

Vincaroseus as anticancer activity

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Date of Submission: 15-12-2024

Date of Acceptance: 25-12-2024

ABSTRACT:

Catharanthusroseus is a highly significant medicinal plant known for its bioactive compounds that have been utilized for decades, particularly in cancer treatment. In Ayurveda, an ancient system of traditional medicine from India, Catharanthusroseus is used for its numerous therapeutic properties. It is particularly known for its antitumor, anti-diabetic, anti-microbial, antioxidant, and antimutagenic effects, making it a vital component in Ayurvedic medicine. The plant is native to the islands of Madagascar, and it is an evergreen shrub with flowers that vary in color from red to pink. The leaves of the plant are arranged in opposite pairs, adding to its distinct appearance. Catharanthusroseus produces a variety of important alkaloids, such as ajmalcine, vincine, reserpine, vincristine, vinblastine, and raubasin. Among these, vincristine and vinblastine are particularly notable for their use in treating several types of cancer, including Hodgkin's disease, skin cancer, breast cancer, and lymphoblastic leukemia. In this review, focuses on the chemical constituents, identification of compound, mechanism and pharmacological activities of plants.

Keywords: Catharanthusroseus, vinblastine, vincristine, Anticancer activity, Alkaloids

I. INTRODUCTION:

Many naturally grown plants have medicinal uses, and one notable example is Catharanthusroseus, it is also called as Madagascar periwinkle. This perennial plant is native to Madagascar and found in tropical regions, including Southern Asia. It features colorful flowers in pink, purple, and white and is often used for ornamental purposes^(1,2)

In Malaysia, it's called KemuntingCina. Catharanthusroseus contains vinca alkaloids, which are important for cancer treatment. the Madagascar periwinkle (Catharanthusroseus) is renowned for its production of a milky sap that contains over 70

indole alkaloids. Among these alkaloids, vinblastine and vincristine are particularly significant for their medicinal properties.⁽³⁾

Different cultures use this plant for various health issues:

In India, leaf extracts help with bee stings and are also used for diabetes. In the Philippines and Africa, leaf infusions treat heavy menstrual bleeding.⁽⁴⁾

In Mauritius, extracts are used for digestive problems. In the Bahamas, flower decoctions are used for tuberculosis treatment and gas. In Malaysia, the West Indies, and Nigeria, it's used for diabetes treatment. Overall, Catharanthusroseus serves both decorative and medicinal roles in various cultures.^(5,6)



Fig.1 Catharanthusroseus.

Scientific classification⁽⁷⁾

1. Botanical Name(s): VincaRosea (CatharanthusRoseus)
2. Family Name: Apocynaceae
3. Kingdom: Plantae
4. Division: Magnoliophyta (Flowering plants)
5. Class: Magnoliopsida
6. Order: Gentianales
7. Genus: Catharanthus
8. Species: C. roseus

Vernacular names:

English: cayenne jasmine, old maid, periwinkle
Hindi: sadabahar, sadabahar
Kannada: batlahoo, kanigalu,
Malayalam: banappuvu, nityakalyani, savanari, usamalari
Marathi: sadaphool, sadaphuli
Sanskrit: nityakalyani, rasna, sadampuspa, sadapushpi
Tamil: cutkattumalli, cutukattumalli, cutukattuppu
Telugu: billaganneru
Gujarati: Barmasi
Bengali: noyontara

Description:

A Periwinkle, known scientifically as *Vinca*, is a versatile and widely distributed shrub that grows to a height of 1 to 3 feet. With its glossy, dark green leaves, it produces flowers throughout the year in various colors, including blue, purple, violet, pink, and white. This hardy plant thrives in tropical and subtropical regions, and it is native to areas including North America, Europe, India, and China. A part from its aesthetic appeal, the periwinkle plant is renowned for its medicinal properties. Various parts of the plant, including its leaves, flowers, and roots, have been used in traditional medicine for centuries. Periwinkle is particularly valued for its potential in treating a range of ailments, such as controlling blood sugar, managing high blood pressure, and even in cancer treatment due to compounds like vincristine and vinblastine found in the plant. These alkaloids are used in chemotherapy for certain types of cancer, showcasing the immense medicinal value of the periwinkle plant. Alkaloids are found in various part of the plant, but they are especially concentrated in certain parts such as the roots and bark. These compounds have notable medicinal properties and are widely used in pharmacology for their therapeutic effects. It contain important alkaloids from the *Rauvolfia* group, including ajmalicine, reserpine, and serpentine. Additionally, vindoline, vincristine, and vinblastine are significant for cancer treatment. The plant is widely used in Ayurvedic and Chinese medicine.

