

A Systematic Review of the Pharmacological and Phytochemical Profiles of Madagascar periwinkle as Potential Dietary Supplement

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Chinese Journal of Applied Physiology, 2023: e20230002

Abstract

Madagascar periwinkle (*Catharanthus roseus*) is a plant species known for its rich pharmacological and phytochemical properties. This systematic review aims to comprehensively evaluate the potential of Madagascar periwinkle as a dietary supplement. A thorough search of relevant databases yielded studies focusing on the pharmacological activities and phytochemical constituents of Madagascar periwinkle. The review highlights the diverse pharmacological effects of Madagascar periwinkle, including anti-cancer, anti-diabetic, anti-inflammatory, and antimicrobial properties, among others. Furthermore, the phytochemical analysis revealed the presence of various bioactive compounds such as alkaloids, flavonoids, terpenoids, and phenolics, which contribute to its medicinal properties. Despite the promising findings, further research is warranted to elucidate the mechanisms of action, safety profile, and potential interactions of Madagascar periwinkle as a dietary supplement. Overall, this systematic review provides valuable insights into the pharmacological and phytochemical profiles of Madagascar periwinkle, suggesting its potential as a natural dietary supplement with diverse health benefits.

Keywords

Madagascar periwinkle, Dietary supplement, Anti-cancer, Anti-diabetic, Anti-inflammatory

Introduction

Madagascar periwinkle (*Catharanthus roseus*), is also known from their several names; Vez Vinca rosea, Ammocalis rosea, Rose periwinkle, Rosy periwinkle, Old maid etc. It is one of the few medicinal plant that have a long history of therapeutic voyage

from Mesopotamian civilization of about 2600 BCE till today¹. At present time, this plant still plays a significant role in the treatment of various diseases such as; Diabetes, Cancer, Diarrhoea, Menorrhagia etc. It belongs to the family of Apocynaceae containing abundant useful Alkaloids.

In ancient period, this plant has been found useful

DOI: 10.62958/j.cjap.2023.002

www.cjap.ac.cn

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Published by CJAP editorial office and Asian BioMed Innovation Press

in Ayurvedic Medicine, traditional Chinese Medicine and other heating systems. During the 20th century, Western medical science had also began researching on Madagascar Periwinkle and they found that this plant contains various pharmacologically active phytoconstituents used for treating various diseases². All parts of this plant, including dried root, leaves, flower, and stalks have been used in regional herbal medicine. Madagascar periwinkle (*Catharanthus roseus*) is a perennial species of flowering plant in the family Apocynaceae. It is native and endemic to Madagascar, **Figure 1**; but is grown elsewhere as an ornamental and medicinal plant. It has glossy green leaves that are oval to oblong, and arranged in opposite pairs. The flowers have five petal-like lobes and are white to dark pink with a darker red center. The fruit is a pair of follicles that contain numerous seeds.

It grows well in dry and nutritionally deficient conditions, and can tolerate partial shade^{3, 4}. It is considered a fast-growing plant that needs repotting every six to eight weeks. It is also a hardy plant that can resist pests and diseases⁵. It is a source of the drugs vincristine and vinblastine, which are used to treat various types of cancer. These drugs are derived from the alkaloids present in the shoots and roots of the plant. It has a long history of medicinal use in traditional systems of medicine, such as Ayurveda and Chinese medicine. It has been used to treat diseases such as malaria, diabetes, Hodgkin's lymphoma, and leukemia⁶. It is also known by many other names, such as bright eyes, Cape periwinkle, graveyard plant, old maid, pink periwinkle, and rose periwinkle. Here are

some details about its morphology:

a. Stem: It has a herbaceous or slightly woody stem that can grow up to 1 m tall. The stem is green, smooth, and cylindrical, with milky sap⁷. It can be erect or sprawling along the ground.

b. Leaves: It has glossy green leaves that are oval to oblong, 2.5–9 cm long and 1–3.5 cm wide. The leaves are hairless, with a pale midrib and a short petiole 1–1.8 cm long⁸. They are arranged in opposite pairs along the stem.

c. Flowers: It has showy flowers that can be white, pink, or red, with a darker red center. The flowers have a basal tube 2.5–3 cm long and a corolla 2–5 cm diameter with five petal-like lobes. The flowers are borne singly or in pairs in the leaf axils⁹. They are pollinated by insects, especially butterflies and moths.

d. Fruits: It has a pair of follicles that are 2–4 cm long and 3 mm wide. The follicles are green, slender, and pointed, containing numerous small seeds^{10, 11}. The seeds are brown, oval, and hairy, with a tuft of white hairs at one end. The seeds are dispersed by wind or water.

However, they also have some side effects that may affect different parts of the body. Here are some of the common and serious side effects of these drugs; Nervous system problems and Blood problems. In the Nervous system problems; Both drugs can cause changes in sensation, such as numbness, tingling, or pain in the fingers and toes¹². They can also affect the muscles, causing weakness, difficulty walking, or drooping eyelids. In rare cases, they can cause seizures, hallucinations, or unconsciousness. And in



Figure 1: Diagrammatically representation of the plant Madagascar periwinkle (*Catharanthus roseus*); (a) Plant, (b) Flower and (c) Fruits

the Blood problems; Both drugs can lower the number of white blood cells, which are important for fighting infections¹³. This can increase the risk of getting sick or developing fever, chills, cough, or sore throat. They can also lower the number of platelets, which are important for clotting. This can increase the risk of bleeding or bruising, especially from the nose, gums, or skin. Some other problems like as Digestive problems; Both drugs can cause nausea, vomiting, diarrhea, or constipation. They can also cause stomach cramps, loss of appetite, or mouth sores^{14,15}.

Hair loss: Both drugs can cause temporary hair loss, which usually grows back after the treatment is over. In the Lung problems; Vinblastine can cause shortness of breath, cough, or chest pain. This can be a sign of lung damage or inflammation, which can be serious. Also in the Urinary problems; Vincristine can cause bed-wetting, painful or difficult urination, or changes in urine output. This can be a sign of kidney damage or bladder irritation, which can be serious.

These are some of the possible side effects of vincristine and vinblastine, but not all of them. Some people may experience other side effects or none at all¹⁶. The severity and duration of the side effects may vary depending on the dose, schedule, and individual response to the drugs. It is important to report any side effects to your doctor, as they may be able to adjust the treatment or prescribe medications to help manage them.

Vincristine and vinblastine are two drugs that are derived from the Madagascar periwinkle plant and are used to treat various types of cancer¹⁷. They are both delivered via intravenous infusion for use in different chemotherapy regimens. Intravenous infusion means that the drugs are given through a thin tube (called a catheter) that is inserted into a vein, usually in the arm or hand. The drugs are mixed with a liquid (called a solution) and flow from a bag through the tube into the vein. The infusion can take from a few minutes to several hours¹⁸, depending on the dose and schedule of the drugs. It is very important that vincristine and vinblastine are given only by intravenous infusion and not by any other route, such as intramuscular injection or intrathecal injection (into the spinal fluid). This is because they can cause severe damage or even death if they are given incorrectly¹⁹. Madagascar periwinkle (*Catharanthus roseus*) is a plant that contains various chemical constituents that have medicinal and pharmacological properties. Some of the main chemical constituents are:

a. Carbohydrates: These are organic compounds that consist of carbon, hydrogen, and oxygen atoms. They are important for energy production, cell

structure, and signaling.

b. Flavonoids: These are a group of plant pigments that have antioxidant, anti-inflammatory, and anti-cancer effects. They also modulate various enzymes and receptors in the body.

c. Saponins: These are glycosides that have detergent-like properties. They can form foam when shaken with water²⁰. They have various biological activities, such as lowering cholesterol, enhancing immunity, and inhibiting tumor growth.

d. Alkaloids: These are nitrogen-containing compounds that have diverse pharmacological effects²¹. They are the most active and valuable constituents of Madagascar periwinkle. There are more than 400 alkaloids present in the plant, but the most important ones are vincristine and vinblastine, which are used to treat various types of cancer^{22,23}.

