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Impacts of ionizing radiations and protective efficacy of phytochemicals: A review

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Abstract

The ionizing radiations have great impact on living cells and damage caused is owing to the multitude of ultra-fast physical and chemical reactions initiated by radiations. Irradiation of a biological system or exposure to radiation causes catastrophic damage. The ionizing radiations initiate free radical generation which causes damage to lipid membranes of the cell and cell organelles, induces strand breaks in DNA and almost every organ damages. There is devoid of commercially available radioprotectors which neutralizes the reactions caused by radiations and completely shields from the radiation induced damage. From few decades, there is search for novel, nontoxic, economically feasible, socially accessible radioprotectors and during time a large number of plants are screened extensively. The search scientifically proved plants as potent protectors against ailments caused by the radiations both *in vitro* and *in vivo*, therefore providing the scope to use against ailments caused by radiations. The phytochemicals like flavonoids, polyphenols, polysaccharides, Vitamins etc., play a significant role in therapeutic purposes and practiced as an alternative medicine in many Asian countries from time immortal. This article extensively reviews the impact of radiations on living tissue and Radioprotective efficacy of phytochemicals against the ionizing radiations.

Keywords: Ionizing Radiation, Phytochemicals, Radioprotection, Oxidative stress, Free radicals

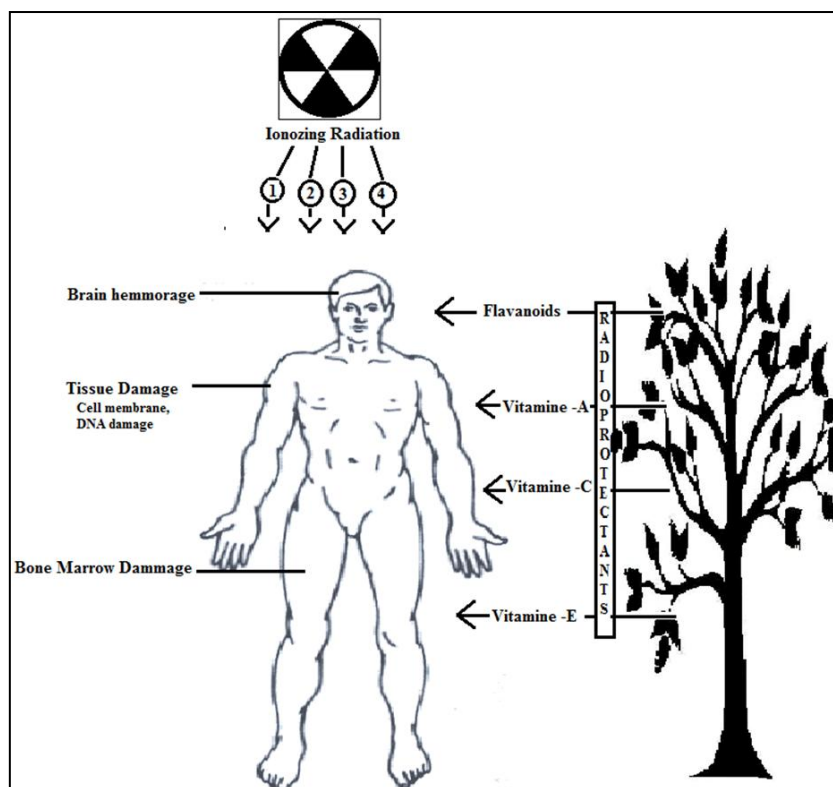
1. Introduction

The ionizing radiations include cosmic rays, gamma rays, X-rays, UV rays of upper vacuum and radiations from radioactive materials. The potential sources of exposure include nuclear power plant disasters such as Chernobyl disaster, Fukushima-Daiichi disasters (Arena C *et al* 2014) [9], chances of using the Nuclear weapons in Wars, highly depending on ionizing radiations in medicine either for diagnosis or treatment (Paul P *et al* 2011) [11, 95], using the radiations for microbial decontamination and to alter physical, chemical properties of foods (Naresh K *et al* 2014) [85]. Every usage or act involved with radiations increases the risk of being exposed either to workers or even the environment. Ionizing radiation at low doses causes a stochastic effect leading to cancers and tissue damage at high doses. Generation of Reactive Oxygen Species (ROS) and formation of free radicals is the most striking effect of radiations on living tissue. DNA damage is the first event immediately after exposure to ionizing radiations followed by cell membrane damage (Tominaga *et al* 2004) [154]. Severity depends on total time of exposure, type of radiation and intrinsic characteristics of the living. A wide range of chemical and synthetic compounds are in practice to shield radiation damage and therefore to provide protection. The WR-2721 [S-2-(3-aminopropylamino) ethyl phosphorothioic acid, amifostine] is the only Food and Drug Administration (FDA, USA) approved Radioprotective drug available which protects the normal tissues against radiation induced damage (Arora R *et al* 2005 [10], Bisht KS *et al* 2000 [14], Shaw L *et al* 1980). The different other chemical and synthetic compounds tested for Radioprotective efficacy include Diethyldithiocarbamate showed protection against γ -radiation to DNA as well as Membrane *in vitro* and *in vivo* (Gandhi NM *et al* 2004). Disulfiram reduced radiation induced cellular lethality and DNA damage may be by scavenging free radicals (Gandhi NM 2003) [28]. Apart from radioprotectors there are radiosensitizers that enhance cells to damage, which can be used to destroy tumor cells. For instance Sanazole (AK-2123) (N-2'-methoxy ethyl)-2-(3''-nitro-1''-triazolyl) acetamide sensitizes the tumour cells and selectively enhances the damage by inducing the Apoptosis (Rajagopalan R *et al* 2003 [105], Raviraj J *et al* 2014) [110]. The usage of chemical radioprotectors is leading to side effects, Nausea, vomiting, diarrhea, hypotension and hypocalcaemia at a therapeutic effective dose (Cairnie 1983 [15], kligerman *et al* 1984 [70], Glover *et al* 1983) [31]. There is a strong need for developing the radioprotectors from natural resources which have nontoxic and socially accessible properties.

