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Medicinal Plants as Potential Source of Anticancer Agents: A Review

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Abstract

Cancer is a major public health burden in both developed and developing countries. Anticancer activity is the effect of natural and synthetic or biological and chemical agents to reverse, suppress or prevent carcinogenic progression. Several synthetic agents are used to cure the disease but they have their toxicity and hence the research is going on to investigate the plant derived chemotherapeutic agents. Therefore an attempt has been made to review some medicinal plants having anticancer properties. In this review, anticancer medicinal plants of Indian origin belonging to various families are reported along with detailed information. All these plants are potential candidates for advanced studies since they are showing good anticancer activity. The present paper is a comprehensive review of different literature sources. It will be helpful to explore the medicinal value of the plants against the cancer and for the new drug discovery from them for the researchers and scientists around the world.

Keywords: Anticancer properties, Medicinal plants, Literature sources

Introduction

In recent years there has been a gradual revival of interest in the use of medicinal plants in the developing countries because herbal medicine have been reported safe and less or without any adverse effect especially when compared with synthetic drugs. Herbal medicines represent one of the most important field of traditional medicines all over the world, To promote the use of herbal medicine and to determine their potential as a source of new drugs. It is essential to study medicinal plants which have folklore reputation in a more intensified way. Human beings have used the plants for medicinal purposes for centuries of the world including countries in the Indian sub-continent like India, Pakistan and Bangladesh [1].

The effort to find anticancer agents from higher plants was launched by the US National Cancer institute (NCI) in 1957. So far plants have been proved to be a novel source of useful anticancer substances. Today many of the most useful and curative anticancer drugs are derived from natural products. Since the initiation of program by NCI more than 35,000 plant species had investigated and resulted in the discovery of anticancer drugs such as Vincristine, Vinblastine, Taxol, Indicine-N-oxide, Etoposide analogs, Camptothecin and analogs etc. However with of knowledge available concerning traditional medicine a new approach could be adopted which combine some or all of above methods [2]. Many of the important and effective drugs derived from higher plants were Vinca alkaloids viz Vinblastine and Vincristine are derived from *Catharanthus roseus* are used to treat leukemia, bladder and testicular Cancer. Paclitaxol (Taxol TM) was originally isolated from *Taxus brevifolia* used in treatment of ovarian and breast cancers which was assumed to bind the tubulin subunit of microtubules and stabilizes the microtubule to normal disassembly [3].

Historically plants with known therapeutics potential have long been used to cure a wide range of diseases. The use of potentially curative plants might be particularly significant for their uses as medicinal herbs. Thus the search for new drugs with better and cheaper substitutes from plant origin is a natural choice. In such situation it is need of time to have new drugs to stop proliferation of cancer from natural origin.

Medicinal plants with anticancer activity

Plants are the chief source of natural products that are used in medicine. Generally, populations that consume a high level of natural herbal products have a reduced incidence of cancer. An example, Soyabeans are the major dietary source of saponins which have been suggested as a possible anticancer agents. There is lately great interest in screening for plants

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to be used in cancer prevention and treatment [4]. For this reason extracts from different plants have been extensively studied. The present study is focused to screen traditionally used medicinal plants for anticancer effect.

Solanum nigrum

Solanum nigrum belongs to family: solanaceae. Commonly it is known as black night shade makoy, deadly night shade. It possess medicinal properties like antimicrobial, antioxidant, cytotoxic properties, antiulcerogenic and hepatoprotective activity. *Solanum nigrum* is a potential herbal alternative as anticancer agent and one of active principles reported to be responsible for this action is Diosgenin. The fruit of *Solanum nigrum* methanolic extract were tested for its inhibitory effect on HeLa Cell Line. The percentage viability of cell line was carried out by using Trypan blue dye exclusion method. The cytotoxicity of *Solanum nigrum* on HeLa cell was evaluated by the SRB assay and MTT assay. *Solanum nigrum* methanolic extract has significant cytotoxicity effect on HeLa cell Line in concentration range between 10mg/ml to 0.0196 mg/ml by using SRB assay and study also showed that inhibitory action on HeLa cell line in concentration range between 10mg/ml to 0.0196 mg/ml by using MTT assay. From the performed assay, methanolic extract of these drug shows greater activity on HeLa cell line and little activity on Vero cell line and that mean *Solanum nigrum* can be used as anticancer activity [5].

