotectors including Amifostine have been found to possess toxicity. This led researchers to develop a novel, economically viable, and efficient therapeutic alternative to radiation therapy. The last two decades have observed a major shift towards investigating natural products as radioprotectors, as these are immensely effective in terms of their potential bioequivalence relative to many of the established synthetic compounds available. Taking into account the limitations of radiation therapy, an approach 'Integrative Oncology' that involves a combination of both traditional and conventional medical treatment are used nowadays to treat patients suffering from cancer and associated mental and psychological disorders.

Keywords: Cancer; Integrative oncology; Natural products; Radioprotection; DNA damage.

Resumen: Los seres humanos, cuando se exponen a radiaciones ionizantes nocivas, sufren diversos trastornos fisiopatológicos, incluido el cáncer. La radioterapia es un tratamiento en el que estas células cancerosas dentro de un tumor son atacadas y destruidas por medio de ondas de alta energía. Esta terapia es muy cara e implica instrumentos muy sofisticados. Además de esto, se ha descubierto que la mayoría de los radioprotectores sintéticos, incluida la amifostina, poseen toxicidad. Esto llevó a los investigadores a desarrollar una novedosa, económicamente viable y eficiente alternativa terapéutica a la radioterapia. En las dos últimas décadas se ha observado un cambio importante hacia la investigación de productos naturales como radioprotectores, ya que son inmensamente eficaces en términos de su potencial bioequivalencia en relación con muchos de los compuestos sintéticos establecidos disponibles. Teniendo en cuenta las limitaciones de la radioterapia, hoy en día se utiliza un enfoque de "Oncología Integrativa" que implica una combinación de tratamiento médico tradicional y convencional para tratar a pacientes que padecen cáncer y trastornos mentales y psicológicos asociados.

Palabras clave: Cáncer; Oncología integrativa; Productos naturales; Radioprotección; Daño en el ADN.

INTRODUCTION

Nowadays, we have become quite familiar with the negative consequences of different kinds of harmful radiations. The intensity of such radiations are increasing daily due to rapid technological advancements caused by human interventions. We are mostly concerned with ionising radiations, and World Health Organization (WHO, 2020) has defined 'ionising radiations' as those radiations which emit enough energy when interacting with an atom, displacing tightly bound electrons from the shells or orbits of an atom, thereby causing the atom to become ionised or charged either positively or negatively. These ionising radiations possess dual characters having both particle nature (electrons, protons, neutrons, etc.) as well as wave nature in the form of electromagnetic waves (X rays, gamma rays, etc.). WHO and Canadian Nuclear Safety Commission (CNSC, 2019) categorised ionising radiations into three main categories – (i) Alpha and beta particles emitted from radioactive isotopes carry their own charge and through coulombic forces interact with the electrons of the atom. Beta particles have high penetrating power when compared with alpha radiations, (ii) Neutrons are considered to be indirectly ionising since they do not carry their own charge, (iii) Gamma rays and X rays are also considered to be indirectly ionising since these electromagnetic waves neither carry their own charge nor interact through the coulombic forces with the electrons of the atom.

Human exposed to these harmful radiations suffer from various pathophysiological disorders related to skin, gut, lungs, eyes, etc., including cancers associated with these organs, and their consequences usually become life threatening ultimately resulting in death. Radioprotection is therefore very significant in terms of medical treatment where cancer patients are exposed to planned radiation therapy (Baskar *et al*., 2012). Around 3.5 million cancer survivors have been reported to undergo radiation therapy as a part of their therapeutic regimen although at recommended doses with minimal side-effects (Bryant *et al*., 2017). Radiotherapy however injures normal tissues causing damaging effects in the genetic material i.e., DNA of a cell. These ionising radiations cause double stranded breaks (DSBs) in DNA directly as well as contribute to base damages. In addition, these radiations are also involved in formation of reactive oxygen species (ROS) that leads to DNA damage by generating apyrimidinic (without base cytosine/thymine) or apurinic (without base adenine/guanine) sites and single stranded breaks (SSBs) in the DNA, and by modifying sugar moieties in the DNA (Aparicio *et al*., 2014, Baselet *et al*., 2019). For several weeks after radiotherapy, a patient experience symptom due to the side-effects of radiation. Several radioprotective measures are now being adopted to minimise the damaging effects of these harmful radiations. Synthetic radioprotectors have been found to possess cumulative toxicity and short self-life, and are therefore unstable, providing only short term protection. Moreover, they are also difficult to administer (Mun *et al*., 2020). These drawbacks have led researchers to investigate natural radioprotective agents that are able to overcome the above mentioned shortcomings, and develop novel approaches to treat cancer patients, thereby providing an alternative solution to orthodox cancer radiotherapy.

Since ancient times, traditional people have been using herbal medicine to cure different types of diseases. Researchers have investigated that plants containing high amounts of polyphenols namely tannins, anthocyanins, flavonoids, lignin etc. possess antioxidant activity with radioprotective and anti-cancer properties (Shahidi & Yeo, 2018). Benkovic *et al*. (2008), reported several flavonoids namely rutin, quercetin, myricetin-flavonol, gallate-flavanol etc. which behave as antioxidants possessing radioprotective abilities. Flavonoids have the potentiality to absorb high energy solar wavelengths and scavenge the free radicals i.e., ROS generated during radiation (Brunetti *et al*., 2013). Natural products with such properties have proven to be non-toxic, providing long term protection and can be administered easily. India is home to a large number of medicinal plants which native tribal people have been using as traditional medicine through their undocumented knowledge, for the cure of different kinds of ailments. Researchers have found an alternative way to treat cancer, a multifaceted illness, using natural radioprotectors, with the aim of developing an economic, viable, and efficient treatment (Mun *et al*., 2020). In addition to this, natural radioprotectors are affordable to a large number of people mostly from the poorer sections of the society. This has given rise to a new concept called 'Integrative Oncology' which is based on a combinatorial approach of both traditional Complementary and Alternative Medicine (CAM) and conventional medical treatment, used to treat cancer patients, along with their mental and psychological disorders associated with this disease (Smith *et al*., 2018). Oncologists should have proper knowledge about natural medicines that have the potentiality to cure cancer, apart from their chemotherapy and radiotherapy approaches. Indian traditional medicine includes Ayurveda, Yoga, Unani, Siddha, Homeopathy (AYUSH), Naturopathy and acupuncture (Shrivastava *et al*., 2015).

The aim of this review is to provide a brief account of radioprotective natural products that have the potentiality in curing cancer. The mechanism by which ionising radiation induces oxidative stress and DNA damage in cells has also been presented along with the preference of natural over synthetic radioprotectors. A concept of Integrative Oncology has been discussed focusing on the role of Indian traditional medicine within context of treatment of cancer.

Consequences of radiation in context of DNA damage and genome instability

The consequences of radiation can be devastating, affecting at the molecular level, and are usually expressed in the form of mutations leading to cancer etc. Ionising radiations, through a series of signaling cascades impose damages at the molecular level. There are direct as well as indirect effects caused as a result of such ionising radiations (Desouky *et al*., 2015).

Firstly, the direct effect of radiation involves damage to macromolecules such as DNA or RNA. These DNA damages can lead to the formation of either SSBs or DSBs, thereby resulting in altered genomic expression and thus genome instability (Kavanagh *et al*., 2013). These genomic instabilities can lead to various birth defects, mutations, and the rise of multifaceted diseases such as cancer. The most fatal outcome of ionising radiations is the formation of DNA DSBs. Besides these, these radiations also damage DNA bases, DNA-DNA interactions, as well as DNA-protein interactions, including dysfunction at cellular and organ level. These damages lead to the induction of highly synchronized pathways referred to as DNA damage response and repair (DRR) pathways (Mota *et al*., 2019).

Secondly, the indirect effect of radiation involves generation of free radicals i.e., ROS (Baselet *et al*., 2019). The ROS namely H, OH, H_2O, H_3O^+ carry out their function by depleting the anti-oxidant stores in the cell and by reacting with macromolecules, membrane lipids, proteins ultimately resulting in cellular dysfunction and death. Besides these, ROS generated from radiolysis from water through different mechanisms namely base damage, cross-linking, de-polymerization, strand breakage, etc. also damage DNA (Tiwari & Wilson, 2019). Improper DNA repair mechanisms induce chromosomal aberrations, life threatening diseases such as cancer and mutations that can generate cellular resistance to cancer radiotherapy.

Need for the natural radioprotectors

Radioprotectors are drugs or chemicals designed to attenuate radiation elicited damages in humans, thereby protecting them from harmful ionising radiations like X-rays, gamma rays, cosmic rays, etc., or from radionuclides like Uranium, Thorium, Strontium – 90, Radon, Radium, Caesium – 137. Therefore, both radiation oncologists and biologists need to formulate and develop pharmacologically dynamic, nontoxic, effective, efficient, and easily administrable radioprotectors to safeguard humans from these hazardous and destructive ionising radiations. To develop efficient radioprotectors, Joshi *et al*. (2010), has outlined the following features which a radioprotector must possess – (i) Must furnish multifaceted defence against harmful consequences of ionising radiations with minimal side-effects in majority of tissues and organs, (ii) Must possess stability with a longer shelf life and are easily administrable either orally or intramuscularly, (iii) Must be accessible, economically viable and must be compatible with a wide range of drugs during clinical care, (iv) Must be used at recommended doses that should reach the targeted organs and are competent enough to cross the blood-brain barrier, and (v) Must maintain its efficacy for longer period of time at the time of emergency.

Radioprotectors can be categorised into chemical radioprotectors and natural radioprotectors (Mun *et al*., 2020). Researchers at the Walter Reed Army Research Institute (Maryland, United States), started screening of around 4500 compounds from the year 1957 onwards to detect potential compounds possessing radioprotective activity (Maurya *et al*., 2006), and they found only one compound that was finally approved by the Food and Drug Administration (FDA) in the United States. The detected compound was Amifostine (WR-2721) (Cassatt *et al*., 2002), an ester of phosphoric acid and thiol (Budavari *et al*., 2006), which is currently the only clinically approved radioprotector used in cancer radiotherapy. Amifostine has been reported to be specifically effective against patients with head and neck carcinoma (Bourhis & Rosine, 2002). However, this radioprotective agent is associated with various side-effects such as diarrhoea, nausea, dizziness, sleeplessness, hypocalcemia, hypotension and so on (Monig *et al*., 1990). Moreover, cumulative toxicity, high cost, limited administration, and lower protection to the Central Nervous System add to the negative side effects of Amifostine (Bourhis & Rosine, 2002). Other synthetic compounds such as 5-aminosalicylic acid (5-ASA) and Sulfasalazine (SAZ) have also been reported to possess the potentiality to behave as radioprotectors, but clinically these compounds have not been approved due to their toxicity (Lans, 2007).

