Traditional Indian Herb *Catharanthus roseus* Used as Cancer Treatment: A Review

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**ABSTRACT**
Cancer is one of the main challenges in human health care which has been recorded as world’s second largest cause of death. Though there are number of therapies available to address the issue but prolonged use of these therapies generally produces severe adversities for example chemotherapy. Therefore, into the realization of finding other alternatives to reduce such adversities and side effects has revealed new horizon in the field of cancer therapy. More interestingly, the use of naturally driven products has been observed as significant alternative with new arrays of hopes to treat cancer. However, the studies on plant possessing anti-cancerous activities have been made but yet have to be evaluated in human. Furthermore, advancement in new technologies to characterize the active biomolecule is another aspect. Presently, we are focusing on the importance of *Catharanthus roseus* for anti-cancerous activity. More interestingly, the identified potential anti-cancerous compounds from this very plant are vincristine and vinblastine. In addition, *C. roseus* is the only plant which produces more than 100 monoterpeneoids and indole alkaloids, which possess two major cytotoxic diametric alkaloids and are commercially available to cure cancer.

**Keywords:** Anticancer, *Catharanthus roseus*, Vinblastine and Vincristine.

**INTRODUCTION**
Cancer can be defined as a mode of cell death which results in erasing healthy cells from the normal tissues and losing their function. The basic of cancer relies on the apoptosis which has been realized with the gene control over the malignant phenotype. The variables of apoptosis are generally seen with rapid condensation, chromatin condensation, nuclear fragmentation and shrinking of cells. The apoptosis are induced by oncogenic factors/mutations which facilitates the uncontrolled cell proliferation or tumor initiation (metastasis). More surprisingly, the treatment of tumor with cytotoxic anticancer agents has been reported as inducer of malignant cells. The most used therapy to treat cancer is exploited by using chemotherapy which indeed has been observed with apopstatic cell death on nearby subset of tissues that suggested as contributing toxicity across normal cells. Therefore, most anticancer agents now in use were developed using empirical screens designed to identify agents that selectively kill tumor cells. Until recently, most research into drug action focused on their intracellular targets, the nature of the cellular damage produced by the drug-target interaction, or resistance mechanisms that prevent the drug target interaction. Among the worldwide 7 million deaths from cancer in 2001, an estimated death in high-income countries were 0·76 million and about 1·67 million were observed in lower middle-income countries. The prevalence of high cancer induced death in less income countries have been reported due to intake of less nutritional value diet.

Amongst various form of cancer, breast cancer is progressively increasing which has been correlated with involvement of certain types of food such as rich animal fat. According to the national cancer database report during the period of 1985-1995, the relative survival rate of U.S patients suffering from papillary, follicular, hurthle cell, medullary and anaplastic carcinoma was 93%, 85%, 76%, 75% and 14 %. The age factor appears to be influencing all the forms of carcinoma mentioned. The excessive smoking, alcohol use and obesity are the other most important causes of cancer, which significantly prevail the risk of more deaths in men than women. Cancer leads to the increase in the restlessness, because of pain in patients of the breast, colon, rectum, prostate and various others. The look for other alternatives to defeat the prevalence of cancer worldwide has stepped out as best approach in today’s scientific field. It cannot be ignored that before emergence of modern medical science, we have been very close to nature and unveil the medicinally important plants to treat various ailments associated with our health. From that point of view the use of modern facilities to understand their chemical constituents and biological activities has contributed a lot in streaming down various challenges associated with life threatening diseases. Such medicinally important properties are exhibited in plants due to presence of phytochemicals which are classified as primary and secondary compounds. More importantly, secondary compounds such as alkaloids, terpenoids, phenolic compounds and coumarins etc. delivers vast array of medical benefits as anticancer.

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ant-inflammatory and anti-bacterial agents\textsuperscript{5,6}. In present study we are reviewing the use medicinally important plant \textit{Cantharantus roseus} in cancer therapy. \textit{Cantharantus roseus} is a traditional medicinal plant which possesses alkaloids known to cure many health problems like cancer, diabetes, blood pressure, asthma etc. The anticancerous compounds of \textit{Cantharantus roseus} namely vinblastin and vincristine are broadly used as medicine to cure various cancers.

\textbf{Scientific classification}

Botanical Name(s): Vinca Rosea (\textit{Cantharantus roseus})

Family Name: Apocynaceae

Kingdom: Plantae

Division- Magnoliophyta (Flowering plants)

Class- Magnoliopsida (Dicotyledons)

Order- Gentianales

Family- Apocynaceae

Genus- Catharanthus

Species: \textit{Catharanthus roseus}

\textbf{Morphology}

\textit{Catharanthus roseus} is an evergreen herb. The presence of oval leaves and white to dark pink flowers makes it unique and centre of the attraction. A corolla is about 2-5 cm in diameter with five petals like lobes. The fruit is a pair of follicles about 2-4 cm long and 3 mm broad\textsuperscript{7}.

\textbf{Phytochemical constituents and their therapeutic uses}

The alkaloids isolated from this plant are known sedative, hypotensive and anti-cancerous. \textit{C. roseus} is traditionally used by folklore to get rid from various health problems like disorders related to central nervous system, body pain and bleeding nose. It is also well established remedy for gastritis, cystitis and diarrhea. The book of pharmacognosy written by Rang et al describes the strong antioxidant properties of this plant which was also proved by many studies\textsuperscript{9}.

