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Herbal Plants as Potential Anticancer Agents: A Review

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ABSTRACT

Cancer is a disease that begins in the cells of the body. Side effects of allopathic drugs and development of resistance to currently used drugs for infectious diseases have led to increased emphasis on the use of plant materials as a source of medicines for a wide variety of human ailments The compounds derived from plants and their semi-synthetic as well as synthetic analogs have been important source of several clinically useful anti-cancer agents. Some of them include vinblastine, vincristine, shatavarin VI, pollen tripdecapeptide PSPP3, essential oils, etoposide and paclitaxel. In the cancer drug discovery program, a paradigm based on ethnobotanical and ethnopharmacological data would be more economic and beneficial for identifying potential anti-cancer molecules than mass screening of plants species. With the advent of combinatorial chemistry and high throughput screening, however, even greater progress may be expected with natural product leads.A number of promising new agents are in clinical development based on selective activity against career related molecular targets. This paper deals with some important medicinal plants used as an anti-cancer activity.

Keywords: Cancer, allopathic drugs, anticancer agents, combinatorial chemistry, high throughput screening.

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INTRODUCTION

In the normal situations, the cells grow and divide as the body needs them. This process is disturbed when new cells form that the body does not require and old cells don't die when they should. These extra cell lumps together form a growth or tumor. Broadly, two types of tumors exists i.e benign and malignant. Benign tumors are not cancerous. They can usually be removed and generally don't grow back. Malignant tumors are cancerous in nature. The cells in malignant tumor are abnormal and divide randomly. The cells attack the tissue around them. The cells of malignant tumor can also enter the blood stream or lymphatic system to form new tumors. This type of spread is known as metastasis. DNA is found in every cell in the body and regulates all of its activities. Cancer is caused by damage to DNA. The body is usually able to repair damaged DNA, but is unable to do so in cancer cells. Some people inherit damaged DNA, but in most cases DNA is damaged by their own lifestyle choices such as smoking, exposure to UV radiations or exposure to cancer causing substances (carcinogens) in the environment. While being infected with certain viruses, such as human papilloma virus (HPV) and human immunodeficiency virus (HIV), can increase the risk of cancer[1]. Cancer is classified into various stages on the basis of severity. There are multiple staging scales in use. One of the most common ranks cancers into five progressively more severe stages: 0, I, II, III, and IV. Stage 0 cancer is cancer that is just beginning, involving just a few cells. Stages I, II, III, and IV represent progressively more advanced cancers, characterized by larger tumor sizes, more tumors, the aggressiveness with which the cancer grows and spreads, and the extent to which the cancer has spread to infect adjacent tissues and body organs. Cancer can be prevented by choosing healthy lifestyle like by avoiding the use of tobacco products, choosing foods low in fats, eating diet rich in vegetables and fruits, exercising regularly, maintaining a healthy weight and avoiding over exposure to sun. Early detection is also a powerful way to prevent cancer, as treatment is more effective when cancer is detected in early stages. Conventional cancer treatment can include surgery, radiation, chemotherapy, hormone therapy and biological therapy. But there are some side effects of conventional therapies like chemotherapy and radiation therapy. Chemotherapy drugs in addition to cancerous cells also kill some regular healthy cells, causing side effects such as the fatigue, nausea, and hair loss. Like chemotherapy, radiation therapy is not perfectly precise in its targeting of cancer cells, and some normal, healthy cells can also become damaged [2].

Every type of cancer is different, and has a unique set of symptoms. Some of types of cancers and symptoms associated with them are enlisted below:

PLANTS AS A SOURCE OF ANTI-CANCER AGENTS

Since long times plants have been provide essential nutritional values, medicinal properties and physiological effect to life and are a good source of food [3]. Traditional medicine refers to the application, approach, knowledge and belief in incorporating plant and animal based properties in remedies for the purpose of treating or preventing disease as well as to maintain the well-being of an individual. Side effects of allopathic drugs and development of resistance to currently used drugs for infectious diseases have led to increased emphasis on the

use of plant materials as a source of medicines for a wide variety of human ailments. Herbal remedies have been used to cure a variety of disorders like diabetes, sexual malfunction, urinary tract infections in females, cardiovascular diseases, weight control and used to cure many other ailments [4]. Plants have a long history of use in the treatment of cancer. Plants have played an important role as a source of effective anti-cancer agents and it is reported that over 60% of currently used anti-cancer agents are derived from natural sources, including plants, marine organisms and micro-organisms. The search for anti-cancer agents from plants started in 1950s with the discovery and development of vinca alkaloids and isolation of cytotoxic podophyllotoxins. In 1960, the United states National Cancer Institute (NCI) started extensive plant collection program. This led to discovery of many novel chemotypes showing a range of cytotoxicity . This plant collection program was terminated in 1982, but the development of new screening technologies led to the revival of collections of plants and other organisms in 1986.

