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## Role of herbal drugs in cancer an Ethnopharmacological Survey

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### ABSTRACT

Cancer is a general term applied of series of malignant diseases that may affect different parts of body. The main causes of cancer are alterations of DNA, mutations, damage, smoking, addiction to liquor, chewing tobacco, imbalance diet, exposure to certain chemicals (carcinogens) etc. Complementary and alternative medicine use is common amongst cancer patients. In many surveys, herbal medicines are amongst the most commonly used group of treatments. Herbal remedies are believed by the general public to be safe, cause less side-effects and less likely to cause dependency. Traditional medicine has a long history of serving peoples all over the world. The use of herbal remedies and dietary supplements is widespread throughout the world, and use may be increasing. These are taken for a wide range of perceived benefits and treatment of specific conditions. Alternatively many herbals and dietary supplements may predispose to control in different types of cancer. In this article, we review the potential anticancer effects of herbal remedies and discuss the potential interaction between these herbal substances and conventional anticancer medications. These herbal medicines along with benefits also include some adverse effects. This review summarizes the role of some pharmaceutically important herbal medicines used in treating cancer.

**Key Words:** Traditional medicine,cancer,Dietary supplements, herbal remedies, potential interaction.

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## INTRODUCTION

Cancer is a disease that arises from abnormal changes in the genetic make-up of cells that cause them to multiply uncontrollably. The abnormal cells then spread locally or to other regions of the body via the lymphatic or blood circulation<sup>1</sup>. These diseases are characterized by a rapid and uncontrolled formation of abnormal cells, which may mass together to form a growth or tumor, or proliferate throughout the body, initiating abnormal growth at other sites. If the process is not arrested, it may progress until it causes the death of the organism. Cancer may affect people at all ages, even fetuses, but the risk for most varieties increases with age. Cancer causes about 13% of all deaths<sup>2</sup>. The main forms of treatment for cancer in humans are surgery, radiation and drugs (cancer chemotherapeutic agents). Cancer chemotherapeutic agents can often provide temporary relief of symptoms, prolongation of life, and occasionally cures. Natural products and related drugs are used to treat 87% of all categorized human diseases including bacterial infection, cancer and immunological disorders<sup>3</sup>. World Health Organisation (WHO) estimated that about three quarters of the world population living in developing countries relies upon traditional remedies (mainly herbs) for the health care of its people<sup>4</sup> and attributed this high patronage of traditional medicine to its accessibility and affordability. The synthetic anticancer remedies are beyond the reach of common man because of cost factor. Herbal medicines have a vital role in the prevention and treatment of cancer and medicinal herbs are commonly available and comparatively economical. A great deal of pharmaceutical research done in technologically advanced countries like USA, Germany, France, Japan and China has considerably improved quality of the herbal medicines used in the treatment of cancer. Some herbs protect the body from cancer by enhancing detoxification functions of the body. Certain biological response modifiers derived from herbs are known to inhibit growth of cancer by modulating the activity of specific hormones and enzymes. Some herbs reduce toxic side effects of chemotherapy and radiotherapy. Scientists all over the world are concentrating on the herbal medicines to boost immune cells of the body against cancer. WHO therefore encourages the inclusion of herbal medicines of proven safety and efficacy in the healthcare programs of developing countries because of the great potential they hold in combating various diseases<sup>5</sup>.

### **Epidemiology**

There are great regional differences in cancer incidence and mortality overall and at specific organ sites in the world. In terms of mortality, lung cancer was still the most common cause of cancer death in both sexes combined, followed by colorectal, breast and stomach cancer. Lung

