WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 4, 195-209. Review Article ISSN 2277– 7105

CATHARANTHUS ROSEUS (VINCA *ALKALOID*): A MEDICINAL HERB

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Article Received on
04 Jan. 2023,

Revised on 24 Jan. 2023,
Accepted on 14 Feb. 2023

DOI: 10.20959/wjpr20234-26918

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ABSTRACT

Vinca alkaloid (derived from *Catharanthus roseus*) are a subset of drugs (anti-mitotic and anti-microtubule alkaloid) obtained from the Madagascar periwinkle plant. They are naturally extracted from the pink periwinkle plant, Catharanthus roseus G. Don and have hypoglycemic as well as cytotoxic effects. They block beta-tubulin polymerization in a dividing cell. The plant is native of Madagascar and is found in many tropical and subtropical countries especially in India, Australia, South Africa and North and South America. The plant is cultivated as garden plant in Europe and India. The vinca alkaloids are also important for being cancer fighters. The Madagascar periwinkle has a reputation in folk remedy in the treatment of diabetes. vinka alkaloid are used as immunosuppressive drugs. Vinca Alkaloid are chemically indole alkaloids and are known to possess anti-cancer, anti-hypertensive and anti- diabetic roles. The principle members of group are vincristine(VCR), vinblastine(VBL), vindesine(VDS), vinorelbine(VRL). Vinflunine is also a new synthetic vinca alkaloid, which has been approved in Europe for the treatment of second-line transitional cell carcinoma of the urothelium is being developed for other malignancies.

KEYWODS: vinka alkaloid, madagascar periwinkle, anti-mitotic, anti-microtubule, beta tubulin, immunosuppressive, vincristine, vinblastine, vindesine, vinorelbine.

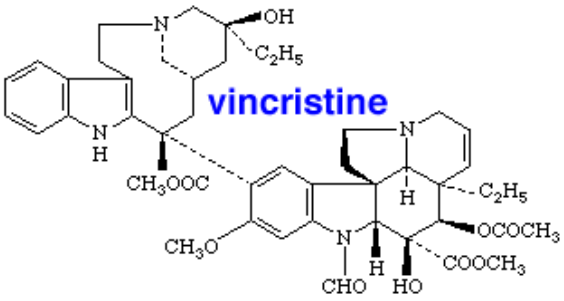
INTRODUCION

Vinca alkaloids are a material of a class of organic compounds made up of carbon, hydrogen, nitrogen and oxygen that is often derived from plants is named alkaloid. Although, the name represents alkali like some do not exhibit alkaline properties. Many alkaloids with having

poisonous characteristics have physiological effects too that make them useful as medicines.[1] Medicinal applications of this plant lead to the monitoring of these compounds for their hypoglycemic activity, which is of little importance compared to their cytotoxic effects.[2] The Madagascan periwinkle *Catharanthus roseus* L. is the source for a number of important natural products,[3] including catharanthine and vindoline[4] and the vinca alkaloids it produces from them: leurosine and the chemotherapy agents vinblastine[5] and vincristine,[6] all of which can be obtained from the plant.[7][8][9][10] However, it can be prepared either from vindoline and catharanthine[9][11] or from leurosine,[11] in both cases by synthesis of anhydrovinblastine, which "can be considered as the key intermediate for the synthesis of vinorelbine.[9] The leurosine pathway uses the Nugent–RajanBabu reagent in a highly chemoselective de-oxygenation of leurosin.[12][13] Anhydrovinblastine is then reacted sequentially with *N*-bromosuccinimide and trifluoroacetic acid followed by silver tetrafluoroborate to yield vinorelbine.

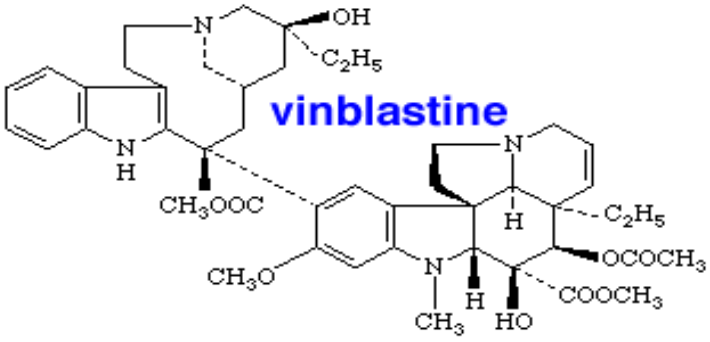
1. Vincristine

Vincristine, a natural vinca alkaloid, was first derived from the leaves of C. roseus[29][30][31] and has been used in tumor therapy since the 1960s as a cell cycle-specific (M-phase) antineoplastic agent.[29][30][31][32][33][34][35] The alkaloid can bind to tubulin, causing microtubule depolymerization, metaphase arrest, and apoptosis in cells undergoing mitosis.[32][34][35][36][37] Vincristine have been used for many years by clinics to treat malignancies including philadelphia chromosome-negative acute lyphoblastic leukemia[38][39] B-cell lymphoma[40][41] metastatic melanoma[42] estrogen-receptor-negative breast cancer,[37] glioma,[43][44] colorectal cancer,[45] non-Hodgkin's lymphoma,[36][46] Hodgkin's lymphoma, neuroblastoma, rhabdomyosarcoma, multiple myeloma, and Wilms' tumor.[47] However, its applications are restricted by severely neurotoxic side effects.