TABLE 1: Different Types of Cancers & their Symptoms

S.no	Type of Cancer	Signs and Symptoms
1	Adult Acute Lymphoblastic Leukemia	Weakness, Fever & night sweats, Bleeding, Shortness of breath, Weight loss & loss of appetite.
2	Bile Duct Cancer	Jaundice, Pain in abdomen, Fever & itchy skin
3	Bladder Cancer	Blood in urine & frequent urination, Pain during urination, Lower back pain
4	Brain Tumors	Morning headache, Loss of balance, Weakness
5	Breast Cancer	A lump or thickening in or near the breast, Change in size & shape of the breast ,A dimple or puckering in the skin of the breast , Fluid other than breast milk, Scaly, red & swollen skin on breast or nipple, A nipple tuned inward into the breast.
6	Cervical Cancer	Vaginal bleeding, Unusual vaginal discharge, Pelvic pain, Pain during sexual intercourse
7	Ewing Sarcoma	Pain & swelling in arms, legs, chest, back or pelvis, A lump in arms, legs and chest, Fever for no reason, A bone breaks for no reason.
8	Hypo pharyngeal Cancer	A sore throat, Ear pain, Painful and difficult swallowing, Change in voice
9	Lip and Oral cavity Cancer	A sore on a lip or mouth, A lump or thickening on the lips, gums or in mouth, A white or red patch on lips, tongue, tonsil, Bleeding, pain or numbness in the lip or mouth, Change of voice, Loose teeth, Swelling of jaw, Trouble in chewing, Sore throat.
10	Lung Cancer	Chest discomfort or pain, A cough that doesn't go away, Trouble in breathing, Blood in sputum, Loss of appetite, Weight loss, Trouble in swallowing, Swelling in face.
11	Pancreatic Cancer	Jaundice, Pain in upper or middle abdomen, Weight loss, Loss of appetite, Fatigue.

Upto early 1990s, the discovery of novel anti-cancer agents from natural sources was largely based on testing for cytotoxic activity against cancer cell lines grown either *in vitro* or using *in vivo* models. Many of the naturally derived anti-cancer agents originally discovered using such assays, have been shown to exert their cytotoxic action through interaction with tubulin and include agents such as vinblastine, vincristine, colchicine and maytansine which promotes the depolarization of tubulin [5].

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TABLE 2: Some Medicinal Plants as Anti-cancer agents

S.No	Botanical Name	Family	Main active components	Parts used
1	*Acrorus calamus*	Araceae	Asarone, eugenol, methyl eugenol, Palmitic acid and camphene	Rhizome
2	*Agrimonia pilosa*	Rosaceae	Agrimonolide, flavnoid, tannin, triterpene and coumarin	Whole plant
3	*Alphitonia zizphoides*	Rhamnaceae	Zizphoisides, triterpene and latex	Whole plant
4	*Alstonia scholaris*	Apocynasaceae	Linalool, cis and trans linalool oxides, α-terpineol	Bark
5	*A. companulatus*	Araceae	Carbohydrates, alkaloids, saponins, steroids and coumarins.	Corm
6	*Andrographis paniculata*	Acanthaceae	Flavnoid, andrographin & andrographolide	Whole plant
7	*Asparagus racemosus*	Asparagaceae	Shatavarins, essential oils, asparagine, arginine, tyrosine, flavonoids resin, (kaempferol, quercetin, and rutin), and tannin.	Whole plant
8	*Avicennia alba*	Avicenniaceae	Napthoquinolines and their analogs	Whole plant
9	*Azardirachta indica*	Meliaceae	Tetranortriterpenoids,azadirone , epoxyazadiradione,nimbin gedunin,azadiradioneand deacetylnimbin	Bark, leaves and flowers
10	*Baccopa monniera*	Scrophulariaceae	Alkaloids, saponins, sterols, betulic acid, Stigmasterol, ß-sitosterol	Leaves
11	*Cissus quadrangularis*	Vitaceae	Tertracyclic triterpenoid and β-sitosterol	Whole plant
12	*Citrus limon*	Rutaceae	Limonoid, limonene, flavnoid, flavone, nobiletin and tangeretin	Fruit
13	*Eugenia caryophyllata*	Myrtaceae	Eugenol, acetyl eugenol, carvacrol, thymol, and cinnamaldehyde.	Flower bud
14	*Equisetum hyemale*	Equisetaceae	Dimethsulfone,kaempferol-diglucoside and caffeic acid	Whole plant
15	*Geranium robertianum*	Geraniaceae	Geranin, tannin and citric acid	Whole plant
16	*Glycerrhiza glabra*	Fabaceae	Glycyrrhizin, glabranin, isoflavone, coumarin, triterpene sterol & eugenol	Root
17	*Mallotus philippensis*	Euphorbaceae	Vitamins (A & C)	Whole plant
18	*Mentha arvenis*	Lamiaceae	Acetaldehyde, amyl alcohol, methyl esters, limonene, β-pinene, β-phellandrene and cadinene	Leaves& root
19	*Moringa oleifera*	Moringaceae	Palmitic and stearic acid, saponins, glycoside, gum, protein Vitamins: A , B1, B2, B3, C	Whole plant
20	*Pandanus odoratissimus*	Pandanaceae	α-terpineol, β-carotene, β-sitosterol stigmasterol, pinoresinol, viridine and vitamin C	Whole plant
21	*Pongamia pinnata*	Fabaceae	Diketonepongamol, glabrin and karanjin	Whole plant
22	Sesbania spieces		Kaempferol	
23	*Taxodium distichum*	Taxaceae	Taxol	Seed
24	*Vernonia cinerea*	Asteraceae	Lupeol, stigmasterol and β-sitosterol	Whole plant