cancer is still one of the biggest public health problems in Europe, accounting for one-fifth of all cancer deaths<sup>6</sup> Breast cancer is the most common form cancer in worldwide.<sup>7,8</sup> Amongst south African women, breast cancer is likely to develop in one out of every 31 women in the country .breast cancer in India is the second most common cancer in women after the cancer of uterine cervix. Multidrug resistance in cancer is sometimes associated with overproduction of growth factors like fibroblast growth factor that provide survival signals to neoplastic cells to overcome the detrimental effects of chemotherapeutic drugs<sup>9</sup>. There is a scant data on the incidence, pattern and genotype of familial cancers or multiple primary neoplasms from India<sup>10</sup>. One hundred and forty six cases of childhood Hodgkin's lymphoma which is caused by Epstein Barr virus was detected immune histo chemically in 91% of childhood in northern india, more often in younger age and lower socio economic status<sup>11</sup>. Non-Hodgkins lymphoma is the 7th most common type of cancer seen in india. Diffuse large Bcell lymphomas represents a clinically and histological diverse group of neoplasms<sup>12</sup>. Cancer of the oral cavity is a disease of acquired occupational, nutritional and environmental insults chronic exposure of the oral cavity to a variety of mutagens/carcinogens present in the betel quid cigarette smoking and alcohol consumption results in the development of clinically a distinct premalignant lesion which got a 5-10% chances of progress towards malignancy in future. Every year, millions of people are diagnosed with cancer, leading to death in the majority of the cases. According to the American Cancer Society, deaths arising from cancer constitute 2-3% of the annual deaths recorded worldwide.

### **Causes of Cancer**

Cancer (a malignant growth) is medically known as neoplasm which means a relatively autonomous growth of tissues and commonly defined as an uncontrolled growth of cells, with loss of differentiation & commonly with metastasis, spread of the cancer to other tissues and organs<sup>13</sup>. The critical difference benign and malignant neoplasm is that benign tumour do not metasize, where as malignant tumour do. A metastasis is a secondary growth originating from the primary tumour and growing elsewhere in the body<sup>14</sup>.Cell division is a genetic process in which a cell passes its genes onto two daughter cells, each of which is a clone or exact of itself. Sometimes, this orderly process goes wrong, the genes in a cell may suffer a mutation or some mistakes may occur in DNA replication and recombination during cell division. Cancer cells continue to divide even in situations in which normal cells will usually wait for a special chemical transduction signal. The tumor cells would ignore such stop signals that are sent out by adjacent tissues. A Cancer cell also has the character of immortality even in vitro whereas normal cells stop dividing after 50-70 generations and undergoes a programmed cell death

(Apoptosis). Cancer cells continue to grow invading nearby tissues and metastasizing to distant parts of the body. Metastasis is the most lethal aspect of carcinogenesis<sup>15</sup>.

- Cancer is a genetic disease. Alterations to the DNA inside cells can endow cells with morbid “superpowers,” such as the ability to grow anywhere and to continue dividing indefinitely. Mutations in a relatively small set of cancer-related genes, as the decisive events in the transformation of healthy cells to malignant tumors<sup>16</sup>.
- Breakdown in DNA duplication or repair leading to many thousands of random mutations in cells.
- Damage to a few “master” genes mangles the chromosomes, which then become dangerous.
- Abnormal numbers of chromosomes in a cell may be the first milestone on the road to cancer.
- Other factors such as tobacco smoking, alcohol consumption, excess use of caffeine and other drugs, sunshine, infections from such oncogenic virus like cervical papillomaviruses, adenoviruses Karposis sarcoma (HSV) or exposure to asbestos.

### **Symptoms**

Cancer is a group of diseases that can cause almost any sign or symptom. The signs and symptoms will depend on where the cancer is, how big it is, and how much it affects the organs or tissues. If a cancer has spread (metastasized), signs or symptoms may appear in different parts of the body. A broad spectrum of non-specific cancer symptoms may include: Persistent Fatigue, Unintentional Weight Loss, Pain, Fever, Bowel Changes, Chronic cough etc. As a cancer grows, it can begin to push on nearby organs, blood vessels, and nerves. This pressure causes some of the signs and symptoms of cancer. If the cancer is in a critical area, such as certain parts of the brain, even the smallest tumor can cause symptoms. But sometimes cancer starts in places where it will not cause any symptoms until it has grown quite large. One example is cancers in the pancreas. They usually do not cause symptoms until they grow large enough to press on nearby nerves or organs (this causes back or belly pain). Others grow around the bile duct and block the flow of bile. This causes the eyes and skin to look yellow (jaundice). By the time a pancreatic cancer causes these signs or symptoms, it is usually in an advanced stage. This means it has grown and spread beyond the place it started the pancreas.

