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A REVIEW: PLANT SOURCES AS POTENTIAL ANTI-CANCER AGENTS

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ABSTRACT

Natural products remain an important source of new drugs, new drug leads and new chemical entities. Cancer known medically as a malignant neoplasm, is a term for a large group of different diseases, all involving unregulated cell growth. The plant based drug discovery resulted mainly in the development of anticancer agents including plants (vincristine, vinblastine, etoposide, paclitaxel, camptothecin, topotecan and irinotecan), marine organisms (citarabine, aplidine and dolastatin 10) and micro-organisms (dactinomycin, bleomycin and doxorubicin). Beside this there is numerous agents identified from fruits and vegetables can used in anticancer therapy. The agents include curcumin (turmeric), resveratrol (red grapes, peanuts and berries), genistein (soybean), diallyl sulfide (allium), S-allyl cysteine (allium), allicin (garlic), lycopene (tomato), capsaicin (red chilli), diosgenin (fenugreek), 6-gingerol (ginger), ellagic acid (pomegranate), ursolic acid (apple, pears, prunes), silymarin (milk thistle), anethol (anise, camphor, and fennel), catechins (green tea), eugenol (cloves), indole-3-carbinol (cruciferous vegetables), limonene (citrus fruits), beta carotene (carrots), and dietary fiber. In this review active principle derived from natural products are offering a great opportunity to evaluate not only totally new chemical classes of anticancer agents, but also novel lead compound and potentially relevant mechanisms of action.

Key Words: Cancer, Active constituents, Plants.

INTRODUCTION

Plants have a long history of use in the treatment of cancer. In his review, Hartwell lists more than 3000 plant species that have reportedly been used in the treatment of cancer, but in many instances, the “cancer” is undefined, or reference is made to conditions such as “hard swellings”, abscesses, calluses, corns warts, polyps, or tumors, to name a few.

The search for anti-cancer agents from plant sources started in earnest in the 1950s with the discovery and development of the vinca alkaloids, vinblastine and vincristine, and the isolation of the cytotoxic podophyllotoxins.

Cancer continues to be one of the major causes of death worldwide and only modest progress has been made in reducing the morbidity and mortality of this disease [1]. Cancers may be caused in one of three ways, namely incorrect diet, genetic predisposition, and via the environment. As many as 95% of all cancers are caused by life style and may take as long as 20–30 years to develop. Current estimates from the American Cancer Society and from the International Union Against Cancer indicate that 12 million cases of cancer were diagnosed last year, with 7 million deaths worldwide; these numbers are expected to double by 2030 (27 million cases with 17 million deaths) [2]. According to a report of World Health Organization, more than 80% of world’s populations depend on traditional medicine for their primary health care needs [3-5]. Naturally occurring drugs that are part of the war against cancer include vinca alkaloids (vincristine, vinblastine, vindesine, vinorelbine), taxanes (paclitaxel, docetaxel), podophyllotoxin and its derivative (etoposide, teniposide), camptothecin and its derivatives (topothecan, irinothecan), anthracyclines (doxorubicin, daunorubicin, epirubicin, idarubicin) and others. In fact, half of all anti-cancer drugs approved internationally were either natural products or their derivatives and were developed on the basis of knowledge gained from small molecules or macromolecules that exist in nature [6,7]. In between 2001

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and 2005, 23 new drugs derived from natural products were introduced for the treatment of disorders such as bacterial and fungal infections, cancer, diabetes, dyslipidemia, atopic dermatitis, Alzheimer's disease and genetic diseases such as tyrosinaemia and Gaucher disease out of these 4 drugs have been approved as anti-cancer agents. The approved anti-cancer agents in 2002 doxorubicin, in 2002 estradiol, in 2004 cholorophyll and l-aspartic acid and taxol nanoparticles in 2005 [8]. Three new drugs also introduced in 2007 originate from microbial sources for the treatment of cancer is marine alkaloid trabectedin, epothilone derivative ixabepilone and temsirolimus [9].

Nature is an attractive source of new therapeutic candidate compounds as a tremendous chemical diversity is found in millions of species of plants, animals, marine organisms and microorganisms as potential anti-cancer agent [10,11]. In this present study the potential anti-cancer agent from plants sources with some recent advancement in the field of cancer research were discussed.

