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Review Article

A Narrative Review on the Anti-genotoxic Potential of Medicinal Plants in Ayurveda

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A B S T R A C T

Genotoxicity is the capacity of drugs to induce DNA damage by chemically modifying either the structure or the sequence of nucleotides. This is most commonly experienced in lifestyle disorders as the medication in these conditions requires long-term administration. As per the WHO's current status, 74% of the current deaths in a year are due to lifestyle disorders. Traditional plant-based medicines play a major role in the prevention of a few communicable diseases. Apart from the prevention of disease, they provide a protective effect against the ill effects induced by oxidative stress due to diet and regimes. The current review contains articles from PubMed, Web of Science, Scopus, and Google Scholar databases from October 2021 – September 2022 by searching keywords including "anti-genotoxicity" or "mutagenicity" or "anti-mutagenicity" and "in vitro" or "in vivo" and "plants" or "medicinal plants". After review, 45 articles were included, which contained information about 38 plants. This article rationalises the long-term usage of medicinal plants in treating various health conditions.

Keywords: Traditional Medicine, Anti-oxidants, Medicinal Plants, Anti-genotoxic Potential, Protective-effect

Introduction

The genotoxicity of a substance is its capacity to induce damage to a DNA by chemically modifying the structure or nucleotide sequence. It can be due to severe repercussions on cellular functions and survival, and can be transmitted to the offspring due to germ cell damage.[1] During the last few decades, cancer, CVD, liver disorders and other lifestyle diseases have constituted a major part of the expenditure in the health sector. The major culprit for the occurrence of these lifestyle disorders is the free radical called Reactive oxygen species (ROS). Among the reactive compounds, ROS are highly reactive, unstable molecules with one or more unpaired electron(s) in the outer shell. They are genotoxic molecules and play a vital role in several pathologies including cancer.

There are many natural antioxidants like polyphenolic compounds that are found to possess protective effects on chronic diseases occurring due to oxidative stress. Epidemiological studies reveal that a high intake of anti-oxidant-rich foods is inversely related to the risk of cancer.[2]

There are a lot of research articles regarding the anti-genotoxic potential of medicinal plants. This article tends to summarise the results of research conducted so far on the anti-genotoxic potential of various medicinal plants used in Ayurveda.

Materials and Method

In the current review, findings were extracted from PubMed, Web of Science, Scopus and Google Scholar databases from October 2021 – September 2022 by searching keywords like "anti-genotoxicity" or "mutagenicity" or "anti-mutagenicity" and "in vitro" or "in vivo" and "plants" or "medicinal plants". Publications in a language other than English language and studies exclusively done on the active compounds were excluded.

Results and Discussion

The articles were selected as per the criteria shown in Figure 1.

Table 1 shows categorisation of anti-genotoxicity activity of medicinal plants.

2AA: 2 amino anthracene, Ac.: Acetone, Ae.: Aerial parts, Al.: Alcoholic, Aq.: Aqueous, Ar.: Arsenic, BAP: Barium amino phosphate, CCl_4: Carbon tetra chloride, $CdSO_4$: Cadmium sulphate, CP: Cyclophosphamide, E: Ethanolic, Fr.: Fruit, Fl.: Flower, Fl. Bud: Flower bud, H_2O_2: Hydrogen peroxide, Hy. Al: Hydro alcohol, L: Leaf, M: Methanolic, MMS: MNNG: N-methyl, N-nitro, N-nitrosoguanidine, P: Pulp, PE: Petroleum ether, R: Root, Rn.: Resin, Rz.: Rhizome, Sd.: Seed, St: Stem, St. Bk: Stem bark, STZ: Streptozotocin, WP: Whole plant

Comet Assay

It's the simplest and a highly versatile method to measure DNA damage and repair at the cellular level. It relies on the 'comet'-like appearance of negatively charged DNA fragments which are pulled in response to an electric field inside an agarose gel. This method adopts the simple biochemical techniques for detecting DNA-single strand breaks, alkali-labile sites and cross-linking approaches in cytogenetic assays. This method is efficient to detect low-level damage, use of proliferating or non-proliferating monodispersed cell populations, single-cell data collection and a smaller number of cells per sample. It is also flexible to use fresh or frozen samples.[49]

Micronucleus Assay

It is the simplest in vitro/ in vivo method to evaluate genotoxic properties in various mammalian models and aquatic models. It is a sensitive model to assess genotoxicity in various mammalian models. Micronuclei are small nuclei which arise in the mitotic cells from chromosomes or chromosomal fragments which lag behind in anaphase and are not integrated into daughter nuclei. These micronuclei harbour chromosomal fragments resulting in direct DNA breakage, replication or inhibition of DNA synthesis. This occurs primarily due to the failure of mitotic spindle, kinetochore or other parts of mitotic apparatus or by chromosomal damage. Thus, an increase in the frequency of micro-nucleated cells is a biomarker of genotoxic effects that can reflect exposure to agents with clastogenic (chromosome breaking; DNA as target) or aneugenic (aneuploidogenic; effect on chromosome number; mostly non-DNA target) modes of action.[50]

