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**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**Available online at: <http://www.iajps.com>**Review Article****PHYTOCHEMICAL AND PHARMACEUTICAL PANORAMA
OF CATHARANTHUS ROSEUS****Kanika Barik, Shweta Sao and Dharmendra K. Parihar***Department of Microbiology Dr. C.V. Raman University, Kargi Road, Kota,
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Abstract:

Madagascar periwinkle Catharanthus roseus is an important tropical medicinal plant, found as a popular ornamental plant in gardens and homes across the warmer parts of the world, also known as “an anticancerous drug yielding plant” is a tropical and subtropical plant belonging to the family Apocynaceae. The plant accumulates an array of diverse compounds comprising over 130 different MIAs. It is a seasonal to perennial garden plant and the exclusive source of the anticancer drugs vincristine and vinblastine. Apart from these, its leaves and roots hyper-accumulate the other terpenoid indole alkaloids, which are required for the economic production of pharmaceutical molecules vindoline, catharanthine, ajmalicine and serpentine. The plant have been used for various other medicinal valued like anti-diabetic, anti-ulcer, anti-bacterial, anti-oxidant and anti-diarrheal properties. The review describes phoarmacological applications and phytochemicals of C. roseus.

Key words: Alkaloids, antioxidant, antibiotic, anticancer, Catharanthus roseus, Vincristine, Vinblastine.

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INTRODUCTION:

The periwinkle *Catharanthus roseus*, is an erect decumbent, deciduous, undershrub upto 100 cm tall and usually with white latex. The plant is displayed indoors in all kinds of geographical locations, especially the temperate locations and grown in gardens in semi- temperate to tropical locations on account of its ability to produce flowers all round the year, small size and perenniality. It occurs in almost every tropical and subtropical region of the world, occurring on every continent except Antarctica and on many islands. It is rarely encountered in temperate environments as low winter temperatures inhibit its growth. The characteristic of wide adaptability to all types of soils facilitates its geographically spread distribution in India. Water logged and highly alkaline soils are not suitable for this plant species. The name *Catharanthus* (L.) G. Don is derived from the Latin words *Katharos* (pure) and *anthos* (flower). Several names such as *Ammocallis rosea*, *Lochnera rosea* and most commonly *Vinca rosea* were used.

Taxonomical Hierarchy

Kingdom	: Plantae
Subkingdom	: Tracheobionta (Vascular Plants)
Division	: Magnoliophyta
Class	: Magnoliopsida
Subclass	: Asteridae
Order	: Gentianales
Family	: Apocynaceae (dog-bane family)
Sub family	: Plumeroideae
Tribe	: Plumerieae
Sub Tribe	: Alstonrieae
Genus	: <i>Catharanthus</i> G. Don
Species	: <i>Catharanthus roseus</i> (L.) G. Don

The genus *Catharanthus* is comprised of eight species of small shrubs and herbs, six of which are predominantly indigenous to Madagascar.

The information about the designations and origins of the 8 species has been shown in Table 1

Table 1: Designations and origins of the *Catharanthus* species

S. No	Name of the <i>Catharanthus</i> species	Origin
1	<i>C. roseus</i> L.G. Don	Madagascar, now naturalized
2	<i>C. ovalis</i> Markgraf	Madagascar
3	<i>C. trichophyllous</i>	Madagascar
4	<i>C. longifolius</i> Pichon	Madagascar
5	<i>C. coriaceous</i>	Madagascar
6	<i>C. lanceous</i> Bojer ex	Madagascar
7	<i>C. saitulus</i> Pichon	Madagascar
8	<i>C. pusillus</i> Murray G.	India and Sri

C. roseus is a diploid plant species with estimated haploid genome size between 696Mbp and 2377 Mbp comprising of 16 chromosomes [1-2]. The floral morphology of *C. roseus* is conducive both for self and insect pollination. The natural populations of *C. roseus* have been observed to harbour considerable genetic variability; natural variability has been used to develop horticulture and drug types. Variations resulting from cross breeding, induced mutagenesis and polyploidy has been variously employed in *C. roseus*. Initial crossing studies have shown that although the plant is self pollinated, frequent out crossing has been observed resulting into different intermediate types. Artificial tetraploids have been produced by a number of workers. Although, some workers reported increased alkaloid content in tetraploids. Tetraploid plants have shorter, thicker stem, larger and thicker leaves. Tetraploids have also been reported to be less susceptible to die back disease.