Plants as source of anti-cancer agents

The history of plant as source of anti-cancer agents started in earnest in the 1950s with the discovery and development of the vinca alkaloids (vinblastine and vincristine) and the isolation of the cytotoxic podophyllotoxins. Vinca alkaloid was responsible for an increase in the cure rates for Hodgkin's disease and some forms of leukemia [12]. Vincristine inhibits microtubule assembly, inducing tubulin self-association into coiled spiral aggregates [13]. Etoposide is a epipodophyllotoxin, derived from the mandrake plant Podophyllum peltatum and the wild chervil Podophyllum emodi [14]. It has also significant activity against small-cell lung carcinoma [15]. Etoposide is a topoisomerase II inhibitor, stabilizing enzyme–DNA cleavable complexes leading to DNA breaks [16]. The taxanes paclitaxel and docetaxel has been show antitumor activity against breast, ovarian and other tumor types in the clinic trial. Paclitaxel stabilizes microtubules and leading to mitotic arrest [17]. In addition, the camptothecin derivatives irinotecan and topotecan, have shown significant antitumor activity against colorectal and ovarian cancer respectively [18,19]. These compounds were initially obtained from the bark and wood of Nyssacea Camptotheca accuminata and act by inhibiting topoisomerase I [20]. The taxanes and the camptothecins are presently approved for human use in various countries.

Rohitukine the plant alkaloid, isolated from the leaves and stems of Dysoxylum binectariferum (Maliaceae) [21,22]. Synthetic flavone derived from rohitukine, Flavopiridol representing the first cyclin-dependent kinase inhibitor to enter the clinical trial [23]. The mechanism of action involves interfering with the phosphorylation of cyclin-dependent kinases and arrest cell-cycle progression at growth phase G1 or G2 [24,25]. Homoharringtonine an alkaloid isolated from the Chinese tree Cephalotaxus harringtonia (Cephalotaxacea) [26]. The mechanism of action is the inhibition of protein synthesis and blocking cell-cycle progression [27]. It has shown efficacy against various leukemias [28]. A lung-cancer-specific antineoplastic agent 4-Ipomeanol is isolated from the sweet potato Ipomoea batata (Convolvulaceae) [29]. The mechanism of action is converted into DNA-binding metabolites upon metabolic activation by cytochrome P450 enzymes that are present in cells of the lung [30]. DNA topoisomerase I inhibitor β-lapachone, that induces cell-cycle delay at G1 or S (synthesis) phase before inducing either apoptotic or necrotic cell death in a variety of human carcinoma cells, including ovary, colon, lung, prostate and breast [31].

Beside this there are so many plants which are used in cancer; following enlist the plant which prevent and target for future studies as potential anticancer agent.

IMPORTANT MEDICINAL PLANTS HAVING ANTICANCER ACTIVITY [32-59]

S No	Botanical name	Family	Common name	Active constituents	Uses
1	*Allium sativum*	Liliaceae	Garlic	Alliin ,allicin alliin, alliinase, S-allylcysteine(SAC), diallyldisulphide(DADS), diallyltrisulphide (DATS)	Lung cancer, sarcoma
2	*Actinidia chinensis*	Actinidiaceae	China gooseber	Polysaccharide known as "ACPS-R"	Sarcoma
3	*Aloe ferox*	Liliaceae	Aloe vera	Aloe-emodin, emodin, aloin acemannan,	Breast cancer
4	*Ananas comosus*	Bromeliaceae	Pine apple, Ananas	Bromelain	Colonic cancer
5	*Angelica sinensis*	Umbelliferae	Angelica	Polysaccharide fraction of known as"AR-4"	Cervical cancer
6	*Annona species*	Annonaceae	Monkey species	Acetogenins	Carcinoma
7	*Arctium lappa*	Compositae	Burdock	Potent anticancer factors	Cancer

