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ANTICANCER MEDICINAL HERBAL PLANTS: A SYSTEMIC REVIEW

Dr. Padma L. Ladda[1]*, Ramchandra M. Dolare[2], Dr. Nilofar S. Naikwade[3], Tabassum S. Shikalgar[4], Gajanan S. Patil[5], Dipak R. Phalle[6]

[1] Associate Professor, Department of Pharmacology, Appasaheb Birnale College of Pharmacy, Sangli, Maharashtra, India. 416416.

[2,5]Post Graduate Student, Department of Pharmacology, Appasaheb Birnale College of Pharmacy, Sangli, Maharashtra, India.416416.

[3]Professor and Head, Department of Pharmacology, Appasaheb Birnale College of Pharmacy, Sangli, Maharashtra, India. 416416.

[4]Assistant Professor, Department of Pharmacology, Appasaheb Birnale College of Pharmacy, Sangli, Maharashtra, India. 416416.

[6]Post Graduate Student, Department of Pharmaceutical Chemistry, Appasaheb Birnale College of Pharmacy, Sangli, Maharashtra, India. 416416.

Corresponding Author: Dr. Padma L. Ladda

Associate Professor, Department of Pharmacology, Appasaheb Birnale College of Pharmacy, Sangli, Maharashtra, India. 416416.

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ABSTRACT

Research on Cancer has predicted that India's cancer burden will nearly double in the next 20 years, from slightly over a million new cases in 2012 to more than 1·7million by 2035. Despite technological and social development, cancer has become one of the most common diseases of concern and a leading cause of human suffering and death. The ever-increasing emergence of the resistance of mammalian tumour cells to chemotherapy and its severe side effects reduces the clinical efficacy of large anticancer agents that are currently in use. In spite of rapid progress and spread of modern medicine & surgery, faith in and popularity of herbal plants & traditional methods has not decreased. Therefore, there is large number of studies which supports the anticancer activity of medicinal plants. Accordingly, Cancer prevention or chemotherapy depending upon bioactive compounds/fractions obtained from medicinal plants with possible known cancer inhibitory properties is a key aspect. In cancer research, these key aspects of research need to be explored by the review articles. So, the aim of this review is to focus on the work on anticancer, cytotoxicity activities of herbal medicine and this article may help in investigation to identify medicinal plants responsible for anticancer potential. This review includes information on scientifically proved anticancer medicinal plants that gives the information on botanical name, family, parts used, chemical constituents, cancer cell lines used for assay and also includes the method of assay which has been used.

KEYWORDS: Anticancer plants, MTT assay, Cytotoxicity assay, Cancer cell lines.

INTRODUCTION

A disease originated & grown by an uncontrolled splitting up of anomalous cells in a fraction of the body is called cancer. Cancer cells basically attack as well as alter cellular functions of normal cells. Cancer is one of the most public health burdens in both developed and in developing countries. In Bangladesh, 13% death due to disease belongs to cancer. Natural Products such as plants have been used for the treatment of different diseases for thousands of years. Globally, plants have been used as medicines in Egypt, China, India and Greece and in many countries from ancient time and an extraordinary number of modern drugs have been developed from them. Medicinal plants remain on to be a central therapeutic assist used for alleviating ailments of human race. Over the last 2500 years, here have been very strongly built traditional systems of medicine such as Ayurvedic, and the Unani.[1]

Following heart disease, cancer is the biggest cause of death in the World. Cancer is a generic term for over 200 diseases, which share a number of characteristics including uncontrolled cellular proliferation. This uncontrolled growth can overcome on surrounding organs, causing disruption of normal bodily functioning which in turn can lead to death. Another feature of cancer is the ability of tumour cells to migrate to other sites in the body. This process (metastasis) also increases the difficulty in treating these diseases as these secondary tumours can also disrupt bodily functions. Under these conditions the removal of tumours by surgery becomes less practicable and other methods of

treatment are needed. Chemotherapy (the use of appropriate drugs) therefore becomes the therapy of choice under these circumstances.[2]