The herb has been used for centuries to treat a variety of ailments and was a favorite ingredient of magical charms it was in the middle ages. Alkaloids and tannins are the two classes of active compounds in *Vinca*. More than 100 monoterpenoids indole alkaloids (TIA) produced by *Catharanthus roseus* in different organs [3]. The leaves and stems of the plant are full of dimeric alkaloids, vinacristine and vinblastine that are indispensable cancer drugs, while roots have antihypertensive, ajmalicine and serpentine[4]. The leaves have been used by diabetic patients. It is reported to reduce blood glucose in normal and alloxan diabetic [5] *C. roseus* was also found to be a good source of the non-enzymatic and enzymatic antioxidants [6]. The *C. roseus* plant has more than 300 alkaloids, some of which are approved as antineoplastic agents to treat leukemia, hodgkin's disease, malignant lymphomas, neuroblastoma, wilm's tumour and other cancers.

Phytochemistry of *Catharanthus Rureus*

Both vegetative as well as root of *Catharanthus ruseus* is very rich in alkanoids, flavonoids, triterpenoids, tannins, saponin, coumarin, carbohydrates, quinine quinine and phenolic compounds[7]. The flowers part of the plant contains abundant amount of tannins, triterpenoids and alkaloids and have been found to be antidiabetic and wound healing property [8]. Leaves of *Catharanthus roseus* are rich in alkaloids and carbohydrates. The root and stem of the plant contains quinones which has antibacterial activities [9]. The alkaloid Alstonine like vincristine and vinblastine are produced from the rootbark part of *C.roseus* traditionally used as calming drug [10]. The leaves of the plant have been used as antibacterial and diabetic agents and contain carbohydrates and alkaloids [11]. It also contains polyphenols responsible for antioxidant activity. *C. roseus* contain a wide range phenolic compounds, including

C6C1 compounds such as 2,3-dihydroxybenzoic acid, as well as phenylpropanoids such as cinnamic acid derivatives, flavonoids and anthocyanins[12].

Catharanthus roseus contain alkaloid (% on dry weight basis) of different parts of *C. roseus plant* are in root: 0.12 - 9.00, Stem; 0.07 - 0.46, Leaf; 0.10-1.16 , Flower; 0.005, Fruit; 0.40, Seed; 0.18 and in Pericarp; 0.14. Out of 130 alkaloid of indole group produced by the plant, 25 are dimeric in nature including two major commercially important cytotoxic dimeric alkaloids vinblastine and vincristine produced by leaves. These are used as indispensable medicine in cancer therapy. The root part of *C. roseus* is rich in ajmalicine and serpentine used as anti-hypersensitive drug. Among the monomeric alkaloids Ajmalicine (Raubacine) found in the roots has been confirmed to have a broad application in the treatment of circulatory diseases, especially in the relief of obstruction of normal cerebral blood flow. Hypoglycemic effects of a number of other indole alkaloids such as lochnerine, tetrahydroalstonine, and vindolidine have also been revealed. Catharanthine is reported to be present in the root tissue and aerial part of the plant and also found effective in treatment of leukaemia, diabetes, hypertension and menorrhagia etc[13].