8	*Astragalus membranaceus*	Papilionaceae	-	Swainsonine	Stomach Cancer
9	*Betula utilis*	Betulaceae	Bhojpatra	Betulin	Cancer
10	*Camellia sinensis*	Theaceae	Tea plant	Epigallocatechin gallate	Tumour
11	*Catharanthus roseus*	Apocynaceae	Vinca	Vinblastine, Vincristine, Alstonine, Ajmalicine and Reserpine.	Sarcoma
12	*Chlorella pyrenoidos*	Oocystaceae	-	Lysine	Prostate cancer, pancreatic cancer
13	*Colchicum luteum*	Liliaceae	Colchicum	Colchicines demecolcine	Malignancy
14	*Combretm caffrum*	Combretaceae	-	Combretastatin	Breast cancer
15	*Curcuma longa Linn.*	Zinziberaceae	Turmeric	Tumerone, curcumine.	Lymphoma, leukaemia
16	*Echinacea angustifolia*	Asteraceae	Black Sampson	Arabinogalactan, Jucogalactoxyloglucans	Leukaemia
17	*Fagopyrum esculentum*	Polygonaceae	Vitamin p	Amygdalin, Rutin	Sarcoma
18	*Ginkgo biloba*	Ginkoaceae	Kew tree	Ginkgolide-B, A, C and J	Cencer, tumour
19	*Glycine max*	Leguminosae	Soyabean	Zinc, selenium, vitamins (A, B1, B2, B12,C, D, E and K), amino acids,isoflavones, protease inhibitors,saponins and phytosterols	Liver cancer
20	*Glycyrrhiza glabra*	Leguminosae	Liquorice	Glycyrrhizin.	Lymphoma
21	*Gossypim barbadens*	Malvaceae	Raw cotton	Gossypol	Tumour
22	*Gyrophoa esculenta*	Umbilicaricea	Mushroom	Polysaccharides β-glucans, α-glucans,and galactomannans	Malignancy, yumour
23	*Lentinus edodes*	Agaricaceae	-	Lentinan	Tumour
24	*Linum usitatissimum*	Linaceae	Flax seed, Linseed	Cynogenetic glycosides, Lignans	Cancer
25	*Mentha species*	Labiateae	Pudina	Monoterpene ketones	Breast cancer
26	*Ochrosia elliptica*	Apocynaceae	-	Ellipticine and 9-methoxy ellipticine are pyridocarbazole (monomeric indole) alkaloid	Lung cancer, cancer
27	*Panax ginseng*	Aralaceae	Ginseng	Ginsenosides, Panaxosides	Cancer
28	*Picrorrhizia kurroa*	Scrophulariaceae	Picrorrhizia (kutki)	Picrosides I, II, III and kutkoside	Tumour
29	*Podophyllum hexandrum*	Berberidaceae	Podophyllum	Podophyllin, astragalin	Pancreatic, lung, liver cancer
30	*Taxus brevifolia*	Taxaceae	Pacific yew	Taxanes, taxol cepholomannine	Cancer, sarcoma
31	*Withania somnifera*	Solanaceae	Ashwagandha	Withanolides, *Withaferin*	Tumour
32	*Zingiber officinale*	Zingiberaceae	Ginger	Curcumin,gingerenone A, Gingeols, shogaols, zingerone	Cancer
33	*Akebia quinata*	Lardizabalaceae	-	Limonene, eugenol, octanol and p-cymene, hexanol monoterpenoids, hexanoic acid, palmitic acid	Sarcoma-180 Sarcoma- 37

34	*Taraxacum mongolicum*	Asteraceae	Taraxacum	Sesquiterpene lactones, phenyl propanoids, triterpenoid saponins, polysaccharides.	Ascites cancer Sarcoma-180 Lung cancer cells
35	*Vitex rotundifolia*	Lamiaceae	Vitex	Essential oils: l-d pinene, alpha-pinene, camphene, terpineol acetylester, diterpene alcohol. Alkaloid: vitricine. Monoterpene glucoside:. Flavonols: vitexicarpin (castisin), camphene, casticin, vitamin A. Iridoid glycosides: agnoside, aucbin. Flavonoids: casticin, isovitexin, orientin.	Lung tumour
36	*Sophora flavescens*	Fabaceae	Sophorac	Alkaloids, Oxymatrine, sophoridine, oxysophocarpine, andsophocarpine	Sarcoma-180
37	*Sophora Subprostrata*	Leguminaceae	Sophorac	matrine and oxymatrine	Leukemia and cervical cancer-14 cells
38	*Scutellaria barbata*	Lamiaceae	-	alkaloids, flavones, steroids, and polysaccharides	Sarcoma-180
39	*Smilax chinensis*	Liliaceae	-	Sucrose, glucose, maltose, and fructose, stearic and palmitic acids. Glutamic acid and potassium, amino acids and minerals Diosgenin, steroidal sapogenin, parillin (also sarsaparillin or smilacin), sarsapic acid, sarsapogenin and sarsaponin.	Sarcoma-180 Ascites sarcoma
40	*Smilax glabra*	Smilacaceae	-	alkaloids, flavones, steroids, and polysaccharides	Sarcoma-180
41	*Solanum lyrati*	Solanaceae	Iyrati	Aristolochic acid I (AA	Sarcoma-180, Sarcoma-37 Ehrlichs ascites carcinom
42	*Agrimonia pilosa*	Rosaceae.	-	Triterpenoid; 19α-hydroxyursolic acid	Intestinal cancer
43	*Ailanthus altissima*	Simaroubaceae	-	Aliphatic acids and their esters, fatty hydrocarbons and steroids e.g.E-oleic acid, (Z,Z)-octadeca-9,12-dienoic acid	Sarcoma-180 Sarcoma-3
44	*Pyrus malus*	Rosaceae	-	C21–29 secondary alcohols; *n*-nonacosan-10-ol; C21–29 ketones; *n*-nonacosan-10-one	Lung, colon, breast and intestinal cancer