A cancer may also cause symptoms like fever, extreme tiredness (fatigue), or weight loss. This may be because cancer cells use up much of the body's energy supply, or they may release substances that change the way the body makes energy from food. Or the cancer may cause the

immune system to react in ways that produce these symptoms. Sometimes, cancer cells release substances into the bloodstream that cause symptoms which are not usually linked to cancer. For example, some cancers of the pancreas can release substances which cause blood clots in veins of the legs. Some lung cancers make hormone-like substances that raise blood calcium levels. This affects nerves and muscles, making the person feel weak and dizzy.

The symptoms of cancer are including an unusual lump or swelling on the neck, armpit, abdomen, grain, testicle or breast area; a change in size; shape or colour of a mole; a sore that won't heal after several weeks; unexplained weight loss; heavy night sweats and an unexplained pain or ache that lasts longer than four weeks<sup>16</sup>.

## TYPES OF CANCERS<sup>10</sup>

### **1. Cancers of Blood and Lymphatic Systems:**

Hodgkin's disease

Leukemias

Lymphomas

Multiple myeloma

Waldenstrom's disease

### **2. Skin Cancers:**

Malignant Melanoma

### **3. Cancers of Digestive Systems:**

Oesophageal cancer

Stomach cancer

Cancer of pancreas

Liver cancer

Colon and Rectal cancer

Anal cancer

### **4. Cancers of Urinary system:**

Kidney cancer

Bladder cancer

Testis cancer

Prostate cancer

### **5. Cancers in women:**

Breast cancer

Ovarian cancer

Gynecological cancer

Choriocarcinoma

#### **6. Miscellaneous cancers:**

Brain cancer,

Bone cancer,

Carcinoid cancer,

Nasopharyngeal cancer,

Retroperitoneal sarcomas

Soft tissue cancer,

Thyroid cancer

#### **The Mechanism on Cancer Therapy**

Oral squamous cell carcinoma is the common malignancy in males and the third most common in females in India. And it is a major cause of cancer morbidity and mortality worldwide. Alterations in the expression of retinoic acid receptors occur early in oral carcinogenesis. Deregulated expression of retinoic acid receptors and cell cycle regulators can serve as a potential predictive marker in the multistep process of development and progression of oral Cancer<sup>17</sup>. Apoptosis is highly regulated process defect in apoptic pathway leads to human disease from neurodegenerative disorder to malignancy. A significant pathway of cell death in squamous cell carcinoma of oropharynx is by apoptosis<sup>18</sup> Malignant disorders are no longer considered as a killer disease owing to continuous refinement of cytogenetic and molecular technologies. Chronic myeloid leukemia is the most known established example with the presence of Philadelphia chromosome in 95% cases<sup>19</sup>.

1. Inhibiting cancer cell proliferation directly by stimulating macrophage phagocytosis, enhancing natural killer cell activity.
2. Promoting apoptosis of cancer cells by increasing production of interferon, interleukin-2 immunoglobulin and complement in blood serum.
3. Enforcing the necrosis of tumor and inhibiting its translocation and spread by blocking the blood source of tumor tissue.
4. Enhancing the number of leukocytes and platelets by stimulating the haemopoietic function.
5. Promoting the reverse transformation from tumor cells into normal cells.
6. Promoting metabolism and preventing carcinogenesis of normal cells.

7. Stimulating appetite, improving quality of sleep,relieving pain, thus benefiting patients health.

## TREATMENT AND MANAGEMENT

### **Synthetic and semi-synthetic anticancer drugs<sup>21,22</sup>**

There are number of synthetic and semi-synthetic medicines used including

**Alkylating agent** like nitrogen mustard (Mechlorethamine, Cyclophosphamide, Chlorambucil), ethylenimine (thiotepa), alkyl sulfonate (busulfan), Nitrosoureas (carmustine, lomustine), Triazine (Dacarbazine);

**Purine antagonist** (6-Mercaptopurine, 6-Thioguanine, fludarabine, azathioprine);

**Pyrimidine antagonist** (5-Fluorouracil, Cytarabine);

**Antimetabolites** (Folate antagonistmethotrexate);

**Antibiotics** (Actinomycin D, Doxorubicin, Daunorubicin, Bleomycin, Mitomycin C);

**Miscellaneous** (Hydroxyurea, Procarbazine, L-Asparaginase, Cisplatin, Imatinib, Carbaplatin);

**Semi-synthetic taxanes analogues** (Paclitaxel, Docetaxel);

**Semisynthetic epidophyllotoxin analogues** (Etoposide);

**Semi-synthetic camptothecin analogues** (Tropotecan, Irinotecan).

Synthetic and semi-synthetic drugs having specific toxicity including bone marrow depression, granulocytopenia, agranulocytosis, thrombocytopenia, aplastic anaemia, lymphocytopenia, nausea, vomiting, diarrhoea, alopecia, amenorrhoea, teratogenesis, abortion, foetal death, hyperuricaemia, oral mucosal ulceration, intestinal denudation ulceration, generalized seizures, cerebellar ataxia, pulmonary fibrosis and many others.