Pharmacological Applications of *C. roseus*

Cytotoxic Activity Effects

The leaves and stem derived anti cancerous alkaloids Vinblastin and vincristine have growth inhibitory effect on animal tumors. The cell division of cancerous cell are interfered by the by Vinblastin and vincristine and their derivatives like deacetyl vinblastine amide (vindesine) marketed as Eldisine They are found effective in both malignant and non malignant platelets and platelets associated disorders. The growth of new blood vessels which are responsible for the supporting tumor growth has been found inhibited by the *C. roseus* alkaloids [14]. They are injectable drugs commercially available as Velban and Oncovian respectively. Vincristine is use for the treatment of leukemia in children whereas Vinblastine choriocarcinoma and Hokin's disease, chorio carcinoma [15]. Vinflunine is a novel alkaloid of *Apocynaceae*, obtained by hemisynthesis. The antitumor activity of vinflunine was evaluated against a range of transplantable murine and human tumors [16].

Hypoglycemic Effect

Different extracts of *C. roseus* have the ability to improve blood supply to the brain resulting in enhanced oxygen and glucose supply to brain. This also limits the nonessential blood clotting. It has been found that this plant is capable of increasing insulin production and utilization of sugar and utilization of sugar in blood. an alkaloid Alastonin found in bark has been used to regulate blood pressure. For diabetic treatment *C. roseus* alkaloid has been marketed under the proprietary name Vinculin [11, 17, 18]. Catharanthine is used as antidiabetic drug.

However, for the treatment of diabetic patients the crude extract instead of purifies active compound is in use. The oral dose chloroform-methnolic extracts of *C. roseus* has been tested in diabetic rates, which showed significant increase in body weight and decreased blood glucose and cholesterol. The increased level of Glucose hexokinase was noted whereas, the decrease in glucose 6- phosphatase and glucose 1,6 bisphosphatase was seen [19].

Antioxidant Effect

The anti oxidant nature of the plant extract is due to the presence of tannins, phenolic and flavonoids. They helpful in eradicating the reactive oxygen species harmful to our body [20]. The antioxidant potentials of these compounds are because of their ability to donate hydrogen, reduce, chelate metals or quench singlet oxygen [21-22]. On comparing a number of plants having antioxidant activity the *C. roseus* was found to be the best oxygen radical absorbance capacity (ORAC). *C. roseus* showed greatest ORAC value of 22.30µmole Trolox equivalent [23]. Although all parts of *C. roseus* contain antioxidant compound, the flower of *Vinca rosea* has highest antioxidant activity of 97.44% at 800 µg which was higher than the standard L-ascorbic acid (94%). The antioxidant potential of the ethanolic extracts of the roots *C. roseus* obtained by [24] using different systems of assay such as Hydroxyl radical-scavenging activity, superoxide radical-scavenging activity, DPPH radical-scavenging activity and nitric oxide radical inhibition method. The results reveal the antioxidant activity of ethanolic extracts of the roots. Rasool et al, [24] demonstrated through the study that *C. roseus* is available source of natural antioxidant which can be exploited for food and nutraceutical applications.

Anti Microbial Effect

Keeping in view the multidrug resistance of microbes and their adverse effect on human, it has become very important to discover new antimicrobial agents. The rate of antibiotic production is much lower than the rate at which the microbes becoming resistant to them [26]. The plant extracts have shown the promising long term health response. Different extracts of *Catharanthus roseus* have been studies a broad spectrum of antimicrobial effect against microbial agents and can be used as a prophylactic agent possess efficient anti-viral [27], anti-bacterial [28] and antifungal [29]) compound. The antibacterial activity of crude extract from different parts of this plant studied against *Salmonella typhimurium* (NCIM2501), *S. aureus* (NCIM5021) and *Pseudomonas aeruginosa* (NCIM2036) which resulted in its high antimicrobial potency [15]. *Bacillus megatarium* and *Staprylococcus albusi* show inhibition by ethanol extract of dried leaves [30]. Water extract of callus culture of micro propagated plant inhibited Tobacco Mosaic Virus [31]. Antifungal effect was shown using different plant part extracts of *C. roseus* and

found active against different fungi like *Tiichophyton mentagrophytes* [32-33], *Candida albicans* [34] and *Aspergillus fumigates* [35]