Hence, it can be concluded that an ideal radioprotector should be non-toxic and should be able to provide a high degree of protection to normal cells, contrarily providing minimal protection to the tumor cells. The failure to develop an effective, efficient, low cost, and low or non-toxic radioprotector has motivated researchers across the globe to focus towards natural products with radioprotective potentiality. Natural products from plants have been used since ancient times to cure various human ailments and recent databases suggest that around 400000 drugs have been reported till date from natural sources (Sorokina & Steinbeck, 2020). Kuruba and Gollapalli (2018), have reported the screening of around 74 natural products with radioprotective properties till date via various *in-vitro* and *in-vivo* experiments to prove the potentiality of these natural products with radioprotective activity. Jagetia (2007), used the combination of natural products along with radiations, and found that there is an enhancement in the death of tumor cells through the process of radiosensitization. This process even protected the normal cells against harmful radiation therapy.

Plants with radioprotective properties

Our mother Earth is gifted with a large number of medicinal plants, and since ancient times, various ethnic groups across the globe have relied on these natural resources, which had the potentiality in curing different human ailments including deadly diseases. According to the latest data available as per Food and Agriculture Organization (FAO, 2019) of the United Nations, around 7500 species of medicinal plants are present in India. Recently researchers have recognized that traditional knowledge from the various ethnic groups need to be documented, because there is a lot of information still unavailable to us regarding the medicinal potential of many native Indian plants. Bhanot & Noolvi (2011), reported that around 60 percent of anticancer drugs namely, taxol, vinblastine, *Vinca* alkaloids, vincristine, topotecan, which are currently being used clinically throughout the world have been derived from natural sources. Most researchers who have conducted their phytochemical studies of medicinal plants to evaluate their radioprotective efficacy, have done it either from polyherbal formulations or from whole extracts, and also from isolated compounds or from fractionated extracts (Hosseinimehr, 2007). A list of few important plants found in West Bengal, India exhibiting both radioprotective and anticancer properties has been presented in **Table No. 1**.

***Aegle marmelos* (L.) Corrêa**

Aegle marmelos (L.) Corrêa (**Figure No. 1A**) is a member of the family Rutaceae (Order: Sapindales) commonly known as ‘Indian bael’ or ‘Bengal quince’ and is considered as one of the sacred trees by Hindus. Secondary metabolites namely furocoumarins, rutin, marmesin, allocryptopine, O-methylhafordinol, etc. have been reported to have been isolated from this plant. Lampronti *et al*. (2003), and Lambertini *et al*. (2004), have reported the anti-proliferative potentiality of ethanol extract of leaves of this plant against tumor and breast cancer cell lines respectively. Jagetia *et al*. (2004), reported the radioprotective activity of hydro-alcohol extract of both leaves and fruits by administrating a dose of 15 mg/kg body weight against 10 Gray (Gy) radiations and a dose of 20 mg/kg body weight against gamma radiations respectively in mouse models. Next year, Jagetia *et al*. (2005a), carried out *in-vivo* experiments in mouse models transplanted with Ehrlich ascites carcinoma (EAC) cell lines where they evaluated the anticancer potentiality of hydro-alcohol leaf extract at 400 mg/kg concentration.

***Justicia adhatoda* L.**

Justicia adhatoda L. (Syn. *Adhatoda vasica* Nees) (**Figure No. 1B**) is a member of the family Acanthaceae (Order Lamiales) commonly known as ‘Vasaka’ in Bengali, and is an excellent Indian traditional medicine, used in the treatment of asthma and chronic bronchitis. Numerous secondary metabolites such as alkaloids, namely vasicine, phenols, tannins, flavonoids, saponins, etc. have been reported till date. Kumar *et al*. (2007), carried out extensive studies by treating radiation induced testes of Swiss albino mice with ethanol extract of leaves of

J. adhatoda, where they monitored the histological changes in the testes, Glutathione (GSH), alkaline phosphatase and lipid peroxidation (LPO) levels, along with chromosomal aberrations in bone marrow cells between 1 to 30 days. After getting exposed to 8 Gy radiation, they observed chromosomal aberrations with 100 percent mortality in bone marrow cells of mice within 22 days. When the leaf extract at a dose of 800 mg/kg body weight concentration was administered orally consecutively for 15 days, they observed the reduction in chromosomal aberrations from 100 to 70 percent within 30 days along with minimal damage to the architectural features of the testes, increased GSH, and alkaline phosphatase levels, decreased LPO levels, thereby proving the potentiality of the plant in terms of radioprotective efficacy. There are also reports regarding the radioprotective activity of *J. adhatoda* in safeguarding mice by providing protection against radiation induced changes in haematological parameters (Kuruba & Gollapalli, 2018).

Figure No. 1
Some examples of plants found in West Bengal, India that possess natural products with radioprotective properties

A **B**

(1A) *Aegle marmelos* (L.) Corrêa (1B) *Justicia adhatoda* L.

Allium cepa L.

Allium cepa L. is a member of the family Amaryllidaceae (Order Asparagales), commonly known as common onion or bulb onion, and is considered as a plant model for carrying out cytological studies during toxicological experiments. *A. cepa* has been found to possess high polyphenol content, with yellow onions and red onions containing high amounts of flavonoid and anthocyanin respectively. The dried bulb at 20 mg/kg concentration is reported to be an excellent radioprotector as it has potentiality in providing protection against X-rays (Arora *et al*., 2005). Ammar (2016), studied the radioprotective activity of onion in Swiss Albino mouse models where they irradiated the mice with single dose of gamma radiations at 10 Gy preceded by administering the mice with 200 mg/5ml/kg/day onion for two weeks, and monitored the levels of GSH, malondialdehyde (MDA), superoxide dismutase (SOD), glutamic pyruvic transaminase (GPT), glutamic oxaloacetic transaminase (GOT) and testosterone in both serum as well as in tissues. Since onions are rich in anti-oxidants, they are able to scavenge the free radicals generated during radiation, thereby protecting the cells from damage at molecular level, and proving its potentiality to act as radioprotective agent, which can protect against cardiovascular diseases and cancer.

Andrographis paniculata (Burm.f.) Nees

Andrographis paniculata (Burm.f.) Nees (**Figure No. 1C**) is a member of the family Acanthaceae (Order Lamiales) and as an Ayurvedic herb, it is commonly known as 'Kalmegh', meaning dark clouds. Major phytochemicals namely andrographolide, neoandrographolide, andrographine, 14-Deoxy-11-dehydroandrographolide, 14-Deoxy-11-oxoandrographolide etc. have been reported to have been isolated from this plant. Rajagopal *et al*. (2003), reported the anti-proliferative activity of the plant in tumor cell lines, where they observed andrographolide capable of arresting the G0/G1 phase of cell cycle via triggering of protein p27 and reducing cyclin-dependent kinase 4 (CDK4). The fraction of methanol extract of the plant in dichloromethane has also been reported to possess anti-stimulatory activity, as well as anticancer activity by prohibiting the escalation of HT-29 cancer cells (Kumar *et al*., 2004). Nantajit *et al*. (2017), isolated and studied the effect of three phytochemicals namely 14-deoxy-11,12-didehydroandrographolide, andrographolide and neoandrographolide on transformed BALB/3T3 cell model, to evaluate the radioprotective as well as anti-neoplastic activity. They observed that these phytochemicals were potent in reducing radiation induced DNA damage in cells and stated that neoandrographolide was the most potent among all the three phytochemicals present in possessing radioprotective activity.

4.5. *Centella asiatica* (L.) Urban

Centella asiatica (L.) Urban (**Figure No. 1D**) is a member of the family Apiaceae (Order Apiales) commonly known as ‘Asiatic pennywort’, and is considered to be an excellent medicinal herb. The phytochemicals present in this plant mainly includes pentacyclic triterpenoids namely asiatic acid, asiaticoside, brahmic acid etc., and also includes centelloside, centellose etc. The acetone fraction of methanol extract of this plant has been reported to inhibit 50 percent of Dalton's lymphoma ascites and EAC cancer cells when treated with 22 mg/ml and 17 mg/ml concentration of plant extract respectively, thereby proving the anti-tumor potentiality of the plant (Babu *et al*., 1995). Yoshida *et al*. (2005), reported anti-proliferative activity of the methanol extract of the plant against different cancer cell lines. Joy & Nair (2009), carried out *in-vitro* and *in-vivo* experiments with the extracts of the plant to evaluate the radioprotective potentiality on mouse bone marrow cells analysed via alkaline comet assay. Moreover, they focussed on the potentiality of the extract in providing protection to radiation induced membrane damage, by evaluating the lipid peroxidation extent through the thio-barbituric acid reacting substances (TBARS) method.

C **D**

(1C) *Andrographis paniculata* (Burm.f.) Nees (1D) *Centella asiatica* (L.) Urban

***Curcuma longa* L.**

Curcuma longa L. (**Figure No. 1E**) is a member of family Zingiberaceae (Order Zingiberales), the powdered rhizome of which is very well known in Indian kitchens in preparing a variety of dishes and is considered as an excellent Ayurvedic medicine. Secondary metabolites, mainly diarylheptanoids like curcumin, bisdemethoxycurcumin, demethoxycurcumin etc., and essential oils, namely zingiberene, atlantone, turmerone, etc. have been reported from this plant. Earlier reports stated curcumin’s potentiality in reducing animal tumor development, where 0.4 mg/ml concentration of turmeric extract inhibited the growth of Chinese Hamster ovary cell line (Kuttan *et al*., 1985). Cheng *et al*. (2001), conducted phase I clinical trials with curcumin at 8000 mg/day concentration and found curcumin to remain non-toxic at this concentration while carrying out their experiments to prove the anticancer potentiality of turmeric against several cancer cell lines. Nada *et al*. (2012), studied the radioprotective effect of plant extract in rats by administering them with a dose of 200 mg/kg body weight concentration before and after exposure to gamma radiations at 6.5 Gy where they reported that an improved anti-oxidant status in rats along with decrease in radiation triggered escalation of inflammatory cytokines.