1.Habit:A perennial herb.

2.Stem:Erect and cylindrical Branched and solid Reddish-green and smooth (glabrous)

3.Root:Tap root that is rarely branched.

4.Leaf: Simple and arranged in pairs (opposite) Petiolate (with a petiole) Entire (smooth edges) with a pointed tip (mucronate apex)

5.Inflorescence:Cymose, with flowers arranged in pairs in the axils of leaves.

6.Flower:Pedicellate (on a stalk), bractate (with bracts)Hermaphrodite (contains both male and female parts) Actinomorphic (symmetrical) and complete, typically pink.

7.Calyx:Composed of 5 green, glandular sepals,Polysepalous (multiple sepals) and inferior,Quincuncial aestivation (specific arrangement of sepals in bud).

8.Corolla:Consists of 5 petals forming a tubular shape.The throat of the corolla tube is hairy,

9.Androecium:Contains 5 stamens that are free and attached to the petals (epipetalous) Anthers are dorsified and yellowish.

10.Gynoecium:Composed of 2 carpels (bicarpellary), syncarpous (fused) Ovaries are free, with nectar glands present Unilocular (one chamber) and marginal placentation (seeds attach along the edge).

11.Fruit:Produces a pair of elongated follicles.

Potentially Active Chemical Constituents⁽⁸⁾

Researchers investigating the medicinal benefits of *Vincarosea* discovered that it contains several alkaloids. While these alkaloids can be extremely toxic, they also have potential applications in treating cancer. *Catharanthusroseus* can produce a variety of chemical compounds that play key biological roles and help protect the plant against threats such as insects, fungi, and herbivores. This plant contains carbohydrates, flavonoids and alkaloids, *vincarosea* has over 400 alkaloids, which are used in pharmaceuticals, agrochemicals, flavors, fragrances, food additives, and pesticides. Some key alkaloids found in the aerial parts of the plant include actinoplastidemic, vinblastine, vincristine, vindesine, vindoline, And Some Alkaloids are found in root and basal stem such as ajmalicine, vincine, vineamine, raubasin, reserpine, and catharanthine. rosindin is anthocyanin pigment which is also found in the flowers of *CatharanthusRosea*.