Wound Healing Property

The antimicrobial property of different extracts from various parts of *C. roseus* has been studied. It is found very useful in many groups of bacteria, fungi and virus as well. This property of the plant extract complement the wound healing ability of the *C. roseus*, because the removing infectious agent from the wound is the primary stage of curing wound. Wound healing is the process of repair that follows injury to the skin and other soft tissues. Following injury, an inflammatory response occurs and the cells below the dermis (the deepest skin layer) begin to increase collagen (connective tissue) production. Later, the epithelial tissue (the outer skin) is regenerated [36-37]. The methanol extract of the *C. roseus* flower has been tested on animal model for treating wound. Nayak and his colleagues [38] evaluated the wound healing property of *C. roseus* in rates. They demonstrated the high rate of wound contraction and decreased epithelialization period. They also noticed significant increased in dry weight in the granulation tissues as compared to the control animal.

Anti Helminthic Property:

Helminthes infections in human and cattle is considered as a chronic infection. *Catharanthus roseus* was being used traditionally for a long period as an anti helminthic agent. The anti helminthic property of *C. roseus* has been evaluated by using *Pherithema postuma* as an experimental model and with Piperazine citrate as the standard reference. The ethanolic extract at the concentration of 250 mg/ml was found to show the significant anti helminthic activity [39]. The aqueous, ethanol, methanol, ethyl acetate extract of *C. roseus* were found anti-helminthic property [40].

Antidiarrheal Activity

Catharanthus roseus plant has been reported for their anti diarrheal activity by some workers in few animal models and found significant role. The ethanolic extracts of leaf were tested on the wistar rats who were induced for diarrhea with castor oil experimentally. The researchers found anti diarrheal effect of ethanolic extracts *C. roseus* as dose dependant inhibition of the castor oil induced diarrhea the result was compared with standard drugs Loperamide and atropine sulphate [41].

Anti Ulcer Property

The anti ulcer property of the *C. roseus* plant leave is reported in ulcer induced test animals [42] Vincamine and Vindoline alkaloids of the plant show anti ulcer property. Vincamine is known for cerebro-vasodilatory and neuroprotective activity [15].

Traditional Remedial Uses

The leave/and root/ their decoction of the *C. roseus* is traditionally used in many countries for various remedy. It is used stomach cramps, in menorrhagia, as anti cancerous in Phillipines. In Madagaskar it is used as vomitive, purgative, vermifugl, depurative, hemostatic and toothache remedies. In India, the leave juice is applied on bee sting and wasp sting. In Africa they are used for menorrhagia and rheumatism. The plant is used in diabetes, hypertension, insomnia and cancer in Malasiya. The juice of *C. roseus* is used in indigestion and dyspepsia in Mauritius. The flower decoction/ extract are used in asthma, flatulence and tuberculosis in Bahmas, aseye wash for infants in Cuba and Jamaica. America uses the plant juice as Gargle ease soar throats, chest ailments and laryngitis. West Indies, Phillipines and Nigeria use plant in diabetes. The boiled plant is also used to arrest bleeding in Hawai [15].

CONCLUSION:

Herbal medicines are the most ancient and undisputed mode of treatment not only in India, China but also in many more developed countries. They are very safe and effective against many diseases, even for those so called incurable. The application of *C. roseus* is described in ancient Indian Sanskrit literature the Ayurveda. The use of *C. roseus* has proven scientifically effective for various illnesses. It contains more than 130 alkaloids, some of which successfully marketed like Vinblastine and Vincristine for cancer treatment. The *C. roseus* alkaloid product is available as Vincula for diabetes patients. Apart from the above listed use is also known for vasodilatory and analgesic use. The *C. roseus* alkaloids Ajmalicine and serpentine found in roots effective in cardiovascular diseases.

The traditional and folk use of *C. roseus* in different countries are very wide, many of which are proven scientifically by bioactive compound analysis and tests, some are in progress and many more need attention. The active compounds responsible for specific remedies are required to be identified in order to make them available in polished and more convenient form. They are also required to be evaluated for the health complication related to the modern lifestyle in the society.

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