Plants have been a prime source of highly effective conventional drugs for the treatment of many forms of cancer. The actual compounds isolated from the plants may not serve as the drugs, but they provide leads for the development of potential novel agents. As new technologies are developed, some of the agents which failed earlier clinical studies are now stimulating renewed interest. With the rapid identification of new proteins having significant regulatory effects on tumor cell cycle progression and their conversion into targets for high throughput screening, molecules isolated from plants are providing to be an important source of novel inhibitors of the action of these key proteins and have the potential for development into selective anti-cancer agents.

Figure 1: *Acorus calamus* (Araceae)

Acorus calamus (Araceae) is a native of eastern countries and indigenous to the marshes of the mountains of India. It is cultivated throughout India in marshy tracts of Kashmir, Nagahills Manipur and in the Koratagere taluka of Karnataka state in peninsular India. *Acorus calamus* (Araceae) is a herbaceous perennial with a rhizome that is long, indefinite branched, smooth, pinkish or pale green. Its leaf scars are brown white and spongy and it possess slight slender roots [6].

TABLE 3: Taxonomical Classification of *Acorus calamus*

Kingdom	Plantae
Phylum	Magnoliophyta
Class	Liliopsida
Order	Acorales
Family	Acoraceae
Genus	Acorus
Species	*A. calamus*

Acorus calamus has the constituents such as alkaloids, flavnoids, gums, lecitins, mucilage, phenols, quinine, saponins, sugars, tannins ans triterpenes. The constituents of the essential oils in *Acorus calamus* are phenylpropanes, mono-terpenes and thermolabile sesquiterpenoids. Methyleugenol, cis-methyleugenol, β-asarone, geranylacetate, β-farnesene, shyobunone and isoshyobunone are the most abundant chemical compounds which are present in the essential oil. The other chemical compounds present are α and β-asarone,

calamenene, asaronaldehyde, acorenone, calamenone, n-heptanic acid, calanendiol and sesquiterpenes .

Acorus calamus exhibits various pharmacological actions such as anti-bacterial activity, anti-fungal activity, anti-oxidant activity, bronchiodilatory effect, anti-diabetic activity, anti-inflammatory activity, anti-hepatotoxic activity, antimutagenic activity, hypolipidemic activity, insecticidal activity, licicidal activity, antiulcer activity, antispasmodic activity, antidiarrheal activity, CNS activity and anti-cancer activity [7]. α-asarone has found to show anti-cancer activity against human carcinoma cells. β-asarone is also responsible for anti-carcinogenic activity [8].

Figure 2: *Agrimonia pilosa* (Rosaceae)

Agrimonia pilosa (Rosaceae), is commonly known as Agrimony. It is perennial herbaceous flowering plant native to temperate regions of the northern hemisphere. *Agrimonia pilosa* has been used as an antidiarrheic, hemostatic and an anti-parasitic in Japan and China.

TABLE 4: Taxonomical classification of *Agrimonia pilosa*

Kingdom	Plantae
Phylum	Magnoliophyta
Class	Magnoliopsida
Order	Rosales
Family	Rosaceae
Genus	Agrimonia
Species	*A. pilosa*

The plant is being used for cancer therapy in China today. *Agrimonia pilosa* had been known traditionally as a plant possessing an anti-tumor effect. However, there are only a few reports on direct cytotoxic activity of certain extracts of this plant against tumor cells in an *in vitro* and *in vivo* test.

