

ANTI-CANCER ACTIVITY OF COMMON HERBS IN AYURVEDIC PERSPECTIVE

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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. 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. This paper deals with the selective medicinal plants having anticancer properties, which could be further designed to produce cancer curing Ayurvedic herbs that can deal with cancer stages at all levels in a very effective manner.

Keywords: Cancer, medicinal plants, antioxidants, anticancer agents, natural sources.

INTRODUCTION

Natural products, especially plants have been used in the treatment of various diseases for thousands of years. Ayurveda, a traditional Indian practice using plant drugs is successful from very early times in using these natural

drugs and preventing or suppressing various tumours with different line of treatment.¹ Cancer is a major public health burden in both developed and developing countries. One of the leading causes of death and globally the num-

bers of cases of cancer are increasing gradually. It is an abnormal growth of cells in body that can lead to death. Cancer cells usually invade and destroy normal cells. Plants, since ancient time, are in use 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. 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. This paper deals with the selective medicinal plants having anticancer properties which could be further designed to produce cancer curing drugs.

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.

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.

Ayurvedic Concept of Cancer:-

Charaka and Sushruta Samhita both described the equivalent of cancer as "*granthi*" and "*arbuda*". "*Granthi*" and "*Arbuda*" can be inflammatory or devoid of inflammation, based on the doshas involved. Three doshas "*Vata, Pitta and Kapha*" in body are responsible for disease and the balanced coordination of these doshas in body, mind and consciousness is the Ayurvedic definition of health. *Tridoshic arbudas* are usually malignant because all three major body humors lose mutual coordination, resulting in a morbid condition. Neoplasm can be classified in Ayurveda depends upon various clinical symptoms in relation to *tridoshas*.

Group I: Diseases that can be named as clear malignancies, including *arbuda* and *granthi*, such as *mamsarbuda* (sarcomas) and *raktarbuda* (leukaemia), *mukharbuda* (oral cancer), and *asadhya vrana* (incurable or malignant ulcers).

Group II: Diseases that are not cancers but can be considered probable malignancies, such as ulcers and growths. Examples of these are *mamsaja oshtharoga* (growth of lips), *asadhya galganda* (incurable thyroid tumour), *tridosaja gulmas*, and *asadhya udara roga*, (abdominal tumours like carcinomas of the stomach and liver or lymphomas).

Group III: Diseases in which there is a possibility of malignancy, such as *visarpa*, *asadhya kamala* (incurable jaundice), *asadhya pradara*.

Plants, since ancient time, are using for health benefits by all cultures as well as source of medicines. It has been estimated that about 80-85% 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 a

good source of polyphenols, flavones, tannins and other bioactive substances.² It is a source of hepatoprotective, antioxidant, immune stimulator and antitumor agent. Pyrogallol an active compound of *E. officinalis* has anti-inflammatory 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 mutagenicity, in mice treated with cyclophosphamide.³

***Moringa oleifera*:-**

Moringa oleifera belongs to the monogeneric family, *Moringaceae*. This rapidly growing tree is also known as horse radish tree or drumstick tree, is native to the sub-Himalayan region tract of India, Pakistan, Bangladesh and Afghanistan. All Parts of *Moringa* tree are edible and have long been consumed by humans. The leaves were used in folk remedies for tumors. *Moringa oleifera* contains a unique combination of isothiocyanate and glucosinolates. Isothiocyanates have antitumor activity in cancers of the lung, breast, skin, esophagus, and pancreas. Studies have found that *Moringa* compounds, benzyl isothiocyanate (BITC) and phenethyl isothiocyanate (PEITC) induced apoptosis in ovarian cancer cells *in vitro*. Beta-sitosterol, glycerol-1-(9-octadecanoate), 3-O-(6'-O-oleoyl-beta-D-glucopyranosyl)-beta-sitosterol and beta-

stosterol-3-O-beta-D-glucopyranoside of *Moringa oleifera* have been identified as anticancer agents.⁴ Benzyl isothiocyanide and the related compound niazimicin were shown to be potent inhibitors of Phorbol ester (TPA)-induced Epstein-Barr-Virus early antigen activation in Lymphoblastoid (Burkitt's Lymphoma) cells. Nair et.al. found that aqueous extract of Moringa tree is cytotoxic against HeLa cell lines.⁵ One of the interesting facts of *Moringa oleifera* is that its root has unique estrogenic, antiestrogenic, progestational and antiprogestational activities. Higher dose of root bark extract of *Moringa* tree can cause toxic hypotensive and violent uterine contraction which can be fatal.⁶

