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# A Herbal Drug of Vinca: Used as an Anti-Cancer Drug

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**ABSTRACT**

Vinca alkaloids are obtained from the Madagascar periwinkle plant. They are naturally occurring or semi synthetic nitrogenous bases extracted from the pink periwinkle plant Catharanthus roseus G. Don. and have a hypoglycemic as well as cytotoxic effects. They have been used to treat diabetes, high blood pressure and have been used as disinfectants. The vinca alkaloids are also important for being cancer fighters. There are four major vinca alkaloids in clinical use: Vinblastine, vinorelbine, vincristine and vindesine. Vinca alkaloids are the second-most-used class of cancer drugs and will stay among the original cancer therapies. The present review work was mainly focused on compilation of data related to extraction of important alkaloids from Vinca (Catharanthus roseus) using different techniques and further their isolation, detection/ identification, and analysis using modern analytical methods.

**Keywords:** Catharanthus roseus , vinblastine, vinca alkaloids, vincristine, Isolation and extraction, Analysis

## Introduction

Vinca Rosea is an important medicinal Plant which is belongs to the family of Apocynaceae. It is a Dicotyledonous Angiosperm and has two terpenes alkaloids that is Vinblastine and Vincristine which is use to treat cancer Vinca grows is whole India up to 500 meter. It is grown freely in tropical & subtropical area in South India & North Eastern States of India. Its flower look white to dark pink with a darker red center & a Basal Tube of 0.2 long with a corolla of about 2.0 – 5.0 cm diameter with five petals like lobes. These fruits follicles are found in pair about 2.0 -4.0 cm long & 3mm broad various synonyms of vinca are Sadabahar, Catharanthus roseus[12].

## Clinical Pharmacology

Vinblastine is a drug used in the elective regime for the metastatic treatment of testicular cancer. The estimates of half-life after vinblastine administration to patients were 4 min, 1.6 h, and 25 h, which indicates a faster drug distribution in most tissues and a subsequent slower terminal elimination process. Distribution and initial cleaning phase for vincristine are kinetically comparable to the ones observed for vinblastine; half-lives for those phases have been reported at 4 min and 2.3 h in studies with vincristine. The terminal elimination phase for vincristine is reported to be three to four times longer than the one estimated for vinblastine, and the slow elimination of vincristine from the neuronal susceptible tissue suggest that it plays a role in neurotoxicity commonly seen in clinical adjustments with vincristine but not with vinblastine. Hepatic metabolism and bile excretion play major roles in the elimination of both vinblastine and vincristine in humans; small quantities of vincristine and vinblastine, in the order of 10% of the administered dose, are excreted with no alterations through urine. The renal clearance of vinblastine is reported as being less than 10% of the total elimination of the serum. It has been reported that vinblastine inhibits a polymorphic cytochrome P-450 in human hepatic microsomes, but the necessary concentrations were higher than those observed in clinical adjustments. It is recommended that vinblastine and vincristine doses must be reduced in patients with liver disease. Vincristine is conventionally administered intravenously, in adults, with a dose of 1.4 mg/$m^2$; the total dose must not exceed 2 mg in each administration. Sulkes and Collins have commented on the adjustments that can be provided for conventional doses of vincristine and other drugs. Of particular importance is the possibility that some patients can show a good clinical response and relatively low toxicity in dose regimes involving the cautious use of large quantities of vincristine. The initial dose of vinblastine for adults is 3.7 mg/m2, with a range of the typical growing dose of 5.5–7.4 mg/m2, administered weekly.

## Application of vinca

Vinca alkaloids are used in chemotherapy for cancer. They are a class of cell cycle specific cytotoxic drugs that work by inhibiting the ability of cancer cells to divide: Acting upon tubulin, they prevent it from forming into microtubules, a necessary component for cellular division. The vinca alkaloids thus prevent microtubule polymerization, as opposed to the mechanism of action of taxanes. The vinblastin sulphate is highly used in the treatment of neoplasm, lymphocytic lymphoma, Hodgkin's disease, testicular carcinoma. Vinblastin can show its potency in its individual form but generally it is dispensed in combination of other drugs to improve its therapeutic efficacy. It is dispensed through intravenous route by considering other factors like body surface, patient age, WBC count etc. Vincristine sulphate is also available in ampoule and stored in refrigerator to improve its stability. It is also useful in lymphosarcoma, small cell lung cancer, neuroblastoma, Hodgkin's disease, cervical and breast cancer. These alkaloids show antimitotic activity

which inhibits cell growth. They disrupt the microtubules which causes the dissolution of cell mitotic spindle and the growth of cell arrest in metaphase. Vinca alkaloids are now produced synthetically and used as drugs in cancer therapy and as immunosuppressive drugs. These compounds include vinblastine, vincristine, vindesine, and vinorelbine. Additional researched vinca alkaloids include vincaminol, vineridine, and vinburnine. Minor vinca alkaloids include minovincine, methoxyminovincine, minovincinine, vincadifformine, desoxyvincaminol, and vincamajine. Vinpocetine is a semi-synthetic derivative of vincamine (sometimes described as "a synthetic ethyl ester of apovincamine".

