

Utilization of cytogenetic biomarkers as a tool for assessment of radiation injury and evaluation of radiomodulatory effects of various medicinal plants – a review

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Abstract: Systematic biological measurement of “cytogenetic endpoints” has helped phenomenally in assessment of risks associated with radiation exposure. There has been a surge in recent times for the usage of radioactive materials in health care, agriculture, industrial, and nuclear power sectors. The likelihood of radiation exposure from accidental or occupational means is always higher in an overburdened ecosystem that is continuously challenged to meet the population demands. Risks associated with radiation exposure in this era of modern industrial growth are minimal as international regulations for maintaining the safety standards are stringent and strictly adhered to, however, a recent disaster like “Fukushima” impels us to think beyond. The major objective of radiobiology is the development of an orally effective radio-modifier that provides protection from radiation exposure. Once available for mass usage, these compounds will not only be useful for providing selective protection against accidental and occupational radiation exposure but also help to permit use of higher doses of radiation during treatment of various malignancies curtailing unwarranted adverse effects imposed on normal tissues. Bio-active compounds isolated from natural sources enriched with antioxidants possess unique immunomodulating properties, thus providing a double edged benefit over synthetic radioprotectors. We aim to provide here a comprehensive overview of the various agents originating from plant sources that portrayed promising radioprotection in various experimental models with special emphasis on studies that used cytogenetic biomarkers. The agents will include crude extracts of various medicinal plants, purified fractions, and herbal preparations.

Keywords: cytogenetic biomarkers, medicinal plants, radioprotectors, radiation exposure

Overview of radiation-induced cytogenetic damage

Radiation is a form of energy that gets converted to other forms on absorption by matter thus resulting in cellular damage after exposure to radiation, however, the degree of damage is dependent on the nature and quality of radiation as well as the type of cells being exposed. Additional factors such as age, sex, and species of the animal also play a great role in variation in degree of radiation damage. In contrast to other forms of radiation, ionizing radiation has the capacity to break chemical bonds, impart energy to living cells through random interactions with atoms, giving rise to ions and reactive radicals, these in turn cause molecular changes that may lead ultimately to biological injury. Due to the high incidence of deaths resulting from exposure to high radiation doses, these effects are prominently analyzed qualitatively and quantitatively. However, harmful biological effects from low doses of radiation cannot easily be detected and analyzed. Moderate doses of radiation are known to increase the likelihood of cancer and birth defects.

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Lower doses may cause temporary cellular changes, but higher doses have a higher incidence of causing abnormalities.

Manifestation of biological effects is preceded by physical and chemical changes caused due to radiation energy deposition in the living materials. Radiation can produce damaging effects by transferring its energy directly to the target molecules of the cells or by deposition of energy to the molecules of water present in surroundings. Radicals are more predominant in causing damage to biological systems since, cells and tissues consist of approximately 80%–90% water.¹ The prominent effect of radiation is by the indirect action of free radical generation in water, which subsequently reacts with vital biological molecules producing a variety of consequences such as genetic effects, cell death, and carcinogenesis.²

Ionizing radiation is an extremely competent potent cytotoxic mediator. It is expected that in cellular systems an X-ray dose of 1.5 Gy results in the production of 10^{-6} radicals.³ Ionizing radiation causes cell death by targeting DNA and thus DNA double-strand breaks are accountable for the damage. However, damage to other biological molecules apart from DNA has also shown potential for cell death.⁴ The structural aberrations can be produced in chromosomes by radiation at any stage of their mitotic cycle. When cells are irradiated just as they enter division, there is apparently some change in the surface properties of the chromosomes, which cause them to stick together. This stickiness has been attributed to a partial dissociation of the nucleoproteins and alterations in their pattern of organization.⁵ Thus, radiation-induced structural chromosomal aberrations are probably due to double-strand breaks.^{6,7}

The radiation-induced double-strand breaks are found to be highly deleterious, interfering with transcription/replication leading to chromosomal rearrangements responsible for various types of cancers.⁸ The double-strand breaks get repaired by non-homologous end joining and homologous recombination repair mechanisms.⁹ The template for repair in homologous recombination repair mechanism is served by homologous chromosome. However, the non-homologous end joining mechanism is a major mechanism and involves several steps. The erroneous repair of double-strand breaks is the cause of cell death, genomic instability, and hereditary diseases including cancer.

Available tools for assessment of radiation injury using cytogenetic biomarkers

It is known that the medical use of low-dose ionizing has a high risk for causing cancer development and children are

more prone to have such exposures. It has been observed that the somatic DNA was found to be damaged in subjects who received low doses of diagnostic X-rays.¹⁰ High-linear energy transfer (LET) radiation exposure during space travel or cancer therapy is more damaging than low-LET radiation and may result in cell inactivation, genetic mutations, cataracts, and cancer. However, these endpoints are interrelated to chromosomal damage and may be utilized as a biomarker for radiation-induced damage (Table 1).

Conventional cytogenetic biomarkers

For assessment of radiation exposure, biological dosimetry utilizing dicentric chromosomes analysis in human lymphocytes is a well-known method practiced since long ago along with physical dosimetry for radiation dose assessment in potentially overexposed people as well as for suspected exposures to estimate risk of health effects.¹¹ Micronuclei, small satellite structures are the chromosomal fragments lacking centromeres. The frequency of micronuclei is also commonly used as a cytogenetic biomarker. Another cytogenetic endpoint, cytokinesis-block micronucleus assay, is considered to be simple in terms of scoring criteria as a reliable and sensitive cytogenetic biomarker. The premature chromosome condensations assay is also being used for biological dosimetry following radiation exposures. The main advantage of the premature chromosome condensations assay is that there is no need for cells to divide for evaluation of cytogenetic damage.¹² Many authors have documented that cells exposed to radiation had significant increase in sister chromatid exchanges. The radiation had great capacity to induce DNA damage and form stable chromosomal aberration. For dose assessment translocations can be used as biological dosimetry.