These are some of the chemical constituents of Madagascar periwinkle, but not all of them. The plant also contains other compounds, such as phenols, tannins, steroids, and terpenoids. The chemical composition of the plant may vary depending on the environmental factors, such as soil, climate, and cultivation methods²⁴.

Pharmacological Properties of the Madagascar periwinkle (*Catharanthus roseus*)

Analgesic Effects

Madagascar periwinkle (*Catharanthus roseus*) is a plant that has analgesic effects, which means it can relieve pain. According to some studies^{25,26}, the plant's extracts have been traditionally used to treat various kinds of pain, such as headache, toothache, menstrual cramps, and rheumatism. The analgesic effects of the plant are mainly attributed to its alkaloids, especially vincamine and vindoline. These alkaloids act on the central nervous system and block the transmission of pain signals²⁷. They also have anti-inflammatory properties, which can reduce the swelling and irritation that cause pain. The plant's extracts can be applied topically as a poultice, ointment, or lotion, or taken orally as a tea, decoction, or tincture²⁸. However, the dosage and safety of the plant's extracts have not been well established, and they may have some side effects, such as nausea, vomiting, dizziness, or allergic reactions.

Antispasmodic Activity

Antispasmodic activity is the ability to prevent or

relieve spasms or contractions of the smooth muscles, such as those in the digestive tract, respiratory system, or urinary system²⁹. Spasms can cause pain, cramps, cough, or difficulty in breathing or urinating. Madagascar periwinkle (*Catharanthus roseus*) is a plant that has antispasmodic activity due to its chemical constituents, especially the alkaloids. Some of the alkaloids that have antispasmodic effects are:^{30,31}

a. Vincamine: This alkaloid relaxes the smooth muscles of the blood vessels, especially in the brain, and improves the blood circulation and oxygen supply. It also reduces the blood pressure and heart rate³². It is used to treat cerebral disorders, such as stroke, dementia, and migraine.

b. Vindoline: This alkaloid inhibits the contraction of the smooth muscles of the intestine and the uterus³³. It also reduces the secretion of gastric acid and bile. It is used to treat gastrointestinal disorders, such as ulcers, colitis, and diarrhea. It also has anti-inflammatory and analgesic properties.

c. Ajmalicine: This alkaloid blocks the calcium channels in the smooth muscles and prevents their contraction. It also dilates the blood vessels and lowers the blood pressure³⁴. It is used to treat hypertension, angina, and asthma.

These are some of the alkaloids that have antispasmodic activity in Madagascar periwinkle, but not all of them³⁵. The plant also contains other compounds, such as flavonoids, saponins, and phenols, that may have antispasmodic effects. The antispasmodic activity of the plant may depend on the dose, route, and duration of administration^{36, 37, 38}, as well as the individual response and interaction with other drugs.

Anti-Allergic Effects

Anti-allergic effects are the ability to prevent or reduce the symptoms of allergic reactions, such as itching, sneezing, swelling, or rashes. Allergic reactions are caused by the immune system's overreaction to certain substances, such as pollen, dust, or animal dander. Madagascar periwinkle (*Catharanthus roseus*) is a plant that has anti-allergic effects due to its chemical constituents, especially the flavonoids³⁹. Flavonoids are plant pigments that have antioxidant, anti-inflammatory, and antihistamine properties⁴⁰. Antioxidants protect the cells from oxidative damage, anti-inflammatories reduce the swelling and irritation, and antihistamines block the release of histamine, a chemical that triggers allergic symptoms. Some of the flavonoids that have anti-allergic effects in Madagascar periwinkle are:^{41,42}

a. Kaempferol: This flavonoid inhibits the production of immunoglobulin E (IgE), a type of antibody that binds to allergens and causes allergic reactions. It also suppresses the activation of mast cells, which are immune cells that release histamine and other inflammatory mediators⁴³.

b. Quercetin: This flavonoid stabilizes the membrane of mast cells and prevents them from releasing histamine and other inflammatory mediators. It also modulates the activity of various enzymes and receptors involved in allergic responses⁴⁴, such as phospholipase A2, cyclooxygenase, and leukotriene receptors.

c. Rutin: This flavonoid enhances the effects of quercetin by increasing its absorption and bioavailability. It also strengthens the capillaries and reduces the leakage of fluid and proteins into the tissues, which can cause swelling and inflammation⁴⁵.

These are some of the flavonoids that have anti-allergic effects in Madagascar periwinkle, but not all of them. The plant also contains other compounds, such as alkaloids, saponins, and phenols, that may have anti-allergic effects⁴⁶. The anti-allergic effects of the plant may depend on the dose, route, and duration of administration, as well as the individual response and interaction with other drugs.

Anticancer Potential

Madagascar periwinkle (*Catharanthus roseus*) is a flowering plant that has been used in traditional medicine for various diseases, such as diabetes and depression⁴⁷. However, it is most famous for its anticancer potential, as it contains compounds that can inhibit the growth and division of cancer cells. These compounds are called vinca alkaloids, and they include vinblastine and vincristine⁴⁸, which are used to treat Hodgkin's lymphoma, leukemia, and other cancers. Vinca alkaloids work by interfering with the formation of microtubules, which are essential for cell division and movement. By disrupting the microtubules, vinca alkaloids prevent cancer cells from dividing and spreading.

Madagascar periwinkle is a valuable source of anticancer phytomedicines, but it is also a challenging plant to study and cultivate⁴⁹. The vinca alkaloids are produced in very low amounts in the plant, and they are difficult to extract and purify. Moreover, the biosynthesis of vinca alkaloids involves a complex pathway that involves many enzymes and intermediate steps. Scientists have been trying to understand how the plant makes these compounds, and how to increase their yield and diversity. One approach

is to use genetic engineering to modify the plant or introduce the pathway into other organisms, such as bacteria or yeast. Another approach is to use informatics and computational methods to predict and evaluate the chemical structures and activities of vinca alkaloids and their derivatives⁵⁰. Madagascar periwinkle is a remarkable plant that has contributed to the development of life-saving drugs for cancer patients. It is also a fascinating example of the diversity and complexity of plant metabolism, and the potential of plant-based natural products for human health, In **Figure 2** shows the active constituents present in the plant Madagascar periwinkle.

Cardioprotective Effects

Madagascar periwinkle (*Catharanthus roseus*) is a plant that has been shown to have cardioprotective effects, meaning that it can protect the heart from damage and disease. Some of the ways that this plant can benefit the heart are, Lowering blood pressure;⁵¹ The plant contains alkaloids, such as reserpine, that can reduce high blood pressure, which is a risk factor for heart attack, stroke, and other cardiovascular

problems. Improving blood circulation; The plant can enhance the blood flow to the heart and other organs, preventing ischemia (lack of oxygen) and improving the delivery of nutrients and oxygen. And the Preventing arrhythmia; The plant can regulate the heartbeat and prevent abnormal rhythms, such as tachycardia (fast heartbeat) and bradycardia (slow heartbeat), that can impair the heart function and lead to cardiac arrest.

Madagascar periwinkle is a natural source of compounds that can support the health and function of the heart⁵². However, it should be used with caution and under medical supervision, as it can also have side effects, such as nausea, vomiting, dizziness, and allergic reactions. Moreover, it can interact with other medications, such as anticoagulants, antidepressants, and antihypertensives, and alter their effects.

