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EXPLORING THE MEDICINAL POTENTIAL OF PERIWINKLE (*CATHARANTHUS ROSEUS*): A COMPREHENSIVE REVIEW

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Abstract– Periwinkle, or *Catharanthus roseus*, is a medicinal plant native to Madagascar that offers significant pharmacological and therapeutic benefits. The plant contains valuable alkaloids such as catharanthine and vindoline, but extracting them can be costly due to their low concentrations. Researchers have employed various breeding techniques to reduce costs. With a repertoire of over 130 alkaloids, periwinkle has the potential to provide treatment for various conditions such as high blood pressure, diabetes, asthama, menstrual issues, and constipation. This review work provides an in-depth discussion on the morphology, chemical composition, pharmacological and therapeutic significance, as well as micropropagation techniques of periwinkle.

INTRODUCTION

Periwinkle, also known as *Catharanthus roseus* L., has a number of aliases, including Madagascar periwinkle, Rose periwinkle, and Cape periwinkle. It is an evergreen herbaceous plant with numerous therapeutic and pharmacological uses. It contributes significantly to global health care and advances research on the metabolites of plant alkaloids. Vinblastine and vincristine, two valuable alkaloids used in the production of anti-cancer medications, are found in abundance in periwinkle. Additionally, the periwinkle has significant bioactive components with anti-diabetic, anti-diarrheal, anti-microbial, and antioxidant activities, including anthocyanins, flavonol glycosides, phenolic acids, saponins, teraponids, and steroids (Lee *et al.,* 2020). Since ancient times, all plant parts have been utilized in local treatments. It is grown in many countries for ornamental purposes in addition to its medical uses. The periwinkle blooms all year long with fragrant pink, purple, or white flowers that are quite beautiful. Due to the low quantities of alkaloids, commercial production is difficult and costly using the traditional technique of propagation. In order to produce it on a big scale, the micropropagation invitro technique was shown to be promising.

MORPHOLOGY

The taxonomical classification of *Catharanthus roseus* species

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Asteridae
Order: Gentianales
Family: Apocynaceae
Genus: Catharanthus
Species: roseus (Linnaeus)

Catharanthus roseus L. is an evergreen herbaceous plant indigenous to Madagascar. It can grow up to 80-100 cm tall and bears pink, purple, or white flowers that bloom throughout the year. The plant has elliptic to oblong leaves that are 2-9 cm long and glossy green with a light midrib. The inflorescence is made up of racemes, and the flowers are actinomorphic and pentamerous, with a cylindrical corolla consisting of five lobes that resemble petals. The fruit of the plant comprises two 2-4 cm long follicles that contain 10-20 tiny, rectangular seeds measuring 2-3 mm long. These seeds have a small endosperm and flat, black cotyledons that are slightly shorter than the radical. Vinblastine and vincristine, two of MP's

economically and pharmacologically significant cytotoxic dimeric alkaloids that are only found in very low yields in the leaves, have been widely employed as cancer chemotherapy agents (Nejat *et al.,* 2015). The existence of many chemical groups, including polyphenols, alkaloids, steroids, flavonoid glycosides, anthocyanins, and iridoid glucosides, in various regions of MP has been established in addition to alkaloids and phenolics (the most significant constituents of MP). However, some evidence suggests the presence of comparable compounds in the plant's leaves and stems, but the same does not hold true for the compounds found in the seeds and petals. As a natural acid-base indicator, MP flower extract has been employed.

Chemical Constitutents

The chemical contents of periwinkle are diverse, including alkaloids, terpenoids, flavonoids, and phenolic chemicals. These chemicals contribute to the therapeutic benefits of the plant. The following is a list of the principal chemical components found in periwinkle:

Alkaloids

Vincristine: This alkaloid is one of the most well-known and useful periwinkle chemicals. It is used to treat a variety of malignancies (Verma and Mishra, 2011). Vincristine causes cell cycle arrest and death by blocking microtubule production during cell division.

Vinblastine: Vinblastine is another significant alkaloid derived from periwinkle that is utilized in cancer treatment. It works on the same anticancer mechanisms as vincristine.

Vinorelbine: This periwinkle alkaloid has anticancer action, notably against lung and breast cancer. It disrupts microtubule assembly and inhibits cell proliferation (Verma and Mishra, 2011).

