

ANTICANCER PLANTS: A REVIEW

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ABSTRACT

Over the last 4-5 decades, biologically active compounds derived from natural resources have provided a number of useful cancer chemotherapeutic drugs. The search for natural products based drug candidates is growing rapidly with the advancements in drug discovery and development techniques in recent years, with the active fractions and isolates of marine organisms along with terrestrial plants and microorganisms. The present review highlights the information about occurrence of such promising leads from natural origin tend to create extensive interest among researchers including medicinal chemists and pharmacologists working in anticancer drug research and therefore the availability of a given brief information about cancer and anticancer drug development focused on natural products.

Keywords: Anticancer; Medicinal Plants.

INTRODUCTION

Cancer is responsible for about 25% deaths caused due to diseases in the developed countries and is a major public health burden and challenge for world health organization and research organizations.^[1-3] It is considered as an adversary of industrial revolution followed by advanced pattern of socio-cultural life dominated by excessive intake of exogenous chemicals and less physical activities. The number of incidences of different types of cancers is also increasing in developing countries, as the extensive technical advancements in the field of drug development and other areas allowed their populations live longer and make negative lifestyle changes leading to increased risk of cancer. Cancer is a broad group of diseases characterized primarily by uncontrolled cell division leading to increase in the number of malignant cells in a tissue, invasion of adjacent tissues by malignant cells, or spread of malignant cells through lymphatic or circulatory system to regional lymph nodes and distant tissues (metastasis). It develops through multi-step process that initiates with small preneoplastic changes, which may subsequently progress to neoplasia.^[4,5] Under certain conditions, neoplastic cells escape the host's

immune surveillance that helps to develop the capacity of growth, invasion and metastasis. Cancer cells behave as independent cells and proliferate continuously with out growth regulation, leading to tumor development through multi step process. An ideal anti cancer drug would restore normal growth regulation and cell cycle control to cancer cells through restoring aberrant molecular signaling pathways and inducing apoptosis in these cells. It should selectively target different components of physiological and biochemical pathways related to different stages of cancer development without affecting the normal cells. The discovery of new compounds with novel mechanisms of action, contribute to improved and highly effective methods for cancer treatment.

A newer dimension in the anticancer drug research is the increasing awareness about natural products based chemotherapy. Several studies have demonstrated that different plant-based foods such as onion, grapes, garlic, ginger, soybean, turmeric, cabbage, cauliflower, broccoli and tomato can offer significant anticancer potential. Natural products have provided four important categories of antitumor agents: taxanes,

camptothecins, bisindole alkaloids also known as vinca alkaloid and epipodophyllotoxins. Microorganisms have also provided several potent anti cancer drugs in form of anti cancer antibiotics such as doxorubicin, actinomycin and mitomycin C.

A natural product is a chemical compound or substance produced by a plant, animal or microorganism and usually has a pharmacological or biological activity which can be utilized in pharmaceutical drug discovery and drug design. Chemically natural products are secondary metabolites, specifically produced by a particular group of organisms and have been postulated to play an important role in self defense against predators as well as in interspecies interactions. Their role is exceptionally pronounced in the field of anti cancer drug research. Roughly 50 % of the new chemical entities introduced during last three decades were either natural products or derived from natural products through structural modifications. Due to enormous advancement in the field of medicinal chemistry, design of natural product or natural product-mimetic scaffolds can be achieved readily in one-step with the help of multi-component reactions. Usually, natural products are isolated only in minute amounts and thus subsequent techniques are required to scale-up of the biologically active molecules.

With reference to above facts, the review has been designed to cover the history of drug development from natural resources, anticancer compounds isolated from different natural resources.

TYPES OF CANCER

Based on the histological characteristics hundreds of different cancers have been identified, which can be classified into six major groups.

1. Carcinomas

Cancers caused due to alteration in epithelial cells covering the surface of skin and internal organs are termed as carcinomas. It is the most common type of cancers, predominantly occurring in the old age, for example breast, prostate, lung, pancreas, and colon cancers. Carcinomas, account for 80 to 90 percent of all cancer cases. These can be further divided into two major subtypes: (i) Squamous cell carcinoma, which

develops in the squamous epithelium and (ii) adenocarcinoma, which develops in an organ or gland.

