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A Review On : Herbal Anticancer Drug

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ABSTRACT

Cancer is major health problem in both developed 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. Plant-derived compounds have been an important source of several clinically useful anti-cancer agents. Plant has been the beacon of therapeutic sources for curing diseases from times immemorial. Medicinal plant with their isolated lead molecules is also used as an alternative medicine for treating cancer. These chemical compounds are formulated with a view to create effective drugs against cancer. Vincristine, Vinblastine, Homoharringtonine, Honokiol, Paclitaxel, Topotecan, Maytansine, Astraguoside, Docetaxel, Elliticine, Lapochel, Oleanolic acid, Cisplatin, Etoposide, Teniposide and Resveratrol this lead molecules isolated from different medicinal plants are in use to treat cancer and chemotherapeutic side effect. In the present review, an attempt has been made to study the plants that have been used in the treatment of cancer.

Keywords: Cancer, Anti-Cancer Drugs, Vincristine, Paclitaxel

I. INTRODUCTION

In recent times, medicinal plants occupy an important position for being the paramount sources of drug discovery, irrespective of its categorized groups- herb, shrub or tree. Plants have been indispensable in treating diverse forms of diseases including cancer. According to World Health Organisation, 80% of the people living in the rural areas depend on medicinal plants as primary health care system. These practices are solely based on the knowledge of traditional use of medicinal plants. Natural products are formulated to generate different types of effective drugs to enhance anticancer activities. Proper understanding of the complex synergistic interaction of various constituent of anticancer herbs would help in formulating the design to attack the cancerous cells without harming the normal cells of the body.

India is the largest producer of medicinal plants and is rightly called the "Botanical garden of the World". And have many of plant used in cancer. The search for this cancer drug discovery from Natural sources began with the investigations done by Hartwell and his co-workers in the late 1960's with the application of Podophyllotoxin and its derivatives from the plant Podophyllium peltatum. Further discoveries lead to isolate anticancer compound from plants like Catharanthus roseus, Camptotheca acuminate, Lapacho,Cephalotaxusharringtonia, Mangnoliagrandifloraand Taxus brevifoliabark are the established potential anticancer agents derived from these plants which are found to be effective against various types of cancer.

To the scientific mind, these translate easily into ideas. Numbers and standard letters such as n are also in the mathematical with 100s of applications and websites, allowing you to put Equations Everywhere and Anywhere.

LEUKEMIA used in leukemia therapy.

Vincristine, Vinblastine, Homoharringtonine and Honokiol this drug are Leukemia is a group of cancers that originate from blood-forming tissues. The name of the disease is derived from the Greek word 'leukos' for 'white blood' Leukemia is classified into four main

categories or subtypes according to cell type and rate of growth: acute lymphocytic leukemia (ALL) derived from immature T- or B-lymphocytes, most common in children; acute myeloid leukemia (AML) from immature myeloid cells, most common in adults; chronic lymphocytic leukemia (CLL) from mature B-lymphocytes, mostly an adult disorder; and chronic myelogenous leukemia (CML) from granulocyte precursors, most common in adults.

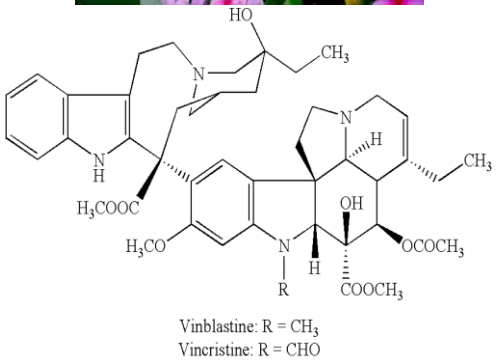
Vincristine works partly by binding to the tubulin protein, stopping the cell from separating its chromosomes during the metaphase; the cell then undergoes apoptosis.[1] **Vinblastine** at very low concentrations they suppress microtubule dynamics and at higher concentrations they reduce microtubule polymer mass.[2]

Homoharringtonine is a protein translation inhibitor. It inhibits protein translation by preventing the initial elongation step of protein synthesis. It interacts with the ribosomal A-site and prevents the correct positioning of amino acid side chains of incoming aminoacyl-tRNAs.[4]

[6]**Honokiol** inhibits phosphorylation of Akt,p44/42 mitogen-activated protein kinase (MAPK), and src. Additionally, honokiol regulates the nuclear factor kappa B (NF-κB) activation pathway, an upstream effector of vascular endothelial growth factor (VEGF), MCL1, and cyclooxygenase 2 (COX-2), all significant pro-angiogenic and survival factors[8-9]

