COMMON INDIAN MEDICINAL PLANTS TRADITIONALLY USED FOR ANTICANCER ACTIVITY—A REVIEW

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Abstract: Cancer is an abnormal growth and proliferation of cells. It is the world second biggest killer after cardiovascular disease. Medicinal plants have been used for healing and preventative health for thousands of years all around the world. The use of herbal medicines in cancer prevention and treatment is increasing worldwide, now days because of their natural origin and lesser side effects. Traditional medicines are widely used in India. There are 21,000 plants which are used for medicinal purposes around the world as listed by World Health Organization. Among these, 2500 species are in India, out of which 150 species are used commercially on a large scale. India is called as botanical garden of the world and is the largest producer of medicinal herbs (Seth *et al.*, 2004) Research indicates several possible mechanisms of action for herbal medicines and their phytochemicals may act alone or in concert to reduce cancer risk through their anti-oxidant (Ahmed *et al.*, 2013), and anti-tumorigenic properties, as well as their direct suppressive effect on carcinogen bioactivities. In this article we gather the information about the easily available plants used previously and recently identified in the treatment of cancer.

Keywords: Ayurveda, Cancer, Medicinal plants, Treatment

INTRODUCTION

ancer is the second leading cause of death, after cardiovascular disease (WHO, 2007; Mathers & Loncar, 2006). Cancer is responsible for one in eight deaths worldwide-more than AIDS, tuberculosis, and malaria together (Sener et al., 2005). Globally, the number of cancer deaths is projected to increase from 7.1 million in 2002 to 11.5 million in 2030 (Mathers & Loncar, 2006). Cancer patients who already got crippled with this disease further burden by drug-induced toxic side effects. Chemotherapy is routinely used for cancer treatment. Cancer cells lose a lot of regulatory functions present in normal cells, they continue to divide but normal cells do not. Recently the discovery of active components from the plant and their biological function in disease control has led to active interest in the plants across the globe. Ayurveda therapy was found to be able to cure these chronic diseases better, which were previously not amenable to treatment by western medical practices. This traditional Ayurvedic Indian therapy with its evolution through centuries has always fascinated practitioners and researchers for its applications in cancer treatment on a scientifically proven research background. Herbal decoctions consists of many herbs each possessing tremendous potential for a cancer cure (Treadway, 1998).

Plants and products derived from them have been proved effective and safe in the treatment of various cancers. Many natural products and plant constituents have been identified as potent anticancer agents. Anticancer properties of various plants and phytochemicals are being identified by many researchers. Several plant-based anticancer agents including taxol, vinblastine, vincristine, camptothecin derivatives, topotecan, and irinotecan are in clinical use all over the world. Plants still have tremendous potential to provide newer drugs and act as reservoir of natural chemicals that may provide chemoprotective agents against cancer. Recently, Taneja and Qazi, have suggested a number of compounds from medicinal plants with potential anti-cancer activities (Murthy, 1987). This review will discuss some of the plants and their products that have recently been tested and may have potential in anticancer therapies.

Comman plants having anticancer properties Ashwagandha

Ashwagandha (Withaniasomnifera), is a widely used medicinal herb in Ayurveda. It is considered to be a *rasayana* herb, an adaptogen (which adapt themselves to the need of the organism), and is commonly referred to as 'Indian ginseng'. The leaf and root extracts of Ashwagandha reduce the growth of breast, central nervous system, colon, and lung cancer cells without affecting normal cells. Ashwagandha also appears to make tumor cells more sensitive to radiation or heat therapies (Devi,1996; Devi & Sharada, 1996). Anticancer effect of Ashwagandha is generally attributable to steroidal lactones collectively referred to as withanolides and among them withaferin A (WA) appears most active against cancer.

