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A REVIEW OF NATURALLY DERIVED COMPOUNDS SHOWING ANTICANCER ACTIVITY

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ABSTRACT

Cancer is the second leading cause of death after Cardiovascular disease Globally. Determining the goals of treatment and palliative care is an important first step, and health services should be integrated and people-centered. The primary goal is generally to cure cancer or to considerably prolong life. Improving the patient's quality of life is also an important goal. Findings newer treatment options for cancer treatments with attention towards naturally-derived compounds as they are considered to have less toxic side effects compared to current treatments such as chemotherapy. Current treatment of cancer includes Chemotherapy, radiation, and surgery. But all of these treatments are well known for the stress patient has to suffer during and after treatment. So lots of work is being done of finding naturally occurring anticancer drugs. This article reviews different types of naturally derived compounds showing anticancer activity. Despite the progress in the field of cancer research, both developing and developed countries are in the grip of this deadly disease, and still, there is a need to discover and develop anti-cancer therapeutic agents. It has long been recognized that natural products represent the richest source of high chemical diversity, providing the basis for the identification of novel scaffold structures that serves as starting points for rational drug design.

Several medicinal plant species and their phytochemicals inhibit the progression and development of cancer. Out of these, there are four major structural classifications of plant-derived anti-cancerous compounds viz., Vinca alkaloids, Epipodophyllotoxin lignans, Taxane diterpenoids, and Camptothecin quinolone alkaloid derivatives discuss here.

Keywords: Phytochemical, anti-cancer, Vinca alakaloid, Taxane diterpenoids, Camptothecin quinolone alkaloid, Epipodophyllotoxin lignans.

INTRODUCTION

Considering the current scenario of the medical field we find that cancer is one of the major issues the whole world is facing. A lot of research is being done on the early diagnosis and treatment part of the disease. Many new theories are being implemented out of which some are being continued and some are being discontinued due to their adverse effects.

So there exists a need to look for some therapy that will have lesser side effects and be easily accessible. In this article, a literature review has been done with a focus on different research articles and texts related to the study of naturally derived articles showing anticancer activity.

Cancer is the second leading cause of death after Cardiovascular disease Globally. Determining the goals of treatment and palliative care is an important first step, and health services should be integrated and people-centered. The primary goal is generally to cure cancer or to considerably prolong life. Improving the patient's quality of life is also an important goal. [1] Finding newer treatment options for cancer treatments with attention towards naturally-derived compounds as they are considered to have less toxic side effects compared to current treatments such as chemotherapy. Current treatment of cancer includes Chemotherapy, radiation, and surgery. But as all of these treatments are well known for stress, patients have to suffer during and after treatment. So lots of work is being done for finding naturally occurring anticancer drugs. This article reviews different types of naturally derived compounds showing anticancer activity. Despite the progress in the field of cancer research, both developing and developed countries are in the grip of this deadly disease, and still, there is a need to discover and develop anti-cancer therapeutic agents. It has long been recognized that natural products represent the richest source of high chemical diversity, providing the basis for the identification of novel scaffold structures that serves as starting points for rational drug design.[2]

Several medicinal plant species and their phytochemicals inhibit the progression and development of cancer.

It has been researched that the plant kingdom is comprised of approximately 250 000 plant species and only around 10% have been studied for the treatment of different diseases. Phytochemicals and their derived analogues are present in different parts of the plant, e.g., flower stigmas, pericarp, sprouts, fruits, seeds, roots, rhizomes, stem, leaf, embryo, and bark, and perform several pharmacological functions. Several plant products such as alkaloids, flavonoids, lignans, saponins, terpenes, taxanes, vitamins, minerals, glycosides, gums, oils, biomolecules, and other primary and secondary metabolites play significant roles in either inhibiting cancer cell activating proteins, enzymes, and signaling pathways.[3]

Out of these, there are four major structural classifications of plant-derived anti-cancerous compounds viz., Vinca alkaloids, Epipodophyllotoxin lignans, Taxane diterpenoids, and Camptothecin quinolone alkaloid derivatives.

Vinca Alkaloids:

Four major vinca alkaloids are in clinical use for cancer: vinblastine, vinorelbine, vincristine, and vindesine.

These are sometimes called monoterpenoid indole alkaloids in scientific literature. All vinca alkaloids are administered intravenously. They are eventually metabolized by the liver and excreted.

Inside the Malignant Cells

The vinca alkaloids are cytotoxics – they halt the division of cells and cause cell death. Specifically, they can be classified as microtubule target agents. During cell division, vinca alkaloid molecules bind to the building blocks of a protein called tubulin, inhibiting its formation. The drugs work during the M-phase of cell reproduction. Tubulin protein normally works in cells to create "spindle fibers" (also called microtubules). These microtubules provide cells with both the structure and flexibility they need to divide and replicate. Without microtubules, cells cannot divide. The vinca alkaloid's mechanism in a nutshell: by occupying tubulin's building block structure, Vinca alkaloids prevent cancer cells from successfully dividing.