Antimicrobial Activity

Madagascar periwinkle (*Catharanthus roseus*)⁵³ is a plant that has antimicrobial activity, meaning that it can fight against bacteria, fungi, and viruses that cause infections^{54, 55}. Some of the ways that this plant

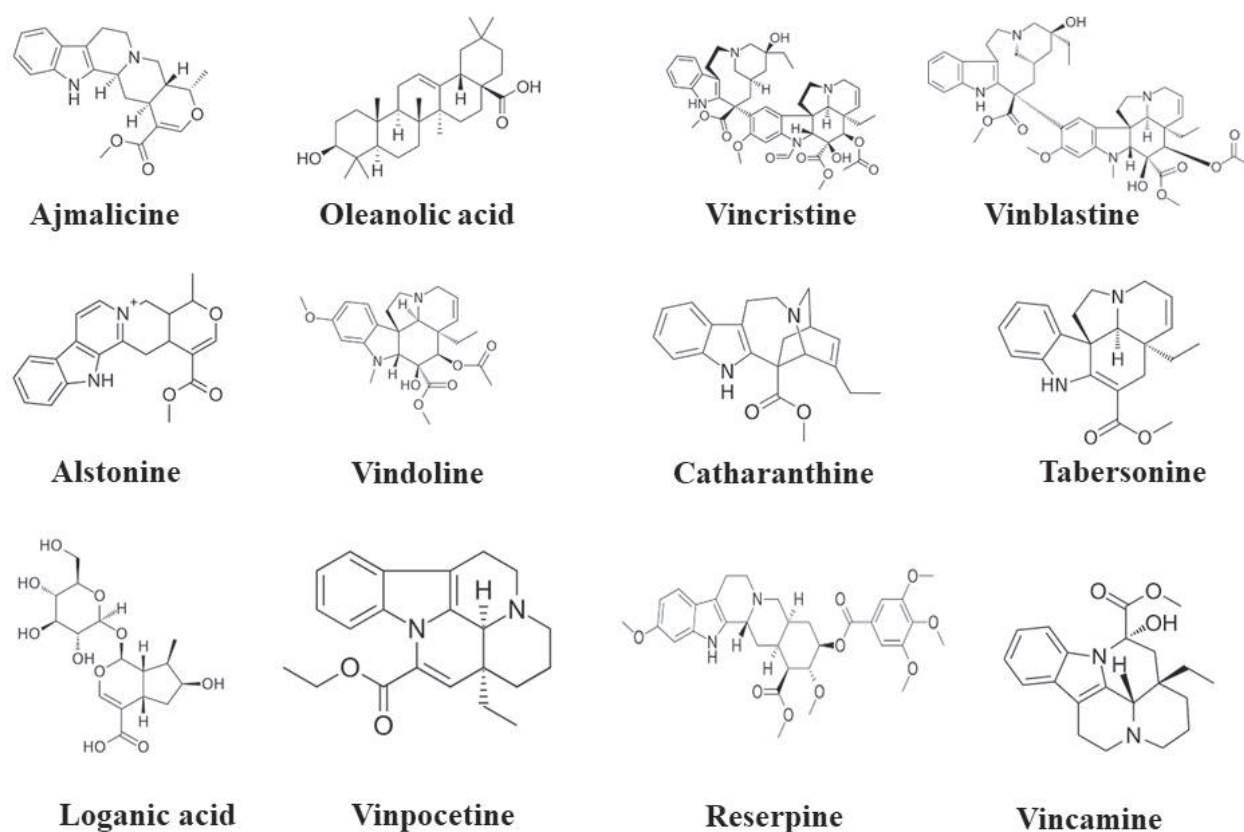


Figure 2: Chemical structure of the various active constituents present in the plant Madagascar periwinkle (*Catharanthus roseus*)

can kill or inhibit microbes are; Producing alkaloids, such as reserpine, vinblastine and vincristine, that can interfere with the metabolism, growth or division of microbial cells.⁵⁶ Modulating the immune system, such as stimulating the production of antibodies, enhancing the activity of macrophages, and increasing the resistance to infections. Inhibiting the attachment, invasion, or replication of viruses, such as herpes simplex virus, human immunodeficiency virus, and hepatitis B virus.⁵⁷ Madagascar periwinkle is a potential source of natural antimicrobial agents that can be used to treat various infectious diseases. However, it should be used with caution and under medical supervision, as it can also have side effects, such as nausea, vomiting, dizziness, and allergic reactions. Moreover, it can interact with other medications, such as anticoagulants,⁵⁸ antidepressants, antihypertensives, and alter their effects.

Antioxidant Properties

Madagascar periwinkle (*Catharanthus roseus*) is a plant that has been used for various medicinal purposes since ancient times. It is also known as Sadabahar, Rose Periwinkle, or Vinca. One of its benefits is its antioxidant properties, which means it can protect the cells from damage caused by free radicals⁵⁹. Antioxidants are important for maintaining health and preventing diseases. According to some studies, Madagascar periwinkle contains several compounds that have antioxidant effects, such as alkaloids, flavonoids, and polyphenols. These compounds can scavenge free radicals, inhibit lipid peroxidation, and modulate the activity of antioxidant enzymes. Some of the alkaloids, such as vinblastine and vincristine, are also used as chemotherapy drugs to treat cancer⁶⁰. The antioxidant properties of Madagascar periwinkle may also help with glucose metabolism, cognitive function, wound healing, stress response, and blood pressure.

Neuroprotective Properties

Madagascar periwinkle (*Catharanthus roseus*) is a herbal plant that has been shown to have neuroprotective properties, which means it can protect the brain and nervous system from damage or degeneration. Some of the compounds that are responsible for this effect are:⁶¹

a. Vincamine: This is an alkaloid that is extracted from the leaves of the plant. It can improve blood flow and oxygen supply to the brain, enhancing cognitive function and memory. It can also prevent or treat conditions such as Alzheimer's disease, dementia, stroke, and vertigo.

b. Vinpocetine: This is a synthetic derivative of vincamine that has similar effects but is more potent and bioavailable. It can also modulate the levels of neurotransmitters such as acetylcholine, dopamine, and serotonin,⁶² which are involved in learning, mood, and motivation.

c. Reserpine: This is another alkaloid that is found in the roots of some periwinkle species. It can lower blood pressure and act as a sedative, reducing stress and anxiety. It can also inhibit the breakdown of catecholamines, which are neurotransmitters that regulate alertness, attention, and arousal.

These compounds can be taken as supplements or extracted from the plant and used as medicine. However, they may also have some side effects or interactions with other drugs, so it is advisable to consult a doctor before using them. Madagascar periwinkle is a remarkable plant that offers many benefits for the brain and nervous system,⁶³ but it should be used with caution and respect.

Hepatoprotective Activity

Hepatoprotective activity is the ability of a substance to prevent or reduce liver damage caused by various factors, such as toxins, drugs, or infections. Madagascar periwinkle is a herbal plant that has been reported to have Hepatoprotective activity in several studies. Madagascar periwinkle contains compounds that can scavenge free radicals, inhibit lipid peroxidation, and enhance the antioxidant defense system of the liver cells. This can protect the liver from oxidative stress and inflammation, which are common causes of liver injury. Madagascar periwinkle can modulate the production of pro-inflammatory cytokines, such as TNF- α , IL-1 β , and IL-6, which are involved in the pathogenesis of liver diseases. It can also suppress the activation of NF- κ B, a key transcription factor that regulates the expression of inflammatory genes. Madagascar periwinkle can inhibit the proliferation and activation of hepatic stellate cells, which are responsible for the deposition of collagen and extracellular matrix in the liver. This can prevent or reverse the fibrosis and cirrhosis of the liver, which are the end-stage consequences of chronic liver damage.⁶⁴ Madagascar periwinkle can induce apoptosis and cell cycle arrest in hepatocellular carcinoma cells, which are the most common type of liver cancer. It can also inhibit the angiogenesis and metastasis of the tumor cells, which are essential for their growth and survival. Madagascar periwinkle is a promising natural source of hepatoprotective agents, but more clinical trials are

needed to confirm its safety and efficacy in humans.