Also, in case of skin cancer and melanoma towards death among world need new modalities in cancer research. Melanoma is the main cause of death in patients with skin cancer around the World. Melanoma is less common than other skin cancers, however, it is much more dangerous if it is not detected early, and is responsible for the majority (75%) of skin cancer-related deaths. The spread of metastatic melanoma (MM) to other organs is one of the most dangerous conditions that are almost uniformly fatal for the majority of patients with the currently available treatment modalities. Since melanoma is an immunogenic tumour, developing novel immune strategies will continue to play a critical role in designing effective treatment modalities for those at high risk of recurrence and those with distant metastasis. The treatment includes surgical removal of the tumour. If melanoma is found early when it is still small and thin, and completely removed, the chances of cure are high. The likelihood of the melanoma coming back or spreading out depends on how deeply it goes into the layers of the skin. For melanomas that come back or spread out, treatments include chemo- and immunotherapy, or radiation therapy. Therefore, there is a need to understand cancer burden on world is necessary. Also requires social health awareness about cancer and its treatments.[3]

One in 4 deaths in the United States is due to cancer. A total of 1,638,910 new cancer cases and 577,190 deaths from cancer are reported in the United States in 2012.[25] Detailed analysis of pathways and mechanisms and structures of antitumour compounds have led to significant developments in the prevention and treatment of cancer. Establishment of tumour cell lines and analysis of the effect of many natural and synthetic antitumour compounds have achieved remarkable success. Despite their severe toxicity, chemotherapy, irradiation and immunotherapy are the gold standard approaches for the treatment of cancer worldwide. Other than these classical ways, use of natural products from plants and animals and their derivatives have produced remarkable leads for the control of cancer. Due to the toxicity of currently used therapeutics for the treatment of various types of tumours, several natural products are being tried as an alternative. Being less toxic, many therapeutic compounds from animal and plant sources have been extensively studied. This review focuses on newly discovered plant-derived chemicals exhibiting anticancer properties.[4]

Table 1: Medicinal plants having potential anticancer & cytotoxicity activity.

Sr. no.	Botanical name of plant	Parts used	Chemical constituent	Cell lines used	Assay performed	Reference
1	*Allium sativum L.* (Liliaceae)	Bulbs	Allicin, S-allylcysteine,	Tumourgenic lymphoid cell line *A. tumefaciens* (strain B6) which contain the Ti (tumour inducing) plasmid	Pottato disc assay	[5]
2	*Acharanthus aspera* (Amaranthaceae)	Leaf & root	Alkaloids, Fagaronine.	Liver (Hep-2) & colon (HT-29).	SRB assay.	[6]
3	*Jatropha curcas* Linn. (Euphorbiaceae)	Root, Stem, bark, Leaf.	Flavonoids.	Human colon adenocarcinoma (HT-29).	MTT assay.	[7]
4	*Balanites aegyptiaca* (Zygophyllaceae)	Fruit	Saponins, Balanitoside	EAC Cell line (In-vivo model)	In-Vivo assay	[8]
5	*Carica papaya* (Caricaceae)	Latex, Fruit, Seed, Flower,Roots.	Glucosinolates and Benzyl isothiocyanate.	Liver cancer (Hep G2), breast cancer cell (MDA-MB-21), (MCF-7), (T47D)	Cell viability assay	[9]
6	*Cannabis sativa* (Cannabidaceae)	Leaf	Anandamide, Cannabinoids.	Breast adenocarcinoma (MCF-7), glioblastoma (SF-268) and the colon Adenocarcinoma (HT-29).	Trypan blue assay	[10]
7	*Camellia sinesis* (Theaceae)	Roots, leaf	Di- and tri-terpenes, Polyphenol, Steroidal saponins (TS1, TS2).	Human cell lines & Cells from leukaemia patients.	Flow cytometry, MTT assay.	[11]
8	*Oroxylum indicum* (Bignoniaceae)	Leaf, young pod, Stem	Chrysin, Baicalein, Oroxylin-B, Baicalin,	Cervical cancer cell line HeLa, kidney epithelial African green monkey cells (Vero), Madin-Darby canine kidney	Methylene blue assay	[12]

