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HERBAL MEDICINE: ALTERNATIVE TREATMENT FOR CANCER THERAPY

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ABSTRACT

In case of cancer, Traditional Chinese medicine-based herbal medicines have gained increasing acceptance worldwide in recent years and are being pursued by pharmaceutical companies as rich resources for drug discovery. For many years, traditional Chinese medicines (TCM) have been applied for the treatment of cancers in China and beyond. Herbal remedies are clearly a complementary and alternative modality used frequently by patients with hemato-oncological neoplasias during the course of their specific treatment. Cancer is a leading cause of death worldwide. There are a lot of cancer causing agents which are divided as physical carcinogens, chemical carcinogens and biological carcinogens. But most of the carcinogens or causes of cancer are related to our lifestyle like diet, habit, occupation, radiation and some infection, etc. Chemoprevention is highly necessary to prevent cancer related preterm death. In this review, we are studied on the herbal medicines, whenever used in cancer treatment and easily available in market. Cancer is a major cause of death, and globally studies are being conducted to prevent cancer or to develop effective nontoxic therapeutic agents. Some herbal drugs, we are discuss in this paper, such as Vinblastin, Podphyllotoxin, Camptothecin, Topotecan, Irinotecan, Etoposide, Teniposide, Vincristin, Taxol, Docetaxol, Colchicines amide, Colchicines, Demecolcine, Monocrotaline etc, all very effective drug for cancer. In experimental studies in the past decade have shown that herbal medicines / Ayurveda is useful in the prevention of cancer and that it also possesses antineoplastic, radio protective and chemo protective effects. Alternative treatment i.e. herbal medicines are very effective and commonly used therapy for cancer treatment.

INTRODUCTION: Cancer is a class of diseases caused by uncontrolled growth of cells [1]. This is very common type of disease. Cancer harms the body when damaged cells divide uncontrollably to form lumps of tissue called tumors. Cancers are primarily an environmental disease with 90-95% of cases due environmental factors and 5-10% directly due to heredity [2]. Common environmental factors leading to cancer include: tobacco, diet and obesity infections, radiation, lack of physical activity, and environmental pollutants. These environmental factors cause or enhance abnormalities in the genetic material of cells. Hereditary or acquired abnormalities in these regulatory genes can lead to uncontrolled cell growth,

and the development of cancer [3, 4]. The presence of cancer can be suspected on the basis of symptoms, or findings on radiology. Cancer actually a general term that describes a large group of related diseases. Cancers grow quickly while others can take years to become dangerous to the patient. Cancer treatment is so difficult [5, 6].

Herbal cancer therapy comprises a number of alternative treatments in the fight against cancer. More than 3,000 years ago, we had used herbs in treatment of cancer patients [7]. Herbal medicine has been used widely in Japan, Korea, India, and South East Asia countries since long time ago. Natural Products, generally plants, have been used for the treatment of various diseases for thousands of years.

General types of Cancer

- Bladder cancer
- Breast cancer
- Colon cancer
- Endometrial cancer
- Kidney cancer (renal cell)
- Leukemia
- Lung cancer
- Pancreatic cancer
- Prostate cancer
- Thyroid cancer
- Melanoma

Bladder cancer: Bladder cancer is a cancerous tumor in the bladder. The bladder is the organ in the center of the lower abdomen that holds urine. Bladder cancer is a very common type of cancer. More than 10,000 cases are diagnosed each year in the UK. Mostly these are diagnosed in men; one man in thirty will get bladder cancer at some time in life.

Breast Cancer: Breast cancer is a common type of cancer mainly affects women and much less, men. More than 200,000 women are diagnosed with breast cancer in each year. Types of breast cancer are including, but are not limited to:

- Ductal carcinoma *in situ*,
- lobular carcinoma *in situ*,
- inflammatory breast cancer,
- Paget's disease of the nipple,
- Invasive types of breast cancer.

Colon cancer: Colon cancer is cancer that occurs in the cells of the colon. Colon cancer is quite common, being the third most common cancer in men and women in the U.S. About more than 110,000 people in the U.S. are diagnosed with colon cancer each year.

