

A Review on Plant and Plant Derived Compounds as Anti-Cancer Agents

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ABSTRACT: Cancer is the cause of death all over the world and the number of deaths due to cancer has been increasing at a very high rate and it has become a global threat. The causes of cancer may be environmental or genetic or other prolonged diseases. 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 problems 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 cancer. These days, most of the research work on cancer drugs is targeted on plants and plant derived natural products. Many natural products and their analogues have been identified as potential anti-cancer agents and day by day, the anti-cancer property of various plants is being identified. Here, an attempt is made to review and analyse some of the plants and their products to look into their anti-cancer activities by targeting the inhibition of the mode of development of cancer cells and their effect on normal cells.

KEYWORDS: Cancer cells, Chemotherapy, Natural products, Anti-cancer agents, Carcinoma.

I. INTRODUCTION

Cancer is a general term applied to a series of malignant diseases that may affect different parts of body. These diseases are characterised by a rapid and uncontrolled formation of abnormal cells which may mass together to form an abnormal mass or tumour and proliferate throughout the body initiating abnormal growth at other sides. If the process is not arrested, it progresses until it causes the death of the organism. 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. Several chemo-preventive agents are used to treat cancer but these cause toxicity, which restricts their usage.

II. RELATED WORK

A. Causes of cancer

Cancer begins with mutation in DNA which instructs the cells how to grow and divide. Normal cells have ability to repair most of the mutations in their DNA, but the mutations that are not repaired and causing the cells to grow and become cancerous [1].

A.1.Environmental factors

Environmental factors which form a scientist's standpoint include tobacco smoking and tobacco chewing for longer durations, exposure to ionising radiations for longer periods, exposure to carcinogenic chemicals, radioactive materials and other specific substances even exposed at low levels. Even passive tobacco smoke [1] increases the risk of cancer.

A.2. Genetic factors

The hereditary transmission of gene mutations may cause the carcinogenic problems in the coming generations. The changes in gene material may occur in people with certain genetic background as illustrated by the findings of genes associated with some cases of cancer and family's prevalence of certain cancer transmissions.

A.3.Other factors

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Persons infected by chronic viruses such as viral hepatitis may lead to liver cancer, HIV may lead to lymphoma. Similarly prolonged infections and wounds could also be carcinogenic.

B. Types of cancers

B.1. Cancers of blood and lymphatic systems

These include Hodgkin's disease, Leukemias, lymphoma, multiple myeloma, waldenstroms disease.

B.2. Skin cancers

It is malignant melanoma.

B.3. Cancers of digestive systems

These include oesophageal cancers, stomach cancer, cancer of pancreas, liver cancer, colon and rectal cancer and anal cancer.

B.4. Cancers of urinary system

These include kidney cancer, bladder cancer, testis cancer and prostate cancer.

B.5. Cancers in women

These include breast cancer, ovarian cancer, gynaecological cancer and chorio-carcinoma.

B.6. Miscellaneous cancers

These include brain cancer, bone cancer, carcinoid cancer, nasopharyngeal cancer, retroperitoneal sarcomas, soft tissue cancer and thyroid cancer.

C. Medical treatment available

C.1. Radiotherapy.

This treatment is used to cure tumours, cancerous malignant tissues, or other outgrowths by irradiating these areas with high energy radiations like gamma rays. These rays break down cancer cells and prevent their proliferation. But this therapy has drawback that radiations affect normal cells also and may cause other ailments.

C.2. Chemotherapy

It is the treatment of cancer by using chemical drugs. A large number of drugs have been synthesised with a wide range of activity for different stages of cancer. A few are listed below. Cis-platin, cis-platin derivatives, Taxol and its derivatives, camptothecin, podophylotoxin, Vinblastin, vincristine, topotecan, etoposide, Teniposide. The problem with synthetic chemotherapeutic drugs is that these exhibit severe toxicity on normal tissues, may cause hair loss, low blood count, liver toxicity and retarded metabolism.