		bark and Fruit.	Dihydrooroxylin, A-7-O-methyl glucuronide	(MDCK) mouse connective tissue cells (L929).		
9	*Terminalia chebula* (Combretaceae)	Fruit	Hydrolyzable tannin, phenolics, ellagic, 2,4-chebulyl-b-D-glucopyranose, chebulinic acid.	Human (MCF-7), mouse (S115) breast cancer cell line, a human osteosarcoma cell line (HOS-1), A human prostate cancer cell line (PC-3), (PNT1A).	[3H]-Thymidine Incorporation, cell viability assay, flow cytometry (DNA stain)	[13]
10	*Withania somnifera* (Anacardiaceae)	Leaf	Steroids, Tannic acid, Phenolic Compound, Flavonoids.	MCF-7, A549 and PA-1 cancer cell line (breast, lung and ovary respectively	MTT assay	[14]
11	*Zingiber officinale* (Zingiberaceae)	Buds	b-Elemene	HCT 116 and HT 29 colon adenocarcinoma cancer cell lines	MTT assay	[15]
12	*Mangifera indica* (Anacardiaceae)	Flesh and peel	Phenols, carotenoids, anthocyanins, tocopherols, flavonoids, ascorbic acid.	Human hepatoma cell line, HepG2,	MTT assay, Comet assay.	[16]
13	*Curcuma longa* L. (Zingiberaceae)	Buds	Curcumin, Capsaicin, Gingerol	Human breast cancer cell line MCF-7	MTT assay.	[17]
14	*Syzygium cumni* (Myrtaceae)	Fruit	Kaempferol, 7-O-Methylether Sitosterol.	Leukemia cancer cells (AML cell line)	(DPPH) free radical assay	[18]
15	*Allium ascolonicum* (Liliaceae)	Bulbs	Furostanol Saponins.	MCF-7 cell lines, HepG2 cell line	MTT assay	[19]
16	*Emilia sonchifolia* (Compositae)	Stem, Leaf	Flavonoids.	Cervical cancer (Bu25TK) Epidermal carcinoma (A 431) Ovarian cancer (AS4, NEO)	MTT Assay	[20]
17	*Croton flavens* (Euphorbiaceae)	Leaf	Viridiflorene, Germacrone,γ-Bisaboline.	Human carcinoma A-549. Colon adenocarcinoma DLD-1.	Resazurin reduction test	[21]
18	*Paris polyphylla* var. (Melanthiaceae)	Rhizome	Steroidal saponins.	LA795 lung adenocarcinoma cell line	MTT & TUNEL assay	[22]
19	*Terminalia bellerica* (Combretaceae)	Fruits	Tannins, Glycosides	MCF-7 breast cancer cells and PC-3 and DU-145 prostate cancer cells.	[3H] Thymidine incorporated into DNA	[23]
20	*Embllica officinalis* (Euphorbiaceae)	Fruits	Glycosides, tannins	S115, MCF-7, PC-3, DU-145	[3H] Thymidine incorporated to DNA	[23]
21	*Terminalia chebula* (Combretaceae)	Fruits	Phenolic content, Glycosides.	S115, MCF-7, PC-3, DU-145	[3H] Thymidine Incorporate into DNA	[23]
22	*Solanum nigrum* (Solanaceae)	Fruit.	Diosgenin.	He-La cells, Vero cells	SRB assay, MTT assay	[24]
23	*Theobroma cacao* (Malvaceae)	Leaf, Bark, Husk.	Gallic acid & Cocao phenolic compounds.	(MDA-MB-231) breast cancer cells; liver (HepG2), colon carcinoma (HT-29), lung (A549), and cervical (HeLa)	MTT assay	[25]