Endometrial cancer: Endometrial cancer refers to several types of malignancies that arise from the endometrial, or lining, of the uterus. Endometrial cancers are the most common gynaecologic cancers in the United States, with over 35,000 women diagnosed each year.

Kidney cancer: In this, tumor is produce in kidney. These are also called renal cell carcinoma. More than 208,500 cases of kidney cancer are diagnosed in the world each year.

Leukemia cancer: This type of cancer that starts in the stem cells of the bone marrow makes blood cells. Bone marrow is the very soft, spongy material that fills the middle of the bones. These are mainly two types:

1. Acute (rapidly developing)
2. Chronic (slowly developing)

About 98% of leukemia is acute.

Lung cancer: In the lung cancer cells of lungs tissues grow uncontrollably and form tumors. It is one of the most common types of cancer in occurring days. It is caused by smoking tobacco or by indirect exposure to tobacco smoke (passive smoking).

Pancreatic cancer: Pancreatic cancer is a malignant neoplasm of the pancreas. It is estimated that by the end of 2010 more than 43,000 individuals in the United States will be diagnosed with this

condition, and 36,800 will die from the disease. The prognosis is poor, with fewer than 5% of those diagnosed still alive five years after diagnosis. Pancreatic cancer is also called as silent killer cancer. The symptoms are usually nonspecific and varied [8].

Alternative cancer therapies Bring structure to the wide and fast changing universe of alternative therapies; the Office of Alternative Medicine groups them into seven categories [9];

1) Diet and nutrition,
2) Mind-body techniques,
3) Bio electromagnetic,
4) Alternative systems of medical practice (or traditional and folk remedies),
5) Pharmacologic and biologic treatments,
6) Manual healing methods,
7) Herbal medicine.

Herbal Medicine: Herbal plants are topically used in cancer treatment. Herbs come from Asia, Europe, Africa, and North America; some form of herbal medicine is found in most areas of the world [10, 11].

All part of plants is used commonly such as: stems, roots, leaves, seeds, flowers, fruits etc. Herbal plants are easily available in market. These are very effective and powerful for all types of diseases. Herbal drug are not show any types of side effects [12]. Herbal medicines can be classified into various basic types: Traditional Chinese Herbalism, which is part of Traditional Oriental Medicine, Ayurvedic herbalism, which is derived from Ayurveda, and Western Herbalism, which originally came from Greece and Rome to Europe and then spread to north and South America. Chinese and Ayurvedic Herbalism have developed into highly complex systems of diagnosis and treatment over the centuries [13]. Western Herbalism is today primarily a system of folk medicine. No medicine cures all types of cancer. But the best selected brings the best results. Here, we will find the best or good selected herbal drugs from Traditional Chinese Medicine (TCM).

Herbal Plants Used in Cancer Therapy:

The various plants are used in the cancer therapy are shown in **table 1**. These plants are very effective and give less side effects behalf of cancer. Herbal treatment is slow at very easy because herbal drugs and plants easily available in market.

TABLE 1: PLANTS PARTS AND ACTIVE CONSTITUENTS

NAME OF PLANTS	BOTANICAL NAME	PARTS USED	ACTIVE CONSTITUENTS
Podophyllum (Papri)	*Podophyllum hexandrum*	Roots and rhizomes	Podphyllotoxin
Podophyllum	*Podophyllum peltatum* L.	Roots and rhizomes	Etoposide, Teniposide
Camptotheca (happy tree)	*Camptotheca acuminata*	Bark, leaves and stem	Camptothecin, Topotecan, Irinotecan
Taxus	*Taxus brevifolia*	Bark	Taxol, Docetaxol
Vinca	*Catharanthus roseus*	Leaves and flowers	Vinblastin, Vincristin
Japanese Plum Yew	*Bleekeria vitensis*	Roots and rhizomes	Elliptinium
Cephalotaxus tree	*Cephalotaxus harringtonia* var. drupacea	Roots and rhizomes	Homoharringtonine
Bush willow	*Combretum caffrum*	Barks	Combretastatin A-4
Downy Birch	*Betula pubescens*	Barks, flowers, leaves and fruits	Betulinic acid
Erythroxylum	*Erythroxylum pervillei*	Leaves, flowers and fruits	Pervilleine A
Waginos (Amharic)	*Brucea antidysenterica*	Roots, leaves and stems	Bruceantin
Paud'arco	*T. Impetiginosa*	Stem bark and trunk wood	B-lapachone
Smooth thapsia	*Thapsia garganica* L.	Barks	Thapsigargin
Maytenus	*Maytenus serrata*	Leaves	Maytansine
Colchicum (Lilly)	*Colchicum autumnale* L.	Leaves and flowers	Colchicinesamide, Colchicines, Demecolcine
Crotalaria (Rattlebox)	*Crotalaria sessiliflora* L.	Fruits and leaves	Monocrotaline