2. Sarcomas

Cancers arising on different connective tissue including bone, cartilage and nervous system are termed as sarcomas. These are known to develop from cells originating in mesenchyma outside the bone marrow. Most important examples of sarcoma include fibro sarcoma (fibrous tissue), rhabdomyosarcoma (skeletal muscle), angiosarcoma or hemangioendothelioma (blood vessels), glioma or astrocytoma (neurogenic connective tissue found in the brain) mesothelial sarcoma or mesothelioma (membranous lining of body cavities)

3. Myelomas

These include the cancers arising in the bone marrow plasma cells. These are also called cancers of antibody producing white blood cells

4. Lymphomas

These are developed in the lymph glands and other organs of lymphatic system including tonsils, thymus gland and spleen playing active role in immune system. Lymphomas may also occur in some other organs including breast, stomach and brain. Lymphomas occurring in these organs are known as extranodal lymphomas. These can be further divided into two major subtypes: (i) Hodgkin lymphomas and (ii) non-Hodgkin lymphomas. Both of these subtypes can be differentiated on the basis of the presence of reed-sternberg cells in Hodgkin lymphoma.

5. Leukemias

The cancers occurring in bone marrow are termed as leukemia. It results in the overproduction of immature white blood cells (WBC) rendering the patients immunodeficient and susceptible to subsequent infections. In some cases it also affects red blood cells (RBC) and platelets leading to anemia as well as defective blood clotting. The important examples of leukemia include chronic myelocytic leukemia (CML) occurring in adults, acute myelocytic leukemia (AML) occurring in children, chronic lymphocytic, lymphatic, or lymphoblastic leukemia (CLL) common in adults, acute lymphocytic, lymphatic, or lymphoblastic leukemia (ALL) common in children and adults.

6. Mixed Types

These comprises of more than one component which may be within one category or from different categories. Examples of mixed type include adenosquamous carcinoma, mixed mesodermal tumor, carcinosarcoma and teratocarcinoma.

NATURAL PRODUCTS AS SOURCE OF THE RAPEUTIC AGENTS

The Mother Nature has been continuously serving the mankind as most efficient arsenal, playing an important role in health care and prevention of diseases. Natural products have traditionally been used in form of plant extracts, dry powders, infusions, or other therapeutic preparations to treat several diseases over centuries and continue to play a highly significant role in the modern drug discovery and development process providing a diverse and unique source of medicinally active molecules. Medicinal plants play a major role and constitute the backbone of almost all the traditional systems of medicine. Ayurveda, known as the science of life is one of the oldest system of medicines. This system of using natural resources for betterment of health was originated in India long ago in the pre-Vedic period through day by day experiences and experimentations with the aim of maintaining health and treatment of various diseases. Several other systems of complementary and alternative medicines including Siddha and Unani are also developed from plant based formulations through experience and interactions with natural resources. The earliest written evidence related to use of plant products as therapeutic agents is available on *Atharvaveda*, one of the four most ancient books of knowledge and culture related to Hindu religion showing the strength of Indian wisdom. As many as 114 different therapeutic formulations have been described for the treatment of different diseases. The therapeutic importance of Indian medicinal plants has been exposed thoroughly in the *Susruta samhita* and *Charaka samhita* during the Vedic period. Indian Materia medica has description of more than 2000 drugs derived from natural resources most of which are originated from different systems of traditional and folk practices. 80 % of these drugs are of plant origin whereas the rest are minerals or

animal products. Indian medicinal plants possess enormous therapeutic potential but only a small proportion of it has been explored by mankind leaving the great opportunity to discover novel drugs from natural origin. Numerous therapeutic preparations have been developed by traditional healers and Ayurvedic practitioners for the treatment of various disorders and diseases. Subsequently after the emergence of natural product chemistry thousands of new medicinal plant were identified with immense therapeutic potential. Natural Products chemistry together with analytical chemistry, spectroscopy, pharmacology, biochemistry and other related disciplines demonstrated its value for drug development. It has not only enriched modern medicine with novel bio-active molecules but also provided valuable leads for drug designing. Since the isolation of morphine from *Papaver somniferum* in 1806, extensive efforts are being done to isolate therapeutically active molecules from medicinal plants. Some important examples include emetine, colchicine, atropine, cocaine, ephedrine and quinidine.