### **Herbal Medicines:**

According to World Health Organization, 80 % of the people living in rural areas depend on medicinal herbs as primary healthcare system. The synthetic anticancer remedies are beyond the reach of common man because of cost factor. Herbal medicines have a vital role in the prevention and treatment of cancer and medicinal herbs are commonly available and comparatively economical. A great deal of pharmaceutical research done in technologically advanced countries like USA, Germany, France, Japan and China has considerably improved quality of the herbal medicines used in the treatment of cancer. Some herbs protect the body from cancer by enhancing detoxification functions of the body. Certain biological response modifiers derived from herbs are known to inhibit growth of cancer by modulating the activity of specific hormones and enzymes. Some herbs reduce toxic side effects of chemotherapy and

radiotherapy. Scientists all over the world are concentrating on the herbal medicines to boost immune cells of the body against cancer. Plants are important sources of medicines and presently about 25% of pharmaceutical prescriptions in the United States contain at least one plant-derived ingredient. In the last century, roughly 121 pharmaceutical products were formulated based on the traditional knowledge obtained from various sources.

### **Goals of Herbal Medicine in Cancer**

- Reduction of toxicity from chemotherapeutic and radiation therapies while enhancing tumor killing capacity.
- Reduction of side effects such as fatigue, hair loss, mouth sores, nausea, vomiting, appetite loss, and organ wasting and failure.
- Enhancement of immunity.
- Prevention from cancer spreading via growth, metastasis and local invasion.
- Protection against developing cancer causing effects of radiation and chemotherapy.
- Protection against development of further cancer in cancer prone individuals.
- Improvement of complete or partial remission by exerting direct effects on the tumor by changing the underlying conditions that allows the cancer to exist.
- Augmentation of duration and quality of life.

Medicinal plants continue to play a central role in the healthcare system of large proportions of the world's population<sup>23</sup>. Recognition and development of the medicinal and economic benefits of these plants are on the increase in both developing and industrialized nations<sup>24</sup>.

PLANTS WITH ANTI-CANCER ACTIVITY<sup>25-65</sup>.

Sr.no.	Botanical name	Family	Common name	Active constituent
1	<i>Acnistus arborescens</i>	<i>Solanaceae</i>	Hollow heart, wild tobacco	Withaferin A
2	<i>Acer negundo</i>	<i>Aceraceae</i>	Box Elder, Boxelder Maple, and Maple Ash	Acer saponin P
3	<i>Actinidia chinensis</i>	<i>Actinidiaceae</i>	China gooseberry, Kiwifruit	Polysaccharide known as "ACPS-R"
4	<i>Acronychia baueri</i>	<i>Rutaceae</i>	Acronychia baueri	Acronycine
5	<i>Allamanda cathartica</i>	<i>Apocynaceae</i>	Golden Trumpet	Allamandin
6	<i>Allium sativum</i>	<i>Liliaceae</i>	Garlic	Alliin, allicin, alliinase, S-allylcysteine (SAC), diallyldisulphide (DADS), diallyltrisulphide (DATS) and methylallyltrisulphide.
7	<i>Aloe ferox</i> ,	<i>Liliaceae</i>	Aloe vera	<i>Aloe barbadensis</i> . Aloe-emodin, emodin, aloin, acemannan,
8	<i>Ananas comosus</i>	<i>Bromeliaceae</i>	Pine apple, Ananas	Bromelain
9	<i>Angelica sinensis</i>	<i>Umbelliferae</i>	Angelica	Polysaccharide fraction of known as "AR-4"
10	<i>Annona species</i>	<i>Annonaceae</i>	Monkey species	Acetogenins
11	<i>Arctium lappa</i> ,	<i>Compositae</i>	Burdock	Potent anticancer factors
12	<i>Astragalus membranaceus</i>	<i>Papilionaceae</i> --	yellow leader	Swainsonine
13	<i>Baccharis megapotamica</i>	<i>Baccharin</i>	<i>Baccharis megapotamica</i>	<i>Compositae</i>
14	<i>Betula utilis</i>	<i>Betulaceae</i>	Bhojpatra	Betulin
15	<i>Bouvardia ternifolia</i>	<i>Rubiaceae</i>	Scarlet bouvardia, Firecracker bush, Trompetilla, Clavillo	Bouvardin, Deoxybouvardin
16	<i>Brucea antidysenterica</i>	<i>Simaroubaceae</i>	<i>Brucea antidysenterica</i>	Bruceantin
17	<i>Camellia sinensis</i>	<i>Theaceae</i>	Tea plant	Epigallocatechin gallate
18	<i>Camptotheca</i>	<i>Nyssaceae</i>		Camptothecin
19	<i>Catharanthus roseus</i>	<i>Apocynaceae</i>	Vinca	Vinblastine, Vincristine, Alstonine, Ajmalicine and Reserpine.
20	<i>Cephaelis acuminata</i>	<i>Rubiaceae</i>	<i>Cephaelis acuminata</i>	Emetine