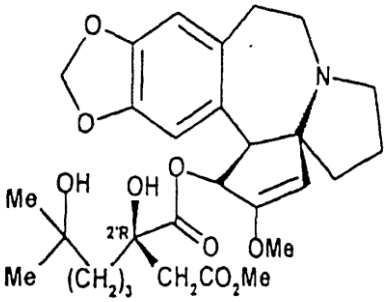
Marketed preparation

1 Vincristine sulph 1mg, methyl paraben 0.13%,propyl paraben 0.02%.[3]
2 Vinblastine sulph. 1mg, sodium chloride 9mg benzyl alcohol 0.9%v/v/ml.[3]
3 Omacetaxine synribo: 1.25 mg/m^2 administered by subcutaneous injection twice daily for 7 consecutive days of a 28-day cycle. 5 mg/m2 for seven days, 7 mg/m2 for seven days, and 5 mg/m2 for nine days.[7]
4 Honokiol90 : 60-330 mg for a 150lb person 220-440 mg for a 200lb person 270-550 mg for a 250lb person.[10]

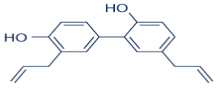


Vinblastine: R = CH_3
Vincristine: R = CHO

CatharanthusroseusVinblastine R=CH_3 Vincristine R=CHO



Cephalotaxusharringtonia Homoharrigtonine



Mangnoliagrandiflora Honokiol

LUNG CANCER

Paclitaxel, Topotecan, Maytansine and Astragalus this drug are used in lung cancer therapy.

Lung cancer starts when cells of the lung become abnormal and begin to grow out of control. As more cancer cells develop, they can form into a tumor and spread to other areas of the body. Lung cancer happens when the cells in your lungs start togrow in an uncontrolled way and form tumours. Tumours are lumps of tissue made up of abnormal cells.There are two main types of lung cancer.Small cell lung cancer (a type of cancer made up ofsmall round cells in the lungs).Non-small cell lung cancer (cancer which grows in cellsother than small cells inside the lungs).

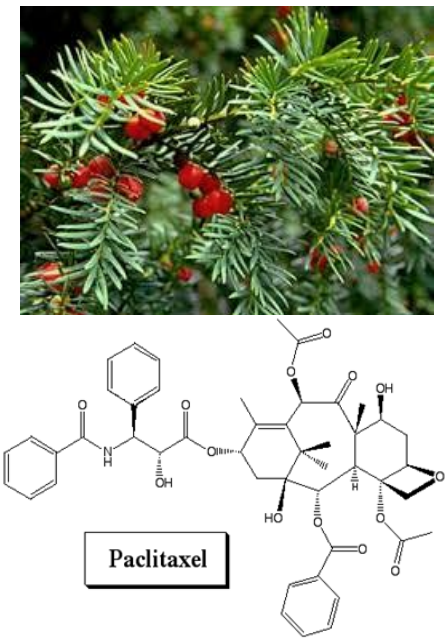
Paclitaxel(Taxol)binds to the N-terminal 31 amino acids of the beta-tubulin subunit of tubulin polymers (3). Unlike the vinca alkaloids, which prevent microtubule assembly, the taxanes decrease the lag time and shift the dynamic equilibrium between tubulin dimers and microtubules toward polymerization, thereby stabilizing microtubules (4). These effects occur even in the absence of GTP- and microtubule-associated proteins, which are usually essential for this function.[12]**Topotecan** binds to the topoisomerase I-DNA complex and prevents religation of these single strand breaks. The cytotoxicity of topotecan is thought to be due to double strand DNA damage produced during DNA synthesis, when replication enzymes interact with the ternary complex formed by topotecan, topoisomerase I, and DNA. Mammalian cells cannot efficiently repair these double strand breaks. [13]

Maytansine inhibits the assembly of microtubules by binding to tubulin at the rhizoxin binding site.[14-15]**Astragalosides**inhibits free radical production, increases superoxide dismutase and decreases lipid peroxidation. It is thought to improve the immune response by potentiating the effects of interferon and it has been confirmed to enhance the immune system in in vitro and in vivo investigations. Astragalus also seems to increase antibody levels of IgA and IgG in nasal secretions.[16-21]