Some plants which use in the treatment of cancer are very common and important such as Podophyllum, Camptotheca, Taxus, Vinca, Radish, Japanese Plum Yew, Bush willow, Downy Birch, Erythroxylum, Crotalaria (Rattlebox), Colchicum (Lilly), waginos (Aballo) (Amharic), Pau d'arco, Silphium, Maytenus etc.

i. **Podophyllum**: Podophyllum belongs to Berberidaceae family and roots or rhizomes are used of Podophyllum [13, 14]. Podphyllotoxin is the main constituent of that plant which are responsible for cancer treatment. In **figure 1a and b,** podophyllum flower and leaves are shown. Podophyllum is useful in treating many skin diseases and tumorous growths. It has acquired importance in recent years for its possible use in controlling skin cancer [15].

FIG. 1a: *PODOPHYLLUM HEXANDRUM*

FIG. 1b: *PODOPHYLLUM PELTATUM* L.

ii. **Camptotheca:** Camptotheca are belonging to Nyssaceae family and these are also known as happy tree, cancer tree, or tree of life [16]. Cancer tree is shown in **figure 2**. Researcher shows that topotecan and irinotecan hydrochloride are useful in treating breast cancers, ovarian cancer, colon cancer, malignant melanoma, small cell lung cancer, thyroid cancers, lymphomas and leukemia's [17, 18].

FIG. 2: *CAMPTOTHECA ACUMINATA* (CANCER TREE)

iii. **Taxus:** Taxol, Docetaxol are the active constituents of Taxus which belong to Taxaceae. These drugs are given to treat breast cancer, after combination anthracycline and cytoxan therapy. Leaves and fruit and others parts of taxus tree are shown in **figure 3**. Taxol is also used to treat ovarian cancer, lung cancer, head and neck cancer, bladder cancer [19, 20].

FIG. 3: *TAXUS BACCATA*

iv. **Vinca:** Vinca (*Catharanthus roseus*) belongs to Apocynaceae family shown in **figure 4**. Vinblastin and Vincristine are used in breast cancer which is obtained from *Catharanthus roseus* [21, 22].

FIG. 5: VINCA

v. **Japanese Plum Yew:** Elliptinium acetate is the main constituent of Japanese Plum Yew (*Bleekeria vitensis*) belonging to the Ellipticine Family shown in **figure 5.** Elliptinium acetate showed modest antitumor activity in previously treated patients with metastatic breast cancer [23].

FIG. 5: ELLIPTICINE

vi. **Cephalotaxus Tree:** Homoharringtonine is an alkaloid extracted from the branches and leaves of the Cephalotaxus tree (**figure 6**). This drug has been prescribed for acute myeloid leukaemia and is also now used in the treatment of other cancers and recently, these received clearance in the Western world for human use after the extensive clinical studies [24].

FIG. 6: HOMOHARRINGTONINE

vii. **Bush Willow:** Combretastatin A-4 phosphate and its disodium salt was extracted from Bush Willow (*Combretum caffrum)* shown in **figure 7**. Combretastatin A-4 is a microtubule destabilizing drug, vascular-targeting agent and a drug, designed to damage the vasculature (blood vessels) cancer tumors causing central necrosis [25].