D. Mechanism of cancer therapy

The drugs used to cure cancer work as per following mechanism:

- a) Inhibiting cancer cell proliferation directly by stimulating macrophage phagocytosis, enhancing natural killer cell activity.
- b) Promoting apoptosis of cancer cells of increasing production of interferon, interleukin-2, immunoglobulin and complement in blood serum.
- c) Enforcing the necrosis of tumour and inhibiting its translocation and spread of blocking the blood source of tumour tissue.
- d) Enhancing the number of leukocytes and platelets by stimulating the haemopoietic function.
- e) Promoting the reverse transformation from tumour cells in the normal cells.
- f) Promoting metabolism and preventing carcinogenesis of normal cells.
- g) Stimulating appetite, improving quality of sleep, relieving pain thus benefiting patient's health.

III PLANTS EFFECTIVE AS ANTI CANCER AGENTS

Considering the toxicity of chemotherapeutic drugs, focus is made on herbal plants for the cure of cancer

a) *Achyranthes aspera* (Family- Amaranthaceae)

It is a common weed found on road sides throughout the India. Its methanol extract containing alkaloid, non-alkaloid and saponious fractions has been found to show significant inhibitory activity[2]. In vivo two-stage mouse skin carcinogenesis test the total methanol extract possessed pronounced cytotoxic activity[3]

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b) **Allium sativum (Family-Allium)**

Allium Sativum (garlic) has been used for thousands of years to treat various diseases. It contains more than 100 biologically useful secondary metabolites which include allin, allinase, allicin, S-allyl cysteine, Di allyl disulphide, etc. Garlic extracts have been found to prevent prostaglandin dependent cancers by inhibiting lipoxygenase and cyclo-oxygenase enzymes. Extracts of *Allium Sativum* inhibit genesis as well as growth of cancer by enhancing activity of the natural killer cells and the macro phages. Studies have shown that the extract increases count of suppressor T cells and make the lymphocytes more cytotoxic to cancerous cells. It also inhibits metastases by preventing adhesion of the circulating cancerous cells to the blood vessels. It also protects DNA from damaging effect of carcinogens, increases activity of detoxifying enzymes, speeds up excretion of chemical carcinogens and enhances immunity of the body. It also inhibits growth of many cancers including those of breast, bladder, skin, colon, oesophagus, stomach and lungs[4]. The research done at National Medical centre and Hospital, Japan has revealed that garlic extract reduces the side effects of radio and chemotherapy.

c) **Actinidia chinensis**

Actinidia chinensis roots are used by Chinese physicians for the treatment of cancer. It contains polysaccharides known as ACPR that possess immunity enhancing and anti-cancer activities[5]

d) **Aloe vera**

Aloe vera contains aloe-emodum which activates the macro phages to fight cancer. *Aloe vera* also contains acemannan which enhances the activity of immune cells against cancer[6]. *Aloe vera* is found to inhibit metastasis[7].

e) **Annona muricata**

Annona muricata is found to contain a class of medicinal compounds, the acetogenins. Acetogenins block production of ATP which inhibits the pump that removes the cancer drugs from the cell, allowing chemotherapy to be more effective. Acetogenins are found to possess significant cytotoxic activity against leukaemia and sarcoma[8].

f) **Arctium lappa**

Arctium lappa contains potential anti-cancer factors that prevent mutations in the oncogens. It has been used in the treatment of malignant melanoma, lymphoma and cancers of pancreas, breast, ovaries, oesophagus, bladder, bile duct, and bone. A study revealed that it reduces the size of tumour, relieves the pain and prolongs the survival period[9].

g) **Betula utilis**

Betula utilis contains botulin that can be easily converted into betulinic acid. Studies have revealed that betulinic acid inhibits the growth of malignant melanoma and cancers of liver and lungs.