Ficus racemosa **L.**

Ficus racemosa L. is a member of the family Moraceae (Order Rosales), commonly known as 'Indian fig tree' or 'gular' and is considered sacred tree by Hindus. Phytochemicals present in this plant mainly include flavonoids, alkaloids, triterpenoids like lanosterol, tannins, gluanol acetate, lupenol, rocemosic acid, etc. Vinutha *et al*. (2015), conducted *in-vitro* experiments to prove the potentiality of *Ficus* plant extracts in inhibiting electron beam induced DNA damage, when plasmid pBR322 was exposed to various doses of electron beam radiation. They also conducted *in-vivo* experiments in mice irradiated with electron beam at 6 Gy radiations, where they used comet assay to monitor the inhibitory effect of 400 mg/kg body weight concentration of plant extract on comet parameters like tail length and percentage of DNA in tail of blood lymphocytes which were initially found to have increased after radiation exposure.

Gingko biloba **L.**

Gingko biloba L. is a member of the family Gingkoaceae (Order Gingkoales), commonly known as 'maidenhair tree', and is currently considered as an endangered plant. Secondary metabolites present include mainly flavonoid glycosides like quercetin, kaempferol, myricetin etc., gingkolides, terpene trilactones, gingko biflavones, and so on. Ethanol extract of dried leaf at 100 μg/mL concentration has been reported to be effective against hydroxyl radical induced neuronal cellular death in rat cerebellar cell culture medium (Ni *et al*., 1996). Khedr *et al*. (2018), reported on the radioprotective efficacy of plant extracts from *G. biloba* in ameliorating radioactive 99m-technetium sestamibi induced oxidative damage in organs of Wistar rats, through its free radical scavenging potentiality. 99m- technetium sestamibi is known to cause cataractogenesis in rats leading to lens injury.

Hippophae rhamnoides **L.**

Hippophae rhamnoides L. is a member of the family Elaeagnaceae (Order Rosales), commonly known as 'sea buckthorn plant'. The fruits (berries) of this plant are rich in polyphenols, malic acid, L-quebrachitol, quinic acid, vitamins C, E, and K, etc. Agrawala and Goel (2002), reported 80 percent radioprotective potentiality of 25-35 mg/kg body weight extract in mice when exposed to 10 Gy radiations. Goel *et al*. (2005), reported around 82 percent survivality chances and life span increment in mice irradiated with 60Co-gamma radiations, after treating them with aqueous-alcohol extract of berries of this plant. The aqueous-alcoholic extract of berries of *H. rhamnoides* increased life span and rendered 82% survival when administered to mice 30 min before 60Co-Gamma irradiation (Goel *et al*., 2005). Chawla *et al*. (2007), reported the radioprotective potentiality of Vitamin E from the fractioned extracts of the berries of this plant.

Mentha arvensis **L.**

Mentha arvensis L. is a member of the family Lamiaceae (Order Lamiales) commonly known as 'corn mint', 'field mint', or 'wild mint' plant. Phytochemicals namely menthol, neomenthol, menthyl acetate, piperitone, limonene, flavonoids, tannins etc., have been isolated from this plant. Jagetia and Baliga (2002a), has reported the radioprotective potentiality of chloroform extracts of this plant, dispensed at a dose of 10 mg/kg body weight in mouse models exposed to radiations. The aqueous extract has been reported to provide radioprotection against chromosomal damages in bone marrow cells of Swiss albino mice irradiated with 8 Gy radiations (Samarth & Kumar, 2003). This plant has also been reported to protect mice irradiated with gamma radiations from sickness and death (Baliga & Rao, 2010).

Ocimum tenuiflorum **L.**

Ocimum tenuiflorum L. (Syn. *Ocimum sanctum* L.) (**Figure No. 1F**) is a member of the family Lamiaceae (Order Lamiales), commonly known as 'holy basil' or 'tulsi' and is widely used as Indian traditional medicine. Phytochemicals namely oleanolic acid, ursolic acid etc., and essential oils namely β-elemene, eugenol, etc. have been reported from this plant. Flavonoids like vicenin and orientin isolated from this plant have been reported to provide protection against radiation induced chromosomal damages when cultured peripheral cells of humans were irradiated with 2 Gy of gamma radiations (Vrinda & Devi, 2001). The aqueous ethanol extract of this plant has been reported to possess radio-protective activity at a concentration of 50 mg/kg body weight along with chemo-preventive and anti-cancer activity (Ranga *et al*., 2005). Pattanayak *et al*. (2010), reviewed a comparative study with mouse, where one group irradiated with 2 Gy of gamma radiations was treated with the flavonoid orientin at a dose of 50 mg/kg body weight, and another group with similar radiations was treated with radioprotective chemical amifostine at a dose of 150 mg/kg body weight, and a similar radioprotective potentiality of these two compounds was evaluated. At non-toxic concentrations, the two flavonoids vicenin and orientin have been reported to provide radioprotection against radiation mediated sickness and death in various animal models (Baliga *et al*., 2016).

E **F**

(1E) *Curcuma longa* L. (1F) *Ocimum tenuiflorum* L.

***Phyllanthus emblica* L.**

Phyllanthus emblica L. (Syn. *Emblica officinalis* Gaertn.) (**Figure No. 1G**) is a member of the family Phyllanthaceae (Order Malpighiales) commonly known as 'Indian gooseberry', 'amla' or 'amlaki' in Sanskrit, and every part of the plant is used in Indian traditional medicine. Phytochemicals namely high amount of Vitamin C (ascorbic acid), emblicanin A and B, ellagitannins, polyphenols, and flavonoids such asellagic acid, kaempferol etc. have been reported from this plant. The extract from *P. emblica* has radioprotective potentiality in providing protection against radiation triggered sickness and cell death in mouse models. Aqueous extract of this plant has been found to possess anti-tumor activity as well as cytotoxic activity in L929 cells (Jose *et al*., 2001). The aqueous extract of fruit pulp of the plant has been shown to possess radioprotective potentiality in Swiss albino mice at a dose of 100 mg/kg body weight against radiation induced 9 Gy of gamma radiations (Singh *et al*., 2005).

***Syzygium cumini* (L.) Skeels**

Syzygium cumini (L.) Skeels (**Figure No. 1H**) is a member of the family Myrtaceae (Order Myrtales), commonly known as 'malabar plum'. Phytochemicals namely flavonol glycosides, triterpenoids, tannins, betulinic acid, quercetin, β-sitosterol, etc. have been reported from this plant. The leaf extract of this plant at 100 μg/mL concentration has shown to cause significant reduction in micronuclei formation when used in treating peripheral bool lymphocytes of human cells before irradiating with gamma radiations at 3 Gy radiations (Jagetia & Baliga, 2002b). Jagetia *et al*. (2005b), reported that hydro-alcohol extract of seeds from *S. cumini* possess radioprotective potentiality in mice irradiated with gamma radiations of 10 Gy in a dose dependent manner. They found that 80 mg/kg body weight concentration of seed extract offered highest radioprotection in reducing radiation induced sickness and death. The *in vivo* assessment of the extract at 80 mg/kg body weight concentration has been reported to act as a radioprotector by reducing gastrointestinal sickness and bone marrow deaths that are induced as a result of radiation (Jagetia, 2007).

G **H**

(1G) *Phyllanthus emblica* L. (1H) *Syzygium cumini* (L.) Skeels.

***Tinospora cordifolia* (Thunb.) Miers.**

Tinospora cordifolia (Thunb.) Miers is a member of the family Menispermaceae (Order Ranunculales), commonly known as 'gaduchi' or 'heart-leaved monsoon seed'. Phytochemicals namely columbin, palmatine, tinosporic acid, tinosporal, choline etc. have been reported to have been isolated from this plant. Pahadiya and Sharma (2003), evaluated radioprotective potentiality of the aqueous extract of this plant administered to Swiss albino mice at a concentration of 10 mg/kg body weight for seven days. Data showed 50 percent survivality chances within 13 days as compared to 100 percent mortality in 13 days. Goel *et al*. (2004), reported the radioprotective potentiality of *T. cordifolia* plant extract administered to male mice irradiated with 2 Gy of gamma radiation at a concentration of 200 mg/kg body weight that showed 76.3 percent survivality chances as compared to 100 percent mortality in control. They also reported that the plant extract provided protection against spleen colony forming units, micronuclei formation, haematological parameters and cell cycle progression.

***Vanilla planifolia* Jacks. Ex Andrews**

Vanilla planifolia Jacks. Ex Andrews is a member of the family Orchidaceae (Order Asparagales), commonly known as 'vanilla' which is the primary source of vanilla flavour resulting from the presence of the phytochemical vanillin. Besides vanillin, other phytochemicals reported from the pods of this plant include vanillic acid, 4-hydroxybenzoic acid, 4-hydroxybenzaldehyde etc. Earlier studies reported the radioprotective ability of *V. planifolia* extract by supressing chromosomal abnormalities induced from X-ray irradiation both in V79 cells and mice *in-vitro* (Keshava *et al*., 1998) and *in-vivo* (Sasaki *et al*., 1990) respectively. The plant extract also provided protection against X-ray induced micronuclei formation in V79 cells (Keshava *et al*., 1998). Kumar *et al*. (2000), also provided similar evidence of attenuating chromosomal aberrations in mice and cells when exposed to radiations.

Natural products as potential radioprotective candidates

In the last few decades, exponential shift has been observed towards the evaluation of natural products as radioprotectors, mainly due to its efficacy and potential bioequivalence comparative to several well established available synthetic compounds. Some plants by virtue of their radioprotective mechanisms can grow even in presence of radiations emitted from harsh sunlight. The innate radioprotective ability of natural products obtained from plants is in part due to the numerous antioxidant possess as a part of their normal secondary metabolic processes. It has been observed from various studies that lower doses of herbal preparations show significant advantage in radioprotective properties over toxic doses of synthetic formulations (Hosseinimehr, 2007). Moreover, the natural products when administered before irradiation, have shown to diminish deleterious effects of infrared radiations in cells. Many researchers have focused on these natural products as promising radioprotective agents against ionizing radiations (Oh *et al*., 2016). The chemical structure of some natural products obtained from plants have been represented in **Figure No. 2**.

