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Plants Helpful in Potential Anticancer Activity

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Abstract – An attempt has been made to review some medicinal plants used for the prevention and treatment of cancer. Plant derived compounds have played an important role in the development of several clinically useful anticancer agents. Several anticancer agents including taxol, vinblastine, vincristine and topotecan are in clinical use all over the world. A number of promising agents such as combrestatin, betulinic acid and silvesterol are in clinical or preclinical development.

Keywords: Medicinal plants, Cancer, Taxol, Chemotherapeutic, Phytochemicals.

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INTRODUCTION

Natural Products, especially plants, have been used for the treatment of various diseases for thousands of years. Terrestrial plants have been used as medicines in Egypt, China, India and Greece from ancient time and an impressive number of modern drugs have been developed from them. The first written records on the medicinal uses of plants appeared in about 2600 BC from the Sumerians and Akkaidians. The "Ebers Papyrus ", the best known Egyptian pharmaceutical record, which documented over 700 drugs, represents the history of Egyptian medicine dated from 1500 BC. The Chinese *Materia Medica,* which describes more than 600 medicinal plants, has been well documented with the first record dating from about 1100 BC. Documentation of the Ayurvedic system recorded in Susruta and Charaka dates from about 1000 BC. The Greeks also contributed substantially to the rational development of the herbal drugs. Dioscorides, the Greek physician (100 A.D.), described in his work " *De Materia Medica*" more than 600 medicinal plants. Phytochemicals have been proposed to offer protection against a variety of chronic ailments including cardiovascular diseases, obesity, diabetes, and cancer. As for cancer protection, it has been estimated that diets rich in phytochemicals can reduce cancer risk by 20%.The compounds that are responsible for medicinal property of the drug are usually secondary metabolites. Plant natural product chemistry has played an active role in generating a significant number of drug candidate compounds in a drug discovery program. Recently, it has been reported in the literature that approximately 49 % of 877 small molecules that were introduced as new pharmaceuticals between 1981 and 2002 by New Chemicals Entities were either natural products or semi-synthetic analogs or synthetic products based on natural product models.

Plants have a long history of use in the treatment of cancer. Hartwell, in his review of plants used against cancer, lists more than 3000 plant species that have reportedly been used in the treatment of cancer. It is significant that over 60% of currently used anticancer agents are derived in one way or another from natural sources, including plants, marine organisms and micro-organisms. Indeed, molecules derived from natural sources (so called natural products)**,** including plants, marine organisms and micro-organisms have played and continue to play, a dominant role in the discovery of leads for the development of conventional drugs for the treatment of most human diseases. The search for anti-cancer agents from plant sources started in earnest in the 1950s with the discovery and development of the vinca alkaloids, vinblastine and vincristine, and the isolation of the cytotoxic podophyllotoxins. These discoveries prompted the United States National Cancer Institute (NCI) to initiate an extensive plant collection program in 1960. This led to the discovery of many novel chemotypes showing a range of cytotoxic activities, including the taxanes and camptothecins.

Cancer, after cardiovascular disease, is the second leading cause of death. Worldwide about 10 million people per year are diagnosed with cancer and more than 6 million die of the disease and over 22 million people in the world are cancer patients. When cancer is diagnosed, therapists face a formidable range of challenges. Treatment usually consists of various combinations of surgery, radiation therapy, and chemotherapy but despite these therapeutic options, cancer remains associated with high mortality. Natural and some synthetic compounds can prevent, suppress, or reverse the progression of cancer. Although tumors have traditionally been treated with