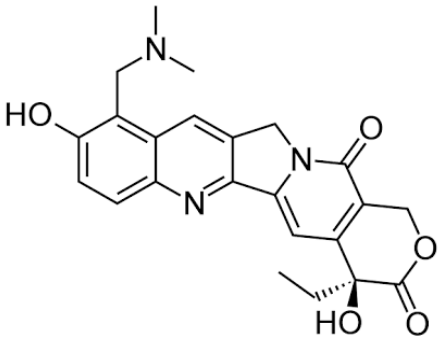
Marketed preparation

1. Paclitaxelis available in 30 mg (5 mL), 100 mg (16.7 mL), and 300 mg (50 mL) multidose vials.[11]
2. Topotecan Injection 1.5 mg/m2 by intravenous infusion over 30 minutes daily on days 1 to 5 of each 21-day cycle.[13]

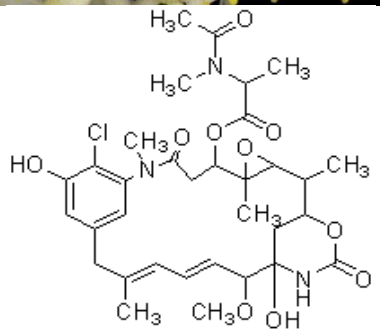
3.



***Taxus brevifolia*bark. Paclitaxel**



Camptotheca Acuminata Topotecan



Maytanus Maytansine

BREAST CANCER

Docetaxel, Elliticine, Lapochel and Oleanolic acid this drug used in breast cancer therapy.

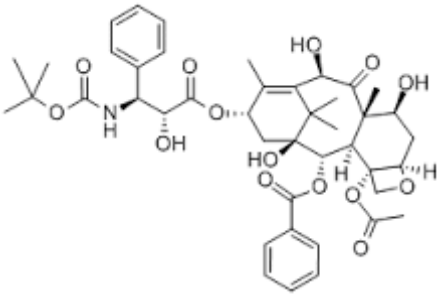
Breast cancer is a malignant tumor that starts in the cells of the breast. A malignant tumor is a group of cancer cells that can grow into (invade) surrounding tissues or spread (metastasize) to distant areas of the body. Most breast cancers are *carcinomas*, a type of cancer that starts in the cells (epithelial cells) that line organs and tissues like the breast. In fact, breast cancers are often a type of carcinoma called *adenocarcinoma*, which is carcinoma that starts in glandular tissue. Other types of cancers can occur in the breast, too, such as sarcomas, which start in the cells of muscle, fat, or connective tissue.[30]

Docetaxel has been shown in vitro to disrupt the microtubular network in cells which is essential for vital mitotic and interphase cellular functions.[23]**Ellipticine** antitumor, mutagenic and cytotoxic activities were suggested to be intercalation into DNA and inhibition of DNA topoisomerase II activity.[25-26]

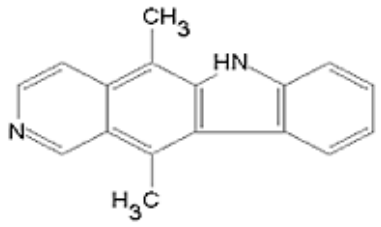
Lapachol has been proposed that interaction of the naphthoquinone moiety between base pairs of the DNA helix occurs with subsequent inhibition of DNA replication and RNA synthesis.[27]**Oleanolic** acid induces metabolic adaptation in cancer cells by activating the AMP-activated protein kinase pathway.

Marketed preparation

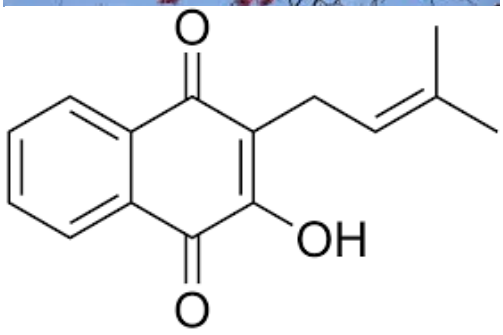
1. Injection containing 20 or 80 mg of docetaxel per 1.0 Or 4.0mL, respectively, in 50/50 (v/v)polysorbate 80/ethanol (anhydrous).[23]
2. Ellipticine-polyvinylpyrrolidone was compared with that of the hydrochloride salt and ellipticine in suspension following oral administration at 250 mg/kg.[24]
3. Lapachol concentration levels (20, 40 or 60 mg/ mxzL).[27]
4. Treated with various concentrations of oleanolic acid (0, 5, 25, 50 μM) for 72 h.[29]



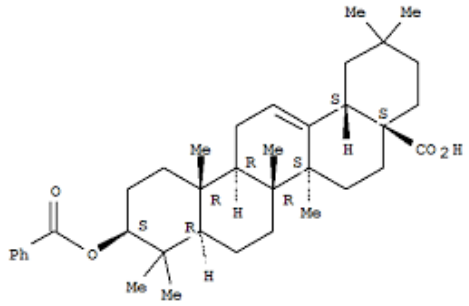
***Taxusbrevifolia*bark. Docetaxel**



Ochorsiaelliptica Ellipticine



Handroanthus Lapochol



Phytolacca Americana Oleanolic acid

SKIN CANCER :

Cisplatin, Etoposide,Teniposide andResveratrol are used in skin cancer therapy.