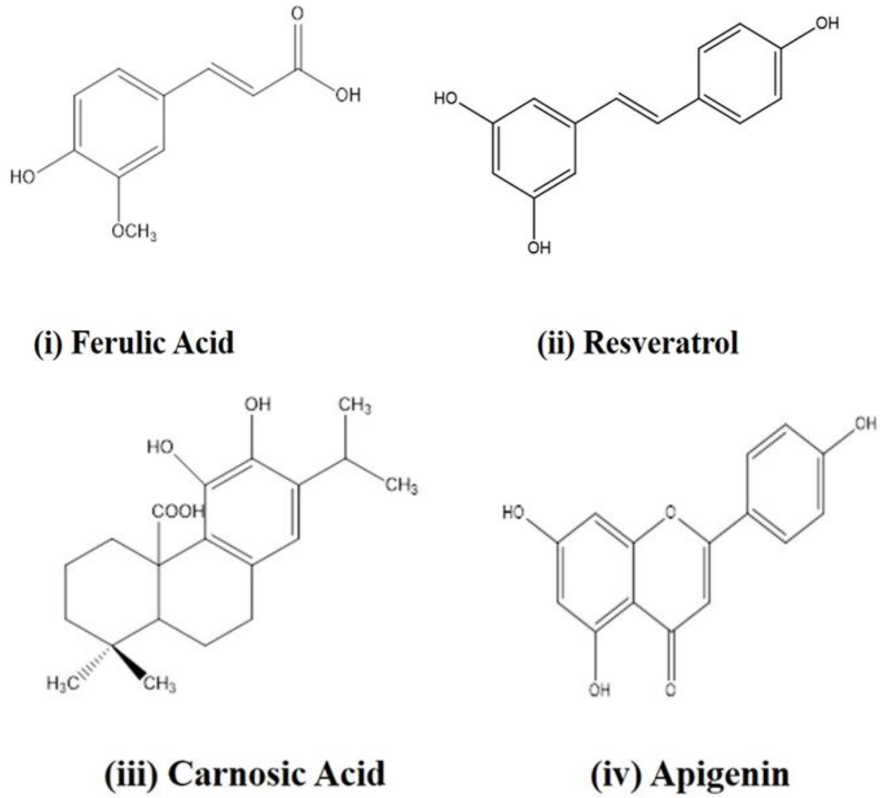
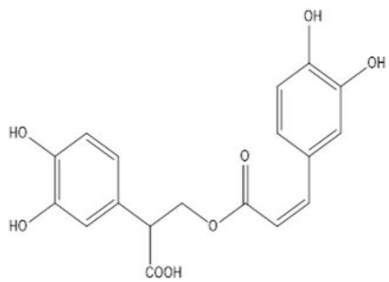


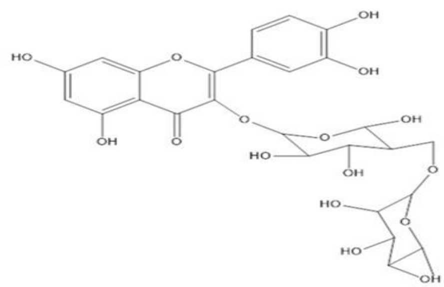
Figure No. 2
Chemical structure of natural products (i – iv) that possesses radioprotective properties.

The whole blood sample of volunteers who drank green tea (*Camellia sinensis* (L) Kunntze) for five days was exposed to gamma radiation. A significant decrease in DNA damage was observed in the lymphocytes collected 3 h after drinking green tea compared to controls (Davari *et al*., 2012). The radioprotective effect of ferulic acid (**Figure No. 2 - i**) was studied on cultured lymphocytes (Prasad *et al*., 2006). In this study, the pre-treated human lymphocytes with varying concentration of ferulic acid were exposed to gamma radiation. The results suggest that, pre-treated lymphocytes with the ferulic acid resulted in a significant reduction in DNA damage compared to non-treated controls. The ferulic acid significantly increases the activity of superoxide dismutase, catalase, and glutathione reductase by preventing the effect of radiation on the pre-treated lymphocytes.

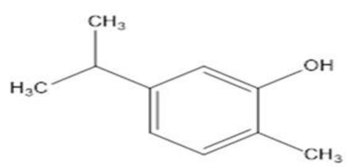
Resveratrol (**Figure No. 2 - ii**), a well-known free radical scavenger and antioxidant was investigated for its effect on growth-inhibitory activity in some human cancer cell lines and pro-apoptic effect on leukemia, mammary and epidermoid cell lines. Firouzi *et al*. (2015), investigated the effect of resveratrol on DNA damage and colony death on treated glioblastoma cells relative to controls. The study proposes that, resveratrol leads to the stabilization of p53 by binding to hypoxia inducible factor-1 (HIF1-α) in hypoxic condition (often found in neoplastic growth), thereby decreased function of the vasculogenic cells. Resveratrol leads to decreased vascular growth in the glioblastoma cells. They also observed that this natural product detects and kills genetically mutated cells. On other hand, Carsten *et al*. (2008), reported that resveratrol decreased the expression of anti-apoptotic proteins like BCL2 and increased the expression of pro-apoptotic proteins like BAX in cancer cells. Thus, it was proved that resveratrol, is a promising natural product in treating cell-cycle or ROS-mediated diseases, including radiation induced cellular damage (Carsten *et al*., 2008; Firouzi *et al*., 2015).



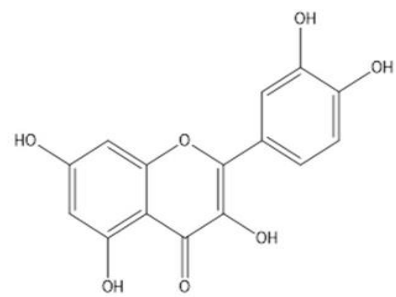
(v) Rosmarinic Acid



(vi) Rutin



(vii) Carvacrol



(viii) Quercetin

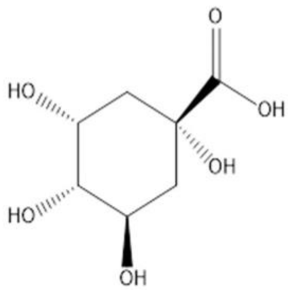
Cont. Figure No. 2
Chemical structure of natural products (v – viii) that possesses radioprotective properties

Wan *et al*. (2006), investigated the radioprotective effect of naturally occurring antioxidant compounds like ascorbic acid, Vitamin E, N-Acetyl cysteine, ascorbic acid, sodium ascorbate, alphalipoic acid, coenzyme Q10, and l-selenomethionine on human breast epithelial cells. The cells were pre-treated with a single and combination of antioxidants on antioxidant-free control groups before radiation. The findings suggest that, the pre-treated antioxidant to human breast epithelial cells provided significant 94.7% and 100% reduction in DNA damage when exposed to X-rays and gamma rays respectively. Studies on different antioxidant compounds such as carnosic acid (**Figure No. 2 - iii**), green tea extract, apigenin (**Figure No. 2 - iv**), diosmine, rosmarinic acid (**Figure No. 2 - v**), l-ascorbic acid, δ-tocopherol, rutin (**Figure No. vi**), amifostine, and dimethylsulphoxide proved themselves as potent radioprotectants in reducing chromosomal damage in cells caused by ionizing radiation (Dillard & German, 2000). Significant inhibition of DNA damage and the greatest degree of protective effect was observed in rosmarinic acid, carnosic acid, δ-tocopherol (vitamin E), and apigenin compared to irradiated controls (Dillard & German, 2000).

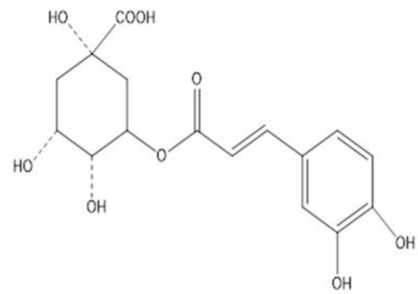
Arivalagan *et al*. (2015), conducted studies on carvacrol (**Figure No. 2 - vii**) to prove it as a potential radioprotective agent due to its antioxidant property. The lymphocytes collected from healthy individuals were pre-treated with DMSO or carvacrol. They exposed the lymphocytes from control groups to the radiations and observed the reduction in the rate of cell survival and increase in DNA damage. The ameliorative effect on pre-treated lymphocytes with carvacrol showed decrease in DNA damage and lipid peroxidation. A significant decrease in apoptosis was observed with rise in the lethal dose of radiation compared to controls. Several naturally occurring plant phenolic glycosides such as sinapoyl-E-glucoside (sEg), quercetin-3-*O*-rhamnoside-7-*O*-glucoside (**Figure No. 2 - viii**), quercetin-3-*O*-rhamnoside (q3Or) and luteolin-7-*O*- (2-apiosyl)-glucoside (l7O2ag) were reported as promising radioprotective agents as well as antioxidants (Materska *et al*., 2015). They collected the lymphocytes from healthy human donors, treated them with the phenolic glycosides before irradiation with X-rays and proposed that q3Or exhibited a promising radioprotective effect with 50% reduction in DNA damage compared to controls on irradiation of X-rays. While, l7O2ag reported to possess significant superoxide radical scavenging capabilities thereby demonstrating its radioprotective potentiality. Cinkilic *et al*. (2013), evaluated *in-vitro* radioprotective potentiality of phenolic glycosides quinic acid and chlorogenic acid (**Figure No. 2 - ix, x**) on human lymphocytes. According to the study protocol, lymphocytes were irradiated with different doses of X-rays and treated with different concentrations of either quinic acid, chlorogenic acid, or a sham control. Data showed that quinic acid and chlorogenic acid prior to irradiation significantly decreased DNA damage as measured by the genetic damage index of lymphocytes. Based on genetic damage index, the magnitude of protection was calculated to be 5.99% – 53.57% for quinic acid and 4.49% – 48.15% for chlorogenic acid. The potential effect of quinic acid and chlorogenic acid as radioprotective compounds of natural origin is comparable to other phenolic compounds such as curcumin, caffeic acid, hesperidin, vanillin, and resveratrol. The finding is in concord due to the presence of vicinal hydroxyl groups on an aromatic residue of both the phenolic glycosides and thus may be responsible for the anti-mutagenic, anti-carcinogenic and antioxidant effects (Cinkilic *et al*., 2013). Some flavonoids that have been investigated for their radioprotective uses include hesperidine (**Figure No. 2 - xi**), curcumin, sesamol, rutin (Yahyapour, 2018). The application of hesperidin in mice at a dose of 100 mg/kg body weight has proved its effectiveness by reducing the healing time of radiation-induced wounds by two days (Jagetia & Rao, 2018). Haddadi *et al*. (2018) also observed similar wound healing property from radiation-induced skin damage by applying similar oral dose of hesperidin.