chemotherapeutic agents, the advents of compounds which prevent malignancies represent an emerging field and offer new options. Cancer is a complex disease that is normally associated with a wide range of escalating effects both at the molecular and cellular levels. It therefore seems unlikely that chemoprevention follows simplistic rules and formulations. The old saying "Prevention is always better than cure" is particularly true in the case of cancer where a cure, if at all possible, is associated with high cytotoxic loads and/or invasive procedures. With our growing understanding of the molecular etiology of cancer, it has become apparent that strategies which limit DNA damage and/or increase the probability of DNA repair by inhibiting aberrant proliferation will decrease cancer incidence. Investigators have identified approximately 400 drugs, vitamins, hormones and other agents that might help in preventing cancer. Clinical trials are underway to investigate an increasing number of agents. Cancer is the abnormal growth of cells in our bodies 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. Most of these trials involve healthy people with a higher than average risk of cancer. Despite the tremendous advancements in the understanding and treatment of cancer, there is no sure fire cure for a variety of cancers to date. Therefore, natural protection against cancer has recently been receiving a great deal of attention not only from cancer patients but, surprisingly, from physicians as well. The major causes of cancer are smoking, dietary imbalances, hormones and chronic infections leading to chronic inflammation. Breast cancer is the most common form of cancer in women worldwide. Amongst South African women, breast cancer is likely to develop in one out of every 31 women in the country. Colon cancer is the second most common cause of cancer deaths in the US. Prostate cancer is the most frequently diagnosed cancer among men in the US, second to skin cancer with an estimated 180,000 new cases and 37,000 deaths expected by American Cancer Society each year. Plants have been used for treating various diseases of human beings and animals since time immemorial. They maintain the health and vitality of individuals, and also cure diseases, including cancer without causing toxicity. More than 50% of all modern drugs in clinical use are natural products, many of which have the ability to control cancer cells. A recent survey shows that more than 60% of cancer patients use vitamins or herbs as therapy. These plants are used against various types of tumors/cancers such as sarcoma, lymphoma, carcinoma and leukemia. Many of these medicinal plants have been found effective in experimental and clinical cases of cancers. Attempts are being made to isolate active constituents from natural sources that could be used to treat this very serious illness.

The first agents to advance into clinical use were the isolation of the vinca alkaloids, vinblastine and vincristine from the Madagascar periwinkle, *Catharanthus roseus* (Apo-cynaceae) introduced a new era of the use of plant material as anticancer agents. They were the first agents to advance into clinical use for the treatment of cancer. Vinblastine and vincristine are primarily used in combination with other cancer chemotherapeutic drugs for the treatment of a variety of cancers, including leukemias, lymphomas, advanced testicular cancer, breast and lung cancers, and Kaposi's sarcoma. The discovery of paclitaxel from the bark of the Pacific Yew, *Taxus brevifolia* Nutt. (Taxaceae), is another evidence of the success in natural product drug discovery. Various parts of *Taxus brevifolia* and other *Taxus* species (e.g., *Taxus Canadensis*, *Taxus baccata*) have been used by several Native American Tribes for the treatment of some noncancerous cases. *Taxus baccata* was reported to use in the Indian Ayurvedic medicine for the treatment of cancer. Paclitaxel is significantly active against ovarian cancer, advanced breast cancer, small and non-small cell lung cancer. Camptothecin, isolated from the Chinese ornamental tree *Camptotheca acuminate* (Nyssaceae), was advanced to clinical trials by NCI in the 1970s but was dropped because of severe bladder toxicity. Topotecan and irinotecan are semi-synthetic derivatives of camptothecin and are used for the treatment of ovarian and small cell lung cancers, and colorectal cancers, respectively. Epipodophyllotoxin is an isomer of podophyllotoxin which was isolated as the active antitumor agent from the roots of *Podophyllum* species, *Podophyllum peltatum* and *Podophyllum emodi* (Berberidaceae). Etoposide and teniposide are two semi-synthetic derivatives of epipodophyllotoxin and are used in the treatment of lymphomas and bronchial and testicular cancers. Homoharringtonine isolated from the Chinese tree *Cephalotaxus harringtonia* (Cephalotaxaceae), is another plant-derived agent in clinical use. Combretastatins were isolated from the bark of the South African tree *Combretum caffrum* (Combretaceae). Combretastatin is active against colon, lung and leukemia cancers and it is expected that this molecule is the most cytotoxic phytomolecule isolated so far. Betulinic acid, a pentacyclic triterpene, is a common secondary metabolite of plants, primarily from *Betula* species (Betulaceae). Betulinic acid was isolated from *Zizyphus* species, e.g. *Zizyphus mauritiana*, *Zizyphus rugosa* and *Zizyphus oenoplia* and displayed selective cytotoxicity against human melanoma cell lines. Silvestrol was first isolated from the fruits of *Aglaila sylvestre* (Meliaceae). Silvestrol exhibited cytotoxicity against lung and breast cancer cell lines. The *Podophyllum* species (Podophyllaceae), *Podophyllum peltatum* (commonly known as the American mandrake or Mayapple), and *Podophyllum emodii* from the Indian subcontinent, have a long history of medicinal use, including the treatment of skin cancers and warts. *Podophyllum peltatum* was used by the Penobscot Native Americans of Maine for the treatment of cancer.

