



Review Article

IMPORTANT HERBS IN TREATMENT OF CANCER

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ABSTRACT

Cancer is a major public health burden in both developed and developing countries. Plant derived agents are being used for the treatment of cancer. Reservoir of bioactive compounds exists in many species of plants of Earth, only a small percentage of which have been examined and continued to be an important source of anticancer agents. Worldwide efforts are ongoing to identify new anticancer compounds from plants. With the current decline in the number of new molecular entities from the pharmaceutical industry, novel anticancer agents are being sought from traditional medicines. In recent years owing to the fear of side effects people prefer more and more use of natural plant products for cancer. This article reveals a detailed review of important herbs in cancer from Indian medicinal plants which will be useful to treat various types of cancer. It will be helpful to explore the medicinal value of the plants and for the new drug discovery from them for the researchers and scientists around the globe.

Keywords: Cancer, Medicinal plants, anticancer agents, bioactive compounds.

INTRODUCTION

CANCER is the abnormal growth of cells in our bodies that can lead to death. Cancer cells usually invade and destroy normal cells. These cells are born due to imbalance in the body and by correcting this imbalance, the cancer may be treated. Billions of dollars have been spent on cancer research and yet we do not understand exactly what cancer is⁸. Cell growth and cell multiply process is known as cell division. It must be extremely controlled that all the cells in the body should grow at the right place, and for all the organs and tissues to function properly. When the cells divide too quickly, consequences can be disastrous. When a cell divides, it first makes an exact copy of its DNA via a process called DNA replication, before splitting into half, to form two

'daughter' cells, that are genetically identical. Hundreds of proteins involve in Cell division. Some proteins inform the cell when or when not to divide. Others were responsible for making sure that the DNA is copied accurately. Yet more were involved physically by pulling the duplicated chromosomes apart as the cell to split into two. Uncontrolled cell division may have many causes, to form any type of cell. But usually results from defects or damage from one or more of the genes involved in cell division. When those genes were damaged (mutated) on some way, for instance on exposure to cigarette smoke or ultraviolet radiation, the cell may start dividing uncontrollably. Those defective cells might multiply to form a lump of abnormal tissue called a tumour.

Cancer – a worldwide snapshot

Cancer is a major public health problem, with significant associated death and disability. It is the second leading cause of death in developed countries and is one of the three leading causes of death for adults in developing countries. There are over 200 different types of cancer but four cancers: lung cancer, breast cancer, prostate cancer and large bowel cancer account for more than half of all cases.^[6] Of the 12.4 million new cancer cases in 2008, the most common cancers in terms of incidence were lung (1.52 million), breast (1.29 million) and colorectal (1.15 million).^[5]

The types of cancer vary around the world and there is significant variation in the risk of different cancers by geographic area. Most of this global variation is due to exposure to known or suspected risk factors related to lifestyle or environment and provides a clear challenge to prevention. In developed countries, almost as many cancer cases are attributable to an unhealthy diet and inactive lifestyle as to smoking. Although a third of all cancer deaths are linked to cigarette smoking, obesity is associated with colon, breast, uterine, oesophageal and kidney cancer.

- One out of every two men and one out of every three women will have some type of cancer at some point during their lifetime.^[2]
- Cancer is one of the leading causes of death in the world and represents a tremendous burden on patients, families and societies.^[3]
 - In 2008 there were 12.4 million new cases of cancer diagnosed and 7.6 million deaths from the disease.^[4]
 - Based on projections, cancer deaths will continue to rise. By the year 2030 the burden is set to more than double: there will be 26.4 million cancer cases, 17 million deaths and 75 million people living with the disease.^[4]
 - More than half of cancer cases and 60% of deaths from cancer occur in less developed countries.^[5]
 - The lifetime risk of developing cancer is now more than one in three and by 2015 this is expected to rise to one in two.^[6]