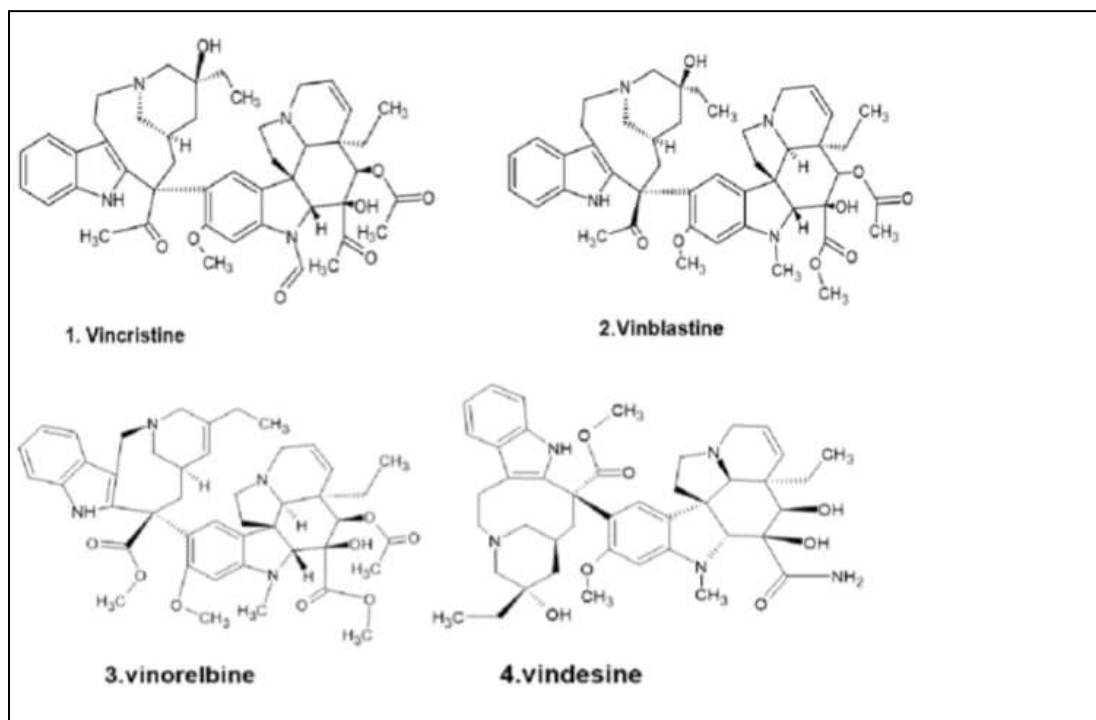


Fig.2 Chemical structure of vincaroseusalkaloids

Chemical Composition, and mechanism of anticancer molecules of vincarosea:

Catharanthusroseus produces a range of indole alkaloids, Vinca alkaloids. These compounds are of significant medical importance due to their ability to inhibit cell division, making them valuable as antimitotic agents in cancer treatment.

Examples: Vinflunine and vinorelbine have a special structure called the velbanamine moiety, which is derived from the precursor alkaloids catharanthine and vindoline to enhance their effectiveness.⁽⁹⁾

Mechanism of Action:

1. Microtubule Inhibition: Vinca alkaloids bind to tubulin, a protein that forms microtubules essential for cell division.
2. Prevention of Mitotic Spindle Formation: By binding to tubulin, these drugs disrupt microtubule assembly, preventing the formation of the mitotic spindle. This causes cells to become stuck in metaphase during mitosis, stopping them from dividing.⁽¹⁰⁾

Production of anticancer molecule's of Vincaroseus in submerged culture system:

Recent research has focused on growing plant cells in controlled environments to produce

anticancer compounds from *Catharanthusroseus* more efficiently than traditional field cultivation.

This method offers several advantages:

1. It Reduces the complexity of extracting compounds.
2. Faster Production: Allows for quicker generation of the desired compounds.
3. Controlled Conditions: Maintains a sterile environment for better consistency.⁽¹¹⁾

To boost alkaloid production, researchers have found that adding certain chemicals to the culture can induce stress on the cells, leading to higher yields of compounds. For example: Chromium: Adding chromium at low concentrations (10-100 μM) can reduce cell growth but significantly increase the production of vinblastine and vincristine.⁽¹²⁾

Sodium Chloride: Increasing osmotic stress by adding sodium chloride also triggers stress responses, enhancing the production of both vinblastine and vincristine.⁽¹³⁾

Fungal Elicitors: Introducing the fungus *Aspergillusflavus* can stimulate cell growth and further increase the production of these alkaloids.⁽¹⁴⁾

Identification by Thin layer chromatography:

Vinblastine can be identified using Thin Layer Chromatography (TLC) by spotting both the standard and sample solutions on the TLC plate. The plate is then developed in the mobile phase consisting of n-Butanol: Acetic acid: Water in the ratio of 5:1:1. After development, the plate is sprayed with a modified Dragendorff's reagent, which reacts with alkaloids like vinblastine, producing a colored spot. The R_f value of 0.24 corresponding to vinblastine in both the standard and sample solutions, indicating that the sample contains vinblastine, as it tracks similarly to the standard.⁽¹⁵⁾

Pharmacological activities:

1. Anticancer activity:

In clinical practice, Catharanthus roseus extracts are administered intravenously, where they are metabolized by the liver and subsequently excreted from the body. To enhance therapeutic efficacy, semi-synthetic alkaloids such as vinorelbine and vinflunine were developed. These alkaloids exert their antitumor effects by binding to tubulin, thereby disrupting cell division. Tumor Growth Inhibition: Vinorelbine and vinflunine inhibit the growth of certain human tumors. Vinblastine is being tested experimentally for the treatment of various neoplasms and is recommended for conditions such as Hodgkin's disease and choriocarcinoma. They have some side effects. Includes Hair loss, Peripheral neuropathy, Constipation, Hyponatremia (low sodium levels)⁽¹⁶⁾