Tinospora cardifolia

Giloy is one of the most useful ayurvedic herb which act as tonic and aphrodisiac, it is also used as anthelmintic, anti-arthritis, anti-pyretic, blood purifier carminative, digestive, diuretic, expectorant, stomachic, rejuvenating, appetizing, and anti-inflammatory. In Ayurvedic literature Giloy is described as Amrita because of its innumerable medicinal properties and it is also said to increase the lifespan of humans by preventing them from many chronic diseases. Starch from the roots of Giloy as well as from its stem can be used for chronic diarrhea and dysentery. The fresh juice used for chronic fever, gouts, vomiting, cardiac debility, skin diseases, leprosy, anemia, cough, asthma, jaundice, seminal weakness and splenopathy. It is also used for cancer prevention, cancer treatment, support, high cholesterol and liver protection. It is used as strong anti-aging factor. The main chemical constituents of plants are tinosporin, perberillin, palmarin, berberine. The fresh stem barks yield giloin, gilonin, and gilosterol. Hypoglycemia agent and phenolic lignin have also been isolated from this plant [6].

Momordica dioica

Momordica dioica is perennial, dioecious climber included in the Cucurbitaceae family which is commonly known as spiny gourd, teasel gourd or small bitter gourd worldwide, whereas in India it is known as kankro, kartoli, kantola, kantroli, ban karola or janglee karela. *Momordica dioica* has been known to have many medicinal properties namely antitumorogenic, analgesic, anti-diabetic, anti-inflammatory and anti-allergic activity. MMT assay was performed to investigate the anti-proliferative activity of *Momordica dioica* methanolic seed coat extract on the growth of human breast and lung carcinoma cell lines which showed increase inhibition toward the both the tested carcinoma cell lines. At a concentration of 100 µg / mL, methanolic seed coat extract of *Momordica dioica* increased (50% cell inhibition at a concentration of 50 µg/ mL) cell growth inhibition in both the treated cancer cell lines [7].

Cynodon dactylon

Cynodon dactylon belongs to the family of Poaceae and is said to have many medicinal properties including anti-helminthic, anti-diuretic, anti-inflammatory, hepatoprotective activity as well as treatment of urinary tract infection, Prostatitis and Dysentery. Traditionally it is used in diabetes, jaundice, kidney problem, urinary diseases, gastro intestinal disorder, constipation and abdominal pain. The whole plant is used for diuretics, dropsy, syphilis, wound infection and piles. *Cynodon dactylon* is used as antihemorrhagic in dysentery and nasal bleeding. The juice of plant is astringent and is applied externally to fresh cuts and wounds. It is used in treatment of catarrhal ophthalmia hysteria, epilepsy, insanity and chronic diarrhea. The plant is folk remedy for anasarca, calculus, carbuncles, cough, hypertension, snake bites, gout, and rheumatic affections. The nontoxic dose of the petroleum ether of *Cynodon dactylon* on normal vero cell line showed that with regard to viability of cell was found to be 97% at a concentration of 0.007 mg/ml which decreased with increase in concentration. The extract showed a potent cytotoxic activity against Hep-2 laryngeal cancer cell line. Cyclophosphamide served as pc-control and 96.2% cancer inhibition was observed. The concentration of petroleum ether extract of *Cynodon dactylon* at 10 mg/ ml showed inhibition percent with regard to cytotoxicity of 93.5% that was comparable to the positive control [8].

Drosera indica

Drosera is a cosmopolitan genus of insectivorous plants and consist of approximately 170 species. In India *Drosera indica* L. family-Droseraceae, *Drosera burmannii* Vahl and *Drosera peltata* J.E. Sm.ex. Wild have been reported to be present at different location. These species are used as vital components in the Ayurvedic preparation Swarnabhasma (Golden ash). Swarnbhasma (golden ash) is used in several clinical manifestation including the loss of memory, defective eyesight, infertility, overall body weakness and incidence of early aging. It is also used for the treatment of diseases like bronchial asthma, rheumatoid arthritis, diabetes mellitus and nervous disorder. The ethanolic and aqueous extract of *D. indica* L. Possess significant anti-oxidant and anticancer activities when tested against different *in vitro* models. The antioxidant ability could be attributed action. Thus *D. indica* L. extracts as promising natural source of antioxidant and anticancer agent can be used in nutritional or pharmaceutical field for the prevention fields for the prevention of free radical mediated disease [9].