h) **Bidens pilosa**

The extracts of *Bidens pilosa* on fractionation has led to isolation and characterisation of potential compound phenyl-1,3,5 hepta triyne, which shows significant anti-tumour activity.[10]

i) **Colchicum luteum**

Colchicum luteum contains tropolone groups of alkaloid colchicines which show antimitotic activity and are used cancer for for the dispersal of tumours and for treatment of various neoplastic diseases[11].

j) **Combretum cafferum**

This plant contains combretastatin which has been isolated recently. Combretastatin executes its therapeutic action against cancer by inhibiting blood supply to the tumour.

k) **Camptotheca acuminata**

From the seeds of plant *Camptotheca acuminata* [12] the compound camptothecin, a pyridoindole alkaloid has been isolated which has good anti-cancer activity. Derivatives of *Camptotheca acuminata* such as 18-OH-camptothecin, 11-OH-camptothecin and 10-OH-camptothecin have been found to possess strong anti leukemic activity [13][14].

l) **Daphne mezereum**

This plant is widely used as remedy for treating cancer like symptoms. A hydro alcohol extract of plant exhibited a potent anti-leukemic activity against lymphocytic leukaemia in mice. Further fractionation studies

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on the extract resulted in the isolation and characterisation of mezerein as a potent anti-leukemic compound[15].

m) **Gyrophora esculenta**

It is a mushroom that inhibits growth of cancer by enhancing activity of natural killer cells. A study revealed that it inhibits carcinogenesis and metastasis[16].

n) **Lentinus edodes**

Lentinan, a β -glucan shiitake mushrooms, has been shown to possess anti-tumour activity. It was active against lung carcinoma [17]. It is thought that lentinan has its effects by activating the host immune system. Lentinin stimulates increased production and activity of natural killer cells and macrophages which destroy tumour cells[18].

o) **Panax ginseng**

Studies suggest that ginseng may lower the risks of cancer in humans. Ginseng inhibits growth of cancer by interfering with DNA synthesis. The plant contains several active constituents; the main active ingredients in ginseng root are thought to be a family of 6-triterpene saponins called ginsenosides[18][19][20].

p) **Mentha species**

Mentha species such as *Mentha piperita*, *Mentha longifolia* and *Mentha aquatic* contain phenolic antioxidants that prevent reoccurrence of cancer. The essential oils exhibit OH radical scavenging activity, reducing OH radical generation in Fenton reaction by 24%. The most powerful scavenging compounds in the *Mentha piperita* oil were mono terpene ketones. Spear mint tea causes inhibition of carcinogen activities by direct effects on activated metabolites. [21]

q) **Zingiber officinalis**

Zingiber officinalis (ginger) rhizomes offer a rich package of gingerols – phenolic antioxidants that possess pronounced anti-inflammatory activity that inhibits various cancers. Ginger also contains curcumin, which assists in the elimination of cancer causing substances from the body. The anti-cancer properties of ginger are attributed to the presence of certain pungent vallinoids like 6-gingerol and 6-paradol as well as some other constituents like shogaols, Zingerone, etc. A number of mechanisms that may be involved in the chemo preventive effects of ginger and its components have been reported from the laboratory studies in a wide range of experimental models [22][23].

IV. SOME PLANT DERRIVED ANTI-CANCER AGENTS

a) **Vinca alkaloids**

The vinca alkaloids- vinblastine and vincristine isolated from the species *Catharanthus roseus* has yielded good result on mice. They prolonged the life of mice suffering from lymphocytic leukaemia. Semi synthetic analogues of vinca alkaloids vinorelbine and vindesine are finding use in treatment of lymphomas, leukaemia, breast cancer, testicular cancer, lung cancer, etc.

b) **Podophyllotoxin derivatives**

The podophyllotoxin derivatives obtained from plants podophyllum peltatum linn has been used to combat lymphomas, bronchial and testicular cancers.

c) **Taxanes**

A more recent advancement in the development of plant derived chemotherapeutic agents in the development of a class of molecules called taxanes. Paclitaxol also named as taxol isolated from the bark of *Texas brevifolia*. Paclitaxol is used in the treatment of wide variety of cancers including breast cancer, ovarian and lung cancer. Docetaxol, a semi-synthetic derivative is primarily used in the treatment of breast cancer.[24]

d) **Camptothecin derivatives**

These are isolated from Chinese tree *Camptotheca acuminata*. Its various plant extracts have been tested for anti-tumour activity.