Causes of cancer

Importantly, 40% of all cancer cases can be prevented by not smoking, eating a healthy diet and by taking physical exercise. Tobacco use is the single largest preventable cause

of cancer and results in many different cancer types, including lung, throat, mouth, pancreatic, bladder, stomach, liver and kidney. Environmental tobacco smoke, or passive smoking, can also cause lung cancer. In developed countries, almost as many cancer cases are attributable to an unhealthy diet and inactive lifestyle as to smoking. Obesity is associated with colon, breast, uterine, oesophageal and kidney cancers. Some cancers are caused by biological carcinogens such as infections by viruses (hepatitis B/C and liver cancer and human papillomavirus [HPV] and cervical cancer) and bacteria (*Helicobacter pylori* and gastric cancer) and parasites (schistosomiasis and bladder cancer). In addition, excessive alcohol consumption is associated with several cancer types, including head and neck, oesophageal, throat, liver and breast cancer. Mortality and morbidity it is estimated that in 2008 there were 7.6 million deaths from cancer.^[4] In 2008, lung cancer was the most common cause of death (1.31 million deaths), followed by stomach (780 000 deaths) and liver cancer (699 000 deaths).^[5]

The table overleaf provides a breakdown of worldwide mortality rates for the top five cancer types^[7] as shown in

Table :1

Table: 1

Cancer Type	Annual Mortality
Lung	1.3 million
Stomach	803 000
Colorectal	639 000
Liver	610 000
Breast	519 000

Among all the cancer, Lung cancer is the most common worldwide and accounts for major death annually. The following Table 2 shows the global scenario for various types of cancer.

Table -2: Global Scenario on Types of Cancer.

S.No	Type of Cancer	No. of Patients affected /year
1.	Colorectal	940000
2.	Stomach	870000
3.	Liver	560000

4.	Cervical	470000
5.	Esophageal	410000
6.	Head and Neck	390000
7.	Urinary Bladder	330000
8.	Malignant Non-Hodgkin lymphomas	290000
9.	Leukemia	250000
10.	Prostate and Testicular	250000
11.	Pancreatic	216000
12.	Ovarian	190000
13.	Kidney	190000
14.	Endometrial	188000
15.	Nervous system	175000
16.	Melanoma	133000
17.	Thyroid	123000
18.	Pharynx	65000
19.	Hodgkin disease	62000
20.	Lung	1.2 million
21.	Breast	Over 1 million

But cells contain many different proteins whose job is to repair the damaged DNA. Thanks to those, scientists think that the vast majority of DNA damage is repaired immediately, with no ill effects. But if the DNA damage occurs to a gene that makes a DNA repair protein, a cell's ability to repair itself will be reduced, and that can allow errors to accumulate in other genes over time. Causes of cancer as follows.

- 1) Viruses such as *Epstein-Barr-Virus* (EBV), *Hepatitis-B-Virus* (HBV), *Human Papilloma Virus* (HPV).
- 2) Environmental and occupational exposure such as ionizing, UV radiation, exposure to chemicals including vinyl chloride, benzene and asbestos.
- 3) Life style factors such as high-fat, low fibres diets, tobacco, ethanol etc.
- 4) Medication such as alkylating agents and immunosuppressant's.
- 5) Genetic factors such as inherited mutations, cancer causing genes, defective tumor suppressor genes.

Free radicals and cancer

A free radical is nothing more than a molecular structure which contains an unpaired electron. Electrons tend to stay in pairs. Electron pairs make up the chemical bonds which keep molecules from flying apart. An unpaired electron, driven by a potent chemical force which compels it to find a mate. Thus molecular instinct that merges with another electron was so powerful that the searching molecule behaves erratically, moving about much like a weapon within cellular structures. Its random and wild molecular movements within cellular material can create cellular damage, which can eventually result in degeneration or mutation.

A free radical can destroy a protein, an enzyme or even a complete cell. To make matters worse, free radicals can multiply through a chain reaction mechanism resulting in the release of thousands of the cellular oxidants. When it happens, cells can become so badly damaged that DNA codes can be altered and immunity can be compromised. Contact with a free radical or oxidant on the scale can create cellular deterioration, resulting in diseases like cancer. Tissue breakdown from the oxidative stress can also occur, which contributes to aging, arthritis and a whole host of other degenerative conditions. Our constant bombardment with

Cancer-causing genes

There are four main types of gene involved in cell division. Most tumours have faulty copies of more than one of the genes viz., **Oncogenes** - Ontogenesis were the genes, under normal circumstances, that play a role tell the cells to start dividing. When oncogenes are activated, they speed up a cell's growth rate. When one of them becomes damaged, causing cancer, it is like the accelerator is becoming stuck down - the cell, and all its daughter cells, are permanently instructed to divide. **Tumour suppressor genes**- This gene was co-discovered in 1979 by the scientist Professor Sir David Lane Cancer Research UK. These genes make proteins whose normal function is the opposite to that of ontogenesis.