				cancer cells; and normal human liver WRL-68 cells. MCF-7, HT-29, MDA-MB-231, and WRL-68 cells MCF-7 cells, liver cell line WRL-68.		
24	*Hibiscus sabdariffa* (Malvaceae)	Leaf	Phlobatannins, Anthraquinones, Flavonoids, Alkanoids, Cardiac Glycosides.	Hepatocellular carcinoma cell line Hep 3B	MTT assay	[26]
25	*Debregeasia salicifolia* (Urticaceae)	Stem	lupeol, β-sitosterol, stigmasterol.	Breast carcinoma MCF-7.	MTT assay.	[27]
26	*Catharanthus roseus* (Apocynaceae)	Arial parts.	Vincristitin, vinblastine, etc.	Human colorectal cancer cell line HCT-116	MTT assay	[28]
27	*Zea mays* (Gramineae)	Leaf	Phenols, Flavonoids.	Hep2 (laryngeal carcinoma) cells	MTT assay.	[29]
28	*Trailliaedoxa gracilis* (Rubiaceae)	Whole plant	Ursolic acid	Small intestine SI-NET cell line KRJ-I and in KRJ-I transplanted mice Human Carcinoid KRJ-I Cells	WST-1 cell proliferation assay, DAPI (4'-6-diamidino-2-phenylindole) staining Luminescence assays.	[30]
29	*Vernonia amygdalina* (Asteraceae)	Leaf	Alkaloids, Glycosides	Human Breast Cancer Cell Lines MCF-7 and MDA-MB-231	MTT & Flow cytometric cell cycle analysis.	[31]
30	*Moringa oleifera* L. (Moringaceae)	Leaf	Steroids, Flavonoids, phenolic compounds etc.	Hep-2 cell line & Daltons lymphoma ascites model in mice	SRB assay.	[32]
31	*Glycyrrhiza glabra* (Fabaceae)	Roots	Triterpenoid saponins.	Breast cancer MCF-7	SRB assay.	[33]
32	*Picrorhiza kurroa Royle* (Scrophulariaceae)	Rhizome	Alkaloids, Glycosides.	MDA-MB-435S (human breast carcinoma), Liver Hep3B and PC-3 (human prostate cancer) cell lines.	XTT assay, TBA assay	[34]
33	*Abrus precatorius* (Fabaceae)	Leaf	Phenols, Flavonoids, Isoflavone, Flavones, Anthocyanins, Catechin, Isocatechin & Carotenoids.	Human colon Adenocarcinoma (Colo-205), retinoblastoma (Y79), hepatocellular (HepG2) Leukemia cells (SupT1).	MTT assay	[35]
34	*Betula utilis* (Betulaceae)	Bark	Triterpenes	DLD-1- Colorectal adenocarcinoma, PLC/PRF/5- Liver hepatoma, A549-Lung carcinoma, SK-OV-3- Ovarian carcinoma, BxPC-3- Pancreatic adenocarcinoma, DU145- Prostate carcinoma.	SRB assay.	[36]
35	*Echinacea angustifolia* (Asteraceae)	Roots	Cynarine, Echinaciside.	HeLa cells & MCF-7 cells.	MTT assay.	[37]
36	*Helicteres angustifolia* (Sterculiaceae)	Root	Phenolic compounds, Flavonoids.	Liver HepG2, Lung A549, colon cancer DLD-1 cells.	Cytotoxic assay.	[38]

