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Review Article,

Phytochemistry and Phytochemical Potential of *Catharanthus Roseus*: A Narrative Review

Arooj Aftab[1], Muhammad Akram[1], Umme Laila[1], Rida Zainab[1], Momina Iftikhar[1], Maghchiche Abdelhak[2] , Gaweł Sołowski[3], Fethi Ahmet Ozdemir[3], Ebrahim Alinia-Ahandani[4], Adonis Sfera[5]

[1]Department of Eastern Medicine, Government College University Faisalabad Pakistan
[2]Department of pharmacy- Batna2 University – Algeria
[3]Department of Molecular Biology and Genetics, Faculty of Science and Art, Bingol University, Bingol, 1200, Türkiye
[4]Department of Biochemistry, Payame Noor University of Tehran, Tehran, Iran
[5]University of California Riverside, Patton State Hospital, USA
Email Address: makram_0451@hotmail.com

Abstract:

Catharanthus roseus is a kind of flowering plant used in conventional medicineto cure a variety of diseases, such as diabetes, hypertension, skin disorders and cancer. Alkaloids are among the many substances present in the plant that shown pharmacological effect. Numerous alkaloids found in the plant, such as vincristine and vinblastine, used in chemotherapy to treat various cancers. Numerous studies on these substances have revealed their efficacy when treating illnesses like Hodgkin's lymphoma and pediatric acute lymphoblastic leukemia. C. roseus has developed as a model organism in order to study plant secondary metabolism and its control in recent years. It used to gain understanding of the genetic and metabolic mechanisms underlying the manufacture of alkaloids as well as other secondary metabolites found in plants.

Keywords: alkaloids, traditional medicine, cancer, vincristine, vinblastine

Introduction:

Secondary metabolites, a broad category of natural compounds produced by plants, are well recognized. Due to their functions as pollinator attractants, for symbiosis, and defense against assaults by microbes, other plants, or animals, they are of utmost significance to the plant. Due to their numerous uses as medications, flavours, scents, insecticides, colors, food additives, poisons, and other things, they are commercially significant to humans (Chaturvedi et al., 2022). It is sound knowledge, nonetheless, that their output is usually insufficient and is influenced by the physiological and developmental stages of the plant. Although various attempts have been undertaken, the bulk of secondary metabolites of medicinal importance are acquired from wild or domesticated plants. Their chemical synthesis has typically not been commercially viable.

Only minimal amounts of the two bisindole alkaloids, or around 0.001%, are accumulated by the plant. Alternative strategies to boost TIA synthesis in plants or plant cell cultures have been studied since there is a high demand for alkaloids, notably anti-cancer alkaloids. Significant strides have been made in manufacturing alkaloids in vitro cell culture systems, although commercializing these methods have not yet been accomplished (Colinas et al., 2021).

Nomenclature and Taxonomy:

In reference to the orderliness and beauty of the flower, The Latin words Katharos (pure) and anthos combine to produce the name *Catharanthus L.G*. Don (flower). In 1935, with the name Lochnera, Reichenbach was the first to recognize and generically separate the pre-existing genus Catharanthus from Vinca.George Don gave its name, Catharanthus L.G.Don, to it in 1935.

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Figure 1.Catharanthus roseus with different eye colour.

Synonyms:

There are two known types:

- Catharanthus roseus

Substitute for this kind of:

AngustusCatharanthus roseus Steenis ex Bakhuizen f.
Albus variant of Catharanthus roseus G.Don
occellatusCatharanthus roseus G.Don
nanusCatharanthus roseus Markgr.
Alba Lochnerarosea (G. Don) Woodson
ocellata variant of Lochnera Rosea (G.Don) Woodson
Catharanthus roseus (Steenis) Angustus Bakh.
Replace with this type of:
nanusCatharanthus roseus Markgr.
Steenis' Lochnerarosea var. angusta

Description

A subshrub or herbaceous plant that is evergreen, Catharanthus roseus grows to 1 m (39 inches). The leaves are (1-3.5) cm wide, oval to rectangular in form, and (2.5-9) cm long.They have a short petiole, a pale midrib, and a glossy, hairless green exterior that are (1.8 cm) in length. The flowers contain a (2.5-3) cm long basal tube, a (2-5) cm wide corolla, and five lobes that resemble petals.The blossoms come in a variety of colors, ranging from white with a yellow or red core to dark pink with a deep red center. The fruit consists of two follicles that are (3 mm) broad and (2-4) cm long. (Paarakh et al., 2019).

