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Mini Review

NANOPARTICLES CARRYING NATURAL PRODUCT FOR DRUG DELIVERY

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ABSTRACT

Camptothecin, Doxorubicin, Paclitaxel, Vincristine, and Etoposide are the naturally occurring anti-cancer drugs that are analyzed in this analysis. It is found that these compounds can be developed as nanomedicine. It has been determined from analyses that nanoparticles are useful in targeted drug delivery to address some of the innate issues. However, there are certain limitations that are found in nanomedicine. There is a need for more research to develop effective drugs in the future. A more detailed analysis of the same has been done in the following.

Keywords: Camptothecin, Doxorubicin, Paclitaxel, Vincristine, Etoposide, Targeted drug delivery, mechanism of action, toxicity, limitations

INTRODUCTION

Nanoparticles have more surfaces to volume ratio. These nanoparticles are found to revolutionize drug delivery.¹ This is because the drugs target the viruses and tumors and they are found to not affect the healthy tissue.^{2,3} The bioavailability of the particles is found to be the reason for the Nanomedicine to gain precedence.

Natural product is one of the best sources for procuring drugs and drug leads.⁴⁻⁶ From the year 1940 onwards, 131 drugs out of 175 small molecule anticancer drugs are found to be based on the natural product.⁷ This is owing to the fact that the natural products are found to have diversity in their physical structure and have chemical diversity. 40% of the chemical scaffolding is found in natural products.^{8,9} One of the most important reasons for considering natural products is that they are optimized evolutionarily as a drug-like molecule.¹⁰⁻¹² This is based on the natural products and these drugs are found to occupy the same molecular volume.¹³

Some of the nanoparticles that have been developed from the natural products are discussed in the following.

Camptothecin

Camptothecin is found to plant alkaloid that is initially isolated from *Camptotheca acuminata*. Camptothecin is found in the bark, leaves, and stem in the Chinese happy tree. *Camptotheca acuminata* is a native breed to China.^{14,15} These are considered to be important for the anticancer properties of Camptothecin.¹⁶⁻¹⁸ This is considered to be the traditional medicine that has been used for many centuries. This Camptothecin compound is found to have an important role in curing of a number of diseases including Nanomedicine treatment for cancer. This Camptothecin compound is found to halt the cell during the S phase mitosis. It is found to have a nanomolar potency to address the issues of cytotoxicity against the human tumor cell lines such as HT29, LOX to name a few. In combination with the TNF, it is found to induce apoptosis. A number of feasible drugs that are developed from the Camptothecin analogs are used in the development of anti-cancer drugs. Some of them are

topotecan and irinotecan.^{19,20} These have been commercially sold as anti-cancer drugs and in chemotherapy.²¹ These compounds are now being used in Nanomedicine. They are found to have long circulation half-lives and localize the tumor cells. The nanoparticles address the tumor cells only and release the CPT and cause them to disassemble the individual polymer chains.²² These are found to be smaller and cleared renally. IT-101 is one such drug that is currently investigated. Hence, this compound with a lot of potentials is found to originate from natural sources. Its complete potential in nanomedicine is yet to be utilized completely.

Etoposide

Etoposide is a compound that is extracted from the *Podophyllum hexandrum*. It is difficult to grow this plant. Owing to this, it was found that they can transfer the enzyme producing gene from *P. hexandrum* to *Nicotiano benthiana*. This is a tobacco-like plant that is easier to grow. The engineered plant is found to produce only nanograms of etoposide aglycone as a precursor to Etoposide. The prolific growth of the yeast cell can lead to better production. Etoposide is anti-cancer chemotherapy drug. This drug is a plant alkaloid and it functions as a topoisomerase II inhibitor. In the current times, it is used as a semisynthetic derivative of podophyllotoxin that is found to exhibit antitumor activity. The Etoposide inhibit DNA is found and is found to form a complex with the topoisomerase II and DNA.²³⁻²⁵ The complex is used to induce the break in the double stranded DNA and is found to prevent repair of the topoisomerase II binding. The accumulated then breaks the DNA into the mitotic phase of cell division. This eventually causes apoptosis. This then enters into the G2 and S phases of cell cycle. Currently, the feasibility of administering the medicine in the form of nanoparticles is being studied.²⁶ The complete potential of the Etoposide is yet to be harnessed completely.