Currently, bioactive compounds isolated from seaweeds especially green, red and brown algae are gaining more interest among numerous scientific groups to study their pharmaceutical and biomedical properties namely radioprotective (Yang *et al*., 2018; Moon *et al*., 2008), antioxidant (Manandhar *et al*., 2019), anti-inflammatory (Hannan *et al*., 2020a; Souza *et al*., 2020), anti-fungal (Righini *et al*., 2019), anti-bacterial (Bhuyar *et al*., 2020), and neuroprotective activities (Zhou *et al*., 2019; Hannan *et al*., 2020b). A large proportion of phenolic compounds such as bromophenols (**Figure No. 2 – xii**), flavonoids, phenolics acids, phenolic terpenoids, and mycosporine-like amino acids are present in green and red seaweeds (Cotas *et al*., 2020) whereas, on other hand, the phlorotannins (**Figure No. 2 – xiii**) are the major polyphenolic phytochemicals found in the marine brown seaweeds (Manandhar *et al*., 2019). These phytochemicals are considered as secondary metabolites since they act as protective agents in response to different stimuli and as key players involved in defensive mechanisms against herbivory and UV radiation (Manandhar *et al*., 2019). The phytoconstituents as for example, colpol (**Figure No. 2 – xiv)** isolated from red sea algae *Colpomenia sinuosa* exhibits cytotoxicity towards different cancer cell lines (Monla *et al*., 2020). The brown algae namely *Ecklonia* species and *Ishige okamurae* have been evaluated for their phlorotannin contents (Yang *et al*., 2018). Eckol (**Figure No. 2 – xv**), a precursor compound illustrating the dibenzo-1,4-dioxin class of phlorotannins, contains phloroglucinol components linked to each other in multiple fashions. Eckol and dieckol were also examined for their radioprotective activity in intestinal stem cells (reference). Moon *et al*. (2008) pre-treated gamma-irradiated mice (3.5 days irradiation (8 Gy)) with phloroglucinol (crypts per circumference 43.73 ± 15.87) and eckol (crypts per circumference 32.08 ± 17.96) and observed a remarkable increase in the jejunal villi height (n = 6 per group) when compared with the irradiated controls (crypts per circumference 8.6 ± 1.7). The researchers suggested the role of both phloroglucinol and eckol in improving the survival rate of the jejunal crypt in irradiated mice (Moon *et al*., 2008).

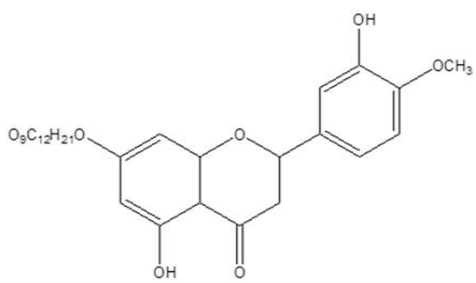
Natural products encompass enormous bioactivities and are examined for their ability to provide health benefits. Nevertheless, various reports on phytochemicals have proved their potential effects and roles against infectious and non-infectious diseases and disorders. Therefore, screening of plants and phytochemicals offers a major avenue towards new drug discovery and drug development. With this backdrop, attention over the past 20 years has shifted towards the evaluation of plant products as promising radioprotective drug candidates. Besides the above discussed radioprotective plants and natural products, there are many other plants available that possess radioprotective potentiality in mitigating a number of radiation triggered damages, not only in mammalian systems but also in various animal models. Hence, these plants provide an insight into being considered as natural radioprotectors in future days to come. Therefore, systematic isolation of phytochemicals or bioactive compounds requires greater attention in those plants showing commitment towards radioprotection and future candidature as an alternative to cancer radiation therapy.



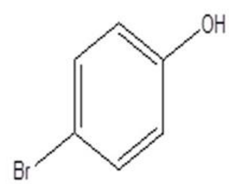
(ix) Quinic Acid



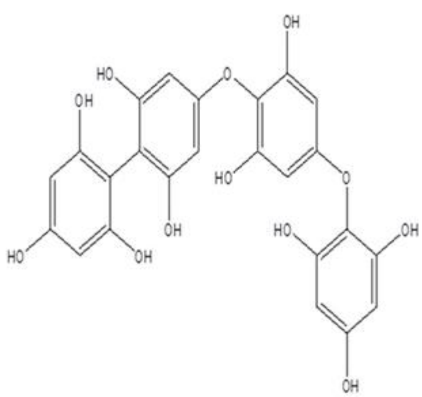
(x) Chlorogenic Acid



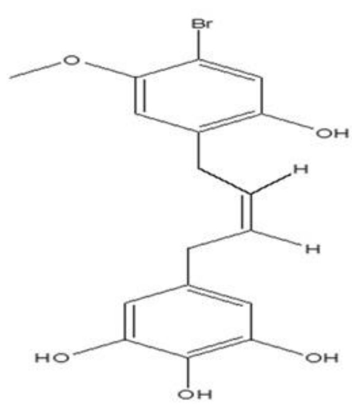
(xi) Hesperidin



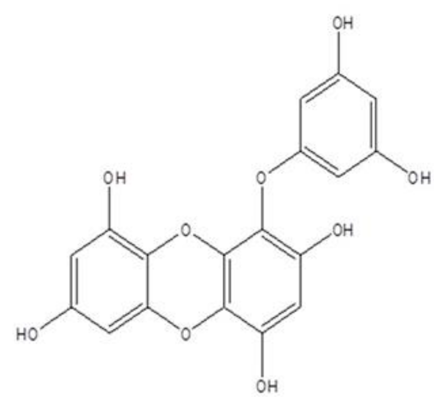
(xii) Bromophenol



(xiii) Phlorotannin



(xiv) Colpol



(xv) Eckol

Cont. Figure No. 2
Chemical structure of natural products (ix – xv) that possesses radioprotective properties

Limitations of orthodox cancer adiotherapy: An introduction to integrative oncology

Cancer radiotherapy is a treatment that uses high energy waves to kill cancerous cells within a tumor and shrink them. Apart from killing cancer cells, the surrounding normal cells also get exposed to radiation from where their side effects originate. The intensity and time of the radiation and the area being exposed to the rays determine the degree of side effect. Usually cancer associated with head, neck, cervix, breast, prostrate, retina have been reported to get cured through this therapy (Arruebo *et al*., 2011). However, this therapy is very expensive. Side effects associated with radiation therapy include fatigue, redness of skin, as well as the chances of developing second cancer, which though very uncommon usually depends on the intensity of radiation and age of the patient. Other side effects include nausea, headache, vomiting, sleep disturbances, diarrhoea, and constipation (Metri *et al*., 2013). The limitations of radiation therapy also include its inability to kill all cancerous cells within a tumor and many other associated side effects which ultimately create panic among cancer patients disturbing their mental state further leading to depression and mental disorders.

Therefore, we should aim for an integrated or combinatorial approach that can alleviate the side effects associated with cancer and can add days to the patient's life improving their mental well-being. This idea has led to the introduction of an approach called 'Integrative Oncology' that focusses on the combinatorial usage of both traditional CAM and conventional radiotherapy in order to ameliorate the mental and health status of cancer patients. Reports suggest that almost half of the cancer patients worldwide are using CAM for their cancer treatments, and the incidence of using CAM worldwide has increased from 25 percent in 1970 to around 49 percent after 2000 (Horneber *et al*., 2012). Very few literatures are available that highlights on the possible use of CAM in combination with conventional cancer radiotherapy to treat patients suffering from cancer and associated disorders (Deng & Cassileth 2014). According to the classification proposed by Rosenthal and Clower (2005), and Cramer *et al*. (2013), CAM in cancer care can be classified as (i) Alternative medical systems that includes Ayurveda, Unani, Siddha, Homeopathy (ii) Medicines providing energy that includes Reiki (iii) practices related to biological importance that includes naturopathy (iv) practices on body and manipulation that includes Ayurvedic massage (v) Medicine based on mind and body.

Table No. 1

List of plants exhibiting radioprotective efficacy and anticancer potentiality has been presented along with their respective family, radioprotective and anti-cancerous uses and recommended doses of plant extract. Gy – Gray, GSH – Glutathione, MDA – Malondialdehyde, SOD – Superoxide dismutase, GPT – Glutamic pyruvic transaminase, GOT – Glutamic oxaloacetic transaminase, EAC - Ehrlich ascites carcinoma. (* indicates – not reported or no information available)

Serial No.	Plants with radioprotective properties	Family	Radioprotective and/or anti-cancer uses	Ionising radiation dose	Plant extract dose	Reference
1	*Aegle marmelos* (L.) Corrêa	Rutaceae	Radioprotective activity of hydro-alcohol extract of leaves in mouse models	10 Gy of gamma radiations	15 mg/kg body weight	Jagetia *et al*. (2004)
			Radioprotective activity of hydro-alcohol extract of fruits in mouse models	10 Gy of gamma radiations	20 mg/kg body weight	
2	*Justicia adhatoda* L.	Acanthaceae	Radioprotective activity with significant reduction in chromosomal aberrations along with minimal damage to	8 Gy of gamma radiations	800 mg/kg body weight	Kumar *et al*. (2007)

			architectural features in radiation induced testis of Swiss albino mice			
3	*Allium cepa* L.	Amaryllidaceae	Radioprotective activity evaluation along with monitoring of GSH, MDA, SOD, GPT, GOT, testosterone levels in both serum and tissues in Swiss Albino mouse models	10 Gy of gamma radiations	200 mg/5mL/kg/day	Ammar (2016)
4	*Andrographis paniculata* (Burm.f.) Nees	Acanthaceae	Radioprotective and anti-neoplastic activity evaluation on transformed BALB/3T3 cell model with reduction in radiation induced DNA damaged cells	*	*	Nantajit *et al*. (2017)
5	*Centella asiatica* (L.) Urban	Apiaceae	Anti-tumor potentiality of acetone fraction of methanol extract with inhibition of 50 percent of Dalton's lymphoma ascites	*	22 mg/mL	Babu *et al*. (1995)
			Anti-tumor potentiality of acetone fraction of methanol extract with inhibition EAC cancer cells	*	17 mg/mL	
6	*Curcuma longa* L.	Zingiberaceae	Anticancer potentiality of turmeric during Phase I clinical trials against several cancer cell lines	*	8000 mg/day	Cheng *et al*. (2001)
			Radioprotective activity evaluation along with improved anti-oxidant status in rats along with decrease in radiation triggered escalation of inflammatory cytokines	6.5 Gy of gamma radiations	200 mg/kg body weight	Nada *et al*. (2012)
7	*Ficus racemosa* L.	Moraceae	Radioprotective activity evaluation by monitoring on comet parameters like tail length, percentage of DNA in tail of blood lymphocytes that	6 Gy electron beam radiations	400 mg/kg body weight	Vinutha *et al*. (2015)