Molecular cytogenetic biomarkers

A relatively new developed technique, fluorescence in situ hybridization, has revealed unique endpoints related to radiation quality. It has now become possible to detect inter-chromosomal and intra-chromosomal exchanges as well as distribution of the breakpoints of aberrations with the help of the mBAND technique. The cytokinesis-block micronucleus cytome assay is also being utilized to measure the cytogenetic damage induced by radiation. The single cell gel electrophoresis or comet assay, developed for the evaluation of DNA single-strand breaks, utilizes the DNA migration as a measure of the DNA damage, however, the DNA double-strand breaks can be measured by neutral comet assay.¹³ With the development of microarray formats, analysis of the chromosome damage of human peripheral lymphocytes is done with the modern technology of integration of techniques.¹⁴ The human

Table I Tools for assessment of radiation injury using cytogenetic biomarkers

Cytogenetic biomarkers	Particulars	References
Conventional cytogenetic biomarkers		
Total number of aberrations	The radiation damage is quantified by scoring different types of chromosomal aberrations, and is considered to be one of the accurate technique among cytogenetic tools used as biological dosimeter. This technique is used to estimate the dose–response curves and is also popular in radiation biology for radioprotective studies.	82–89,160
Dicentrics and ring chromosomes	For assessment of radiation exposure, biological dosimetry utilizing dicentric chromosomes analysis in human lymphocytes is a well-known method practiced since long ago, along with physical dosimetry for radiation dose assessment in potentially overexposed people as well as for suspected exposures to estimate risk of health effects.	11,90–101
Micronuclei assay/cytokinesis-block micronucleus assay	Micronuclei, small satellite structures, are the chromosomal fragments lacking centromeres. The frequency of micronuclei is variously used as cytogenetic biomarker. The cytokinesis-block micronucleus assay is simple in terms of scoring criteria and is a reliable and sensitive cytogenetic biomarker.	102–117
Sister chromatid exchanges	Many authors have documented that cells exposed to radiation had significant increase in sister chromatid exchanges.	87,88, 118,119
Translocations	Irradiation causes various types of DNA damage that lead to stable chromosomal aberration. Translocation chromosomal aberration is stable and can be used as biological dosimetry for dose assessment.	120–127
Premature chromosome condensation	The premature chromosome condensations assay is being used for biological dosimetry following radiation exposures. The main advantage of the premature chromosome condensations assay is that there is no need for cells to divide for evaluation of cytogenetic damage.	128–140
Molecular cytogenetic biomarkers		
FISH/chromosome painting/mBAND analysis	A relatively newly developed technique, FISH has revealed unique endpoints related to radiation quality. It has now become possible to detect inter-chromosomal and intra-chromosomal exchanges as well as distribution of the breakpoints of aberrations with the help of mBAND technique.	121,122, 141,142
DNA-PK	Double-strand break repair pathways are responsible for maintaining genomic integrity, genetic instability, and neoplastic transformation. It has been speculated that DNA-PK plays an essential role in DNA double-strand break repair and maintaining genomic integrity.	143–147
hTERT (telomerase reverse transcriptase) and genomic instability	The hTERT-immortalized cells have been found to be useful for determining the effects of radiation.	148–151, 159
Cytokinesis-block micronucleus cytome assay	Development of microarray formats analysis of the chromosomal damage of human peripheral lymphocytes is done with the modern technology of integration of techniques. The cytokinesis-block micronucleus cytome assay is being utilized as radiation biological dosimetry specifically developed to assess various forms of chromosomal damage.	10,152–155
The single cell gel electrophoresis assay/comet assay	The single cell gel electrophoresis or comet assay, developed for the evaluation of DNA single-strand breaks utilizes DNA migration as a measure of the DNA damage, however, the DNA double-strand breaks can be measured by neutral comet assay.	13,15,156, 157

Abbreviations: FISH, fluorescence in situ hybridization; mBAND, high resolution multicolor chromosome banding.

telomerase reverse transcriptase (hTERT)-immortalized cells have been found to be useful for determination of the effects of radiation. Double-strand break (DSB) repair pathways are responsible for maintaining genomic integrity, genetic instability, and neoplastic transformation. It has been speculated that DNA-PK plays an essential role in DNA double-strand break repair and maintenance of genomic integrity.

Modulation of radiation-induced cytogenetic damage by various medicinal plant products

It is well-known that ionizing radiation damages DNA through direct and indirect action. In the direct mechanism, the DNA structure is altered due to disrupted chemical

bonds, whereas in the indirect mechanism, DNA interacts with the reactive free radicals like $\cdot\text{OH}$, $\cdot\text{H}$, and e^-_{aq} generated by radiolysis of water. These reactive free radicals can be scavenged by compounds called scavengers thus having the ability to provide protection against damage caused by radiation. Therefore, it is of special interest to identify and develop effective agents which could be used for protection against radiation-induced genetic damage especially in humans. A series of chemicals like WR2721, WR1065, and S-(2-aminoethyl)isothiuronium bromide hydrobromide (AET) were studied but these chemical radioprotectors were found to have limitations in medicine due to their toxic side effects at effective doses. One of the avenues for non-toxic radioprotectors of plant origin has been explored

in recent years, with the advantage of low or no toxicity at the effective doses.

Radioprotective effects of medicinal plants

Plant parts such as fruits, roots, stem/bark, leaves, and medicinal herbs have been found to have antioxidant capacity due to the presence of phenolic compounds, vitamins, nitrogen compounds, terpenoids, and other metabolites. These compounds have been shown to possess antioxidant, immunostimulatory, and antimicrobial activity and to impart radioprotective effects (Table 2). Several studies have focused on screening of herbal-/plant-based drugs for the development of drug discovery.¹⁶

Adhatoda vasica

The radiomodulatory effect of *A. vasica* extract was studied through chromosomal analysis in bone marrow as well as histological and biochemical alterations in testis of mice.¹⁷ *A. vasica* extract pretreatment was effective in increasing survival rate (dose reduction factor [DRF]=1.43) and reducing cytogenetic damage in irradiated mice. Thus, *A. vasica* extract was found to possess radioprotective properties.

Aegle marmelos

The protective effects of *A. marmelos* extract against radiation were evaluated using micronucleus test.^{18,19} An increase in micronuclei frequency was noticed in an “irradiated alone” group while *A. marmelos* extract pretreatment was found to be effective in significantly reducing the cytogenetic damage in lymphocytes.

Alstonia scholaris

The cytogenetic alterations in mouse bone marrow were studied to assess the radioprotective effects of *A. scholaris*.²⁰ Increased frequencies of dicentrics and chromosomal aberrations were reported after radiation exposure but *A. scholaris* bark extract pretreatment was effective in reducing the percentage of dicentrics and chromosomal exchanges significantly, thus providing evidence for radioprotective potential.