Vincristine

Vincristine is a vinca alkaloid that is isolated from the *Vinca Rosea*. It has been marketed under many brand names. These are found in many formulations. This is used in the treatment of acute leukemia, Hodgkin's disease, malignant lymphoma and acute erythraemia. This vincristine sulfate is used as a part of the polychemotherapy as it stems from the lack of significant bone-marrow suppression. It has a unique clinical toxicity. This inhibits the mitosis at the metaphase stage that stems from the interaction with the tubulin. They interfere with the amino acid, glutathione metabolism, calmodulin-dependent Ca²⁺ or transport the ATPase activity or impact the cellular respiration and lipid biosynthesis. Currently, the lower solubility of the compound is causing a detrimental impact. This has impeded the process of nanomedicine. A number of clinical trials are being undertaken to understand the impact of the compound.²⁷

Paclitaxel

Paclitaxel is one of the compounds for cancer drug in the United States. This is found to be derived from the bark

of the *Taxus brevifolia*. It is used in the treatment of Kaposi sarcoma and a number of cancers.⁽²⁸⁻³⁰⁾ In this, the complex of α , β tubulins subunits along with Paclitaxel is used to correct the issues in mitotic spindle assembly, cell division, and chromosome segregation.^{31,32} This medicinal compound is used in Nanomedicine. The encapsulation of Paclitaxel is found to be biodegradable and has non-toxic Nano-delivery systems that reduce the toxicity of the company and increases the circulation half-life. It has found to yield a better result. This is also found in improved pharmacokinetic profiles. Paclitaxel along with the albumin-bound nanoparticles is used as a commercial medicine to treat the metastatic breast cancer. This drug is currently being used for the treatment of breast cancer on a commercial scale. This is one of the few nanomedicine drugs that have managed to address all the issues.³³ There are a number of novel paclitaxel nanoparticles that are current being analyzed.

Doxorubicin

Doxorubicin is found to be extracted from the anthracycline antibiotic that is cytotoxic and isolated from the *Streptomyces peucetius* cultures. These compounds are found to bind to the nucleic acid based on the specific intercalation of the planar anthracycline nucleus along with the double-helical structure of the DNA. It is found to impede the growth of the Cancer cells in the body.³⁴ The doxorubicin blocks the function of the enzyme topoisomerase 2. This is needed by the cancer cells to proliferate.³⁵⁻³⁷ Some of the factors that are considered in this situation are the efficacy of the drug based on the exposure of the tissue. The commerce and the toxicity are some of the other factors that are considered.³⁸ There has been an improved comprehension of the heterogeneity of clinical cancers and its biological factors. There is a transition that has been observed in the case of formulation-driven research to it being disease driven development. The nanomedicine needs to be developed and the potential needs to be fully harnessed.

SUMMARY

Camptothecin, Doxorubicin, Paclitaxel, Vincristine, and Etoposide are some of the naturally occurring anti-cancer drugs that are discussed in this analysis. The mechanism of action, sources of the compounds and the limitation during commercial production of the compounds are discussed. From this, a number of insights are gained. These are natural medicines and they are found to be optimized evolutionarily as a drug-like molecule that makes it feasible for the commercial production of the compounds. These medicines are mostly administered as chemotherapy drugs. These medicines are found to have the potential to be administered as nanomedicine into the body. However, its complete potential is yet to be harnessed. Each of these five compounds is found to be naturally occurring and has a number of properties to impede the growth of the anti-cancer cells. In the case of nanomedicine, there can be targeted drug delivery and the toxicity of the medicine can be prevented in this process. There are a number of ongoing clinical trials that are being undertaken to commercially produce the

compounds on a large scale. To conclude, the complete potential of the naturally occurring compounds that can be used as nanomedicines is yet to be harnessed.

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