In a study it was found that, withanone obtained from leaf extracts of ashwagandha, act as tumor inhibitory factor, its components kill cancer cells by at least by five different pathways, including, GM-CFS, p53, apoptosis and death receptor signaling and G2-M

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DNA damage regulation pathway (Widodo et al., 2008) It has been found that naturally occurring withanone cause inactivation of the TPX2-Aurora A complex, which has an effective role during mitosis and cytokinesis and found to be up regulated in several cancer types (Grover et al., 2011), It prevents cancer proliferation by interrupting cell division and by inhibiting the development of new blood vessels. A research on animal model for lung cancer, showed that ashwagandha supported the chemotherapeutic activity of medicine paclitaxel and its antioxidant properties reduced the oxidative stress caused by tumors (Ahmed et al., 2013). During study on pancreatic cancer, researcher found that Withaferin, significantly stimulates cell death in a number of pancreatic cancer cell lines. It appears to target and limit the activity of a specific protein like (Hsp90) which helps other proteins in maturing, stimulating and promoting the growth and survival of cancer cells (Yu Yanke et al., 2011). The water extracts from ashwagandha leaves, containing Withaferin A, may offer a treatment option for another deadly cancer-Glioma, the most prevalent types of brain tumor (Shah et al., 2009; Kataria Hardeep et al., 2011). In another experiment tumor cells (Sarcoma 180) were transplanted into mice. Administration of Ashwagandha extracts to these mice at 400 mg/Kg produced complete regression of the tumor growth (Devi et al., 1992). The effect of Ashwagandha have been observed on in vitro human cancer cells or in vivo on animals, showed the potential use of ashwagandha as anticancer agent.

Aloe Vera

Aloe Vera has been used in Avurveda from ancient time. It is a popular houseplant in India and is often called the 'miracle plant' and the 'natural healer'. Aloe Vera (inner gel) contains the 8 essential amino acids that the human body needs but cannot manufacture, complex carbohydrates, enzymes, steroids, antibiotic agents and minerals. Research shows strong immunomodulatory and antitumor properties for Aloe Vera polysaccharides. It boosts immune system function while destroying cancer tumors. One study published in International Immunopharmacology (1995) showed that Aloe Vera polysaccharides exhibited potent macrophageactivating activities by producing increased volumes of nitric oxide (which has antitumor potential). Aloe constituents Emodin and Rhein also produced anticancer effects, which included the halting of tumour progression and cell death among cancer cells The polyphenols, glucans and alkaloids give Aloe its tremendous anti-inflammatory and antioxidant properties, along with its ability to stimulate healing.

In the books entitled "Cancer can be cured" (2000) and "Aloe in not medicine yet it cures" (2009), Father Romano Zago showed the world that curing cancer does not have to be expensive. His simple 3

ingredient formula when prepared correctly has been reported to cure many types of cancers (EJerome, 2011) It is known to reduce radiation induced damage. The majority of cancer patients who have steadily used an Aloe Vera gel throughout their radiotherapy treatment have experienced great relief as it helped to heal and sooth their skin that's why many specialist nurses and radiotherapists recommend its use, during and for a few weeks after radiotherapy treatment (Richardson et al., 2005; Surjushe et al., 2008). Researcher studied the effect of Aloe Vera crude extract (ACE) alone or in combination with cisplatin in human breast (MCF-7) and cervical (HeLa) cancer cells and found that Aloe Vera may be an effective anti-neoplastic agent to inhibit cancer cell growth.It increases the therapeutic efficacy of conventional drugs like cispolatin (Hussain et al., 2015).

Papaya

Carica papaya is a fast growing, soft woody, herbaceous plant reaching 3-10 m in height. In some places it is known by the name pawpaw. Its leaves have been used in traditional medicines for treatment of various types of diseases like malaria, dengue fever, asthma, beriberi and cancer (Rahman et al., 2011; Ahmad et al., 2011). Researchers have found that papaya leaf extract and its tea have dramatic cancer-fighting properties against a broad range of tumour's including cervix, breast, liver, lung, and pancreatic (Fauziya et al., 2013). Papaya Leaves have a milky sap that's great for preventing and killing cancer cells because it contains acetogenin, that supports the body's normal cells during the time of cellular stress. University of Florida, United States researcher Nam Dang and colleagues in Japan, in a report published in the Journal of reported Ethnopharmacology, the papaya's anticancer effect against tumours of the cervix, breast, liver, lung and pancreas. Dang and the other scientists showed that the leaf extracts of papaya boosts the production of key signaling molecules called Th1-type cytokines, which helps in regulating the immune system. This could lead to therapeutic treatments that use the immune system to fight cancers (Otsuki et al., 2010).

