








REVIEW PAPER

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Plants – a source of therapeutic material?

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ABSTRACTS

Introduction. The use of plants with therapeutic or medicinal properties is as ancient as human civilization and for many years prior to the 20th century, plants and animal products were the main source of therapeutic medicinal drugs.

Aim. The discovery of new plant-derived drugs continues to be an active field of research in medical science today. The aim of this article is to describe several main classes of natural products currently under investigation.

Material and methods. Analysis of literature.

Keywords. plants, natural products, drug, therapeutic material

Introduction

The isolation and evaluation of natural products from plants have made an enormous impact on the discovery of new drugs and has led to advances in medical science.^{1,2} Many natural plant substances are used for general health maintenance or for serious conditions such as cancer, asthma, AIDS, multiple sclerosis, and arthritis.³⁻⁵

Plant Anticancer Agents

Plants are an excellent source of anticancer agents.⁶ Each year, more evidence for their use against tumors in traditional systems of medicine is reported in the lit-

erature. Several main types of natural products derived from plants that are especially of interest in anticancer research are listed below:

- The alkaloids⁶⁻¹⁴
- The terpenes¹⁵⁻²⁰
- The lignans²¹⁻²³
- The macrolides²⁴⁻²⁵

Historical evidence for the use of plants used as anticancer agents is well known. Over the past 40 years, major chemotherapy agents derived from this source have been introduced to the pharmacy market. Several examples of anticancer substances and their plant source are

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as follows: alkaloids from *Vinca* species (vinblastine, vincristine, vindesine, vinorelbine), camptothecin derived cytotoxics (topotecan and irinotecan) and more recently homoharringtonine from *Cephalotaxus* trees, lignans based on the podophyllotoxin class (etoposide and teniposide), terpenes like betulin and taxanes (paclitaxel and taxotere and ingenol mebutate, and the macrolide maytansine from *Gymnosporia* spp. Plants are a rich sources of cytotoxic agents and given the likelihood of a vast number of active substances which are still unknown, their continued discovery and investigation are warranted pursuits in medicinal chemistry. In addition, advances in genome biology and target selection will ensure that plants will continue to provide new anticancer drugs.

The alkaloids

Alkaloids are an immensely important group of naturally occurring bioactive compounds and contain one or more amine functional groups.⁶⁻⁸ In addition, they are easily extracted and purified with simple partition and precipitation methods and they were isolated in high purity very early on in the history of drug discovery.⁹⁻¹² This group includes some compounds with neutral and even weakly acidic properties. Molecules of alkaloids, depending on the pH, mimic the chemistry of endogenous amines acting as physiological compounds. Many alkaloids are endowed with an exquisite selectivity for their targets, allowing them to exert their effects at very low concentrations. Ironically, many alkaloids were also used as poisons in ancient times.

Important anticancer alkaloids have been derived from *Vinca* species.¹²⁻¹⁶ Bioassays performed on Madagascar periwinkle (*Catharanthus roseus*, *Vinca rosea*) led to the discovery of the active alkaloidal compounds vincristine and vinblastine. Both, vincristine and vinblastine are dimeric indole alkaloids and their laboratory synthesis is difficult and expensive. The yield of alkaloids from *Vinca rosea* is low and equals 0.0002% for the alkaloid vincristine only. Vincristine, is also known as leurocristine and is marketed under the trade name Oncovin[®]. Vinblastine is marketed under the trade name Velbe[®] and is used to treat acute Hodgkin's disease. These alkaloids cause M phase specific cell cycle arrest by disrupting microtubule assembly and proper formation of the mitotic spindle and the kinetochore, each of which are necessary for the separation of chromosomes during the anaphase of mitosis. The alkaloid Vindesine (a synthetic derivative of vinblastine) is used to treat leukemia and lung cancers. Vinorelbine (marketed as Navelbine[®]) is used as a treatment for non-small cell lung cancer and breast cancer in combinations with cisplatin.¹⁶

The terpenes

Terpenes are class of organic compounds, produced by a variety of plants. They alter anticancer therapy; how-

ever there are still difficulties isolation and characterizations. Terpenes do not precipitate or form crystals easily. Terpenes are the essential oils of many types of medicinal plants and flowers.¹⁷⁻²⁰ They are complex mixtures with very low polarity making their separation difficult. Commonly known medicinal plants which possess terpenes are *Taxus brevifolia* (the source of Taxol) and *Euphorbia* (the source of the diterpene known as ingenol mebutate). Betulic acid is a well-known topoisomerase inhibitor with antiretroviral and antimalarial properties extracted from the bark of White birch (*Betal alba*).

The lignans

Lignans are wide variety of polyphenols present in more than 55 plant families. Due to numerous arrangements of these polymerized polyphenols, they provide a wide array of chemical functionality. Lignans consists of two phenylpropane units linked by a C-C bond between the central atoms of the respective side chains.²¹⁻²³ Lignans have been implicated in reduction in the occurrence of certain types of estrogen-related tumors. They found in sesame seeds, black tea, soy milk and coffee, garlic, asparagus and carrots, lentils and beans.

The macrolides

Macrolides are microbial secondary metabolites. Those compounds have antibiotic and cytotoxic properties.²⁴⁻²⁵ Today, they are recognized to be plant-derived natural products with anticancer properties synthesized by endophytic microorganisms.

Microbial Anticancer Agents²⁴

- The anthracyclines
- The bleomycines
- The actinomycins

Marine anticancer natural products

The ocean covers 70% of the Earth's surface and is a vast reserve for the discovery of new natural products drugs. This huge environment is home to a fantastic range of diverse organisms and of the 28 major animal classes, 26 exist in aquatic regions and eight are exclusively aquatic. The discipline of marine natural product chemistry is comparatively young compared to phytochemistry with relatively small numbers of natural products having been reported.²⁶ At present, Ecteinascidin-743 is a marine natural product that is used as an anticancer drug clinically for soft-tissue sarcoma branded under the name Yondelis[®]. Ecteinascidin-743 is also under clinical trial for breast and prostate cancer.²⁷⁻²⁸

Further strategy

There are a number of potential strategies that can be applied to attempts to discover new natural product cytotoxic agents, such as: to obtain biomass in previously

unexplored environments and the collection of marine organisms. Many marine natural products have shown antimicrobial and anticancer activity but are not yet approved for clinical use.²⁹

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