Chromosomal Aberration Assay

This assay identifies the agents which produce structural chromosome aberrations like chromatid formation. An increase or decrease in the number of chromosomes suggests the potential of the agent to induce aberrations.[51]

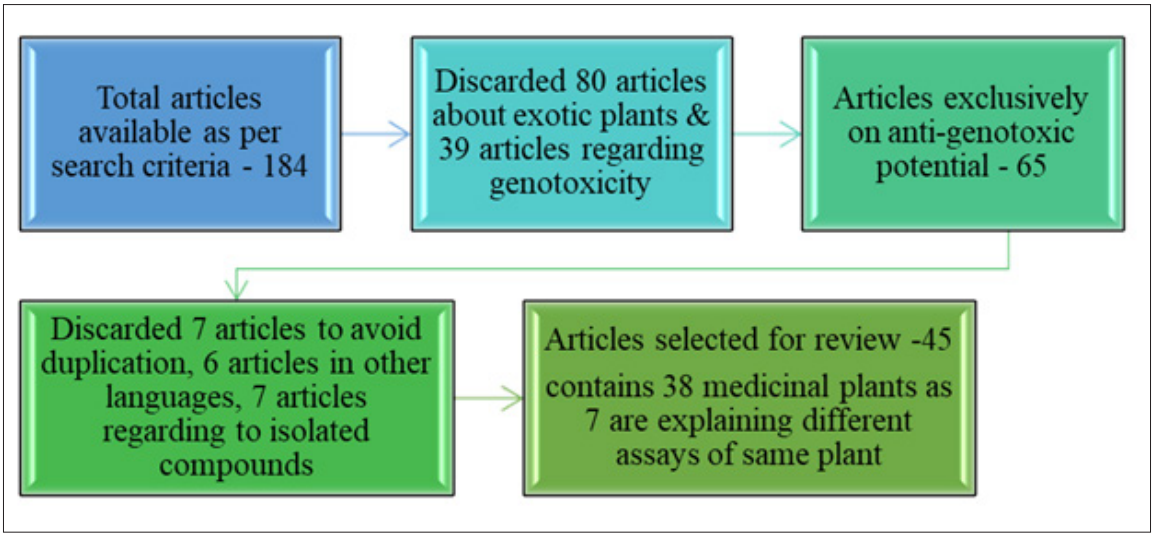

Figure 1.Selection Criteria for the Articles describing Anti-genotoxicity of Medicinal Plants

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Table 1.Categorisation of Anti-genotoxicity Activity of Medicinal Plants

S. No.	Botanical Identity	Plant Part	Ex.	Conc.	Ind. Agent	Conc.	Test	Result	
								Observation	Toxicity
1.	*Aegle marmelos [Bilwa]*[3]	Fr	M, Ac, Aq.	50, 100, 150, 200 µg/ml	H_2O_2	1.0 mM	SOS chromo test using *E. coli* PQ37	Reduced the oxidative stress induction factor induced by H_2O_2 in a dose-dependent manner	Anti-genotoxic
					Aflatoxin B1	10µg/assay	SOS chromo test using *E. coli* PQ37	Reduced the oxidative stress induction factor induced by H_2O_2 in a dose-dependent manner	
2.	*Alstonia scholaris* Linn. *[Saptaparna]*[4]	WP	M	In vitro - 150, 200, 250, 300 µg/ml in vivo - 200, 250, 300, 350, 400 mg/kg	MMS	5 µg/ml	Chromosomal aberration test	Reduced total frequencies of cell-aberration	Anti-genotoxic
3.	*Amaranthus spinosus* Linn. *[Tanduleeyaka]*[5]	L	Aq.	0.05 g/L, 0.1 g/L, 0.5 g/L, 1 g/L	H_2O_2	3%, 7%	Allium cepa assay	Significant reduction of nuclear lesions, prevented oxidative damage at tested conc.	Anti-mutagenic
4.	*Azadirachta indica [Nimba]*[6,7]	L	E	200 mg/kg	MNNG	40 mg/kg	Schmid Micronucleus test	Significantly reduced micronuclei and lipid peroxides	Anti-genotoxic
		L	E	200 mg/kg	DMBA	35 mg/kg	Micronucleus test	Significantly reduced micronuclei and lipid peroxides	Anti-genotoxic