21	<i>Cephalotaxus harringtonia</i>	<i>Cephalotaxaceae</i>	Japanese Plum Yew	Harringtonine, Homoharringtonine
22	<i>Chlorella pyrenoidosa</i> --	<i>Oocystaceae</i>	Algue Verte d'Eau Douce, Bulgarian Chorella	Lysine
23	<i>Colchicum luteum</i>	<i>Liliaceae</i>	Colchicum	Colchicines demecolcine
24	<i>Combretum caffrum</i>	<i>Combritaceae</i>	Bushwillow tree	Combretastatin
25	<i>Crotalaria spectabilis</i>	<i>Leguminosae</i>	Rattlebox, showy crotalaria	Monocrotaline
26	<i>Curcuma longa</i> Linn.	<i>Zinziberaceae</i>	Turmeric	Tumerone, curcumine
27	<i>Cyclea peltata</i>	<i>Menispermaceae</i>	Raj Patha	Tetrandrine
28	<i>Echinacea angustifolia</i>	<i>Asteraceae</i>	Black sampson	Arabinogalactan, Jucogalactoxyloglucans.
29	<i>Fagara zanthoxyloides</i> , <i>F. macrophylla</i>	<i>Rutaceae</i>	Fagara	Nitidine
30	<i>Fagopyrum esculentum</i> ,	<i>Polygonaceae</i>	Vitamin p	Amygdalin, Rutin
31	<i>Ginkgo biloba</i>	<i>Ginkgoaceae</i>	Kew tree	Ginkgolide-B, A, C and J
32	<i>Glycine max</i>	<i>Leguminosae</i>	Soyabean	Zinc, selenium, vitamins (A, B1, B2, B12,C, D, E and K), amino acids, isoflavones, protease inhibitors, saponins and phytosterols
33	<i>Glycyrrhiza glabra</i>	<i>Leguminosae</i>	Liquorice	Glycyrrhizin
34	<i>Gnidia lamprantha</i>	<i>Thymelaeaceae</i>	Gnidia lamprantha	Gnidin
35	<i>Gossypium barbadense</i>	<i>Malvaceae</i>	Raw cotton	Gossypol
36	<i>Gyrophora esculenta</i>	<i>Umbelicariaceae</i>	Mushroom	Polysaccharides $\beta$ -glucans, $\alpha$ -glucans, and galactomannans.
37	<i>Helenium autumnale</i>	<i>Compositae</i>	Sneezeweed, Helen's Flower, Dogtooth Daisy	Helenalin
38	<i>Heliotropium indicum</i>	<i>Boraginaceae</i>	Indian heliotrope	Indicine-N-oxide
39	<i>Holacantha emoryi</i>	<i>Simaroubaceae</i>	Burro thorn	Holacanthone
40	<i>Ipomoea batatas</i>	<i>Convolvulaceae</i>	The sweet potato	4-ipomeanol
41	<i>Jacaranda caucana</i>	<i>Bignoniaceae</i>	Jacaranda	Jacaranone
42	<i>Jatropha gossypiiifolia</i>	<i>Euphorbiaceae</i>	Tuba-tuba	Jatrophone
43	<i>Lentinus edodes</i>	<i>Agaricaceae</i>	Shiitake	Lentinan
44	<i>Liatris chapmanii</i>	<i>Compositae</i>	Chapman's gayfeather	Liatrin

