



HYGEIA
JOURNAL FOR DRUGS AND MEDICINES
www.hygeiajournal.com



ETHNOMEDICINAL PLANTS FOR CANCER THERAPY – A REVIEW

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Article history: Received: 17August, 2010, revised: 14 November, 2010, accepted: 03 December, 2010, Available online: 14 April 2011

Abstract

A huge 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 effects 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. This article reveals a detailed review of ethno medicinally important plants 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.

Key words: Cancer, Medicinal plants, bioactive compounds, Anticancer.

1. Introduction

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.

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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.

1.1. 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 p53. *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 damage, 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. 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 fiber 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.

1.2. 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 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 include: 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 overload can occur. Supplementing the diet with effective antioxidant compounds.

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.

1.3. Cancer - Indian scenario

Every year about **8,50,000** new cancer cases being diagnosed, India resulting about **5,80,000** cancer related death every year. India had the highest number of the oral and throat cancer cases in the world. Every third oral cancer patient in the world is from India. In males Oral, Lungs and Stomach cancers was the three most common causes of cancer incidence and death whereas In females Cervical, Breast and Oral cancers were the three main causes of cancer related illnesses and death. Overall cervical cancer was the number one cause of cancer death in India. That was really unfortunate as cervical cancer can be easily prevented and also relatively easy to diagnose and treat at an early stage. Compared to developed countries overall there were less cancer cases in India but that could be due to under diagnosis and under reporting. At the same time regional, ethnic, dietary and socio-economic factors might also results in difference in the cancer susceptibilities and the incidence. Also cancer was mainly a disease of old ages. World wide median age at diagnosis was about 60 years. Average life span was about 58 yrs in India compared to 75 yrs in the developed world.

1.4. Cancer- global scenario

Among all the cancer, Lung cancer is the most common worldwide and accounts for major death annually. The following Table 1 shows the global scenario for various types of cancer.

The three leading cancer killers were different than the three most common forms, (i) Lung cancer responsible for 17.8 per cent of all cancer deaths. (ii) Stomach 10.4 per cent and (iii) Liver 8.8 percent. Industrial nations with the highest overall cancer rates include: U.S.A, Italy, Australia, Germany, The Netherlands, Canada and France. Developing countries with the lowest cancer were in Northern Africa. Cancer rates could further increase by 50% to 15 million new cases in the year 2020. According to the World Cancer Report, the most comprehensive global examination of the disease to date. However, the report also provides clear evidence that healthy lifestyles, and public health action by governments and health practitioners could stem this trend, thus prevent as many as one third of cancers worldwide.

1.5. Plant phytochemicals on cancer – an overview

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-tribydroxy isoflavone) inhibit the growth of transplantable human prostate carcinoma.¹ 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.² Andrographolide the potential cancer therapeutic agent isolated from *Andrographis paniculata*.³

In the screening of Yemeni plants used in folk medicine for the anticancer potential, the methanolic extracts of *Dendrosicyos Socotrana*, *Withania aduensis*, *Withania riebeckii*, *Dracena Cinnabari* and *Buxus hildebrandlii* exhibited the highest toxicity on all tumor cell lines.⁴ The four varieties of muscadine grape extract had the ability to inhibit the activity of matrix metalloproteinases implying that those could be good inhibitors of carcinogenesis.⁵ The limonoids isolated from the methanol extract of *Khaya Senegalensis* proved good anticancer activity.⁶ The leaf extract of Ashwagandha selectively killed tumor cells and thus it was a natural source for safe anticancer medicine.⁷ The fruit of deerberry (*Vaccinium stamineum*) exhibited the anticancer capability of human lung and leukemia cancer cells.⁸ 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.⁹