Immunomodulatory Actions

Immunomodulatory actions are the effects of a substance on the immune system, either enhancing or suppressing its function. Madagascar periwinkle is a herbal plant that has been reported to have immunomodulatory actions in some studies.⁶⁵ Some of the possible mechanisms of action are:

a. Stimulation of immune cells: Madagascar periwinkle can activate various types of immune cells, such as macrophages, natural killer cells, T cells, and B cells, and increase their proliferation, differentiation, and cytokine production. This can enhance the immune response against pathogens and tumors.

b. Regulation of immune balance: Madagascar periwinkle can modulate the balance between Th1 and Th2 cells, which are subsets of helper T cells that produce different cytokines and mediate different immune responses. Th1 cells are involved in cellular immunity, while Th2 cells are involved in humoral immunity. Madagascar periwinkle can increase the Th1/Th2 ratio, which can improve the resistance to intracellular infections and autoimmune diseases.

c. Inhibition of inflammation: Madagascar periwinkle can inhibit the expression of inflammatory mediators, such as nitric oxide,⁶⁶ prostaglandins, and leukotrienes, which are involved in the initiation and propagation of inflammation. It can also suppress the activation of transcription factors, such as NF- κ B and AP-1, which regulate the expression of inflammatory genes.

Madagascar periwinkle is a potential source of immunomodulatory agents, but more research is needed to confirm its safety and efficacy in humans.

Anti-Diabetic Effects

Madagascar periwinkle (*Catharanthus roseus*) has emerged as a significant botanical resource in the realm of diabetes management due to its multifaceted pharmacological properties. Extensive research has unveiled a spectrum of mechanisms through which this herbaceous plant exerts its anti-diabetic effects.

One of the primary avenues through which Madagascar periwinkle aids in diabetes management is its hypoglycemic activity. Several bioactive compounds found in the plant, including alkaloids such as vincristine and vinblastine, have been implicated in lowering blood glucose levels. These compounds operate by stimulating insulin secretion from pancreatic beta cells, thereby facilitating the uptake of glucose into cells and subsequently

reducing blood sugar levels. Additionally, Madagascar periwinkle has demonstrated the capacity to enhance insulin sensitivity in peripheral tissues, enabling more efficient glucose utilization and contributing to glycemic control.⁶⁷

Moreover, Madagascar periwinkle exhibits a modulatory effect on glucose metabolism pathways. Research suggests that it can increase glucose uptake by skeletal muscle cells and adipocytes, primarily through the translocation of glucose transporter proteins such as GLUT4. By enhancing glucose uptake, Madagascar periwinkle assists in reducing postprandial hyperglycemia, a hallmark of diabetes.

Furthermore, the plant's bioactive constituents have shown promise in regulating hepatic glucose production. Madagascar periwinkle appears to inhibit gluconeogenesis, the process by which the liver synthesizes glucose from non-carbohydrate precursors such as amino acids and glycerol. By suppressing excessive glucose production by the liver, Madagascar periwinkle helps maintain blood glucose homeostasis.⁶⁸

In addition to its direct effects on glucose metabolism, Madagascar periwinkle possesses antioxidant and anti-inflammatory properties. Chronic hyperglycemia in diabetes is associated with increased oxidative stress and inflammation, leading to tissue damage and the development of diabetic complications. Madagascar periwinkle's antioxidant compounds, including flavonoids and phenolic acids, help scavenge free radicals and attenuate oxidative stress. Furthermore, it exerts anti-inflammatory effects by inhibiting pro-inflammatory cytokines and enzymes involved in the inflammatory cascade.⁶⁹ By mitigating oxidative stress and inflammation, Madagascar periwinkle may offer protection against diabetic complications such as neuropathy, nephropathy, and retinopathy.

The potential of Madagascar periwinkle in diabetes management extends beyond its standalone use. It has been explored as a complementary therapy alongside conventional anti-diabetic medications, with studies suggesting synergistic effects when used in combination. However, while Madagascar periwinkle shows promise as a natural remedy for diabetes, further clinical research is warranted to elucidate optimal dosage, long-term safety, and potential drug interactions. Individuals with diabetes should exercise caution and consult healthcare professionals before incorporating Madagascar periwinkle or any herbal supplement into their treatment regimen. Madagascar periwinkle is a herbal plant that has been traditionally used in many Asian folk medicines to treat diabetes.⁷⁰

In the **Table 1** summaries the Pharmacological profile of the plant Madagascar periwinkle. Some of the anti-diabetic effects of Madagascar periwinkle are:

a. Insulin secretion: Madagascar periwinkle can stimulate the secretion of insulin from the pancreatic beta cells, which can lower the blood glucose levels and improve glucose tolerance.

b. Insulin sensitivity: Madagascar periwinkle can enhance the sensitivity of the insulin receptors on the target cells, which can increase the uptake and utilization of glucose and reduce insulin resistance.

c. Glucose metabolism: Madagascar periwinkle can modulate the activity of various enzymes involved in glucose metabolism, such as hexokinase, glucokinase, glucose-6-phosphatase, and glycogen synthase. This can regulate the synthesis and breakdown of glycogen, the storage form of glucose, and prevent hyperglycemia and hypoglycemia.

d. Antioxidant: Madagascar periwinkle can scavenge free radicals, inhibit lipid peroxidation, and enhance the antioxidant defense system of the body. This can protect the cells from oxidative stress and

Table 1: Pharmacological profile of the plant Madagascar periwinkle (*Catharanthus roseus*)^{18, 25, 46}

Pharmacological Profile	Description	Potential Health Benefits
Anticancer Activity ⁵	<ul style="list-style-type: none"> •Vincristine: Disrupts microtubule formation by binding to tubulin, inhibiting cell division and inducing apoptosis in cancer cells. •Vinblastine: Similar mechanism to vincristine, used in the treatment of various cancers including leukemia, lymphoma, and testicular cancer. •Alkaloids: Other alkaloids like ajmalicine and serpentine also demonstrate cytotoxic effects against cancer cells, making Madagascar Periwinkle a potential source of anticancer agents. 	<ul style="list-style-type: none"> •Treatment of various cancers, including leukemia, lymphoma, and solid tumors. •Reduction of tumor growth and metastasis. •Potential alternative or adjunctive therapy to conventional chemotherapy with potentially fewer side effects.
Hypotensive Effects ⁹	<ul style="list-style-type: none"> •Ajmalicine: Acts as a calcium channel blocker, leading to vasodilation and reduction of blood pressure. •Serpentine: Exhibits antihypertensive effects by relaxing smooth muscles in blood vessels. •Alkaloids: Other alkaloids present in Madagascar Periwinkle contribute to its hypotensive properties, making it useful in managing hypertension. 	<ul style="list-style-type: none"> •Management of hypertension and prevention of related cardiovascular complications. •Potential adjunctive therapy to conventional antihypertensive medications.
Antidiabetic Potential ¹⁴	<ul style="list-style-type: none"> •Vindoline: Shows potential antidiabetic effects by improving insulin sensitivity and glucose metabolism. •Alkaloids: Other alkaloids in Madagascar Periwinkle may contribute to its antidiabetic properties by regulating glucose levels. •Flavonoids and Polyphenols: Certain flavonoids and polyphenols also exhibit hypoglycemic effects, aiding in blood sugar control. 	<ul style="list-style-type: none"> •Management of diabetes mellitus and regulation of blood glucose levels. •Potential prevention of diabetic complications such as neuropathy and retinopathy.
Anti-inflammatory Effects ²⁶	<ul style="list-style-type: none"> •Terpenoids: Possess anti-inflammatory properties by inhibiting pro-inflammatory enzymes and mediators. •Flavonoids and Polyphenols: Exhibit anti-inflammatory effects through modulation of inflammatory pathways such as NF-κB and COX-2. •Alkaloids: Certain alkaloids also show anti-inflammatory activities, contributing to the overall anti-inflammatory profile of Madagascar Periwinkle. 	<ul style="list-style-type: none"> •Alleviation of inflammation associated with various chronic conditions, including arthritis, inflammatory bowel disease, and cardiovascular diseases. •Reduction of pain, swelling, and tissue damage. •Potential treatment for inflammatory-related disorders.

