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Some medicinal plants as natural anticancer agents

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ABSTRACT
India is the largest producer of medicinal plants and is rightly called the "Botanical garden of the World". The medicinal plants, besides having natural therapeutic values against various diseases, also provide high quality of food and raw materials for livelihood. Considerable works have been done on these plants to treat cancer, and some plant products have been marketed as anticancer drugs, based on the traditional uses and scientific reports. These plants may promote host resistance against infection by re-stabilizing body equilibrium and conditioning the body tissues. Several reports describe that the anticancer activity of medicinal plants is due to the presence of antioxidants in them. In fact, the medicinal plants are easily available, cheaper and possess no toxicity as compared to the modern (allopathic) drugs. Hence, this review article contains 66 medicinal plants, which are the natural sources of anticancer agents.
KEY WORDS : Cancer, medicinal plants, natural anticancer agents, antioxidants.

INTRODUCTION

Cancer (malignant tumour) is an abnormal growth and proliferation of cells. It is a frightful disease because the patient suffers pain, disfigurement and loss of many physiological processes. Cancer may be uncontrollable and incurable, and may occur at any time at any age in any part of the body. It is caused by a complex, poorly understood interplay of genetic and environmental factors (1-2). It continues to represent the largest cause of mortality in the world and claims over 6 millions. Cancer kills annually about 3500 per million population around the world. A large number of chemopreventive agents are used to cure various cancers, but they produce side effects that prevent their extensive usage. Although more than 1500 anticancer drugs are in active development with over 500 of the drugs under clinical trials, there is an urgent need to develop much effective and less toxic drugs (3).

The plant kingdom plays an important role in the life of humans and animals. India is the largest producer of medicinal plants and is rightly called the "Botanical garden of the World". Medicinal plants have been stated (4) to comprise about 8000 species and account for approximately 50% of all the higher flowering plant species of India. In other words, there are about 400 families of the flowering plants; at least 315 are represented by India. Medicinal properties of few such plants have been reported but a good number of plants still used by local folklore are yet to be explored. Ayurveda, Siddha and Unani systems of medicine provide good base for scientific exploration of medicinally important molecules from nature. The rediscovery of Ayurveda is a sense of redefining it is modern medicines. Emerging concept of combining Ayurveda with advanced drug discovery programme is globally acceptable. Traditional medicine has a long history of serving peoples all over the world. The ethnobotany provides a rich resource for natural drug research and development. In recent years, the use of traditional medicine information on plant research has again received considerable interest. The Western use of such information has also come under increasing scrutiny and the national and indigenous rights on these resources have become acknowledged by most academic and industrial researchers (5).

According to the World Health Organization (WHO), about three quarters of the world's population currently use herbs and other forms of traditional medicines to treat diseases. Traditional medicines are widely used in India. Even in USA, use of plants and phytomedicines has increased dramatically in the last two decades (6). It has been also reported (7) that more than 50% of all modern drugs in clinical use are of natural products, many of which have been recognized to have the ability to include apoptosis in various cancer cells of human origin.

SOME ANTICANCER MEDICINAL PLANTS

With the above background, this review article enumerates 66 medicinal plants (Tables 1 & 2) possessing anticancer properties[3,8-44], and are used against various types of cancer. The chemopreventive potential of an 80% hydroalcoholic extract (50 and 180 mg/kg/day for 14 days) of *Andrographis paniculata* has been reported (8) against chemotoxicity, including carcinogenicity. The authors observed the modulatory influence of *A. paniculata* on hepatic and extrahepatic carcinogen metabolizing enzymes (viz. cytochrome P450), antioxidant enzymes, glutathione (GST) content, lactate dehydrogenase (LDH) and lipid peroxidation in Swiss albino mice. Some other workers (9) also reported the anticancer and immunostimulatory activities of *A. paniculata.*