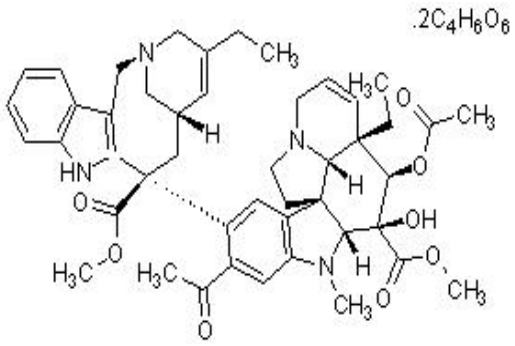
2. Vinblastine

Vinblastine is a mitotic inhibitor that has been used in the clinical treatment of leukemia, non-Hodgkin's disease, Hodgkin's disease, breast cancers such as breast carcinoma, Wilm's tumor, Ewing's sarcoma, small-cell lung cancer, testicular carcinoma, and germ cell tumors.[48][49][50][51] Vinblastine restrains not only the tumor growth, but malignant angiogenesis,[48][49-53] and can bind specifically to tubulin, inhibiting its polymerization and the subsequent association of microtubules. Side-effects of vinblastine consist of toxicity to white blood cells, nausea, vomiting, constipation, dyspnea, chest or tumor pain, wheezing, fever, and rarely, antidiuretic hormone secretion.[48]



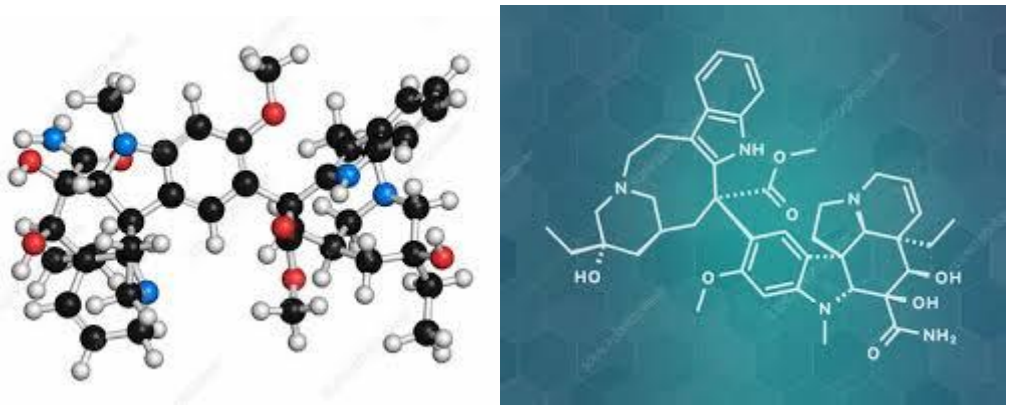
3. Vinorelbine

Vinorelbine is a semi-synthetic vinca alkaloid with a wide antitumor spectrum of activity, especially active in advanced breast cancer and advanced/metastatic non-small-cell lung cancer. Compared with vincristine and vinblastine, vinorelbine is more active and relatively less neurotoxic An injectable form of vinorelbine (Navelbine® IV, Medicament, France) developed by Pierre Fabre is now widely used in clinics. Because vinorelbine is well known to cause venous irritation and phlebitis when directly administered intravenously, new drug delivery systems are urgently required.[54-58]