Antioxidant Protection ³²	<ul style="list-style-type: none"> •Flavonoids, Polyphenols, and Carotenoids: Act as potent antioxidants, scavenging free radicals and reducing oxidative stress. •Alkaloids: Some alkaloids also possess antioxidant properties, contributing to the overall antioxidant capacity of Madagascar Periwinkle. •Tannins: Exhibit antioxidant activity, protecting cells from oxidative damage. 	<ul style="list-style-type: none"> •Protection against oxidative stress and age-related degenerative diseases. •Support for immune function and overall health. •Potential prevention of chronic diseases such as cancer, cardiovascular diseases, and neurodegenerative disorders.
Immunomodulatory Effects ³⁶	<ul style="list-style-type: none"> •Saponins: Demonstrate immunomodulatory properties by enhancing immune responses and regulating immune function. •Alkaloids and Polyphenols: Certain alkaloids and polyphenols also exhibit immunomodulatory effects, contributing to the overall immunomodulatory profile of Madagascar Periwinkle. 	<ul style="list-style-type: none"> •Strengthening of the immune system, reducing susceptibility to infections. •Potential treatment for autoimmune disorders by modulating immune responses. •Support for overall health and well-being.
Neuroprotective Effects ⁴⁶	<ul style="list-style-type: none"> •Alkaloids and Polyphenols: Exhibit neuroprotective effects by reducing neuroinflammation, oxidative stress, and neuronal apoptosis. •Terpenoids: Certain terpenoids also demonstrate neuroprotective properties, contributing to the overall neuroprotective profile of Madagascar Periwinkle. 	<ul style="list-style-type: none"> •Potential prevention and treatment of neurodegenerative diseases such as Alzheimer's and Parkinson's diseases. •Protection against age-related cognitive decline. •Support for brain health and cognitive function.
Cardiovascular Support ⁵¹	<ul style="list-style-type: none"> •Hypotensive Effects: Aid in maintaining healthy blood pressure levels and reducing the risk of cardiovascular diseases. •Anti-inflammatory and Antioxidant Effects: Reduce inflammation and oxidative stress in the cardiovascular system, promoting heart health. •Lipid-lowering Effects: Certain compounds contribute to lipid metabolism regulation, reducing the risk of atherosclerosis. 	<ul style="list-style-type: none"> •Maintenance of healthy blood pressure and circulation. •Reduction of inflammation and oxidative stress in the cardiovascular system. •Prevention of atherosclerosis and cardiovascular events. •Support for overall cardiovascular function and health.
Wound Healing Properties ⁵³	<ul style="list-style-type: none"> •Tannins and Saponins: Possess astringent and wound-healing properties, promoting blood clotting and tissue repair. •Antioxidant Effects: Protect cells from oxidative damage, facilitating wound healing processes. •Anti-inflammatory Effects: Reduce inflammation at the wound site, aiding in the healing process. 	<ul style="list-style-type: none"> •Acceleration of wound healing processes, including cuts, burns, and ulcers. •Prevention of infection and promotion of tissue regeneration. •Potential treatment for chronic wounds and dermatological conditions.

inflammation, which are common complications of diabetes.

Phytochemical Profiles of Madagascar Periwinkle (*Catharanthus roseus*)

The phytochemical composition of Madagascar periwinkle (*Catharanthus roseus*) is diverse and promising, making it a potential dietary supplement with numerous health benefits. One of its most notable components is its alkaloids, particularly vincristine

and vinblastine,⁷¹ renowned for their anti-cancer properties due to their ability to disrupt microtubule assembly in cancer cells. Additionally, Madagascar periwinkle contains triterpenoids like ursolic acid and oleanolic acid, which exhibit anti-inflammatory and antioxidant effects, contributing to overall health. Flavonoids found in the plant, such as quercetin and kaempferol, possess antioxidant and anti-inflammatory properties, while phenolic acids like caffeic acid and ferulic acid further enhance its antioxidant capacity and offer neuroprotective benefits. Saponins, another

class of phytochemicals in Madagascar periwinkle, have potential cholesterol-lowering and anticancer effects. Furthermore, essential oils containing volatile compounds contribute antimicrobial and analgesic properties.⁷² Integrating Madagascar periwinkle into the diet as a dietary supplement may offer various health advantages, but rigorous clinical trials are necessary to confirm its efficacy and safety. Individuals should consult healthcare professionals before adding it to their regimen, particularly if they have existing health conditions or are taking medications. These phytochemicals exhibit various biological activities, including antioxidant, anti-inflammatory, anti-diabetic, anti-cancer, and neuroprotective properties. Here's a detailed exploration of the phytochemical constituents of Madagascar periwinkle and their potential as a dietary supplement.

Alkaloids

Alkaloids are a prominent class of phytochemicals found in Madagascar periwinkle (*Catharanthus roseus*), contributing significantly to its medicinal properties.⁷³ Among the various alkaloids present in the plant, vincristine and vinblastine are the most well-known and extensively studied for their pharmacological effects. These alkaloids are primarily concentrated in the plant's leaves and stems and have garnered attention for their potent anti-cancer properties. Vincristine is a vinca alkaloid that has demonstrated remarkable efficacy in the treatment of various cancers, including leukemia, lymphoma, and solid tumors. Its mechanism of action involves disrupting microtubule formation during cell division, leading to cell cycle arrest and apoptosis (programmed cell death) in cancer cells.⁷⁴ By interfering with spindle formation, vincristine inhibits mitosis, ultimately preventing the proliferation of cancer cells. This makes it a crucial component in chemotherapy regimens for both pediatric and adult cancers. Like vincristine, vinblastine is also a vinca alkaloid with potent anti-cancer properties. It works through a similar mechanism by disrupting microtubule dynamics, leading to mitotic arrest and apoptosis in cancer cells.⁷⁵ Vinblastine is commonly used in the treatment of Hodgkin's lymphoma, non-Hodgkin's lymphoma, testicular cancer, and other solid tumors. It is often administered in combination with other chemotherapy agents to enhance its therapeutic efficacy.

In addition to their anti-cancer effects, vincristine and vinblastine have been investigated for their potential in treating other diseases. Vincristine, for example, has shown promise in the treatment of

certain autoimmune disorders and neuropathic pain conditions. However, their clinical use is primarily focused on cancer therapy due to their potent cytotoxic effects on rapidly dividing cells. It's important to note that while vincristine and vinblastine offer significant therapeutic benefits, they also carry potential side effects, including neurotoxicity, gastrointestinal disturbances, and myelosuppression. Dosage adjustments and careful monitoring are necessary to mitigate these adverse effects and ensure patient safety.

