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REVIEW ARTICLE

A REVIEW ON COMMON MEDICINAL PLANTS OF ANTICANCER ACTIVITY

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ABSTRACT

Cancer is a major public health burden in both developed and developing countries. One of the leading causes of death and globally the numbers of cases of cancer are increasing gradually. Cancer chemo-preventive agents, many of which are natural products, are capable of preventing or inhibiting the process of carcinogenesis.Plants, since ancient time, are using for health benefits by all cultures as well as source of medicines. Over the past decade, herbal medicines have become a topic of global importance, making an impact on both world health and international trade. Medicinal plants continue to play a central role in the healthcare system of large proportions of world's population. This is particularly true in developing countries, where herbal medicine has a long and uninterrupted history of use. 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, which are the natural sources of anticancer agents.

Key words: Cancer, medicinal plants, antioxidants, anticancer agents, natural sources.

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INTRODUCTION

Cancer is an abnormal growth of cells that grows and spreads through uncontrolled cell division. These 'malignant' cells may invade other tissues and spread (metastasize) to more distant parts of the body. Cancer is not one disease but a group of more than 100 distinct disorders. It is the world's second biggest killer after cardiovascular disease and was responsible for the death of 7.6 million people in 2005 (World Health Organisation, 2017). Globally the number of people diagnosed with cancer is estimated at around 11 million people, a figure that is set to rise to 16 million by 2020. Of all new cancer cases, it is estimated that one third could be cured if they were adequately diagnosed and treated (Bernard *et al.,* 2003). Natural Products, especially plants, have been used for the treatment of various diseases for thousands of years. Terrestrial plants have been used as medicines in Egypt, China, India and Greece from ancient time and an impressive number of modern drugs have been developed from them. 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. Despite many therapeutic advances in the understanding of the processes in carcinogenesis, overall mortality statistics are unlikely to change until, it is believed, There is a reorientation of the concepts for the use of natural products as new chemo-preventive agents (Abdulla and Gurber, 2000). 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 (Fan *et al.,* 1998). 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 (Abdulla and Gurber, 2000). 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.

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What causes cancer?

Cancer begins with mutations in DNA, which instructs the cells how to grow and divide. Normal cells have the ability to repair most of the mutations in their DNA, but the mutation which is not repaired and causing the cells to grow becomes cancerous. Cancer may affect people of all ages, but risk tends to increase with age, due to the fact that DNA damage becomes more apparent in aging DNA. Statistics indicate that men are largely plagued by lung, colon, rectum, and prostate cancer, whilst women increasingly suffer from breast, colon, rectal, and stomach cancer (Belman, 1983).

Environmental factors: Environmental factors which, from a scientist's standpoint, include smoking, diet, and infectious diseases as well as chemicals and radiation in our homes and workplace along with trace levels of pollutants in food, drinking water and in air. Other factors which are more likely to affect are tobacco use, unhealthy diet, not enough physical activity, however the degree of risk from pollutants depends on the concentration, intensity and exposure. The cancer risk becomes highly increased where workers are exposed to ionizing radiation, carcinomas chemicals, certain metals and some other specific substances even exposed at low levels. Passive tobacco smoke manifold increase the risk in a large population who do not smoke but exposed to exhaled smoke of smokers.

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 to be used in cancer prevention and treatment (Zhang *et al.,* 2001). Plants, since ancient time, are using for health benefits by all cultures as well as source of medicines. It has been estimated that about 85% of global population rely on traditional medicines for their primarily health care needs and it is assumed that a major part of traditional therapy involves the use of plant extracts or their active principles,. Although a lot of recent investigations have been carried out for advancements in the treatment and control of cancer progression, significant work and room for improvement remain. The main disadvantages of synthetic drugs are the associated side effects. However natural therapies, such as the use of the plants or plant derived natural products are being beneficial to combat cancer. Most of the medicinal plants, which are screened for anti-cancer and anti-tumour activity, are not indicated in the treatment of Arbuda in the original texts. This confirms that cancer is not merely dealt under Arbuda. This paper has been made to explain the rationality behind the ancient approach on cancer.