The anti-tumor activity of the methanolic extract from roots of *Agrimonia pilosa* against some transplantable rodents were carried out by Ryozo Koshiura *et al.* As per the results of

Ryozo Koshiura *et al* , it is thought that the anti-tumor activity of methanol extract of *Agrimonia pilosa* may be due to host-mediated actions so that the extract stimulates macrophages and induces cytotoxic macrophages and the stimulated macrophages activate immune charging and cytotoxic lymphocytes [9]. Further studies on the isolation of the effective constituents from this plant and on mechanisms related to the anti-tumor activity are in progress.

Figure 3: *Alstonia scholaris* (Apocynaceae)

Alstonia scholaris (L.) is an evergreen tropical tree native to Indian sub-continent and south East Asia. This plant is native of India, Sri Lanka, Pakistan, Nepal, Burma, Malaysia, Thailand, South East Asia, Africa, Northern Australia and Southern China. The plant is large evergreen tree, growing upto 17-20m in height and about 1.1m in diameter. The bark of *Alstonia scholaris* is grayish brown, rough, lenticellate, bitter in taste and secreting white milky latex. The leaves are 4-7 in a whorl, coriaceous, elliptic-oblong. Flowers are small, greenish white, corolla tube is short and very strongly scented. Fruits are 30-60cm long. Seeds are papillose with brownish hair at each end [10].

TABLE 5: Taxonomical Classification of *Alstonia scholaris*

Kingdom	Plantae
Phylum	Magnoliophyta
Class	Magnoliopsida
Order	Gentianales
Family	Apocynaceae
Genus	Alstonia
Species	*A. scholaris*

Alstonia scholaris is known to be rich source of alkaloids. The volatile oils which are present in the flower of *Alstonia scholaris* are linalool, cis and trans linalool oxides, α- terpineol and terpinen-4-ol [11]. The bark has been reported to have triterpenoids α-amyrin acetate and lupeol [12]. The leaves of *Alstonia scholaris* have been reported to have alkaloids, coumarins, flavnoids, leucoanthocyanins, reducing sugars, simple phenolics, steroids, saponins and tannins [13].

Alstonia scholaris has been used in traditional systems of medicine for treating various ailments. The plant has been reported to have antituberculosis, antibacterial, radioprotective, antitussive, anti-inflammatory, antidiabetic, antihyperlipidemic, antihypertension, antidiarrheal, anti-anxiety, antimalarial, antifertility, hepatoprotective and anticancer activities [10].

Sharma vikas *et al*, has reported the anticancer potential of leaf extracts from the plant *Alstonia scholaris*. The extracts of leaves were screened *in vitro* cytotoxicity by means of SRB assay on five human cancer lines i.e lung cancer cells, oral cancer cells, breast cancer cells, neuroblastoma cancer cells and colon cancer cells. The ethanolic extract of *Alstonia scholaris* indicated the potent anticancer effect against all human cancer cell lines [14].

Figure 4 :*Andrographis paniculata* (Acanthaceae)

Andrographis paniculata (Kalmegh) is commonly known as 'King of Bitters'. It is distributed in tropical Asian countries. It can be found in a variety of habitats like plains, hill slopes, wastelands, farms, dry or wet lands and sea shores. The herb is also available in Northern India, Java, Malaysia, Indonesia, West Indies, Hong kong, Thailand and Singapore [15, 16]. *Andrographis paniculata* is an annual, profusely branched, erect herb having 0.5-1.0m height. Leaves are green, lanceolate, 3-7cm long and 1-2.3cm wide, glabrous with slightly undulate margin, acuminate apex with a tapering base. Flowers are small and solitary, corrola is whitish or pink in colour with hairs. Fruit is a capsule, linear, oblong and acute at both ends.

TABLE 6: Taxonomical Classification of *Andrographis paniculata*

Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Lamiales
Family	Acanthaceae
Genus	Andrographis
Species	*A.Paniculata*

Andrographis paniculata contains active compounds such as andrographolide, oxoandrographolide, 14-deoxyandrographolide, neoandrographolide, homoandrographolide, andrographosterol, andrographane, andrographone, andrographosterin, stigmasterol, α-sitosterol, monohydroxy terimethyl flavones; andrographin [17].