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5.	*Boswellia serrata [Sallaki]*[8]	Rn	Dry	5, 2.5, 1.25, 0.625, 0.312 mg/plate	4-nitroquinolene-1-oxide, 2-aminofluorene, mitomycin C, sodium azide, benzo alpha pyrene	5 µg/plate, 20 µg/plate, 0.02 mg/plate, 5 µg/plate	Anti-mutagenicity test	Exhibited protection against the mutagenicity induced by 4-nitroquinolene-1-oxide, 2-aminofluorene, sodium azide in TA98 and TA100 strain	Anti-genotoxic
6.	*Brassica juncea [Rajika]*[9,10]	Sd	Ch.	0.1, 0.25, 0.50, 0.75, 1.0%	Hg	0.1, 0.25, 0.50, 0.75, 1, 2 ppm	Allium cepa chromosomal aberration assay	A dose-dependent increase in root number and root growth in Hg-treated groups	Dose-dependent anti-genotoxic
			Aq.	0.1, 0.25, 0.50, 0.75, 1.0%	Hg	0.1, 0.25, 0.50, 0.75, 1, 2 ppm	Allium cepa chromosomal aberration assay	Dose-dependent protective effect	Anti-genotoxic
7.	*Calotropis procera [Arka]*[11]	R	E	500 mg/kg	DMBA	30 mg/kg	Micronucleus assay	Increase in the % MNCPE in test groups, inhibition of bone marrow cell multiplication, decrease in PCE:NCE ratio	Anti-genotoxic
8.	*Capparis spinosa L. [Himsra]*[12]	Fl. bud	Aq.	10, 20, 30 g/L	EMS	3.10^{-2} M	Micronucleus assay	Growth retardation, a significant decrease in mitotic index and chromosomal aberrations observed in a dose-dependent manner	Anti-mutagenic
9.	*Centella asiatica Linn. [Mandukaparni]*[13]	L	Ac	[1.075, 2.127, 3.15, 4.17] × 10^{-4}	CPA	20, 30 µM	Chromosomal aberration analysis	Dose-dependent protective effect	Anti-genotoxic

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10.	*Citrullus colocynthis (L.) [Indravaruni]*[14]	Fr	Hy.Al.	0.5-3 mg/ Ml	CP	10, 50, 100, 200 mg/kg as i.p inj.	Micronucleus assay	Suppressed the action of CP in clastogenic effects	Anti-mutagenic
11.	*Citrus reticulata [Naranga]*[15]	P, Ae	E, PE	20 mg/kg	BaP	50 mg/kg	Comet assay	Effective in preventing DNA damage induced by BaP and showed good antigenotoxic activities	Anti-mutagenic
12.	*Coriandrum sativum* Linn. *[Dhanyaka]*[16]	Sd	M	0.1, 0.5, 1.0%	CT	2-10 ppm	Allium cepa assay	Protection against CT-induced physiological and clastogenic aberrations	Anti-genotoxic
13.	*Costus speciosus [Ketaki]*[17]	WP	Aq.	50, 100, 150 mg costus	STZ	80 mg/kg	Comet assay	Significantly reduced DNA damage	Anti-genotoxic
							Micronucleus assay	Lowered the incidence of micronucleated polychromatic erythrocytes	
							Chromosomal aberrations	Lowered the percentage of all types of structural aberrations and numerical variations	
14.	*Cuminum cyminum* Linn. *[Sweta jeeraka]*[16]	Sd	M	0.1, 0.5, 1.0%	CT	2-10 ppm	Allium cepa assay	Protection against CT-induced physiological and clastogenic aberrations	Anti-genotoxic

ISSN: 2278-2044
DOI: https://doi.org/10.24321/2278.2044.202312

15.	*Curcuma longa* Linn. *[Haridra]*[18]	Rz	E	50, 100, 200, 400 mg/kg	Mytomycin-C	2 mg/kg	Micronucleus assay, chromosomal aberration	Showed a protective effect of about 90% for mitotic index, 97.55% for chromosome aberrations, and 97.65% for reduction of micronucleus	Anti-genotoxic
16.	*Cyperus rotundus* Linn. *[Mustha]*[19,20]	Ae	Aq., EA, M, TOF	50, 200, 500 µg/ assay	BAP	200 µg/ assay	SOS chromo test strain *E. coli* PQ37	A dose-dependent decrease in mutagen genotoxicity	Anti-mutagenic
		Rz	Aq., EA, M, TOF	50, 200, 500 µg/mL	Aflatoxin B1, Nifuroxazide	10 µg/ assay	AME's *Salmonella* tester strains TA98, TA100; SOS chromo test strain *E. coli* PQ37	Dose-dependent inhibitory effect	Anti-mutagenic
17.	*Foeniculum vulgare* Mill. *[Misreya]*[21-23]	Sd	Aq.	2,4,8%	MMS	1 mM	SMART assay of Drosophila melanogaster – eye spot test	A dose-dependent decrease in mutation frequency at an inhibition rate of 41.16%	Anti-mutagenic
			Aq.	0.5, 5 mg/ ml	Mytomycin C Colchicine		Chromosomal aberration Drosophila assay	Decreased the chromosomal aberrations induced by the mutagens	Anti-mutagenic
		Essential oil	Oil	1, 2 ml/kg	CP	40 mg/kg	Bone marrow CA assay, Micronucleus assay, Sperm abnormality assay	Inhibited genotoxicity and oxidative stress induced by CP	Anti-mutagenic