Azadirachta indica (Neem) has been used in buccal carcinogenesis, skin carcinogenesis, prostate cancer, mammary carcinogenesis, gastric carcinogenesis, Ehrlich carcinoma and B16 melanoma. Dietary neem flowers caused a marked increase in glutathione S-transferase (GST) activity in the liver, while resulting in a significant reduction in the activities of some hepatic P450-dependent monooxygenases. These results strongly indicate that neem flowers may have chemopreventive potential. Young animals were fed with

AIN-76 purified diets containing either 10-12.5% ground freeze-dried neem flowers for 1 week prior to, during, and for 1 week after the administration of each carcinogen. Interestingly, it was found that neem flowers resulted in a marked reduction of the incidence of mammary gland (about 35.2%) and liver tumours (61.7% and 80.1% for benign and malignant tumours, respectively). Furthermore, the multiplicity of tumours per rat was also lower in the neem flower groups, i.e. those for mammary gland tumours and benign and malignant liver tumours were reduced to 44.0%, 87.9% and 88.9%, respectively. These results clearly demonstrated that neem flowers contain some chemopreventive agents capable of inhibiting liver and mammary gland carcinogenesis in rats (10). Administration of ethanolic neem leaf extract (ENLE) inhibited DMBA-induced hamster buccal pouch carcinogenesis, as revealed by the absence of neoplasm. These results suggest that the chemopreventive effect of ENLE may be mediated by induction of apoptosis (11). The modulatory effect of neem leaf with garlic on hepatic and blood oxidant-antioxidant status may play a key role in preventing cancer development at extrahepatic sites (12). The ethanolic extract of neem has been shown to cause cell death of prostate cancer cells (PC-3) by inducing apoptosis, as evidenced by a dose-dependent increase in DNA fragmentation and a decrease in cell viability (13).

Camellia sinensis (Tea) is one of the most popular beverages in the world. The consumption of tea has been associated with a decreased risk of developing cancers of the ovary (14), oral cavity (15), colon (16), stomach (17) and prostate (18). This beneficial health effect has been attributed to the catechins (flavonoids) in tea. Their biological benefits are due to their strong antioxidant and antiangiogenic activity as well as their potential to inhibit cell proliferation and modulate carcinogen metabolism (19-20). *Citrus limon* (Nibu) fruit contains flavonoid, flavone, limonoid, limonene, nobiletin and tangeretin. The flavonoid, tangeretin and nobiletin are potent inhibitors of tumor cell growth and can activate the detoxifying P450 enzyme system. Limonoids inhibit tumour formation by stimulating the GST enzyme. The limonene (a terpenoid) also possesses anticancer activity. Nibu fruit is used for inhibition of human breast cancer cell proliferation and delaying of mammary tumorigenesis. It is also used in metastasis and leukemia (21-22).

The derivatives (viz. chlorogenic, dicaffeoylquinic and tricaffeoylquinic acids) of caffeoylquinic acid contained in *Ipomoea batatas* tubers (Shakarkand) have potential cancer chemoprotective effect (23-26). 4-Ipomeanol (a furanoterpenoid) isolated from *I. batatas* has been found to exhibit anticancer activity against non-small cell lung cancer lines (27). Further, leaves of *Martynia annusa* (28), bark of *Prunus* spp. (28), and stem of *Rhaphidophora pertusa* (29) have been used against neck, lung and abdominal cancers, respectively.

It has been reported that medicinal plants may promote host resistance against infection by re-stabilizing body equilibrium and conditioning the body tissues (1). Several reports (2-3, 41) describe that the anticancer activity of these plants is due to antioxidants such as vitamins (A, C, E), carotene, enzymes (e.g., superoxide dismutase, catalase and glutathion peroxidase), minerals (e.g., Cu, Mn, Se and Zn), polysaccharides, polyphenols (e.g., ellagic acid, gallic acid and tannins), flavonoids (e.g., quercetin, anthocyanins, catechins, flavones, flavonones and isoflavones), lignins, xanthones, etc. Many medicinal plants mentioned in Tables 1 and 2 contain several of these antioxidants.