Plants are the richest source of many compounds like flavonoids, polyphenols, polysaccharides, alkaloids, Vitamins, tannins and lignin etc., represented as phytochemicals and these compounds played a vital role in scavenging the free radicals and shielding against ailments caused by the ionizing radiations. Plants are proven to be the best alternative remedy against maladies caused by ionizing radiations. Free radical scavenging property, antioxidant property, protecting DNA from strand breaks and lipid membrane from peroxidation are the main attributes for Radioprotective efficacy of phytochemicals. This article reviews the implications of radiations on living tissue and Radioprotective efficacy of phytochemicals.

Effects of ionizing radiations on living cells: The effect of ionizing radiations on living tissue is dependent on various factors like total time of exposure, Source of radiation, distance from radiation and physical, biochemical properties of the living tissue. Whenever radiations strike the living tissue excitation and ionization of atoms and molecules will take place in 10^{-10} Sec. free radical formation occurs within 10^{-6} Sec. if the exposure is for seconds to hours DNA oxidation occurs, leading to DNA breaks, cell death and if cell

survives causes the mutations in genetic material (Citrin D *et al* 2010) [21]. The main effects on DNA include Chromosomal aberrations such as Acentric fragments, Chromatid and chromosome breaks, Centric rings, Dicentrics, DNA strand breaks (Harper JV *et al* 2010) [39] and Micronuclei formation (Jagetia GC and Reddy TK 2002 [49], Jagetia GC *et al* 2003) [53, 55]. The effects on cell and cell organelles are Gastro intestinal injury, Bone marrow injury/damage, Cerebral haemorrhage, Radiation induced increased lipid peroxidation (Agrawal A and Kale RK 2001) [3], Haemopoietic damage, Mitochondrial SOD damage (Bhattacharya S 2006), Hydroxyl radical induced apoptosis, Mucous damage, Decrease in erythrocyte count, leucocyte, thrombocyte count (Firuzi O *et al* 2005) [26], WBC, Decline in GSH, Radiation evoked sickness, Clastogenic and biochemical alterations (Shimoi K *et al* 1996 [130], Emerit I *et al* 1995 [24], Harikumar KBN *et al* 2007) [38], Radiation induced pulmonary fibrosis (R. Shapira *et al* 1957) [123], Protein carbonylation (Daly MJ 2012) [22], Testicular damage/injury (Sharma P *et al* 2011) [126, 161], Hyperplastic response, Radiation elicited free radical formation. This affects the every organ and damages all tissues.



1= Radiations from Sun

2= Nuclear power plant disasters and Nuclear wars

3=use of radiations for diagnosis and treatment

Radioprotective efficacy of phytochemicals: Plants are the richest source of different compounds which are produced as primary or secondary metabolites. A large number of phytochemicals obtained from plant sources have been reported to be Radioprotective in various animal models. Few of phytochemicals studied so far to mitigate the Radioprotective efficacy are: Arabino galactan polysaccharide from *Tinospora cordifolia* (Subramanian M *et al* 2003) [147], Allicin (Jaiswal SK and Bordia A 1996) [58], Alpha-Santalol, [1-oxo-5 beta, 6beta epoxy-with a-2-enolide] (S. Mathur *et al* 2004) [81], Caffein (Vaidya PJ *et al* 2001) [158], Chlorogenic acid (Hosseinimehr SJ *et al* 2008) [44], cinnamic acid (Cinkilic

N *et al* 2014) [20] Hesperidin (Kalpana KB *et al* 2009) [63], Magniferin (Jagetia GC *et al* 2005) [48, 50 54], Morin (Parihar VK *et al* 2007) [91, 99], Oleuropein (Kimura Y and Sumiyoshi M. 2009) [68], Plumbagin (Sand JM *et al* 2012) [119], Sesamol (Parihar VK *et al* 2006) [92, 100], Vitexina (Hien TV *et al* 2002 [41]), and Zingerone (Rao BN *et al* 2009) [108, 8], etc. The studied phytochemicals include polysaccharide fractions, polyphenols, flavonoids, lignins, tannins etc., which are diverse in physical and biochemical properties, but all showed great potential in mitigating the radiation induced damages either *in vitro* or *in vivo* or in both experimental systems.