***Biological source:***

It is dried whole plant of *Vinca rosea*

***Geographical Source:***

It is indigenous to Madagascar. Vinca plant is cultivated for the decorating plant and found in tropical regions like Africa, Australia, Eastern Europe Taiwan and Thailand.

***Botanical Classification***

- **Botanical Name(s)** ; *Vinca Rosea ( Catharanthus Roseus)*
- **Family Name**: Apocynaceae
- **Kingdom**: Plantae
- **Division:** Magnoliopsida (Flowering plants)
- **Class**: Magnoliopsida (Dicotyledons)
- **Order**: Gentianales
- **Genus**: Catharanthus
- **Species**: C. roseus

***Vernacular names***

- **English**: Cayenne, jasmine, old maid
- **Hindi**: Sada-bahar
- **Malayalam**: Banappuva,Nityakalyani
- **Marath**i: Sadaphool, Sadaphul
- **Sanskrit**: Nityakalyani, Rasna,
- **Tamil**: Cutkattu malli, Cutukattu malli
- **Telugu**: Billaganneru
- **Gujarati**: Barmasi
- **Bengali**: Noyontara

***Morphological Character:***

A Vinca is found in blue, purple and white color. It is a type of annular or corneal plant. Vinca is near about 0.52 to 1 cm in length and its leaves is oblong, ovate, glossy and bitter in taste with slight odour.

## Chemical Constituents:

In vinca plant constitute of vinblastin and vincristine, on the chemotherapy medication it is used for several types of cancers. These are the biosynthesized from the compuling on the cantharanthine and vindoline alkaloids). Vinorelbin agent are semi synthetic chemotherapeutic which are used to treat non small cell of lung cancer.(They can be prepared either from vindline and catharthine or from the vinca alkaloid leurosine), in both case via anhydrovinblastin . vinca flower is constitute of Rosinidin pink anthracynidin pigments which are responsible for the flower color.

There are following chemical constituents of vinca as follows.

**1.Vinblastin:**

Vinblastin, under the marketed brand name Velban amongst others, is chemotherapy. It is topically used combined with other medications. These are treat various type of cancer includes non-small cell lung cancer, hodgkin's lymphoma, bladder cancer, brain cancer, testicular cancer and melanoma. It is administered by injection into a vein (Vinblastine Sulphate).

**2.Vincristin:**

Vincristin is also called leurocristine and under marketed brand name is Oncovin among other,in a chemotherapy . It should bemused in the treat o different types of cancer .These include acute lymphocytic leukemia, acute myeloid leukemia, hodgkin's disease, neuroblastoma, and small cell lung c amongst other. It is administered by intravenously. These are also used as immunosuppressant (Vincristine Sulphate).

**3. Vindesine**:

Vindesine is used in Chemotherapy, Vindesine is the anti-mitotic Vinca alkaloid . It should be used in the treatment of various type of cancer including or under the leukemia, multiple melanoma, Lymphoma, breast cancer and lung cancer. It is administrated by the intravenous.

**4.Tabersonine:**

Tabersonine is the terpenes of indole alkaloid which are found in the medicinal plant of vinca rosea. These are hydroxylated at the 16 position by the enzyme tabersonine 16-hydroxylase (T16H) was form16- hydroxytabersonine. It is first intermediate leading to form the vindoline one of the two precursors are required for vinblastine biosynthsis[6].

**5. Vinpocetine**:

These are the chemical syntheticaly derivative of the vinca alkaloid vincamine[14] . These are the extracted from the leaves of vinca minor (lesser periwinkle-2008)[13] or the seeds of voacangan africona. Vinpocetin supplement was banned for the sale in New Zealand, Australia and Canada because it is potentially harmful nootropic characteristics (https://en.m.wikipedia. org/wiki/vinpocetine).