45	*Pteris multifida*	Pteridaceae	Pterus	Sesquiterpenoid, 3β-caffeoxyl-1β,8α-dihydroxyeudesm-4(15)-ene (1), together with two known compounds including ludongnin V (2) and isoneorautenol (3),	Sarcoma-37 Yoshidas sarcoma
46	*Fritillaria thunbergii*	Liliaceae	Fritillaria	Steroidal alkaloids, as well as diterpenoids	Throat, chest, neck and breast cancer
47	*Phaleria macrocarpa*	Thymelaeaceae	-	Kaempferol, myricetin, naringin, and rutin, naringin and Quercetin	Esophageal cancer
48	*Nidas vespae*	Vespidae	Nidas	Quercetin	Gastric and liver cancer
49	*Aegle marmelos*	Rutaceae	-	Mono-terpene hydrocarbons, sesquiterpene, Limonene, Z)-β- ocimene, and one phenolic compound.	Cancer
50	*Agave americana*e	Agavaceae	-	Leaf contains steroidal saponin, alkaloid, coumarin, isoflavonoid, hecogenin and vitamins (A, B, C)	Brain cancer Prostate cancer
51	*Agropyron repens*	Poaceae	-	Rhizome contains essential oil, polysaccharide and mucilage	Breast cancer
52	*Agrimonia pilosa*	Rosaceae	-	Herb contains agrimonolide, flavonoid, triterpene, tannin and coumarin	Stomach cancer
53	*Ailanthus altissima*	Simaroubaceae	-	Bark contains triterpene, tannin, saponin and quercetin-3-glucoside	Tumour, malignancy
54	*Akebia quinata*	Lardizabalaceae	Akebia	Fruit contains flavonoid and saponin	Stomach cancer,Tumour
55	*Alpinia galanga*	Zinziberaceae	Alpinia	Rhizome contains kaempferide and flavones	Malignancy
56	*Aristolochia contorta*	Aristolochiaceae	-	Root and fruit contain lysicamine and oxaaporphine	Lymphoma, sarcoma
57	*Aster tataricus*	Asteraceae	Aster	Whole plant and root contain triterpene, monoterpene and epifriedelanol	Liver cancer
58	*Broyonia dioica*		-	Root contains cucurbitacin and glycoside	Brain cancer, tumour
59	*Cannabis sativa*	Cannabinaceae	Cannabis	Leaf contains stereo isomers of cannabitriol	Colon cancer
60	*Chelidonium jajus* var. *asiaticum*	Papaveraceae	-	Herb contains alkaloids (sanguinarine, chelerythrine, berberine)	Cervical, prostate cancer
61	*Chimaphila umbellate*	Ericaceae	-	Whole plant contains ericolin, arbutin, urson and tannin	Tumour

62	*Coix lachryma jobi*	Poaceae	Coix jobi	Seed contains trans-ferulyl stigmasterol	Malignancy, cancer
63	*Dryopteris crassirhizoma*	Polypodiaceae	-	Rhizome contains filicinic and filicic acids, aspidinol and aspidin	Cancer
64	*Echinops setifer*	Asteraceae	-	Whole plant contains echinopsine	Stomach Cancer
65	*Erythronim americanum*	Liliaceae	-	Whole plant contains alpha-methylenebutyrolactone	All types of cancer
66	*Euonymus alatus*	Celastraceae	-	Whole plant contains triterpene, euolatin, steroid and sesquiterpene .	Sarcoma
67	*Eupatorium cannabinum*	Asteraceae	-	Whole plant contains sesquiterpene, lactone, pyrrolizidine alkaloid	Breast,prostate cancer
68	*Fragaria vesca*	Rosaceae	Veasca	Leaf and fruit contain flavonoid, tannin, borneol and ellagic acid	Tumour
69	*Fritillaria thunbergii*	Liliaceae	-	Whole plant contains alkaloid and peimine	Cancer
70	*Galium aparine*	Rubiaceae	Gallium	Cleaver contains iridoid, polyphenolic acid, tannin, anthraquinone	Leukaemia
71	*Hydrastis Canadensis*	Ranunculaceae	-	Whole plant contains isoquinoline alkaloids resin and lactone	Leukaemia, lymphoma
72	*Lantana camara*	Verbenaceae	Lantana	Whole plant contains alkaloids (camerine, isocamerine, micranine,	Stomach Cancer
73	*Larrea tridentate*	Zygophyllacae	-	Whole plant contains resin	Tumour

CONCLUSION

Natural products have been a prime source for the treatment of many forms of cancer, many of which are consumed daily with the diet. They provide significant protection against various cancers and many other diseases. The antioxidant medicinal plants and their products prevent from the cancer and other diseases by protecting cells from damage. Thus, consuming a diet rich in antioxidant fruits, vegetables, herbs etc. will provide health-protective effects. Microbes and marine organisms also have been offering the great role in the prevention and treatment of cancer. All the natural products discussed in this review exhibit anticancer activities. Natural products offer a great opportunity to evaluate not only totally new chemical classes of anticancer agents, but also novel and potentially relevant mechanisms of action.

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