One of the most important tumour suppressor genes is called **Suicide genes** - Apoptosis or cell suicide, which was a highly complex and hugely important process. Cells usually have the ability to commit suicide whenever something goes wrong, to prevent damage to their neighbours. There are many different genes involved. If the 'suicide genes' become damaged, then a faulty cell can keep dividing and become cancerous. **DNA-repair genes** -The DNA in every cell in the body is under constant assault from a variety of directions.

free radicals had been likened to being irradiated at low levels all the time.

Unfortunately, because of the damage free radicals cause within our cellular structures, the sad fact was that many of us will die prematurely from one of a wide variety of degenerative diseases. Free radical damage has been associated with over 60 known diseases and disorders. An important fact to remember that the act of breathing oxygen activates those reactive chemical structures known as free radicals. To make matters worse, as because in our generation more than any other had been exposed to a number of potentially harmful environmental substances, free radical formation can reach what has been referred to as epidemic proportions. Some of the more dangerous free radical producing substances includes: cigarette smoke, herbicides , high fats, pesticides, smog car exhaust , certain prescription drugs, diagnostic and therapeutic x-rays , ultra-violet light , gamma radiation , rancid foods, certain fats , alcohol some of our food and water supplies , stress, poor diets etc. Even exercising, as beneficial as it is, can initiate the release of free radicals within our cellular systems. Aerobic exercising produces damaging oxidation by-products. Many of these are not completely neutralized by internal safety mechanisms and an over load can occur. Supplementing the diet with effective antioxidant compounds etc. Numerous research studies support the fact that many cancers, in particular breast cancer- diet related. Moreover, the risks of certain kinds of cancer could be significantly reduced with dietary changes. While most of us are aware of the wonders of a low-fat diet, a tremendous amount of data conceding other cancer preventative nutrients never reaches the average consumer. For instance, recent studies suggested that just reducing dietary fat may not be enough to prevent certain cancers. Perhaps more and more research suggested that, lack of certain protective nutrients appeared to originate from dietary sources that increase risk of cancer and other degenerative diseases. The role of certain bioflavonoid compounds were the exceptional free radical scavengers that just begin to emerge, and the protective potential of those flavonoids was impressive, to say the least.

Plant phytochemicals on cancer

Plant materials was been used for the treatment of malignant diseases for centuries. Recent phytochemical examination of plants which have a suitable history of use in folklore for the treatment of cancer had induced often resulted in the isolation of principles with antitumour activity. An intensive survey of plants, micro organism and marine animals for antitumour activity began in the later 1950s mainly because the United States National Cancer Institute (NCI) instigated and fund a major screening programme. Random selection screening programme was adopted, since novel compounds may be found anywhere from plant or animal kingdom. Soybean phytochemicals such as genistein (4',5,7-trihydroxy isoflavone) inhibit the growth of transplantable human prostate carcinoma. Epidemiological studies have consistently shown that regular consumption of fruits and vegetables strongly associated with reduced risk of developing chronic diseases such as cancer as the phytochemical extracts from it exhibit strong antioxidant activity.^[9] Andrographolide the potential cancer therapeutic agent isolated from *Andrographis paniculata* .^[10]

In the screening of Yemeni plants used in folk medicine for the anticancer potential, the methanolic extracts of *Dendrosicyos socotranus*, *Withania aduensis*, *Withania riebeckii*, *Dracena cinnabari* and *Buxus hildebrandii* exhibited the highest toxicity on all tumor cell lines.^[11] The four varieties of muscadine grape extract had the ability to inhibit the activity of matrix metalloproteinase's implying that those could be good inhibitors of carcinogenesis.^[12] The limonoids isolated from the methanol extract of *Khaya senegalensis* proved good anticancer activity.^[13] The leaf extract of Ashwagandha selectively killed tumor cells and thus it was a natural source for safe anticancer medicine.^[14] The fruit of deerberry (*Vaccinium stamineum*) exhibited the anticancer capability of human lung and leukemia cancer cells.^[15] Polyphenolic extracts from *Vaccinium macrocarpon* inhibited the growth and proliferation of breast, colon, prostate, lung, and other tumors as do flavonols, proanthocyanidin, oligomers, and triterpenoids isolated from the fruits of the same.^[16] *Morinda citrifolia* showed of cancer preventive

effective on both clinical practice and laboratory animal models.^[17]