***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.⁷ Ethanolic extract of *B. diffusa* showed cytotoxicity against HeLa cell line and inhibits the S-phase of the cell cycle. It also suppressed the growth of cancer cells in DMBA- induced

cancer carcinogenesis in mice by preventing the promotional events in the mouse skin through free radical scavenging mechanism.⁸ Two rotenoids isolated from *B. diffusa*, boeravinones G and H, have been found to potentially inhibit the drug efflux activity of breast cancer resistance protein (BCRP/ABCG2), a multidrug transporter responsible for cancer cell resistance to chemotherapy.⁹

***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. [6]-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, [6]-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 [6]-paradol and other structurally related derivatives like [10]-paradol, [3]-dehydroparadol, [6]-dehydroparadol and [10]-dehydroparadol, induced apoptosis in an oral squamous carcinoma cell line, in a dose dependent manner through a caspase-3-dependent mechanism.¹⁰ 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.¹¹ Results from pharmacological experiments indicate that ginger might inhibit the growth of tumors in humans.¹² 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.¹³ 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.¹⁴

Vitex negundo:-

Vitex negundo (Nirgundi in Hindi) which is a species of *Verbenaceae* family, is a large evergreen, climbing, much branched shrub and ascending up to an altitude 1100-1400 ft, is found almost throughout India. Although all parts of *V. negundo* are used as medicine in the indigenous system of medicine, the leaves are the most potent part for medicinal use. It is used for treatment of eye disease, toothache, inflammation, leucoderma, enlargement of the spleen, skin- ulcers, in catarhal fever, rheumatoid arthritis, gonorrhoea and bronchitis. They are also used as tonics, vermifuge, lactagogue, emmenagogue, antibacterial, antipyretic and antihistaminic agents. Ethanolic extract of *Vitex negundo* treatment was found to enhance nonviable counts in peritoneal exudates and decrease

the viable cell count.¹⁵ This extract is effective against the major problems, myelosuppression and anaemia, that are being encountered during chemotherapy and can bring back hemoglobin and RBC count to normal.

The antitumour activity of the ethanolic extract of leaves of *Vitex negundo* (EVN) has been evaluated against Dalton's ascitic lymphoma (DAL) in Swiss albino mice at the dose of 250 & 500 mg/kg, body weight. The experimental parameters used were tumour volume, tumour cell count, viable tumour cell count, mean survival time and increase in life span to assess antitumour activity. The extract administered orally for 14 consecutive days to tumor bearing group of animals. The extract increase the life span of DAL treated mice and restore the hematological parameters as compared with the DAL bearing mice in dose dependant manner. The study revealed that the EVN showed significant antitumour activity in tested animals. (Nandu Kaynde, Dr. R Patel et.al.2015).¹⁶

Withania somnifera:-

Withania somnifera (also known as ashwagandha), belongs to the family Solanaceae, is an important medicinal plant that is widely used as a home remedy for several diseases in the Indian subcontinent and other parts of the world. *W. somnifera* is a dietary supplement composed of various nutrients, polyphenols and alkaloids that have free radical scavenging capacity as well as other chemical constituents that possess anti-inflammatory, antitumor, anti-aging, anti-stress, antioxidant, immunomodulatory, and rejuvenating properties. Over 35 chemical constituents have

been identified from *Withania*. The biologically active chemical constituents are alkaloids- isopelletierine and anaferins, steroidal lactones- withanolides and withaferins, saponin containing an additional acyl group-sitoidoside VII and VIII and withanolides with a glucose at carbon 27- sitoindoside IX and X. *Withania somnifera* is also rich in iron.¹⁷ *W. somnifera* decreases NF-kB levels, suppresses intercellular tumor necrosis factor and potentiates apoptotic signaling in animal cancerous cell lines. In vitro and in vivo studies of *W. somnifera* has showed stimulatory effects on cytotoxic T lymphocyte generation has demonstrated the potential to reduce tumor growth.¹⁸ The chemo preventive effect of *W. somnifera* root extract was demonstrated in a study on induced skin cancer in Swiss albino mice. A study of an alcohol extract of dried *W. somnifera* roots and the active component withaferin A isolated from the extract showed significant antitumor and radio sensitizing effects in in-vivo experimental tumors and lacked any noticeable systemic toxicity. These isolated compounds of *W. somnifera* could provide a potential and relatively safe radio sensitizer or chemotherapeutic agent.¹⁹