Allium sativum (garlic)

The extract of *A. sativum* was evaluated for its radioprotective effects in mice.²¹ The extract of *A. sativum* was found to be effective in significantly reducing the frequencies of radiation-induced micronucleated polychromatic erythrocytes. Also, different concentrations were studied against the clastogenic

Table 2 Modulation of radiation-induced cytogenetic damage by various medicinal plants

Name of plant	Family	Doses		Radiation dose	Animal/tissue studied	Cytogenetic parameters studied	References
		Plant extract dose					
<i>Adhatoda vasica</i> <i>Aegle marmelos</i>	Acanthaceae	800 mg/kg bwt orally		8 Gy	Mouse bone marrow cells	Chromosomal aberrations	17
	Rutaceae	1.25–100 µg/mL treatment in culture		3 Gy	Human peripheral blood lymphocytes	Micronuclei frequency	18
<i>Alstonia scholaris</i>	Apocynaceae	0–300 mg/kg bwt orally		0.5, 1, 2, 3, and 4 Gy	Mouse bone marrow cells	Frequency of MnPCE	19
		100 mg/kg bwt orally		2.5 Gy	Mouse bone marrow cells	Chromosomal damage and micronuclei	20
<i>Allium sativum</i>	Amaryllidaceae	25–500 mg/kg bwt orally		0.5, 1, and 2 Gy	Mouse bone marrow cells	Micronucleus test	21
		25–100 mg/kg bwt orally		Mitomycin C	Mouse bone marrow cells	Chromosomal aberrations	22
<i>Aphanamixis polystachya</i> <i>Brassica campestris</i> <i>Biophyllum sensitivum</i>	Meliaceae	7.5 mg/kg bwt orally		1.5 mg/kg bwt ip			
	Brassicaceae	50–250 mg/kg bwt orally		1–5 Gy	Mouse bone marrow cells	Chromosomal aberrations	23
		50 mg/kg bwt orally		0.5–4 Gy	Mouse bone marrow cells	Micronuclei frequency	24
		Oxalidaceae	50 mg/kg bwt ip		6 Gy	Swiss albino mice	Hemopoietic damage and immunomodulation
<i>Bixa orellana</i> <i>Citrus aurantium</i> <i>Coleus aromaticus</i> <i>Crataegus microphylla</i>	Bixaceae	500–1,000 mg/kg bwt ip		2 and 4 Gy	Mouse bone marrow cells	Chromosomal aberrations	26
	Rutaceae	250 mg/kg ip		1.5 Gy	Mouse bone marrow cells	Clastogenic effect	27
	Lamiaceae	5 µg/mL treatment in culture		0.5, 1, 2, and 4 Gy	V79 cells	Clastogenic effect	28
	Rosaceae	200 mg/kg bwt ip		2 Gy	Mouse bone marrow cells	Frequency of MnPCE	29

<i>Crotalaria retusa</i>	Fabaceae	0.3–2.5 gm/kg bwt ip	Cyclophosphamide 20 mg/kg bwt ip	Mouse bone marrow cells	Chromosomal aberrations	30
<i>Crotalaria mucronata</i>	Poaceae	40 and 50 µg/mL treatment in culture	0.5, 1, 2, 3, and 4 Gy	V79 cells and human peripheral blood lymphocytes	Micronuclei frequency	31
<i>Cynodon dactylon</i>	Ginkgoaceae	100 µg/mL treatment in culture	γ-radiation	Whole blood from healthy volunteers	The anticlastogenic effect	32
<i>Ginkgo biloba</i>	Gesneriaceae	1.0, 4.0, and 8.0 µL/mL treatment in culture	2 Gy	Rabbit peripheral lymphocytes	Chromosomal aberrations	33
<i>Haberlea rhodopensis</i>		0.03, 0.06, or 0.12 g/kg im	1, 2, or 3 Gy	Rabbit peripheral lymphocytes	Dicentric/chromosomal aberrations	34
		0.03, 0.06, and 0.12 g/kg bwt im	2 Gy	Rabbit peripheral lymphocytes	Chromosomal aberration test/ cytokinesis blocked micronucleus assay	35
<i>Hippophae rhamnoides</i>	Elaeagnaceae	25–35 mg/kg bwt ip	2 Gy	Mouse bone marrow cells	Micronuclei frequency	36
<i>Mangifera indica</i>	Anacardiaceae	50–1,000 µg/mL treatment in culture	5 Gy	Human lymphocytes	DNA damage, DNA repair/comet assay	37
<i>Mentha piperita</i>	Lamiaceae	1 g/kg bwt orally	8 Gy	Mouse bone marrow cells	Chromosomal aberrations/ micronuclei frequency/ EPO level	38,39
<i>Moringa oleifera</i>	Moringaceae	150 mg/kg bwt ip	4 Gy	Mouse bone marrow cells	Percent aberrant cells	40
<i>Nelumbo nucifera</i>	Nelumbonaceae	200 mg/kg bwt ig	4 Gy	Mouse bone marrow cells	Micronucleated cells	41
<i>Nigella sativa</i>	Ranunculaceae	0–100 mg/kg bwt orally	2 Gy	Mouse splenic lymphocytes	DRF, CFU-S, MnPCE, NCE, and P/N ratio	42
<i>Ocimum sanctum</i>	Lamiaceae	10 mg/kg bwt ip	1–6 Gy	Mouse bone marrow cells	Micronuclei frequency	43
<i>Panax ginseng</i>	Araliaceae	100, 200, or 300 mg/kg bwt ip	1.5 Gy	Mouse bone marrow cells	Percent aberrant cells	44
					Frequency of MnPCE	
<i>Panax quinquefolius</i>	Araliaceae	50–1,000 µg/mL treatment in culture	1 and 2 Gy	Human peripheral blood lymphocytes	PCE/NCE ratio	45
					Micronuclei frequency	
<i>Phyllanthus niruri</i>	Phyllanthaceae	50–250 mg/kg bwt ip	4 Gy	Mouse bone marrow cells	Chromosomal aberrations	46
<i>Podophyllum hexandrum</i>	Berberidaceae	200 mg/kg bwt im	9 Gy	Mice strain “A”	Micronuclei frequency	47
		Different concentrations treatment in culture	1, 2, 3, 4, and 5 Gy	Human peripheral blood lymphocytes	Dicentric, micronuclei, nucleoplasmic bridges, and nuclear buds	48
<i>Plumbago rosea</i>	Plumbaginaceae	5 mg/kg bwt ip	2 Gy	Swiss albino mice	CFU-S	49
<i>Spirulina platensis</i>	Lichinaceae	1–5 mg/g bwt orally	2.5 Gy	Mouse bone marrow cells	Micronuclei frequency	50
<i>Withania somnifera</i>	Solanaceae	30 mg/kg bwt ip	2 Gy	Swiss albino mice	CFU-S	49

Abbreviations: ig, intra-gastric administration; im, intramuscular injection; ip, intraperitoneal injection; bwt, body weight; CFU-S, colony forming units in spleen; MnPCE, micronucleated polychromatic erythrocytes; EPO, erythropoietin level; DRF, dose reduction factor; NCE, normochromatic erythrocytes; P/N, ratio of polychromatic and normochromatic erythrocytes; PCE, polychromatic erythrocytes.

effects of known toxicants.²² A dose-dependent effect on the frequencies of damaged cells and chromosomal aberrations was observed. It has been recommended that administration of the extract for 30 days is required for protection against the clastogenic effects of genotoxicants used in the study.