Genetics

- Cathharanthus roseus is a diploid plant with 16 chromosomes in its karyotype; eight bivalents are visible during meiosis.
- C. roseus's flower shape is conducive to insect and self-pollination.
- It has been noted that C. roseus shows significant genetic variability.
- The indigenous variation has been brought forth through crossbreeding.
- Numerous applications of n- polyploidy and mutagenesis have been made in it.
- Preliminary crossover experiments have revealed that although the plant is self-pollinating, there has been regular outcrossing, leading to several intermediary categories.
- A large number of workers generated synthetic tetraploids.
- It has bigger and thicker leaves and a shorter, thicker stem (Kaushik et al., 2017).

Chemical Constituents

Researchers looking into its medical characteristics found that it included a class of alkaloids that, despite being exceedingly poisonous, could be useful in treating cancer. Plants may synthesis various chemical compounds to carry out crucial biological processes and protect themselves from predators like insects, fungi, and herbivorous animals. Alkaloids, flavonoids, saponins, and carbohydrates are present in C. roseus. The Catharanthus roseus plant's principal chemically active components are alkaloids. The plant contains more than 400 alkaloids, which are utilised as insecticides, flavours& fragrances, ingredients, medicines, and agrochemicals. Although the aerial sections of plants are where most alkaloids, including catharanthine, raubasine, vineamine, reserpine, ajmalicine, and vinceine are foundin the aerial parts of plants, alkaloids like actineoplastidemeric, vinblastine, vincristine, vindesine, and vindelinetabersonine are mainly found there (Mishra, J. N., & Verma et al., 2017).

Alkaloids in C. roseus

Essentially created by plants, bacteria, fungi, and mammals, alkaloids are a broad range of naturally occurring chemical compounds. Mainly, they are composed of simple nitrogen atoms. Alkaloids have various pharmacological effects, such as analgesics, anti-cancer, anti-arrhythmic,

bactericidal, and hypoglycemic effects. Alkaloids are the substance responsible for the pharmacologically powerful actions that are the basis for many medications (Barrales-Cureño et al., 2019).

Leaf

Yohimbine, raubasine, vinblastine, vincristine, catharanthine, vindoline, vindolidine, vindolicine, vindolinine, and ibogaine. 0.12 – 9.00% of alkaloids are present in dry weight of leaves.

Stem:

Vindoline, Leurosine, Lochnerine, and Catharanthine. These alkaloids are about 0.07 – 0.46% of the dry content of the stem.

Flower

Vindoline, Leurosine, Lochnerine, Tricin, Catharanthine. They account for ~ 0.005% offlowers of dry weight content.

Roots

Alstonine, Tabersonine, Horhammericine, Lochnericine, Echitovenine, Serpentine, Catharanthine, Vindoline, Leurosine, Lochnerine, Reserpine. Alkaloids make up 0.12 – 9.00% of the dry-weight content in roots.

Types of Alkaloids

From C. roseus, a variety of alkaloids have been found. More than 130 indole and dihydro-indole group alkaloids have been isolated and studied from various plant parts. The following are a few crucial ones:

Vinblastine

Vinblastine is a useful alkaloid obtained from C. roseus leaves. Vinblastine extraction and purification used to be quite expensive. However, new protocols for quick manufacturing have been established due to the development of diverse biotechnological techniques.

