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Review Article

Catharanthus Roseus Linn—A Review

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Abstract

Cancer, the most dreaded six letter bomb afflicting mankind in the worst possible ways. Over few decades, there is an excellent progress made but treatment of cancer still remains an enigma. However, nature always has its way of maintaining balance and we have been blessed with the boon of plants producing exceptionally promising anti-cancerous activities. The most successful higher plant material used in cancer chemotherapy are alkaloids of *Catharanthus roseus*, commonly known as the Madagascar periwinkle or rosy periwinkle, a species of flowering plant in the dogbane family-Apocynaceae. It is native and endemic to Madagascar, but frequently grown as an ornamental and medicinal plant, the storehouse of the very famous oncolytic alkaloids - vincristine and vinblastine, used effectively to treat cancer. In this review, we have highlighted the pharmacognostical characteristics, cultivation, chemical constituents and pharmacological uses of the plant.

Keywords: *Catharanthus Roseus*; Ethnobotany Uses; Pharmacognosy; Pharmacological Activity; Review

Introduction

Catharanthus roseus Linn (synonym: *Vinca rosea*; Madagascar periwinkle; Apocynaceae) a perennial plant is commonly seen in tropical counties and are native to Madagascar and Southern Asia [1,2]. The plant has spread all over tropical and subtropical parts of India and grows wild all over the plains and lower foothills in Northern and Southern hills of India. In Malaysia it is locally called as Kemunting Cina. The periwinkle logo as a symbol for hope for cancer patients is used by National Cancer Council of Malaysia [3]. The flowers produced by these plants are planted for decorative purposes are of colours such as pink, purple and white Madagascar periwinkle is used traditionally for number of ailments such as high blood pressure, infection and diabetes mellitus. Stem produces a milky sap which is a source for more than 70 indole alkaloids. Vincristine and vinblastine were isolated from this plant are well known anti cancer drugs for Hodgkin's lymphoma and childhood leukemia respectively. The mechanism of action being bindIng to tubulin thus inhibit the metaphase of cellular mitosis. Hair loss, peripheral neuropathy, constipation and hyponatremia are the major side effects of this drugs [4,5].

Scientific classification [6]

Kingdom: Plantae
Division: Magnoliophyta (Flowering plants)
Class: Magnoliopsida (Dicotyledons)
Order: Gentianales
Family: Apocynaceae
Genus: *Catharanthus*
Species: roseus

Vernacular names [7]

Sanskrit: Nityakalyani, rasna, sadampuspa, sadapushpi
English: Cayenne jasmine, old maid, Madagascar periwinkle, Red periwinkle
Hindi: Sada suhagan, sadabahar
Kannada: Batla hoo, bili kaasi kanigalu, ganeshana hoo, kempu kaasi kanigalu

Telugu: Billaganneru
Malayalam: Banappuvu, nityakalyani, savanari, usamalari
Tamil: Cutkattu malli, Sudukadumallakai
Gujarathi: Barmasi
Bengali: Nayantara

Botanical description

It is an herbaceous plant or an evergreen subshrub growing to 32 in 80 cm high. It has glistening, dark green, and flowers all summer long. The flowers of the naturally appear pale pink with a purple "eye" in their centres.Erect or accumbent suffrutex, to 1 m, usually with white latex. Stems is green, often permeate with purple or red.

Leaves: Oval leaves (1-2in long) decussate, petiolate; lamina variable, elliptic, obovate or narrowly obviate; apex mucronate.

Flowers: 4-5 cm, classy, white or pink, with a purple, red, pale yellow or white centre Follicle 1.2-3.8 × 0.2-0.3 cm, susceptible on the axial side.
Seeds 1-2 mm, are numerous and grooved on one side.

Climate, soil and propagation

Flowering period: Throughout the year in equatorial conditions, and from spring to late autumn, in warm temperate climates.

Soil: Full sun and well-drained soil is preferred.

Light: Bright light, included three or four hours of direct sunlight daily, is essential for good flowering.

Temperature: Normal room temperatures is suitable at all times. It cannot tolerate temperatures less than 10°C (50°F).

Watering: Water the potting mixture plentifully, but do not allow the pot to stand in water.

Feeding: As the flowering begins, apply standard liquid fertiliser every two weeks. Plants are not tolerant of excessive fertiliser.

Irrigation: They need regular moisture, but avoid overhead watering. It should be watered tolerably during the growing season, but it is relatively drought resistant once entrenched. They will regain after a good watering.

Fertilising: The plants is not heavy breeders. If necessary, feed biweekly or once monthly with a fair amount liquid fertilizer. Too much fertilizing will produce abundant foliage instead of more blooms [1,2,7].