- **Emblica Officinalis:** Emblica officinalis belongs to the family Euphorbiaceae. It is commonly known as amla or Indian gooseberry. Emblica has been used as an important traditional herbal medicine in Southeast Asia since ancient times. It is extensively found all over India, as well as Sri Lanka, Malaysia, China, Pakistan and Bangladesh. The fruits contain constituents with variable biological activity. Emblica is agood source of polyphenols, flavones, tannins and other bioactive substances (Haque *et al.,* 2001). It is a source of hepatoprotective, antioxidant, immune stimulator and antitumor agent. Pyrogallol an active compound of E. officinalis has antiinflammatory effect. Eighteen compounds found in Emblica inhibit the growth of gastric, uterine and breast cancer. It enhances natural killer (NK) cells in various tumors and reduced the ascites and solid tumor induced by Dalton's lymphoma ascites cells in mice. Cyclophosphamide is one of the most popular alkylating anticancer drugs inspite of its toxic effects. Haque et.al found that aqueous extract of Emblica officinalis reduced the toxic effect, such as immunotoxicity, hematotoxicity and mutagenecity, in mice treated with cyclophosmamide (Manu and Kuttan, 2007).

Boerhaavia Diffusa: Boerhaavia diffusa L. is a perennial creeping herb which belongs to the family Nyctaginaceae. It is commonly known as "Punarnava" in the Indian system of medicine. The various parts of the plant are used in the treatment of cancer, jaundice, dyspepsia, inflammation, enlargement of spleen, abdominal pain and as an anti-stress agent. Punarnava possesses punarnavoside, which exhibits a wide range of properties such as diuretic, antifibrinolytic, anticonvulsant and antibacterial. Liriodendrin isolated from the methanol extract of the roots of B. diffusa exhibits significant calcium channel antagonistic activity. Punarnavine, an alkaloid from B. diffusa enhanced the immune response against metastatic progression of B16F-10 melanoma cells in mice (Bharali *et al.,* 2003). Ethanolic extract of B. diffusa Showed cytotoxicity against HeLa cell line and inhibits the Sphase of the cell cycle. It also suppressed the growth of cancer cells in DMBA- inducedcancer carcinogenesis in mice by preventing the promotional events in the mouse skin through free radical scavenging mechanism (Ahmed-Belkacem *et al.,* 2007). Two rotenoids isolated from B. diffusa, boeravinones G and H, have been found to potently inhibit the drug efflux activity of breast cancer resistance protein (BCRP/ABCG2), a multidrug transporter responsible for cancer cell resistance to chemotherapy (Keum *et al.,* 2002).

Zingiber Officinale: Zingiber officinale (Ginger), belonging to the family Zingiberaceae, is a commonly used medicinal herb throughout the world. It is a natural dietary component with antioxidant and anticarcinogenic properties. Active phenolic compounds of ginger such as shagaol and gingerol, have antioxidant, anti-angiogenesis, anti-inflammatory, anti-atherosclerotic and anticancer properties. Gingerol, a compound of ginger can inhibit angiogenesis of human endothelial cells and cause cell cycle arrest in the G1 phase through the down regulation of cyclin D1. The oleoresin from the roots of ginger also contains a structurally related vanilloid, paradol. These compounds suppress the proliferation of human cancer cells through the induction of apoptosis and exert inhibitory effects on the viability of human HL-60 (promyelocytic leukemia) cells. Keum et.al, found that paradol and other structurally related derivatives like paradol, dehydroparadol, dehydroparadol and dehydroparadol, induced apoptosis in an oral squamous carcinoma cell line, in a dose dependent manner through a caspase-3-dependent mechanism (Wichtl, 2004). Beta- Elemene is a novel anticancer drug, which is extracted from the ginger plant. It triggers apoptosis in non-small cell lung cancer cells through a mitochondrial release of the cytochrome c- mediated apoptotic pathway. Beta-Elemene also induced caspase-3, -7 and -9 activities and decreased Bcl-2 expression. Results from pharmacological experiments indicate that ginger might inhibit the growth of

tumors in humans (Jeong *et al.,* 2009). Gingerol, the active component in ginger, has been the focus of clinical trials determining its potential to prevent certain cancers. Researchers determined that in cases of ovarian cancer, administration of gingerol contributed to cancer-cell death. In cases of ovarian cancer, gingerol was found to reduce inflammation and boost immune function. It has been stated by researchers that gingerol might protect against colon cancer (Cho, 2011).