Andrographis paniculata is extensively used in Ayurveda, Uniani and Siddha medicines as home remedy for various diseases. The therapeutic value of *Andrographis paniculata* is due to its mechanism of action by enzyme induction. It is used to treat gastrointestinal tract and upper respiratory tract infections, fever, sore throat, hepatitis [15].The herb and its isolates like andrographolide, neoandrographolide, dehydroandrographolide etc are reported to possess anti-inflammatory, hepatoprotective, astringent, anti-pyretic and anti-cancer properties [16]. Flavnoids present in plant are reported to inhibit collagen, arachidonic acid, thrombin and platelet activation factor induced platelet aggregation.

Andrographolide suppresses the adhesion of gastric cancer cells which express high level sialyl Lewis to human vascular endothelial cells by blocking E-selection expression. The effect of ethanolic extract and andrographolide on cell-mediated immune responses in normal and tumor-bearing control animals was reported. Authors observed that treatment with extract and andrograholide significantly elevated the production of interleukin-2 and interferon-gamma in normal and Ehrlich ascites carcinoma-bearing animals. The effect of two doses (50 and 100mg/kg body weight/day for 14 days) of 80% hydroalcohol extract of plant and butylated hydroxyanisole were studied on swiss alboni mice (6-8 weeks old) and a significant increase in the levels of acid soluble sulphydryl content, cytochrome P450, cytochrome P450 reductase, cytochrome b5 reductase at both dose levels of extract treatment. The catalase glutathione peroxidase and glutathione reductase showed significant increases only at higher doses in the liver. Jada *et al* reported anti-tumor activity against two human cancer cell lines i.e breast cancer cell line and colon cancer cell line [18]. It is reported that andrographolide is able to efficiently block T cell activation *in vitro* as well as *in vivo* [19].

Figure 5: *Annona Glabra* (Annonaceae)

Annona glabra is native to Florida in United States, Central and South America and west Africa. The growth requirements of the plant are that it grows in swamps and it cannot grows in dry soil. The tree grows upto the height of around 10-12m. The trunk is thin and leaves are elliptic oblong with appointed tip, 8-15 cm long & 4-6 cm wide. Flowers are about 2-2.5 cm long and 2.5 cm wide, thick and fleshy. Sepals are triangular in shape about 5-8mm long and 5-7mm

wide. The fruit is oblong or may be spherical about 7-15cm long and up to 9cm across. It is edible and can be used as jam [20].

TABLE 7: Taxonomical Classification of *Annona glabra*

Kingdom	Plantae
Phylum	Magnoliophyta
Class	Magnoliopsida
Order	Mangoliales
Family	Annonaceae
Genus	Annona
Species	*A.glabra*

Annona glabra has been reported to have a group of compounds called Acetogenins. Some of the acetogenins which were isolated are annonacin, annonacione, corossolone, annomontacin, squamosine. Acetogenins are reported to possess potent cytotoxic activity and are potent inhibitors of mitochondrial complex I respiratory chain [21]. The leaves and bark of *Annona glabra* are used in Chinese medicine against cancer and other ailments. If the extracts of leaf, pulp and seed are compared, the seed extracts are more potent than other extracts. Li *et al* isolated four cytotoxic cytopeptides i.e Glabrin A, B, C and D from seeds [22].

Cochrane *et al* has been reported the anti-cancer activity of *Annona glabra* extracts in human leukemia cell line. The results reported by Cochrane *et al* showed that the total ethanolic extract of *Annona glabra* seeds induced apoptosis when analyzed by annexin-V. A concentration-dependent increase in the percentage of apoptotic cells was observed with increasing concentrations of extract. The cytotoxicity measurments of *Annona glabra* leaf, pulp and seed extracts are significantly better than other anti-cancer compounds [23].

Figure 6: Apium graveolens (Apiaceae)

The dry food of *Apium graveolens* is known as celery. Celery is available as celery seed, celery flakes, vegetable and celery seed oleoresin. The celery is native to the lowland of Italy. It is also grown in Sweden, Egypt, Algeria and India. In India it is cultivated in Punjab, Haryana, north-western Himalayas and western Uttar Pradesh.

Celery is herbaceous annual or bionomical herb. It grows upto height of 60-90cm. The stem is branched and ridged. The leaflets are ovate to sub orbicular three lobes 2-4.5cm long. The flowers are small and white in colour.There are five petals ovate acute within floured tips. The fruit is schizocarp with two mericarps, sub-orbicular to ellipsoid, 1-2mm is diameter, aromatic and slightly bitter

TABLE 8: Taxonomical Classification of *Apium graveolens*

Kingdom	Plantae
Phylum	Spermatophytes
Class	Mangnolisisa
Order	Apicedes
Family	Apiceae
Genus	Apium
Species	*A.graveolens*

Celery has reported to contain β-carotene, folic acid, vitamin C, magnesium, potassium, sodium and fiber. The seeds also contain essential oils limonene, salience, linalool and vitamin B. Celery has been reported to possess anti-fungal, antiseptic, diuretic, carminative, anthelmintic, laxative, sedative, stimulant, anti-arthritis and anti-cancer properties [24].