ISSN: 2278-2044
DOI: https://doi.org/10.24321/2278.2044.202312

18.	*Glycyrrhiza glabra* Linn. *[Yashtimadhu]*[24,25]	R	M	0.1, 5, 10, 20 µg/ml	Mitomycin-C Cytochalasin B	0.1 µg/ml 6 µg/ml	Chromosome aberration assay, Cytokinesis-block micronucleus (CBMN) assay	Significantly reduced the formation of micronucleus and chromosomal aberrations	Anti-genotoxic
			Aq,M	300, 450, 600 mg/kg	CP	50 mg/kg	Chromosomal aberration test	Dose-dependent protective effect against chromosomal aberration	Anti-genotoxic
19.	*Hemidesmus indicus R Br [Sariba]*[26]	R	E	2, 4, 8, 16, 32 µg/ml	Cisplatin	0.05 µg/ml	Sister Chromatid analysis Chromosome aberration assay, Cytokinesis – block micronucleus assay	Significantly reduced the frequency of sister chromatid exchange, chromosome aberration and micro-nucleated binuclear cells at lower conc. 4 and 8 µg/ml	Anti-genotoxic
20.	*Hibiscus rosa-sinensis [Japa]*[27]	Fl.	E	250 mg/kg	CP	40 mg/kg	Micronucleus assay, Comet assay – Single cell gel electrophoresis - SCGE	A dose-dependent increase in radical scavenging ability against various free radicals and significant inhibition of lipid peroxidation in vitro	Anti-genotoxic
21.	*Myristica fragrans* Houtt. *[Jatiphala]*[28]	Fr	Aq.	1, 2, 4, 8%	CP	0.1%	Allium cepa test	Suppresses cytotoxicity and chromosomal aberrations	Anti-genotoxic

ISSN: 2278-2044
DOI: https://doi.org/10.24321/2278.2044.202312

22.	*Nigella sativa [Kalajaji]*[29,30]	Sd	Aq.	1, 4, 8 mg/ plate 2, 4, 9 mg/ ml 0.5265, 1.125, 2.25, 4.5, 9, 18 mg/ml	2AA	1 µg/plate	Vitotox test – TA104 Ame's assay – TA98, TA100 Comet assay, Micronucleus assay, Neutral red uptake test in human C3A cells	Lowers the genotoxicity induced by the mutagens in a dose-dependent manner	Anti-genotoxic
			E	8.3%	MNNG	0.5 µM	Cytogenetic studies	Significantly reduced the formation of micronucleus and chromosomal aberrations	Anti-genotoxic
23.	*Ocimum sanctum [Karpoora thulasi]*[31,32]	L	Aq. & E	50 mg/kg	Ch. py	75 µg/mml	Comet assay, Chromosomal aberrations, Micronuclei frequency Mitotic index	Reduced the manifestation of chromosomal aberrations, even though the mitotic index remained increased	Anti-genotoxic
			Aq.	50, 100, 200 µl/ml	CP	100 µg/ml	Chromosomal aberration assay	All the treated doses significantly reduced the chromosomal aberrations induced by cyclophosphamide and there is an increase in mitotic index.	Anti-genotoxic
24.	*Phyllanthus emblica Linn. [Amalaki]*[33]	Fr	Aq.	170, 340, 680 mg/kg	CP	50 mg/kg	Chromosomal aberration assay	Decrease in the frequency of chromosomal aberrations	Anti-genotoxic

ISSN: 2278-2044
DOI: https://doi.org/10.24321/2278.2044.202312

25.	*Phyllanthus maderaspatensis* Linn. *[Bhoomyamalaki]*[34]	WP	E	400, 600 mg/kg	Cisplatin	5 mg/kg	Bone marrow micronucleus assay	The number of MNCPE's Micro nucleated polychromatic erythrocytes formed was less in the treated groups.	Anti-genotoxic
26.	*Phyllanthus niruri* Linn. *[Bhoomyamalaki]*[35]	WP	Aq.	50, 150, 250 mg/Kg	CP	50 mg/kg	Micronucleus assay	There's no significant decrease in micro-nucleated polychromatic erythrocytes.	Non-genotoxic, protective effect
27.	*Phyllanthus orbicularis [Krishna kamboji]*[36]	WP	Aq.	0, 10, 100, 500, 1000 µg/ml	H_2O_2	5 Mm	Chromosome aberration assay	Significantly reduced the chromosome aberrations caused by hydrogen peroxide.	Anti-genotoxic
28.	*Plumbago zeylanica [Sweta chitraka]*[37]	R	E	250, 500 mg/kg	CP	40 mg/kg	Micronucleus test	Results show a dose-dependent reduction in micronucleated polychromatic erythrocytes formed in treated groups.	Anti-genotoxic
29.	*Punica granatum Linn. [Dadima]*[38]	P, Sd.	E	0.3 g/kg	CCl_4	5%	Chromosome aberration assay, Sperm morphology assay	Significantly decreased the number of cells with chromosomal aberrations and percentage of abnormal sperms induced by CCl_4	Anti-genotoxic

ISSN: 2278-2044
DOI: https://doi.org/10.24321/2278.2044.202312

30.	*Quercus infectoria [Mayaphala]*[39]	Gall	Aq.	2, 5, 7 gm/ kg	2AA	750 mg/kg	Bone marrow index, Chromosomal aberration, Micronucleus assay	Significantly decreased the chromosomal aberrations, micronuclei formation frequency and stimulated cell proliferation in bone-marrow cells at 2 gm/kg	Anti-genotoxic
31.	*Spondias dulcis* Forst F. *[Amrataka]*[40]	St Bk.	E	500, 1000, 1500 mg/kg	BAP, CP	9 mg/kg 40 mg/kg	Micronucleus assay, Comet assay	The extracts effectively reduced the formation of micronucleated polychromatic erythrocytes and reduced the chromosomal aberration induced by testing compounds.	Anti-genotoxic
32.	*Syzygium cumini [Jambu]*[41,42]	Sd.	M	200, 400 mg/kg	Ar.	100 ppm	Comet assay	The mean value of tail per cent DNA, tail length, and tail moments were significantly less in treated groups.	Anti-genotoxic
		Fr.	M	100, 200 mg/kg	CP	40 mg/kg	Micronucleus assay, Chromosomal aberration	The treated groups significantly inhibited the frequencies of aberrant metaphases, chromosomal aberrations and mono-nuclear formation	Anti-genotoxic

