



Review Article

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A Brief Overview of Plant-Derived Chemotherapeutic Agents for Cancer Therapy

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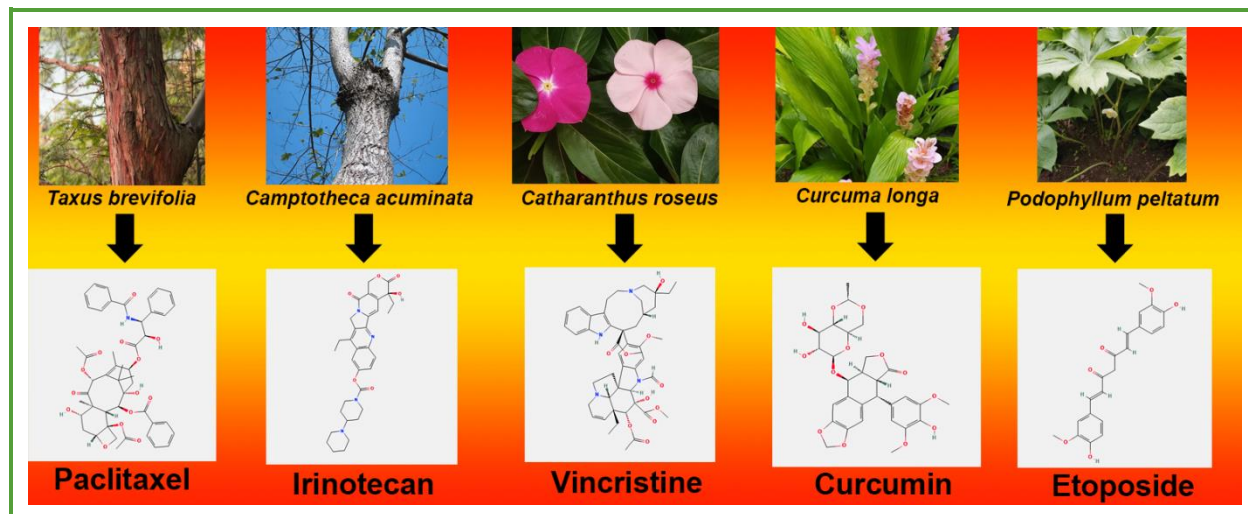
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ABSTRACT

Plants are the inexhaustible source of biologically active compounds. For thousands of years, humans have been using plants to treat diseases. In the past decades, a large number of researches have made many efforts to extract medicinal molecules from plants to treat diseases. The use of pure medicinal compounds has advantages over the use of medicinal plants in the traditional way. Pure compounds allow for better drug dose management and combination therapy. In addition, by focusing on the main therapeutic molecules, the unwanted effects of thousands of complex molecules in medicinal plants are eliminated. On the other hand, by determining the structure of pure pharmaceutical compounds, it is possible to manipulate them to improve therapeutic efficiency or reduce the side effects of the drug. In recent decades, some compounds have been extracted from plants that are the source of a number of important chemotherapy drugs for cancer treatment. This article provides a brief review of some chemotherapy drugs derived from plants.

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Graphical Abstract



Introduction

Medicinal plants have been used to treat diseases for thousands of years [1-8]. With the progress in biomolecules separation techniques in the past decades, it has become possible to discover pure effective compounds from medicinal plants for the treatment of diseases. The use of pure compounds has advantages over the use of medicinal plants in traditional way. Pure compounds allow for better drug dose management. Using pure compounds, it is possible to prescribe high doses of medicinal compounds. The administration of these high doses through the main source of medicinal plants is not possible in the traditional way. Likewise, the use of pure pharmaceutical compounds provides the possibility of better prescription of combination therapy through different pure drugs. Medicinal plants have a complex composition of thousands of biological molecules. By purifying the main therapeutic molecules, the unwanted effects of thousands of complex molecules in medicinal plants are eliminated. In addition, after purification of medicinal compounds from plants, it is possible to determine their structure. After

determining the chemical structure of these therapeutic molecules, it is possible to manipulate them to improve efficiency or reduce side effects.

In recent decades, some compounds have been extracted and purified from plants, which are the source of a number of important chemotherapy drugs for cancer management in the clinic. In this article, an overview of some of these chemotherapy drugs will be discussed.

Paclitaxel

Paclitaxel was discovered as a result of a joint work of the United States Department of Agriculture and the National Cancer Institute in the United States through the use of a plant screening program to discover a new effective drug for the management of cancer diseases [9].

