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Review Article

REVIEW OF PHYTO-MEDICAL EXTRACTS' AND COMPOUNDS' ANTI-RADIATION PROPERTIES

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ABSTRACT

Humans are routinely exposed to radiation when receiving cancer treatment, fighting nuclear weapons, exploring space, and flying. Radiation exposure damages biological components such as protein, lipids, and cell membranes because it causes oxidative stress and inflammatory mediators, which can lead to DNA destruction even at low concentrations. Protecting people from the harmful effects of radiation is a challenging task due to the plethora of side effects of the chemical compounds used to mitigate DNA damage in normal cells. Hospitals continue to utilize radiotherapy for cancer treatment; yet, the adverse effects of the radiation they emit have outweighed the benefits. Plant phytochemicals and their derivatives exhibit diverse biological functions, often perceived as innocuous due to their non-toxic nature within subcellular and cellular environments. Moreover, they possess the capability to mitigate radiation-induced damage. This review aims to delineate the radioprotective attributes of plant polyphenols and extracts, elucidating their mechanisms of action across various models.

Keywords: Ionizing radiation, Radioprotective, Phytochemicals, Plants extracts, Radiotherapy, DNA damage.

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INTRODUCTION

Humans are exposed to radiation on a daily basis as they seek treatment for disease, as well as in nuclear conflicts, industries, and air travel [1]. Ultraviolet (UV) radiation from the sun induces hyperplasia, erythema, edema, sunburn cells, and photocarcinogenesis. Photoaging is caused by UVA (320–400 nm), while UVB (280–320 nm) causes sunburn and skin cancer [2]. Radioimaging aids early patient diagnosis, but ionizing radiation can cause DNA damage, cancer, carcinogenicity, and teratogenicity. X-rays and CT scans expose patients to radio-associated pathology, nucleotide dimerization, and fatal mutations [3,4]. Internal and external risk factors may produce irreversible alterations in DNA structure, which may aid in the onset and advancement of the carcinogenesis process [5]. Radiation has an impact on immune system cells and organs, as well as systemic impacts on proinflammatory cytokines and macrophage phenotypic alterations. Radiotherapy induces acute to chronic complicated toxicities to healthy tissues in close proximity [6,7] leading in long-term alterations such as fibrosis, renal failure, and xerostomia [8]. Radiation causes abnormalities in ROS homeostasis, which causes DNA damage when produced in excess, producing genomic disorganization and hence promoting cancer progression [9]. Although radiotherapy is highly effective and employed in treating nearly 60% of cancer patients, it entails significant adverse effects, such as heart disease, cystitis, infertility, erectile dysfunction, and stenosis. Radiation exposure diminishes testicular germ cells, leading to the onset of azoospermia [10]. Mucositis on the oral mucosa cells is caused by radiotherapy, which is especially common during head-and-neck cancer treatment. Inflammation causes ulceration, edema, and erythema in the oral mucosa [11], which is uncomfortable for the patients. Unlike the detrimental effects of reactive oxygen species (ROS), which can impair the activities of antioxidant enzymes (such as superoxidase, catalase, and glutathione [GSH] peroxidase) in both serum and tissues, radioprotective agents interact with free radicals, enhancing the levels of antioxidant enzymes in serum and tissues, thereby inhibiting their formation [12]. Oxidative stress also produces other harmful compounds such as malondialdehyde (MDA) and protein peroxidants [13]. Chemical compounds employed to safeguard the genomes of normal cells from radiation-induced damage often entail numerous adverse effects. Therefore, researchers are focusing on non-nutritive dietary antioxidants found in foods and plants to enhance therapeutic outcomes [14]. Due to their efficacy and low toxicity, as well as multiple underlying processes in giving protection, plant chemicals have been examined by several researchers and found to confer protective function in several cellular and animal models. During radiotherapy, drugs with radio-mitigating capabilities can be used to protect normal tissues from the negative effects of post-irradiation exposure [15,16]. This review aims to elucidate the radioprotective potential of plant extracts and phytochemicals across various models, along with their underlying mechanisms of action.

PLANT POLYPHENOLS WITH RADIOPROTECTIVE ACTIVITIES

An overview of several plant-derived substances with putative radioprotective qualities, produced from diverse botanical sources, is described in this section. This review addresses the potential effects of these substances on various physiological systems using both *in vitro* and *in vivo* studies. The documented mechanisms of action of these substances on certain target regions, organs, and cellular constituents are compiled in Table 1.

Plumbagin

An effective anti-tumor agent, plumbagin, is a quinone that is present in plants belonging to the *Plumbaginaceae*, *Droseraceae*, *Ancistrocladaceae*, and *Dioncophyllaceae* families. A study evaluated the radioprotective potential of plumbagin to protect normal lymphocytes against radiation-induced apoptosis. The findings indicated that plumbagin provided protection to lymphocytes for up to 4 h following irradiation by preventing DNA fragmentation and preserving mitochondrial membrane potential. However, its efficacy diminished with time. Nonetheless, it did not confer protection against irradiated A549 lung cancer cells [8].

Chrysin

Chrysin (5, 7-dihydroxyflavone), a flavonoid found in honey, honeycomb, and plants, has anti-apoptotic, anti-cancer, antioxidant, and anti-inflammatory properties. In a study on female rats exposed to gamma radiation, Mantawy and Abdel-Aziz found that chrysin enhanced estradiol levels, maintained ovarian weight, reduced TNF-α, and downregulated NF-kβP65 expression, inhibiting apoptotic protein production [10].