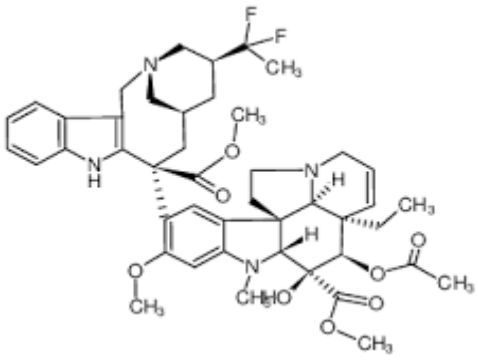


4. Vindesine and Vinflunine

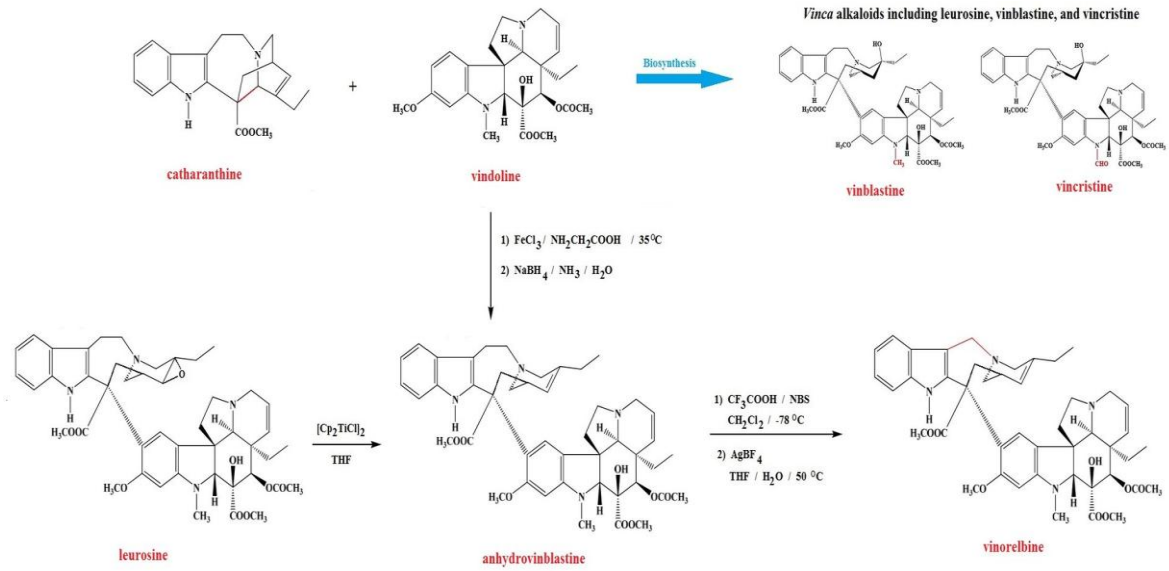
Vindesine, desacetyl-vinblastine-amide, is a semisynthetic vinca alkaloid with effects similar to those of vinblastine.[48][59] Vindesine inhibits net tubulin addition at the assembly ends of microtubules and treats pediatric solid tumors; malignant melanoma; blast crisis of chronic myeloid leukemia; acute lymphocytic leukemia; metastatic colorectal; and breast, renal, and esophageal carcinomas.[48][60][61] Although vindesine is useful for treating many types of cancer, it is not approved by the FDA.[48] Vinflunine, a semi-synthetic vinca alkaloid, is currently being clinically evaluated.[48][62] Both second-generation vinca alkaloid, vinorelbine, and third-generation compound vinflunine have shown promising results in cancer therapy.[62] Vinflunine is emerging as an effective anticancer agent because it is less neurotoxic than vinorelbine and has superior antitumour activity (preclinical) compared to that of other vinca alkaloids. Although vindesine and vinflunine are promising antitumor agents used clinically, research on related drug delivery systems is limited.



[Vindesine: Cancer chemotherapy drug]



[Vinflunine]



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(Redirected from Anhydrovinblastine)

Scientific Classification	
Kingdom	*Plantae*
Division	*Magnoliophyta (flowering plant)*
Class	*Magnoliopsida*
Order	*Gentianales*
Family	Apocynaceae
Genus	*Catharanthus*
Species	*C.roseus*
	Vernacular Names
English	old maid, periwinkle, cayenne jasmine
Hindi	sadabahar
Kannada	batla hoo, bili kasi kanigalu, ganeshana hoo, kempu kaasi kanigalu
Marathi	sadaphul, sadaphool, sadaphuli
Sanskrit	nityakalyani, rasana, sadampuspa, sadapushpi
Tamil	cutkatu malli, cutukatu malli, cutukattupuu
Telugu	billaganneru
Gujarati	Barmasi
Bengali	noyontara

Pharmacological Activities

Anti – cancer activity

The anticancer alkaloids Vinblastine and Vincristine are derived from stem and leaf of Catharanthus roseus. These alkaloids have growth inhibition effect to some human tumors. Vinblastine is used experimentally for treatment of neoplasmas and is recommended for Hodgkins disease, chorio carcinoma. Vincristine another alkaloids is used for leukemia in children. Different percentage of the methanolic crude extracts of Catharanthus was found to show the significant anticancer activity against numerous cell types in [the in vitro condition and especially greatest activity was found against the multidrug resistant tumor types. Vinblastine is sold as Velban or Vincristine as oncovin.[15][16]