Terpenoids

Ajmalicine: it's an indole alkaloid having antihypertensive action. Ajmalicine works by dilating blood arteries, lowering blood pressure.
Vindoline: Vindoline is an essential precursor for the manufacture of vinblastine and is found in quite high amounts in periwinkle (Singh *et al.,* 2014). Vindoline has been explored for its anticancer properties.
Catharanthine: Catharanthine is an intermediary chemical in the production of vindoline and the vinca alkaloids vincristine and vinblastine (Jain *et al.,* 1996).

Flavonoids

Quercetin: This flavonoid has antioxidant and anti-inflammatory effects. It also has anticancer action and may have a function in the prevention of chronic illnesses (Lee *et al.,* 2020).
Kaempferol: It's Known for its antioxidant and anti-inflammatory characteristics, kaempferol has been researched for its potential in cancer prevention and neuroprotective capabilities (Mukherjee *et al.,* 2013).

Phenolic Compounds

Chlorogenic Acid: Chlorogenic Acid: This phenolic acid is well-known for its antioxidant and anti-inflammatory properties. It may possibly have anti-diabetic properties and help to cardiovascular health (Mukherjee *et al.,* 2013)
Ferulic acid: Ferulic acid is an antioxidant with neuroprotective properties. Ferulic acid has been examined for its involvement in the prevention of oxidative stress-related diseases (Verma and Mishra, 2011).
Caffeic Acid: This phenolic acid has antioxidant and anti-inflammatory effects. It has also been researched for its possible anticancer properties.

Biological Activities

The biological actions of periwinkle components have been examined in vitro and *in vivo*. Vinca alkaloids have been found to decrease cell division in cancer cells *in vitro*. Vinca alkaloids have been found *in vivo* to be effective in the treatment of leukemia and lymphoma. Periwinkle flavonoids contain antioxidant and anti-inflammatory effects (2). Periwinkle glycosides have been proven to have anti-cancer, anti-inflammatory, and antibacterial effects.

Vinca alkaloids: Vinca alkaloids are a group of compounds that are found in periwinkle. They are known for their anti-cancer properties. Vinca alkaloids work by inhibiting microtubule assembly, which is essential for cell division. This inhibition of cell division leads to the death of cancer cells. Vinca alkaloids are used to treat a variety of cancers, including leukemia, lymphoma, and breast cancer (Rao *et al.,* 2016).

Flavonoids: Flavonoids are a group of compounds that are found in many plants. They have a variety of biological activities, including antioxidant, anti-

inflammatory, and anti-cancer properties (Sankar *et al.,* 2005). Antioxidants help to protect cells from damage by free radicals. Free radicals are unstable molecules that can damage cells and lead to cancer. Anti-inflammatory compounds help to reduce inflammation, which is a major risk factor for cancer. Anti-inflammatory compounds help to reduce inflammation, which is a major risk factor for cancer. Anti-cancer compounds can kill cancer cells or prevent them from growing (Verma and Mishra, 2011).

Glycosides: Glycosides are a group of compounds that are found periwinkle. They have a variety of biological activities, including anti-cancer, anti-inflammatory, and antimicrobial properties (Verma and Mishra, 2011). Anti-cancer glycosides can kill cancer cells or prevent them from growing. Anti-inflammatory glycosides help to reduce inflammation, which is a major risk factor for cancer. Antimicrobial glycosides can inhibit the growth of bacteria and fungi (El-Sayed *et al.,* 2019).

PHARMACOLOGICAL ACTIONS OF PERIWINKLE

Periwinkle includes a variety of chemicals with therapeutic effects. These include alkaloids, flavonoids, and glycosides. Alkaloids are chemicals that can stimulate or depress the central nervous system. Flavonoids are plant chemicals with antioxidant and anti-inflammatory effects. Glycosides are substances that can be broken down into sugar and a non-sugar component. The non-sugar component of periwinkle glycosides possesses anti-cancer effects.

Anticancer Activity: Periwinkle is well-known for its powerful anticancer effects. It includes the alkaloids vincristine, vinblastine, and vinorelbine, which are commonly used in chemotherapy to treat a variety of cancers (El-Sayed *et al.,* 2019). These chemicals suppress cancer cell development by interfering with mitotic spindle formation, resulting in cell cycle arrest and death. Periwinkle extracts have been demonstrated to be effective in the treatment of leukemia, lymphoma, breast cancer, lung cancer, and colon cancer (Saravanan *et al.,* 2013).