Table 1: Radio protective mechanism of plant compounds

Plant compound	Class	Targets	Mechanism of action	Reference
Plumbagin	Quinone	Normal lymphocytes	Inhibiting caspase-3 activity in radiation-induced apoptosis normal cells. Modification of thiol antioxidants in radiation Induced apoptosis normal cells. Modification of thiol antioxidants	[8]
Chrysin	Flavone	Ovary	Reducing the levels of the inflammatory markers NF-κB, TNF-α, iNOS, and COX-2	[10]
Lycopene	Carotenoid	Lymphocytes	Protect DNA damage	[15]
		oral mucosa	Prevention of membrane lipid peroxidation o and free radicals scavenging	[16]
Ginseng	Peptide	Intestinal and immune system	Reducing concentration of plasma LPS and inflammatory cytokines (IL-1 and TNF-α) Reducing oxidative stress Reducing expression of the apoptosis-related proteins (Bax and Caspase-3)	[17]
Genistein	Phytoestrogen	Liver	Protecting liver tissue injury	[18]
Crocin	carotenoid	Liver tissue Pancreatic cancer cells	Restoration liver enzymes near to normal levels Pancreatic tumor remission	[19]
		Hematopoietic cells	Free radical scavenging	[20]
Ursolic acid	pentacyclic triterpenoid	HaCaT cells plasma cells	Attenuates lipid peroxidation and prevented DNA oxidative damage. Down regulating the expression of pro inflammation cytokines (TNF-a, IL-6, and IL-1β) levels. Inactivating NF-kB DNA binding activity. Increasing the counts of hematopoietic cells.	[21]
Jervine	steroidal alkaloids	Liver and intestinal tissues	Lessing intraepithelial inflammation and lymphoid infiltration	[22]
Lutein	carotenoid	Blood, liver, brain, and lungs	Increasing hematological anti-oxidation and anti-peroxidation.	[23]
Rutin Quercetin	flavonoid flavonoid	Human Lymphocytes	Reducing micro nucleated binucleate cells (MNBNC) reducing DNA strand breaks	[26]
Curcumin and Silymarin	curcuminoid	Kidney	Reducing oxidative stress level and blood urea nitrogen (BUN), creatinine, cystatin-C (CYT-C), neutrophils gelatinase-associated lipocalin (N-GAL), and kidney injury molecule-1 (Kim-1) decrease in inflammatory cytokines (interleukin-18, tumors necrosis factor-alpha, and C-reactive protein), Bax protein, and Fas	[28]
		Normal and colon cancer cells.	Restoration of radiation induced-migrarion	[29]
Resveratrol	stilbene	peripheral human blood lymphocytes, CHO-k1and A549 cell	decrease in cell viability	[32]
		Bone marrow	Reduced clastogenic effect	[33]
Thymoquinone	Benzoquinone	Blood	Have effect on sulfide/thiol ratio	[36]
Grape seed proanthocyanidns	Plant pigments	Lung cancer cells	regulation of the MAPK signaling pathway regulated secretion of cytokines IL-6 and IFN-γ and expression of p53 and Ki67	[40]
Amentoflavone	biflavonoid	Blood and bone marrow	Down regulating the expression ofTNFAIP-2 genes	[41]
Pine Cone Polyphenols	Polyphenol	Blood and bone marrow	Maintaining the level of antioxidant enzyme, inhibition of lipid peroxidation, and prevention of DNA damage	[42]
Dosimin	Flavone	Kidney and liver	Oxidative stress inhibition and apoptosis deactivation	[43]
CAPE	polyphenol	Adenocarcinomas and PCLS	Reducing proinflammatory gene expression and NF-κB activity	[44]
p-coumaric acid	polyphenol	Rat Liver	Decreasing ALT and AST, and suppressing BAX	[46]
Baicalein	flavone	Cancer cell lines	Radio sensitizer	[47]
Baicalin	flavone	Spleen RAW264.7 cells	Immunomodulation, anti-inflammatory, and antioxidant	[48]
OrychophragineD	alkaloid	HUVECs, peripheral blood	Improves survival rate and enhances blood cell count	[49]

Lycopene

Tomatoes and other red fruits contain lycopene, a carotenoid with anti-free radical qualities. Research has demonstrated that lycopene can shield human blood cells from X-ray radiation [5]. The radioprotective of lycopen was investigated on mice reticulocytes. After administering different dosages of X-rays and lycopene to the mice, the frequency of micronuclei (MN) in the reticulocytes was comparable to that of control animals [15]. In rats exposed to radiation, lycopene also exhibited antioxidant properties on the oral mucosa. Following treatment, the mucositis in all the rats was reduced, and 75% of the animals given 50 mg/kg of lycopene recovered fully [16].

Ginseng oligopolysaccharide

Panax ginseng is utilized in restorative medicine and possesses anti-oxidative, anti-cancer, immunoregulatory, and anti-diabetic qualities. It also shields mice's intestinal tissue from radiation-induced damage. The study evaluated the radioprotective effects of Ginseng oligopolysaccharide (GOP) on intestinal injury and immune dysfunction in mice. Oral treatment with GOP improved liver and thymus indexes, restored plasma diamine oxidase and membrane lipopolysaccharide levels, and enhanced endogenous antioxidants [17].

Genistein

Genistein is an isoflavone known to have radioprotective property. Genistein's ability to shield mice's livers from damage inflicted by radiation therapy was investigated. The mice were given genistein before the full radiation treatment, and the liver tissues were then graded histopathologically using a light microscope. Genistein shielded the livers of mice from necrosis, resulting in a grade of 0 [18].

Crocin

Crocin is a carotenoid isolated from the dietary herb *Crocus sativus* L (saffron). It has been reported to have several properties such as anti-hyperlipidemic, cardioprotective, anticancer activity hypertensive, and antidepressant properties. Crocin's hepatoprotective activity on irradiated Swiss albino mice was investigated. Results showed that crocin brought the liver enzymes near to normal (GSH-50±0.18 (PBS), 3.33±0.03 (PBS+RT (4 Gy.), and 46.6±0.059 crocin (100 mg/kg body weight)+RT (4Gy [19]. Wang *et al*. research on 4-pentylphenylboronic acid nanodrug of crocin (PBA-Crocin), a nanodrug of crocin, demonstrated its biocompatibility in human umbilical vein endothelial cells (HUVECs) and radioprotective potential in mice exposed to 4 Gy radiations. PBA-Crocin significantly increased white blood cells (WBC) and red blood cells (RBC) counts, and its specific radiation protective effects suggest potential use in acute radiation injury [20].

Ursolic acid (UA)

Numerous herbal plants, including *Rosemarinus officinalis*, *Eugenia jambolana*, and *Ocimum sanctum,* contain UA. UA is a potent antioxidant that lowers blood pressure and inflammation. UA's ability to protect irradiated human epidermal keratinocyte (HaCaT) cells and Blab/c female mice was investigated. After treatment with 10 and 15 mM, the viability of HaCaT-irradiated cells fell considerably and was effectively reversed. UA also reduced ROS and lipid peroxidation levels, decreased interleukin-6 and 1β, tumor necrotic factor-alpha levels, and blocked the binding activity of NF-kB DNA induced by gamma radiation on HaCaT skin cells. UA therapy alleviated the mayelosuppression syndrome in irradiated mice and raised hematopoietic cell numbers [21].

Jervine

Jervine (J) is a steroidal alkaloid isolated from *Veratrum album*, reported to have antitumor antioxidant and anti-inflammatory activities. A study was conducted on Wistar-Albino female rats receiving abdominopelvic irradiation to ascertain the gastrointestinal side effects and protective effect of jervine. Histopathological analysis revealed that mice that were treated with jervine before and after exposure to 8 Gray (Gy) irradiation had low intraepithelial lymphoid infiltration 4.4±1.0, 3.3.4±0.8 compared to RT rats (16.0±2.8) intraepithelial inflammation behaved similarly 2±2.8, 4 (RT) 1.3±1.9, 3 (J+RT), and 0.6±1.1, 2.5 (J+RT+J) [22].

Lutein

Lutein, an antioxidant carotenoid, shields the intestines from anticancer drug-induced damage and accumulates in the skin, guarding against UV-induced oxidative stress. A study on Swiss albino mice investigated lutein's protective effects against electron beam radiation (EBR). Mice were orally given varying lutein concentrations alongside controls. Continuous EBR exposure for 15 days, followed by a critical dose of 10 Gy and a sub-lethal 6 Gy, preceded euthanization. Hematological parameters were assessed, and antioxidant assays were conducted on liver, lung, and brain tissues. Lutein, even at doses up to 20 g/kg, proved safe. EBR reduced WBC counts, while lutein and gallic acid elevated counts significantly. Granulocytes and monocytes increased, whereas lymphocytes decreased compared to controls (p<0.001) [23].