***Cultivation of vinca :***

Vinca is a decorative plant, it is appreciated for its hardiness in dry and nutritionally deficient condition, famous subtropical gardens these temperature never fall below 5-7 Cº (41-45 7980 Ravikant Vishwakarma et al. A herbal drug of Vinca: Used as a anticancer agent degree Fº), and as a summer season bedding plant in temperature gardens .It's flowering period was long, throughout the year in tropical conditions, spring to late autumn, in summer temperature climates .To choice the full sun and well-drained soil. Various cultivars have been selected, for the variation in flower color (white, mauve, pink, peach, scarlet and reddish orange), and also for tolerance of cooler growing conditions in temperate regions. The famous cultivars include "Albus "(white flowers),"Grape cooler"(rose pink,cool – tolerant ), the ocellatus group (various colors), and "peppermint cooler " (white with red centre, cool-tolerant)(Chathopadhay)[7].

***Mechanism of action of Vinca:***

Vinca causes cytotoxicity is due to their interactions with disruption of microtubule function and tubulin, especially of microtubules comprising the mitotic spindle fiber and causing metaphase arrest. They can perform some other biochemical response which can be effective or may not be effective on microtubules. Have some effect which do not interrupted the microtubule only after treatment of cells with clinically irrelevant doses of the vinca.

Vinca and other anti-microtubule drug are also shows effect on both malignant cells and non-malignant cells in the non-mitotic cell cycle, because microtubules are involved in various nonmitotic functions. Vinca are connected to binding sites of tubulin which is separate from the taxanes, colchicine, podophyllotoxin and guanosin-5'- triphosphate. Binding occur rapidly and can reverse too. Maintains the existence of vinca binding site / mole of tubulin dimer. 16-17 high affinity binding sites in each microtubule which is located at the end of per microtubule. The vinca bind at the binding site and interrupts microtubule congregations,but low drug concentration can be decreasing the rates of both growth and shortening at the assembly end of the microtubule that can cause produces a " kinetic cap "and suppresses function .

The distributing effects of the vinca on microtubules dynamics, particularly at the ends of mitotic spindle, which causes metaphase arrest, occur at drug concentrations below those that decrease microtubule mass. The vinca and other microtubule distort agents have power to inhibit malignant angiogenesis in vitro.

## Pharmacological Value:

1. **Anticancer Property:** The anticancer active ingredients Vinblastin and Vincristine are derived from the leaf and stem of vinca. They inhibit the growth of human tumors. Vinblastine is used experimental or treatment of neoplasmas and for Hodakins disease, choric carcinoma. Vincristine and anothers active ingredients are used for leukemia in children (Banskota, 2002[2]; Wang, 2004).

2. **Memory Enhancement Property**: Vinpocetine produces various actions that would hypothetically be beneficial in Alzheimser disease (AD). When study investigating this agent in a well-defined cohort of AD patients found no benefit. Vinpocetine has been well tolerated at doses up to 60 mg/d in clinical trials of dimention and stroke and no significant adverse events.

3. **Wound Healing Property:** Vinca is useful for management of wound healing when wound contraction together with increased tensile strength and hydroxyproline (Nayak, 2007)[15].

4. **Hypolipidiemic Property**: Important anti-atherasclerotic activity as suggested by reduction in the serum level of total cholesterol, triglycerides, LDLc, VLDLc and histology of aorta,liver and kidney with the action of leaf juice of vinca.

5. **Hypotension Property:** The vinca leaves extract play significant role in hypotension[11] .The leaves have been contain 150 useful alkaloids among other pharmacologically active compound.

6. **Anti-dibetic property:** The ethanolic extracts of vinca leaves showed a dose dependept lowering of blood sugar in comparable to the standard drug and lower the blood sugar in camparable to the standard drug glibendamide.

7. **Anti-microbial property[9]**: The extract from different parts of vinca is tested for anti-microbial property and the vinca leaf extract showed significantly higher efficacy .The anti- bacterial property of the leaf extract of the vinca was checked agonist micro-organism and found that the extracts could be used as the prophylactic agent in the treatment of many of the disease.

8. **Antioxidant Property**: The antioxidant potential[3] of the ethanolic extract of the roots of the varieties of vinca namely rosea (pink flower) and alba (white flower).

9. **Anti-helminthic Property:** Helminthes infection are the chronic illness which affects the human beings and cattle. In vinca found to be used from the traditional period as an anti – helmenthic agent. The ethanolic extract of the vinca concentration of 250mg/ml was found to show the significant anti-helmenthic property.

10. **Anti- ulcer property:** Vincamine and Vindoline alkaloids of the plant showed anti-ulcer property[10]. The vincamine are present in the leaves of vinca plant shows cerebrovaso dilatary and neuro-protective property.