Morinda citrifolia showed of cancer preventive effective on both clinical practice and laboratory animal models.¹⁰ 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.¹¹ 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.¹² Nimbolide, a triterpenoid extract from the flowers of the neem tree was found to have antiproliferative activity against some cancer cell lines.¹³ *Semecarpus anacardium* Linn nut milk extract exerts its anticancer effect through quenching - reactive oxygen species.¹⁴ The cytotoxic activities of two medicinal herbs *Linum persicum* and *Euphorbia cheradania* that are native to Iran showed cytotoxic activity on tumor cell lines.¹⁵ The Pomegranate extracts inhibits the growth of breast cancer cells.¹⁶ Brassinosteroids, steroid plant hormones are promising leads for potential anticancer drugs.¹⁷ The *careya arborea* bark significantly reduced the solid tumor volume induced by DLA cells.¹⁸ The methanol extract of *Bauhinia racemosa* stem bark exhibited antitumor effect in EAC bearing mice.¹⁹ The antitumor activity of the ethanol extract of *Indigofera aspalathoides* was established.²⁰

The extract of 12 Chinese medicinal herbs such as *Anemarrbena asphodeloides* (Root), *Artemisia argyi* (leaf), *Commiphora Myrrh* (Resin), *Duchesnea indica* (Aerial Plants), *Gleditsia sinensis* (Fruit), *Ligustrum lucidum* (fruit), *Rheumpalmatum* (Root and Rhizome),

Rubia cordifolia (Root), *Salvia Chinesis* (Aerial parts), *Scutellaria barbata* (Aerial Parts), *Uncaria rhychopylla* (Stem), *Vaccaria segetails* (seed) showed anticancer effects invitro and those effects were markedly greater on cancer cells compared with normal cells.²¹

Phytoconstituents extracted from a large number of plants belonging to the genus *Hypericum* are known to possess potent anticancer nature²² cytotoxic activity of *Sarris cernuss* extract on human colon and breast carcinoma cultures was proved.²³ 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.²⁴ 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, shogaolsand zingerone attributed to the anticancer properties of ginger.²⁵

The antineoplastic activity of methanolic extracts of five medicinal plants that 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.²⁶ *Panax ginseng* and its extracts have long been used for medical purposes and there increasing interest in developing ginseng products as cancer preventive agents.²⁷ Purified bioactive compounds derived from medicinal mushrooms were potentially important for new source of anticancer agents.²⁸

The Saponins from the plant of china, *clematis manshrica* has obvious antitumor effects against various transplanted tumor on mice.²⁹ The Embelin derivatives such as 1,4 - benzoquinone derivative 5-0 ethyl embelin(1) and 5-0 methyl embelin are promising antimitotic and anti cancer molecules.³⁰ 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.³¹

The anticancer activity from *Platycodon grandiflorum* was proved and established.³² The methanol extract of stem bark of *Dillenia pentagons* appears to be more active against Dalton's lymphoma.³³ *Limonium Vulgare*, *Artemisia Maritima* and *Salicornia europaea* showed antineoplastic activities. The extracts of *Ononis spinosa*, *Trifolium fragiferum* and *Trifolium repen* showed tumor growth inhibiting activities.³⁴ Methanol extract *Ledum groelandicum* Retzius (Labrador tea) leaf twig extract showed anticancer activity.³⁵ The anti-neoplastic activity of guduchi (*Tinospora cordifolia*) on Ehrlich ascities carcinoma was proved.³⁶ Some of the other plants of anticancer activities are shown in Table-2.

Table -1: Global Scenario on Types of Cancer.

S.No	Type of Cancer	No. of Patients affected /year
1.	Lung	1.2 million
2.	Breast	Over 1 million
3.	Colorectal	9,40,000
4.	Stomach	8,70,000
5.	Liver	5,60,000
6.	Cervical	4,70,000
7.	Esophageal	4,10,000
8.	Head and Neck	3,90,000
9.	Urinary Bladder	3,30,000
10.	Malignant Non-Hodgkin lymphomas	2,90,000
11.	Leukemia	2,50,000
12.	Prostate and Testicular	2,50,000
13.	Pancreatic	2,16,000
14.	Ovarian	1,90,000
15.	Kidney	1,90,000
16.	Endometrial	1,88,000
17.	Nervous system	1,75,000
18.	Melanoma	1,33,000
19.	Thyroid	1,23,000
20.	Pharynx	65,000
21.	Hodgkin disease	62,000