Dried papaya leaf powder contain papain enzyme, which have powerful digestive action . Researchers while doing their research on action of different enzymes in treatment of cancer , found that papain will work more aggressively than the pancreatic enzymes in attacking and destroying cancer cells (Indran *et al.*, 2008). The dried leaves of papaya have been boiled for preparing tea for cancer patients. Papain enzyme was found to be effective at 150-160 degree F. The seeds of Papaya contains agents that stop the growth of cancer cells and tumors. Papaya Seeds contain isothiocyanate which works well for colon, breast, lung, leukemia and prostate cancer (Nguyen *et al.*, 2013).

Giloy

Tinosporacordifolia, also known as guduchi in Sanskrit, giloya in Hindi and heartleaf moonseed plant in English, it is a climbing deciduous shrub. The most commonly used part of the shrub is the stem and its roots are also comprise important alkaloids. This shrub is commonly found in India, Myanmar, Sri Lanka and China. A variety of active components like alkaloids, diterpenoid lactones, aliphatics, glycosides, steroids like tinosporine, tinosporide, tinosporaside, cordifolide, cordifol, clerodanefuranoditerpene, heptacosanol. diterpenoidfuranolactonetinosporidine, columbin and β-sitosterol. have been isolated from the different parts of the plant body, including root, stem, and whole plant. The plant may also contain phytoandrogen, which means it can protect against DNA damage induced by the environment and radiation therapy.

T. cordifolia efficaciously kills HeLa cells in vitro, suggesting its potential as an anticancer agent. In a study on HeLa cells, a dose-dependent increase in HeLa cell death was observed when treated with T. cordifolia extract as compared to the control cells (Jagetia, 1998). Enhancement in nitric oxide (NO) production by stimulation of splenocytes and macrophages indicative of anti-tumor effects (Upadhyaya et al., 2011). In another study it has been shown to block the G1 phase in EAC mice and cause apoptosis by the formation of apoptotic bodies, nuclear condensation, by activating caspase-3, increased expression of pro-apoptotic gene, Bax, and decreased expression of anti-apoptotic gene, Bcl-2 (Thippeswamy et al., 2007). Its extracts are capable in reduction of papilloma's, tumour yield, tumour burden, and tumor weight by increasing phase II detoxifying enzymes in skin carcinoma animal models (Chaudhary et al., 2008). In another report by Singh et al, who investigated the effect of in vivo application of alcoholic extract of T. cordifolia ,on the proliferation of cancerous cells and myeloid differentiation of bone marrow hematopoietic precursor cells on a mice bearing a transplantable T cell lymphoma of spontaneous origin called as Dalton's lymphoma (DL). Their study indicates that the T. cordifolia can influence the myeloid differentiation of bone marrow progenitor cells and the recruitment of macrophages in response to tumor growth in situ. Dichloromethane extracts of TC shows cytotoxic effects owing to lipid peroxidation and release of LDH and decline in GST (Verma et al., 2011). Methanolic extract of TC that were cytotoxic to human breast cancer cells failed to induce apoptosis in Vitro cell (Rumana Ahmad et al., 2015).

Tulsi

'Tulsi' is considered to be the most sacred herb of India.It is called as "TheMother medicine of nature" in Ayurveda. It improves energy levels, decreases