Table 1

Name of plant	Family	Common name	Radio protective efficacy	Optimum radio protective dose mg/kg b. wt.	Reference
<i>Acanthopanax senticosus</i>	Araliaceae	Siberian ginseng	The extract lowered the frequency of Brain haemorrhage and increased leucocyte count in mice. 80% survival rate pre irradiation administration.	5	Miyanomae. T and Frindel E <i>et al</i> 1988 [83]
<i>Acorus calamus</i> Linn.	Araceae	Sweet flag, Calamus	The water: ethanol, 1:1 fraction of the extract scavenged free radicals, protected DNA from radiation evoked strand breaks and increased the DNA repair process	*	Sandeep D and Nair CKK 2010 [120]
<i>Adhatoda vasica</i> Nees	Acanthaceae	Malabar nut	Leaf extract pretreated irradiated animals exhibited radioprotection by an increase in GSH content and decrease in Lipid Peroxidation (LPO) level. A significant increase in the serum alkaline phosphatase activity and decrease in acid phosphatase activity was also observed. Dose Reduction Factor (DRF) 1.6	800	Kumar A <i>et al</i> 2005 [10, 73, 74]
<i>Aegle marmelos</i> (L.) Correa	Rutaceae	Bel, Beli fruit, stone apple, wood apple, Bengal quince	Administering mice with extract before irradiation reduced the symptoms of radiation sickness and delayed death	15	Jagetia GC <i>et al</i> , 2003 [53, 55] (a)
<i>Ageratum conyzoides</i> Linn.	Asteraceae	Goat weed, Tropical white weed	Alcoholic extract administration one hour pre irradiation protected mice against radiation induced gastrointestinal and bone marrow related death	75	Jagetia GC <i>et al</i> , 2003 [53, 55] (b)
<i>Allium cepa</i> (Linn.)	Alliaceae	Onion	Provided protection against X-ray induced chromosomal aberrations	20	Larsson B and Kihlman BA 1960 [75]
<i>Allium sativum</i> (Linn.)	Alliaceae	Garlic	Pre-treatment with garlic extract before γ -irradiation showed significant dose-related reductions in frequencies of micro nucleated polychromatic erythrocytes; S-allyl cysteine sulphoxide, a sulphur containing amino acid of garlic is the precursor of allicin and has been showed significant radioprotection in albino rats by markedly reducing radiation induced mortality	Dose dependent studies against 125, 250 and 500 *	Singh SP <i>et al</i> 1995 [133]; Jaiswal SK and Bordia A. 1996 [58]
<i>Aloe arborescens</i>	Liliaceae	Krantz aloe, candelbara aloe	Protected skin of mice against soft x-rays by altering enzymes and by hydroxyl radical scavenging	*	Sato Y <i>et al</i> 1990 [121]
<i>Aloe vera</i>	Xanthorrhoeaceae	Aloe vera	Administering the mice with <i>Aloe</i> before γ -Irradiation delayed the onset and reduced the severity of radiation sickness. DRF 1.47; <i>Aloe vera</i> extract treatment pre and post irradiation resulted in protection against radiations by restoring the levels of Fe and Cu in the liver and intestine, intestinal Zn. Protected against oxidative stress	750 300	Saini DK <i>et al</i> 2011 [114] Nada AS <i>et al</i> 2013 [84]
<i>Alstonia scholaris</i>	Apocyanaceae	Blackboard tree, Indian devil tree, Ditebark, Milkwood pine,	Extract oral administering for 5 consecutive days, 30minutes before irradiation provides protection against radiation-induced chromosomal damage and micronuclei induction in the bone marrow of mice	100	Jahan S <i>et al</i> 2010 [57]
<i>Amaranthus paniculatus</i>	Amaranthaceae	Red amaranth	Oral administering the aqueous extract of leaves before irradiation of Swiss albino mice exhibited modulation of radiation induced decrease in reduced glutathione and radiation induced increase in lipid peroxidation with a Dose Reduction Factor of 1.36. ; Absent or less severe symptoms of Diarrhea, ruffled hairs, epilation and facial edema in Rajgira leaf extract treated mice	* 800	Maharwal J <i>et al</i> 2003; Krishna A and Kumar A 2005 [10, 73, 74]
<i>Angelica sinensis</i>	Apiaceae	Dong quai, female ginseng	inhibited the progress of radiation-induced pulmonary fibrosis, Possibly by down-regulating the expression of the pro	*	Zhong YH <i>et al</i> 2007 [165]