ISSN: 2278-2044
DOI: https://doi.org/10.24321/2278.2044.202312

33.	*Terminalia catappa [Ingudi]*[43]	L	Aq.	25, 50, 75, 100 µg/ml	BMS	2.25 mU/ml	Comet assay, Chromosomal aberration	The extracts prevent the intracellular DCF fluorescence intensities induced by bleomycin sulphate.	Anti-genotoxic
34.	*Tinospora cordifolia [Guduchi]*[44]	St	E	80 mg/kg	Na_2HAsO_4	4 mg/kg	Micronucleus assay	Minimises the clastogenic effect. The numbers of micronuclei formed were much less in extract-treated groups.	Anti-genotoxic
35.	*Terminalia arjuna Linn. [Arjuna]*[45]	St. Bk.	E	120, 180, 240 mg/kg	CP	50 mg/kg	Micronucleus assay, Chromosomal aberration	Significantly prevented the micronucleus formation and chromosomal aberrations induced by CP	Anti-genotoxic
36.	*Trigonella foenum-graecum[Methika]*[46]	L	M, E	0.1, 0.5, 1%	$CdSO_4$	250 ppm	Allium cepa assay	The extracts significantly modulated the genotoxic and clastogenic aberrations induced by the cadmium sulphate.	Anti-genotoxic
37.	*Withania somnifera [Aswagandha]*[47]	Rz.	DEE	0.25, 0.50, 0.75%	MNNG	0.1%	Allium cepa assay	The treated extracts exhibited a dose-dependent protective effect on MNNG-induced chromosomal aberrations.	Anti-genotoxic
38.	*Withania coagulans [Rishyagandha]*[48]	Fr	M	500, 1000, 1500 mg/kg	CP	50 mg/kg	Micronucleus assay	In a dose-dependent manner, the extracts prevent the formation of micronuclei.	Anti-genotoxic

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SOS Chromo Text

This is a rapid, short-term, colorimetric biological assay to assess the genotoxic potential of chemical compounds. It measures the expression of genes in *E. coli* when exposed to genotoxic agents, by means of a fusion with the structural gene for β-galactosidase. It compliments Ame's assay in such a way that it detects genotoxic agents like estradiol, which may yield false negative results with the previous one.[52]

Allium Cepa Assay

The test is a widely applicable screening test for chemicals and in situ monitoring of environmental contaminants. This test employs the exposure of apical meristems of *Allium cepa* to monitor for any chromosomal aberrations.[53]

Ame's Assay

This is a rapid, easy and inexpensive way to conduct an initial screening test for genotoxicity.[54] It is conducted by using amino acid requiring strains of *Salmonella typhimurium* and *Escherichia coli* to detect the mutation points like deletion, addition or substitution of one or more base pairs of DNA.[55] The principle behind the test is that if the bacterial strains are kept in a medium with minimal or no histidine and mutant, the mutant will revert the DNA so as to produce histidine, which is essential for the growth of bacterial strains.[54,56]

Conclusion

This article contains the anti-genotoxic properties of 38 plants assessed using Comet assay (8 plants), Micro nucleus assay (21 plants), Chromosomal aberration assay (18 plants), SOS chromo text (3 plants), Allium cepa assay (8 plants), Sperm abnormality test (2 plants), and Anti-mutagenicity test, Ame's assay, Drosophila melanogaster eye spot test, and Vitotox assay (one each). This article has aimed to briefly describe the medicinal plants with anti-genotoxic properties along with the tests performed to assess them.