An alcoholic extract of *Biorhythms sensitivum* for antitumor activity could inhibit the solid tumor development on mice induced with Dalton's lymphoma ascites (DLA) cells and increase the life span of mice bearing Ehrlich ascites carcinoma (EAC) tumors.^[18] Edible fruits and berries served the source for novel anticancer agents, given that extracts of those foods have demonstrated cytotoxic activity against tumor cell lines.^[19] Nimbolide, a triterpenoid extract from the flowers of the neem tree was found to have antiproliferative activity against some cancer cell lines^[20]. *Semecarpus anacardium* Linn nut milk extract exerts its anticancer effect through quenching - reactive oxygen species.^[21]

The cytotoxic activities of two medicinal herbs *Linum persicum* and *Euphorbia cheradania* that are native to Iran showed cytotoxic activity on tumor cell lines.^[22] The Pomegranate extracts inhibits the growth of breast cancer cells.^[23] Brassinosteroids, steroid plant hormones are promising leads for potential anticancer drugs.^[24] The *careya arborea* bark significantly reduced the solid tumor volume induced by DLA cells.^[25] The methanol extract of *Bauhinia racemosa* stem bark exhibited antitumor effect in EAC bearing mice.^[26] The antitumor activity of the ethanol extract of *Indigofera aspalathoides* was established.^[27]

The extract of 12 Chinese medicinal herbs such as *Anemarrbena asphodeloides* (Root), *Artemisia argyi* (leaf), *Commiphora Myrrh* (Resin), *Duchesnea indica* (Aerial Plants), *Gleditsia sinesis* (Fruit), *Ligustrum lucidum* (fruit), *Rheumpalmatum* (Root and Rhizome), *Rubia cordifolia* (Root), *Salvia Chinesis* (Aerial parts), *Scutellaria barbata* (Aerial Parts), *Uncaria rhynchophylla* (Stem), *Vaccaria segetails* (seed) showed anticancer effects invitro and those effects were markedly greater on cancer cells compared with normal cells.^[28] Phytoconstituents extracted from a large number of plants belonging to the genus *Hypericum* are known to possess potent anticancer nature^[29] cytotoxic activity of *Sarris cernuss* extract on human colon and breast carcinoma cultures was proved.^[30] The natural antioxidant gallic acid (GA) isolated from the fruits of an Indonesian medicinal Plant, *Phaleria Macrocarpa* was proved to be a potent anticancer compound.^[31] The rhizome *Zingiber officinalis*, one of the most widely used species of the ginger family is a

common condiment for various foods and beverages. The pungent vallinoids i.e., 6-gingerol and 6-paradol, shogaols and zingerone attributed to the anticancer properties of ginger.^[32] The antineoplastic activity of methanolic extracts of five medicinal plants those are native to Iran including *Galium mite*, *Ferula angulata*, *Stachys obtuscrena*, *Grsium bracteosum*, and *Echinophora cinerea* was investigated and proved to have anti tumor activity.^[33] *Panax ginseng* and its extracts have long been used for medical purposes and there increasing interest in developing ginseng products as cancer preventive agents.^[34]

Purified bioactive compounds derived from medicinal mushrooms were potentially important for new source of anticancer agents.^[35] The Saponins from the plant of china, *clematis manshrica* has obvious antitumor effects against various transplanted tumor on mice.^[36] The Embelin derivatives such as 1,4 – benzoquinone derivative 5-O ethyl embelin(1) and 5-O methyl embelin are promising ant mitotic and anti cancer molecules.^[37] Sesquiterpenes the class of naturally occurring molecules that are 15-carbon isoprenoid compounds. Those typically found on plants and marine life. They have therapeutic potential in decreasing the progression of cancer.^[38]

The anticancer activity from *Platycodon grandiflorum* was proved and established.^[39] The methanol extract of stem bark of *Dillenia pentagons* appears to be more active against Dalton's lymphoma.^[40] *Limonium vulgare*, *Artemisia maritima* and *Salicornia europaea* showed antineoplastic activities. The extracts of *Ononis spinosa*, *Trifolium fragiferum* and *Trifolium repens* showed tumor growth inhibiting activities.^[41] Methanol extract *Ledum groelandicum* Retzius (Labrador tea) leaf twig extract showed anticancer activity.^[42] The anti-neoplastic activity of guduchi (*Tinospora cordifolia*) on Ehrlich ascites carcinoma was proved.^[43] Some of the other plants of anticancer activities are shown in Table-3

