

Herbal Drugs Used in Treatment of Cancer

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ABSTRACT

Cancer is one of the leading causes of death and globally the numbers of cases of cancer are increasing gradually. There are several medicines available in the market to treat the various types of cancer but no drug is found to be fully effective and safe. The major problem in the cancer chemotherapy is the toxicity of the established drugs. However plants and plant derived products have proved effective and safe in the treatment and management of cancers. These days most of the research work on cancer drugs is targeted on plants and plants derived natural products. Many natural products and their analogues have been identified as potent anti-cancer agents and day by day the anti-cancer property of various plants is being identified. Here an attempt is being made through this review to highlights the natural products and their analogues established as anti-cancer agents and the new plant species identified with anti-cancer properties either in vivo or in vitro.

Keywords: Cancer, Chemotherapy and anti-cancer agents.

INTRODUCTION

Cancer is a major public health burden in both developed and developing countries. It is an abnormal growth of cells in body that can lead to death. Cancer cells usually invade and destroy normal cells. These cells are born due to imbalance in the body and by correcting this imbalance, the cancer may be treated. Billions of dollars have been spent on cancer research and yet we do not understand exactly what cancer is. Every year, millions of people are diagnosed with cancer, leading to death. According to the American Cancer Society, deaths arising from cancer constitute 2–3% of the annual deaths recorded worldwide. Thus cancer kills about 3500 million people annually all over the world. Several chemo preventive agents are used to treat cancer, but they cause toxicity that restricts their usage¹.

What is cancer?

Cancer is malignant growth, formed by the abnormal rapid reproduction of cell. Cancerous cell invasiveness particular properties. The first known as invasiveness is the capacity in filtrate and destroy adjacent organ.

For example - A cancer of the bowel may spread into bladder. The second is ability to form a secondary deposited in distant part of body. Cancer cell break off from the parent growth and

are carried usually in the blood stream to another organs, where they begin to reproduced and form addition tumor masses².

What Causes Cancer?

Cancer begins with mutations in DNA, which instructs the cells how to grow and divide. Normal cells have the ability to repair most of the mutations in their DNA, but the mutation which is not repaired and causing the cells to grow becomes cancerous³.

➤ Types of Cancer

Cancers may be classified by their primary site of origin or by their histological or tissue types.

Classification by site of origin

By primary site of origin, cancers may be of specific types like breast cancer, lung cancer, prostate cancer, liver cancer renal cell carcinoma (kidney cancer), oral cancer, brain cancer etc.

➤ Classification by tissue types

The international standard for the classification and nomenclature of histologies is the International Classification of Diseases for Oncology, Third Edition (ICD-O-3). This classification is based on the ICD-O-3.

Based on tissue types cancers may be classified into six major categories:

1. Carcinoma⁴



This type of cancer originates from the epithelial layer of cells that form the lining of external parts of the body or the internal linings of organs within the body.

Carcinomas, malignancies of epithelial tissue, account for 80 to 90 percent of all cancer cases since epithelial tissues are most abundantly found in the body from being present in the skin to the covering and lining of organs and internal passageways, such as the gastrointestinal tract. Carcinomas usually affect organs or glands capable of secretion including breast, lungs, bladder, colon and prostate.

Carcinomas are of two types

Adenocarcinoma and squamous cell carcinoma. Adenocarcinoma develops in an organ or gland and squamous cell carcinoma originates in squamous epithelium. Adenocarcinomas may affect mucus membranes and are first seen as a thickened plaque-like white mucosa. These are rapidly spreading cancers.