Rutin

Numerous plants, fruits, and vegetables contain the flavonoid rutin. It has been demonstrated to have anti-inflammatory and antioxidant effects in animal studies [24]. The alkaline comet and cytokinesis block micronucleus assays were used to evaluate its defense against radiation-induced DNA damage to human lymphocytes. The findings revealed that 2Gy gamma radiation damaged lymphocyte DNA, resulting in the formation of micronucleated binucleate cells in contrast to non-irradiated and treated lymphocytes, which reduced MN significantly (p<0.01) in a dose-dependent manner, with 25 μg/mL rutin showing the greatest mononuclei reduction (29.9%) among the doses used. The cytokinesis blocked proliferation index increased as rutin doses increased in pre-treated groups, indicating that rutin had an effect on proliferative activity. Rutin at 25 g/mL reduced the proportion of tail DNA (p<0.01) from 26.32–1.97 to 13.92–1.25 while considerably reducing the olive tail moment (P<0.01) from 16–2.67 to 15.77–1.36 [25]. Rutin and iron rutinate were reported by Mammadli *et al*., to reduce chromosomal aberration in onions exposed to 200 Gy gamma radiations [26].

Quercetin (QRT)

QRT, a flavonoid polyphenol with a biphenyl propane structure, was investigated for its protective effects against radiation-induced genetic damage in human lymphocytes. The study assessed comet and MN parameters. Results indicated that at a concentration of 25 μg/mL, QRT significantly (p<0.001) decreased MN compared to the group exposed to radiation alone (78.25±8.84–142.65±3.68). Comet parameters also exhibited a similar reduction (p<0.01). Neutron radiation absorption capacities were measured using a 241 Am-Be 4.5 MeV energy neutron source and a portatif-type Canberra brand BF3 gas neutron detector. Samples were compared with paraffin to evaluate their absorption capability. It was observed that the samples absorbed 31.76% of the dose (1.1094 μSv/h) from the source [26].

Curcumin

Curcumin (1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-Dione) is a polyphenolic diketone derived from the rhizome of turmeric *Curcuma longa* L plants. Curcumin possesses anti-inflammatory, radioprotective to normal cells, and radiosensitizer to cancers, protects the skin [27]. On male albino rats, a study was done to assess its protective impact against kidney radiation-induced damage. The rats were administered with a daily dose of 100 mg/kg for 14 days after receiving an acute dose of 8 Gy gamma radiations for 1 h. The animals were slaughtered the next day, blood was taken, and the kidneys were dissected and homogenized for further examination. MDA, H_2O_2, and AOPP, redox status markers, dropped significantly (41%, 34%, and 34%, respectively) on CUR-treated rats, whereas GSH content and total antioxidant capacity (TAC) increased by 144% and 125%, respectively, when compared to irradiation rats without treatment. Treatment of the irradiated rats with CUR resulted in a significant (p≤0.01) decrease in serum levels of BUN (by 35%), creatinine (by 31%), cystatin-C (by 36 %), N-GAL (by 45%), and Kim-1 (by 45%). Similarly, after treatment with CUR, the injured rats' apoptotic and inflammatory markers dropped dramatically (p≤0.01) [28]. Kim *et al*. discovered that radiation exposure notably decreased the survival and migration capacity of colon cancer cells and also impeded endothelial tube elongation. Treatment with curcumin restored 32% of migrating cancer cells, although it decreased cell viability following radiation exposure. Interestingly, a combination of Rh1 and curcumin amplified cell migration by 54% and enhanced the length of endothelial tubes, implying a synergistic effect between these compounds [29].

Silymarin (SLM)

SLM, a kind of flavonoid, is found in *Silybum marianum*. On male albino rats, a study was done to assess its protective impact against kidney radiation-induced damage. The rats were administered with a daily dose of 100 mg/kg for 2 weeks after receiving an acute dose of 8 Gy gamma radiations for 1 h. On the following day, the animals were sacrificed, blood was drawn and kidneys were dissected and homogenized for further analysis. Redox state markers MDA, H_2O_2, and AOPP decreased significantly(36%, 34%, 34%), respectively, on rats that received SLM and tremendous rise in GSH content and TAC by 135% and 100%, respectively, compared to irradiated rats without treatment. Treatment of the irradiated rats with SLM resulted in a significant (p≤0.01) decrease in serum levels of BUN (by 27%), creatinine (by 28%), cystatin-C (by 35%), N-GAL (by 42%), and Kim-1 (by 43). Similarly, the apoptotic and inflammatory markers of the injured rats decreased significantly ($p \leq 0.001$) upon treatment with SLM [28].

Resveratrol (RSV)

RSV, a naturally occurring trans-stilbene found in raspberries, blackberries, plums, peanuts, blueberries, and red grapes, has a chemical designation of 3, 5, 4'-trihydroxytrans-stilbene [30,31]. A study was undertaken using conventional and hypofractionated techniques to assess its radiomodulatory and genotoxic effects in peripheral human blood lymphocytes, CHO-k1, and A549 cell lines. The A549 cells were subjected to an extra dose of 16Gy X-ray at 300cGy/min, whereas the lymphocytes from non-smoking healthy women (age range, 22–30 years) and CHO-k1 cell lines were treated with 15 µM and 60 µMRSV and exposed to 4 Gy X-rays. Comet assays were used to assess genotoxic damage, while the MTT and Trypan blue exclusion assay were used to assess cell viability. RSV at 60 µM significantly damaged the genomes of CHO-k1 cells and A549 cells. There was no genotoxic effect observed within 15min in both cells neither in the lymphocytes treated with 60 µMRSV [32]. The ability of RSV to protect the genome from extremely low-frequency electromagnetic fields induced clastogenic or mutagenesis effects in mice bone marrow was investigated. When compared to irradiated animals, RSV dramatically reduced the frequency of bone marrow MN [33].

Thymoquinone (TQ)

TQ is the major compound of the black cumin seed (*Nigella sativa*). TQ is a strong antioxidant that inhibits inflammatory mediators and cancer cells from proliferation [34] and has wound healing action [35]. A study was conducted to examine the potential effects of TQ to check on the balancing effect of sulfides homeostasis of irradiated rats and to evaluate its radioprotective effectiveness. TQ treatment showed that disulfide and native thiol to that of total thiol ratio to be significantly different ($p=0.003$) from the sham and irradiated groups [36].

Grape seed proanthocyanidins (GSP)

Condensed tannins, or proanthocyanidins, are present in foods including cereals, tea, and cocoa, chocolate, wine, peanuts, almonds, and barks, as well as in fruits, seeds, flowers, nuts, and barks from different plant kingdoms [37]. GSP has been found to have anti-tumor effects on several cancer cells [38,39]. An investigation was carried out to study that the radioprotective effects of GSP on the normal lung as well as radiosensitizing effects on lung cancer were conducted *in vitro* and *in vivo* using lung cancer cells and tumor-bearing mice models. All the cancer cells and normal cells remained viable on treatment with 20 µg/mL GSP, apoptosis decreased significantly in normal cells treated with GSP and increased in A549 cells while the viability of irradiated normal cells improved significantly but reduced similarly in both lung cancer cells although the difference between the two was not significant. GSP was found to significantly increase the ratio of Bax to BCl-2 after irradiation in A549 cells and decrease the expression of p-JNK and p-P38 protein in normal lung epithelial cells in tumor-bearing mice. GSP also significantly decreased serum interleukin-6 level and increased interferon-γ level compared to tumor mice and irradiated without treatment [40].