			inflammatory cytokine Tgfb1		
<i>Aphanamixis polystachya</i>	Meliaceae	Pithraj tree	Ethyl acetate fractions of plant reduced LPO in bone marrow cells of mice, significantly reduced the frequencies of aberrant cells and chromosomal aberrations	7.5	Jagetiya GC and Venkatesha VA 2006 [56]
<i>Archangelica officinalis</i>	Apiaceae	Mountain angelica	<i>Archangelica officinalis</i> and <i>Ledum palustre</i> caused a significant protection against radiation injuries caused to gastrointestinal tract and haemopoietic system	*	Narimanov AA 1993 [86]
<i>Aspalathus linearis</i>	Fabaceae	Rooibos plant, bush tea	plant flavonoids (Luteolin) showed, anticlastogenic activity, Radioprotective efficacy which may be attributed to its hydroxyl radical scavenging	1 ml	Shimoi K <i>et al</i> 1996 [130]
<i>Asparagus racemosus</i>	Asparagaceae	Satavar, Shatavari, Shatamull	Crude extract and purified aqueous fraction protected against membrane damage induced by free radicals generated by gamma irradiation	10µg/ml	Kamat JP <i>et al</i> 2000 [64]
<i>Azadirachta indica</i>	Meliaceae	Indian Lilac, Neem, Nim tree	Neem leaf extract may exert radio sensitization by activating pro-apoptotic signaling and negating survival signaling	50	Veeraraghavan J <i>et al</i> 2011 [160]
<i>Biophytum sensitivum</i>	Oxalidaceae	Little tree plant, sensitive plant	the protective effect of methanolic extract on Radiation induced hematopoietic damage is mediated through immune modulation as well as sequential induction of IL-1β, GM-CSF and IFN-γ	50	Guruvayoorappan C and Kuttan G. 2008 [35]
<i>Bixa orellana</i>	Bixaceae	Aploppas	Pretreatment with hydro alcoholic extract of seeds protected mice with significant reduction in aberrant metaphases	500 and 1000	Karchuli MS and Ganesh N 2009 [65]
<i>Boerhaavia diffusa</i>	Nyctaginaceae	red spiderling, spreading hogweed and tarvine	Hydro alcoholic extract of plant protected mice against lowering of white blood count ailments due to irradiation	20	Manu KA <i>et al</i> 2007 [79]
<i>Brassica oleracea</i>	Brassicaceae	Cabbage, Broccoli	Provided protection against X- ray induced mortality	*	Spector H and Calloway DH 1959 [143]
<i>Brassica oleracea wild</i>	Brassicaceae	Wild cabbage	Provided protection against UV radiation induced skin carcinogenesis in SKH-1 hairless mice	Extracts and 10µmol of glucoraphanin against 30mJ cm ² of UV-B.	Dinkova-Kostova <i>et al</i> 2010
<i>Caesalpinia digyna</i>	Fabaceae	Teri pod	The extracts from the root exhibited free radical scavenging and radioprotection <i>in vitro</i>	*	Singh U <i>et al</i> 2009 [134, 76]
<i>Camellia sinensis</i>	Theaceae	Tea	The tea flavonoids (-)-Epicatechin and (+)-Catechin presence in solution during gamma irradiation protected the damage of macromolecules probably by scavenging the water radiolysis products	*	Ershov DS <i>et al</i> 2011 [25]
<i>Centella asiatica</i>	Apiaceae	Centella, gotu kola	Oral administration of the extract increased the survival time, reduced body weight loss in irradiated animals The extract significantly reduced the radiation induced damage to DNA	100 *	Sharma J and Sharma R 2002 [124]; Joy J and Nair CK 2009 [62]
<i>Chelidonium majus</i>	Papaveraceae	Greater celandine, swallow wort	Injecting the plant extract increased the number of bone marrow cells, Spleen cells, GM-CFC and platelets in irradiated mice	*	Song JY <i>et al</i> 2003 [141]
<i>Citrus aurantium var. amara</i>	Rutaceae	Bitter Orange, Seville Orange, Sour orange	i.p administration of extract reduced the frequencies of micro nucleated polychromatic erythrocytes and normochromatic erythrocytes.	250	Hosseinimer SJ <i>et al</i> 2003 [43]
<i>Coronopus didymus</i>	Brassicaceae	Lesser swine- cress	Free radical scavenging activity protected mice against radiations	400	Prabhakar KR <i>et al</i> 2006 (a, b, c) [92, 100, 101]
<i>Curcuma longa</i> Linn.	zingiberaceae	Turmeric	Curcumin (Diferuloyl methane) restored the specific activity of glyoxalase system in irradiated mice, probably due to free radical scavenging. Pretreatment with curcumin analog protects the hepatocytes against γ radiation induced cellular damage. Curcumin: copper(II) complex protected against irradiation by reducing the decline in	5, 25 and 50 6.91µM of Curcumin analog 50 * 100	Choudhary D <i>et al</i> 1999; Srinivasan M <i>et al</i> 2007, 2008 [144]; Koiram PR <i>et al</i> 2007 [71]; Aktas C <i>et al</i> 2011;

			levels of GSH, GST, SOD, Catalase and total thiols, and reduced lipid peroxidation Curcumin prevents follicular Artesia in radiation induced apoptosis in ovarian follicles Curcumin pretreatment accelerated healing of irradiated wound		Jagetia GC <i>et al</i> 2012 [4]
<i>Drypetes Roxburghii</i> Wall.	Euphorbiaceae	Putranjiva, lucky bean tree	Pretreatment with ethanolic extract of seeds delayed the onset of mortality and increased survival rate up to 40%.	400	Shastry CS <i>et al</i> 2014 [127]
<i>Echinodorus macrophyllus</i> Mich.	Alismataceae	**	The reduction of phenolic fractions such as trans-ferulic acid, E-caffeoyltartronic acid, 6-C-(1-hexitol)-luteolin and 6-C-(1-hexitol)-apigenin, when absorbed dose was increased indicates an important Radioprotective effect.	the studies was on antimicrobial and anti-fungal property of irradiated phenolic fractions	Silva TM <i>et al</i> 2012 [131]
<i>Elaeocarpus sylvestris</i>	Elaeocarpaceae	Woodland Elaeocarpus	Provided protection against radiation induced injuries	*	Park E <i>et al</i> 2008 [93]
<i>Eleutherococcus senticosus</i>	Araliaceae	ginseng	Panax ginseng saponins and Eleutherococcus senticosus extract applied to cells in culture prior irradiation exhibited protection by morphologically altering the cells	*	Ben hur and fulder 1981 [12]
<i>Emblica officinalis</i>	Phyllanthaceae	Amla, Indian gooseberry	Prevented γ ray induced LPO and also protected mitochondrial SOD. The free radical scavenging activity may be attributed to Radioprotective nature; Administering extract before irradiation caused a significant depletion in lipid peroxidation and elevation in glutathione and catalase levels	* 100	Bhattacharya S <i>et al</i> 2006 [113]; Jindal A <i>et al</i> 2009 [61]
<i>Empetrum nigrum</i> Var. <i>japonicum</i>	Ericaceae	Crowberry, black crowberry	Ethyl acetate fraction recovered Bcl-2 expression reduced by irradiation. Anti-apoptotic effect was due to inhibition of mitogen activated protein kinase 4 (MKK4/SEK 1)-c-Jun NH ₂ – terminal Kinase (JNK) cascades induced by γ -radiation	*	Kim KC <i>et al</i> 2011 [67]
<i>Ficus racemosa</i>	Moraceae	Indian fig tree, Goolar fig, cluster fig tree	Pretreatment with Ethanol extract protected V79 cells from radiation and acted as potent antioxidant	0.2	Veerapur VP <i>et al</i> 2009 [161]
<i>Genista sessilifolia</i> DC	Leguminaceae	**	Showed protective effect against UV light and Nitric oxide mediated plasmid DNA damage.	*	Rigano D <i>et al</i> 2009
<i>Genista tinctoria</i> L.	Leguminaceae	Dyers broom	Showed protective effect on UV light and Nitric oxide mediated plasmid DNA damage.	*	Rigano Det <i>et al</i> 2009
<i>Gentiana Dinarica</i>	Gentianaceae	Trumpet Gentian	Plant extracts protected Cultured human peripheral blood lymphocytes against radiation induced damage.	0.1	Petrovic S <i>et al</i> 2008 [96]
<i>Ginkgo biloba</i>	Ginkgoaceae	Maidenhair tree	Showed complete disappearance of Clastogenic factors after regular use of the extract for 2 months post irradiation	0.1 *	Emerit I <i>et al</i> 1995 [24]; Ni Y <i>et al</i> 1996 [89]
<i>Glycyrrhiza glabra</i>	Fabaceae	Licorice	70% methanolic extract protected rat microsomal membranes from γ radiation induced lipid peroxidation	0.1	Kovalenko PGet <i>et al</i> 2003
<i>Grewia asiatica</i>	Malvaceae	Phalsa, falsa	Radiation induced augmentation in the levels of lipid peroxidation of mice cerebrum was significantly ameliorated by pretreatment	700	Sisodia R 2008 [137]
<i>Haberlea rhodopensis</i> (Friv.)	Gesneriaceae	*	Pretreatment with plant leaf extract decreased Chromosome aberrations, Micronucleus formation and MDA levels. Increased the SOD and CAT activity	1200	Georgieva Set <i>et al</i> 2013 [30]
<i>Hemidesmus indicus</i>	Apocynaceae	Kshirini, karala	Root extract showed radioprotective property of microsomal membranes by reduction in lipid peroxidation and also protected DNA from radiation induced strand breaks	*	Shetty TK <i>et al</i> 2005 [129]
<i>Hippophae rhamnoides</i> Linn.	Elaeagnaceae	Common sea-buckthorn	An aqueous alcohol extract of berries protected against radiation by increasing survival time; The alcoholic extract exhibited the immunostimulatory activity against radiations	30 30	Goel HC <i>et al</i> 2002 [32]; Prakash H <i>et al</i> 2005 [102]