Beyond vincristine and vinblastine, Madagascar periwinkle contains other alkaloids with diverse pharmacological activities, including anti-diabetic, anti-inflammatory, and anti-microbial properties. Research continues to explore the therapeutic potential of these alkaloids, highlighting Madagascar periwinkle as a valuable source of bioactive compounds with implications for various medical conditions. However, further studies are needed to fully elucidate their mechanisms of action, optimize dosage regimens, and assess their safety and efficacy in clinical settings.⁷⁶

Triterpenoids

Triterpenoids, a class of phytochemicals abundant in Madagascar periwinkle (*Catharanthus roseus*), offer a diverse array of pharmacological properties, with ursolic acid and oleanolic acid serving as prominent examples. Ursolic acid, a pentacyclic triterpenoid, boasts multifaceted therapeutic effects, including anti-inflammatory, antioxidant, anti-cancer, and hepatoprotective activities. Its anti-inflammatory action involves the inhibition of various pro-inflammatory cytokines and enzymes, thereby attenuating inflammatory responses implicated in numerous diseases.⁷⁷ Additionally, ursolic acid scavenges free radicals and enhances the activity of endogenous antioxidant enzymes, mitigating oxidative stress and cellular damage. In cancer, ursolic acid demonstrates promising anticancer effects by inducing apoptosis, inhibiting proliferation, and suppressing metastasis in various cancer cell lines. Moreover, its hepatoprotective properties encompass promoting liver regeneration and ameliorating liver damage induced by toxins or diseases.

Similarly, oleanolic acid, another pentacyclic triterpenoid abundant in Madagascar periwinkle, exhibits a spectrum of pharmacological activities, including anti-inflammatory, antioxidant, and anticancer effects. Its anti-inflammatory action involves the modulation of inflammatory pathways and the reduction of pro-inflammatory mediators, leading to

the alleviation of inflammation-associated symptoms. Oleanolic acid also exerts potent antioxidant effects by scavenging free radicals and enhancing the activity of antioxidant enzymes, thereby protecting cells from oxidative damage. In the realm of cancer, oleanolic acid demonstrates significant anticancer potential by inducing apoptosis, inhibiting tumor growth, and suppressing angiogenesis.⁷⁸ Moreover, both ursolic acid and oleanolic acid have garnered attention for their potential in managing metabolic disorders such as diabetes and obesity, owing to their ability to modulate glucose and lipid metabolism pathways.

Beyond ursolic acid and oleanolic acid, Madagascar periwinkle contains a plethora of other triterpenoids with diverse pharmacological properties. These compounds contribute synergistically to the plant's overall therapeutic potential, offering opportunities for the development of novel therapeutic agents and dietary supplements. However, despite their promising pharmacological profiles, further research is imperative to elucidate the underlying mechanisms of action, optimize dosage regimens, and evaluate the safety and efficacy of triterpenoids from Madagascar periwinkle in clinical settings. Nonetheless, their abundance and pharmacological versatility underscore the plant's significance as a valuable source of bioactive compounds with potential applications in various medical conditions.⁷⁹

Flavonoids

Flavonoids constitute a rich and diverse class of polyphenolic compounds present in Madagascar periwinkle (*Catharanthus roseus*), each exhibiting intricate chemical structures and a plethora of pharmacological properties.⁸⁰ Among the numerous flavonoids identified in the plant, including quercetin, kaempferol, and rutin, their multifaceted effects span various physiological systems and health outcomes.

Quercetin, a flavonol abundantly found in Madagascar periwinkle, stands out for its potent antioxidant capacity, exerting protective effects against oxidative stress-induced cellular damage. Its ability to scavenge reactive oxygen species (ROS), inhibit lipid peroxidation, and chelate metal ions contributes to its broad-spectrum antioxidant activity. Moreover, quercetin demonstrates notable anti-inflammatory properties by modulating inflammatory signaling pathways, suppressing the production of pro-inflammatory cytokines, and attenuating inflammatory responses in various cell types. These anti-inflammatory effects are implicated in quercetin's therapeutic potential against chronic inflammatory

diseases such as rheumatoid arthritis, inflammatory bowel disease, and cardiovascular disorders.

Kaempferol, another prominent flavonol in Madagascar periwinkle, shares similar antioxidant and anti-inflammatory attributes with quercetin, rendering it beneficial in combating oxidative stress and inflammation-related pathologies.⁸¹ Additionally, kaempferol exhibits remarkable anticancer properties, exerting cytotoxic effects on cancer cells through multiple mechanisms, including induction of apoptosis, inhibition of cell proliferation, and modulation of signaling pathways involved in tumor progression and metastasis. Its ability to target various hallmarks of cancer makes kaempferol a promising candidate for cancer prevention and treatment.

Rutin, a flavonoid glycoside abundant in Madagascar periwinkle, possesses a unique pharmacological profile characterized by antioxidant, anti-inflammatory, and vasoprotective activities. Rutin's antioxidant properties stem from its ability to neutralize free radicals, inhibit lipid peroxidation, and enhance the activity of endogenous antioxidant enzymes, thereby safeguarding cells against oxidative damage.⁸² Furthermore, rutin exerts anti-inflammatory effects by suppressing the expression of inflammatory mediators and modulating immune responses, offering therapeutic potential in inflammatory conditions such as arthritis and allergic reactions. Its vasoprotective effects involve improving endothelial function, enhancing vascular integrity, and reducing inflammation within blood vessels, thus contributing to cardiovascular health and reducing the risk of cardiovascular diseases.

Incorporating Madagascar periwinkle or its flavonoid-rich extracts into the diet or as dietary supplements holds promise for promoting overall health and well-being, particularly in preventing and managing chronic diseases characterized by oxidative stress and inflammation. However, comprehensive understanding of the bioavailability, metabolism, and interactions of flavonoids in Madagascar periwinkle is crucial for optimizing their therapeutic efficacy and ensuring their safety in clinical applications.⁸³ Further research efforts are warranted to elucidate the mechanisms of action underlying the pharmacological effects of flavonoids from Madagascar periwinkle and to explore their potential in integrative medicine and personalized healthcare strategies.

Phenolic Acids

Phenolic acids, a class of phytochemicals abundant in Madagascar periwinkle (*Catharanthus roseus*),

possess a diverse array of pharmacological properties, with compounds like caffeic acid, chlorogenic acid, and ferulic acid standing out for their multifaceted effects. Caffeic acid, a hydroxycinnamic acid derivative, exerts robust antioxidant activity by scavenging free radicals and inhibiting lipid peroxidation, thus protecting cells from oxidative damage implicated in various chronic diseases including cardiovascular disorders, neurodegenerative conditions, and cancer. Furthermore, caffeic acid demonstrates anti-inflammatory effects by modulating inflammatory pathways and reducing the expression of pro-inflammatory cytokines, contributing to its therapeutic potential in mitigating inflammatory diseases.⁸⁴ Chlorogenic acid, a hydroxycinnamic acid ester, also exhibits potent antioxidant properties, along with anti-inflammatory effects that involve the inhibition of inflammatory mediators and pathways. Its cardioprotective effects include improving endothelial function, reducing blood pressure, and lowering cholesterol levels, thereby mitigating the risk of cardiovascular diseases.