Amentoflavone (AMF)

AMF, a bioflavonoid from *Selaginella tamariscina*, has been studied for its radioprotective effect against damage from cobalt-60 gamma irradiation male mice. The study found that male mice (C57BL/6) treated with 6 mg/kg AMF had a high survival rate of 40%. AMF improved hematopoietic cell counts, protecting the system from irradiation. It also decreased MN frequency, while radiation increased it. The study also found that radiation downregulated the expression of the TNFAIP2 gene [41].

Pine cone polyphenols (PP)

Polyphenols from *Pinus koraiensis* have a powerful antioxidant activity that can inhibit oxidative stress inflammatory and related effects such as type 2 diabetes, cancers, radiation-induced damages, and bacterial infections. A study to explore the radiation protection effect of PP coated with chitosan microsphere (PPM) was conducted in a mice model and compared to free PP. Male and female mice were exposed to 6 Gy 60Co-rays and they were administered with PP and PPM intragastrially, they were examined for body weight changes for 15 days, thymus and spleen indices were determined, and bone marrow MN frequency was quantified. The thymus and spleen indices considerably decreased ($p<0.01$) after irradiation and significantly rose ($p<0.05$) in the PP and PPM administered groups; however, the indices in the PP group were lower than those in the PPM group. Administration of PP and PPM, further, protected the mice by restoring the depleted SOD activity caused by radiation, reducing MDA levels, and by inhibiting MN production induced by radiation [42].

Diosmetin 7-O-rutinoside

A flavone called diosmetin 7-O-rutinoside **(**diosmin) is widely distributed in the pericarp of numerous citrus fruits. Diosmin's potential to prevent radioactively exposed rats was investigated. Male Wistar albino rats weighing between 150 and 200 g were given a single gamma radiation treatment of 8Gy or 10Gy fractioned for 5 days at a rate of 0.54 Gy/min after receiving daily doses of 100 or 200 mg/kg diosmin for a month. Liver homogenates were used to determine the level of GSH, TBARS, and SOD while hepatic tissues were used to determine the level of MDA using biodiagnostic assay kits. Results showed that irradiation altered the levels significantly ($p<0.05$) compared to control by 89%, 666%, and 82%, respectively, while diosmin reversed the level by 66%, 55%, and 21%, respectively. Kidney (urea and serum creatinine) and liver (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) injury biomarkers increased significantly on irradiation while administration of diosmin before irradiation of rats improved the injury biomarkers dose-dependently. Irradiation again caused an increase in comet parameters significantly but with diosmin treatment, the parameters reduced significantly ($p<0.05$), thus preventing DNA radiation-induced damage. Furthermore, diosmin prevented DNA damage by inhibiting apoptotic signal caspase 3 [43].

Caffeic acid phenethyl ester (CAPE)

Prades-Sagarra *et al.* evaluated the radioprotective properties of CAPE on lung cancer cell lines and normal tissue. The study found that CAPE may lengthen treatment window by down regulating proinflammatory genes in precision cut lung slices and NF-κB activity in adenocarcinomas [44].

***p-c*oumaric acid (p-CA)**

p-CA (4-hydroxycinnamic acid) is a phenolic compound found to exist naturally in various plants, cereals, fruits, and vegetable with multiple health benefits such as anticancer, anti- diabetes, anti-inflammatory, and antiulcer [45]. The hepatoprotective impact of p-CA on radiation-induced liver damage in male C57BL/6 mice was examined in by Li *et al*. The outcomes demonstrated enhanced hematopoietic function, reduced serum levels of AST and ALT, suppressed expression of the BAX protein, and improved liver shape. The best results were obtained with a dose of 100 mg/kg body weight. Radiation-induced weight loss in mice was reversed and hematological parameters improved with CA administration, suggesting that CA may be able to repair radiation-induced damage [46].

Baicalein

Sisin *et al.* studied baicalein-rich fraction (BRF), Cisplatin (Cis), and Bismuth Oxide nanoparticles (BiONPs) on MCF-7, MDA-MB-231, and NIH/3T3 cell lines with 6 MV photon and 6 MeV electron beams. Combinations of BRF-BiONPs and BRF-Cis-BiONPs were assessed for interactions using the Combination Index. According to the findings, there was less toxicity to NIH/3T3 normal cells and higher toxicity to MCF-7 and MDA-MB-231 breast cancer cells [47].

Baicalin

The active component of Scutellaria root, baicalin (5, 6, 7-Trihydroxyflavone), has been utilized in traditional Chinese medicine to treat fever and asthma. Its bioactivities include anti-inflammatory, anti-tumor, anti-bacterial, and antioxidant. Research on the radioprotective qualities of baicalin *in vitro* revealed that it protects cells from radiation in a concentration-dependent manner. Over 70% of cells died when exposed to 4 Gy radiations, compared to those in the unirradiated and baicalin-treated control groups. Baicalin also improved mouse survival and the number of endogenous spleen colonies. Baicalin's anti-inflammatory qualities were demonstrated by the fact that it decreased the amount of NO released by RAW 264.7 macrophage cells [48].

Orychophragine D

Orychophragine D (extracted from *Orychophragmus violaceus* seeds) was assessed for radiation protection of SPF C57BL male mice and HUVECs. Compared to cells treated with Ex-RAD, the Orychophragine D treated cells exhibited considerably greater survival rates, indicating radioprotective properties. Similar to the positive group, hemoglobin red blood cells and platelets all showed considerable enhancement following irradiation [49].

PLANTS WITH RADIOPROTECTIVE ACTIVITIES

This section provides an overview of different plants from various botanical origins that may have radioprotective properties. Using both *in vitro* and *in vivo* investigations, this review discusses the possible effects of these drugs on different physiological systems. Table 2 compiles the recent plants 'reported modes of action on specific target regions, organs, and or cellular components.

***Chlorophytum borivilian* (CB)**

Ayurvedic medicine uses CB, a member of the *Liliaceae* family, for its antibacterial and anti-inflammatory qualities, as well as its ability to cure cardiac disorders and impotence. The protective effect of CB-derived silver nanoparticles (CB-AgNp) and CB root extract (CBE) against radiation-induced testicular injury was evaluated in a study conducted on fertile male Swiss albino rats. Significant decreases in body and testicular weight were seen with CBE treatment compared to the control group after 7 days of treatment and 6 Gy gamma radiation exposures. CB-AgNp, on the other hand, displayed a less dramatic weight loss. The CB-treated group experienced a progressive drop in sperm count, but the CB-AgNp or combination-treated groups experienced a reverse in sperm count, suggesting possible radioprotective properties [9].

***Aloe barbadensis* miller**

A. barbadensis Miller (family: *Asphodelaceae*/*Liliaceae*) normally referred to as *Aloe vera* ago. Reports in anti-aging [50], immunomodulation, anti-inflammation, antimicrobial, and radioprotection properties of this plant also exist [51,52]. Male Blab/c mice were used to test the anti-radiation efficacy of aloe gel extract against kidney and liver damage. Injury markers together with chromosomal aberration of the heart tissues were assayed on respective homogenates. Results showed a decrease in renal LDH level in the irradiated treated group when compared to the irradiated alone group while the hepatic LDH level remains unchanged. When compared to the untreated group, ROS and LPO levels in the treated group's tissues reduced dramatically ($p \leq 0.001$). The reduced GSH level and SOD activity in hepatic tissue raised in the treated group when compared to untreated irradiated group. The hepatic antioxidant enzymes decreased significantly but renal GSH increased in the treated group when compared to the untreated group ($p \leq 0.05$) [53].