Aphanamixis polystachya

The radioprotection of mice by *A. polystachya* extract was studied using cytogenetic biomarkers.²³ The study demonstrated that *A. polystachya* extract pretreatment resulted in a reduction of the cytogenetic damage in mice exposed to radiation.

Brassica campestris

The extract of *B. campestris* was found to be effective in protecting mice from chromosomal damage after irradiation.²⁴ The *B. campestris* extract pretreatment effectively reduced the frequencies of micronuclei in irradiated mouse bone marrow. The protection afforded by *B. campestris* was due to its antioxidant capacity.

Biophytum sensitivum

The extract of *B. sensitivum* was evaluated to study radioprotection in mice.²⁵ The animals pretreated with extract of *B. sensitivum* and exposed to radiation showed cytogenetic protection in terms of colony forming units in spleen (CFU-S) and immunomodulation was responsible for hematopoietic protection.

Bixa orellana

The radioprotective effects of *B. orellana* seed extract have been studied in mouse bone marrow through chromosomal aberration analysis.²⁶ *B. orellana* extract pretreatment was found to be effective in significantly reducing aberrant metaphases and chromosomal aberrations in irradiated mice.

Citrus aurantium

The protective effects of citrus extract against irradiation have been studied in mouse bone marrow.²⁷ It was observed that citrus extract pretreatment greatly reduced the cytogenetic damage in bone marrow. It was speculated that the flavonoid contents of citrus extract may be responsible for the protective activity against irradiation in mice.

Coleus aromaticus

The extract of *C. aromaticus* was evaluated for its radioprotective effect in Chinese hamster fibroblast V79 cells.²⁸ It was revealed that *C. aromaticus* extract treatment before

irradiation offered significant protection from DNA damage induced by irradiation in terms of cytogenetic biomarkers.

Crataegus microphylla

The extract of *C. microphylla* (hawthorn) was studied for radiation-induced genotoxicity in mouse bone marrow cells.²⁹ Administration of hawthorn extract before irradiation showed significant reduction in micronucleated polychromatic erythrocyte frequency in bone marrow cells of mice. It was speculated that radioprotection offered by hawthorn extract could be due to its antioxidant activity that helps in reducing the radiation-induced genotoxicity in mice.

Crotalaria retusa and *Crotalaria mucronata*

The extracts from *C. retusa* and *C. mucronata* were evaluated for their anticlastogenic effects against irradiation in mice.³⁰ The study showed that fruit extract of *C. retusa* caused a dose-dependent increase in chromosomal aberration frequency in mouse bone marrow. The clastogenic effect of *C. retusa* fruit extracts in mouse bone marrow cells was attributed to the alkaloids.

Cynodon dactylon

The radiomodulatory potential of *C. dactylon* extract was studied.³¹ A significant reduction in micronucleated binucleated cells was observed in *C. dactylon* extract pretreated irradiated V79 cells and lymphocytes. Also, *C. dactylon* extract pretreatment resulted in the significant reduction of percentage of micronucleated binucleated cells. Thus, the radioprotective effect of *C. dactylon* has been demonstrated.

Ginkgo biloba

The *G. biloba* extract was evaluated for its anticlastogenic activity.³² It has been demonstrated that clastogenic factors in the blood showed significant reduction after treatment of *G. biloba* extract for 60 days.

Haberlea rhodopensis

The radiomodulatory effect of *H. rhodopensis* extract was studied against gamma irradiation in peripheral blood lymphocytes of rabbits.³³ It has been demonstrated that *H. rhodopensis* extract pretreatment was useful in reducing radiation-induced cytogenetic damage. Further it was demonstrated that the radioprotective as well as antioxidant potential of *H. rhodopensis* in rabbits suggested the need of in-depth investigations for identification of the protective compounds.³⁴ The different concentrations of *H. rhodopensis* extract were injected into rabbits. The rabbits were exposed to

gamma-radiation, which showed dose-dependent reduction in frequency of chromosomal aberrations and micronuclei.³⁵

Hippophae rhamnoides

The protective effect of *H. rhamnoides* extract against radiation-induced cytogenetic damage was studied in mice.³⁶ The *H. rhodopensis* extract treatment increased the survival rate in irradiated mice. It was observed that administration of *H. rhamnoides* alone did not enhance the micronuclei frequency but showed a dose-dependent decrease in micronuclei frequency in pretreated irradiated mice, thus protecting against radiation-induced cytogenetic damage.

Mangifera indica

The *M. indica* extract was studied for evaluation of radioprotection in human peripheral blood lymphocytes and lymphoblastoid cells.³⁷ Dose-dependent DNA damage was observed after *M. indica* extract treatment in human peripheral blood lymphocytes and lymphoblastoid cells, without altering the DNA repair capacity.

Mentha piperita

Administration of *M. piperita* extract before radiation exposure in mice was found to provide protection in bone marrow cells.³⁸ Pretreatment with *M. piperita* extract significantly reduced the number of aberrant cells and different chromosomal aberrations in irradiated mice. Also, *M. piperita* extract pretreatment was found to be effective in protecting against hematopoietic damage in bone marrow of irradiated mice by maintaining the erythropoietin level.³⁹

Moringa oleifera

The radioprotective property of *M. oleifera* extract in mice has been studied.⁴⁰ A significantly reduced number of micronuclei and aberrant cells in *M. oleifera* extract pretreated irradiated animals was reported. However, fractionated administration of *M. oleifera* extract offered more protection in terms of survival of animals and chromosomal damage in bone marrow cells.

Nelumbo nucifera

Pretreatment with *N. nucifera* extract has been shown to provide protection against sickness and mortality in mice exposed to radiation.⁴¹ It was observed that *N. nucifera* extract effectively maintained spleen index and stimulated endogenous spleen colony forming units in mice. Also, a significant reduction in cytogenetic damage was noticed in bone marrow cells of *N. nucifera* extract pretreated irradiated animals.