37	*Mentha arvensis* (Lamiaceae)	Leaf	Flavonoids, Phenolic compound.	Human liver cancer cell line Hep-2.	MTT assay.	[39]
38	*Alpinia oxyphylla* (Zingiberaceae)	Fruits	Phenolic compounds	Human breast cancer cell line (MCF-7), human cervix Carcinoma (HeLa), human liver carcinoma (HepG2), human gastric (MNK-45), human lung adenocarcinoma (A549), human colon cancer (SW480).	SRB assay.	[40]
39	*Lentinus edodes* (Marasmiaceae)	Mushroo ms.	Polysaccharides	Seven day-Old Sarcoma 180 ascites.	In-Vivo model	[41]
40	*Xanthium strumarium* L. (Asteraceae)	Burs	Xanthatin and xanthinosin, 2-sesquiterpenelactones.	MDA-MB-231 ATCC (breast) and NCI-417 (lung).	MTT assay	[42]
41	*Artemisia indica* (Asteraceae)	Leaf & Young Shoot	α-pinene, camphene, β-pinene, α-phellandrene, p-cymene, limonene.	Human breast adenocarcinoma cell line (MCF 7), human Hepatocarcinoma cell line (HepG2).	MTT assay, Trypan blue cell exclusion assay	[43]
42	*Eupatorium odoratum,* (Asteraceae)	Aerial parts	α-pinene, pregeijerene, geijerene, β-pinene, germacrene-D.	Human breast adenocarcinoma cell line (MCF 7), human Hepatocarcinoma cell line (HepG2).	MTT assay, Trypan blue cell exclusion assay	[43]
43	*Eupatorium adenophorum* (Asteraceae)	Leaf	Monoterpenes, Sesquiterpens.	Human breast adenocarcinoma cell line (MCF 7), human Hepatocarcinoma cell line (HepG2).	MTT assay, Trypan blue cell exclusion assay	[43]
44	*Maesama crophylla* (Myrsinaceae)	Bark, fruit, leaf.	Quinones	Human breast adenocarcinoma cell line (MCF 7), human Hepatocarcinoma cell line (HepG2).	MTT assay, Trypan blue cell exclusion assay	[43]
45	*Phlogacanthus thyrsiformis* (Acanthaceae)	Leaf, bark.	Terpinoidal glycosides, β-Sitosterol.	Human breast cell line (MCF 7), human cell line (HepG2).	MTT assay, Trypan blue cell exclusion assay.	[43]
46	*Ocimun basilicum* (Lamiaceae)	Leaf, Flower.	Vinblastine, vincristine, podophyllotoxins, colchicine.	Human cancer HL60 cell lines.	MTT assay.	[44]
47	*Mentha spicata* (Lamiaceae)	Aerial parts	Essential oil, phenols, Flavonoids.	Human cancer HL60 cell lines.	Trypan blue, MTT assay.	[44]
48	*Leucas aspera* (Labiatae)	Leaf	Phenolics, flavonoids, stilbenes.	He-La cell line	MTT assay	[45]
49	*Ononis hirta* (Fabaceae)	Aerial parts	Phenyl Propanoids, Terpenoids.	Hep-2, MCF-7, and Vero cell lines	MTT assay	[46]
50	*Inula viscosa* (Asteraceae)	Flowers	Alkaloids, Tepenoides.	Hep-2, MCF-7, and Vero cell lines	MTT assay	[46]

Note: MTT*-3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide.*
SRB*-2-(3-dimethylamino-6-diethylazaniumylidene-xanthen-9-yl)-5-sulfo-benzenesulfonate.*
TBA*- Thiobarbituric acid.*
DPPH*-di(phenyl)-(2,4,5-trinitrophenyl)iminoazanium.*
XTT*-2,3-bis[2-Methoxy-4-nitro-5-sulfophenyl]-2H-tetrazolium-5-carboxanilide*

CONCLUSION

The knowledge of medicinal plants used by the people is popular in various culture & traditions. Therefore, taking herbal medicine concerns, not always or almost 100% effective, and should not take with prescribed medication or having existing health problems. Taking herbal medication as long term may or may not cause health concern. Despite the availability of various anticancer modalities, one of the most challenging research area of pharmaceutical & medical sciences is the search for newer, most potent, additionally safe & less expensive drugs that require infrequent & self-administration & should have long lasting but anticancer effects. From, this review it reveals that phenols, flavonoids, phytoconstituents may be mostly responsible for anticancer activity.

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