Costus speciosus

C. speciosus is a medicinal herb in India with many pharmacological properties due to its powerful antioxidant activity [54,55]. Research demonstrated that costus has the potential to lower WBC count while boosting ICAM adhesion factor levels. This prompted investigations into its hematological protective effects in rats against gamma radiation. Rats were administered 3.75 g/kg of *C. speciosus* through intraperitoneal injection 1 h before exposure to 7.5Gy gamma radiation. Blood samples were analyzed for hematological changes. The results indicated a significant decrease in all hematological parameters following irradiation ($p<0.05$), while costus administration notably reversed these effects ($p<0.05$), except for MHC levels, which showed no significant difference [56].

***Washingtonia robusta* (EWR) and *Washingtonia filifera* (EWF)**

These plants, belonging to the Arecaceae (Palmae) family and found in tropical and subtropical regions, are mainly used for decoration. Researchers investigated the effectiveness of ethanol extracts from EWR and EWF leaves in protecting the liver from radiation damage. Albino rats were exposed to 7.5Gy radiation and then treated with doses of 100 and 300 mg/kg body weight of the plant extracts. Liver samples were collected and analyzed for levels of MDA and ROS, indicators of oxidative stress. The results showed a significant increase ($p \leq 0.05$) in MDA and ROS levels in rats exposed to radiation compared to the control group. However, treatment with the plant extracts reduced these levels, bringing them closer to normal. The liver/body weight ratio decreased significantly in treated rats compared to the control group. In addition, liver biomarkers such as ALT, cholesterol, and triglycerides showed a significant decrease ($p \leq 0.05$) after treatment, approaching normal levels. Treatment also led to a reduction in the expression of the STING gene [57].

Pterocarpus santalinus

P. santalinus (Family: *Fabaceae*) is a deciduous tree spreading in two hill ranges of the Eastern Ghats of India, Seshachalam and Velikonda. A study investigated the radioprotective effects of *P. santalinus* hydroalcoholic extract (PSHE) against gamma radiation-induced damage by assessing Nrf2 expression. Male BALB/c mice had spleens removed, and splenic lymphocytes were exposed to Cobalt-60 gamma rays. PSHE inhibited membrane lipid peroxidation in a dose-dependent manner (2.5, 5, 10, and 2 μg/mL), protecting cells from DNA damage compared to controls. Plasmid DNA damage was evident, but PSHE restored plasmid DNA integrity dose-dependently, reducing comet parameters significantly ($p<0.001$) and increasing Nrf2 expression. These findings suggest PSHE's potential as a radioprotective agent by mitigating DNA damage through Nrf2-mediated mechanisms [58].

***Psidium guajava* L.**

P. guajava L. (Family: *Myrtaceae*) is an evergreen shrub widely cultivated all over the world. Many disorders and infections such as diarrhea, stomach upsets, diabetes, high blood pressure, ulcers, and itchy scabies rashes can be treated using it [59-61]. Its radioprotective activity was studied in albino Wistar rats. The rats were treated with 200 mg/kg *P. guajava* extract and double-distilled water, irradiated with 4 Gy X-ray at of 3.5Gy/min, killed by dislocation of neck 24 h post-exposure to the last dose of radiation. Blood and liver homogenates were used for various biochemical assays. Results revealed a significant increase in cyclooxygenase-2 (COX-2) levels in the irradiated group compared to the control group. *P. guajava* (200 mg/kg body weight) treatment reduced significantly ($p \leq 0.01$) the COX-2 levels almost equal to the control group compared to DDW+X-ray. A significant decrease of IL-6 ($p \leq 0.05$) and increase of IL-10 ($p \leq 0.01$) levels were observed on treatment with *P. guajava* compared to (DDW+X-ray) group. Red blood cell levels of CAT and SOD decreased significantly on irradiation when compared with control $p \leq 0.01$ and $p \leq 0.05$, respectively. Treatment with *P. guajava* did not show a significant difference in both enzymes, catalase ($p=0.848$), and SOD ($p=0.536$). TBARS and protein carbonyl levels increased significantly when the rats were exposed to 4 Gy radiation, pre-treatment with 200 mg/kg body weight of *P. guajava* reduced the levels to a lesser extent but not significant in comparison with the X-ray-treated group. Bone marrow micronucleus polychromatic erythrocytes in the animals increased significantly ($p \leq 0.001$) on radiation exposure but reduced significantly ($p \leq 0.01$) once pre-treated with 200 mg/kg body weight *P. guajava* 1 h before radiation [62].

***Ilex paraguariensis* (Ip)**

The leaves of Ip have a longstanding history of use by the Guarani Indians for preparing mate, a traditional infusion. This South American plant has attracted considerable scientific attention due to its rich composition of

Table 2: Radioprotective mechanism of medicinal plants

Plant name	Target Organ/tissue	Mechanism	References
Chlorophytum borivilian (CB) Sant	Testicles	Increase sperm count	[9]
Aloe vera	Kidney livers	Radical scavenging action	[53]
Costus speciosus	Blood	Radical scavenging action	[56]
Washingtonia robusta	Liver	Restoring elevated liver index, ALT, albumin, and reactive oxygen species (ROS) levels, and reduction of STING gene expression	[57]
Pterocarpus santalinus	Splenic lymphocytes	Up regulation of Nrf2, HO-1, and GPX-reducing lipid peroxidation levels, IL-6 and TNF-α and increasing GSH levels	[58]
Psidium guajava	Erythrocytes	Regulation of COX-2 IL-6, and IL-10 levels. Improvement of antioxidant enzymes and preventing DNA damage	[62]
Ilex paraguariensis	Yeast cells	Prevention of DNA-induced breakages	[66]
Phoenix dactylifera L	Blood	Anti-oxidation, anti-inflammatory, and reduction of DNA damage	[68]
	Lymphocytes and hepatocytes	Lymphocytes hepatocytes	[69]
Costu safer	Kidney, liver and blood	Improving hematological parameters and decrease body organ weight	[76]
Musa acuminata	Blood	Improving hematological parameters, preventing lipid peroxidation, and up regulating P53 gene expression	[79]
Pycnanthus angolensis	Human lymphocytes	Decreasing micronuclei frequency and increasing survival rate	[81]
Rhodiola crenulata	HaCaT and cancer cell lines	Attenuation of radiation-induced oxidative stress markers, cell apoptosis, MMP levels, and expression of cytokine genes. Down regulating P53 and P21genes.	[85]
Trianthema portulacastrum	Red blood cells	Stimulation of ATPase activities	[90]
	Hepatocytes and murine macrophages	Modifying cellular redox status and prevention of inflammation by restoring Nrf2 transcription factor	[91]
Punica granatum	Human	Preventing mucotitis	[94]
Triticum aestivum	Blood	Anti-lipid peroxidation, antiradical scavenging activity	[3]
Rosmarinus officinalis	CHO cells human peripheral blood lymphocytes	antiradical scavenging activity reduces apoptosis and necrosis	[102,103]
Ferulago angulata	Human blood lymphocytes	Decrease MDA levels, increase of superoxidase , preventing DNA damage	[106,107]
Actinidia deliciosa	Human peripheral blood lymphocytes	antioxidative	[110]
Leea manillenis	Human lymphocytes	Reduction in micronuclei	[113]
Malva sylvestris L	Abdomen	Improved histopathological parameters	[119]
Brownea grandiceps	Rat liver	Reduction of liver enzymes	[121]
Bamboo	human peripheral blood lymphocytes	minimizes chromosomal aberrations	[122]
Olea europaea L. *cv. Caiazzana*	Normal cell and cancer cell lines	Decreased DNA damage in normal cell lines and enhance radiation penetration in cancer cells	[123]
Drymaria Cordata	Mice blood cells	Increased blood cells	[124]
Allium cepa Linn	Renal and blood tissues	Increase antioxidant enzymes and restore renal function	[125]
Mentha-Pulegium	Peripheral blood mononuclear cells	Decreased apoptosis and necrosis, increased survival rate	[126]