Curcuma Longa: Native to the Indian subcontinent and Southeast Asia, turmeric has been used - since 1900 BC - by Ayurvedic physicians to alleviate the symptoms of allergies and inflammation, liver complications, and rheumatism. As a medicine, turmeric is taken as a tea or as an ingredient in chai, the traditional Indian preparation of black tea. The component in turmeric with anticancer potential - curcumin - has been researched in depth. In clinical trials, turmeric proved to be effective in preventing colon and pancreatic cancers. While studies have been far reaching, few conclusions have been drawn as to whether turmeric should be used to treat cancer. It is reported that curcumin induces apoptosis (cell death) of cancer cells without cytotoxic effects on healthy cells. Curcumin achieves this via suppression of the nuclear factor-kappa B activation pathway, the activation of nuclear factor-kappa B being linked to a number of inflammatory diseases - including cancer. Recent studies indicate that curcumin might have anticancer potential. When administered orally to rats, curcumin proved to be effective in preventing cancer of the skin, stomach, colon, lung, and breast. According to an in vivo study in 2001, the rodent specimens that were given curcumin as a dietary supplement throughout their life cycle showed a significant reduction in potentially cancerous cellular activity as compared to those in the control group. Recently, curcumin was determined to be a regulator of genes involved in cancer formation - in clinical trials, it was found to inhibit the migration of lung cancer cells. The idea that curcumin might inhibit cancer cell growth has prompted the formation of subsequent hypotheses. Most recently, curcumin has been studied for its potential to treat myeloma and breast cancer (Aggarwal and Shishodia, 2004; Anticancer Potential of Plants and Natural Products).

Allium Sativum: Allium sativum (garlic, lasun) is used to treat a wide variety of diseases in India. Allicin is a major component of raw garlic and ajoene is a product of the rearrangement of allicin. Its cytotoxic effect has been tested using human primary fibroblasts, a permanent, non-tumorgenic cell line derived from baby hamster kidney cells and a tumorgenic lymphoid cell line derived from a Burkitt lymphoma. The cytotoxic action was in the range 2-50 µg/ml. Some organo-sulfur compounds from garlic, like S-allylcysteine, are reported to retard the growth of chemically induced and transplantable tumors in several animal models. Administration of garlic (250 mg/kg, p.o., thrice a week) in male wistar rats, has significantly suppressed 4-nitroquinoline-1-oxide induced tongue carcinogenesis as revealed by the absence by the carcinomas in the initiation phase and their reduced incidence in the post initiation phase. Thus the consumption of garlic may beneficial providing some kind of protection from cancer.

Azadirachta Indica: 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. 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. 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. 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.

Tinospora Cardifolia: Giloy is one of the most useful ayurvedic herb which act as tonic and aphrodisiac, it is also used as anthelmintic, anti- arthritic, 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 antiaging 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 [xx].

Cynodon Dactylon: Cynodon dactylon belongs to the family of Poaceae and is said to have many medicinal properties including anti-helmintic, 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, urinay 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 antihaemorrhagic 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.

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.

Conclusion

These plants possess good immunomodulatory and antioxidant properties leading to anticancer activity. Many medicinal plants described in this paper contain several of these antioxidants. Many herbs play chemo protective action, a combination of ayurvedic medicine and conventional therapy could also be recommended to inhibit the growth of cancer cells and to reduce the side effects of radiation and chemotherapy. Aswagandha has already proven to be a constituent of anti- aging property. Vitex negundo is an important plant with lots of medicinal properties. According to earlier studies it has been shown that Vitex negundo possess antioxidant properties. This proper exploration would develop in introducing a site specific and safe anticancer drug with higher therapeutic properties to eradicate cancer. Medicinal plants maintain the health and vitality of individual and also cure various diseases including cancer without causing toxicity. Natural products discovered from medicinal plants have played an important role in treatment of cancer.

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