stress and also acts as an immune-booster. Its active constituent eugenol is responsible for its anticancer potential which inhibits the multiplication, migration and invasion of cancer cells and will also induce apoptosis (programmed cell death of tumors). Moreover, holy basil has a host of cancer-fighting phytochemicals such as, apigenin, rosmarinic acid, myretenal, beta-sitosterol ,carnosic acid and luteolin, These phytochemicals in tulsi increase antioxidant activity, alter healthy gene expressions, induce cancer cell death, prevent blood vessel growth contributing to cell growth and stop metastasis, which is the spread of cancer from one organ to another. (Baliga MS et al., 2013; Shimizu T et al., 2013)According to a recent 2013 research published in Nutrition and Cancer. It was shown that flavonoid compounds present in water extracts of holy basil like, orintin and vicenin protected mice against radiation-induced tumour (Uma Devi P, 2001). According to Karthikeyan et al., 1999 Holy basil (Ocimum sanctum) may have the ability to prevent the early events of carcinogenesis. Studies also indicate that holy basil can repair cells damaged by oxidation and radiation, demonstrating the potential to destroy precancerous lesions and tumours. Leaves and flowering tops are used for extracting essential oil. Oil of O. sanctum has revealed the presence of five fatty acids (stearic, palmitic, oleic, linoleic and linolenic acids). It is a good source of beta carotene, calcium and vitamin C and it also contains volatile substances including estragol, linalool, eugenol, methyl chavicol, methyl cinnamate, cineole, and some other terpenes, tannins, urolic acid etc The leaves contain an essential oil, which contains eugenol, eugenal, carvacrol, methylchavicol, limatrol and caryophylline. The oil extracted from its seeds contained fatty acids and sitosterol. The roots contain sitosterol and three triterpenes Urosolic acid and oleanlic acid possess anticancer property (Zhang et al., 2004; Bhavana J. et al., 2016; Prakash P & Gupta. N, 2005)

Tulsi protects against toxic chemical-induced injury by increasing the body's levels of antioxidant molecules, such as glutahione, and enhancing the activity of antioxidant enzymes. These enzymes organelles and protect cellular membranes by fighting free radical damage caused by a lack of oxygen and other toxic agents (Banerjee et al., 1996). Kim et al., 2010 found that ethanolic extract of O. sanctum can be a potent anti-metastatic candidate which inactivate matrix metalloproteinase-9 (MMP-9) and enhance antioxidant enzymes. Magesh et al., 2009 demonstrated thatethanolic extract of O. sanctum induces apoptosis in A549 cells via a mitochondrial caspase-dependent pathway and inhibits the in vivo growth of Lewis lung carcinoma animal model. Tae-kyungKwak et al., 2014 also favour anti-metastatic mechanism of EEOS mediates inhibition of PI3K/Akt in Osteopontin (OPN) treated NCI-H460 non-small cell lung cancer cells.

Turmeric

Turmeric has been used for centuries in Ayurvedic and Chinese medicines to treat inflammation and cure infections.Turmeric contains a class of compounds known as the curcuminoids, comprised of curcumin, demethoxycurcumin and bisdemethoxycurcumin (Jurenka JS, 2009). Curcumin is the principal curcuminoid and comprises approximately 2-5% of turmeric; it is responsible for the yellow color of the spice as well as the majority of turmeric's therapeutic effects (Chattopadhyay et al., 2004). Aside from being employed as a flavoring and coloring agent in food, turmeric has also been widely used in Ayurvedic medicine for its anti-oxidant, antiseptic, analgesic, anti-inflammatory antimalarial and properties (Aggarwal et al., 2007). Studies have shown that curcumin helps prevent several forms of cancer including oral, breast, lung, stomach, liver, and colon because of its anti-inflammatory and antioxidant properties (Coleman et al., 2015; Nahar et al., 2014; Elattar & Virji, 2000). Epidemiological studies attribute the low incidence of colon cancer in India due to the chemopreventive and antioxidant properties of diets rich in curcumin (Mohandas KM & Desai DC, 1999). Curcumin has been shown to suppress the expression of cyclin D1 in many types of cancer including head and neck, colon, bladder, cervical, breast, and pancreatic. And this attributes the effect of curcumin's in inhibition of NF-KB activation and subsequent suppression of downstream gene products (Liu Q et al., 2009).

Cucurmin stops the development of cancer by interfering with the cellular signalling pathways. It has the ability to block cancer cells at every stage of cancer development, from cell mutation, to tumour growth, and up to metastasis. In another study it was found effective inhibitor of cancer cells by triggering apoptosis (programmed cell death) without affecting normal cells (O'Sullivan-Coyne et al., 2009; Aoki H et al., 2007). Ludwig Maximilians University in Munich, Germany in 2012 wshowed that curcumin can inhibit the formation of metastases in prostate and breast cancer. Both cancers spread throughout the body by releasing some chemical messengers like, pro-inflammatory cytokines CXCL1 and CXCL2, and curcumin alters the expression of these two damaging proteins.