2. Anti-diabetic activity:

The ethanolic extracts of the leaves and flowers of vincaroseus lower blood sugar levels in a dose dependent manner, similar to the standard drug glyburide.⁽¹⁷⁾ The hypoglycemic effect occurs because of increased glucose utilization in the liver. The aqueous extract decreased blood glucose levels by approximately 20% in diabetic rats, whereas the dichloromethane and methanol extracts resulted in a more significant reduction, lowering blood glucose levels by 49-58%^(18,19)

3. Anti-oxidant property:

The study evaluating the antioxidant potential of ethanolic extracts obtained from the roots of two varieties of Catharanthus roseus—rosea and alba, using various assays such as Hydroxyl radical scavenging activity, Superoxide radical

scavenging activity, DPPH radical scavenging activity, suggests a comprehensive approach to understanding their ability to neutralize harmful free radicals and oxidative stress. It showed that the ethanolic extracts obtained from both varieties exhibited a good scavenging effect across all tests, with effectiveness increasing with higher concentrations. However, Catharanthus roseus (pink flower) demonstrated greater antioxidant activity compared to Catharanthus alba (white flower).⁽²⁰⁾

4. Anti-helminthic activity:

Helminth infections are chronic diseases that affect both humans and livestock. Vincarosea has been traditionally used as an anti-helminthic agent in various cultures. Research evaluating its effectiveness by using *Pheretima posthuma* as an experimental model, comparing its effect to those of Piperazine citrate as a standard reference drug. The ethanolic extract of vincaroseus at a concentration of 250 mg/ml demonstrated significant anti-helminthic activity, indicating its potential as a natural treatment option for helminth infections.⁽²¹⁾

5. Anti-ulcer property:

Vincamine and Vindoline these both are derived from Catharanthus roseus, have been studied for their potential anti-ulcer properties. The plant leaves demonstrated anti-ulcer activity by reducing experimentally induced gastric damage in rats, showing potential for ulcer prevention and healing through mechanisms like reducing ulcer size, increasing mucus production, and inhibiting gastric acid secretion.⁽²²⁾

6. Hypotensive property:

The leaf extracts of Catharanthus roseus have been shown to exhibit significant hypotensive effects in several studies. The leaves contain around 150 beneficial alkaloids and other bioactive compounds. Research has reported notable anti-hyperglycemic and hypotensive activities of these leaf extracts, particularly in hydroalcoholic and dichloromethane-methanol preparations, when tested in laboratory animals. These findings suggest the plant's potential for managing blood pressure and blood sugar levels.⁽²³⁾

7. Anti-diarrheal property:

The anti-diarrheal effects of vincaroseus were tested using ethanolic extracts from its leaves. Wistar rats were utilized, and diarrhea was induced by administering castor oil. The rats were pretreated with the leaf extract prior to the test. The

extracts showed that the reduction in diarrhea was dependent on the dose given, effectively inhibiting the diarrhea caused by castor oil.⁽²⁴⁾

8. Memory enhancement activity:

Vinpocetine is believed to have several actions that could potentially help with Alzheimer's disease (AD). However, the only study focusing on a clearly defined group of AD patients found no benefits from using vinpocetine. A meta-analysis of older studies with poorly defined dementia populations found insufficient evidence to support its clinical use. On a positive note, vinpocetine has been generally well tolerated in clinical trials, with doses up to 60 mg per day showing no significant side effects in patients with dementia (loss of memory) and stroke.⁽²⁵⁾

II. CONCLUSION:

Vinca is a highly accessible plant known for its life-saving properties. One of the most

prevalent diseases today is cancer, and vinca has anti-cancer and anti-tumor characteristics. Typically, cancer is only diagnosed at an advanced stage, leading to treatment challenges due to delayed detection. Effective cancer treatment is possible only when cellular abnormalities are identified in the body. Similar to vinca, there are various plants believed to have anticancer properties. While synthetic drugs often come with numerous side effects, traditional medicine, such as vinca, has been utilized since ancient times. Nowadays, vincarosea is commonly employed as a secondary treatment option.

Several cytotoxic agents that have received approval in the US include vinblastine, vincristine, and vinorelbine. In Europe, vinflunine, an alkaloid, has been approved for treating urothelium carcinoma. With swift progress in treatment and ongoing research, there is renewed hope for a complete cure for cancer, suggesting that the era of effectively curing cancer is approaching.

Marketed preparations:



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