			were initially found to increase after radiation exposure.			
8	*Gingko biloba* L.	Gingkoaceae	Radioprotective efficacy of plant extract in ameliorating the radioactive 99m-technetium sestamibi induced oxidative damage in organs of Wistar rats	*	*	Khedr *et al*. (2018)
9	*Hippophae rhamnoides* L.	Elaeagnaceae	Radioprotective potentiality in mice by around 80 percent	10 Gy of gamma radiations	25-35 mg/kg body weight	Agrawala and Goel (2002)
10	*Mentha arvensis* L.	Lamiaceae	Radioprotective potentiality of the chloroform extract in mouse models	*	10 mg/kg body weight	Baliga (2002)
11	*Ocimum tenuiflorum* L.	Lamiaceae	Comparative study of radioprotective potentiality of flavonoid orientin and radioprotective chemical amifostine in mouse models	2 Gy of gamma radiations	50 mg/kg body weight	Pattanayak *et al*. (2010)
12	*Phyllanthus emblica* L.	Phyllanthaceae	Radioprotective potentiality of aqueous extract of fruit pulp of the plant in Swiss albino mice	9 Gy of gamma radiations	100 mg/kg body weight	Singh *et al*. (2005)
13	*Syzygium cumini* (L.) Skeels	Myrtaceae	Radioprotective potentiality of leaf extract with significant reduction in micronuclei formation when treated on radiation induced peripheral bool lymphocytes of human cells	3 Gy of gamma radiations	100 µg/ml	Jagetia and Baliga (2002b)
			Radioprotective potentiality of hydro-alcohol extract of seeds with reduction in radiation induced sickness and death in mice	10 Gy of gamma radiations	80 mg/kg body weight	Jagetia *et al*. (2005b)
14	*Tinospora cordifolia* (Thunb.) Miers.	Menispermaceae	Radioprotective potentiality with 76.3 percent survivality chances in male mice along with protection against spleen colony forming units, micronuclei formation,	2 Gy of gamma radiations	200 mg/kg body weight	Goel *et al*. (2005)

			haematological parameters and cell cycle progression			
15	*Vanilla planifolia* Jacks. Ex Andrews	Orchidaceae	Radioprotective ability of the plant extract by supressing chromosomal abnormalities induced due to X-ray irradiation both in V79 cells and mice; protection against micronuclei formation in V79 cells	* (used X rays)	*	Keshava *et al*. (1998); Sasaki *et al*. (1990)

Conclusion and Future Perspectives

The presence of different phytochemicals has given plants their inherent ability to combat different kinds of human diseases thereby paving the way for an alternative to conventional treatments. Most of the plants discussed above have been found to possess abundant flavonoids and phenolics which make them radioprotective and potent anticancer agents. The medicinal plant *Ocimum sanctum* L. (family- Lamiaceae), which is almost found in every household in India is an excellent example of a radioprotective plant that is currently at the preclinical trial stage (Jamshidi & Cohen, 2017). The flavonoid orientin isolated from this plant has been shown to possess radioprotective efficacy comparable to the radioprotective chemical amifostine. Besides these, the plants discussed in this review are mostly present around us and possesses both radioprotective and anticancer properties. Our mother Earth is a home to a large number of medicinal plants and special attention is required to investigate the radioprotective and anticancer potentiality of these plants, which we see every day, but are unaware of their strength towards curing deadly diseases. These can become alternatives to conventional cancer radiotherapy treatments all over the world, which might be accessible to even poorer sections of the society, suffering from cancer, who are still not capable of accessing modern cancer treatment due to its high cost. A combinatorial approach of CAM along with conventional cancer treatment play an important role in palliative management of cancer that has given rise to a concept of Integrative Oncology which mostly relies on ethnic medicines. More focus is required for conducting research activities along with courses, workshops and conferences for conventional physicians regarding CAM and conventional medicines. The motto of Integrative Oncology is not just to make cancer patients exist in the world but to make them live with a positive mental attitude towards combating such a deadly disease.

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REFERENCES

Agrawala PK, Goel HC. 2002. Protective effect of RH-3 with special reference to radiation induced micronuclei in mouse bone marrow. **Indian J Exp Biol** 40: 525 - 530.

Ammar AA. 2016. Use of onion and curcumin as radioprotectors against ionizing radiation induced hepato-testicular alterations in rats. **Egyp J Hosp Med** 65: 468 - 473. **https://doi.org/10.12816/0033754**

Aparicio T, Baer R, Gautier J. 2014. DNA double-strand break repair pathway choice and cancer. **DNA Repair** 19: 169 - 175. **https://doi.org/10.1016/j.dnarep.2014.03.014**

Arivalagan S, Thomas NS, Kuppusamy T, Namashivayam N. 2015. Radioprotective effect of carvacrol against X-radiation-induced cellular damage in cultured human peripheral blood lymphocytes. **J Environ Pathol**

Toxicol Oncol 34: 263 - 275. **https://doi.org/10.1615/jenvironpatholtoxicoloncol.2015013548**

Arora R, Gupta D, Chawla R. 2005. Radioprotection by plant products: present status and future prospects. **Phytother Res** 19: 1 - 22.

Arruebo M, Vilaboa N, Sáez-Gutierrez B, Lambea J, Tres A, Valladares M, González-Fernández A. 2011. Assessment of the evolution of cancer treatment therapies. **Cancers (Basel)** 3: 3279 - 3330. **https://doi.org/10.3390/cancers3033279**

Babu TD, Kuttan G, Padikkala J. 1995. Cytotoxic and anti-tumor properties of certain taxa of Umbelliferae with special reference to *Centella asiatica* (L.) Urban. **J Ethnopharmacol** 48: 53 - 57. **https://doi.org/10.1016/0378-8741(95)01284-k**

Baliga MS, Rao S. 2010. Radioprotective potential of mint: A brief review. **J Can Res Ther** 6: 255 - 262. **https://doi.org/10.4103/0973-1482.73336**

Baliga MS, Rao S, Rai MP, D'souza P. 2016. Radio protective effects of the Ayurvedic medicinal plant *Ocimum sanctum* Linn. (Holy Basil): A memoir. **J Can Res Ther** 12: 20 - 27. **https://doi.org/10.4103/0973-1482.151422**

Baselet B, Sonveaux P, Baatout S, Aerts A. 2019. Pathological effects of ionizing radiation: endothelial activation and dysfunction. **Cell Mol Life Sci** 76: 699 - 728. **https://doi.org/10.1007/s00018-018-2956-z**

Baskar R, Lee KA, Yeo R, Yeoh KW. 2012. Cancer and radiation therapy: current advances and future directions. **Int J Med Sci** 3: 193 - 199. **https://doi.org/10.7150/ijms.3635**

Bhanot AR, Noolvi MN. 2011. Natural sources as potential anti-cancer agents: a review. **Int J Phytomed** 3: 9 - 26.

Bhuyar P, Rahim MHA, Sundararaju S, Ramaraj R, Maniam GP, Govindan N. 2020. Synthesis of silver nanoparticles using marine macroalgae *Padina* sp. and its antibacterial activity towards pathogenic bacteria. **Beni-Suef Univ J Basic Appl Sci** 9: 3. **https://doi.org/10.1186/s43088-019-0031-y**

Benkovic V, Knezevic A, Dikic D. 2008. Radioprotective effects of propolis and quercetin in gamma-irradiated mice evaluated by the alkaline comet assay. **Phytomedicine** 15: 851 - 858. **https://doi.org/10.1016/j.phymed.2008.02.010**

Bourhis J, Rosine D. 2002. Radioprotective effect of amifostine in patients with head and neck squamous cell carcinoma. **Semin Oncol** 29: 61 - 62. **https://doi.org/10.1053/sonc.2002.37349**

Brunetti C, Di Ferdinando M, Fini A, Pollastri S, Tattini M. 2013. Flavonoids as antioxidants and developmental regulators: relative significance in plants and humans. **Int J Mol Sci** 14: 3540 - 3555. **https://doi.org/10.3390/ijms14023540**

Bryant AK, Banegas MP, Martinez ME, Mell LK, Murphy JD. 2017. Trends in radiation therapy among cancer survivors in the United States, 2000–2030. **Cancer Epidemiology, Biomarkers & Prevention**. **https://doi.org/10.1158/1055-9965.EPI-16-1023**

Budavari S, O'Neil MJ, Smith A, Heckelman PE. 2006. **The Merck index - an encyclopedia of chemicals, drugs and biologicals** 14th Ed. Whitehouse Station New Jersey, Merck and Co. Inc, New Jersey, USA.

Carsten RE, Bachand AM, Bailey SM, Ullrich RL. 2008. Resveratrol reduces radiation-induced chromosome aberration frequencies in mouse bone marrow cells. **Radiat Res** 169: 633 - 638. **https://doi.org/10.1667/rr1190.1**

Cassatt D, Fazenbaker C, Bachy CM, Hanson MS. 2002. Preclinical modelling of improved amifostine (Ethyol) use in radiation therapy. **Semin Radiat Oncol** 12: 97 - 102. **https://doi.org/10.1053/srao.2002.31382**

Chawla RR, Arora S, Singh RK. 2007. Radioprotective and antioxidant activity of fractionated extracts of berries of *Hippophae rhamnoides*. **J Med Food** 10: 101 - 109. **https://doi.org/10.1089/jmf.2006.007**

Cheng AL, Hsu CH, Lin JK. 2001. Phase I clinical trial of curcumin, a chemopreventive agent, in patients with high-risk or premalignant lesions. **Anticancer Res** 21: 2895 - 2900.