Neem

Neem (*Azadirachta indica*) is a member of the Meliaceae family. It has been widely used in Chinese, Ayurvedic, and Unani medicines worldwide in the treatment and prevention of various diseases. Earlier finding confirmed that neem and its constituents play a vital role in the scavenging of free radical generation and prevention of disease pathogenesis (Amritpal Singh *et al.*, 2008). The active constituent of neem is azadirachtin and the others constituents like nimbin, nimbidol, sodium nimbinate,

nimbolinin, gedunin, and quercetin are also effective against many diseases (Zong A et al., 2012). The various components extracted from neem plant were used in traditional medicine for the cure of many diseases including cancer for centuries. The extracts obtained from its seeds, leaves, flowers, and fruits, have consistently act as chemopreventive agents and show antitumor effects in different types of cancer. . Neem ingredient shows impressive role in the management of cancer by regulating cell cycle and cell signaling pathways (Wu Chia-Mao et al., 2009). Neem extracts modify the activity of various tumour suppressor genes (e.g., p53, pTEN), angiogenesis (VEGF), transcription factors (e.g., NF-kB), and apoptosis (e.g., bcl2, bax) (Elumalai P. et al., 2012; Raja Singh et al., 2014) Another study was carried out to examine the effects of nimbolide neem constituent on apoptosis and insulin-like growth factor (IGF) signaling molecules on androgenindependent prostate cancer (PC-3) cells lines.The results of the study suggested that nimbolide acts as a potent anticancer agent by i inhibiting cell proliferation and inducing apoptotic pathway via PI3K/Akt pathway in PC-3 cells (Gunadharini et al., 2011).

Azadirachtin and nimbolide bioactive components of neem have been studied extensively. The key anticancer effects of these components on malignant cells include inhibition of cell proliferation and induction of cell death The studies based on animal model established that neems chief constituents play pivotal role in anticancer management by modulating various molecular pathways including p53, pTEN, NF-*k*B, PI3K/Akt, Bcl-2, and VEGF as mentioned above also. It is considered as safe medicinal plants which modulates the number of metabolic processes without any adverse effect on normal cells. Neem also plays role as anti-inflammatory via regulation of proinflammatory enzyme activities of cyclooxygenase (COX), and lipoxygenase (LOX) enzyme (Hossain et al., 2013).

Sheesham

Dalbergia sissoo is known as Indian rosewood which is a deciduous forest tree. It is natively found in Indian subcontinent. It is called as Sheesham in comman language and is best known as premier timber tree. A number of phytochemicals like tannins, steroids, terpenoids, saponins, flavonoids and alkaloids including isoflavonoids, neoflavonoids, O-Prenylated flavonoids were extracted from it and found effective against different types of tumours. Glycosides. phenols, quinones, furans. oligosaccharides, trisaccharides and some other compounds have also been isolated from various parts of the D. Sissoo (Chihiro Ito, 2003; Rana V et al., 2009). In addition to uses in day today life D. sissoo plant consists of a large number of reputed medicinal properties (Shah et al., 2010). The extract of D. sissoo leaves contains a large amount of flavanoids. D. sissoo leaves extract can be used with poise to treat colorectal cancer alongwith other usual treatments with chemotherapeutic agents (Shaltout *et al.*, 2011; Ghogare Pradip *et al.*, 2014).

Palash

Palash (Buteamonosperma) from family Fabaceae popularly known as 'flame of the forest'. It has been widely used in the traditional Indian Ayurvedic medical system . Its various parts like leaves, stem bark, fruits, seeds, flowers and their extracts contain bioactive compounds such as triterpene, butein, butin, isobutrin, coreopsin, tannins, chalcones, glucosides, gallic acid, linoleic acid, palmitic and lignoceric acid were used against various disorders like diabetes, cancer and helminthic infections (Choedon T *et al.*, 2010; Sehrawat *et al.*, 2012; Mishra MK, 2016).

Aqueous extract of Buteamonosperma inhibit cell proliferation and arrest cells in G1 phase. This was accompanied by a marked reduction in the levels of activated Erk1/2 and SAPK/JNK which induces apoptotic cell death. In MCF-7 cancer cells, 1µM of butein is able to reduce mRNA levels of COX2 at baseline (associated with reduced ERK1/2 and PKC phosphorylation) (Lau GT et al., 2010). Intraperitonial application of the aqueous extract from flowers of Butea monosperma tested on X-15myc onco mice, this study showed antitumorgenic activity, these results suggest that the extracts may have potential chemopreventive efficacy (Rasheed Z et al., 2010). J.Banu Rekha et.al., in 2011 reported the antitumor activity of the ethanol extract of leaves of Butea monosperma (L) Taub in Ehrlich ascites carcinoma (EAC) cells bearing mice.