45	<i>Linum usitatissimum</i>	<i>Linaceae</i>	Flax seed, Linseed	Cynogenetic glycosides, Lignans
46	<i>Marah oreganus</i>	<i>Cucurbitaceae</i>	the Oregon Manroot, Coastal Manroot, Western Wild-cucumber	Cucurbitacin
47	<i>Maytenus buchananii</i> , <i>M.serrata</i>	<i>Celastraceae</i>	Maytenus buchananii	Maytansine, Maytanacine, Maytanvaline
48	<i>Mentha species</i>	<i>Labiataeae</i>	Pudina	Monoterpene ketones
49	<i>Ochrosia elliptica</i>	<i>Apocynaceae</i>	Elliptic Yellow wood, Kopsia	Ellipticine and 9-methoxy ellipticine are pyridocarbazole (monomeric indole) alkaloids
50	<i>Panax ginseng</i>	<i>Aralaceae</i>	Ginseng	Ginsenosides, Panaxosides
51	<i>Penstemon deutus</i>	<i>Scrophulariaceae</i>	hotrock penstemon, scabland beardtongue	Penstimide
52	<i>Phyllanthus acuminatus</i>	<i>Euphorbiaceae</i>	the Jamaican gooseberry tree	Phyllanthoside
53	<i>Picrorrhizia kurroa</i>	<i>Scrophulariaceae</i>	Picrorrhizia (kutki)	Picrosides I, II, III and kutkoside
54	<i>Podophyllum hexandrum</i>	<i>Berberidaceae</i>	Podophyllum	Podophyllin, astragaline
55	<i>Simarouba glauca</i>	<i>Simaroubaceae</i>	Laxmi Taru	Glaucarubinone
56	<i>Steganotaenia araliaaceae</i>	<i>Umbelliferae</i>	Carrot Tree	Steganacin
57	<i>Stereospermum sauveolens</i>	<i>Bignoniaceae</i>	Trumpet	Lapachol
58	<i>Taxus brevifolia</i>	<i>Taxaceae</i>	Pacific yew	Taxanes, taxol cepholomannine
59	<i>Thalictrum dasycarpum</i>	<i>Ranunculaceae</i>	Purple meadow-rue	Thalicarpine
60	<i>Tripterygium wilfordii</i>	<i>Celastraceae</i>	Thunder god vine	Triptiodide
61	<i>Tylophora crebiflora</i>	<i>Asclepiadaceae</i>	Tylophora	Tylocrebine
62	<i>Vernonia hymenolepis</i>	<i>Compositae</i>	Vernonia hymenolepis	Vernolepin
63	<i>Withania somnifera</i>	<i>Solanaceae</i>	Ashwagandha	Withanolides, <i>Withaferin</i>
64	<i>Zingiber officinale</i>	<i>Zingiberaceae</i>	Ginger	Curcumin, gingerenone A, Gingeols, shogaols, zingerone