Cinkilic N, Cetintas SK, Zorlu T. 2013. Radioprotection by two phenolic compounds: chlorogenic and quinic acid, on X-ray induced DNA damage in human blood lymphocytes *in vitro*. **Food Chem Toxicol** 53: 359 - 563. **https://doi.org/10.1016/j.fct.2012.12.008**

CNSC. 2019. **A report on types and sources of radiation**. **Http://nuclearsafety.gc.ca/eng/resources/radiation/introduction-to-radiation/types-and-sources-of-radiation.cfm**

Cotas J, Leandro A, Monteiro P, Pacheco D, Figueirinha A, Gonçalves AAM, Silva GJD, Pereira L. 2020. Seaweed phenolics: From extraction to applications. **Mar Drugs** 18: 384. **https://doi.org/10.3390/md18080384**

Cramer HL, Cohen GD, Witt CM. 2013. Integrative oncology: best of both worlds - theoretical, practical, and research issues. **Evid Based Compl and Alt Med** 38: 31 - 42. **https://doi.org/10.1155/2013/383142**

Davari HF, Haddad A, Moghimi M, Rahimi F, Ghavamnasiri MR. 2012. Study of radioprotective effect of green tea against gamma irradiation using micronucleus assay on binucleated human lymphocytes. **Iran J Basic Med Sci** 15: 1026 - 1031.

Deng G, Cassileth B. 2014. Integrative oncology: An overview. **Am Soc Clin Oncol Educ Book** 233 - 242.

Desouky O, Ding N, Zhou G. 2015. Targeted and non-targeted effects of ionizing radiation. **J Radiat Res App Sci** 8: 247 - 254. **https://doi.org/10.1016/j.jrras.2015.03.003**

Dillard CJ, German JB. 2000. Phytochemicals: Nutraceuticals and human health. **J Sci Food Agric** 80: 1744 - 1756. **https://doi.org/10.1002/1097-0010(20000915)80:12<1744::aid-jsfa725>3.0.co;2-w**

FAO. 2019. **Status of medicinal plants in India**. **http://www.fao.org/3/ad871e/ad871e09.htm**

Firouzi F, Khoei S, Mirzaei HR. 2015. Role of resveratrol on the cytotoxic effects and DNA damages of iododeoxyuridine and megavoltage radiation in spheroid culture of U87MG glioblastoma cell line. **Gen Physiol Biophys** 34: 43 - 50. **https://doi.org/10.4149/gpb_2014023**

Goel HC, Prasad J, Singh S. 2004. Radioprotective potential of an herbal extract of *Tinospora cordifolia*. **J Radiat Res** 45: 61 - 68.

Goel HC, Gupta D, Gupta S, Garg AP, Bala M. 2005. Protection of mitochondrial system by *Hippophae rhamnoides* L. against radiation-induced oxidative damage in mice. **J Pharm Pharmacol** 57: 135 - 143. **https://doi.org/10.1211/0022357055218**

Haddadi G, Abbaszadeh A, Mosleh-Shirazi MA, Okhovat MA, Salajeghe A, Ghorbani Z. 2018. Evaluation of the effect of hesperidin on vascular endothelial growth factor gene expression in rat skin animal models following cobalt-60 gamma irradiation. **J Cancer Res Ther** 14: S1098 - S1104. **https://doi.org/10.4103/0973-1482.202892**

Hannan MA, Sohag AAM, Dash R, Haque MN, Mohibbullah M, Oktaviani DF, Hossain MT, Choi HJ, Moon S. 2020a. Phytosterols of marine algae: Insights into the potential health benefits and molecular pharmacology. **Phytomedicine** 69: 153201. **https://doi.org/10.1016/j.phymed.2020.153201**

Hannan MA, Dash R, Haque MN, Mohibbullah M, Sohag AAM, Rahman MA, Uddin MJ, Alam M, Moon IS. 2020b. Neuroprotective potentials of marine algae and their bioactive metabolites: pharmacological insights and therapeutic advances. **Mar Drugs** 18: 347. **https://doi.org/10.3390/md18070347**

Horneber M, Bueschel G, Dennert G, Less D, Ritter E, Zwahlen M. 2012. How many cancer patients use complementary and alternative medicine: A systematic review and meta-analysis. **Integr Cancer Ther** 11: 187 - 203. **https://doi.org/10.1177/1534735411423920**

Hosseinimehr SJ. 2007. Trends in the development of radioprotective agents. **Drug Discov Today** 12: 794 - 805. **https://doi.org/10.1016/j.drudis.2007.07.017**

Jagetia GC. 2007. Radioprotective potential of plants and herbs against the effects of ionizing radiation. **J Clin Biochem Nutr** 40: 74 - 81. **https://doi.org/10.3164/jcbn.40.74**

Jagetia GC, Baliga MS. 2002a. Influence of the leaf extract of *Mentha arvensis* Linn. (mint) on the survival of mice exposed to different doses of gamma radiation. **Strahlenther Onkol** 178: 91 - 98. **https://doi.org/10.1007/s00066-002-0841-y**

Jagetia GC, Baliga MS. 2002b. *Syzygium cumini* (Jamun) reduces the radiation-induced damage in the cultured human peripheral blood lymphocytes: a preliminary study. **Toxicol Lett** 132: 19 - 25. **https://doi.org/10.1016/s0378-4274(02)00032-2**

Jagetia GC, Venkatesh P, Baliga MS. 2004. Evaluation of the radioprotective effect of bael leaf *Aegle marmelos* extract in mice. **Int J Radiat Biol** 80: 281 - 290. **https://doi.org/10.1080/09553000410001679776**

Jagetia GC, Venkatesh P, Baliga MS. 2005a. *Aegle marmelos* (L.) Correa inhibits the proliferation of transplanted Ehrlich ascites carcinoma in mice. **Biol Pharm Bull** 28: 58 - 64. **https://doi.org/10.1248/bpb.28.58**

Jagetia GC, Baliga MS, Venkatesh P. 2005b. Influence of seed extract of *Syzygium cumini* (Jamun) on mice exposed to different doses of gamma-radiation. **J Radiat Res** 46: 59 - 65. **https://doi.org/10.1269/jrr.46.59**

Jagetia G, Rao K. 2018. Hesperidin treatment abates radiation-induced delay in healing of deep cutaneous excision wound of mice hemi-body exposed to different doses of γ-radiation. **Clin Dermatol Dermatitis** 1: 104.

Jamshidi N, Cohen MM. 2017. The clinical efficacy and safety of Tulsi in humans: A systematic review of the literature. **Evid Based Complement Alternat Med** 2017: 9217567. **https://doi.org/10.1155/2017/9217567**

Jose JK, Kuttan G, Kuttan R. 2001. Antitumor activity of *Emblica officinalis*. **J Ethnopharmacol** 75: 65 - 69.

https://doi.org/10.1016/s0378-8741(00)00378-0
Joshi Y, Jadhav T, Kadam V. 2010. Radioprotective and pharmacological intervention for protection against ionizing radiations: a review. **Int J Intern Med** 8: 1 - 11.
Joy J, Nair CK. 2009. Protection of DNA and membranes from gamma-radiation induced damages by *Centella asiatica*. **J Pharm Pharmacol** 61: 941 - 947. **https://doi.org/10.1211/jpp/61.07.0014**
Kavanagh JN, Redmond KM, Schettino G, Prise KM. 2013. DNA double strand break repair: A radiation perspective. **Antioxid Redox Signal** 18: 2458 - 2472. **https://doi.org/10.1089/ars.2012.5151**
Keshava C, Keshava N, Nath TO. 1998. Protective effect of vanillin on radiation induced micronuclei and chromosomal aberrations in V79 cells. **Mutat Res** 397: 149 - 159. **https://doi.org/10.1016/s0027-5107(97)00203-0**
Khedr MH, Shafaa MW, Abdel-Ghaffar A, Saleh A. 2018. Radioprotective efficacy of *Ginkgo biloba* and *Angelica archangelica* extract against technetium-99m-sestamibi induced oxidative stress and lens injury in rats. **Int J Radiat Biol** 94: 37 - 44. **https://doi.org/10.1080/09553002.2018.1407463**
Kumar M, Samarth R, Kumar M, Selvan SR, Saharan B, Kumar A. 2007. Protective effect of *Adhatoda vasica* nees against radiation-induced damage at cellular, biochemical and chromosomal levels in Swiss Albino mice. **Evid Based Complement Alternat Med** 4: 343 - 350. **https://doi.org/10.1093/ecam/nel098**
Kumar RA, Sridevi K, Kumar NV, Nanduri S, Rajagopal S. 2004. Anticancer and immunostimulatory compounds from *Andrographis paniculata*. **J Ethnopharmacol** 92: 291 - 295. **https://doi.org/10.1016/j.jep.2004.03.004**
Kumar SS, Ghosh A, Devasagayam TP, Chauhan PS. 2000. Effect of vanillin on methylene blue plus light-induced single-strand breaks in plasmid pBR322 DNA. **Mutat Res** 469: 207 - 214. **https://doi.org/10.1016/s1383-5718(00)00074-7**
Kuruba V, Gollapalli P. 2018. Natural radioprotectors and their impact on cancer drug discovery. **Radiat Oncol J** 36: 265 - 275. **https://doi.org/10.3857/roj.2018.00381**
Kuttan R, Bhanumathy P, Nirmala K, George MC. 1985. Potential anticancer activity of turmeric (*Curcuma longa*). **Cancer Lett** 29: 197 - 202. **https://doi.org/10.1016/0304-3835(85)90159-4**
Lambertini ER, Piva MT, Khan I, Lampronti N, Bianchi M, Gambari R. 2004. Effects of extracts from Bangladeshi medicinal plants on in vitro proliferation of human breast cancer cell lines and expression of estrogen receptor alpha gene. **Int J Oncol** 24: 419 - 423. **https://doi.org/10.3892/ijo.24.2.419**
Lampronti ID, Matello N, Bianchi M, Borgatti E, Lambertini R, Piva S, Jabbar MS, Choudhuri MT, Gambari R. 2003. *In vitro* antiproliferate effects on human tumor cell lines of extract from the Bangladesh medicinal plant *Aegle marmelos* Correa. **Phytomedicine** 10: 300 - 308. **https://doi.org/10.1078/094471103322004794**
Lans C. 2007. Ethnomedicines used in Trinidad and Tobago for reproductive problems. **J Ethnobiol Ethnomed** 3: 13.
Manandhar B, Wagle A, Seong SH, Paudel P, Kim HR, Jung HA, Choi JS. 2019. Phlorotannins with potential anti-tyrosinase and antioxidant activity isolated from the marine seaweed *Ecklonia stolonifera*. **Antioxidants** 8: 240. **https://doi.org/10.3390/antiox8080240**
Manandhar B, Paudel P, Seong SH, Jung HA, Choi JS. 2019. Characterizing eckol as a therapeutic aid: A systematic review. **Mar Drugs** 17: 361. **https://doi.org/10.3390/md17060361**
Materska M, Konopacka M, Rogoliński J, Ślosarek K. 2015. Antioxidant activity and protective effects against oxidative damage of human cells induced by X-radiation of phenolic glycosides isolated from pepper fruits *Capsicum annuum* L. **Food Chem** 168: 546 - 553. **https://doi.org/10.1016/j.foodchem.2014.07.023**
Maurya D, Devasagayam T, Nair C. 2006. Some novel approaches for radioprotection and the beneficial effect of natural products. **Indian J Exp Biol** 44: 93 - 114.
Metri K, Bhargav H, Chowdhury P, Koka PS. 2013. Ayurveda for chemo-radiotherapy induced side effects in cancer patients. **J Stem Cells** 8: 115 - 129.
Monla RA, Dassouki Z, Kouzayha A, Salma Y, Gali-Muhtasib H, Mawlawi H. 2020. The cytotoxic and apoptotic effects of the brown algae *Colpomenia sinuosa* are mediated by the generation of reactive oxygen species. **Molecules** 25: 1993. **https://doi:10.3390/molecules25081993**
Moon C, Kim SH, Kim JC, Hyun JW, Lee NH, Park JW, Shin T. 2008. Protective effect of phlorotannin components phloroglucinol and eckol on radiation-induced intestinal injury in mice. **Phytother Res** 22: 238 - 242. **https://doi.org/10.1002/ptr.2298**

