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Vinca roseus as anticancer activity

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Abstract:

Catharanthus roseus is a medicinal plant native to Madagascar, renowned for its bioactive compounds, particularly alkaloids like vincristine and vinblastine, which are used in cancer treatments. In Ayurveda, it is valued for its antitumor, anti-diabetic, antimicrobial, antioxidant, and antimutagenic properties. The plant produces alkaloids such as ajmalcine, vincine, resperine, and raubasin, with vincristine and vinblastine being effective against cancers like Hodgkin's disease, breast cancer, and leukemia. This review highlights its chemical constituents, mechanisms of action, and pharmacological activities, underscoring its importance in modern and traditional medicine.

Keywords:

Catharanthus roseus, leaf extract, vinblastine,vincristine,Anticancer activity, vinca Alkaloids

Introduction:

Catharanthus roseus, commonly known as Madagascar periwinkle, is indeed a remarkable plant with both ornamental and medicinal value. Native to Madagascar, it thrives in tropical climates, particularly in Southern Asia, and is well-known for its vibrant pink, purple, and white flowers. Beyond its aesthetic appeal, this plant has significant medicinal uses, particularly in traditional and modern medicine.

The plant contains alkaloids such as vincristine and vinblastine, which have been isolated for their anticancer properties. These compounds are crucial in the treatment of various cancers, including leukemia, lymphoma, and testicular cancer. They work by inhibiting cell division, thus preventing the spread of cancer cells.

In addition to its cancer-fighting capabilities, parts of the plant have been traditionally used to treat other ailments such as diabetes, hypertension, and infections. Despite its beneficial uses, it's important to note that the plant should be used with caution, as it can be toxic if not properly prepared or administered. [1,2]

In Malaysia, it's called Kemunting Cina. Catharanthus roseus contains vinca alkaloids, which are important for cancer treatment. the Madagascar periwinkle (Catharanthus roseus) 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, Catharanthus roseus serves both decorative and medicinal roles in various cultures. [5,6]

Fig.1 Catharanthus roseus.

Scientific classification [7]

Botanical Name(s): Vinca Rosea(Catharanthus Roseus)

Family Name: Apocynaceae

Kingdom: Plantae

Division:Magnoliophyta (Flowering plants)

Class: Magnoliopsida

Order: Gentianales

Genus: Catharanthus

Species: C. roseus

Synonym:

English: old maid, periwinkle

Hindi: sada bahar, sadabahar

Kannada: batla hoo, kanigalu,

Malayalam:nityakalyani, savanari,

Marathi: sadaphool, sadaphuli

Sanskrit: nityakalyani, rasna,

Tamil: cutkattu malli, cutukattu malli,

Telugu: billaganneru

Gujarati: Barmasi

Bengali: noyontara

Description:

A Periwinkle (Vinca), a versatile and widely distributed shrub, is known for its aesthetic and medicinal properties. This shrub grows to a height of 1 to 3 feet and is characterized by its glossy, dark green leaves. It produces flowers throughout the year in a variety of colors, including blue, purple, violet, pink, and white. Native to tropical and subtropical regions such as North America, Europe, India, and China, periwinkle thrives in diverse climates.

Beyond its ornamental value, periwinkle is widely recognized for its medicinal benefits. Various parts of the plant, such as the leaves, flowers, and roots, have been used in traditional medicine for centuries. It has been employed to treat a range of ailments, including blood sugar control, high blood pressure, and certain cancers. The plant contains powerful alkaloids like vincristine and vinblastine, which are utilized in chemotherapy for specific types of cancer. These alkaloids, especially concentrated in the roots and bark, have significant pharmacological effects, with applications in cancer treatment and other therapeutic fields.

Periwinkle also contains alkaloids from the Rauvolfia group, such as ajmalicine, reserpine, and serpentine, which have beneficial effects in traditional treatments for hypertension and mental health issues. In addition, compounds like vindoline, vincristine, and vinblastine have been pivotal in cancer therapies, highlighting the immense medicinal value of this plant. Periwinkle's use spans various traditional medicine systems, including Ayurveda and Traditional Chinese Medicine, cementing its status as a valuable herb in both historical and modern contexts.

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 Researchers studying Vinca rosea (Catharanthus roseus) have identified a range of alkaloids in the plant, which, despite being highly toxic in large quantities, hold significant potential for medicinal use, especially in cancer treatment. This plant produces a variety of chemical compounds that serve vital biological functions, including defense against environmental threats such as insects, fungi, and herbivores. Among the key bioactive compounds, Vinca rosea contains over 400 alkaloids, which are utilized in pharmaceuticals, agrochemicals, fragrances, food additives, and pesticides.

Some of the prominent alkaloids found in the aerial parts of the plant include vinblastine, vincristine, vindesine, and vindoline, which are widely known for their anticancer properties and have been incorporated into chemotherapy treatments. Additionally, the roots and basal stem of the plant contain alkaloids such as ajmalicine, vincine, vineamine, raubasin, reserpine, and catharanthine, which contribute to its therapeutic potential. Furthermore, rosindin, an anthocyanin pigment, is present in the flowers of Catharanthus roseus, adding to the diversity of bioactive compounds within the plant. These compounds continue to be of great

interest for their role in both medicine and other industries.