<i>Hypericum perforatum</i> L.	Hypericaceae	St John's wort, Tipton's weed, Rosin rose, Goat weed, Chase devil	Decreased the intensity of enzymatic and non-enzymatic process of lipid peroxidation, increased number of SH groups <i>in vivo</i>	*	Smyshliaeva AV <i>et al</i> 1992 ^[140]
<i>Isatis indigotica</i>	Brassicaceae	Indigo Wood, glastum	Extract treated mice showed recovery of hematopoietic system, reduction in inflammatory cytokines and intestinal toxicity.	*	You WC <i>et al</i> 2009 ^[164]
<i>Ledum palustre</i> L.	Ericaceae	Wild rosemary, Marsh Labrador tea	Injecting mixture of extracts from <i>Archangelica officinalis</i> and <i>Ledum palustre</i> showed a significant protection to gastrointestinal tract and haemopoietic system	*	Narimanov AA 1993 ^[86]
<i>Lycium chinense</i>	Solanaceae	Chinese boxthorn, Chinese matrimony vine, wolfberry	extract supplementation protected mice against the X- irradiation either by enhancing post irradiation repair or increasing proliferation of hematopoietic stem cells	500	Hsu HY <i>et al</i> 1999 ^[45]
<i>Mangifera indica</i> L.	Anacardiaceae	Mango	Mangiferin, a gluosylxanthone, present in the <i>Mangifera indica</i> protected mice against the radiation induced sickness and mortality; Invitro Plasmid DNA protection was observed in presence of mango juice against radiation induced damage	2 *	Jagetia GC <i>et al</i> 2005 ^[48, 50 54] , Naresh K <i>et al</i> 2014. ^[85]
<i>Mentha arvensis</i>	Lamiaceae	Field mint, wild mint, corn mint	Mint extract treatment protected the mice against gastrointestinal death and bone marrow related death. DRF is 1.2	10	Jagetia GC <i>et al</i> 2001
<i>Mentha piperita</i> (Linn.)	Lamiaceae	peppermint	Oral administering of <i>M. piperita</i> before γ irradiation provided protection against radiation induced chromosomal damage in bone marrow of Swiss albino mice. Increase in GSH and decrease in LPO was also observed	1	Samarth RM and Kumar A 2003 ^[116] .
<i>Mentha spicata</i>	Lamiaceae	Spearmint	<i>Mentha spicata</i> oil administration one hour prior irradiation showed gastroprotective and calcium channel antagonizing properties and can be utilize for preventing radiation induced behavioural changes	Mint oil 10% (v/v)	Haksar A <i>et al</i> 2009 ^[36]
<i>Moringa oleifera</i>	Moringaceae	Drum stick plant	One hour prior i.p administration of 50% leaf methanolic extract showed significant radiation protection to bone marrow chromosomes in mice; Leaf extract treatment restored GSH in liver and prevented radiation induced augmentation in hepatic lipid peroxidation.	150 300	Rao AV <i>et al</i> 2001 ^[107] ; Sinha M <i>et al</i> 2011 and 2012 ^[135] .
<i>Myristica fragrans</i>	Myristicaceae	Nutmeg	Pretreatment decreased Lipid peroxidation. DRF 1.3	*	Sharma M and Kumar M 2007 ^[125]
<i>Nelumbo nucifera</i>	Nelumbonaceae	Indian lotus, sacred lotus, bean of India	Procyanidins extracted with acetone- water from seedpod prevented spleen and skin damage in irradiated mice	200	Duan Y <i>et al</i> 2010 ^[23]
<i>Nigella sativa</i>	Ranunculaceae	Fennel flower, nutmeg flower, black caraway, and roman coriander	Pre administration of Oil from the plant Protected Sprague-Dawley mice from radiation by reducing the oxidative stress markers	1000	Cikman OMD <i>et al</i> 2014 ^[19]
<i>Ocimum sanctum</i>	Lamiaceae	Holy basil, tulasi	Flavonoids orientin and vicenin isolated from plant protected mice when either compound administered i.p. 30 minutes before irradiation, protected against the gastrointestinal syndrome and bone marrow syndrome. DMF 1.37 (vicenin), 1.30 (orientin). Radical scavenging property was also observed Patients suffering from the squamous cell carcinoma of oral cavity and oropharynx undergoing radiotherapy were used in study by providing flavonoid capsules from holy basil plant, significant increase in SOD was observed	0.05 1.32	Umadevi Pet <i>et al</i> 1999, 2000; Reshma K <i>et al</i> 2008 ^[111]
<i>Olea europaea</i>	Oleaceae	Olive plant	Oleuropein a component protected mice against chronic UV B, induced skin damage	Oleuropein 10and 25	Kimura Y <i>et al</i> 2009 ^[68]