Hemp

The Hemp (Cannabis sativus) is an annual herb that may reach 5 meters in height and its leaves form a

Table 1. List of Plants Having Anti-Cancer Properties

fan-like structure with jagged edges. It belongs to family Cannabinaceae. This plant can be used as fibre, in medicine, as a narcotic and now a day it is used to relieve cancer pain and treat depression. It is popularly known as medical marijuana. Chemical constituents of Cannabis are many hydrocarbons, sugars, terpenes, steroids ,flavonoids, nitrogenous compounds and amino acids among these cannabinoids such as tetrahydrocannabinol (THC) and cannabidiol (CBD), are mostly used in medical therapy to treat disease or alleviate symptoms, and delta-9-tetrahydrocannabinol (known as THC) is the primary psychoactive ingredient. Indian hemp is known as Cannabis indica, tends to have a higher concentration of CBD than Cannabis sativa. Cannabinoids activate canabinoid receptors in human body. The human body also produces endocannabinoids which plays an important role in creating healthy environment within body cells Cannabidiol is thought to have significant painrelieving and anti-inflammatory activity without the psychoactive effect of delta-9-THC (Tariq A.L. and A. L. Reyaz, 2012a). Cannabis oil is considered as a cancer preventer because it decreases the size of tumours and alleviate nausea, pain, lack of appetite and weakness. However, the U.S. Food and Drug Administration has not approved cannabis as a treatment for cancer but research shows that it has some anticancer properties. Both dronabinol and nabilone prepared from phytochemicals obtained from cannabis are approved for prevention and treatment of chemotherapy-induced Nausea/ Vomiting in cancer patients. In another study researchers found that cannabinoids inhibit cancer cell invasion via increasing tissue inhibitor of matrix metalloproteinases-1 (TIMP-1) in lung cancer cell lines (Ramer R et al., 2012).

S	Common Name	Botanical Name	Family	Part Used	Tumor Inhibitory
No.		Dotanical Manie	T anni y	I alt Oscu	Factor
1	Ashwagandha	Withania somnifera	Solanaceae	Leaves	Withafarin-A
2	Aloe vera	Aloe barbadensis	Asphodelaceae	Leaves	Emodin,
					Cispolatin
3	Papaya	Carica papaya	Caricaceae	Whole	Papain,
				Plant	Acetogening
4	Giloy	Tinospora cardifolia	Menispermaceae	Whole	Cordifolide,
				Plant	Tinosporide
5	Tulsi	Ocimum sanctum	Lamiaceae	Leaves	Euginol, Epigenin
6	Turmeric	Curcuma longa	Zingiberaceae	Rhizome	Cucurmin
7	Neem	Azadirachta indica	Meliaceae	Bark, Leaf,	Nimbidol,
				Seeds	Quercetin
8	Sheesham	Dalbergia sissoo	Fabaceae	Bark,	Terpenoids,
				Leaves	Flavanoids
9	Palash	Butea monosperma	Fabaceae	Bark, Leaf,	Butein
				Fruits	
10	Bhang	Cannabis sativa	Cannabaceae	Leaves	Cannabinoids

CONCLUSION

Nowadays many people are learning and doing research on ancient medicinal systems like Unani, Ayurveda and Chinese for treating various diseases. Among them the use of medicines obtained from the herbal source is found to be most effective (The Ayurveda). Ayurveda means 'the science of life'. It focuses on balancing all aspects of a human's mind, body and spirit. According to Ayurveda unbalanced Doshas (or homeostasis) affects gene expression, leading to disease like Cancer. When Dosha is in balance, Cancer doesn't occur. Due to adverse effects of chemotherapy and radiotherapy treatments and the huge cost associated with them, the use of easily available and cost effective Ayurvedic herbs that deal with all type of cancer is an effective way of treating cancer.

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