Skin cancerare two types of skin cancer: malignant melanoma of the skin and non-melanoma skin cancer (NMSC). Malignant melanoma is the most serious type of skin cancer. NMSC is much more common than malignant melanoma, and in the vast majority of cases it is detected early and is not life-threatening. Malignant melanoma is a cancer that develops from melanocytes (cells found in the deep layers of the epidermis). Melanocytes produce the ultraviolet (UV)-protective pigment melanin, which is responsible for the colour of skin. NMSC most commonly develops from the epidermal cells keratinocytes, which produce the waxy skin-strengthening substance keratin.[31]

Cisplatin binds with DNA to form intrastrand crosslinks and adducts that cause changes in the conformation of the DNA and affect DNA replication. Other mechanisms of cisplatin cytotoxicity include mitochondrial damage, decreased ATPase activity, and altered cellular transport mechanisms.**Etoposide** forms a ternary complex with DNA and the topoisomerase II enzyme (which aids in DNA unwinding), prevents re-ligation of the DNA strands, and by doing so causes DNA strands to break.Cancer cells rely on this enzyme more than healthy cells, since they divide more rapidly. Therefore, this causes errors in DNA synthesis and promotes apoptosis of the cancer cell.

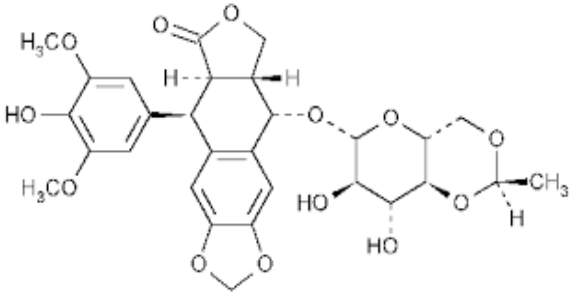
Thymoquinone Induces Mitochondria-Mediated Apoptosis inAcute Lymphoblastic.

Resveratrol activates Sirtui1and PGC-1α and improves the functioning of the mitochondria.[34]

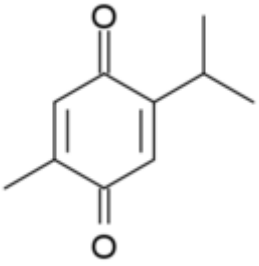
Resveratrol's ability to directly activate sirtuin 1 has been called into question, although newer attempts tried to reconfirm this link,latest research demonstrated that resveratrol binds to TyrRS to potentiate a PARP1/NAD+ driven signaling cascade to activate p53 and AMPK by inhibiting SIRT1.[37]

Marketed preparation

1. Cisplatin 70 mg/m2 (days 1, 8, 15, 29, 36, 43) in combination with escalating doses of paclitaxel.[36]
2. Etoposide daily administrationof 100 mg/m2 for 4 to 5 days.[35]
3. Thymoquinone: 20, 30 and 40 mg/kg body weight for intraperitoneal injection and 200, 300 and 500 mg/kg body weight for oral ingestion.[34]



Podophyllum hexandrumEtoposide



Nigella Sativa Thymoquinone

II. CONCLUSION

Cancer is major health problem in both developed 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. Plant-derived compounds have been an important source of several clinically useful anti-cancer agents. Plant have been the beacon of therapeutic sources for curing diseases from times immemorial. Medicinal plant with their isolated lead molecules are also used as an alternative medicine for treating cancer. These chemical compounds are formulated with a view to create effective drugs against cancer.Vincristine, Vinblastine, Homoharringtonine, Honokiol , Paclitaxel, Topotecan, Maytansine, Astraguoside , Docetaxel, Elliticine, Lapochel, Oleanolic acid,Cisplatin, Etoposide,Teniposide and Resveratrolthis lead molecules isolated from different medicinal plants are in use to treat cancer and chemotherapeutic side effect. In the present review, an attempt has been made to study the plants that have been used in the treatment of cancer.

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