phytochemicals such as phenolic compounds, saponins, and methylxanthines [63]. Recent studies have explored its potential anti-obesity properties [64] and antifungal activity [65]. A particular investigation focused on analyzing the effects of Ip extract and its rutin fraction on radiation-induced damage at both cellular and molecular levels, utilizing yeast strains SJR751 and mutant sml1. Cells were cultured and irradiated with 200 Gy 60Co, with or without Ip treatment. Results demonstrated that Ip significantly increased survival fractions of both strains post-irradiation, indicating protection against DNA-induced breakages [66].

Phoenix dactylifera L.

P. dactylifera L commonly known as date palm or Siwa date palm is a cash crop in arid regions of Egypt. Studies were conducted to investigate the protective effect of date syrup against radiation in rats. Sixty male albino rats (200±10 g) were acclimatized to laboratory conditions. They were divided into four groups each containing 15 rats. Group1 (control) was given 1 ml of normal saline solution, group 2 (irradiated) was exposed to one severe dose of 6 Gy and sacrificed after 48 h, group 3 (Date syrup) was given 4 mL/kg body weight of date syrup daily for 28 days, and the last group (irradiated date syrup) was irradiated with the same dose strength, given date syrup by stomach intubation and sacrificed after 48 h. Blood samples were collected for biochemical analysis. Results of irradiation revealed elevated levels of serum ALT, AST, ALP, and LDH and reduced levels of HDL with a significant increase in serum cholesterol, triglycerides, LDL-C, and VLDL-C levels in irradiated rats. Liver MDA was raised and hepatic GSH and catalase depleted. These parameters were significantly reversed ($p \leq 0.05$) in group 3 and group 4 increased DNA strand breakage and DNA-protein crosslink depicted the further impact of radiation DNA damage [67]. In another investigation of Siwa date aqueous extract radioprotection effect, 6-week-old male BalB/C mice aged 20–25 g were acclimatized in laboratory condition and irradiated at 6Gy gamma rays with or without Siwa date aqueous extract of 4 mL/kg body weight. The following assay; cytokinesis-blocked micronucleus, apoptotic, matrix metallopeptidase 9, and tissue inhibitor matrix metalloproteinase (TIMP) 1, proinflammatory cytokines, and MDA were performed. Results revealed that the irradiation increased mean nucleated cells significantly ($p<0.05$) while Siwa dates administration decreased the levels. Radiation exposure increased the number of apoptotic cells; however, no significant difference was observed in the Siwa-irradiated group though the decreased the total aberration significantly when compared to unprotected mice. Regarding the inflammatory cytokines, irradiation raised their level and Siwa dates reduced the cytokine levels significantly ($p<0.05$) when compared to the unprotected group. Finally, the levels of MMP 9 and TIMP 1 in liver samples were elevated on radiation and decreased significantly on administration of Siwa dates before irradiation [68]. Another study by Khezerloo *et al*. [69] showed that rats exposed to gamma radiation (7.5Gy) were able to survive when administered 500 mg/kg of date palm seed extract, which is attributed to the presence of phenolic compounds, tocopherols, and sterols.

Costus afer

C. afer is a perennial rhizomatous monocot distributed in the moist and shady forest belts of Africa, belonging to the family *Costaceae*

[70]. It has been shown to protect against testicular damage induced by lead [71], prevent lipid peroxidation in the liver, kidney, and brain induced by ferrous/ascorbate [72], and exhibit anti-sickling properties [73]. The biological activity may be attributed to the presence of diverse phytochemicals such as terpenoids, alkaloids, cardiac glycosides, phenols, and tannins [74]. However, silver nanoparticles have shown deteriorating effects on kidney and liver biomarkers in Wistar rats [75]. A study was conducted to investigate the radioprotective ability of the *C. afer* plant against whole-body radiation-induced serum and tissue disorder in mice. The animals were irradiated at 3Gy and 6Gy of X-ray at 4000MU/min. Three groups were designated as CAE, CAE-3Gy, and CAE-6Gy were orally administered with 250 mg/kg body weight of *C. afer* 6 days before irradiation. Results revealed a decrease in kidney and liver body mass on irradiation and a slight increase in treated mice. Hematological parameters (RBC, PCV, Hb, WBC, and Neutrophils) decreased significantly (p<0.05) compared to control on irradiation. CAE treatment before irradiation increased PCV, Hb, and WBC significantly (p<0.005) at both 3Gy and 6Gy exposure, neutrophils significantly increased on the 6Gy treated group [76].

Musa acuminata

Banana is a plant from Musa species with several pharmacological activities having antioxidative properties due to the presence of phenolic components [77,78]. Mice were used to test the potential of banana peels as a radioprotectant against gamma radiation damage. A single dose of 3 Gy was administered to mice throughout their entire bodies at a repetition rate of 0.664 rad/S. The animals were grouped as follows: Normal (N), exposed (IR), treated (BPEx), and exposed/treated (IR+BPEx). Treatment was done orally or by tube with ethanol banana peels extract (300 mg/Kg/day) for 3 weeks after which the mice group were exposed to a single dose of 3.0 Gy of γ-rays accordingly. Blood samples were obtained from the decollated mice for hematological investigation. Using the western blotting technique, the level of P53 expression was assessed. All hematological parameters evaluated showed a substantial decline (p<0.05) with the exception of RBCs, which did not significantly vary from the normal groups. The results for, N, IR, BPEx, and IR+BPEx groups, were as follow: 7.50±0.11, 4.77±0.11, 4.77±0.11, 4.77±0.11 (WBC), 4.76±0.11, 13.52±0.11, 4.20±0.11, 4.58±0.1 (RBCs), 14.27±0.11, 36.43±11, 12.41±0.11, and 13.71±0.06 (Hbg), respectively. Irradiation increased the levels of MDA from 0.84±0.01to1.76±0.11, whereas BPEx decreased the MDA levels to 1.28±0.08 group. Furthermore, the peels significantly upregulated P53 gene expression level as compared to the normal and irradiated alone groups [79].