Barleria grandiflora

Barleria grandiflora (Family-Acanthaceae) commonly known as Dev koranti in Marathi which is frequently distributed in central India especially in Vidarbha area of Maharashtra. Ethnobotanical survey reveals the leaf juice is used for treating the mouth ulcer. The principle constituents of leaf and stem circumscribe the presence of glycoside i.e barlein. shanzhiside, methyl ester. *In-vitro* cytotoxicity study of MeBG extract and WtBG extract, MeBG showed direct cytotoxic effect on the A-549 and DLA cell line in a concentration dependant manner and IC 50 value was found to be 143.4 µg/ml (MeBG) and 210.8 µg/ml(WtBG) 137.2 µg/ml (MeBG) and 217.8µg/ml(WtBG) respectively. While both the extract were less toxic to Vero cell line and IC50 value was found to be 148.7 µg/ml (MeBG) and 152.6 µg/ml (WtBG). *In-vitro* cytotoxicity study shows that MeBG is more cytotoxic for

DLA tumour cells and less cytotoxic for normal cell line i.e. A-549 cell line [10].

Moringa oleifera

Moringa oleifera (M.oleifera) or drumstick is a member of Moringaceae and it is grown extensively in many Southeast Asian countries particularly in Thailand, India, Philippines, and Pakistan. It has long been known as a food plant in Thai cuisine and as an ingredient of Indian traditional medicine. The leaves contain nutrients especially essential amino acids, vitamins, minerals and beta-carotene. For this reason it is used as an alternative source for nutritional supplements and growth promoter in some countries. Apart from nutritional benefits *M.oleifera* is reported to be used for the treatment of rheumatism, Ascites, infection, hiccough, influenza and internal abscess. Many recent reports on diseases prevention by *M.oleifera* have been reported. The leaf extract is capable of reducing hyperglycemia and dyslipidemia. The antiproliferation was tested on HepG2, Caco-2, MCF-7 and human fibroblast cells. It was found that both extracts (0-250µg/ml) contributed to similar cancer cell viability patterns. It showed IC₅₀ of 120.37±2.55, 112.46±3.74 and 133.58±2.47 µg/ml for HepG2, Caco-2 and MCF-7 respectively. According to the results *M.oleifera* extracts not only exhibit antiproliferation on cancer cells but also showed no cytotoxicity on normal cells [11].

Terminalia chebula

Terminalia chebula is a rich medicinal value herb which is widely employed for many diseases. The methanolic extract of *T. chebula* reduced the silver nanoparticle biologically and ecofriendly. The biosynthesized silver nanoparticle were explored against colon cancer cells and multi drug resistant (MDR) broad spectrum micro-organism. The silver nanoparticles from *T.chebula* methanolic extract exhibit significant antibacterial and anticancer activity. This study insights the *T.chebula* synthesized silver NP's could be and effective applicability drug candidate for colon cancer and applied externally for the MDR bacteria wound infection [12].

Cucurbita maxima

The plant *Cucurbita maxima* (commonly known as pumpkin) belongs to family-Cucurbitaceae. The family is widely cultivated throughout the world for use as vegetable as well as medicine. Both of its fruits and the aerial parts are commonly consumed as vegetable. The plant has been used traditionally as medicine in many countries such as China, India, Yugoslavia, Brazil and America. Traditionally it is used in most countries as anti-diabetic, antitumor, antihypertensive, anti-inflammatory, immune modulator and antibacterial agents. Constituents of medicinal plants such as flavonoids and phenols play a significant role in cancer control through the regulation of genetic pathways without any side effect. The MTT assay of the compound isolated from isolated ethyl acetate fraction of *Cucurbita maxima* flowers shows that all concentration are having anticancer activity. The sample concentration of 1000 µg/ml, 500µ/ml, 250µg/ml, 125µg/ml and 62.5µg/ml showed 72.05µg/ml, 68.94µg/ml, 54.22µg/ml, 43.19µg/ml and 37.80µg/ml of CTC50 (212µg/ml) value against the human cancer HePG2 cell line respectively [13].

Cassia auriculata

The *Cassia auriculata* belongs to family-Cesalpiniaceae which has been claimed to possess the wound healing and antioxidant activities. Traditional background of Indian medicine shows widespread use of plant product in cancer. Fresh flower of *Cassia auriculata* is widely used in traditional system of medicine as a cure for rheumatism. The plant has been reported to possess antipyretic, hepatoprotective, antidiabetic, antiperoxidative, antihyperglycemic and microcidal activity. *Cassia auriculata* plant contains preliminary phytochemical constituents such as alkaloids, phenols, glycoside, flavonoids, tannin, saponins, protein, carbohydrate and anthraquinone derivatives are responsible for the pharmacological activities. The MTT assay of ethanolic extract of flowers of *Cassia auriculata* shows that all concentration are having anticancer activity [14].