2. Sarcoma⁵

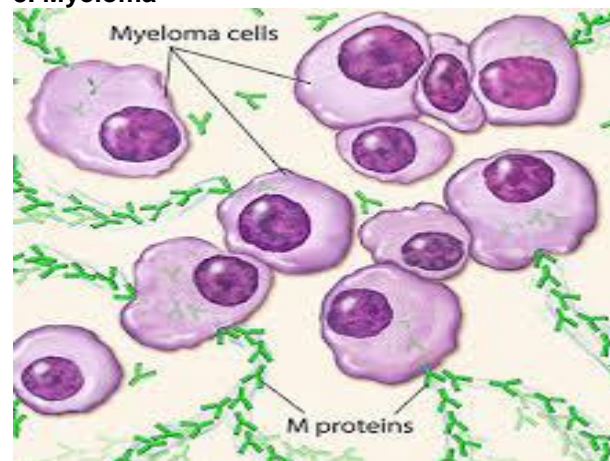


These cancers originate in connective and supportive tissues including muscles, bones, cartilage and fat. Bone cancer is one of the sarcomas termed osteosarcoma. It affects the

young most commonly. Sarcomas appear like the tissue in which they grow.

Other examples include chondrosarcoma (of the cartilage), leiomyosarcoma (smooth muscles), rhabdomyosarcoma (skeletal muscles), Mesothelial sarcoma or mesothelioma (membranous lining of body cavities), Fibrosarcoma (fibrous tissue), Angiosarcoma or hemangioendothelioma (blood vessels), Liposarcoma (adipose or fatty tissue), Glioma or astrocytoma (neurogenic connective tissue found in the brain), Myxosarcoma (primitive embryonic connective tissue) and Mesenchymous or mixed mesodermal tumor (mixed connective tissue types).

3. Myeloma⁶



These originate in the plasma cells of bone marrow. Plasma cells are capable of producing various antibodies in response to infections. Myeloma is a type of blood cancer.

4. Leukemia⁷



This is a group of cancers that are grouped within blood cancers. These cancers affect the bone marrow which is the site for blood cell

production. When cancerous, the bone marrow begins to produce excessive immature white blood cells that fail to perform their usual actions and the patient is often prone to infection.

Types of leukemia include

Acute myelocytic leukemia (AML) – these are malignancy of the myeloid and granulocytic white blood cell series seen in childhood.

Chronic myelocytic leukemia (CML) – this is seen in adulthood.

Acute Lymphatic, lymphocytic, or lymphoblastic leukemia (ALL) – these are malignancy of the lymphoid and lymphocytic blood cell series seen in childhood and young adults.

Chronic Lymphatic, lymphocytic, or lymphoblastic leukemia (CLL) – this is seen in the elderly. Polycythemia Vera or erythremia – this is cancer of various blood cell products with a predominance of red blood cells.

5. Lymphoma⁸



These are cancers of the lymphatic system. Unlike the leukemias, which affect the blood and are called “liquid cancers”, lymphomas are “solid cancers”. These may affect lymph nodes at specific sites like stomach, brain, intestines etc. These lymphomas are referred to as extranodal lymphomas.

Lymphomas may be of two types – Hodgkin's lymphoma and Non-Hodgkin's lymphomas. In Hodgkin lymphoma there is characteristic presence of Reed-Sternberg cells in the tissue samples which are not present in Non-Hodgkin lymphoma.

6. Mixed types

These have two or more components of the cancer. Some of the examples include mixed mesodermal tumor, carcinosarcoma,

adenosquamous carcinoma and teratocarcinoma. Blastomas are another type that involves embryonic tissues.

Classification by grade

Cancers can also be classified according to grade. The abnormality of the cells with respect to surrounding normal tissues determines the grade of the cancer. Increasing abnormality increases the grade, from 1–4.

Cells that are well differentiated closely resemble normal specialized cells and belong to low grade tumors. Cells that are undifferentiated are highly abnormal with respect to surrounding tissues. These are high grade tumors.

Grade 1 – well differentiated cells with slight abnormality

Grade 2 – cells are moderately differentiated and slightly more abnormal

Grade 3 – cells are poorly differentiated and very abnormal

Grade 4 – cells are immature and primitive and undifferentiated.

Classification by stage

Cancers are also classified individually according to their stage. There are several types of staging methods. The most commonly used method uses classification in terms of tumor size (T), the degree of regional spread or node involvement (N), and distant metastasis (M). This is called the TNM staging.