\textbf{Anticancerous compounds of \textit{C. roseus}}

The most potent and commercially available molecules characterized from \textit{C. roseus} are Vincristine and Vinblastin. In vitro studies of these molecules have shown significant anti-tumour activity as elaborated below.

\textbf{Vincristine and Vinblastin}

According to the reports shown by The American Society of Health System Pharmacists in 2015, vincristine and vinblastin are known for inhibiting mitosis i.e it stops the division of the cells and results in killing of the cells\textsuperscript{10}. Vincristine formulation helps in binding to the tubulin protein and stops the cells from separating its chromosomes at the time of metaphase which is responsible for cell death\textsuperscript{11}. It binds tubulin which results in inhibiting the microtubule assembly. According to a survey conducted on the 13 children suffering from acute leukemia showed remission rate of 54\% after the treatment with vincristine sulfate\textsuperscript{12}. On the other hand vinblastin results in the arresting of M phase specific cell cycle by inhibiting the microtubule assembly by improper mitotic spindle formation and kinetochore, which is important for the separation of chromosome at the time of anaphase.

\textbf{Mode of delivery of Vinblastine and Vincristine}

Vincristine and vinblastine both are delivered by intravenous infusion for use in many chemotherapy regimens. In case of Hodgkin lymphomas stage IA or IIA the Vinblastin is used with bleomycin and methotrexate in VBM chemotherapy. But in the case of Vincristine the chemotherapy regimen CHOP is used for non-Hodgkin lymphomas. For Hodgkin lymphomas the regimen used are MOPP, COPP, and BEACOPP. Stanford V chemotherapy regimen is rarely used in acute lymphoblastic leukemia and nephroblastom\textsuperscript{16}.

\textbf{Mode of action and Pharmacology}

Vincristine is known for binding to the tubulin dimmers which results in the inhibition of microtubule assembly and restricts mitosis at metaphase. The side effect associated with vincristine is that it targets all frequently dividing cell types which can also shows effects on the intestinal epithelium and bone marrow. Vinblastine at very low concentration is able to suppress the microtubule dynamics, whereas at high concentration it reduces the polymer mass of microtubule. It also causes the microtubule fragmentation\textsuperscript{13}. \textit{C. roseus} contains carbohydrates, flavonoids, alkaloids and saponins. Among all the most important constituents are alkaloids, which are about 400 in number present in \textit{C. roseus}. The majority of alkaloids are used in pharmaceutical, pesticides and food industry. The anti-cancerous compound vinblastine is an alkaloid by nature whereas vincristine is formed by the coupling of indole alkaloids namely vindoline and cantharidine present in the \textit{C. roseus}.

\textbf{Medicinal Properties}

Plants contain alkaloids, terpenoids, coumarins and many other phyto-compounds which are responsible for various therapeutic uses\textsuperscript{14}. The Vinblastine and Vincristine are two alkaloids of \textit{C. roseus}, which are responsible for the anticancer activity\textsuperscript{15}. The growths of some human tumours are suppressed by these alkaloids of \textit{C. roseus}. The use of Vinblastine is recommended for chorio carcinoma and Hodgkins disease. The other alkaloid namely Vincristine is used for leukemia in children. The Vinblastine is available under the name of Velban in the market, whereas Vincristine is sold as onconvin. The various extracts of \textit{C. roseus} are known for curing many diseases, like the ethanolic extract of leaves and flower of \textit{C. roseus} showed anti-diabetic property because it helps lowering of blood sugar\textsuperscript{16,17}. The extracts of \textit{C. roseus} leaf were known for its anti-bacterial activity against like \textit{Salmonella typhimurium NCIM2501}, \textit{Pseudomonas aeruginosa NCIM2036}, \textit{Staphylococcus aureus NCIM5021\textsuperscript{18}}. The ethanolic root extract of \textit{C. roseus} were observed to have anti-oxidant property\textsuperscript{19}. The anti- helmenthic property is also shown by this plant to cure chronic illness caused by the helminthes infections. Vincamine and Vindoline alkaloids of the plant have anti ulcer property to great extent. The ethanolic leaf extracts shows the anti diarrheal activity which was tested in the wistar rats with castor oil as an experimental diarrrhea inducing agent in addition to the pretreatment of the extract. The anti diarrheal effect of ethanolic extracts \textit{C. roseus} showed the dose dependant inhibition of the castor oil induced diarrrhea\textsuperscript{20}. This plant also used in phyto remediation by bioaccumulates heavy metal like cd etc. \textit{Catharanthus roseus} was found to be used from the traditional period as an anthelmintic agent. The ethanolic
CONCLUSION
The emergence of cancer is very fast since last decade. Many chemotherapies and herbal formulation are used extensively to reduce the risk of cancer. *C. roseus* is an effective name in the cure of cancer through the herbal approach. The study of its potential compounds against cancer is still going on. These studies to find the herbal alternative to beat cancer can be the most effective to reduce the side effects of chemotherapy. There is much more to analyze the importance of various medicinal plants for the treatment of cancers. In the coming years, as *C. roseus* and curcumin (compound extracted from *Curcuma longa*) more potential herbal formulations are expected to be discovered, which will prove to be the best treatment for cancer with minimum side effects.

REFERENCES