Vinblastine prevents cancer cells' cell cycles. It attaches to tubulin and prevents the growth of microtubules by doing so. Cell cycle arrest in the M phase results from no chromosomal segregation during mitosis's anaphase because of the inhibition of microtubule production (Almagro et al., 2015).

Vincristine

The alkaloid vincristine, also known as leurocristine and sometimes referred to as "VCR», is taken from Catharanthus roseus (Madagascar periwinkle). Typically, it is used in cancer chemotherapy. Vinblastine and vincristine have relatively similar chemical structures; however, they have different actions. Acute lymphoblastic leukaemia is treated with vincristine, while particular cancers like Hodgkin's disease are treated with vinblastine (ALL). The survival percentage for children with ALL increases to 80% when vincristine is included in the treatment plan.

Volatile Oils

Citronellol, geraniol, (Z, E)-pentadecanal, (E, E)-2, 4-hexagonal, and phytol from the leaf, and tetracosane, heneicosane, and tricosane the flower, were the principal volatile chemicals detected from a sample. An additional investigation discovered plenty of palmitic acid, methyl myristic acid, and palmitatein the leaf, palmitic acid, and methyl geranylacetonepalmitate residues at the Marcs industrial plant. Aside from that 2, 3-benzaldehyde, -ionone. Ethyl hexanoate, dihydroactinidiolide, epoxy-ionone, and plamitic acid. The stem contains isobutyl-3-methoxypyrazine and 2-phenylethanol, 1-phenylethanol. Limonene and phenyl acetadelhyde are the primary components in the sample from the flowers examined in Portugal.

Essential oils

According to analysis performed using Gas Chromatography-Mass Spectrometry (GC-MS), it contains the following essential oils: Pinene, (Z)-oximene, phenandrene (E, Z) 2,6-Nonadienal, Terpinene, Pinene, and Trans-Sabinene Hydrate Isopulegol, Terpinen-4-ol, Camphor, Limonene, Linalool, Terpineol, n-Dodecane, iso-dihydro carveol, neral, geraniol, and geranial perilla aldehyde are among the compounds. terpinylacetate, eugenol, n-tridecane, 2,6,11-trimethyl dodecane, Widdrol, n-Tetradecane, methyl eugenol, Elemol, Isoamyl laurate, Farnesyl, acetone B, n-Hexadecene, n-Heptadecane, 3-Phenyldodecane, Hexadecanal, Hexadecanol, Phytol, 2,4-bis(n-hexadecanoic acid, bisabolene) (1,1-dimethyl ethyl) Phenol, Oleic acid ethyl ester, Linolenic acid ethyl ester, Linoleic acid, Linolenic acid methyl ester, Stearic acid, Dehydroabietic acid, (Z)-9-Tricosene, Oxygenated sesquiterpenes, non-terpenes, monoterpene hydrocarbons, sesquiterpene hydrocarbons, tocopherol, dotriacontane, sitosterol, tetracontane, diterpenes, triterpenes, phenylpropanoids, alkanes, and fat(Lawal et al., 2015).

Medicinal Uses

The identified C. roseus alkaloids have been shown to have hypotensive effects, sedative, and possess characteristics that are calming and anti-cancerous. The herb has used to treat wasp stings, central nervous system depression and muscle pain. It is applied to nose bleeds, gum bleeding, mouth ulcers, and sore throats. Additionally, it has been used internally to treat hypertension, memory loss, cystitis, gastritis, enteritis, diarrhea, and high blood sugar levels. Its uses encompass a broad-spectrum, including cancer treatment, antidiabetic, stomachic, and cancer prevention.

Through discovery, C. roseus has a significant amount of alkaloid-class compounds. Alkaloids are bitter-tasting plant chemicals with a high nitrogen content; several have been shown to have analgesic or anti-cancer effects. Specifically, two significant alkaloids from C. roseus, vinblastine and vincristine, were developed into prescriptions for anti-cancer medications. It discovered that these injectable medications and their derivatives, such as vinflunine, interfere with the division of cancer cells through several mechanisms. Additionally, some compounds in C. roseus play a role in preventing the development of new blood vessels, which support the growth of tumours. Fusarium oxysporum, an endophyte of this host, was reported to generate vincristine, whereas vinblastine was isolated from an endophytic fungus by another group.