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Conflict of Interest: None

References

1. Turkez H, Arslan ME, Ozdemir O. Genotoxicity testing: progress and prospects for the next decade. Expert Opin Drug Metab Toxicol. 2017;13(10):1089-98. [PubMed] [Google Scholar]
2. Greenwald P, Clifford CK, Milner JA. Diet and cancer prevention. Eur J Cancer. 2001;37(8):948-65. [PubMed] [Google Scholar]
3. Kaur P, Walia A, Kumar S, Kaur S. Antigenotoxic activity of polyphenolic rich extracts from *Aegle marmelos* (L.) Correa in human blood lymphocytes and E. coli PQ 37. Rec Nat Prod. 2009;3:68-75. [Google Scholar]
4. Ahmad S, Ahmad S, Ali A, Afzal M. Anticarcinogenic and antimutagenic activity of *Alstonia scholaris* on the albino mice bone marrow cells and peripheral human lymphocyte culture against methyl methane sulfonate induced genotoxicity. Adv Biomed Res. 2016;5:92. [PubMed] [Google Scholar]
5. Prajitha V, Thoppil JE. Genotoxic and anti-genotoxic potential of the aqueous leaf extracts of *Amaranthus spinosus* Linn. using *Allium cepa* assay. South Afr J Bot. 2016;102:18-25. [Google Scholar]
6. Subapriya R, Kumaraguruparan R, Abraham SK, Nagini S. Protective effects of ethanolic neem leaf extract on N-methyl-N'-nitro-N-nitrosoguanidine-induced genotoxicity and oxidative stress in mice. Drug Chem Toxicol. 2004;27(1):15-26. [PubMed] [Google Scholar]
7. Subapriya R, Kumaraguruparan R, Abraham SK, Nagini S. Protective effects of ethanolic neem leaf extract on DMBA-induced genotoxicity and oxidative stress in mice. J Herb Pharmacother. 2005;5(4):39-50. [PubMed] [Google Scholar]
8. Magesh V, Raman D, Pudupalayam KT. Genotoxicity studies of dry extract of *Boswellia serrata*. Trop J Pharm Res. 2008;7(4):1129-35. [Google Scholar]
9. Sharma S, Nagpal A, Vig AP. Genoprotective potential of *Brassica juncea* (L.) Czern. against mercury-induced genotoxicity in *Allium cepa* L. Turk J Biol. 2012;36(6):622-9. [Google Scholar]
10. Sharma S, Nagpal A, Vig AP. Genoprotective potential of Brassica juncea (L.) Czern. against mercury-induced genotoxicity in Allium cepa L. Turk J Biol [Internet]. 2012 [cited 2022 Aug 27];36:622-9. Available from: https://journals.tubitak.gov.tr/cgi/viewcontent.cgi?article=1740&context=biology
11. Dayana K, Manasa MR. Evaluation of antigenotoxic activity of ethanolic extract of *Calotropis procera* root in 7,12-dimethylbenz[a]anthracene induced genotoxicity in Wistar rats. Natl J Physiol Pharm Pharmacol. 2018;8(12):1617-21. [Google Scholar]
12. Sultan AO, Celik TA. Genotoxic and antimutagenic effects of *Capparis spinosa* L. on the Allium cepa L. root tip meristem cells. Caryologia Intl J Cytol Cytosyst Cytogenet. 2009;62(2):114-23. [Google Scholar]
13. Siddique YH, Ara G, Beg T, Faisal M, Ahmad M, Afzal M. Antigenotoxic role of *Centella asiatica* L. extract against cyproterone acetate induced genotoxic damage in cultured human lymphocytes. Toxicol in Vitro. 2008;22:10-7. [PubMed] [Google Scholar]
14. Shokrzadeh M, Chabra A, Naghshvar F, Ahmadi A. The mitigating effect of *Citrullus colocynthis* (L.) fruit extract