			and carcinogenesis due to inhibition of expression of VEGF, MMP-2, MMP-9, and MMP-13 through a reduction in COX-2 levels		
<i>Oroxylum indicum</i> (L.) Vent.	Bignoniaceae	Midnight horror, oroxylum, kampong or Indian trumpet flower	I.p injecting of ethanol extract protected DNA from radiation induced damage by scavenging free radicals and providing antioxidant properties	1-2 g/kg	Thokchom DS <i>et al</i> 2014 [152]
<i>Paeonia suffruticosa</i>	Paeoniaceae		Aqueous extract of seeds protected HEK 293 cells from irradiation induced cell damage		He C <i>et al</i> 2012
<i>Panax ginseng</i>	Araliaceae	**	Radioprotective effect exhibited against radiation induced hematological and biochemical alterations in blood and liver of mice	*	Preeti Verma <i>et al</i> 2011
<i>Phyllanthus amarus</i>	Phyllanthaceae	Stone breaker, seed under leaf	Protected against clastogenic effects of radiation as seen from decreased number of micronuclei	250-750	Harikumar KBN <i>et al</i> 2007 [38]
<i>Phyllanthus niruri</i>	Phyllanthaceae	Stone breaker, seed under leaf	Alcoholic extract showed highly significant decrease in chromosomal aberrations	250	Thakur I <i>et al</i> 2011 [151]
<i>Pilea microphylla</i>	Urticaceae	Artillery plant, gun powder plant	Protected hematopoietic system, inhibited iron induced lipid peroxidation, scavenged free radicals	900	Prabhakar KR <i>et al</i> 2007 [91, 99]
<i>Pinus caribaea</i>	Pinaceae	Caribbean pine	Pre or co treatment with extract and exposure to γ -rays showed anti genotoxic action in <i>E. coli</i> cells	*	Fuentes JL <i>et al</i> 2006 [27]
<i>Pinus maritima</i>	Pinaceae	Maritime pine, cluster pine	When exposed to UV-B, bark extract Flavangenol Inhibited increase in skin thickness, formation of wrinkles and melanin granules. The anti photo aging and anti carino genetic activities may be due to inhibition of expression of ki-67, VEGF and scavenging the reactive oxygen species	*	Kimura Y <i>et al</i> 2010 [69]
<i>Piper betle</i>	Piperaceae	Betle plant	Leaf extract administration before irradiation enhanced radiation abated antioxidant potential of plasma, GSH level, lowered lipid peroxidation, and decline in radiation induced micro nucleated cells	225	Verma S <i>et al</i> 2010 [34, 162]
<i>Piper longum</i>	Piperaceae	Long pepper, Indian long pepper	Ethanollic extracts of fruit reduced the elevated levels of Glutathione Pyruvate Transaminase, Alkaline phosphatase and lipid peroxidation in liver and serum of irradiated swiss mice	*	Sunila ES <i>et al</i> 2005 [148]
<i>Plumbago zeylanica</i>	Plumbaginaceae	Ceylon Leadwort, Doctor bush	Plumbagin a naphthoquinone from roots showed protection against UV radiation induced development of squamous cell carcinomas by inhibiting the Nuclear factor kappa B, Stat 3 transcription factors, protein levels of Bcl 2, Bcl xL,.	*	Sand JM <i>et al</i> 2012 [119]
<i>Podophyllum hexandrum royale</i> (syn. <i>P.emodi wall</i>)	Berberidaceae	Himalayan may apple, Indian may apple	i.p administration of extract showed protection against the radiation induced damage in different types of cells present in testicular region. Partially purified fraction protected mice against lethal doses of γ irradiation Scavenged radiation inflicted free radicals and protected mice	200 * *	Samanta N <i>et al</i> 2004 [115]; Latha M <i>et al</i> 2009; Gupta ML <i>et al</i> 2010 [34, 162]
<i>Potentilla alba</i>	Rosaceae	white cinquefoil	70% methanolic extract protected rat microsomal membranes from γ radiation induced lipid peroxidation	100 μ g/ml	Kovalenko PG <i>et al</i> 2003
<i>Pothomorphe umbellata</i>	Piperaceae	Pariparoba	Extract inhibited the hyperplasia response and induced an increase in p53 positive cells against UV B induced skin lesions	*	Silva VVD <i>et al</i> 2009 [132]
<i>Prunus avium</i>	Rosaceae	Wild cherry, sweet cherry, bird cherry, gean	Before and after the irradiation administration of extract reduced radiation induced deficit in blood sugar, cholesterol and modulated hematological constituents	450	Sisodia R <i>et al</i> 2011 [138]
<i>Punica granatum</i>	Lythraceae	Pomegranate	Peel extract administering Protected mice against damage caused due to X- ray irradiation by reversing the leucocyte apoptosis and cell death reduction	50	Toklu HZ <i>et al</i> 2009 [153]
<i>Pyrus malus</i>	Rosaceae	Apple	<i>In vitro</i> studies of Radioprotective properties	2	Chaudhary P <i>et al</i>