BIOASSAY GUIDED DRUG DISCOVERY

Bioassay-directed fractionation supported by several recent techniques is extensively used to identify the active principles/pure compounds present in crude natural products preparations. This approach can be used systematically to reduce the complexity of the extracts/fractions in order to locate the biological activities of complex materials. It resolves the complex mixtures to more simple and pure form.^[6,7] Considering on therapeutic preparation obtained from crude extracts, only a specific portion of the extract-the active principles/bioactive molecules with specific biological targets is of interest. In view of this fact, a bio-molecular interaction step should be included into analytical methods to achieve bio-selectivity and to purify the compounds with specific therapeutic activity.

POTENTIAL ANTICANCER AGENTS OBTAINED FROM NATURAL PRODUCTS

Citrus fruits and green vegetables provide a rich source of vitamins, flavonoids and other polyphenolic compounds, adequate consumption of these plant products reduce the risk of cancer.

More than 1,000 non-nutritive plant derived compounds are known to have cancer-preventive activity. More than 400 plant derived compounds with anticancer potential are under investigation. . Most of the species of higher plants, microorganisms, arthropods, and marine invertebrates are still not studied and thus these

diverse natural resources can be explored to provide novel anticancer agents. Recent studies have identified new species of bacteria, algae, fungi, and vertebrates which are able to provide new anticancer molecules. Some important medicinal plants possessing anticancer potential are listed in table 1.

Table 1: Some important Medicinal Plants possessing anticancer activity

Plant name	Family	Active part	Plant name	Family	Active part
<i>Acacia xanthophloea</i>	Leguminosae	Fruit	<i>Ipomea batata</i>	Convolvulaceae	Rhizome
<i>Adenium obesum</i>	Apocynaceae	Leaf	<i>Juncus acutus</i>	Juncaceae	Leaf
<i>Adiantum macrophyllum</i>	Pteridaceae	Entire	<i>Lansea stuhlmannii</i>	Anacardiaceae	Root
<i>Aeonium arboretum</i>	Crassulaceae	Leaf	<i>Lavandula angustifolia</i>	Meliaceae	Leaves
<i>Aglaiia foveolata</i>	Meliaceae	Fruit	<i>Lep tadenia hastate</i>	Asclepiadaceae	Bark
<i>Alnus japonica</i>	Betulaceae	Wood	<i>Ligustrum lucidum</i>	Oleaceae	Seed
<i>Aphanamixis polystachya</i>	Meliaceae	Stem bark	<i>Maytenus canariensis</i>	Celastraceae	Fruit juice
<i>Arisaema erubescens</i>	Araceae	Root	<i>Ma ytenus macrocarpa</i>	Celastraceae	Stem bark
<i>Aster amellus</i>	Compositae	Entire	<i>Maytenus serrata</i>	Celastraceae	Seed
<i>Azadirachta indica</i>	Meliaceae	Leaf	<i>Monnina obtusifolia</i>	Polygalaceae	Aerial parts
<i>Begonia glabra</i>	Begoniaceae	Entire	<i>Morinda ci trifolia</i>	Rubiaceae	Root
<i>Carapa guianensis</i>	Meliaceae	Seed oil	<i>Ocotea foetens</i>	Lauraceae	Branchlets
<i>Cassia quinquangulata</i>	Caesalpiniaceae	Root	<i>Pinus parviflora</i>	Pinaceae	Strobilus
<i>Celastrus orbiculatus</i>	Celastraceae	Entire	<i>Piper latifolium</i>	Piperaceae	Leaf
<i>Crassocephalum bojeri</i>	Compositae	Entire	<i>Plantago asiatica</i>	Plantaginaceae	Leaf
<i>Combretum caffrum</i>	Combretaceae	Bark	<i>Pleione bulbocodioides</i>	Orchidaceae	Tuber
<i>Cyathea fauriei</i>	Cyatheaceae	Shoot	<i>Pratia nummularia</i>	Campanulaceae	Entire