### Mechanism of herbs with anticancer activity

*Studies of Allium sativum* revealed presence of bioflavonoids quercetin and cyanidin are responsible for antioxidant properties of garlic. Ajoene, a sulphurcontaining compound, found in garlic oil, inhibits mutagenesis. Garlic oil prevents prostaglandindependent cancers by inhibiting lipoxygenase and cyclo-oxygenase enzymes. Garlic contains a rich content of selenium, which is a cellular antioxidant. Diallyltrisulphide, diallyldisulphide and S-allylcysteine, found in *Allium sativum*, have anticarcinogenic properties. Diallyltrisulphide prevents metastases in the lung cancer<sup>[29]</sup>. *Actinidia chinensis* contains a polysaccharide known as “ACPSR” that possesses immune-enhancing and anticancer activities<sup>31</sup>. *Aloe vera* also contains acemannan, which enhances activity of the immune cells against cancer. *Aloe vera* is found to inhibit metastases<sup>31</sup>. *Ananas comosus* contains bromelain, Bromelain stimulates defence mechanism of the body against cancer by enhancing cytotoxic activity of the monocytes and the macrophages, thus inhibiting growth of cancer<sup>31</sup>. The polysaccharide fraction of *Angelica sinensis*, known as “AR-4” possesses immunostimulating activities such as induction of interferon production, stimulation of the immune cell proliferation and enhancement of antitumour activity of the immune cell. *Annona species* contain acetogenins, Acetogenins are found to be effective in the treatment of nasopharyngeal carcinoma<sup>31</sup>. *Arctium lappa* contains potent anticancer factors that prevent mutations in the oncogenes. Swainsonine, a derivative of *Astragalus membranaceus*, is known to prevent metastases. *Betula utilis* contains betulin that can be easily converted into betulinic acid. Studies have revealed that betulinic acid inhibits growth of malignant melanoma and cancers of the liver and the lung<sup>33</sup>. *Betula utilis* contains betulin that can be easily converted into betulinic acid. Studies have revealed that betulinic acid inhibits growth of malignant melanoma and cancers of the liver and the lung<sup>33</sup>. *Camellia sinensis* contains polyphenolics which are known to possess antimutagenic and anticancer activity. *Vinca rosea* contains vinca alkaloids, which were the first phytoconstituents ever used to treat cancer. *Chlorella pyrenoidosa* contains a very effective detoxifying agent, known as lysine. *Chlorella pyrenoidosa* also contains high content of albumin that neutralizes free radicals. *Chlorella pyrenoidosa* protects the body from cancer<sup>40</sup>. *Colchicum luteum*, *C. autumnale* contains tropolone groups of alkaloid colchicines. Colchicine shows antimitotic activity and used in cancer. *Combretum caffrum* contains combretastatin, Combretastatin executes its therapeutic action against cancer by inhibiting blood supply to the tumour. *Curcuma longa* contains curcumin, which inhibits the growth of cancer by preventing production of harmful eicosanoid such as PGE-2. The anticancer effect of curcumin has been demonstrated in all the steps of cancer development. *Echinacea*

*angustifolia* contains arabinogalactan, which protects the body from cancer by activating the macrophages. Amygdalin, which is derived from *Fagopyrum esculentum*. Amygdalin is one of the nitrilosides (natural cyanide-containing substances), which consists of two molecules, i.e. benzaldehyde and cyanide. *Ginkgo biloba* contains Ginkgolide-B, which protects the body against cancer. It inhibits growth of cancer by regulating activity of the platelet-activating factor. *Glycine max* (Soya bean) is rich in zinc, selenium, vitamins (A, B1, B2, B12, C, D, E and K), amino acids, isoflavones, protease inhibitors, saponins and phytosterols. Studies have shown that isoflavones convert the cancerous cells to normal cells by inducing Cell-differentiation. Glycyrrhizin an active constituent of *Glycyrrhiza glabra* specifically reduces the activity of two enzymes that break down prostaglandin E. Liquorice shows anti-infective and anticancer properties. *Gossypium barbadense* contains gossypol. gossypol possesses selective toxicity towards cancerous cells<sup>50</sup>. *Gyrophora esculenta* is a mushroom that inhibits growth of cancer by enhancing activity of the natural killer cells. Lentinan, a  $\beta$ -glucan found in shiitake mushrooms, has been shown to have antitumor activity; it was active against lung carcinoma. *Linum usitatissimum* (Flaxseed) contains a rich supply of lignans. These plant lignans are converted to mammalian lignans (enterolactone and enterodiol) by bacterial fermentation in the colon<sup>46</sup> and they can then act as estrogens. Mammalian lignans appear to be anticarcinogenic; lignan metabolites bear a structural similarity to estrogens and can bind to estrogen receptors and inhibit the growth of estrogen-stimulated breast cancer<sup>57,58</sup>. *Mentha species* such as *Mentha piperita*, *Mentha longifolia* and *Mentha aquatica* contain phenolic antioxidants that prevent recurrence of cancer. Ellipticine and 9-methoxy ellipticine are pyridocarbazole (monomeric indole) alkaloids that have been isolated from *Ochrosia elliptica*, which acts as potent anticancer agent. Ginseng inhibits growth of cancer by interfering with the DNA synthesis. *Panax ginseng* contains several active constituents; the main active ingredients in ginseng root are thought to be a family of 6 triterpene saponins called ginsenosides<sup>61</sup>. *Picrorrhiza kurroa* (Kutki) has shown to reduce formation of liver cancer due to chemical exposures. *Podophyllum peltatum* and *P. hexandrum* contain podophyllin, which has similar therapeutic action on the dividing cancerous cells as that of the vinca alkaloids. *Taxus brevifolia*, *Taxus yunnanensis*, *Taxus baccata* and *Taxus wallichiana* contain taxanes, which include paclitaxel (Taxol) and docetaxel (Taxotere). Taxanes arrest multiplication of cancerous cells by cross-linking the microtubules. *Withania somnifera* contains withanolides, which possess immuno-modulatory activity. Withaferin A and withanolide D found in *Withania somnifera* are known to inhibit growth of cancer<sup>63</sup>. *Zingiber*