Authors have observed that the crude extracts of seeds of *Apium graveolens* significantly inhibited the proliferation of human cancer cell line RD and its activity was in a concentration-dependent manner [25]. The celery seed extracts have growth inhibition action on various cancer cell lines including acute lymphoblastic leukemia cell line CEM-C7H2 and human neuroblastoma SH-SY5Y cells [26, 27]. According to Momin *et al* and Sultana *et al* anti-cancer effects of celery may be due to phthalide constituents found in celery seeds [28, 29]. Apigenin, a chemical constituent of *Apium graveolens* has been reported to possess antioxidant. Apigenin is found to inhibit the growth of many human cancer cell lines like cervical carcinoma cells, breast cancer cells and leukemia by the mechanism of apoptosis of cancer cells [30, 31]. The anticancer effect of apigenin has been suggested by authors to be mediated through induction of p53 expression, which causes cell cycle arrest and apoptosis [32]. Tannins isolated from the seeds of *Apium graveolens* has been reported to have cancer preventive properties. Many bioactive constituents like luteolin, linolenic acid, psoralen and oleic acid are isolated from the seed of *Apium graveolens* and has been reported to possess growth inhibition on various cancer cell lines through inhibition of tumor cell proliferation by inducing cell cycle arrest and by inducing apoptosis [33, 34]. It has been reported that Apium graveolens also contains vitamins A, B and C. These vitamins are antioxidants and helps in reducing the oxidative stress caused by toxic agents [35]. From the above discussion it is revealed that the extracts showed inhibitory effects on cancer cell lines and the plant may be promising anti-cancer drug.

Figure 7: *Asparagus racemosus* (Asparagaceae)

Asparagaus racemosus (Asparagaceae), commonly known as shatavari is a branched shrub found growing wild in tropical and sub-tropical regions of India. The plant is a woody climber growing to 1-2m height. The leaves are small and uniform. The inflorescence has tiny white flowers, in small spikes and roots are finger like and clustered [36].

TABLE 9: Taxonomical classification of *Asparagus racemosus*

Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Asparagales
Family	Asparagaceae
Genus	Asparagus
Species	*A.racemosus*

Asparagus racemosus has been reported to contain steroids saponins-shatavarins (I,IV), sarsasapogenin, adscendin (A,B), asparanin (A,B,C). Shatavarin-I is major glycoside with 3 glucose and rhamnose moieties attached to sarsasapogenin. Shatavarin IV have 2 rhamnose and 1 glucose moieties attached to sarsasapogenin.This plant has been also reported to contain Vitamins A, B1, B2, C, E and minerals such as Mg, P, Ca, Fe and folic acid. Chemical analysis indicate that *Asparagus racemosus* also contains essential oils, asparagine, arginine, tyrosine, flavnoids such as kaempferol, quercetin and rutin, resins and tannins.

Asparagus racemosus has been reported to possess gastrointestinal effects to treat gastric ulcers and dyspepsia. It has been also used for nervous disorders, inflammation, liver diseases and in cancer treatment [37].

The major steroidal glycosides such as shatavarin I to X were reported from the roots. The total extract, polar or non-polar extracts exhibit immuno-pharmacological activity in cancer chemotherapy [38]. The extracts of *Asparagus racemosus* also reported to have inhibitory action on 7, 12-dimethylbenzanthracene (DMBA)-induced mammary carcinogenesis in rats [39]. The most important criteria for determining the potency of anticancer drug is prolongation of life span of tumor bearing animals. There is also a significant increase in body weight in EAC tumor bearing mice due to the rapid increase in the ascetic tumor volume [40].

Mitra *et al* isolated chroloform extract of *Asparagus* roots (AR-1), choloform: methanol extract (AR-2) and methanol extract (AR-3). Further these dried extracts were subjected to fractionation by maceration at room temperature. Authors fractionate AR-1 with hexane and separated hexane soluble faction (AR-1A) & hexane insoluble fraction AR-1B. AR-2 was fractionated with ethyl acetate and separated ethyl acetate soluble fraction (AR-2A) & ethyl acetate insoluble fraction (AR-2B). Similarly, AR-3 was fractionated with butanol and separated butanol soluble fraction (AR-3A) & butanol insoluble fraction (AR-3B). The mice bearing EAC tumor has been reported to show significant increase in life span and decrease in body weight when administered orally with AR-2B fraction. It also showed a significant decrease in the tumor volume, packed cell volume and viable tumor cell count indicating the anti-cancer activity of AR-2B [41]. From the above findings by Mitra *et al* it could be concluded that shatavarins rich fraction AR-2B from Asparagus racemosus exhibited potent anti-cancer activity.