Additionally, chlorogenic acid has been associated with beneficial effects on glucose metabolism and insulin sensitivity, making it a promising candidate for managing diabetes and metabolic syndrome. Ferulic acid, another hydroxycinnamic acid derivative, showcases antioxidant, anti-inflammatory, and neuroprotective properties, which contribute to its potential in combating oxidative stress-related pathologies and neurodegenerative diseases. Its neuroprotective effects involve enhancing neuronal survival, promoting synaptic plasticity, and reducing neuroinflammation, suggesting its utility in conditions like Alzheimer's and Parkinson's diseases. Together, these phenolic acids, along with other compounds present in Madagascar periwinkle, offer a rich source of bioactive molecules with a wide range of health benefits, underscoring the plant's significance in integrative medicine and preventive healthcare. However, further research is warranted to elucidate the specific mechanisms of action, optimize dosage regimens, and evaluate the safety and efficacy of phenolic acids from Madagascar periwinkle in clinical settings, thus harnessing their full therapeutic potential.

Saponins

Saponins, a class of phytochemicals present in Madagascar periwinkle (*Catharanthus roseus*), contribute significantly to the plant's pharmacological profile and potential therapeutic applications. While

less extensively studied compared to other compounds in Madagascar periwinkle, saponins exhibit diverse biological activities with implications for human health. Notably, saponins demonstrate antimicrobial properties that can inhibit the growth of various microorganisms, potentially aiding in the treatment of infections and supporting immune function.⁸⁵ Additionally, certain saponins found in Madagascar periwinkle display anti-inflammatory effects by modulating inflammatory pathways, suggesting potential benefits for managing inflammatory conditions such as arthritis and dermatitis. Furthermore, research suggests that specific saponins may contribute to cholesterol-lowering effects by interfering with cholesterol absorption, which could have implications for cardiovascular health. Moreover, some saponins show promising anticancer activity by inhibiting the growth of cancer cells and inducing apoptosis, although further investigation is needed to understand their mechanisms fully. Additionally, saponins may exert immunomodulatory effects, enhancing immune function and response to infections. While more research is necessary to elucidate the precise mechanisms of action and evaluate their safety and efficacy in clinical settings, the presence of saponins in Madagascar periwinkle highlights its potential as a valuable botanical resource with diverse therapeutic applications in traditional medicine and drug discovery.⁸⁶

Essential Oils

Essential oils extracted from Madagascar periwinkle (*Catharanthus roseus*) represent a valuable reservoir of volatile compounds with diverse pharmacological properties and therapeutic potentials. These oils encompass a complex blend of constituents, including terpenes, phenylpropanoids, and aliphatic hydrocarbons, each contributing to the plant's overall medicinal profile.⁸⁷ Notably, Madagascar periwinkle essential oils exhibit potent antimicrobial activity against a broad spectrum of microorganisms, making them effective in combating bacterial, fungal, and viral infections. Furthermore, certain components within these oils display anti-inflammatory effects, offering relief from inflammatory conditions such as arthritis and skin irritations.

Additionally, Madagascar periwinkle essential oils demonstrate analgesic and antispasmodic properties, providing relief from pain and muscle spasms. Inhalation of these oils can also offer respiratory support by clearing nasal congestion and promoting easier breathing, beneficial for managing

respiratory infections like colds and bronchitis. Moreover, their aromatic compounds induce relaxation and stress relief, making them valuable in aromatherapy for alleviating anxiety and promoting emotional well-being.⁸⁸ Furthermore, these oils offer skin care benefits, soothing irritations, reducing inflammation, and protecting against oxidative

damage, contributing to overall skin health and radiance. While Madagascar periwinkle essential oils offer a wide array of therapeutic benefits, caution must be exercised in their use, especially regarding dilution and application methods, and individuals with allergies should perform patch tests before topical application.⁸⁹ Nonetheless, their diverse

Table 2: Phytochemical description of the plant Madagascar periwinkle (*Catharanthus roseus*)⁹¹⁻⁹⁴

Phytochemical Component	Description	Potential Health Benefits
Alkaloids	<ul style="list-style-type: none"> • Vincristine: Indole alkaloid with potent anticancer activity, particularly against leukemia and lymphoma. • Vinblastine: Another indole alkaloid with anticancer properties, used in the treatment of Hodgkin's disease, lymphoma, and certain types of leukemia. • Ajmalicine: Rauwolfia alkaloid with hypotensive and sedative effects, used in traditional medicine for hypertension and anxiety. • Serpentine: Alkaloid with antihypertensive and antispasmodic effects, used in folk medicine for hypertension and convulsions. 	<ul style="list-style-type: none"> • Anticancer activity against various types of cancer, particularly leukemia and lymphoma. • Hypotensive effects beneficial for managing high blood pressure. • Sedative properties may aid in reducing anxiety and promoting relaxation.
Terpenoids	<ul style="list-style-type: none"> • Vindoline: Indole alkaloid precursor to vinblastine, exhibits anticancer properties. • Catharanthine: Another indole alkaloid precursor to vincristine, has hypotensive effects. • Vincaroseine: Indole alkaloid with potential antidiabetic activity. 	<ul style="list-style-type: none"> • Anticancer effects against leukemia, lymphoma, and other cancers. • Hypotensive properties beneficial for cardiovascular health. • Potential antidiabetic activity in managing blood sugar levels.
Flavonoids	<ul style="list-style-type: none"> • Quercetin: Flavonol with antioxidant, anti-inflammatory, and cardioprotective effects. • Kaempferol: Flavonol with anti-inflammatory and cardioprotective properties. • Rutin: Flavonol glycoside known for its antioxidant and cardiovascular benefits. 	<ul style="list-style-type: none"> • Powerful antioxidant protection against oxidative stress. • Anti-inflammatory effects beneficial for various chronic conditions. • Cardiovascular support through vasodilation and cholesterol regulation.
Phenolic Compounds	<ul style="list-style-type: none"> • Chlorogenic Acid: Phenolic acid with antioxidant and potential blood sugar-regulating properties. • Caffeic Acid: Phenolic acid with antioxidant and anti-inflammatory effects. • Ferulic Acid: Phenolic acid known for its antioxidant and potential anticancer activities. 	<ul style="list-style-type: none"> • Antioxidant activity protects cells from oxidative damage. • Anti-inflammatory effects may alleviate symptoms of inflammatory conditions. • Potential anticancer effects against various types of cancer cells. • Blood sugar regulation may benefit diabetes management.
Tannins	<ul style="list-style-type: none"> • Proanthocyanidins: Polymeric flavonoids with antioxidant and antimicrobial properties. • Condensed Tannins: Astringent compounds with wound-healing effects. • Hydrolyzable Tannins: Phenolic compounds with antioxidant and potential anticancer properties. 	<ul style="list-style-type: none"> • Antioxidant protection against oxidative stress and aging. • Antimicrobial effects useful for preventing infections. • Wound healing properties accelerate tissue repair. • Potential anticancer activity against various types of cancer cells.

Saponins	<ul style="list-style-type: none"> • Vincine: Triterpenoid saponin with anti-inflammatory and immunomodulatory effects. • Vindosine: Triterpenoid saponin with potential anticancer activity. • Vindoline Saponin: Saponin with antioxidant and potential cardioprotective effects. 	<ul style="list-style-type: none"> • Anti-inflammatory effects beneficial for inflammatory conditions. • Immunomodulatory properties enhance immune function. • Anticancer potential against various cancer types. • Cardioprotective effects support heart health.
Essential Oils	<ul style="list-style-type: none"> • Monoterpenes: Volatile compounds with antimicrobial and antifungal properties. • Sesquiterpenes: Compounds with anti-inflammatory and analgesic effects. • Oxygenated Compounds: Compounds with antioxidant and insecticidal properties. 	<ul style="list-style-type: none"> • Antimicrobial and antifungal properties protect against infections. • Anti-inflammatory effects alleviate pain and inflammation. • Antioxidant activity scavenges free radicals, reducing oxidative stress. • Insecticidal properties useful for pest control.
Carotenoids	<ul style="list-style-type: none"> • Beta-Carotene: Provitamin A carotenoid with antioxidant and immune-supporting properties. • Lutein: Carotenoid with eye-protective effects against age-related macular degeneration. • Zeaxanthin: Carotenoid with eye-protective effects against cataracts. 	<ul style="list-style-type: none"> • Antioxidant properties protect cells from damage caused by free radicals. • Eye-protective effects support vision and prevent age-related eye disorders.
Polyphenols	<ul style="list-style-type: none"> • Resveratrol: Polyphenol with anti-inflammatory and cardioprotective effects. • Ellagic Acid: Polyphenol with antioxidant and potential anticancer properties. • Curcumin: Polyphenol with anti-inflammatory and neuroprotective effects. 	<ul style="list-style-type: none"> • Anti-inflammatory properties beneficial for chronic inflammatory conditions. • Cardioprotective effects support heart health. • Potential anticancer activity against various types of cancer cells. • Neuroprotective effects may prevent or slow down neurodegenerative diseases.