*officinalis* (ginger) rhizomes offer a rich package of gingerols-phenolic antioxidants that possess pronounced anti-inflammatory activity-that inhibit various cancers<sup>64,65</sup>

### **Herb-Drug interaction**

With the use of herbal drugs in combination with conventional chemotherapeutics, there is an increasing risk for unwanted interactions, especially because of the narrow therapeutic index of most oncolytic drugs. Although, as a result of a lack of investigations, reports about clinically relevant pharmacokinetic (PK) interactions. In cancer patients using SJW in combination with irinotecan, the plasma levels of SN-38, the active metabolite of irinotecan, were 42% lower<sup>66</sup>. The degree of myelosuppression was substantially worse in the absence of SJW. Similarly, in the rat, gastrointestinal and hematological toxicities after irinotecan injection were alleviated in the presence of SJW. SJW and irinotecan or imatinib, induction of the enzymes involved in the metabolism and transport of these chemotherapeutic drugs is responsible for the lower plasma levels. SJW has been shown to induce both CYP3A4 as well as Pgp in vitro and in vivo and CYP2C19 in healthy subjects<sup>67</sup>. Constituents of *Ginkgo biloba*, kava, ginseng, *Echinacea purpurea*, milk thistle (silybin), and evening primrose oil (*cis*-linoleic acid). Pgp activity was shown to be inhibited by curcumin, ginsenosides, piperine, some catechins from green tea, quercetin, and silymarin<sup>68</sup>.

### **Future prospects of herbal medicine market**

Medicinal plants continue to play a central role in the healthcare system of large proportions of the world's population. It is estimated that nearly three fourths of the herbal drugs used worldwide were discovered following leads from local medicine. According to WHO about 25% of modern medicines are descended from plants first used traditionally. Many others are synthetic analogues built on prototype compounds isolated from plants. Almost, 70% modern medicines in India are derived from natural products. The basic uses of plants in medicine will continue in the future, as a source of therapeutic agents, and as raw material base for the extraction of semi-synthetic chemical compounds such as cosmetics, perfumes and food industries. Though the efficacy of herbal requires development of quality consciousness in respect of the evaluation related evidences, supplying the demand for botanicals and herbals is a booming business This means that scientists, doctors and pharmaceutical companies will be looking at countries like China, India, etc. for their requirements, as they have the most number of medicinal plant species and are the top exporters of medicinal plants. Medicinal herbs are also significant source of synthetic and herbal drugs. So far, pharmaceutical companies have screened more than 25,000 plants for anti-cancer drugs<sup>69</sup>.

## CONCLUSIONS

The principles underlying herbal medicines are relatively simple, although they are quite distinct from conventional Medicine. Medicinal herbs as potential source of therapeutics aids has attained a significant role in health care system all over the world for human beings not only in the diseased condition but also as potential material for maintaining proper health<sup>70</sup>. A major factor impeding the development of the medicinal plant based industries in developing countries has been the lack of information on the social and economic benefits that could be derived from the industrial utilization of medicinal plants. Except for the use of these plants for local health care needs, not much information has been available on their market potential and trading possibilities. As a result, the governments or entrepreneurs have not exploited the real potential of these plants. This should tell us that looking for single ingredients to attack cancer might be missing the point. Just as cancers are a product of disturbances in the body, so herbs can correct the disturbances as well as control many cancers. Herbal system of medicine has been practiced for thousands of years.

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