Oxidative stress caused by excessive production of free radicals causes damage of macromolecules such as lipids and induce lipid peroxidation *in vivo*. Lipid peroxide formed in the primary site would be transferred through circulation and cause damage to the tissues. It has been reported that cancer tissues contains high quantity of malondialdehyde (MDA), the end product of lipid peroxidation than healthy tissues. Asparagus racemosus root induced elevation of antioxidant activity could be responsible for its anti-cancer activity [42, 43].

Figure 8*: Azadirachta indica* (Meliaceae)

Azadirachta indica is native of India and naturalized in most of tropical and sub-tropical countries. In India it occurs naturally in Siwalik Hills, dry forests of Andhra Pradesh, Tamil Nadu and Karnataka. It is also cultivated in tropical and sub-tropical regions of Sri Lanka, Pakistan, Thailand, Indonesia, Malaysia, Singapore, Australia, Saudi Arabia and Tropical Africa [44]. It grows upto the height of 40-50 feet with a straight, rough dark brown trunk and long spreading branches. The leaves are compound, each comprising 5-15 leaflets. It bears many flowered panicles in the leaf axils. Fruits are green when unriped and turns yellow when riped. Fruits are having aromatic garlic like odour. Fruits mature between April and August [45].

The different parts of *Azadirachta indica* has been reported to contain azadirachtin, maliacin, gedunin, nimbidin, nimbolides, salanin, nimbin and valassin [46]. The kernels of

Azadirachta indica contains triterpene or limnoids [47]. The four best limnoids are azadirachtin, salanin, meliantriol and nimbin [48].

TABLE 10: Taxonomical Classification of *Azadirachta indica*

Kingdom	Plantae
Phylum	Magnoliophyta
Class	Magnoliopsida
Order	Sapindales
Family	Meliaceae
Genus	Azadirachta
Species	*A.indica*

All the parts of the plant have been reported to have medicinal value. It has been used in Ayurvedic medicine for more than 4000 years. It has been reported to be useful in various ailments such as chickenpox, fever caused by malaria, diabetes, heart diseases, neuromuscular pains, psoriasis and ulcers. It is also used in pest control and cosmetics. *Azadirachta indica* has been reported to possess various pharmacological activites such as larvicidal activity, antibacterial activity, antioxidant activity, anti-HIV activity, antiulcer activity, antimalarial activity, antifertility activity, antihypertensive activity and anti-cancer activity [49].

Researchers in India, Japan and Europe have found that polysaccharides and limonoids present in the bark, leaves and seed oil of *Azadirachta indica* reduce tumor and cancers. In Japan hot water extracts from neem bark showed significant effectiveness against several types of tumors. It has been reported that ethanolic extract of *Azadirachta indica* leaves, when administered at doses of 250-500mg/kg, suppressed the average number of papilomas as well as overall tumor burden induced by BαP and DMBA in the 7-week old swiss albino mice model [50]. Subapriya *et al* investigated molecular pathways of anticancer effects of the ethanolic extract of *Azadirachta indica* leaves on DMBA-induced carcinogenesis in bucal pouch of hamster. Their observations suggest the involvement of the PCNA (Proliferating cell nuclear antigen), mutant p53 and bcl2 genes [51]. *Azadirachta indica* has been reported to induce apoptosis in cancer cells. The extracts and its purified products of *Azadirachta indica* have been examined for induction of apoptosis among cancer cells. The ethanolic extract of *Azadirachta indica* has been shown to induce apoptosis in prostate cancer cells (PC-3) in a dose-dependent manner [52]. According to the observations of Kumar *et al* nimbolide, which is active anti-cancer principle of leaves and flowers induces apoptosis through engagement of the mitochondrial pathway [53].

Figure 9: *Bacopa monnieri* (Scrophulariaceae)

Bacopa monnieri is a perennial, creeping herb. It is grown in wetlands and muddy shores. It is grown in India, Nepal, Sri Lanka, China, Florida, Hawaii and other southern states of USA. *Bacopa monnieri* have thick leaves. Leaves are arranged oppositely on the stem. The flowers are small and white in clour with four or five petals.

TABLE 11: Taxonomical Classification of *Bacopa monnieri*

Kingdom	Plantae
Phylum	Magnoliophyta
Class	Magnoliopsida
Order	Scrophulariales
Family	Scrophulaceae
Genus	Bacopa
Species	*B.monnieri*

Bacopa monnieri has been reported to contain tetracyclic triterpenoid saponins, bacosides A and B, hersaponin, alkaloids such as herpestine and brahmine, flavonoids [54], sterols such as bacosterol [55] and triterpine such as bacosine [56].

