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A Review on Medicinal Plants for Cancer Therapy

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Abstract : Cancer is major health problem in both developed and developing countries. Cancer after cardiovascular disease is the second leading cause of death. Cancer is the abnormal growth of cells in our bodies that can lead to death. 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 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 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.

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

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 *Anemarrhena asphodeloides* (Root), *Artemisia argyi* (leaf), *Commiphora Myrrh* (Resin), *Duchesnea indica* (Aerial Plants), *Gleditsia sinensis* (Fruit), *Ligustrum lucidum* (fruit), *Rheum palmatum* (Root and Rhizome), *Rubia cordifolia* (Root), *Salvia Chinesis* (Aerial parts), *Scutellaria barbata* (Aerial Parts), *Uncaria rhychopylla* (Stem), *Vaccaria segetalis* (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, shogaols and 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 antimetabolic 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.³²The 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.³⁵The 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 2. List of Anticancer plants:

Sr.No:	Plant Name/Family	Habitat	Active constituent	Class
1.	<i>Agapanthus africanus</i> Agapanthaceae	S.Africa	Isoliquiritigenin	Chalcone [7]
2.	<i>Aglaila sylvestre</i> Meliaceae	India	Silvesterol	-
3.	<i>Ailanthus Altissima</i> Simaraubaceae	China	Ailnthon, Ailantenol	Quassinoids [18]
4.	<i>Apium graveolens</i> Umbelliferae	N.America	Apigenin	Flavonoid [19]
5.	<i>Bleckeria vitensis</i> Apocynaceae	France	Ellipticine	Alkaloid [20]
6.	<i>Brucea antidysenterica</i> Simaraubaceae	Africa	Bruceantin	Quassinoid [20]
7.	<i>Bursera microphylla</i> Burseraceae	Mexico	Burseran	Lignan
8.	<i>Camptotheca acuminata</i> Nyssaceae	China	Camptothecin	Alkaloid [20]
9.	<i>Catharanthus roseus</i> Apocynaceae	India,Africa	Vincristine, Vinblastine	Alkaloid [20]
10.	<i>Centaurea montata</i> Asteraceae	Europe	Montamine	Alkaloid
11.	<i>Centaurea schischkinii</i> Asteraceae	-	Schischkinnin	Alkaloid
12.	<i>Cephalotaxus harringtonia</i> Cephalotaxaceae	Japan	Homoharringtonine	Alkaloid [20]
13.	<i>Cleistanthus collinus</i> Euphorbiaceae	India	Cleistanthin, Collinusin	Lignan
14.	<i>Combretum caffrum</i> Combretaceae	S.Africa	Combrestatins	Stilbenes
15.	<i>Croton lechleri</i> Euphorbiaceae	S.America	Taspine	Alkaloid [21]
16.	<i>Daphne mezereum</i> Thymelaeaceae	Asia, Europe	Mezerein	-
17.	<i>Diphylleia grayi</i> Berberidaceae	Japan	Diphyllin	Lignan [20]
18.	<i>Dysoxylum binectariferum</i> Meliaceae	India	Rohitukine	Alkaloid [20]
19.	<i>Erythroxylum pervillei</i> Erythroxylaceae	Madagascar	Pervilleine	Alkaloid
20.	<i>Euphorbia semiperfoliata</i> Euphorbiaceae	Europe	Jatrophone	Terpenoid [20]

Table 2. conti...				
Sr.No:	Plant Name/Family	Habitat	Active constituent	Class
1.	<i>Fritillaria thunbergii</i> Liliaceae	China,Japan	Zhebeinone	Alkaloid
2.	<i>Gunnera perpensa</i> Gunneraceae	Brazil	2-methyl-6(3-methyl 2-butenyl) benzo 1-4 quinone	Quinone
3.	<i>Hypericum perforatum</i> Clusiaceae	Europe	Hypericin	Anthraquinone
4.	<i>Hypoxis colchicifolia</i> Hypoxidaceae	S.Africa	Hypoxoside, Rooperol	Glycoside
5.	<i>Indigofera tinctoria</i> Leguminosae	Asia	Indirubins	Indigoids [20]
6.	<i>Justicia procumbens</i> Acanthaceae	India	Justicidin A,B	Lignan
7.	<i>Lantana camara</i> Verbenaceae	America	Verbascoside	Glucoside
8.	<i>Larrea tridentate</i> Zygophyllaceae	Mexico	Terameprocol	Lignan [22]
9.	<i>Linium album</i> Linaceae	-	Podophyllotoxin	Lignan
10.	<i>Lonicera japonica</i> Caprifoliaceae	Japan	Luteolin	Flavanoid [23]
11.	<i>Paris polyphilla</i> Trilliaceae	China	Polyphyllin	[24]
12.	<i>Pestemon deustus</i> Serophulariaceae	U.S.A	Liriodendrin	Lignan
13.	<i>Phaleria macrocarpa</i> Thymelaeaceae	Indonesia	Pinoresinol, Laricinesinol	Lignan
14.	<i>Podophyllum emodii</i> Berberidaceae	India	Epipodophyllotoxin	Alkaloid
15.	<i>Polygonum cuspidatum</i> Polygonaceae	Japan,China	Resveratrol	Flavanoid
16.	<i>Pteris multifida</i> Pteridaceae	Japan	Pterokaurane	Terpenoid [25]
17.	<i>Pygeum africanum</i> Rosaceae	Africa	Amygdalin	Glycoside
18.	<i>Vitex rotundifolia</i> Verbenaceae	India, Korea	Casticin	Flavanoid [31]
19.	<i>Wikstroemia viridi</i> Thymelaeaceae	China	Wikstromol	Caumarin

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 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. this article also provides the knowledge about anticancer medicinal plants of foreign origin, which are used by people all over the world. Also it is of significance to exploit novel anticancer drugs from medicinal plants.

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