Camptothecin isolated from *Camptotheca acuminata* (Nyssaceae), also known as tree of joy in China is a possible source of steroidal precursors for the production of cortisone. The extract of *C. acuminata* was the only one of 1000 of the plant extracts tested for anti-tumor activity which showed efficacy and camptothecin was isolated as an active constituent. Other plant derived agents in clinical use are homoharringtonine isolated from the Chinese tree, *Cephalotaxus harringtonia* (Cephalotaxaceae), and elliptinium, a derivative of ellipticine isolated from species of several genera of the Apocynaceae family including *Bleekeria vitensis,* a Fijian medicinal plant with reputed anti-cancer properties. Several *Terminalia* species have reportedly been used in the treatment of cancer. The combretastatins are a family of stilbenes which act as anti-angiogenic agents causing vascular shutdown in tumors and resulting in tumor necrosis. Species of the genus *Tabebuia* (Bignoniaceae) have a history of use in the Amazonian region for the treatment of several diseases including syphilis, fevers, malaria, cutaneous infections and stomach disorders. Claims for clinical efficacy in the treatment of cancers started in the 1960s, particularly in Brazil and these led to widespread sales of the stem bark and trunk wood of *Tabebuia impetiginosa, Tabebuia rosea* and *Tabebuia serratifolia* in health food stores under various names such as pau d'arco or lapacho. They possess numerous bioactive compounds, but the naphthaquinones particularly lapachol and β-lapachone have received most attention. Lapachol showed significant *in vivo* anti-tumor activity in some early mouse models.

Dragon's blood is the popular name for a dark red viscous sap produced by *Croton lechleri*. This herb is used in folk medicine as an anti-inflammatory, antimicrobial and anticancer. Crude extracts from plants like *Colubrina macrocarpa*, *Hemiangium excelsum* and *Acacia pennatula* have been shown to possess a selective cytotoxic activity against human tumor cells. In the Palestinian and Israeli territories, extracts of *Teucrium polium* and *Pistacia lentiscus*, among others are known to treat liver disease, jaundice, diabetes, fertility problems and cancer. In Saudi Arabia, aerial parts of *Commiphora opobalsamum* are commonly used to treat various diseases. However, its potential use in stomach problems and cancer has been reported only recently. Historic medicinal practice used Cat's Claw also known *Uncaria tomentosa*, as an effective treatment for several health disorders which include chronic inflammation, gastrointestinal dysfunction such as ulcers, tumors and infections. The efficacy of Cat's Claw was originally believed to be due to the presence of oxindole alkaloids. Some *Astragalus* species are used to treat leukemia and promote wound healing. Chinese medicinal herb *Paris polyphylla* has been used to treat liver cancer in China for many years and has been reported as a potent anticancer agent that can overcome drug resistance. *Salvia officinalis* is the most popular herbal remedy in the Middle East to treat common health complications. Salvia species (Labiatae) are known for their antitumor effects. Phytochemically, the whole plant contains several antioxidants that protect against cellular peroxidative damage. *Lantana camara* possesses several medicinal properties and is commonly used in folk medicine for its antipyretic, antimicrobial and antimutagenic properties. *Solanum nigrum* is a common herb that grows wildly and abundantly in open fields. It has been used in traditional folk medicine because of its diuretic and antipyretic effects. More specifically, it has been used for a long time in oriental medicine to cure inflammation, edema, mastitis and hepatic cancer.

CONCLUSION

Medicinal plants maintain the health and vitality of individual and also cure various diseases including cancer without causing toxicity. Natural products discovered from medicinal plants have played an important role in treatment of cancer. In this review some anti-cancer plants have been presented. These plants possess good immunomodulatry and antioxidant properties leading to anticancer activity. In conclusion this article provides the knowledge about anticancer medicinal plants of foreign origin, which are used by people all over the world. Also it is of significance to exploit novel anticancer drugs from medicinal plants.

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