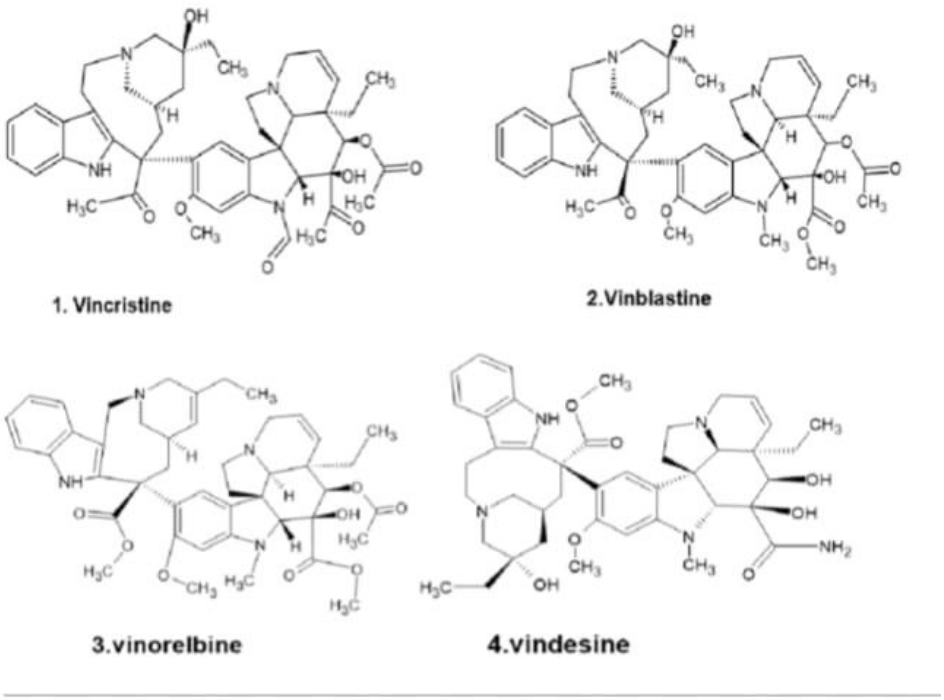

Fig.2 Chemical structure of vinca roseus alkaloids

Chemical Composition, and mechanism of anticancer molecules of vinca rosea:

Catharanthus roseus 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, such as vincristine, vinblastine, and vinorelbine, target tubulin, a globular protein that is essential for forming microtubules. Microtubules are dynamic structures made from tubulin dimers, which are involved in various cellular processes. One of their critical roles is in cell division, specifically during mitosis, where they form the mitotic spindle—a structure that separates chromosomes into the daughter cells.

Tubulin Structure: Tubulin exists in two forms, alpha and beta, which combine to form heterodimers. These heterodimers polymerize into long, linear chains that make up microtubules. The microtubules are continuously undergoing polymerization (growth) and depolymerization (shrinking), which is crucial for their dynamic role in cellular functions, including mitosis.

Vinca Alkaloids' Action: Vinca alkaloids bind to the β-tubulin subunit of the tubulin dimers. This binding prevents polymerization, effectively disrupting the dynamic assembly of microtubules. Because microtubules cannot form or maintain their structure, the cell loses its ability to create functional microtubule networks.

2. Prevention of Mitotic Spindle Formation:

The mitotic spindle is a structure composed of microtubules that is essential for the separation of chromatids during mitosis. Microtubules grow out from structures called centrosomes (or spindle poles) and attach to kinetochores on chromosomes. These microtubules help align the chromosomes at the metaphase plate and then pull them apart during anaphase.

Disruption of Spindle Formation: When vinca alkaloids bind to tubulin and prevent the assembly of microtubules, the mitotic spindle fails to form properly. This leads to a failure in chromosome alignment at the metaphase plate and an inability to segregate the chromosomes during anaphase. Without functional microtubules, the spindle cannot exert the forces needed to pull the chromosomes apart.

Metaphase Arrest: The inability to complete spindle formation causes cells to become arrested in metaphase, the stage of mitosis where chromosomes are aligned at the metaphase plate but cannot be separated. This mitotic arrest prevents the cell from progressing into anaphase, halting cell division.

Cell Death: Because cell division is halted, the affected cells eventually undergo apoptosis (programmed cell death), particularly if the arrest is prolonged. This is especially effective in cancer cells, which typically divide rapidly, making them more susceptible to disruption of mitosis. [10]

Production of anticancer molecule's of Vinca roseus in submerged culture system:

Recent research has focused on growing plant cells in controlled environments to produce anticancer compounds from Catharanthus roseus more efficiently than traditional field cultivation.[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 Aspergillus flavus can stimulate cell growth and further increase the production of these alkaloids. [14]

Identication 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 Rf 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 vinca roseus lower blood sugar levels in a dosedependent 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. Vinca rosea 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 Piperazine citrate as a standard reference drug. The ethanolic extract of vinca roseus 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 are 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 antidiarrheal effects of vinca roseus 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]

Conclusion:

Vinca is a valuable plant known for its life-saving properties, particularly in the treatment of cancer. With its anti-cancer and anti-tumor characteristics, vinca offers a promising approach to fighting cancer, a disease that is often diagnosed at advanced stages, complicating treatment. Unlike synthetic drugs, which can come with severe side effects, vinca, a traditional medicine, has been used for centuries and remains an important secondary treatment option today. Cytotoxic agents derived from vinca, such as vinblastine, vincristine, and vinorelbine, are approved for use in the US, while vinflunine is used in Europe for urothelial carcinoma. The ongoing progress in cancer treatment research brings renewed optimism that a complete cure for cancer may soon be within reach.

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