11. **Anti-diarrheal property**: The ethanolic leave extract of vinca is show the anti- diarrheal[11] property as tested in the wistar rats with castor oil which are the experimental diarrhea inducing agent by addition of pretreatment of the extract. These effects of ethanol extracts C.roseus are showed for the dose dependant inhibition on the castor oil decrease diarrheal.

## Conclusion

In this review, discussed about the vinca. It is broadly used in medical field. These are consisting of following chemical constituents and each and every constituents are play a vital role like vinblastine and vincristins have anticancer property[4]. Vinca is popular for anticancer property but as well as it have memory enhancement, anti helmentic, antioxidant properties. As the synthetic drug have many side effects but we also have the traditional medicine like vinca which is been used from the ancient times.mostly the vinca rosea is been used as the second line therapy now –a-days. The cytotoxic agents which were been approved by the US are vinblastin, vincristine, vinorelbine.European have been approved the alkaloid, vinflunine which is used for the treatment of second-line transitional cell carcinoma of the urothelium. With rapid advancement in treatment and prolonged research the complete cure for cancer has hope after all and the days of curing cancer are not very far.

**REFERENCES**


**1)** Ajaib M., Khan ZUD., Khna N., Wahab M. 2010. 2Ethnobotonical studies on useful shrubs of District kotli, Azad Jammu and Kashmir, Pakistan. Pak Bot.,1407-1415. 7981

**2)** International Journal of Current Research, Vol. 11, Issue, 10, pp.7979-7982, October, 2019 Banskota A.H. 2002. Antiproliferrtive activity of vietnamose medical plants

**3)** Alba Bhutkar MA, Bhise SB. Comparative Studies on Antioxidant Properties of Catharanthus Rosea and Catharanthus. International Journal of Pharmaceutical Techniques, 2011, 3(3): 1551-1556.

**4)** Brogan C. Alkaloids cancer treatments. 2010. Jun 7, [Cited on 2010 Sep 23]. Available from: http://www.Vinca alkaloids\AlkaloidsCancer Treatment Livestrong_com.mh.

**5)** Mithun Singh Rajput, Veena Nair, Akansha Chauhan.Evaluation of Antidiarrheal Activity of Aerial Parts of Vinca major in Experimental Animals. Middle-East Journal of Scientific Research.2011, 7 (5): 784-788.

**6)** Sekar P. “Vedic clues to memory enhancer”. The Hindu 21 (1996).

**7)** Chattopadhyay RR., et al. “Hypoglycemic and antihyperglycemic effect of leaves of Vinca rosea Linn”. Indian Journal of Physiology and Pharmacology 35.3 (1991): 145-151.

**8)** Yogesh P. "Evaluation of hypolipidemic activity of leaf juice of Catharanthus roseus (Linn.)". Acta Poloniae Pharmaceutica - Drug Research 68.6 (2011) :927-935.

**9)** Prajakta J Patil and Jai S Ghosh. "Antimicrobial Activity of Catharanthus roseus – A Detailed Study". British Journal of Pharmacology and Toxicology 1.1 (2010): 40-44.

**10)** The Wealth of India-Raw Materials New Delhi: Publication and Information Directorate, Council of Scientific and Industrial Research has found anti- ulcer property. 3 (1985): 391-395.

**11)** P. P. Pillay, C. P. M. Nair, and T. N. Santi Kumari. Lochnera rosea as a potential source of hypotensive and other remedies.Bulletin of Research Institute of the University of Kerala, 1959, 1:51–54.

**12)** Asma N., et al. "An updated Review on Catharanthus Roseus:Phytochemical and Pharmacological Analysis". Indian Research Journal of Pharmacy and Science 3.2 (2016): 631-653.

**13)** CatharantusRoseus– periwinkle. Tropiclab Inc.www.tropilab.com/periwinkle.html(accessed 20 July 2008).

**14)** Babulova A, Machova J, Nosalova V. Protective action of vinpocetine against experimentally induced gastric damage in rats. Arzneimittel forschung, 2003, 43:981-985. 14) P. P. Pillay, C. P. M. Nair, and T. N. Santi Kumari. Lochnera rosea as a potential source of hypotensive and other remedies.Bulletin of Research Institute of the University of Kerala, 1959, 1:51–54.

**15)** Nayak BS., et al. "Evaluation of wound-healing potential of Catharanthus roseus leaf extract in rats". Fitoterapia 78.7-8 (2007): 540-544