All plant components of Catharanthus roseus L. are a substantial source of the indole alkaloids. The plant used to cure diabetes, fever, malaria, chest pain, throat infections, and menstrual cycle irregularities and to induce euphoria. The roots contain three alkaloids linked to hypertension: ajmalicine, serpentine, and reserpine. Both vincristine and vinblastine, two physiologically relevant antineoplastic alkaloids, found in the leaves. It found that the alkaloids vincristine and vinblastine are effective in treating different forms of lymphoma and leukaemia. It has been discovered that these Catharanthus alkaloids help treat both malignant and nonmalignant diseases as well as platelet and disorders linked with platelets. The production of such a broad range of complex alkaloids by a single plant species has not seen in any other species, according to reports.Ajmalicine and serpentine, two key ingredients in medications used to treat cardiovascular disorders and excessive blood pressure, were discovered to concentrate in the plant's roots. Vinblastine and vincristine, two economically significant bisindole alkaloids found in the plant's leaves, are determined to be powerful antineoplastic agents. These are essential components inmost cancer chemotherapies. Vindoline was explicitly discovered in the plant's green portions, and neither the roots nor the cultured cell suspensions found to be biosynthesized from the intermediate branch point tabersonine.

Pharmacological Activities:

Anthelminthic Activity

Humans and cattle are both affected by helminthes infections, which are chronic diseases. It discovered that Catharanthus roseus was used from the conventional era as an anthelminthic substance. Catharanthus' anthelminthic properties Roseus has been assessed as an experiment, pheretima posthuma, using an ethanolic extract as the model reference standard, the 250 mg/ml concentration of piperazine citrate resulted in death. And considerable anthelminthic activity time of 46.33 min. At the same time, the typical medication that takes the time of death found to be indicated by 50 mg/ml at 40.67 minutes. This study provided evidence for ethno medicine, Catharanthus roseus astheplant that fights anthelminths (Agarwal et al., 2011).

Antidiabetic Activity

An equivalent dose-dependent reduction in blood sugar was seen using the ethanolic extracts of C. roseus leaves and flowers. Blood sugar lowering is equivalent to the standard medicationglibenclamide. The increased hepatic glucose utilization has led to the appearance of ahypoglycemicimpact. Comparing the aqueous extract to the methanol and dichloromethane extracts, it was found to decrease blood sugar levels by around 20%, it resulted in a 49–58% reduction in the levels of glucose in the blood in diabetic rats. Because the liver consumes more glucose, the hypoglycemic impact has become apparent. An herbal treatment made from the plant C. roseus has been researched pharmacologically for its ability to lower blood sugar levels (Mishra, J. N., & Verma et al., N2017).

Anti-Cancer Activity

Vinblastine and vincristine, two anti-cancer alkaloids, are present in the leaves and stems of Catharanthus roseus. These alkaloids prevent the growth of specific people’s tumors. Vinblastine is utilized in research to treat neoplasms

Choriocarcinoma, and Hodgkin's disease. Vincristine, another alkaloid, is used to treat paediatricleukaemia. Various portions of the methanolic crude Catharanthus extracts demonstrated significant anti-cancer activity in many cell types in the in-vitro environment. The multidrug was determined to have the most active forms of resistant tumours (Arora, R., Malhotra et al,. 2010).

Anti-Ulcer Activity

The plant's alkaloids vindoline and vincamine have been demonstrated to have anti-ulcer properties. Vincamine, an alkaloid found in plant leaves, has cerebrovasodilatory and neuroprotective properties. Rats with artificially produced gastric damage were protected against ulcers by the plant's leaves (Mishra, J. N., & Verma et al., 2017).