***Pycnanthus angolensis* Warb**

P. angolensis has been used customarily in Africa and many Asia countries to treat various diseases [80,81]. Its extracts have been used in several pharmacological activities such as antibacterial, antiparasitic, anti-inflammatory, analgesic, anti-hemorrhagic agents, antidote against poisons, hyperglycemia, antifertility, and antimycobacterium due to its strong antioxidant potential [80-82]. An investigation of radioprotective and genoprotective capability of *P. angolensis* seed extract (PASE) against x-ray induced damage was carried out in mouse and human lymphocytes. These experiments were carried out on 12-week-old male Swiss albino rats that had been treated and exposed to X-rays 1 week before receiving the extract. The frequency of bone marrow MN was measured after 24 h of 2Gy X-ray exposure at 1.3cGy/s. When compared to the unirradiated control, the frequency of MN rose considerably (p<0.001). PASE treatment reduced MN frequency, indicating that it has anti-genotoxicity properties. *In vitro* tests were carried out with normal epithelial prostatic cell line (PNT2) and mouse metastatic melanoma cell line (B16F10) cell lines, which were exposed to a similar X-ray dose as *in vivo* but for 48 h after PASE treatment. The MTT assay was used to determine the cell survival rate following irradiation. Non-irradiated cells showed a survival range of 95–105% throughout various incubation times, although PASE treatment did not significantly affect cell survival when compared to unirradiated cells [81].

Rhodiola crenulata

R. crenulata plant derivatives are commonly used in Asian herbal medicine, display antioxidant and anti-inflammatory properties. In addition, they have shown antimicrobial activity [83] and can mitigate hypoxia [84]. A recent study investigated its efficacy on normal human skin cells and cancer cells. After exposure to γ-ray radiation, HaCaT cells exhibited a significant decrease in viability compared to the control. However, pre-treatment with *R. crenulata* extract (RCE) significantly protected the cells, with viability ranging from 83% to 89% at varying concentrations. In addition, RCE demonstrated a dose-dependent reduction in intracellular ROS levels and protein carbonyl content. Furthermore, RCE effectively mitigated radiation-induced apoptosis by decreasing apoptotic markers (P53, P21, caspase-3, and caspase-8). Moreover, it attenuated the inflammatory response by reducing levels of proinflammatory cytokines, TNF-α, and IL-6, in a dose-dependent manner [85].

***Trianthema portulacastrum* (TP)**

TP, a natural herb found in Africa and India [86], has demonstrated cardioprotective effects against chemical toxins such as thioacetamide, paracetamol, and carbon tetrachloride (CCl4) by enhancing endogenous antioxidant enzymes [87-89]. In a study investigating TP's protective role in gamma radiation-induced alterations of red blood cell membrane transport markers, TP extracts significantly stimulated ATPase activities compared to the irradiated group [90]. Das *et al*. evaluated the radioprotective and anti-inflammatory effects of TP on hepatocytes and murine macrophages exposed to 4Gy radiation. Results showed reduced lipid peroxidation, cytotoxicity, and cell proliferation. TP extract significantly rescued colony formation and decreased ROS levels [91].

***Punica granatum* (pomegranate)**

Supported by multiple scientific studies, *P. granatum* (pomegranate) extracts have been observed to contain potent phenolic antioxidant compounds suitable for nutraceutical applications, offering benefits to human health [92,93]. Pomegranate extract was studied for radioprotective ability against dermatitis and mucositis induced by radiation in humans with head and neck cancers. The patients were under radiotherapy. One group was given whole pomegranate fruit extract (300 mg) in form of a capsule every day for 6 to 7 weeks after which the skin and its mucosa changes were scored following RTOG criteria from grade 0 to 4. Results showed that four-fifth of the patient in the treated group had less mucositis and dermatitis and at least 90% of the control group had severe mucositis [94].

Triticum aestivum

T. aestivum commonly known as wheatgrass is a natural herb rich in flavonoids, vitamins, and minerals. Due to its richness in antioxidant compounds, several medicinal properties such as anti-inflammatory, anti-carcinogenic, and antibacterial activities have been studied [95-99]. A study to explore the role of *T. aestivum* to attenuate the harmful effects of radiation exposure on rats' lymphocytes was carried out. The whole body of the rats was irradiated with a daily dose of 3Gy for 7 days. Blood samples were drawn, centrifuged and lymphocytes were isolated were utilized for biochemical assays of antioxidant defense system. Radiation exposure raised the MDA and ROS levels significantly and decreased the antioxidant enzyme activities. When the irradiated rats were supplemented with wheatgrass, the antioxidant enzymes increased significantly (p<0.001) and the levels of MDA and ROS decreased similarly when compared to the irradiated rats [3].

***Rosmarinus officinalis* L.**

The therapeutic herb *R. officinalis* L (rosemary) has many health advantages, such as anti-inflammatory, antibacterial, antioxidant, and anticarcinogenic qualities [100]. Strong antioxidant activity in both cultivated and wild forms inhibits acetylcholinesterase and BChE. Extractions have the potential to be used as natural medicines since *in vitro* studies show that they can regulate NF-kB and COX-2, as well as lower the generation of ROS and proinflammatory cytokines [101]. Hasanzadeh *et al.* demonstrated that while the radioprotective effects of rosemary aqueous extract and its nanocomposites of selenium nanoparticles on Chinese Hamster Ovary (CHO) were similar, their combination did not demonstrate a synergistic effect on CHO exposed to different doses of ionization radiation at varying times of 6, 12 and 24 h [102]. Zhaeintan *et al*. investigated the radioprotective properties of rosemary essential oil (R-EO) on human peripheral blood mononuclear cells (PBMCs). They exposed the cells to radiation doses of 25 and 200 cGy in the presence of R-EO and observed a notable increase in cell survival compared to the control group. In addition, the percentages of apoptosis and necrosis in the cells significantly decreased when treated with R-EO, indicating its potential as a radioprotective agent [103].

Ferulago angulata

F. angulata, a plant belonging to the Umbelliferae family, has a number of chemicals with anti-amnesic, antioxidant, antidiabetic, hypolipidemic, larvicidal, and other health advantages [104,105]. Moshafi *et al.* assessed the radioprotective effects of *F. angulata* on human blood lymphocytes. Their findings demonstrated that the 200 μg plant protected the cells from oxidative damage and gene toxicity, as demonstrated by a decrease in MDA and micronuclear frequency and an increase in superoxidase enzyme levels [106]. Similarly, Seyedi *et al*. demonstrated that a bionanocomposites of Chitosan-Co-Silver complex synthesized from *F. angulata* as a reducing agent, decreased MN frequency of human lymphocytes exposed to ionization radiation, possibly due to its antioxidant activity [107].

Actinidia deliciosa

A. deliciosa is also known to be Green Kiwi, kiwi fruit, Chinese. It is distributed throughout the world, especially in eastern Asia. A member of the *Actinidiaceae* family, kiwi fruit, is grown commercially in China, New Zealand, and Italy. It has a wealth of nutrients, vitamins, minerals, and phytochemicals and is well-known for its ability to treat conditions related to the heart, kidney, diabetes, cancer, digestive system, bones, and eyes. Pharmacological characteristics of its constituents include anti-tumor, anti-inflammatory, hypoglycemic, antidiabetic, and antioxidant actions [108,109]. Ribeiro *et al*., demonstrated that 400 μg/mL of freeze-dried kiwi fruit significantly reduces the frequency of chromosomal aberrations caused by phenolic compounds and antioxidant present rather than their quantity, protecting human peripheral blood cells against damage caused by gamma radiation [110].