Based on the results of clinical trials, paclitaxel was selected as an effective biological agent for the effective management of cancer diseases [10].

Paclitaxel was obtained from a medicinal plant, particularly from the bark of the yew tree (*Taxus brevifolia* Nutt), which belongs to the *Taxaceae* family. Paclitaxel, as an

anticancer drug, targets microtubules, and thereby disrupts the process of mitosis [11]. Paclitaxel is used in chemotherapy, especially for AIDS-related Kaposi's sarcoma and various solid tumors [12].

Irinotecan

Irinotecan is a chemotherapy drug derived from natural compound camptothecin that inhibits topoisomerase 1. Camptothecin was discovered and isolated from the bark of the Chinese happy tree (*Camptotheca acuminata* Decne) [13].

Topoisomerase 1 is an essential enzyme for DNA replication and cell proliferation. Irinotecan inhibits cell division by inhibiting topoisomerase 1 [14].

Irinotecan is the first-line chemotherapy drug for the treatment of metastatic colorectal cancer worldwide [15].

It is also used in other cancers in combination with other drugs for chemotherapy. This drug is among the essential drugs of the World Health Organization (WHO).

Vinblastine and vincristine

Monoterpene indole alkaloids are plant secondary metabolites mostly found in Gentianales plants, which have remarkable structural diversity as well as valuable pharmacological and biological activities, of which more than 3000 compounds have been derived from their common precursor strictosidine. Chemotherapy drugs vinblastine and vincristine are derivatives of monoterpene indole alkaloids obtained from the dried leaves of *Catharanthus roseus* plant [16].

Vinblastine and vincristine have anti-mitotic properties and inhibit the proliferation of cancer cells. These drugs are still used to treat various types of cancer [12].

These two drugs are among the essential drugs of the World Health Organization (WHO) [16].

Curcumin

Curcumin is a polyphenolic pigment extracted from *Curcuma longa* plant. Curcumin has several biological effects, including antioxidant, anti-inflammatory, antimicrobial, antiviral, and anticancer effects, among which the potential of its anticancer effects is the most described and is still under investigation.

Curcumin has been reported to modulate growth factors, enzymes, transcription factors, kinases, inflammatory cytokines, as well as pro-apoptotic and anti-apoptotic proteins. This polyphenol compound alone or together with other agents can be an effective drug for cancer treatment [17].

Etoposide and teniposide

Etoposide and teniposide are lignan derivative compounds widely used in chemotherapy for testicular cancer, lung cancer, lymphoma, leukemia, neuroblastoma, and ovarian cancer. Both of these drugs are now obtained by chemical modifications of the podophyllotoxin skeleton, a lignan that accumulates at low levels in the roots of Mayapple plant (*Podophyllum peltatum*) [12].

Noscapine

Papaver somniferum plant is a source of potent medicinal compounds that show diverse activities. Among the complex compounds related to the family of benzyloquinoline alkaloids, noscapine shows an exciting anticancer potential, but it is produced only in small amounts in this plant [12].

Noscapine targets microtubules and thereby inhibits cell proliferation [18].

Cannabidiol

Cannabidiol is a cannabinoid compound extracted from the *Cannabis sativa* plant. There is the extensive preclinical research showing that cannabidiol is effective as an anticancer agent alone or in combination with other cannabinoids, chemotherapy drugs, and radiation therapy in cancer treatment [19].

Conclusion

Medicinal plants are a rich source of biological compounds that have been used in the treatment of diseases for thousands of years. Various medicinal compounds are obtained from medicinal plants that have been effective in cancer treatment. Currently, some of these compounds such as paclitaxel, irinotecan, vinblastine, vincristine, etoposide, and teniposide are used for the treatment of various cancers in the clinic and they are considered as the most important chemotherapy drugs for cancer. Preclinical and clinical studies on the anticancer properties of other compounds extracted from plants, such as curcumin, noscapine, and cannabidiol, have been extensively conducted with success, and in the future, they can be used as potent chemotherapy drugs. In the future, we could devise new medicinal plant compounds for cancer treatment. We need to study chemical synthesis or semi-chemical synthesis of these anticancer compounds. In addition, it is essential to discover the main enzymes in the synthesis process of these compounds in plants. In the next step, we could clone the coding genes of these enzymes in bacteria and use these engineered bacteria to produce these anticancer medicinal plant compounds.

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