Table-3: Indian Medicinal plants having anticancer activity

S. No.	Parts used	Name of the plant Family
1.	<i>Calotropis gigantean</i> , Asclepiadaceae	Whole plant
2.	<i>Cajanus cajan</i> , Fabaceae	Leaves

3.	<i>Butea monosperma</i> , Fabaceae	Bark	25	<i>Jatropha curcas</i> , Euphorbiaceae	Leaves, seed, oils
4.	<i>Bauhinia variegata</i> , Caesalpiniaceae	Root	26	<i>Kaempferia galanga</i> , Zingiberaceae	Rhizome
5.	<i>Bacopa monnieri</i> , Scrophulariaceae	Whole plant	27	<i>Kaempferia rotunda</i> , Zingiberaceae	Tubers
6.	<i>Azadirachta indica</i> , Meliaceae	Bark	28	<i>Lanata camara</i> , Verbanaceae	Whole plant
7.	<i>Asparagus racemosus</i> , Liliaceae	Liliaceae			
8.	<i>Aphanamixis polystachya</i> , Meliaceae	Bark	29	<i>Lens culinaris medikus</i> , Fabaceae	Seed
9.	<i>Aloe barbadensis</i> , Liliaceae	Leaf juice	30	<i>Limonia acidissima</i> , Rutaceae	Fruit
10.	<i>Alium cepa</i> , Liliaceae	Bulb			
11.	<i>Acorus calamus</i> , Araceae	Rhizome	31	<i>Macrotyloma uniflorum</i> , Fabaceae	Seed
12.	<i>Cassia absus</i> , Caesalpiniaceae	Leaves			
13.	<i>Cassia auriculata</i> , Caesalpiniaceae	Root	32	<i>Mimosa pudica</i> , Mimosaceae	Whole plant
14.	<i>Cassia senna</i> , Caesalpiniaceae	Leaves	33	<i>Nicotiana tabacum</i> , Solanaceae	Leaves
15.	<i>Catunaregum spinosa</i> , Rubiaceae	Bark/Fruit	34	<i>Operculina turpethum</i> , Convolvulaceae	Root
16.	<i>Citrullus colocynthis</i> , Cucurbitaceae	Root	35	<i>Rhinacanthus nasuta</i> , Acanthaceae	Whole plant
17.	<i>Citrus medica</i> , Rutaceae	Root			
18.	<i>Cissus quadrangularis</i> , Vitaceae	Whole plant	36	<i>Zanthoxylum armatum</i> , Rutaceae	Bark,Fruit
19.	<i>Clerodendrum serratum</i> , Verbanaceae	Root	37	<i>Xanthium strumarium</i> , Compositae	Root
20.	<i>Clerodendrum viscosum</i> , Verbanaceae	Leaves	38	<i>Salvadora persica</i> , Salvadoraceae	Bark, Leaf,
21.	<i>Crinum asiaticum</i> , Amaryllidaceae	Bulb	39	<i>Symplocos cochinchinensis</i>	Shoot, Fruit
22.	<i>Daucus carota</i> , Apiaceae	Root	40	<i>Tylopora indica</i> , Asclepiadaceae	Root, Leaf
23.	<i>Embelia ribes</i> , Myrsinaceae	Fruit	41	<i>Vernonia cinerea</i> , Asteraceae	Whole plant
24.	Symplocaceae	Bark	42	<i>Vitex trifolia</i> , Verbanaceae	Leaf

CONCLUSION

From the present review, it can be concluded that cancer is the leading cause of death in developing countries like India. As there is an enormous increase in the population day by day, the alternative therapy in the market is getting its glimpse. 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. Based on that the siddha medicines are coming up in combination with metals and other essential supplements to improve the immune status of the cancer patients in India. The above survey reveals the role of Indian medicinal plants and the various phytochemicals that may be used effectively for cancer treatment. The available literature finds to be very impressive which may give an indication for the therapeutic usefulness. Only few of the plants listed here and there are hundreds of plants unexplored need much detailed survey. The isolation, identification of active principles and pharmacological studies of the active phytoconstituents may be considered and studied elaborately to treat effectively various types of cancer.

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