***Curcuma longa*:-**

Native to the Indian subcontinent and South-east 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 re-

searched 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-kappaB activation pathway, the activation of nuclear factor-kappaB 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.^{20,21}

***Achyranthes aspera*:-**

Achyranthes aspera Linn.(Family- Amaranthaceae) is a commonly found herb as a weed on road sides throughout India. The methanol extract of *Achyranthes aspera*, its alkaloid, non-alkaloid and saponin fractions has been exhibited significant inhibitory ef-

fects on the Epstein-Barr virus early antigen activation induced by the carcinogen 12-O-tetradecanoylphorbol-13-acetate in Raji cells (at a concentration of 100µg). In in-vitro study the non-alkaloid fraction containing mainly nonpolar compounds showed the most significant inhibitory activity. In in- vivo two-stage mouse skin carcinogenesis test the total methanol extract possessed a pronounced cytotoxic activity.²²

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, nontumorigenic cell line derived from baby hamster kidney cells and a tumorigenic 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 be beneficial providing some kind of protection from cancer²².

Azadirachta indica²³:-

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.

Table 1: Important drugs mentioned with anticancerous activity and their indications-

S.No.	Drug Name	Arbuda related conditions	Rakta Vikaras	Kapha hara & Medo hara	Rasayana
1.	<i>Gunja</i>	-	+	-	-
2.	<i>Sirisha</i>	<i>Vrana</i>	+	+	+
3.	<i>Lasuna</i>	-	+	+	+
4.	<i>Kumari</i>	<i>Granthi</i>	+	+	-
5.	<i>Saptrparni</i>	<i>Vrana</i>	+	+	-
6.	<i>Rohitaka</i>	-	+	-	-
7.	<i>Iswari</i>	<i>Vrana</i>	+	-	-
8.	<i>Shatavari</i>	-	+	-	+
9.	<i>Brahmi</i>	-	+	-	+
10.	<i>Danti</i>	-	+	+	-
11.	<i>Kanchanara</i>	<i>Gandamala</i>	+	+	-
12.	<i>Daruharidra</i>	<i>Vrana</i>	+	+	-
13.	<i>Paashanabhedi</i>	<i>Gulma, Vrana</i>	-	-	-
14.	<i>Shallaki</i>	<i>Vrana</i>	+	+	-
15.	<i>Arka</i>	<i>Vrana</i>	+	++	-
16.	<i>Devadaru</i>	<i>Vrana</i>	-	+	-
17.	<i>Mandukaparni</i>	<i>Vrana</i>	+	-	+
18.	<i>Haridra</i>	<i>Vrana</i>	+	+	-
19.	<i>Dhattura</i>	<i>Vrana</i>	+	+	-
20.	<i>Dugdika</i>	-	+	+	-
21.	<i>Kutaja</i>	-	+	+	-
22.	<i>Kampillaka</i>	<i>Gulma, Vrana</i>	+	+	-
23.	<i>Nimba</i>	-	+	-	-
24.	<i>Shigru</i>	<i>Vrana, Gulma, Apachi, Ganda</i>	+	++	-
25.	<i>Karaveer</i>	<i>Vrana</i>	+	+	-
26.	<i>Tulasi</i>	-	+	+	-
27.	<i>Bhumyamalaki</i>	-	+	+	-
28.	<i>Katuki</i>	-	+	-	-
29.	<i>Chitraka</i>	-	+	+	-
30.	<i>Manjishtha</i>	<i>Ganda, Vrana</i>	+	+	-
31.	<i>Ashoka</i>	<i>Apachi</i>	+	-	-
32.	<i>Bhallataka</i>	<i>Vrana</i>	+	+	+
33.	<i>Aswagandha</i>	-	+	+	+
34.	<i>Talisapatri</i>	<i>Gulma</i>	-	+	-
35.	<i>Sahadevi</i>	-	+	-	-

Note: + indicates Kapha hara & ++ indicates Kapha-Medo hara.

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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