For example, T0 signifies no evidence of tumor, T 1 to 4 signifies increasing tumor size and involvement and T is signifies carcinoma in situ or limited to surface cells. Similarly N0 signifies no nodal involvement and N 1 to 4 signifies increasing degrees of lymph node involvement. Nx signifies that node involvement cannot be assessed. Metastasis is further classified into two – M0 signifies no evidence of distant spread while M1 signifies evidence of distant spread.

Stages may be divided according to the TNM staging classification. Stage 0 indicates cancer being in situ or limited to surface cells while stage I indicates cancer being limited to the tissue of origin. Stage II indicates limited local spread; Stage II indicates extensive local and regional spread while stage IV is advanced cancer with distant spread and metastasis^{9, 10, 11}.

ROLE OF HERBAL PLANTS AS MEDICINAL AND ANTI-CANCER AGENT

Plants, since ancient time, are using for health benefits by all cultures as well as source of medicines. It has been estimated that about 80-

85% of global population rely on traditional medicines for their primarily health care needs and it is assumed that a major part of traditional therapy involves the use of plant extracts or their active principles^{12, 13, 14}. Although a lot of recent investigations have been carried out for advancements in the treatment and control of cancer progression, significant work and room for improvement remain. The main disadvantages of synthetic drugs are the associated side effects. However natural therapies, such as the use of the plants or plant derived natural products are being beneficial to combat cancer. The search for anti-cancer agents from plant sources started in the 1950s when discovery and development of the vinca alkaloids (vinblastin and vincristine), and the isolation of the cytotoxic podophyllotoxins was carried out¹⁵.

Example of Herbal Drugs Using Anti-cancer Agent

1. *Catharanthus roseus* (Vinca Alkaloid)
2. *Adhatoda zeylanica*
3. *Acorus calamus*
4. *Anona squamosa*
5. *Bacopa monnieri*

1. Vinca Alkaloids¹⁶

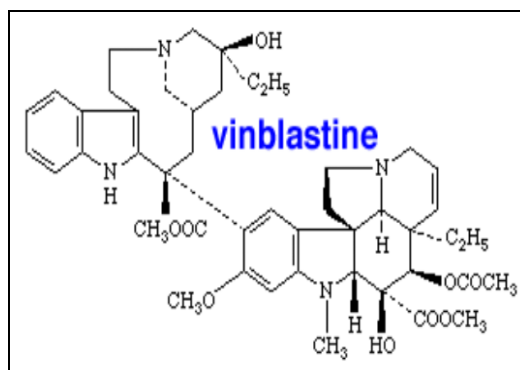
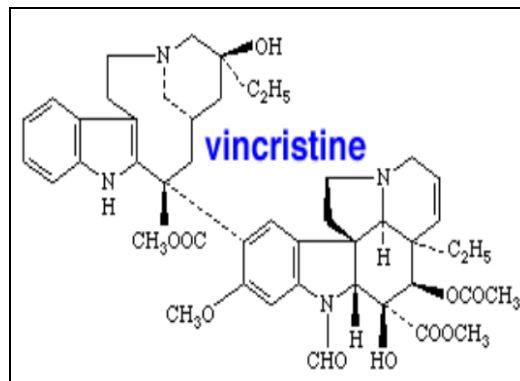


Fig- Flowers of Vinca

Synonym: - Catharanthus and Periwinkle.

Biological source: - It is dried whole plant of *Catharanthus roseus*, belonging to family Apocynaceae.

Chemical constituents: - A large no. of Indol alkaloids is present in vinca. Vinblastin and Vincristine¹⁷ are major constitution of vinca.



Uses- Vinca is used to extract Vincristine and Vinblastin. Vincristine sulphate is an anti-neoplastic agent which act by arresting mitosis at the metaphase¹⁸.