Antioxidant Activity

Utilizing a variety of test methodologies, like the activity to scavenge DPPH radicals, active hydroxyl radical scavenging, nitric oxide radical inhibition and superoxide radical scavenging activities, The ethanolic extracts of the roots of the two C. roseus species, Rosea (pink flower) and Alba (white flower), were evaluated for their antioxidant potential.. The findings demonstrated that the ethanolic extract of various Periwinkle kinds' roots had an excellent scavenging result throughout the whole essay in a manner dependent on the concentration. Yet, it was discovered that C. roseus has more antioxidant activity than C. Alba (Bhutkar & Bhise et al., 2011).

Hypolipidemic Effect

Significant anti-atherosclerotic activity with Catharanthus roseus (Linn.) G. Don as demonstrated by a reduction in the serum levels of triglycerides, LDL-c, VLDL-c, total cholesterol, and the histology of the aorta, hepatic, and renal. Leaf liqueur may have been the reason due to the antioxidant properties of flavonoids and perhaps a vinpocetine-like substance that was present (Ara et al,.2009).

Memory-improving Activity

There have been several effects attributed to vinpocetine that may be helpful for Alzheimer's patients (AD).The one trial that looked at this medication in a specific group of AD patients did not find any advantages. There is not yet enough data to support vinpocetine's clinical use, according to a meta-analysis of previous studies on populations with ill-defined dementia. Up to 60 mg/d of vinpocetine has been well tolerated in clinical trials for dementia and stroke with no discernible side effects (Sekar et al., 2010).

Injury Healing Property

Rats given 100 mg/kg/day of the ethanol extract of Catharanthus roseus displayed a quicker rate of wound repair than the controls a significantly reduced epithelization period, a considerable growth in dry weight and an increased concentration of hydroxyproline in the tissue granulation. Every indication suggests that C. roseus is excellent at controlling healing of wounds due to its higher tensile strength, hydroxyproline content, and other factors (Nayak et al., 2007).

Catharanthus roseus leaf extract for the production of nanoparticles

Several bioactive chemicals produced by *catharanthus roseus*, and an increased interest in employing *catharanthus roseus* leaf extracts as a source of biosynthetic agents for the creation of nanoparticles in recent years.Several techniques that can used to extract bioactive substances from *Catharanthus roseus* leaves, incorporating microwave-assisted extraction, solvent extraction, and ultrasonic extraction. Alkaloids, flavonoids, tannins, and phenolic acids are some of the biologically active substances found in the leaf extract that can act as reducing and stabilizing agents during the creation of nanoparticles. The extract combined with a metal salt solution, to create a combination, which then treated to specific physical or chemical conditions, such as heating, stirring, or the addition of a stabilizing agent, in the biogenesis of nanoparticles. The metal ions in the salt solution can then interact with the bioactive chemicals in the extract to create nanoparticles. There are several advantages to using Catharanthus roseus leaf extract to make nanoparticles. For instance, the extract obtained is abundant, regenerative, and non-toxic, making it an economical and sustainable substitute for conventional chemical synthesis techniques. In addition, depending on the specific bioactive components contained in the extract, the extract can give the nanoparticles particular capabilities, such as antioxidant and antibacterial properties (Vanlalveni et al., 2021).

Conclusion:

Catharanthus roseus, additionally called Madagascar periwinkle, is a plant local to Madagascar. The leaves of this plant incorporate diverse compounds with medicinal properties, which includes alkaloids, only Catharanthus roseus is used economically for the monoterpenoid indole alkaloids (MIAs), catharanthine and vindoline, which are substances that make up the commercially important anticancer dimers vinblastine and vincristine. Vinblastine and vincristine used with inside the remedy of cancers that includes Hodgkin's sickness and leukemia. Extracts from C. roseus leaves have additionally proven anti-inflammatory, anti-tumor, and anti-diabetic results in laboratory and animal studies.

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