			was studied for Epicarp and mesocarp of apple and polyphenols showed radioprotection properties against DNA damage and Cell death in murine thymocytes		2006 ^[17]
<i>Rhodiola imbricata</i> Edgew	Crassulaceae	**	Increased survival time with very high therapeutic window by reducing oxidative stress, chelating metal ions, scavenging free radicals and inhibiting lipid oxidation	400	Arora R <i>et al</i> 2005 ^[10]
<i>Rosmarinus officinalis</i>	lamiaceae	Rosemary	Pretreatment with extract considerably protected against radiations by altering the biochemical parameters; Treatment with extract before irradiation caused a major depletion in lipid peroxidation and elevation in glutathione levels	*	Soyal D <i>et al</i> 2007 ^[142] Jindal A <i>et al</i> 2010 ^[60] .
<i>Rubia cordifolia</i> Linn.	Rubiaceae	Common Madder, Indian Madder	Alcoholic extract of root provided protection against lipid peroxidation, hemopoietic injury and Geno toxicity	1200	Bhusan Y <i>et al</i> 2007
<i>Saccharum officinarum</i> L	Poaceae	Sugar cane	Sugar cane extract was orally administered to 3 week old chickens for 3 consecutive days before or after X-ray irradiation , survival rate increased	500	Amer S <i>et al</i> 2005 ^[6]
<i>Santalum album</i>	Santalaceae	Indian sandal wood	α -santalol effectively prevented UV –B evoked skin cancer development in CD-1, Sencar and SKH-1 mice, reduced tumor incidence and multiplicity, increase in apoptosis proteins, caspase-3 and -8 levels and tumor suppressor protein P ⁵³ .	0.1ml, 5% w/v in acetone	Arasada BL <i>et al</i> 2008 ^[7]
<i>Saraca indica</i>	Fabaceae	<i>Saraca asoca</i> , Ashoka tree	Pretreatment with Hydro alcoholic extract of the plant increased levels of Glutathione S-Transferase, Catalase and lowered lipid peroxidation. The protection mechanism may be attributed to free radical scavenging and elevating in antioxidants. DRF 1.39	400	Satish Rao BS <i>et al</i> 2010
<i>Syzygium cuminii</i>	Myrtaceae	Jambul, jambolan, jamblang, jamun	Jamun extract protected mice against radiation induced DNA damage and inhibited formation of radiation induced free radicals	50	Jagetia GC <i>et al</i> 2011
<i>Tephrosia purpurea</i>	Fabaceae	Wild indigo, wasteland weed	Showed selective effect on erythroid compartment by protecting against haemopoietic injury Showed free radical scavenging property	200*	Taraphdar AK <i>et al</i> 2002 ^[150] ; Patel A <i>et al</i> 2010 ^[94]
<i>Terminalia chebula</i>	Combretaceae	Yellow myrobalan	I.p administrating aqueous extract of fruit showed decrease in radiation induced damage to DNA and free radical scavenging properties	80	Gandhi NM and Nair CK 2005 ^[29]
<i>Thymus vulgaris</i>	Lamiaceae	Common thyme, garden thyme	Thymol, the main constituent of plant protected Chinese hamster lung fibroblast (V79) cells from Oxidative stress, lipid peroxidation and increased cell viability	25 μ g/ml	Archana PR <i>et al</i> 2009 ^[8] .
<i>Tinospora cordifolia</i>	Menispermaceae	Guduchi, Giloy	Oral administration of plant extract protected mice against radiation sickness such as anorexia, lethargy, ruffled hair, Diarrhea and Death. The arabino galactan polysaccharide fraction of plant protected the yeast cells against radiation damage; Protected mice against the radiations and increased survival time, decreased radiation induced weight loss. Plant root extract protected testicular constituents against γ radiation	5 and 10 10; 200 75	Pahadiya S <i>et al</i> 2003 ^[90] ; Subramanian M <i>et al</i> 2003 ^[147] ; Goel HC <i>et al</i> 2004 ^[33, 115] ; Sharma P <i>et al</i> 2011 ^[126, 161]
<i>Vernonia cinerea</i>	Asteraceae	Little iron weed	I.p administration of plant extract protected bal b/c mice from radiation induced ailments like reduction in WBC, bone marrow cellularity and α -esterase positive cells, elevation of serum enzymes etc.,	20	Kumar PP and Kuttan G 2011
<i>Vicia faba</i>	Fabaceae	Broad bean, fava bean, faba bean, bell bean	Provided protection against X-ray evoked chromosomal aberrations	*	Larsson B and Kihlman BA 1960 ^[75]
<i>Vigna radiata</i>	Fabaceae	Mung bean, moong bean, green gram,	Vitexina, a product containing flavonoid Vitexin provided a significant protection to peripheral blood cells and to lymphocyte	*	Hien TV <i>et al</i> 2002 ^[41]

		golden gram	blast transformation function against damage caused due to radiation		
<i>Viscum album</i>	Santalaceae	European mistletoe, common mistletoe	Showed reduction in aspect effects caused by radiation	*	Kienle GS <i>et al</i> 2010 [66]
<i>Vitis vinifera</i>	Vitaceae	Common grape vine	Pro antho cyanidins play a vital role in interference of ROS-induced oxidative lymphocyte damage by decreasing DNA damage, lowering membrane lipid peroxidation and increasing activity of AOP enzymes	*	Stankovic M and Horvat A 2008 [146]
<i>Withania somnifera</i>	Solanaceae	Ahwagandha, indian ginseng, poison gooseberry, winter cherry	Root extract prevented the incidence of malignancy in cutaneous tissue and prevented incidence of skin cancer	20	Mathur S <i>et al</i> 2004 [81]
<i>Xylopi aethiopica</i>	Annonaceae	Bitter wood	Dried fruit extract increased the antioxidant defense systems in liver and kidney of irradiated animals	250	Adaramoye OA <i>et al</i> 2011 [1]
<i>Zingiber officinale</i>	Zingiberaceae	Ginger	Hydro alcoholic extract exhibited radical scavenging capability and protected mice against radiation induced injury.	250	Jagetia GC <i>et al</i> 2004 [46]