The first agents introduced in clinical use were vinca alkaloids, Vinblastin (VLB) and Vincristine (VCR), isolated from the *Catharanthus roseus* G. Don. (Apocynaceae). These drugs were discovered during an investigation for oral hypoglycemic agents. While research investigators could not confirm this activity, it was noted that plant extracts reduced significantly white blood cell counts and also caused bone marrow depression in rats. Plant extract also prolong the life of mice bearing a transplantable lymphocytic leukemia. Further extraction and fractionation led to the isolation of two active alkaloids namely Vincristine and Vinblastin. The plant was originally endemic to Madagascar, but the samples used in the discovery of Vincristine and Vinblastin were collected in Philippines and the Jamaica. Recently semi-synthetic analogues of vinca alkaloids are Vinorelbine (VRLB) and vindesine (VDS). These are primarily using alone or in combination with other chemotherapeutic drugs to combat a variety of cancers. VLB is using for the treatment of lymphomas, leukemias, breast cancer, testicular cancer, lung cancers, and

Kaposi's sarcoma. VCR had also showed efficacy against leukemia, particularly acute lymphocytic leukemia in childhood. Of over 2069 anti-cancer clinical trials recorded by the National Cancer Institute as being in progress as of July 2004, over 160 are drug combinations including these agents against a range of cancers¹⁹.

2. *Adhatoda zeylanica*²⁰



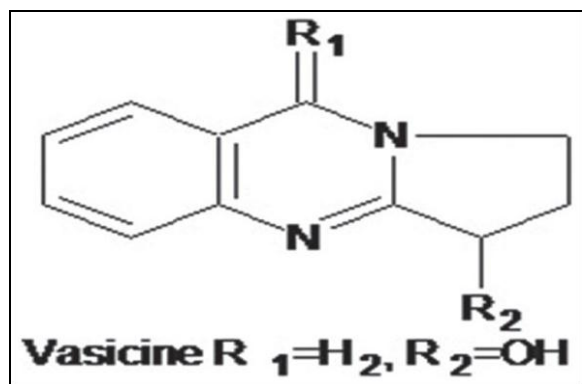
Fig- Flowers of Vasaka.

Synonym- *Justica adhatoda*.

Biological source:- It consists of dried, as well as fresh leaves of the plant *Adhatoda vasica* belonging to family *acanthaceae*, and contain not less than 0.6% of vasicine on dried basis.

Chemical constituents:- *vasaka* leaves contain quinazolin derivatives such as vasicine, vasicinon and 6-hydroxy vasicin. This drug also contains volatile oil, betain and vasakin²¹.

Plant is occurring commonly in wasteland, stony land, scrub forest and road side almost throughout India, ascending to 1204-1300 meter in the Himalayas generally in tropical and sub tropical region²².



Uses- The drug is considered to possess anti-cancer property as it is recommended in chest cancer. given specifically for checking the

complications in stage of blood vomiting and other symptoms²³.

3. *Acorus calamus*²⁴



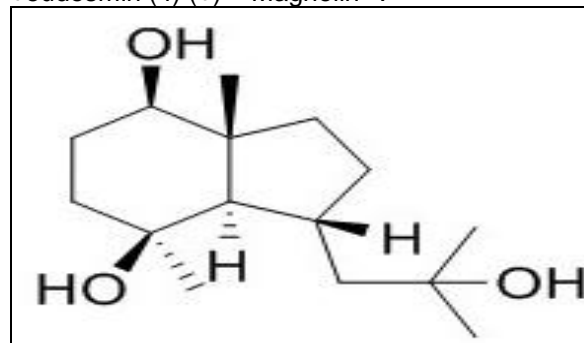
Fig- *Acorus calamus*

Synonyms- Calais, Bach, Ghoda Vaj.

Biological source- These are the dried rhizomes of the plant as *Acorus calamus* Linn, belonging to family *Araceae*. It contains not less than 1.5% of volatile oil.

Chemical Constituents:- The drugs contain 1.5% to 3.5% of volatile oil. Volatile oil contains Asaraldehyde and the other constituents of the oil are Asaroni and Eugenol²⁵.

Major Chemical constituents- (1) 4 Beta, 7 Alpha trihydroxyindenesunane (2) Bullatantriol (3) + eudesmin (4) (+) - Magnolin²⁶.