Nigella sativa

The extract of *N. sativa* was studied in mice to evaluate its protection against radiation damage.⁴² It was observed that *N. sativa* extract pretreatment resulted in significant reduction in lipid peroxidation and intracellular reactive oxygen species in splenocytes. Also it was reported that *N. sativa* extract pretreatment increased the survival rate of irradiated animals indicating the radioprotective ability of *N. sativa*.

Ocimum sanctum

Chromosomal aberration analysis was carried out in mice to evaluate the radiation protective property of extract of *O. sanctum*.⁴³ The pretreatment of mice with extract of *O. sanctum* provided faster recovery and helped in removal of aberration from the cell. It was found that extract of *O. sanctum* afforded in vivo protection against radiation and suggested free radical scavenging as a probable mechanism for radioprotection.

Panax ginseng

The radioprotective effect of *P. ginseng* extract (ginsan) was evaluated in bone marrow cells of mice.⁴⁴ It has been shown that ginsan pre- or post-treatment resulted in a significant dose-dependent increase in frequency of micronucleated polychromatic erythrocytes in bone marrow cells, thus reducing radiation injury in mice.

Panax quinquefolius

The extract of *P. quinquefolius* has been studied for its radioprotective potential on human peripheral lymphocytes through cytogenetic biomarkers.⁴⁵ It has been observed that ginseng extract treatment resulted in concentration-dependent declined micronuclei yield in lymphocytes. Therefore, ginseng extract is considered to be a non-toxic natural product for dietary supplements as countermeasure for radiation risk.

Phyllanthus niruri

The extract of *P. niruri* has been evaluated in mouse bone marrow through chromosomal aberration analysis.⁴⁶ It was noticed that administration of extract of *P. niruri* caused a significant decrease in chromosomal aberrations in irradiated mice.

Podophyllum hexandrum

The extract of *P. hexandrum* was evaluated for its radioprotective effects in mice.^{47,48} The studies showed that *P. hexandrum* provided cytogenetic protection in terms of

decreased radiation-induced micronuclei frequency and chromosomal aberrations in mouse bone marrow.

Spirulina platensis

Administration of extract of *S. platensis* before radiation exposure has shown significant protection in mouse bone marrow cells.⁵⁰ It has been reported that *S. platensis* extract treatment reduced micronuclei frequency significantly in irradiated mice.

Withania somnifera and *Plumbago rosea*

The extracts of *W. somnifera* and *P. rosea* were studied for their effects on tumors.⁴⁹ It was observed that extracts of *W. somnifera* and *P. rosea* had significantly reduced the CFU-S. Further these results have revealed that the effects of extracts of *W. somnifera* and *P. rosea* were radiosensitizing and tumor non-specific in nature.

Radioprotective effects of certain phytochemicals

It has been revealed that chromosomal aberrations are formed by interaction of free radicals with DNA and cause cytogenetic damage (Table 3). Such damage can be reduced significantly by agents that scavenge the free radicals, which are called antioxidants. Radiation is responsible for the production of free radicals in cells, therefore, this damage can be minimized by antioxidants. Plants are abundantly available and contain a variety of flavonoids with antioxidant capacity and have become the prime focus of research in recent years in order to develop an effective radioprotector for use in the medical field. Therefore, researchers gained momentum to work for active principles of plants and isolated compounds. Also, it was more convenient, as it greatly reduced the amount to use, and determined the possible mechanisms involved in radioprotection at a cellular level.

Apigenin

Apigenin was evaluated for radioprotective effects on cell cultures exposed to radiation and showed a significant dose-dependent elevation in the number of micronuclei, it was speculated that apigenin may further be studied to illustrate its possible role as promising radioprotective drug.⁵¹

Beta carotene

The radiation-induced cytogenetic damage in bone marrow of mice after beta carotene administration was evaluated by micronucleus test.^{55,161,163,164} It has been demonstrated that a significant decline in the number of micronucleated

Table 3 Modulation of radiation-induced cytogenetic damage by various phytochemicals and herbal formulations

Name of phytochemical	Chemical/other name	Origin/source	Doses		Animal/tissue studied	Cytogenetic parameters studied	References
			Phytochemical dose	Radiation dose			
Modulation of radiation-induced cytogenetic damage by various phytochemicals							
Apigenin	4',5,7-trihydroxyflavone or 5,7-dihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one	Plants	0, 2.5, 5, 10, and 25 µg/mL treatment in culture	2 Gy	Human peripheral blood lymphocytes	Micronuclei frequency	51
Beta carotene	1,3,3-Trimethyl-2-[3,7,12,16-tetramethyl-18-(2,6,6-trimethylcyclohex-1-en-1-yl)octadec-1,3,5,7,9,11,13,15,17-nonaen-1-yl]cyclohex-1-ene	Plants and fruits	0.5 and 2.5 mg/kg bwt orally	1.15 Gy	Mouse bone marrow cells	Micronuclei frequency	55
Caffeine	1,3,7-Trimethylpurine-2,6-dione	Coffee seeds, tea	1–5 µg/mL treatment in culture Caffeine treatment in culture 5 and 15 mg/kg bwt ip	2 Gy 1.75 and 4.38 Gy 1.5 Gy	Human peripheral blood lymphocytes V79 cells Mouse bone marrow cells	Micronuclei frequency Aberrations per cell Frequency of chromosomal aberrations	161 53 52
Chlorophyllin	Natural green 3, E141	Green leafy vegetables	50, 100, and 200 mg/kg bwt orally	1.15 Gy	Mouse bone marrow cells	Micronuclei frequency	54
Chlorogenic acid	(1S,3R,4R,5R)-3-[[[(2E)-3-(3,4-dihydroxyphenyl)prop-2-en-1-yl]oxy]-1,4,5-trihydroxycyclohexanecarboxylic acid	Bamboo, potato, and many other plants	50, 100, and 200 mg/kg bwt orally	1.15 Gy	Mouse bone marrow cells	Micronuclei frequency	55