Table 1: Some medicinal plants as anticancer agents[3,8-41]

Botanical name (with Hindi/common name)	Family	Main active components	Parts used
Acrorus calamus (Bach)	Araceae	Asarone, eugenol, methyl eugenol, palmitic acid and champhene	Rhizome
Agrimonia pilosa (Hairy agrimony)	Rosaceae	Agrimonolide, flavonoid, tannin, triterpene and coumarin	Whole plant
Alphitonia zizphoides	Rhamnaceae	Zizphoisides (A, C, D, E triterpenoid saponins)	Whole plant
Alstonia scholaris (Devil tree)	Apocynasaceae	Triterpene and latex	Bark
Amorphophallus companulatus (Suran)	Araceae	Leucine, isoleucine, lysine stigmasterol and β-sitosterol	Corm
Andrographis paniculata (Kalmegh)	Acanthaceae	Flavonoid, andrographin and andrographolide	Whole plant
Avicennia alba	Avicenniaceae	Napthoquinolines and their analogues (avicequinones A, B, C)	Whole plant
Azadirachta indica (Neem)	Meliaceae	Tannin, β-sitosterol, nimbin, quercetin and carotene Alkaloid and inositol Tannin and phenolic compounds	Bark, leaf, flower
Bruguiera exaristata	Rhizophoraceae	Caesalpins ($\alpha, \beta, \gamma, \delta, \varepsilon$) and homoisoflavone	Whole plant
Bruguiera paviflora	Rhizophoraceae		Whole plant
Caesalpinia bonduc (Kantkarej)	Caesalpiniaceae	Many essential amino acids	Whole plant
Cajanus cajan (Arhar)	Fabaceae	Quercetin, xanthone, biflavonoid, neoflavonoid, benzophenone and β-sitosterol	Leaf, seed
Calophyllum inophyllum (Sultanachampa)	Clusiaceae		Whole plant
		Polyphenols, epigallo-catechin-3-gallate, carotene,	

		ascorbic acid, xanthine and inositol	
Camellia sinensis (Green tea, black tea)	Theaceae	Chrysophanol, isochrysophanol, rhein and β-sitosterol	Leaf
Cassia absus (Chaksu)	Caesalpiniaceae	Hydrocyanic acid, delphinidin and cyaniding	Leaf
Cayratia carnosa (Amalbel)	Vitaceae	Sesquiterpene lactone and lignin	Whole plant
Ceiba pentandra (Saphed simal)	Bombacaceae	Tetracyclic triterpenoid and β-sitosterol	Root, bark
Cissus quadrangularis (Hadjod)	Vitaceae	Flavonoid, flavone, limonoid, limonene, nobiletin and tangeretin	Whole plant
Citrus limon (Nibu)	Rutaceae	Resin	Fruit
Cycas rumphii (Kama)	Cycadaceae	Plant contains essential oil, coumarins (ellagic acid derivatives)	Bud, flower
Decaspermum fructico-sum (Christmas bush)	Myrtaceae	Volatile oils (eugenol, actyl eugenol, pinene) and tannin	Whole plant
Eugenia caryophyllata (Laung, clove)	Myrtaceae	Dimethlsulfone, kaempferol-diglucoside and caffeic acid	Whole plant, flower bud
Equisetum hyemale (Common horsetail)	Equisetaceae	Geranin, tannin and citric acid	Whole plant
Geranium robertianum (Herb Robert)	Geraniaceae	Triterpenoid saponin (glycyrrhizin, glabranin), isoflavone, coumarin, triterpene sterol (β-amerin stigmasterol), eugenol and indole	Whole plant
Glycerrhiza glabra (Mulathi)	Fabaceae	Monophenolase, catalase, cytochrome c-oxidase, anthocyanins and caffeic acid	Rhizome
		Kamlolenic, conjugated dienoic, oleic, lauric, plmitic and stearic acids	
Ipomoea batatas (Sakkarkand)	Convolvulaceae	Essential oils (menthol, menthone, limonene).	Stem (tuber)
Mallotus philippensis (Sindur, kamala)	Euphorbiaceae	Vitamins (A, C)	Whole plant
Mentha arvensis (Podina)	Lamiaceae	Quercetin, β-sitosterol, saponin and glucoside	Whole plant
Moringa oleifera (Mungana)	Moringaceae	Dipentene and d-linalool	Leaf, root
Mussaenda raiateenisis	Rubiaceae	Plant contains essential oil and crystalline furocoumarin	Bark
Pandanus odoratissimus (Kevda)	Pandanaceae	Dikitonepongamol, glabrin and karanjin	Whole plant, leaf
Pastinaca sativa (Parsnip)	Umbelliferae	Selenium, ayanin (flavonoid) and β-sitosterol	Whole plant
Pongamia pinnata (Karanj)	Fabaceae	Monocyclic sesquiterpene	Root, fruit
Physalis angulata (Wild tomato)	Solanaceae	Alkaloids (premnine, ganiarine, ganikarine)	Whole plant, leaf
Piper longum (Pipli)	Piperaceae	Ca, Fe and vitamins (A, B, C)	Whole plant
Premna obtusifolia (Agetha)	Verbenaceae	Glycosides of quercetin, isoquercitrin, kaempferol 3-flucoside, lupenone and β-sitosterol	Whole plant
Tetragonia tetragonioides	Tetragoniaceae	Taxol (diterpene)	Stem
Thespesia populnea (Paras-papal)	Malvaceae	Lupeol, stigmasterol and β-sitosterol	Seed
Taxodium distichum	Taxaceae		Whole plant
Vernonia cinerea (Sahadeyi)	Asteraceae		