Anti – diabetic avtivity

The ethanolic extacts of the leaves and flowers of C.roseus showed a dose dependent lowering of blood sugar in comparable to the standard drug. Lowering of blood sugar in comparable to the standard drug glibenclamine. The Hypoglycemic effect has appread due to the result of the increase glucose utilization in the liver. The aqueous extract was found to lower the blood glucose of about 20% in diabetic rats when compared to that of the dicloromethane and methanol extracts which lower the blood glucose level to to the 49-58%. The hypoglycemic effect appeared due to the result of the increased glucose utilization in the

liver. The hypoglycemic activity of alkaloids isolated from C.roseus have been studied pharmacologically and a remedy derived from the plant has been marketed under the propritery name Vinculin as a treatment for diabetes.[17][18][19]

Anti – microbial activity

Crude extracts from different parts of the plant was tested for anti-bacterial activity. Extract from leaves showed significantly higher efficacy. The anti-bacterial activity of the leaf extract of the plant was checked against microorganism like Pseudomonas aeruginosa NCIM2036, Salmonella typhimuruim NCIM2501, Staphylococcus aureus NCIM5021 and was found that the extracts could be used as the prophylactic agent in the treatment of many of the disease.[20]

Anti-helminthic activity

Helminthes infections are the chronic illness, affecting human beings and cattle. Catharanthus roseus was found to be used from the traditional period as an anti-helminthic agent. The anti-helminthic property of C. roseus has been evaluated by using Pheretima posthuma as an experimental model and with Piperazine citrate as the standard reference. The ethanolic extract of the concentration of 250 mg/ml was found to show the significant anti helminthic activity.[21]

Anti-oxidant property

The anti-oxidant potential of the ethanolic extract of the roots of the two varieties of C. roseus namely rosea (pink flower) and alba (white flower) was obtained by using different system of assay such as Hydroxyl radical-scavenging activity, uperoxide radical-scavenging activity, DPPH radical- scavenging activity and nitric oxide radical inhibition method. The result obtained proved that the ethanolic extract of the roots of Periwinkle varieties has exhibited the possess satisfactory scavenging effect in the entire assay in a concentration dependent manner but C. roseus was found to more antioxidant activity than that of C. alba.[22]

Anti-ulcer property

Vincamine and Vindoline alkaloids of the plant showed anti- ulcer property. The alkaloid vincamine, present in the plant leaves shows cerebrovasodilatory and neuroprotective activity. The plant leaves proved for anti-ulcer activity against experimentally induced gastric damage in rats.[23]

Hypotensive property

Extract of leaves of the plant made significant change in hypotensive. The leaves have been known to contain 150 useful alkaloids among other pharmacologically activecompounds. Significant antihyperglycemic and hypotensive activity of the leaf extracts (hydroalcoholic or dichloromethane-methanol) have been reported in laboratory animals.[24]

Anti-diarrheal property

The anti-diarrheal activity of the plant ethanolic leaf extracts as tested in the wistar rats with castor oil as a experimental diarrhea inducing agent in addition to the pretreatment of the extract. The anti-diarrheal effect of ethanolic extracts C. roseus showed the dose dependant inhibition of the castor oil induced diarrhea.[25]

Hypolipidimic effect

In study, significant anti atherosclerotic activity as suggested by reduction in the serum levels of total cholesterol, triglycerides, LDL-c, VLDLc and histology of aorta, liver and kidney with the leaf juice of Catharanthus roseus (Linn.) G. Donn. Could have resulted from the antioxidant effect of flavonoid, and probably, vinpocetine like compound present in leaf juice of Catharanthus roseus (Linn.) G. Donn.[26]

Wound healing property

Rats treated with 100 mg /kg/day of the Catharanthus roseus ethanol extract had high rate of wound contraction significantly decreased epithelization period, significant increase in dry weight and hydroxyproline content of the granulation tissue when compared with the controls. Wound contraction together with increased tensile strength and hydroxyproline content support the use of C. roseus in the management of wound healing.[27]

Memory enhancement activity

Vinpocetine has been reported to have a variety of actions that would hypothetically be beneficial in Alzheimer's disease (AD). The only study investigating this agent in a well-defined cohort of AD patients found no benefit. Meta- analysis of older studies of vinpocetine in poorly-defined dementia populations concluded that there is insufficient evidence to support its clinical use at this time. Vinpocetine has been well tolerated at doses up to 60 mg/d in clinical trials of dementia and stroke, and no significant adverse events.[28]

Acknowledgement

Authors like to express their sincere thanks to Hon. Shri. Padma Nandkumar Shinde, President, Shriram Dyan Shikshan Prasarak Mandal, Vaijapur, Maharashtra, India for their contant encouragement and support.

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