Monig H, Messerschmidt O, Streffer C. 1990. Chemical radioprotection in mammals and in man. In Schere E, Streffer C, Trott KR, Eds. **Radiation exposure and occupational risks**. Heidelberg: Springer, Germany pp 97-143. **https://doi.org/10.1007/978-3-642-83802-6_5**

Mota MBS, Carvalho MA, Monteiro ANA, Mesquita RD. 2019. DNA damage response and repair in perspective: *Aedes aegypti*, *Drosophila melanogaster* and *Homo sapiens*. **Parasites Vectors** 12: 533. **https://doi.org/10.1186/s13071-019-3792-1**

Mun GI, Kim S, Choi E, Kim CS, Lee YS. 2020. Pharmacology of natural radioprotectors. **Arch Pharm Res** 43: 272 - 274. **https://doi.org/10.1007/s12272-019-01194-1**

Nada AS, Hawas AM, Nel D, Amin MM, Elnashar ZY, Abd E. 2012. Radioprotective effect of *Curcuma longa* extract on γ-irradiation-induced oxidative stress in rats. **Can J Physiol Pharmacol** 90: 415 - 423. **https://doi.org/10.1139/y2012-005**

Nantajit D, Jetawattana S, Suriyo T, Grdina DJ, Satayavivad J. 2017. *Andrographis paniculata* diterpenoids protect against radiation-induced transformation in BALB/3T3 cells. **Radiat Res** 188: 66 - 74. **https://doi.org/10.1667/rr14698.1**

Ni Y, Zhao B, Hou J, Xin W. 1996. Preventive effect of *Ginkgo biloba* extract on apoptosis in rat cerebellar neuronal cells induced by hydroxyl radicals. **Neurosci Lett** 214: 115 - 118. **https://doi.org/10.1016/0304-3940(96)12897-4**

Oh JY, Feranando IP, Jeon YJ. 2016. Potential applications of radioprotective phytochemicals from marine algae. **Korean Soc Phycol Algae** 31: 403 - 414. **https://doi.org/10.4490/algae.2016.31.12.1**

Pahadiya S, Sharma J. 2003. Alteration of lethal effects of gamma rays in Swiss albino mice by *Tinospora cordifolia*. **Phytother Res** 17: 552 - 554. **https://doi.org/10.1002/ptr.1156**

Pattanayak PP, Das BD, Panda SK. 2010. *Ocimum sanctum* Linn. A reservoir plant for therapeutic applications: an overview. **Pharmacogn Rev** 4: 95 - 105. **https://doi.org/10.4103/0973-7847.65323**

Prasad NR. Srinivasan M, Pugalendi KV, Menon, VP. 2006. Protective effect of ferulic acid on gamma-radiation-induced micronuclei, dicentric aberration and lipid peroxidation in human lymphocytes. **Mutat Res.** 603: 129 - 134. **https://doi.org/10.1016/j.mrgentox.2005.11.002**

Rajagopal S, Kumar RA, Deevi S, Satyanarayana C, Rajagopalan R. 2003. Andrographolide, a potential cancer therapeutic agent isolated from *Andrographis paniculata.* **J Exp Ther Oncol** 3: 147 - 158. **https://doi.org/10.1046/j.1359-4117.2003.01090.x**

Ranga RS, Sowmyalakshmi S, Burikhanov R, Akbarsha MA, Chendil D. 2005. A herbal medicine for the treatment of lung cancer. **Mol Cell Biochem** 280: 125 - 133. **https://doi.org/10.1007/s11010-005-8518-3**

Righini H, Baraldi E, Fernández GY, Quintana MA, Roberti R. 2019. Different antifungal activity of *Anabaena* sp., *Ecklonia* sp., and *Jania* sp. against *Botrytis cinerea*. **Mar Drugs** 17: 299. **https://doi.org/10.3390/md17050299**

Rosenthal DS, Clower ED. 2005. Integrative medicine in hematology/oncology: benefits, ethical considerations, and controversies. **Hematology Am Soc Hematol Educ Program** 2005: 491 - 497. **https://doi.org/10.1182/asheducation-2005.1.491**

Samarth RM, Kumar A. 2003. *Mentha piperita* (Linn.) leaf extract provides protection against radiation induced chromosomal damage in bone marrow of mice. **Indian J Exp Biol** 41: 229 - 237. **https://doi.org/10.1269/jrr.07052**

Sasaki YF, Ohta T, Imanishi H, Watanabe M, Matsumoto K, Matsumoto K, Kato T, Shirasu Y. 1990. Supressing effects of vanillin, cinnamaldehyde, and anisaldehyde on chromosome aberrations induced by X-rays in mice. **Mutat Res** 243: 299 - 302. **https://doi.org/10.1016/0165-7992(90)90146-b**

Shahidi F, Yeo J. 2018. Bioactivities of phenolics by focusing on suppression of chronic diseases: A Review. **Int J Mol Sci** 19: 1573. **https://doi.org/10.3390/ijms19061573**

Shrivastava SR, Shrivastava PS, Ramasamy J. 2015. Mainstreaming of Ayurveda, Yoga, Naturopathy, Unani, Siddha, and Homeopathy with the health care delivery system in India. **J Tradit Complement Med** 5: 116 - 118. **https://doi.org/10.1016/j.jtcme.2014.11.002**

Singh I, Sharma A, Nunia V, Goyal PK. 2005. Radioprotection of Swiss albino mice by *Emblica officinalis*. **Phytother Res** 19: 444 - 446. **https://doi.org/10.1002/ptr.1600**

Smith CA, Hunter J, Delaney GP, Ussher JM, Templeman K, Grant S, Oyston E. 2018. Integrative oncology and complementary medicine cancer services in Australia: findings from a national cross-sectional survey. **BMC Complement Altern Med** 18: 289. **https://doi.org/10.1186/s12906-018-2357-8**

Sorokina, M., Steinbeck, C. 2020. Review on natural products databases: where to find data in 2020. **J Cheminform** 12: 20. **https://doi.org/10.1186/s13321-020-00424-9**

Souza CRM, Bezerra WP, Souto JT. 2020. Marine alkaloids with anti-inflammatory activity: Current knowledge and future perspectives. **Mar Drugs** 18: 147. **https://doi.org/10.3390/md18030147**

Tiwari V, Wilson DM. 2019. DNA damage and associated DNA repair defects in disease and premature aging. **Am J Hum Genet** 105: 237 - 257. **https://doi.org/10.1016/j.ajhg.2019.06.005**

Vinutha K, Vidya SM, Suchetha NK, Sanjeev G, Nagendra HG, Pradeepa VC. 2015. Radioprotective activity of *Ficus racemosa* ethanol extract against electron beam induced DNA damage *in vitro*, *in vivo* and *in silico*. **Int J Pharm Pharmaceut Sci** 7: 110 - 119.

Vrinda B, Devi PU. 2001. Radiation protection of human lymphocyte chromosomes *in vitro* by orientin and vicenin. **Mutat Res** 498: 39 - 46. **https://doi.org/10.1016/s1383-5718(01)00263-7**

Wan XS, Ware JH, Zhou Z, Donahue JJ, Guan J, Kennedy AR. 2006. Protection against radiation-induced oxidative stress in cultured human epithelial cells by treatment with antioxidant agents. **Int J Radiat Oncol Biol Phys** 64: 1475 - 1481. **https://doi.org/10.1016/j.ijrobp.2005.11.024**

WHO. 2020. **A report on ionising radiation: What is ionising radiation?** **https://www.who.int/ionizing_radiation/about/what_is_ir/en**

Yahyapour R, Shabeeb D, Cheki M, Musa AE, Farhood B, Rezaeyan A, Amini P, Fallah H, Najafi M. 2018. Radiation protection and mitigation by natural antioxidants and flavonoids: Implications to radiotherapy and radiation disasters. **Curr Mol Pharmacol** 11: 285 - 304. **https://doi.org/10.2174/1874467211666180619125653**

Yang HK, Jung MH, Avunje S, Nikapitiya C, Kang SY, Ryu YB, Lee WS, Jung SJ. 2018. Ecacy of algal *Ecklonia* cava extract against viral hemorrhagic septicemia virus (VHSV). **Fish Shellfish Immunol** 72: 273 - 281. **https://doi.org/10.1016/j.fsi.2017.10.044**

Yoshida M, Fuchigami M, Nagao T, Okabe H, Matsunaga K, Takata J, Karube Y, Tsuchihashi R, Kinjo J, Mihashi K, Fujioka T. 2005. Antiproliferative constituents from Umbelliferae plants VII. Active triterpenes and rosmarinic acid from *Centella asiatica*. **Biol Pharm Bull** 28: 173 - 175. **https://doi.org/10.1248/bpb.28.173**

Zhou X, Yi M, Ding L, He S, Yan X. 2019. Isolation and purification of a neuroprotective phlorotannin from the marine algae Ecklonia maxima by size exclusion and high-speed counter-current chromatography. **Mar Drugs** 17: 212. **https://doi.org/10.3390/md17040212**