Table-2: Indian Medicinal plants having anticancer activity

S.no.	Name of the plant	Family	Parts used
1.	<i>Calotrophis gigantea</i>	Asclepiadaceae	Whole plant
2.	<i>Cajanus cajan</i>	Fabaceae	Leaves
3.	<i>Butea monosperma</i>	Fabaceae	Bark
4.	<i>Bauhinia variegata</i>	Caesalpinaceae	Root
5.	<i>Bacopa monnieri</i>	Scropulariaceae	Whole plant
6.	<i>Azadirachta indica</i>	Meliaceae	Bark
7.	<i>Asparagus racemosus</i>	Liliaceae	Root
8.	<i>Aphanamixis polystachya</i>	Meliaceae	Bark
9.	<i>Aloe barbadensis</i>	Liliaceae	Leaf juice
10.	<i>Alium cepa</i>	Liliaceae	Bulb
11.	<i>Acorus calamus</i>	Araceae	Rhizome
12.	<i>Cassia absus</i>	Caesalpinaceae	Leaves
13.	<i>Cassia auriculata</i>	Caesalpinaceae	Root
14.	<i>Cassia senna</i>	Caesalpinaceae	Leaves
15.	<i>Catunaregum spinosa</i>	Rubiaceae	Bark/Fruit
16.	<i>Citrullus colocynthis</i>	Cucurbitaceae	Root
17.	<i>Citrus medica</i>	Rutaceae	Root
18.	<i>Cissus quadrangularis</i>	Vitaceae	Whole plant
19.	<i>Clerodendrum serratum</i>	Verbanaceae	Root
20.	<i>Clerodendrum viscosum</i>	Verbanaceae	Leaves
21.	<i>Crinum asiaticum</i>	Amaryllidaceae	Bulb
22.	<i>Daucus carota</i>	Apiaceae	Root
23.	<i>Embelia ribes</i>	Myrsinaceae	Fruit
24.	<i>Flacourtia jangomos</i>	Flacourtiaceae	Bark/Leaf
25.	<i>Jatropha curcas</i>	Euphorbiaceae	Leaves,seed,oils
26.	<i>Kaempferia galanga</i>	Zingiberaceae	Rhizome
27.	<i>Kaempferia rotunda</i>	Zingiberaceae	Tubers
28.	<i>Lanata camara</i>	Verbanaceae	Whole plant
29.	<i>Lens culinaris medikus</i>	Fabaceae	Seed
30.	<i>Limonia acidissima</i>	Rutaceae	Fruit
31.	<i>Macrotyloma uniflorum</i>	Fabaceae	Seed
32.	<i>Mimosa pudica</i>	Mimosaceae	Whole plant
33.	<i>Nicotiana tabacum</i>	Solanaceae	Leaves
34.	<i>Operculina turpethum</i>	Convolvulaceae	Root
35.	<i>Rhinacanthus nasuta</i>	Acanthaceae	Whole plant
36.	<i>Salvadora persica</i>	Salvadoraceae	Bark,Leaf,Shoot,Fruit
39.	<i>Symplocus cochinchinensis</i>	Symplocaceae	Bark
40.	<i>Tylopora indica</i>	Asclepiadaceae	Root, Leaf
41.	<i>Vernonia cinerea</i>	Asteraceae	Whole plant
42.	<i>Vitex trifolia</i>	Verbanaceae	Leaf
43.	<i>Zanthoxylum armatum</i>	Rutaceae	Bark,Fruit
44.	<i>Xanthium strumarium</i>	Compositae	Root

2. 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 may be treated effectively for cancer. 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 for various types of cancer.

Acknowledgement

We greatly acknowledge Dr. T.K. Ravi, Principal, College of Pharmacy, Sri Ramakrishna Institute of Paramedical Sciences, Coimbatore for the support and encouragement throughout the study.

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