<i>Dillenia suffruticosa</i>	Dilleniaceae		Fruit	<i>Phymatosorus diversifolium</i>	Polydiaceae	Root
<i>Dioscorea collettii</i>	Dioscoreaceae		Rhizome	<i>Phytolacca esculenta</i>	Phytolaccaceae	Root
<i>Dyosma pleiantha</i>	Berberidaceae		Root	<i>Rabdo sia rubescens</i>	Labiatae	Leaf
<i>Caragana cuneata</i>	Leguminosae		Leaf	<i>Ruellia tuberosa</i>	Acanthaceae	Bark
<i>Croton flavens</i>	Euphorbiaceae		Leaf	<i>Salvia chinensis</i>	Labiatae	Entire
<i>Croton lechleri</i>	Euphorbiaceae		Latex	<i>Salvia officinalis</i>	Labiatae	Leaves
<i>Cynanchum hancoekianum</i>	Asclepiadaceae		Entire	<i>Scirpus holoschoenus</i>	Cyperaceae	Inflorescence
<i>Deeringia amaranthoides</i>	Amaranthaceae		Fruit	<i>Scutellaria barbata</i>	Labiatae	Entire
<i>Echinops grijisii</i>	Compositae		Root	<i>Scutellaria indica</i>	Labiatae	Root
<i>Echinops latifolius</i>	Compositae		Root	<i>Sempervivum armenum</i>	Crassulaceae	Leaf
<i>Echites vucatanensis</i>	Apocynaceae		Latex	<i>Sempervivum arvense</i>	Crassulaceae	Leaf
<i>Epilobium hirsutum</i>	Onagraceae		Entire	<i>Swietenia humilis</i>	Meliaceae	Seed
<i>Euphorbia ebracteolata</i>	Euphorbiaceae		Aerial parts	<i>Tabebuia impetiginosa</i>	Bignoniaceae	Stem bark and wood
<i>Euphorbia heterophylla</i>	Euphorbiaceae		Stem	<i>Tabebuia rosea</i>	Bignoniaceae	Stem bark and wood
<i>Euphorbia marginata</i>	Euphorbiaceae		Entire	<i>Tabebuia serratifolia</i>	Bignoniaceae	Stem bark and wood
<i>Euphorbia kansui</i>	Euphorbiaceae		Root	<i>Thalictrum fabri</i>	Ranunculaceae	Root
<i>Euphorbia prolifera</i>	Euphorbiaceae		Latex	<i>Thevetia ahouia</i>	Apocynaceae	Leaf and Stem
<i>Ficus pretoiiae</i>	Moraceae		Sap	<i>Thevetia gaumeri</i>	Apocynaceae	Leaf and Stem
<i>Hedyotis chrysotricha</i>	Rubiaceae		Entire	<i>Thevetia peruciana</i>	Apocynaceae	Leaf and Stem
<i>Hippophae salicifolia</i>	Elaeagnaceae		Fruit	<i>Uncaria tomentosa</i>	Rubiaceae	Bark
<i>Hypoxis nyasica</i>	Hypoxiaceae		Rhizome	<i>Viola bicuhyba</i>	Myristicaceae	Seed
<i>Hypoxis rooperii</i>	Hypoxiaceae		Tuber	<i>Viscum album</i>	Loranthaceae	Leaves
<i>Inula linariaefolia</i>	Compositae		Flowers	<i>Viscum calcaratum</i>	Loranthaceae	Entire

CONCLUSION

Research work done up to date has shown the importance of medicinal plants in the field of different human diseases including cancer, intense efforts and multiple approaches have fructified in form of number of anti-cancer drugs in the area but the main problem associated with these drugs is the toxicity, solubility and lack of specificity as healthy cells are also become the target, most of the modern anti-cancer drugs available are either inspired from natural product or their analogues, efforts are still required to keep the delicate balance between toxicity, bio-availability and efficacy, drugs available are not good enough to treat cancer at advance stage though may prolong the life span of person, other drawback is the cost of anti-cancer drugs which must also be taken into account for the countries like India, a lot need to be done and nature has given the direction. More clinical trials are also needed to validate the usefulness of these agents either alone or in combination with existing therapy.

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