Antibacterial action: Periwinkle has antibacterial action against a wide range of pathogens, including bacteria, fungi, and viruses (Verma and Mishra, 2011). Periwinkle alkaloids exhibit antibacterial properties against both Gram-positive and Gram-negative microorganisms. Periwinkle extracts have also been demonstrated to exhibit antifungal action against *Candida* species (Verma and Mishra, 2011). These antibacterial capabilities imply that periwinkle might be used to treat infectious disorders.

Antidiabetic effect: Periwinkle extracts have been demonstrated to exhibit hypoglycemic effect, making them potentially beneficial in the control of diabetes (Bhadra *et al.,* 2016). They can increase glucose absorption, induce insulin secretion, and improve insulin sensitivity. Periwinkle alkaloids have been discovered to have an important role in its anti-diabetic effect by modulating glucose metabolism (Verma and Mishra, 2011).

Antihypertensive Activity: Periwinkle has been shown to have antihypertensive effects, which can aid in the management of high blood pressure (Bhadra *et al.,* 2016). The alkaloid ajmalicine found in periwinkle has vasodilatory properties, causing blood vessels to relax and blood pressure to fall (Verma and Mishra, 2011).

Antioxidant Activity: Periwinkle is high in antioxidants such as flavonoids and phenolic substances, which scavenge free radicals and minimize oxidative stress(25). These antioxidants help protect cells from damage produced by reactive oxygen species and may contribute to the prevention of chronic illnesses related with oxidative stress, such as cardiovascular disease and neurological disorders (El-Sayed *et al.,* 2019)

Neuroprotective Activity: Periwinkle has been found to have neuroprotective qualities, which may be linked to its antioxidant and anti-inflammatory capabilities(Verma and Mishra, 2011). It has showed promise in preventing neurodegenerative disorders and increasing cognitive function. (Mavundza *et al.,* 2020)

Immunomodulatory Activity: Periwinkle extracts have shown immunomodulatory effects through influencing immunological responses (Tewari *et al.,* 2021). They have the ability to modify immune cell activity and increase immunological defense mechanisms, which can be useful in the treatment of immune-related illnesses (Mavundza *et al.,* 2020)

MEDICINAL PROPERTIES

Periwinkle has a wide range of medicinal applications due to its diverse pharmacological properties. Here are some of the notable medicinal

applications of periwinkle:

Cancer Treatment: Cancer therapy: Periwinkle is most recognized for its usage in cancer therapy (Saravanan *et al.,* 2013). The periwinkle alkaloids vincristine and vinblastine have been used in chemotherapy to treat a variety of cancers, including leukemia, lymphoma, breast cancer, lung cancer, and testicular cancer. These alkaloids suppress cancer cell development by affecting microtubule production during cell division, resulting in cell cycle arrest and death (Bhadra *et al.,* 2016).

Infectious Diseases: Periwinkle has antibacterial action against bacteria, fungi, and viruses. It has traditionally been used to treat a variety of infectious disorders, including malaria, diarrhea, and urinary tract infections (Verma and Mishra, 2011). Periwinkle's antibacterial characteristics make it a promising option for the development of novel antimicrobial medicines.

Diabetes Control: Periwinkle extracts have been demonstrated to have anti-diabetic effect by increasing glucose absorption, boosting insulin production, and improving insulin sensitivity. They can help control blood sugar levels and may have a role in diabetes treatment (El-Sayed *et al.,* 2019).

Hypertension Management: Periwinkle has long been used as a hypertension treatment. Periwinkle contains the alkaloid ajmalicine, which has vasodilatory properties, causing blood vessels to relax and blood pressure to fall. It might help with high blood pressure control (Mavundza *et al.,* 2020).

Oxidative Stress-Related Disorders: Periwinkle's antioxidant capabilities aid in the prevention of oxidative stress, which is linked to a variety of chronic illnesses (Tewari *et.al.,* 2021). Periwinkle contains flavonoids and phenolic substances that scavenge free radicals and prevent oxidative damage. As a result, periwinkle may be advantageous in illnesses such as cardiovascular disease, neurodegenerative disorders, and age-related macular degeneration (El-Sayed *et al.,* 2019).

Inflammatory Disorders: Periwinkle extracts have anti-inflammatory and analgesic effects. They can decrease inflammation by inhibiting the synthesis of inflammatory mediators. As a result, periwinkle may be effective in the treatment of inflammatory disorders such as arthritis and inflammatory bowel disease (Niranjan *et al.,* 2019).