Bullatantriol

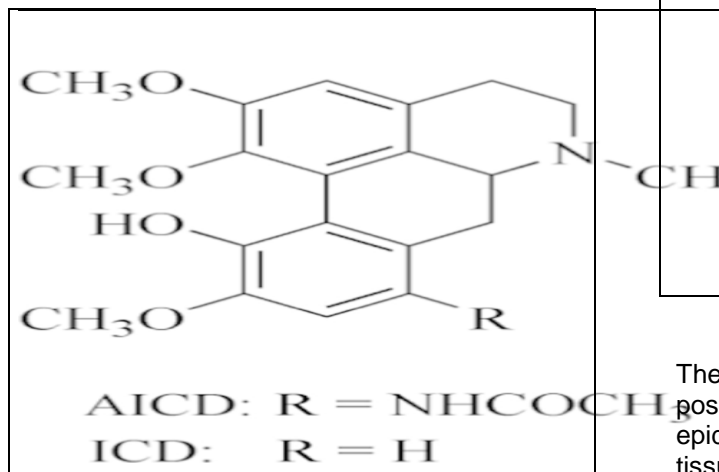
Uses- The drug is considered to possess anti-cancer properties and it is used in the treatment of cancer²⁷.

4. *Anona squamosa* Linn.²⁸



Fig- Sitaphala

The Plant contain a large number of compounds anonaine, reomerine, norcordine, cordine, norisocorydile, isocorydine²⁹, giaucine (+) – xylopine, (+) –o-mehtydrmepavine, lanuginosine.



ISOCORYDINE

Amongst above apocrine alkaloids anonaine, recmerine, norcodyne and corydine reported to anti-cancer activity against human epidermal carcinoma of the naasopharynsxc in tissue culture³⁰.

5. *Bacopa monnieri* (L.) Pennel.³¹



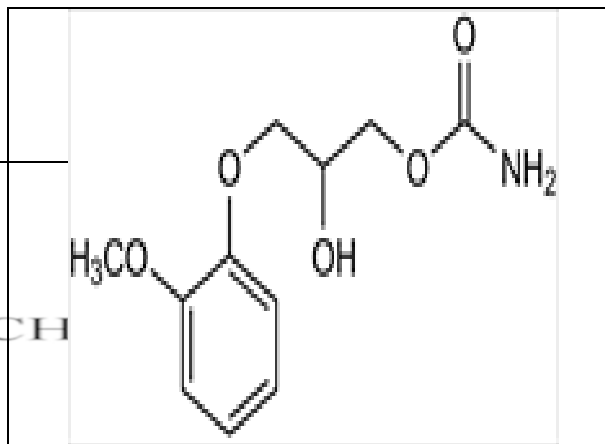
Fig-Flowers of Brahmi

Scrophulariaceae

Brahmi and Aindri.

Brahmi, Birmi, Jainim and Brahmi Booti

The Alkaloids brahmine, herpestine are reported in earlier Phytochemical investigations. Beside these alkaloids betulic acid, sigmasterol, B-sitosterol, d-memitol and two types of sapsins namely bacoside A and bacoside B are found in further screenings which record other data on chemical constituents.



D-MEMITOL

The alcoholic extract of the whole plant possesses anti-cancer activity in human epidermal carcinoma of the nasopharynx in tissue culture³².

CONCLUSION

This review paper provides information on herbs and natural products with potential to decrease growth of cancer or be used as adjuvant with cancer treatments for patients who already have or have had cancer. Review of literature indicates that medicinal herbs have rich anti-cancer potential and on the forefront whenever we talk about anti-cancer remedies, are significant source of synthetic and/or herbal origin. Natural products discovered from medicinal plants have played an important role in the treatment of cancer. They have exhibited anti-cancer activity in animal models of leukemia, skin cancer and sarcomas. Through generating awareness regarding usage of herbs and exploring natural product properties, healthcare professionals, can play significant clinical roles as knowledge resources for masses. From information from this review health care professionals can initiate discussion with colleagues to determine whether patient may benefit from taking a specific herb or natural product. Cancer being associated with high mortality rates if herbs can be used even in the palliative care or to reduce the side effects associated with cancer would be of great relief for the sufferer.

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