Table 2: Additional list of anticancer plants[28-31,42-44]

Botanical Name	Family	Parts used
Allium bakeri	Liliaceae	Bulb
Berberis aristata	Berberidaceae	Whole plant
Cedrus deodara	Pinaceae	Seed

Celitis africana	Ulmaceae	Bark, root
Curtisia dentata	Cornaceae	Bark, leaf
Eucomis autumnalis	Hyacinthaceae	Bulb
Euphorbia ingens	Euphorbiceae	Latex
Ganoderma lucidum	*Bacidiomycetes*	Whole plant
Gentiana spp.	*Gentianaceae*	Root
Gynura pseudochina	Compositae	Root
Hypoxis hemerocallidea	Hypoxidaceae	Corm
Luisia tenuifolia	Orchidaceae	Whole plant
Lynghya gracilis	Ocillatoriaceae	Fruit
Martynia annusa	Martyniaceae	Leaf
Periploca aphylla	Asclepiadaceae	Whole plant- milky juice
Pittosporum viridiflorum	Pittosporaceae	Bark, root
Polygala senega	Polygalaceae	Root
Prunus spp.	Rosaceae	Bark
Psychotria insularum	Rubiaceae	Whole plant
Pterospermum acerifolium	Sterculiaceae	Flower
Rhaphidophora pertusa	Araceae	Stem
Seasamum indicum	Padaliaceae	Seed
Sonchus oleraceus	Compositae	Whole plant
Sutherlandia frutescens	Fabaceae	Stem, leaf, flower, seed
Tetrastigma serrulatum	Vitaceae	Aerial parts
Trapa natans	Trapaceae	Stem
Tricosanthes kirilowi	Cucurbitaceae	Root

CONCLUSION

Considerable works have been done on the medicinal plants to treat cancer, and some plant products have been marketed as anticancer drugs. These plants may promote host resistance against infection by re-stabilizing body equilibrium and conditioning the body tissues. Several reports describe that the anticancer activity of these plants is due to presence of antioxidants (viz., vitamins, carotene, enzymes, minerals, polysaccharides, polyphenols, flavonoids, lignins, xanthones, etc.). Many medicinal plants described in this article contain several of these antioxidants. Thus, the various combinations of the active components of these plants after isolation and identification can be made and have to be further assessed for their synergistic effects. Preparation of standardized dose and dosage regimen may play a critical role in the remedy of cancer. The rate with which cancer is progressing, it seems to have an urgent and effective effort for making good health of humans as well as animals. There is a broad scope to derive the potent anticancer agents from medicinal plants, which need thorough research.

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