Curcumin	(1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione	Rhizome of <i>Curcuma longa</i>	5, 10, and 20 mg/kg bwt orally	1.15 Gy	Mouse bone marrow cells	Micronuclei frequency	55
Eugenol	4-Allyl-2-methoxyphenol	Basil, cinnamon, clove oil, nutmeg	2.5, 5, and 10 µg/mL treatment in culture	2.5 Gy	CHO cells	Chromosomal damage frequency	69
Hesperidin	(2S)-5-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-7-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-[[[(2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxymethyl]oxan-2-yl]oxy-2,3-dihydrochromen-4-one	Citrus fruit	75, 150, and 300 mg/kg bwt orally	0.5, 1, 1.5, and 2 Gy	Mouse bone marrow cells	Micronuclei frequency	56
			10, 20, 40, 80, and 160 mg/kg bwt, ip	2 Gy	Mouse bone marrow cells	Micronuclei frequency	57
			3.27, 6.55, 9.83, 13.10, 16.38, and 19.65 µM treatment in culture	1, 2, 3, and 4 Gy	Human peripheral blood lymphocytes	PCE/PCE + NCE ratio Micronuclei frequency, dicentric aberration, comet assay, DNA fragmentation assay	58
Lycopene	(6E,8E,10E,12E,14E,16E,18E,20E,22E,24E,26E)-2,6,10,14,19,23,27,31-octamethyldotriaconta-2,6,8,10,12,14,16,18,20,22,24,26,30-tridecaene	Tomatoes, red fruits, red carrots, papaya, and watermelons	0.001–0.020 µM treatment in culture	10 Gy	Human peripheral blood lymphocytes	Mitotic index frequency of chromosomal aberrations	59,162
Mangiferin	(1S)-1,5-anhydro-1-(1,3,6,7-tetrahydroxy-9-oxo-9H-xanthen-2-yl)-D-glucitol	Mangoes, <i>Bombax ceiba</i> , <i>Salacia</i> , <i>Cyclopia</i> , rhizomes of iris and <i>Anemarrhena</i>	0–100 µg/mL treatment in culture	0, 1, 2, 3, or 4 Gy	Human peripheral blood lymphocytes	Micronucleated binucleated cell frequency	60
			50–1,000 µg/mL	5 Gy	Human lymphocytes and lymphoblastoid cells	proliferation index DNA damage/repair; comet assay	37
			5–100 µg/mL treatment in culture				
Melatonin	N-[2-(5-methoxy-1H-indol-3-yl)ethyl]acetamide	Found in animals, plants, fungi, and bacteria	2.5 mg/kg bwt ip	4.0 Gy	Mouse bone marrow cells	Mitotic index, MnPCEs, chromosomal aberrations	61,158
Naringin	7-[[2-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2,3-dihydro-5-hydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one	Grapefruit, citrus fruits	2 mg/kg bwt ip	Different doses	Mouse bone marrow cells	Frequencies of aberrant cells, chromosomal aberrations	62
Orientin	8-C-β-D-glucopyranosyl-luteolin or 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-8-[(2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]chromen-4-one	<i>Adonis vernalis</i> , <i>Anadenanthera colubrina</i> , <i>Phyllostachys nigra</i> Bamboo leaves and <i>Ocimum</i>	50 µg/kg bwt ip	0–6 Gy	Mouse bone marrow cells	CFU-S, chromosomal aberrations	63,165
Propolis	Propolis had approximately 50 constituents, primarily resins and vegetable balsams (50%), waxes (30%), essential oils (10%), and pollen (5%)	Resinous mixture collected by honey bees from tree buds, sap flow, or other plants	20–2,000 µg/mL treatment in culture	2 Gy	Human peripheral blood lymphocytes	Frequency of chromosomal aberrations, frequency of dicentric	65
			20 mg/kg bwt ip	6 Gy	BALB/c mice	Leukocyte count, spleen's plaque-forming activity	64
Quercetin	2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one	Oak tree and red onions	3, 6, 12, 24, and 48 µM treatment in culture	1–4 Gy	Human peripheral blood lymphocytes	Micronuclei frequency, dicentric aberration, comet assay	66
			10–20 mg/kg bwt orally	3 Gy	Swiss albino mice	Chromosomal aberrations, micronuclei frequency, comet assay	67

(Continued)

Table 3 (Continued)

Name of phytochemical	Chemical/other name	Origin/source	Doses		Animal/tissue studied	Cytogenetic parameters studied	References
			Phytochemical dose	Radiation dose (Gy)			
Resveratrol	3,5,4'-Trihydroxy-trans-stilbene	Naturally produced by several plants in response to injury, also found in grapes, blueberries, raspberries, and mulberries	100 mg/kg bwt, orally	3 Gy	Mouse bone marrow cells	Total chromosomal aberration frequency per metaphase	68
Rutin	2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-3-[α -L-rhamnopyranosyl-(1 \rightarrow 6)- β -D-glucopyranosyloxy]-4H-chromen-4-one	Orange, lemon, lime, grapefruit, and berries	10–20 mg/kg bwt orally	3 Gy	Swiss albino mice	Chromosomal aberrations, micronuclei frequency, comet assay	67
Turmeric	Diferuloylmethane, demethoxycurcumin, and bisdemethoxycurcumin	<i>Curcuma longa</i>	100, 250, and 500 μ g/mL treatment in culture	2.5 Gy	CHO cells	Frequencies of chromosomal aberrations	69
Vanillin	4-Hydroxy-3-methoxybenzaldehyde	Seed and pods of <i>Vanilla planifolia</i>	5, 50 or 100 μ g/mL treatment in culture	1–12 Gy	V79 cells	Micronucleated binucleated cells, aberrant cells	70
Vicenin	6-C- β -D-xyllopyranosyl-8-C- β -D-glucopyranosyl-apigenin	<i>Ocimum sanctum</i>	50 μ g/kg bwt ip	0–6 Gy	Mouse bone marrow cells	CFU-S chromosomal aberrations	63, 165
Vinblastine	Dimethyl (2 β ,3 β ,4 β ,5 α ,12 β ,19 α)-15-[(5S,9S)-5-ethyl-5-hydroxy-9-(methoxycarbonyl)-1,4,5,6,7,8,9,10-octahydro-2H-3,7-methanoazacycloundecino[5,4-b]indol-9-yl]-3-hydroxy-16-methoxy-1-methyl-6,7-didehydroaspidoispermidine-3,4-dicarboxylate	<i>Vinca rosea</i> (<i>Catharanthus roseus</i>)	0.05 mg/kg bwt ip	1–4 Gy	Mouse bone marrow cells	Micronuclei frequency, P/N ratio	71
Vitamin C	2-Oxo-L-threo-hexono-1,4-lactone-2,3-enediol or (R)-3,4-dihydroxy-5-((S)-1,2-dihydroxyethyl)furan-2(5H)-one	Plants, fruits, and vegetables	1 μ g/mL treatment in culture	2 Gy	Human peripheral blood lymphocytes	Micronuclei frequency	161
Vitamin E	(2R)-2,5,7,8-tetramethyl-2-[(4R,8R)-(4,8,12-trimethyltridecyl)]-6-chromanol	Wheat germ oil, sunflower oil, safflower oil, corn oil, soybean oil, and margarine	2 μ g/mL treatment in culture	2 Gy	Human peripheral blood lymphocytes	Micronuclei frequency	161
Zingerone	4-(4-Hydroxy-3-methoxyphenyl)-2-butanone	Cooked ginger	20 mg/kg bwt orally	1–4 Gy	Swiss albino mice	CFU-S, MnPCE, NCE and PCE/NCE ratio	72
Modulation of radiation-induced cytogenetic damage by various herbal formulations							
Abana	<i>Terminalia arjuna</i> , <i>Withania somnifera</i> , <i>Nepeta hindostana</i> , <i>Dashamoola</i> , <i>Tinospora cordifolia</i> , <i>Embellica officinalis</i> , <i>Terminalia chebula</i> , <i>Eclipta alba</i> , <i>Glycyrrhiza glabra</i> , <i>Asparagus racemosus</i> , <i>Boerhaavia diffusa</i>		5, 10, and 20 mg/kg bwt ip	0–3 Gy	Mouse bone marrow cells	Micronuclei frequency, PCE/NCE ratio	73
Brahma Rasayana	<i>Terminalia chebula</i> , <i>Phyllanthus emblica</i> , <i>Cinnamomum zeylanicum</i> , <i>Elettaria cardamomum</i> , <i>Cyperus rotundus</i> , <i>Curcuma longa</i> , <i>Piper longum</i> , <i>Aquilaria agallocha</i> , <i>Santalum album</i> , <i>Centella asiatica</i> , <i>Atropa belladonna</i> , <i>Convolvulus pluricaulis</i> ,		50 mg/day orally	Radio/chemo-therapy	Cancer patients	Total leukocytes, lymphocytes, and neutrophils	74