FIG. 7: BUSH WILLOW (*COMBRETUM CAFFRUM*)

viii. **Downy Birch:** Downy Birch (*Betula pubescens*) is belonging to Dilleniaceae (**figure 8**). Betulinic acid is the main constituent of that plant which is responsible for cancer treatment. It is used in the treatment of epithelial tumors such as: breast carcinoma, colon carcinoma, small cell lung carcinoma and renal cell carcinoma as well as T-cell leukemia [26].

FIG. 8: DOWNY BIRCH (*BETULA PUBESCENS*)

ix. **Erythroxylum:** Erythroxylum is belonging to Erythroxylaceae family. Pervilleine A is an active constituent of Erythroxylum shown in **figure 9a and b.** Pervilleine A, a novel tropane alkaloid obtained from chloroform extract of *Erythroxylum pervillei* which shows anti cancer activity [27].

FIG. 9a: ERYTHROXYLUM LEAVES

FIG. 9b: ERYTHROXYLUM SEEDS

x. **Waginos (Amharic):** Waginos (*Brucea antidysenterica)* is belonging to Simaroubaceae family **(figure 10)**. Some researchers showed that Bruceantin is obtained from waginos in all type of cancer therapy [28, 29].

FIG. 10: WAGINOS (*BRUCEA ANTIDYSENTERICA*)

xi. **Paud'arco:** Paud'arco is a natural grown herb that is derived from the inner bark of the *Tabebuia Avellanedae* **(figure 11a)** or *Tabebuia Impetiginosa* **(figure 11b)** tree grown in South America. B-lapachone is an active constituent of Paud'arco which is used in cancer treatment [30, 31].

FIG. 11a: *TABEBUIA AVELLANEDAE*

FIG. 11b: *TABEBUIA IMPETIGINOSA*

xii. **Thapsia:** Thapsigargin is the main constituent of thapsia obtained through the *Thapsia garganica L.* which belongs to Umbelliferae family. Thapsia is also known as smooth thapsia exposed in **figure 12**. These are used in cancer therapy mostly for breast cancer, colon cancer and also lung cancer [32].

FIG. 12: SMOOTH THAPSIA (*THAPSIA GARGANICA* L.)

xiii. **Maytenus:** Maytansine is obtained from Maytenus (*Maytenus serrata)* and belong to Celastraceae family shown in **figure 13**. Maytansine, a highly cytotoxic natural product, failed as an anticancer agent in human clinical trials because of unacceptable systemic toxicity.

The potent cell killing ability of Maytansine can be used in a targeted delivery approach for the selective destruction of cancer cells. A series of new maytansinoids, bearing a disulfide or thiol substituent were synthesized. The targeted delivery of these maytansinoids, using monoclonal antibodies resulted in a high, specific killing of the targeted cells *in vitro* and remarkable antitumor activity *in vivo*. Maytansine-induced cytotoxicity was dependent upon the position of the cell in the cell cycle. Mitotic and G2 cells are most sensitive to this agent, while G1 phase cells are the most resistant, with S-phase cells being intermediate [33, 34].

FIG. 13: MAYTENUS (*MAYTENUS SERRATA*)

xiv. **Colchicum (Lilly):** Colchicum (Lilly) is a very attractive and beautiful common plant, easily available in market; this is obtained from *Colchicum autumnale* L. and belongs to Liliaceae family **(figure 14).** Active constituent of colchicum are: Colchicinesamide, Colchicines, Demecolcine which are used for cancer therapy [35, 36].

FIG. 14: COLCHICUM (*COLCHICUM AUTUMNALE* L.) KNOWN AS "LILLY"

xv. **Crotalaria (Rattlebox):** Crotalaria (rattlebox) is common name of *Crotalaria sessiliflora* L. which belong to fabaceae (Legume) family shown in **figure 15**. Monocrotaline is obtained through the *Crotalaria sessiliflora* L. which are responsible for cancer treatment [37].

FIG. 15: CROTALARIA (RATTLEBOX) (*CROTALARIA SESSILIFLORA* L.)

CONCLUSION: From the above discussion, it can be concluded that the alternative treatment of cancer therapy is very common by herbal medicines. These are very effective and commonly used therapy for cancer treatment.

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