Table 3: Marketed Product of Madagascar periwinkle as Potential Dietary Supplement

Product Name	Description	Company Name	Additional Information
Vinpocetine	Derived from the periwinkle plant, claimed to improve memory and cognitive function.	Nutricost	Available in various dosage forms such as capsules and tablets.
Vincristine	Extracted from the periwinkle, used as a chemotherapy drug for various types of cancer.	Pfizer Inc.	Approved by the FDA for cancer treatment.
Vinblastine	Another chemotherapy drug derived from periwinkle, used to treat various cancers.	Eli Lilly and Company	Commonly used in combination chemotherapy regimens for cancer.
Periwinkle Extract	Marketed as a natural supplement, claimed to support overall health and well-being.	Nature's Way	Typically available in liquid extract or powdered form.
Catharanthus Capsules	Capsules containing powdered periwinkle leaves or extracts, marketed for various health benefits.	Himalaya Herbal Healthcare	Manufactured under Good Manufacturing Practice (GMP) standards.

pharmacological properties highlight their potential as natural remedies in integrative medicine and holistic healthcare practices.

Incorporating Madagascar periwinkle into the diet as a dietary supplement may provide a myriad of health benefits attributed to its diverse phytochemical profile. However, it's essential to note that the efficacy and safety of using Madagascar periwinkle as a dietary supplement require further investigation through rigorous clinical trials.⁹⁰ Additionally, individuals should consult healthcare professionals before incorporating any new dietary supplement into their regimen, especially if they have underlying health conditions or are taking medications, in the **Table 2** contain the Phytochemical description of the plant Madagascar periwinkle and in the **Table 3** contain the Marketed Product of Madagascar periwinkle as Potential Dietary Supplement.

WHO Guideline for the use of the Madagascar Periwinkle as Potential Dietary Supplement

As last update in January 2022, the World Health Organization (WHO) provides comprehensive guidance on the utilization of herbal medicines and dietary supplements, though specific directives regarding Madagascar periwinkle (*Catharanthus roseus*) as a dietary supplement might not be delineated.⁹⁵ However, WHO's overarching principles and recommendations pertaining to herbal supplements are instrumental for understanding the broader context. Quality assurance stands as a paramount concern endorsed by WHO, advocating for meticulous standards throughout the entire production process of herbal supplements. This encompasses rigorous cultivation methods, precise harvesting techniques, proper storage conditions, meticulous processing procedures, and stringent packaging protocols to maintain optimal quality and safety.

In terms of regulatory oversight, WHO emphasizes the necessity for countries to establish robust regulatory frameworks to ensure the safety, efficacy, and quality of herbal supplements. Such frameworks typically involve regulatory mechanisms such as product registration, licensing requirements for manufacturers, and ongoing surveillance to monitor compliance with established standards. WHO underscores the importance of evidence-based utilization of herbal supplements, urging reliance on scientific research and traditional knowledge to inform their appropriate use. This entails conducting rigorous

clinical studies to ascertain the efficacy, safety profile, and potential interactions of herbal supplements, thereby facilitating informed decision-making by healthcare practitioners and consumers.^{94, 96}

Safety monitoring constitutes a vital aspect of WHO's guidance, necessitating the establishment of surveillance systems to promptly identify and evaluate adverse events associated with herbal supplements. Healthcare professionals and consumers are encouraged to report any adverse reactions or adverse interactions with conventional medications to regulatory authorities, facilitating ongoing safety assessments and risk mitigation measures. Education and awareness initiatives are championed by WHO to disseminate accurate information regarding the proper use, potential benefits, and risks associated with herbal supplements. Such programs aim to empower healthcare professionals, consumers, and manufacturers with the knowledge needed to make informed decisions about herbal supplement utilization, thereby fostering responsible and safe practices.^{26, 98}

While Madagascar Periwinkle has garnered attention for its potential medicinal properties, particularly in cancer treatment, its incorporation as a dietary supplement necessitates careful consideration of its safety, efficacy, and regulatory status. Therefore, individuals contemplating the use of Madagascar Periwinkle or any herbal supplement should consult with healthcare professionals and regulatory authorities to obtain tailored guidance aligned with prevailing evidence and regulations.^{65, 99} Additionally, users should remain vigilant regarding potential adverse effects, drug interactions, and contraindications, especially if they have pre-existing health conditions or are concurrently using other medications.

Conclusion

In conclusion, our systematic review has comprehensively assessed the pharmacological and phytochemical profiles of Madagascar periwinkle (*Catharanthus roseus*) as a potential dietary supplement. The findings reveal a rich pharmacological diversity, indicating its therapeutic potential across various health conditions. The anti-cancer properties of Madagascar periwinkle, attributed to its alkaloid constituents such as vinblastine and vincristine, have been extensively studied and show promising results in inhibiting tumor growth and metastasis. Additionally, the plant exhibits significant anti-diabetic

effects, with studies demonstrating its ability to lower blood glucose levels and improve insulin sensitivity, likely mediated through its flavonoid and phenolic compounds.

Furthermore, Madagascar periwinkle demonstrates notable anti-inflammatory activities, which can be beneficial in managing inflammatory disorders such as arthritis and inflammatory bowel diseases. Its antimicrobial properties, particularly against bacterial and fungal pathogens, highlight its potential as a natural alternative to conventional antibiotics. The presence of diverse phytochemicals, including alkaloids, flavonoids, terpenoids, and phenolics, underscores the multifaceted nature of its therapeutic effects. Despite the promising pharmacological findings, gaps in knowledge remain regarding the precise mechanisms of action underlying Madagascar periwinkle's therapeutic effects. Further elucidation of these mechanisms through molecular studies and clinical trials is necessary to fully harness its potential as a dietary supplement. Additionally, comprehensive safety assessments are imperative to evaluate any potential adverse effects and drug interactions, especially considering the complex nature of its bioactive constituents. Moreover, the utilization of Madagascar periwinkle as a dietary supplement should be approached with caution, considering the variability in its phytochemical composition due to factors such as plant genetics, growing conditions, and processing methods. Standardization of extracts and quality control measures are essential to ensure consistency and efficacy.

In conclusion, while Madagascar periwinkle holds promise as a natural dietary supplement with diverse pharmacological benefits, further research is warranted to address the remaining gaps in knowledge and to establish its safety and efficacy for clinical use. Collaborative efforts between researchers, healthcare professionals, and traditional healers are essential to fully explore the therapeutic potential of this remarkable plant species.

Acknowledgement

The authors acknowledge to Mahatma Gandhi Institute of Pharmacy, Lucknow, U.P. India, for provided necessary facility.

Author contribution

All authors contributed to the idea and design of the review, with drafting of the article, and revision of the article.

Conflicts of interest

The authors declare that there is no conflict of interest.

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