Liv. 52	500 mg/kg bwt orally	4.5 Gy	Mouse bone marrow cells	Frequency of chromatid and chromosomal aberrations	75
<p><i>Acorus calamus</i>, <i>Cyperus scariosus</i>, <i>Glycyrrhiza glabra</i>, <i>Embelia ribes</i>, Ghee, Sesamum oil, Milk, Sugar candy, <i>Desmodium gangeticum</i>, <i>Uraria picta</i>, <i>Solanum indicum</i>, <i>Solanum xanthocarpum</i>, <i>Tribulus terrestris</i>, <i>Aegle bruhat</i>, <i>Clerodendron premnos</i>, <i>Oroxylum indicum</i>, <i>Gmelina arborea</i>, <i>Pterospermum suaveolens</i>, <i>Sida cordifolia</i>, <i>Boerhavia diffusa</i>, <i>Ricinus communis</i>, <i>Phaseolus trilobus</i>, <i>Teramnus labialis</i>, <i>Asparagus racemosus</i>, <i>Tinospora cordifolia</i>, <i>Leptadenia reticulata</i>, <i>Withania somnifera</i>, <i>Bambusa arundanacia</i>, <i>Imperata cylindrica</i>, <i>Saccharum spontaneum</i>, <i>Oryza sativum</i>, <i>Saccharum officinalis</i>, <i>Capparis spinosa</i>, <i>Cichorium intybus</i>, Ferric Oxide Calx, <i>Solanum nigrum</i>, <i>Terminalia arjuna</i>, <i>Cassia occidentalis</i>, <i>Achillea millefolium</i>, <i>Tamarix gallica</i></p>					
<p>Abbreviations: ip, intraperitoneal injection; bwt, body weight; CHO, Chinese hamster ovary; PCE, polychromatic erythrocytes; NCE, normochromatic erythrocytes; MnPCE, micronucleated polychromatic erythrocytes; CFU-S, colony forming units in spleen; P/N, ratio of polychromatic to normochromatic erythrocytes.</p>					

polychromatic erythrocytes (MnPCE) occurred when beta carotene was given orally to mice before radiation exposure.

Caffeine

The radioprotective property of caffeine was evaluated in mice with acute and chronic dosing as well as caffeine treatment given before or after irradiation.⁵² It has been reported that acute doses of caffeine before or after irradiation were responsible for a reduction in the number of chromosomal aberrations. The different doses of caffeine were also studied for cytogenetic biomarkers in Chinese hamster V79 cells.⁵³ The various types of chromosomal aberrations were significantly decreased with caffeine treatment.

Chlorogenic acid

The radiation-induced cytogenetic damage in bone marrow of mice after chlorogenic acid administration was evaluated by micronucleus test.⁵⁵ It has been demonstrated that a significant decline in the number of MnPCE occurred when chlorogenic acid was given orally to mice before radiation exposure.

Chlorophyllin

The effect of chlorophyllin was studied in mouse bone marrow using cytogenetic biomarkers to evaluate its radioprotective properties.⁵⁴ Radiation-induced micronucleated polychromatic erythrocytes were found to be significantly reduced in chlorophyllin treated irradiated animals.

Curcumin

The radiation-induced cytogenetic damage in bone marrow of mice after curcumin administration was evaluated by micronucleus test.^{55,69} It has been demonstrated that a significant decline in the number of MnPCE occurred when curcumin was given orally to mice before radiation exposure.

Eugenol

The radiation-induced genetic damage in bone marrow of mice after eugenol administration was determined using micronucleus test.⁵⁶ Eugenol was found to afford significant radioprotection through reduction in MnPCEs at post-irradiation interval. It has been revealed that eugenol provides radioprotection against oxidative stress and its possible role as radioprotector has been suggested.

Hesperidin

The radioprotective effects of hesperidin using micronucleus test in irradiated mice were demonstrated.^{57,58} It has

been observed that hesperidin treatment had significant radioprotective activity in terms of cytogenetic biomarkers assessed in the bone marrow of mice.

Lycopene

The radioprotective potential of lycopene was assessed by cytogenetic biomarkers.^{59,162} It has been reported that lycopene-supplemented lymphocytes had a lower chromosomal aberration frequency.

Mangiferin

The radioprotective effects of mangiferin were evaluated by cytogenetic biomarkers in lymphocytes⁶⁰ and lymphoblastoid cells.³⁷ The results of cytogenetic studies revealed that mangiferin has significant radioprotective potential and has the capacity to suppress radiation-induced DNA damage via free radicals in lymphocytes and lymphoblastoid cells.