Bacopa monnieri has been reported to have pharmacological activites in nervous disorders such as insanity, epilepsy, neuroasthenia and nervous breakdown. The anti-cancer activity of *Bacopa monnieri* has been also revealed by various workers. E.P Kumar *et al* revealed the potential cytotoxic and anti-tumor activity of *Bacopa monnieri*. According to them, the ethanolic extract of *Bacopa monnieri* has shown significant cytotoxicity towards transformed cell lines. In solid tumor reduction studies, ethanolic extract of *Bacopa monnieri* exhibited significant tumor reducing property. E.P Kumar *et al* proposed the possible mechanism of anti-tumor activity of ethanolic extract of *Bacopa monnieri* against DLA cells may be due to radiomimetic, nucleotoxic and cytotoxic effect and inhibits cell mitosis [57].

Figure 10: *Euphorbia neriifolia* (Euphorbiaceae)

Euphorbia neriifolia is found in throughout the Deccan peninsula of India. The plant is a large succulent shrub, with stipular thorns. Leaves of the plant are succulent, deciduous, 6-12 inch long, terminal on the branches, waved narrowed into a very short petiole. The arrangement of flowers in a bunch on the plant is 'cyathium' type, means one female and several male flowers are found on a same bunch. Female flowers consist of a trichambered ovary. Fruits are three chambered and tricoccaus [58, 59]. The plant has been reported to contain triterpenes such as nerifolione and cycloartenol [60].

TABLE 12: Taxonomical Classification of *Euphorbia neriifolia*

Kingdom	Plantae
Phylum	Magnoliophyta
Class	Magnoliopsida
Order	Euphorbiales
Family	Euphorbiaceae
Genus	Euphorbia
Species	*E.neriifolia*

The plant has been reported to possess various medicinal properties such as antibacterial, antifungal, antiviral, antiparasitic, antiarthritic, antidiabetic, anticonvulsant, antioxidant, radioprotective, spasmodic, diuretic and anti-cancer [61].

Free radical damage is one of the major processes that contribute to degenerative diseases such as cancer. Free radical scavengers protect cellular DNA against indirect effect of ionizing radiation where hydroxyl radicals are believed to be the primary active species responsible for the damage [62]. Yen GC *et al* demonstrate the antioxidant activity of the sapogenin isolated from the leaf extract of *Euphorbia neriifolia*. The good reducing power of sapogenin means that triterpenoidal compounds, especially euphol, are electron donors and therefore act as antioxidants [60]. Peripheral blood lymphocytes are extensively used biomonitoring of populations exposed to various mutagenic or carcinogenic compounds. γ-radiations produces morphological changes in lymphocytes by decaying their proliferation. γ-

rays generate hydroxyl radicals in cells and induce DNA damage that leads to mutations and chromosomal aberrations. Total sapogenin at a concentration of 75µg/ml significantly decreased total chromosomal aberration. This revealed that sapogenins reduce gamma radiation-induced genomic instability. Total sapogenin exhibits cytotoxic activity on murine F1 B16 melanoma cell line [63].

CONCLUSIONS

Plants have been a prime source of highly effective conventional drugs for the treatment of many forms of cancer. Plants provide active constituents which acts directly against various ailments or indirectly by providing leads for the development of potential novel agents. Large number of herbal species has been used traditionally or as folk medicines against cancer. Many of them have been studied scientifically and proved to be beneficial anti-cancer agents. In medicine, particularly in the field of cancer, the use of herbs is increasingly enhanced especially with the excessive use of synthetic drugs and awareness of their toxicity, which contributed in oncology, leading to a favorable reconsideration of the medicinal practices made from natural herbal. Despite the divergent bioactivities of the plant medicines against various diseases, active components of most plant extracts have not been elucidated thoroughly, due their complex mixtures. The ability of agents to attach to carrier molecules directed to specific tumors, shows highly cytotoxic natural products to the tumors. A better understanding of the characteristics of tumor cells has recently led to the development of more targeted treatments, and therefore generally less toxic. In conclusion, the use of naturally occurring molecules in the treatment of cancer has greatly contributed to the improvement of the therapeutic efficacy of drugs used today in cancer chemotherapy. In this review some anti-cancer plants with their phytochemical and pharmacological profile are presented. These plants exhibit good antioxidant and cytotoxic activities leading to anticancer activity. This article provides the knowledge of anti-cancer medicinal plants.

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