Geographical distribution

Catharanthus roseus is originated from the Indian Ocean Island of Madagascar. It was believed to be an endangered plant in the wild. However in many tropical and subtropical regions worldwide, including the Southern United states, it is now a common plant [1,2].

Pharmacognostical studies

Macroscopical characteristics

The leaves are opposite, simple, petiolate; petioles long, glabrous or softly pubescent; lamina elliptic, obovate or oblong-elliptic, obtuse or retuse, mucronulate, base cuneate or subcuneate, often oblique, slightly decurrent; margin entire, may or may not be hairy, membranous or thinly conspicuous. Upper surface puberulus or glabrescent, dark shining green, lower surface pubescent or nearly glabrous, light green, main lateral nerves rather close, arcuate, nervation not conspicuous.

Microscopic and powder characteristics [12]

Leaf is dorsiventral. The lower epidermal cells have sinous walled, upper slightly sinuous walled or walls slightly curved. Stomata on lower surface is ranunculaceous type. Trichromes unicellular of septate, uniseriate, nonglandular and unbranched.

Transverse section of the petiole of *C. roseus* shows the epidermal cells which have thin-walled with a thick cuticle in the outer walls. The cells are of different sizes and shapes such as either oval or elliptical. Next is the hypodermis which consists of thin walled parenchymatous cells. This is followed by the cortex. Next to the upper epidermal cells are much elongated palisade cells which are filled with chloroplasts. The lower epidermal cells are more or less same in size and shape as those of the upper ones. In between the palisade cells and the lower epidermal cells are the spongy arenchymatous cells. Cells are oval, elliptical, oblong or polygonal in shape and are filled up with cell contents.

Powder characteristics

It shows fragments of upper epidermis in surface view wiith straight anticlinal walls and anomocytic and anisocytic stomata, patches of lower epidermis with sinuous anticlinal walls and same types of stomata [8].

Chemical constituents

Major being Alkaloids from 0.74 to 0.82%; important being vincristine, vinblastine, catharanthamine, vincoline. Other alkaloids viz, deoxyvinblastine, leurosine, pleurosin, leurocristine, leurosidine, vincolinine, vinacardine, roseadine, vindolicine, rosicine, etc are isolated [9-13].

Vinca alkaloids are having poisonous activities have physiological effects too that makes them useful as medicines. The alkaloids are distributed in all parts of the plant. The maximum being in the root bark particularly during flowering. The physiologically important alkaloids are antineoplastic dimeric alkaloids, vinblastine, vincristine in the aerial parts and ajmalicine, serpentine in the roots. Another alkaloid, vinflunine, not universally accepted except in Europe and said to possess anti-tumour activity. Vinblastine and vincristine are chemotherapy medications used to deal with several types of cancers and are biosynthesised from the linking of the alkaloids catharanthine and vindoline. The newer semisynthetic chemotherapeutic agent vinorelbine is used to deal with non-small-cell lung cancer, can be prepared either from vindoline and catharanthine or from the vinca alkaloid leurosine in both cases via anhydrovinblastine. Rosinidin is an anthocyanidin pigment found in the flowers of *C. roseus* [14-17].

Identification by TLC

Vinblastine is identified by TLC by spotting standard and sample and developed in mobile phase n-Butanol: Acetic acid: Water: 5:1:1 and spraying with modified Dragondroff's reagent. Rf value of 0.24 corresponds to Vinblastine in both standard and sample solution track.

Analytical methods

The analytical method is similar as identification by TLC except Precoated plates of Silica gel 60 F254 are used and after developing, densitometric scan of the plate is done at 560 nm. Percentage of vinblastine can be calculated from peak area under the curve.

Quantitative standards [7]

Foreign organic matter: Not more than 2.5%
Ash: Not more than 14.6%
Acid Insoluble ash: Not more than 1.0%
Alcohol soluble extractive: Not less than 12.0%
Water soluble extractive: Not less than 40.0%

Pharmacological activities

Anticancer activity

In clinical practice, the administration of *C. roseus* is carried out intravenously, after which they are eventually metabolized by the liver and excreted. Hair loss, peripheral neuropathy, constipation and hyponatremia are the major side effects of this drugs. To improve the therapeutic index, Semi-synthetic *Catharanthus* alkaloids such as vinorelbine and vinflunine were developed. Vinorelbine and vinflunine exert their antitumor effect by binding to tubulin.

These alkaloids have growth inhibition affect some human tumors. Vinblastine is used experimentally for treatment of neoplasmas and is recommended for Hodgkin's disease, chorio carcinoma. C. roseus was found to show the significant anticancer activity against numerous cell types in vitro condition and especially greatest activity was found against the multidrug resistant tumor types.