against genotoxicity induced by cyclophosphamide in mice bone marrow cells. ScientificWorldJournal. 2013;2013:980480. [PubMed] [Google Scholar]
15. Hassan AZ, Ahmed KM, Abu-Gabal NS, Mahrous KF, Shalaby NM. Phytochemical and genotoxicity studies of *Citrus reticulata* aerial part in mice. Egyptian Pharm J. 2017;16:87-97. [Google Scholar]
16. Sharma A, Kumar M, Kaur S. *Cuminum cyminum* Linn. and *Coriandrum sativum* Linn. extracts modulate chromium genotoxicity in Allium cepa chromosomal aberration assay. Nucleus. 2011;54:99-105. [Google Scholar]
17. Giris SM, Shoman TM, Kassem SM, El-Din AE, Abdel-Aziz KB. Potential protective effect of *Costus speciosus* or its nanoparticles on streptozotocin-induced genotoxicity and histopathological alterations in rats. J Nutr Food Sci. 2015;5(3):1-7. [Google Scholar]
18. Mohammed MS. In-vivo cytogenetic and genotoxic effects of curcumin on mouse bone marrow. QMJ. 2013;9(16):245-60. [Google Scholar]
19. Kilani-Jaziri S, Bhouri W, Skandrani I, Limem I. Phytochemical, antimicrobial, antioxidant, and antigenotoxic potentials of *Cyperus rotundus* extracts. South Afr J Bot. 2011;77(3):767-76. [Google Scholar]
20. Kilani S, Bouhlel I, Ben R, Abdelwahed A, Hayder N, Mahmoud A, Ghedira K, Chekir-Ghedira PL. Evaluation of the antimutagenic and antiradical potentials of extracts from the tubers of (Tunisian) *Cyperus rotundus*. Toxicol Environ Chem. 2014;87:415-25. [Google Scholar]
21. Amkiss S, Dallouh A, Idaomar M, Amkiss B. Genotoxicity and anti-genotoxicity of fennel plant (*Foeniculum vulgare* Mill.) fruit extracts using the somatic mutation and recombination test (SMART). Afr J Food Sci. 2013;7:193-7. [Google Scholar]
22. Ebeed NM, Abdou HS, Booles HF, Salah SH, Ahmed ES, Fahmy K. Antimutagenic and chemoprevention potentialities of sweet fennel (*Foeniculum vulgare* Mill.) hot water crude extract. J Am Sci. 2010;6(9):831-42. [Google Scholar]
23. Tripathi P, Tripathi R, Patel RK, Pancholi SS. Investigation of antimutagenic potential of *Foeniculum vulgare* essential oil on cyclophosphamide induced genotoxicity and oxidative stress in mice. Drug Chem Toxicol. 2013;36(1):35-41. [PubMed] [Google Scholar]
24. Kocaman AY, Guzelkokar M. The genotoxic and antigenotoxic potential of the methanolic root extract of *Glycyrrhiza glabra* L. on human peripheral blood lymphocytes. Drug Chem Toxicol. 2018;41:368-75. [PubMed] [Google Scholar]
25. Sharma V, Agarwal RC. Evaluation of anti-clastogenic effects of *Glycyrrhiza glabra* root extract against cyclophosphamide induced chromosomal aberration in Swiss Albino mice. J Appl Pharma Sci. 2015;5(6):127-32. [Google Scholar]
26. Ananthi R, Chandra N, Sathiya ST, Ramesh A. Genotoxic and antigenotoxic effects of *Hemidesmus indicus* R. Br. root extract in cultured lymphocytes. J Ethnopharmacol. 2010;127(2):558-60. [PubMed] [Google Scholar]
27. Khatib NA, Ghoshal G, Nayana H, Joshi RK, Taranalli AD. Effect of *Hibiscus rosa-sinensis* extract on modifying cyclophosphamide induced genotoxicity and scavenging free radicals in Swiss Albino mice. Pharmacologyonline. 2009;3:796-808. [Google Scholar]
28. Akeem A, Mohamed KB, Asmawi MZ, Sofiman OA. Mutagenic and antimutagenic potentials of fruit juices of five medicinal plants in *Allium cepa* L.: possible influence of DPPH free radical scavengers. Afr J Biotechnol. 2011;10:10248-57. [Google Scholar]
29. Nguyen T, Talibi H, Hilali A, Anthonissen R, Maes A. In vitro toxicity, genotoxicity and antigenotoxicity of *Nigella sativa* extracts from different geographic locations. South Afr J Bot. 2019;126:132-41. [Google Scholar]
30. Khader M, Bresgen N, Eckl PM. Antimutagenic effects of ethanolic extracts from selected Palestinian medicinal plants. J Ethnopharmacol. 2010;127(2):319-24. [PubMed] [Google Scholar]
31. Khanna A, Shukla P, Tabassum S. Role of *Ocimum sanctum* Linn. as a genoprotective agent on chlorpyrifos induced genotoxicity. Toxicol Int. 2011;18(1):9-13. [PubMed] [Google Scholar]
32. Vijaya PP, Rekha B, Mathew AT, Ali MS, Yoganath N, Anuradha V, Parveen PK. Antigenotoxic effect of green-synthesised silver nanoparticles from *Ocimum sanctum* Linn. leaf extract against cyclophosphamide induced genotoxicity in human lymphocytes-in vitro. Appl Nanosci. 2014;4:415-20. [Google Scholar]
33. Rao K, Devi KR. The protective effects of *Phyllanthus emblica* Linn. in cyclophosphamide induced genotoxicity in mice. Int J Pure Appl Biosci. 2016;4(5):90-7.
34. Chandrasekar MJ, Bommu P, Nanjan MJ, Suresh B. Chemoprotective effect of *Phyllanthus maderaspatensis* Linn. in modulating cisplatin-induced nephrotoxicity and genotoxicity. Pharma Biol. 2006;44(2):100-6. [Google Scholar]
35. de Queiroz FM, de Oliveira Matias KW, da Cunha MM, Schwarz A. Evaluation of (anti)genotoxic activities of *Phyllanthus niruri* L. in rat bone marrow using the micronucleus test. Braz J Pharm Sci. 2013;49(1):135-48. [Google Scholar]
36. Sanchez-Lamar A, Fiore M, Cundari E, Ricordy R, Cozzi R, de Salvia R. *Phyllanthus orbicularis* aqueous extract: cytotoxic, genotoxic, and antimutagenic effects in the CHO cell line. Toxicol Appl Pharmacol. 1999;161(3):231-9. [PubMed] [Google Scholar]
37. Sivakumar V, Devaraj SN. Protective effect of *Plumbago*