In addition to interfering in the multiplication of malignant cells, **Vinblastine** inhibits angiogenesis or the process by which new blood vessels grow from pre-existing ones. Angiogenesis is an essential step in a tumor's transition to malignancy. Vinblastine is most often applied to treat Hodgkin's disease, non-Hodgkin's lymphoma, breast cancer, and germ cell tumors. Side effects of vinblastine include toxicity to white blood cells, nausea, vomiting, constipation, dyspnea, chest or tumor pain, wheezing, and fever. Vinblastine sometimes causes antidiuretic hormone secretion and angina.[4]

Epipodophyllotoxin lignans :

Epipodophyllotoxin in clinical use for cancer: Etoposide & Teniposide.[5] All Epipodophyllotoxins are administered orally & intravenously. They are eventually metabolized by the liver and excreted.

Inside the Malignant Cells

Etoposide is a commonly used chemotherapy agent with a broad range of antitumor activity. Etoposide and teniposide, the epipodophyllotoxins, stabilize the double-stranded DNA cleavage normally catalyzed by topoisomerase II (topo II) and inhibit faithful relegation of DNA breaks. These double-strand DNA breaks subsequently trigger the desired antitumor effects of the drugs. Metabolism of etoposide is mediated by CYP3A4 and CPY3A5 (Fig. 1) [3,4], both of which are transcriptionally regulated by NR1I2 (i.e., pregnane X receptor). [6]

Epipodophylolotoxin appears to be involved in the production of DNA single & double-strand interaction between drug and heat-labile internuclear compounds. Type 2 topoisomerase is likely an intracellular target for the DNA strand-breaking effect of epipodophyllotoxins.[7]

Taxane diterpenoids :

Taxanes are a class of diterpenes. Docetaxel (Taxotere) & Paclitaxel (Taxol) are used as chemotherapy agents.[8] Cabazitaxel is used to treat hormone-refractory prostate cancer. All Taxane are administered intravenously. They are eventually metabolized by the liver and excreted. [9]

Inside Malignant Cells. The principal mechanism of action of the taxane class of drugs is the disruption of microtubule function. Microtubules are essential to cell division, and taxanes stabilize GDP-bound tubulin in the microtubule, thereby inhibiting the process of cell division as depolymerization is prevented. Thus, in essence, taxanes are mitotic inhibitors.[10] Taxanes are to be radiosensitizing.

In contrast to the taxanes, the vinca alkaloids prevent mitotic spindle formation through the inhibition of tubulin polymerization. Both taxanes and vinca alkaloids are, therefore, named spindle poisons or mitosis poisons, but they act in different ways.

Camptothecin quinoline alkaloid :

Quinoline alkaloids are in clinical use for cancer: Camptothecin and 9-methoxycamptothecin. Camptothecin quinoline alkaloids are administered orally. [11] They are eventually metabolized by the liver and excreted. [12]

The Camptothecin (CPT) class of compounds has been demonstrated to be effective against a broad spectrum of tumors. Their molecular target has been firmly established to be human DNA topoisomerase I (topo I). CPT inhibits topo I by blocking the rejoining step of the cleavage/relegation reaction of topo I, resulting in the accumulation of a covalent reaction intermediate, the cleavable complex. The primary mechanism of cell killing by CPT is S-phase-specific

killing through potentially lethal collisions between advancing replication forks and topo-I cleavable complexes. Collisions with the transcription machinery have also been shown to trigger the formation of long-lived covalent topo-I DNA complexes, which contribute to CPT cytotoxicity. The activation of the ubiquitin/26S proteasome pathway leads to the degradation of topo-I (CPT-induced topo-I downregulation) & involves SUMO conjugation to topo-I. The potentials roles of these new mechanisms for repair of topo-I-mediated DNA damage in determining CPT sensitivity/resistance in tumor cells. [13]

CONCLUSION

The review manifests that there are many naturally derived compounds which show anti-cancer activity. Various derivatives work as anti-cancer action in different ways. Vinca Alkaloids interfere in the division of cancerous cells and inhibits angiogenesis which ultimately caused cessation of the growth of cancerous cells. Epipodophyllotoxin lignans exhibit their anticancer activity via inhibition of tubulin polymerization. Taxane diterpenoids interfere with cell division by disruption of microtubules which are essential for cell division. Camptothecin quinoline alkaloids prevent DNA relegation and therefore cause DNA damage which ultimately results in apoptosis. Thus, preventing cancer spread.

This article takes a review of some of the important naturally occurring anticancer compounds. We can conclude from the above review that there are many natural derivatives which are being used as anticancer agents and there is wide scope to study more such agents and do systematic research on their anticancer activity.

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