Melatonin

The possible role of melatonin as radioprotector has been demonstrated through bone marrow chromosomal aberration analysis in mice.^{61,158} It has been observed that melatonin treatment before irradiation caused a decrease in aberrant cells as well as structural chromosomal aberrations. These cytogenetic biomarkers have provided the evidence for melatonin as radioprotector.

Naringin

Cytogenetic analysis was carried out to evaluate the radioprotective effect of naringin in mice.⁶² It was observed that naringin pretreatment had a protective effect on cytogenetic endpoints.

Orientin

A radioprotective study was carried out in mouse bone marrow for evaluating orientin as radioprotector.⁶³ It was observed that pretreatment with orientin provided significant radioprotective activity in terms of DRF (1.6) based on CFU-S number. Thus it was demonstrated that orientin had protective effects against radiation-induced bone marrow damage and had great potential for protection of normal tissues during radiotherapy.

Propolis

Propolis was studied for radioprotection using cytogenetic biomarkers.^{15,64,65} It was noticed that the frequency of dicentrics was concentration-dependent and showed great potential in reducing the chromosomal aberration frequency. Thus,

propolis had radioprotective effects probably through the enhancement of antioxidant and free radical scavenging activities.

Quercetin

Quercetin was evaluated for cytogenetic protection against radiation in plasmid DNA and lymphocytes by scoring micronuclei frequency.⁶⁶ It was observed that quercetin treatment significantly decreased the micronuclei and dicentric frequencies, demonstrating the anti-genotoxic potential of quercetin.

Resveratrol

Resveratrol was evaluated for protection against irradiation using cytogenetic endpoints in mice.⁶⁸ The resveratrol treatment had protective effects *in vivo* against irradiation in mice.

Rutin

Rutin was evaluated for protective effects against radiation damage.⁶⁷ A significant decline in dicentric formation in the rutin treated group was observed, thus showing its anti-genotoxic potential. It has been demonstrated that administration of rutin prior to radiation exposure decreased DNA damage significantly.

Turmeric

The protective effect of turmeric against radiation-induced cytogenetic damage was evaluated in Chinese hamster ovary cells.⁶⁹ It was demonstrated that turmeric had a radiomodulatory effect in Chinese hamster ovary cells.

Vanillin

Vanillin was evaluated for cytogenetic protection against radiation in V79 cells by scoring micronuclei frequency and chromosomal aberration analysis.⁷⁰ It was observed that vanillin treatment decreased the percentage of structural chromosomal aberrations and percentage of micronucleated binucleated cells, thus indicating protection against cytogenetic damage induced by X-ray.

Vicenin

The radioprotective study was performed in mouse bone marrow to elucidate vicenin as radioprotector.⁶³ It was observed that pretreatment with orientin had significant radioprotective activity evident from DRF (1.7) value. Thus it was demonstrated that vicenin had protective effects against radiation-induced bone marrow damage and had great potential for protection of normal tissues during radiotherapy.

Vinblastine

The cytogenetic analysis was carried out to evaluate the radioprotective effect of vinblastine in mouse bone marrow cells.⁷¹ The vinblastine pretreatment showed increased frequency of micronuclei with increasing radiation dose. It was noted that vinblastine pretreatment provided protection against cytogenetic damage induced by radiation in mice.

Vitamin C and E

Pre- and post-treatment with vitamin C and E was found to be effective in protecting human lymphocytes against gamma irradiation in terms of micronuclei frequency.¹⁶¹ Furthermore, vitamin treatment did not show any adverse effects.

Zingerone

Zingerone was evaluated for its protective effects against radiation-induced cytogenetic damage in mice by micronucleus test.⁷² It has been demonstrated that zingerone had a role in protecting against cytogenetic damage in mice as evident in survival assay and CFU-S studies.

Radioprotective effects of certain herbal preparations

Abana

A herbal preparation, abana, was studied to evaluate the radioprotective effect in mice using micronucleus test.⁷³ The results of the cytogenetic study revealed that pretreatment with abana had prevented radiation-generated damage in bone marrow of mice, which was evident in micronuclei frequency and ratio of polychromatic erythrocytes to normochromatic erythrocytes.

Brahma Rasayana

The hematopoietic protection effect of Brahma Rasayana on cancer patients undergoing radio/chemotherapy was demonstrated.⁷⁴ It was observed that administration of Brahma Rasayana prevented the hematopoietic damage in terms of increase in total leukocytes, thus finding application as an adjuvant in cancer therapy.

Liv. 52

Cytogenetic analysis was carried out to evaluate the radioprotective effect of Liv. 52 in mouse bone marrow cells.⁷⁵ It was observed that Liv. 52 pretreated irradiated animals had significant recovery in cytogenetic endpoints studied.

Future perspectives

In recent years there has been a surge in the use of plant products for treatment of various illnesses including cancer.

The use of plant-based medicine has limitations in terms of systematic studies carried out for each plant product. Therefore, research must be done to acquire knowledge about the safe use of plant-based drugs before their possible use in medicine.⁷⁶ Studies on pharmacokinetics and pharmacodynamic properties including toxicity are essentially needed.⁷⁷ Quality control studies must focus on proper elucidation regarding evaluation process to report defined effects of the drug and factors such as age, sex, and species of the animal must also be considered.⁷⁸ The damage induced by ionizing radiation in cells is modulated by various mechanisms and pathways.⁷⁹ It has been suggested that radioprotectors protect cells by scavenging free radicals, or by hydrogen atom donation to repair sites of DNA damage.^{3,80} The deleterious effects of radiation are minimized by radioprotective agents, these agents are known to scavenge the reactive oxygen species thus preventing their immediate interaction with biochemical molecules.¹⁶⁵ The plants have varied antioxidant capacities probably due to differences in their contents of chemical constituents thus resulting in inconsistent radioprotective effects.⁸¹ For instance, in human studies with carotenoids it was shown that carotenoids can protect against radiation but a high dose of single compound carotenoid led to high mortality.¹⁶⁴ Several scientific studies¹⁶ have demonstrated the role of plants and phytochemicals for prevention of radiation-induced toxicity and damage thus demonstrating the significance, and demanding more attention.¹⁶ However, most of the studies have used either animal models or cell cultures and therefore, it is difficult to extend their validity in clinical settings thus causing a major limitation.¹⁶⁶ In fact these studies throw light on the mechanism of action. Apart from applications in clinics, plants, herbal formulations, and phytochemicals may have a use in case of accidental exposure to radiation. However, considering relevance of the field of plant-based radioprotectors, plant extracts and plant-derived compounds must be stringently analyzed in different models of radiation injury.

Disclosure

The authors report no conflicts of interest in this work.

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