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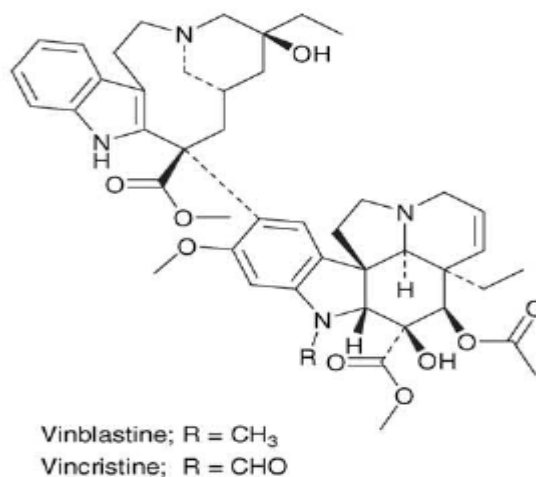
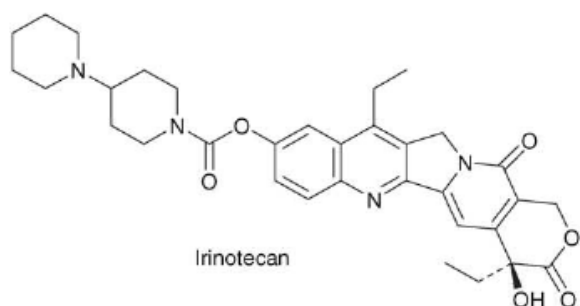
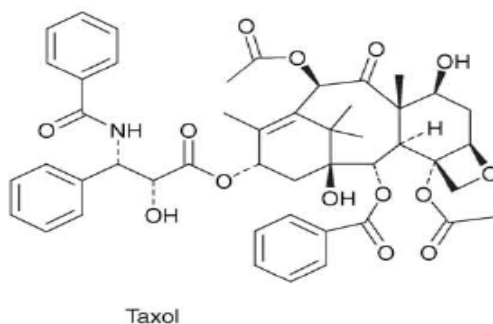
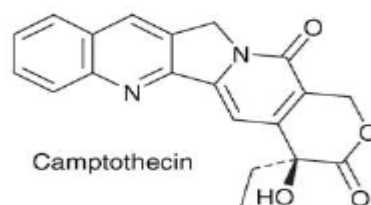
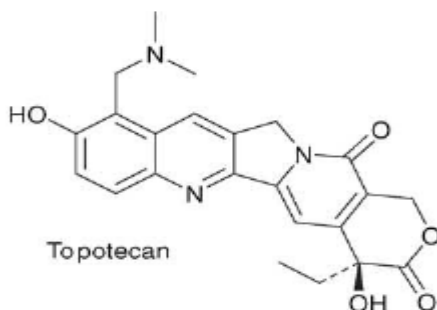
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e) Homoharringtonine

This is obtained from the tree *Cephalotaxa harringtonia*. Purified homoharringtonine has shown efficiency against various leukaemias including some resistant to standard treatment and has been reported to produce complete hematologic remission in patients with late chronic phase chronic myelogenous leukaemia.