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zeylanica against cyclophosphamide induced genotoxicity and oxidative stress in Swiss albino mice. Drug Chem Toxicol. 2006;29(3):279-88. [PubMed] [Google Scholar]
38. Abdou HS, Salah SH, Boolesand HF, Abdel Rahim EA. Effect of pomegranate pretreatment on genotoxicity and hepatotoxicity induced by carbon tetrachloride (CCl_4) in male rats. J Med Plant Res. 2012;6(17):3370-80. [Google Scholar]
39. Mohammed BM. Anti-mutagenic protection of *Quercus infectoria* galls against 2-Aminoanthracene induced genotoxicity in mice bone marrow. World J Pharm Sci. 2017;5(5):78-202. [Google Scholar]
40. de S Arajuo C, Brito LD, Tarifa MO, Silva NJ, Rodrigues KS, Cavalcante DG, Gomes AS, Zocoler MA, Yoshihara E, Camparoto ML, Job AE, Kerche LE. Protective effects of bark ethanolic extract from *Spondias dulcis* Forst F. against DNA damage induced by benzo(a)pyrene and cyclophosphamide. Genet Mol Biol. 2019;42(3):643-54. [PubMed] [Google Scholar]
41. Kumar M, Thakur R. *Syzygium cumini* seed extract ameliorates arsenic induced blood cell genotoxicity and hepatotoxicity in Wistar albino rats. Rep Biochem Mol Biol. 2018;7(1):110-8. [PubMed] [Google Scholar]
42. Tripathi P, Patel RK, Tripathi R, Kanzariya NR. Investigation of antigenotoxic potential of *Syzygium cumini* extract (SCE) on cyclophosphamide induced genotoxicity and oxidative stress in mice. Drug Chem Toxicol. 2013;36(4):396-402. [PubMed] [Google Scholar]
43. Chen PS, Li JH, Liu TY, Lin TC. Folk medicine *Terminalia catappa* and its major tannin component, punicalagin, are effective against bleomycin-induced genotoxicity in Chinese hamster ovary cells. Cancer Lett. 2000;152(2):115-22. [PubMed] [Google Scholar]
44. Ambasta SK, Trivedi I, Kumari S, Kumar A, Verma P, Prasad B, Kumar R, Sinha UK. Anticlastogenic effects of *Tinospora cordifolia* against arsenic induced genotoxicity using micronucleus assay in Swiss albino mice peripheral blood erythrocytes. IOSR J Environ Sci Toxicol Food Technol. 2017;11(1):97-100. [Google Scholar]
45. Scassellati-Sforzolini G, Villarini LM, Moretti LM, Marcarelli LM, Pasquini R, Fatigoni C, Kaur LS, Kumar S, Grover IS. Antigenotoxic properties of Terminalia arjuna bark extracts. J Environ Pathol Toxicol Oncol. 1999;18(2):119-25. [PubMed] [Google Scholar]
46. Mekki L. Genoprotectivity of methanol and ethanol extracted leaf sap of *Trigonella foenum-graecum* in Allium cepa root assay. Acta Biol Hung. 2014;65(1):85-95. [PubMed] [Google Scholar]
47. Kaur M, Sharma A, Soodan RK, Chahal V, Kumar V, Katnoria JK, Nagpal AK. Allium cepa Root Chromosomal Aberration assay: a tool to assess genotoxicity of environmental contaminants. In: Sharma A, Kumar M, Kaur S, Nagpal AK, editors. Evaluation of environmental contaminants and natural products: a human health perspective. Springer International Publishing; 2019. p. 65-93. [Google Scholar]
48. Mathur D, Agarwal RC. Evaluation of in vivo antimutagenic potential of fruits extracts of *Withania coagulans*. Schol Res Lib. 2011;3(4):373-76. [Google Scholar]
49. Costa C, Teixeira JP. Biomentoring. In: Wexler P, Abdollahi M, Peyster AD, Gad SC, Greim H, Harper S, Moser VC, Ray S, Tarazona J, Wiegand TJ, editors. Encyclopedia of toxicology. 3rd ed. Academic Press; 2014. p. 483-4.
50. D'Costa A, Kumar MK, Shyama SK. Genotoxicity assays: the micronucleus test and the single-cell gel electrophoresis assay. In: Meena SN, Naik MM, editors. Advances in biological science research. Academic Press; 2019. p. 291-301. [Google Scholar]
51. OECD guideline for the testing of chemicals [Internet]; [cited 2022 Aug 27]. Available from: https://www.oecd.org/chemicalsafety/testing/50108781.pdf
52. Wikipedia [Internet]. SOS chromotest; [cited 2022 Aug 27]. Available from: https://en.wikipedia.org/wiki/SOS_chromotest#Advantages
53. Feretti D, Zerbini I, Zani C, Ceretti E, Moretti M, Monarca S. Allium cepa chromosome aberration and micronucleus tests applied to study genotoxicity of extracts from pesticide-treated vegetables and grapes. Food Addit Contam. 2007 Jun;24(6):561-72. [PubMed] [Google Scholar]
54. Richardson C, Allen J, Amphlett G, Chanter D, Phillips B, Richardson C, Williams DA, Allen JA, Chanter DO, Phillips B, Richardson C, Allen JA, Amphlett GE, Changer DO, Chanter C. Analysis of data from in-vitro cytogenetic assays. In: Kirkland DJ, editor. Statistical evaluation of mutagenicity test data. Cambridge: Cambridge University Press; 1989. p. 141-54.
55. Morita T, Nagaki T, Fukuda I, Okumura K. Clastogenicity of low pH to various cultured mammalian cells. Mutat Res. 1992;268(2):297-305. [PubMed] [Google Scholar]
56. Scott D, Galloway SM, Marshall RR, Ishidate Jr M, Brusick D, Ashby J, Myhr BC. International Commission for Protection Against Environmental Mutagens and Carcinogens. Genotoxicity under extreme culture conditions. A report from ICPEMC Task Group 9. Mutat Res. 1991;257(2):147-204. [PubMed] [Google Scholar]

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