Note: Optimum dose not available=*, Common name not available =**. DRF= Dose Reduction Factor. DMF= Dose Modification Factor

Vitamins as radioprotectors: Vitamins are the phytochemical constituents with diverse biological functions. Radioprotective efficacy of Vitamin A, C, E and their derivatives was extensively studied and their role as antioxidants and radioprotectors were determined.

Vitamin A: The role of β - Carotene and Vitamin A in radiation protection with relation to antioxidant properties was studied by Seifter E *et al* 1988 [122]. These compounds showed great protection against damage caused by radiations by scavenging free radicals and exhibiting great antioxidant properties.

Vitamin C: The vitamin C or ascorbic acid is a potent antioxidant vitamin and free radical scavenger in both *in vitro* and *in vivo*. The Vitamin C and different derivatives of ascorbic acid are tested for their radiation protection properties. The Vitamin C potentiality to prevent the damage of the radiosensitive spermatogonial cells in the testes of mouse against radiation was studied by Narra VR *et al* 1994 [37, 87]. The derivatives include Ascorbic acid monoglucoside (Mathew D *et al* 2007) [80], a palmitoyl derivative of ascorbic acid 2-glucoside, 6 palmitoyl ascorbic acid -2- glucoside (PAsAG) (Chandrasekharn DK *et al* 2009), are experimentally proved that they prevent the damage of genetic material and the membrane of the cells against radioactivity. Ascorbic acid along with other phytochemicals like polyphenols protected the DNA integrity and reduced the Nucleic acid damage Jimenez L *et al* 2011) [59].

Vitamin E: The water soluble derivative of vitamin E, Alpha-tocopherol monoglucoside (TMG) has antioxidant and Radioprotective properties (Rajagopalan R *et al* 2002) [104]. Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) a structural analogue of Vitamin E also have antioxidant properties similar to Vitamin E. Trolox is also a free radical scavenger and protects DNA from damage (Santosh Kumar S *et al* 1999). However the natural derivative of Vitamin E has higher protective properties than the synthetic chemical compounds.

Flavonoids as radioprotectors: Flavonoids, a group of

phytochemicals with a polyphenolic structures. Over 4000 flavonoids have been identified; many of them are available in fruits, vegetables, green vegetables and beverages. Most of the studies are suggesting that flavonoids act as antioxidants as well as radioprotectants. (Pietta PG 2000) [97]. Based on the chemical nature of flavonoids are categorized into – flavonols, flavones, flavanones, isoflavones and flavanols. Flavonoids affect Oxidative stress and enhance genomic stability by intercalating with DNA (Hosseinimehr SJ 2010) [42]. A large number of flavonoids were studied to elicit the Radioprotective efficacy. Few of them include flavonoids orientin and vicenin isolated from *Ocimum sanctum* protected against chromosome aberrations, hematopoietic syndrome and enhanced survival in irradiated mice (Uma Devi P *et al* 2000) [157]. Naringin a flavonoid found in grapefruit and in many citrus fruits was studied to evaluate the protection against radiation induced damage and found to be a potent protector against radiations (Jagetia GC and Reddy TK 2005) [48, 50, 54]. The studies of flavonoids Naringinin, Scutellarein, rutin and nepitrin have demonstrated the survival time increase in irradiated mice (Agarwal OP and Nagaratnam A. 1981) [2]. Flavonoids from tea and coffee (-) Epicatechin and (+)-Catechin acted as scavengers of free radicals and their presence reduced the damage to DNA when irradiated with radiations (Ershov DS *et al* 2011) [25].

Polysaccharides as radioprotectors: Apart from large number of phytochemicals, polysaccharides also contributed for the protection against radiation induced damage. Lipopolysaccharide protected the intestine and bone marrow from radiation injury in mice. The detailed studies showed lipopolysaccharides protected mice from radiations through prostaglandin dependent pathway (Riehl T *et al* 2000) [112]. The polysaccharide fractions isolated, purified from *Tinospora cordifolia* and tested for Radioprotective property. The results showed polysaccharide fraction acted as polyclonally mitogenic to mouse B-lymphocytes and showed protection through immune modulatory activity as like many of radioprotection compounds (Subramanian M *et al* 2002).

Conclusions: Plants are natural gift to humans with diverse functions and abilities. Plants are used as the best alternative

sources for therapeutic purposes in many Asian countries. They are well equipped with defense mechanisms to protect from biotic and abiotic stress and damages induced from radiations. The self-protecting ability, mechanisms to scavenge free radicals and large number of diverse compounds which can ameliorate the damage induced by radiations are advantages of plants as far as radiations exposure and protective mechanisms are considered. Easy availability, nontoxic nature at therapeutic effective doses, potentiality to be as good radioprotectors with long shelf life and success in preclinical trials owing to screen plants for radioprotectors. A large number of plants are screened in search of a novel, nontoxic and natural compounds which can work effectively and gives relief from radiation induced damage. Many phytochemicals extracted with different procedures and solvents, either in crude or purified fractions are identified as potential protectors against the radiations in vitro, in vivo and ex vivo. Thus, plants can be the alternative, natural, nontoxic sources for safeguarding from radiations induced damage.

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