Plant derived anti-cancer agents

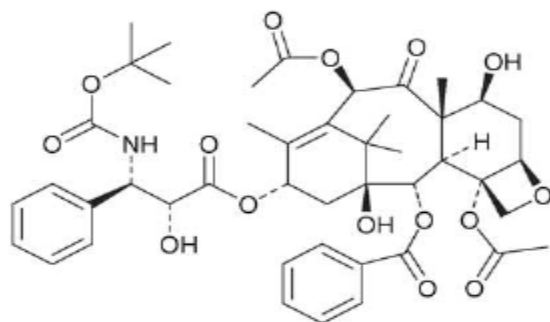


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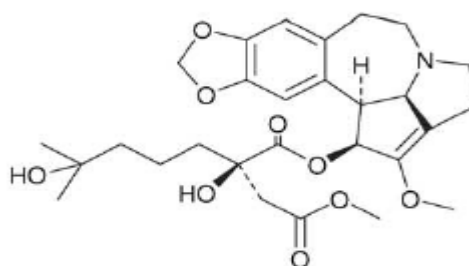
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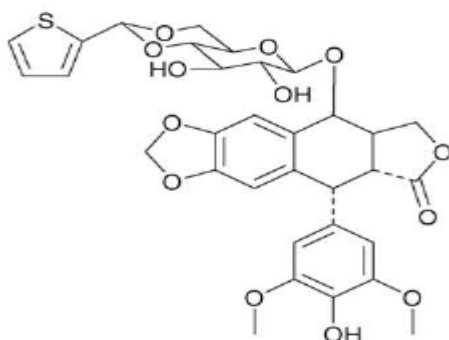
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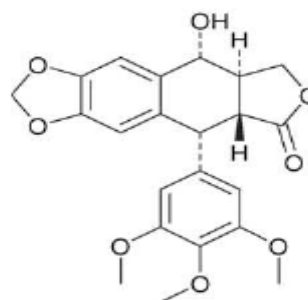
Docetaxel



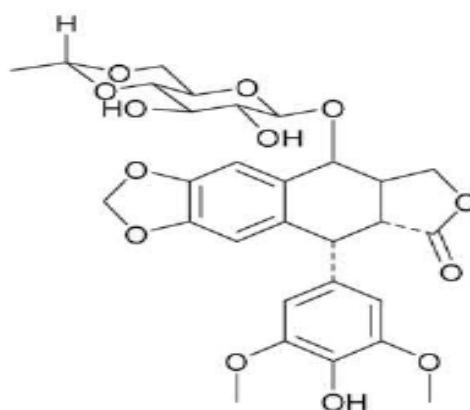
Homoharringtonine



Teniposide



Podophyllotoxin



Etoposide

V. DISCUSSION

Science has long acknowledged the value of healing substances found in nature. Experiments on living cells and animals demonstrated the anti-cancer role of herbal drugs by inducing apoptosis and differentiation, thereby enhancing the immune system, inhibiting angiogenesis and reversing multi drug resistance. However, the mechanism of anticancer role has not yet been fully elucidated. Further research is needed to explore the molecular mechanism of

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herbal drugs. Although clinical trials have showed that herbs were helpful against cancer, these outcomes require further confirmation with controlled trials focussing on anti-cancer effects of herbal formulae. Some herbs may cause serious toxicity when taken excessively or under inappropriate circumstances. Rigorous research is needed to discover the derivatives which can potentially control the DNA causing carcinogenic activity, breakdown of carcinogenic cells and to save the normal cells from the attack of carcinogenic cells. The algorithm automatically generates mask image without user interaction that contains only text regions to be inpainted.

VI. CONCLUSION

Medicinal plants maintain the health and vitality of individual and also cure various diseases. It is documented that medicinal herbs have rich anti-cancer potential. Natural products discovered from medicinal plants have played an important role in the treatment of cancer. These have exhibited anticancer activity in animal models leukaemia, skin cancer and sarcomas. Through generating awareness regarding the usage of herbs and exploring natural product properties. Selected plants have been explored for biological activity and further investigation into anticancer activity of plants is showing promising activity. The alkaloids such as vinca alkaloids, podophyllotoxin derivatives, taxanes, camptothecin derivatives and homoharringtonine derivatives have figured high in the therapeutic segment of cancer. Since cancer being associated with high mortality rate, if herbs can be used even in the palliative care or to reduce the side-effects associated with cancer, it would be a great relief for the sufferer.

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