Leea manillensis

The Vitaceae family plant *L. manillensis* is used medicinally for treating a variety of ailments, including arthritis, stomach-aches, and diarrhea. It is also recognized for its volatile oils. These oils have a variety of uses that are increasing their relevance across a range of industries, such as food and beverage, nutraceuticals, and pharmaceuticals [111,112]. Marasigan *et al*. used micronucleus assay to assess the radioprotective effects of *L. manillensis* extract on human lymphocytes exposed to gamma radiation. Results show a significant decrease in MN, with the highest concentration demonstrating the most substantial reduction, indicating a dose-dependent relationship, highlighting the extract's potential as a radioprotector [113].

***Malva sylvestris* L.**

Native to Europe, Asia, and Africa, *M. sylvestris* (mallow) is a plant that is used in traditional medicine to cure conditions such as sore throats, rashes, peptic ulcers, coughs, and diabetes [114-118]. The radioprotective properties of *M. sylvestris L*. against radiation damage to the abdomen region in mice were assessed by Azmoonfar *et al*. Mallow therapy was administered to the irradiation group for 1 week at doses of 200, 400, and 600 mg/kg daily. Significant improvements were observed in the radiation-induced histological parameters of the liver and kidney based on histopathological examinations. Mallow treatment improved radiation-induced liver fibrosis and kidney damage effectively [119].

Brownea grandiceps

B. grandiceps in recent studies has shown to posse's anti-mycobacterial as well as inflammatory activity [120]. The ability of *B. grandiceps* leaf hydroalcoholic extract (BGE) and ethyl acetate soluble fraction (EAF) to shield rats from enteritis caused by ϒ radiation was investigated. The locomotor activity of irradiated rats did not significantly change, but animals receiving dosages of BGE and EAF exhibited enhanced locomotor activity, according to the results. In addition, the study showed that radiation exposure resulted in acute liver damage, as seen by elevated serum ALT and AST enzyme activity. Serum AST activity was significantly reduced in rats treated with BGE and EAF [121].

Bamboo

Bamboo leaf extracts (BLE) from *Bambusa arundinaceae* (BA), *Bambusa vulgaris* (BV), *Dendrocalamus strictus* (DS), and *Phyllostachys parvifolia* (PP) were assessed for their ability to prevent γ-radiation-induced chromosomal aberrations, specifically dicentric chromosomes (DCs), which are vital for radiation dosimetry, using short-term cultured human peripheral blood lymphocytes. The BLE of all the bamboo species understudy markedly reduced γ-radiation-induced chromosome abnormalities in human peripheral blood over a period of time. At 4 Gy and 6 Gy, genetic damage was decreased by BA and BV extracts, and comparable effects were observed by PP and DS extracts. Reduced complex aberrations were connected with higher extract concentrations. Dicentric chromosomes (DCs) showed a decrease in frequency in all extract-treated cultures, with DS extract showing the greatest reduction. In addition to reducing the frequency of DCs, the extracts also inhibited the production of DCs by preventing DNA oxidation, double-strand breaks, telomere loss, and the degradation of the shelterin complex, which is essential for preserving telomere integrity. Chromosome abnormalities in structure were depicted in photomicrographs [122].

***Olea europaea* L.**

The effect of *O. europaea* (olive leaf extract [OLC]) on the radio-response of normal and cancer cell lines exposed to graded doses of X-rays was assessed, focusing on the modulation of radiation-induced cyto-genotoxicity, particularly DNA damage-associated MN induction in all cell lines and the onset of radiation-induced premature senescence (PS) in one normal cell line**.** The OLC showed distinct radiomodulating effects on both normal and cancer cells. While it significantly reduced radiation-induced damage in normal cell lines (HUVEC and MCF-10A) at a concentration of 12.5 μg/mL, it exacerbated damage in cancer cell lines (DU145 and PANC-1). Furthermore, compared to untreated irradiated samples, which showed accelerated senescence beginning as early as 24 h post-irradiation, OLC delayed the onset of X-ray-induced PS in HUVECs. In addition, OLC significantly decreased the frequency of MN after radiation-induced DNA damage in normal cell lines (MCF-10A and HUVECs), especially at more intense doses (2 Gy and 4 Gy) in HUVECs relative to MCF-10A [123].

Drymaria cordata

Drymaria cordata (DC) (Linn.) Willd, a member of the Caryophyllaceae family, is widely distributed across West and Central Africa, Asia, and America, with its presence spanning diverse regions. A study investigated the potential radioprotective effects of *Drymaria cordata* (DC) extract on irradiated mice. Mice treated with 250 mg of DC extract were exposed to 4 and 8 Gy radiation. The hematological parameters (red blood cell count, hematocrit, leukocyte count, and platelet count) of the mice significantly increased compared to the control group. Administering *Drymaria cordata* extract resulted in a decrease in hematological indicators throughout a 30-day observation period, indicating its potential as a protective agent against radiation-induced hematological damage [124].

***Allium cepa* Linn**

Onion (*A. cepa* Linn) is a highly valued vegetable and field crop with extensive applications in food, medicine, as well as spices and condiments globally over centuries. This study assesses the potential of *A. cepa* (ACE) to protect renal tissues in Wistar rats subjected to total body irradiation at varying doses. Enzyme levels were measured in rats that received ACE therapy and were also subjected to X-ray radiation. In comparison to non-irradiated groups, the results revealed decreased levels of SOD, CAT, GST, and GSH and increased levels of MDA. MDA levels were lowered and SOD, CAT, GST, and GSH levels were raised after ACE treatment. Furthermore, radiation raised the levels of creatinine, urea, and the protein cystatin C, all of which sharply dropped after ACE therapy [125].

Mentha-Pulegium

Hamzian *et al*. conducted research examining the radioprotective properties of *M. Pulegium* essential oil (MP-EO) on PBMCs. At irradiation dosages of 25 and 200 cGy, experiments showed a considerable decrease in necrosis and apoptosis along with a significant increase in survival rates. Furthermore, MP-EO, administered at both doses, reduced the percentage of PBMCs exhibiting necrosis, indicating a potential radioprotective benefit [126].

CONCLUSION

Ionizing and non-ionizing radiation both have major and frequently inescapable consequences on the body. Even with efforts to reduce exposure with medicine, available solutions are still expensive and unsatisfactory. The increase in X-ray procedures carried out for diagnosis and treatment raises questions about radiation exposure. However, numerous plant polyphenols, including carotenoids, flavonoids, steroids, quinones, proanthocyanidins, curcuminoids, stilbenes, phytoestrogens, and triterpenoids, have shown promise in protecting against radiation-induced damage. These compounds exert powerful antioxidative and anti-inflammatory effects, modulating apoptotic markers and safeguarding the central dogma of life from radiation-induced harm. Future research should focus on developing formulations that enhance the synergistic effects of plant compounds, facilitating targeted delivery to organs. Plants offer diverse mechanisms of radioprotection, encompassing radical scavenging, inflammation regulation, antioxidant enhancement, DNA damage prevention, and cellular redox modulation. These mechanisms collectively promote improved hematological parameters, reduced organ weight, mitigated mucositis, decreased lipid peroxidation, chromosomal aberrations, and liver enzyme levels, while also preventing testicular, renal damage, and enhancing histopathological parameters. Further, purification, structural identification, formulation development, and clinical trials are essential steps to harnessing the full potential of plant extracts for radioprotection.

AUTHORS' CONTRIBUTIONS

The authors equally contributed in writing of the review paper.

CONFLICTS OF INTEREST

The authors declared no conflicts of interest.

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