Table1: Medicinal Plants with Anti-Cancer activity.¹⁵⁻⁴¹

Sr.No.	Botanical name	Family	Active constituent
1	<i>Allium sativum</i>	Liliaceae	Alliin, allicin alliin, alliinase
2	<i>Actinidia chinensis</i>	Actinidiaceae	Polysaccharide known as "ACPS-R"
3	<i>Aloe ferox,</i> <i>Aloe barbadensis</i>	Liliaceae	Aloe-emodin, emodin, aloin
4	<i>Ananas comosus</i>	Bromeliaceae	Bromelain
5	<i>Angelica sinensis</i>	Umbelliferae	Polysaccharide fraction "AR-4"
6	<i>Annona species</i>	Annonaceae	Acetogenins
7	<i>Arctium lappa,</i>	Compositae	Potent anticancer factors.
8	<i>Astragalus membranaceus</i>	Papilionaceae	Swainsonine
9	<i>Agapanthus africanus</i>	Agapanthaceae	Isoliquiritigenin
10	<i>Aglaila sylvestre</i>	Meliaceae	Silvesterol
11	<i>Betula utilis</i>	Betulaceae	Betulin
12	<i>Camellia sinensis</i>	Theaceae	Epigallocatechin gallate
13	<i>Catharanthus roseus</i>	Apocynaceae	Vinblastine, Vincristine
14	<i>Chlorella pyrenoidosa</i>	Oocystaceae	Lysine
15	<i>Colchicum luteum</i>	Liliaceae	Colchicines demecolcine
16	<i>Combretum caffrum</i>	Combretaceae	Combretastatin
17	<i>Corcus sativus</i>	Iridaceae	Safranal, Crocetin, Crocin.
18	<i>Echinacea angustifolia</i>	Asteraceae	Arabinogalactan,
19	<i>Fagopyrum esculentum,</i>	Polygonaceae	Amygdalin, Rutin
20	<i>Ginkgo biloba</i>	Ginkgoaceae	Ginkgolide-B, A, C and J
21	<i>Glycine max</i>	Leguminosae	Zinc, selenium, vitamins (A, B1, B2, B12, C, D, E and K),
22	<i>Glycyrrhiza glabra</i>	Leguminosae	Glycyrrhizin.

23	<i>Gossypium barbadense</i>	Malvaceae	Gossypol
24	<i>Gyrophora esculenta</i>	Umbelicariaceae	Polysaccharides β -glucans, α -glucans,
25	<i>Lentinus edodes</i>	Agaricaceae	Lentinan
26	<i>Linum usitatissimum</i>	Linaceae	Cynogenetic glycosides, Lignans
27	<i>Mentha species</i>	Labiataeae	Monoterpene ketones
28	<i>Ochrosia elliptica</i>	Apocynaceae	Ellipticine and 9-methoxy ellipticine
29	<i>Panax ginseng</i>	Aralaceae	Ginsenosides, Panaxosides
30	<i>Picrorrhizia kurroa</i>	Scrophulariaceae	Picrosides I, II, III and kutkoside
31	<i>Podophyllum hexandrum</i>	Berberidaceae	Podophyllin, astragalin
32	<i>Taxus brevifolia</i>	Taxaceae	Taxanes, taxol cepholomamine
33	<i>Withania somnifera</i>	Solanaceae	Withanolides, Withaferin
34	<i>Zingiber officinale</i>	Zingiberaceae	Curcumin, gingerenone A, Gingeols, shogaols, zingerone

Conclusion

From the present review, it can be concluded that herbal medicinal plants and its derivatives are active against different type of cancers like lymphomas, breast, ovarian, lung, liver, stomach, prostate and testicular cancers. The cheap herbal drug treatment may highly be recommended to the rural and poor people to treat effectively the cancers of various type is an ideal choice. This review has shown that plants like *Terminalia chebula*, *Moringa oleifera*, *Tinospora cordifolia* etc. which were used in ayurveda possess potential anticancer activity. The above survey reveals the role of Indian medicinal plants and the various phytochemicals may be treated effectively for cancer. In an attempt of screening the traditional medicinal plants for anticancer activity the presence of several bioactive compounds such as flavonoids, polyphenols, saponins, etc. with specific anticancer activity against particular type of cancer, hence the huge space are available for development of strong anticancer agents from plant derivatives.

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