Neurological Disorders: Periwinkle has demonstrated neuroprotective benefits, probably due to its antioxidant and anti-inflammatory characteristics. It may assist to prevent against neurodegenerative disorders including Alzheimer's and Parkinson's, as well as improve cognitive performance (39).

Immunomodulation: Periwinkle extracts contain immunomodulatory properties that regulate immunological responses. They have the ability to modify immune cell activity and improve immune defense systems. This implies that it might be used to treat immune-related illnesses (Patil *et al.,* 2012).

MICROPROPAGATION TECHNIQUES

Micropropagation is an important technology for mass producing homogeneous and disease-free plantlets. Plant cells, tissues, or organs are grown and multiplied in a controlled laboratory setting. Periwinkle may be grown well using various micropropagation techniques. Here are several ways for periwinkle micropropagation:

Shoot Tip Culture: In this technique, shoot tips from periwinkle plants are removed and cultured (Yang *et al.,* 2018). The apical meristem and shoot tips are put on a nutritional medium that also contains auxins and cytokinin's, two plant growth regulators. The shoot tips grow into several shoots under controlled circumstances, and these shoots may then be subculture to create a huge number of plantlets.

Axillary Bud Culture: This method involves isolating and cultivating axillary buds, which are found in the periwinkle's leaf axils, on an appropriate nutritional media. The axillary buds develop many shoots through shoot proliferation. To produce a lot of plantlets, these shoots can be subculture on a regular basis (Naaz *et al.,* 2014).

Callus Culture: In callus culture, undifferentiated cells from periwinkle explants, such as leaf or stem segments, are induced and grown on a nutritional media that has been treated with plant growth regulators. To encourage the regeneration of new shoots, the callus tissue can be subcultured (43). When branch tips or axillary buds are unavailable or when genetic transformation experiments are being done, this method is very helpful for periwinkle propagation.

Somatic Embryogenesis: Somatic embryogenesis is the process of inducing the development of embryos from somatic cells. Periwinkle may go through somatic embryogenesis, in which explants like leaf, stem, or root segments are used to produce

embryogenic cells. The somatic embryos created by these embryogenic cells can grow and germinate to form plantlets (44).

Temporary Immersion System: In this method, plantlets are cultivated in liquid media in temporary immersion bioreactors. Periodically submerging the plantlets improves nutrient absorption and aeration (Bhadra *et al.,* 2016). By creating the ideal conditions for plant development, this technique boosts the effectiveness and productivity of micropropagation.

Micropropagation techniques for periwinkle offer several advantages, including rapid multiplication, production of disease-free plantlets, and the ability to maintain genetic uniformity (Verma and Mishra, 2011). These techniques have been widely employed for the commercial production of periwinkle plants and for the preservation of valuable cultivars. They have also been used in research for the production of valuable secondary metabolites and for genetic transformation studies.

CONCLUSION

In conclusion, periwinkle (*Catharanthus roseus*) is a valuable medicinal plant with diverse chemical constituents and pharmacological properties. Its bioactive components, which include alkaloids, flavonoids, and phenolic compounds, contribute to its medicinal potential. The review study focused on the chemical composition, biological activities of key chemicals, pharmacological properties, therapeutic uses, and micropropagation techniques of periwinkle. Periwinkle's chemical ingredients, such as the alkaloids vincristine and vinblastine, have demonstrated strong anticancer activity and are commonly employed in chemotherapy. Periwinkle also has antibacterial, antihypertensive, antioxidant, anti-inflammatory, neuroprotective, and immunomodulatory properties, indicating its potential utility in a variety of medical situations (El-Sayed *et al.,* 2019). Cancer treatment, infectious disease management, diabetes, hypertension, oxidative stress-related illnesses, inflammatory conditions, neurological disorders, and immune-related disorders are among the therapeutic uses of periwinkle. These uses demonstrate periwinkle's vast medicinal potential as a source of novel medications and therapy choices. Micropropagation techniques such as shoot tip culture, axillary bud culture, callus culture, somatic embryogenesis, and the temporary immersion system provide an effective method for mass producing periwinkle plantlets (Niranjan *et al.,* 2019). These approaches offer benefits like as quick multiplication, disease-free propagation, and genetic homogeneity preservation. Overall, periwinkle is a potential therapeutic plant with a diverse chemical profile and pharmacological characteristics. Further study and investigation of its bioactive constituents, pharmacological mechanisms, and therapeutic uses can lead to the creation of novel medications, improve healthcare practices, and increase the well-being of humans globally (Sankar *et al.,* 2005).

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