Vinca alkaloids also called as mitotic spindle poisons they inhibit assembly of the spindle forms from microtubules, there by inhibiting mitosis in cell cycle. Vinca alkaloids hence successfully prevent cancer cells from dividing. Different Vinca alkaloids have their own unique properties [17].

Antidiabetic activity

Hypoglycemic activity was found by using the dichloromethane: methanol extract (1:1) of the leaves and twigs of *C. roseus* plant in streptozotocin induced diabetic rat model at the dose of 500 mg/kg that has been administered orally for 7 and 15 days. 48.6 and 57.6% hypoglycemic activity was observed and further treatment for a period of 30 days has provided complete protection against STZ challenge (75 mg/kg/i.p.).

Enzymes activities of glycogen synthase, glucose 6-phosphate-dehydrogenase, succinate dehydrogenase and malate dehydrogenase were found to be decreased in the liver of diabetic animals which would be significantly improved after treatment with extract at dose 500 mg/kg p.o. for 7 days. Results indicated the increased metabolization of glucose in treated rats with the increased levels of lipid per oxidation.

The ethanolic extracts of the leaves and flower of C. roseus revealed that a dose dependent decreasing of blood sugar is similar to the standard drug. Decreasing of blood sugar in comparable to the

standard drug glibenclamide. The Hypo glycemic action has been aroused due to the result of the increase glucose utilization in the liver [18-20].

Antimicrobial activity

C. roseus has been discovered to be an important medicinal plant for the creation of the novel pharmaceuticals as most of the bacterial pathogens were improving resistance against many of the available anti microbial drugs. Plants have been justified to be valuable natural resources for the active chemotherapeutic agents and suggest a broad spectrum of action with the greater emphasis on the preventive action [21]. It is demonstrated that mutant leaf extracts had good antibacterial potential against *S. aureus*, *S. citreus*, and *E. coli* and *P. aeruginosa* bacteria while *B. subtilis* was not influenced. The fluctuation in antibacterial activity between mutant and control plant leaves might be due to the genomic changes, aroused by the mutagen correspondingly influencing the fusion and level of bio-active compounds like vincristine, Vinblastine, vindoline in tissue, which might be obligation for antibacterial property of periwinkle leaves as also reported earlier [22].

Antioxidant activity

The antioxidant activity of *C. roseus* was assured by DPPH assays at distinct concentrations (200, 400, 600, 800 and 1000 µg). Among the five concentrations tested, 800 µg shows the apex antioxidant activity [23,24].

Anti diarrheal activity

The *in vivo* anti diarrheal action of *C. roseus* ethanolic leaf extract was tested in the Wistar rats with castor oil as an experimental diarrhea inducing agent in addition to the pretreatment of the extract. Loperamide and atropine sulphate were used as the standard drugs. The anti diarrheal effect of ethanolic extract of *C. roseus* showed the dose dependent inhibition of the castor oil induced diarrhea at the doses of 200 and 500 mg/kg.

The extracts significantly reduced the number and weight of wet fecal pellets with extract treated groups showing lower diarrheal severity than control rats induced diarrhea in Wistar rats. A further doses of 200 and 500 mg/kg of the extract inhibited castor oil induced diarrhea as well as inhibited gastrointestinal propulsion of charcoal meal. This data corroborates the traditional usage of C. roseus in the treatment and management of diarrhea [25,26].

Anthelminthic activity

Helminthes infections causes chronic diseases in human beings and cattle. The evaluation of anthelminthic property of *C. roseus* was carried out by using *Pherithema posthuma* as an experimental model and with Piperazine citrate as the standard reference. Significant anthelminthic activity was observed in the ethanolic extract in the concentration of 250 mg/ml with death time of 46.33 min and the standard drug at 50 mg/ml was found to show the death time of 40.67 min This investigation bears assistance to the ethnomedical claims of *C. roseus* as an anthelminthic plant [27].

Hypotensive activity

Extract obtained from the leaves of the *C. roseus* plant made significant change in hypotensive property. Remarkable antihyperglycemic and hypotensive activity of the leaf extracts (hydroalcoholic or dichloromethane-methanol) have been outlined in laboratory animals [28].

Wound healing property

The wound healing property was carried out using 100 mg / kg/day of *C. roseus* ethanol extract in rats. High rate of wound contraction was observed which significant decrease in epithelization period, marked increase in dry weight and hydroxyproline content of the granulation tissue as compared with the controls. Wound contraction together with increased tensile strength and hydroxyproline content provides evidence to the use of C. roseus in the management of wound healing [29].

Hypolipidimic activity

The leaf juice of *C. roseus* proved Significant anti atherosclerotic as observed by decline in the serum levels of total cholesterol, triglycerides, LDL-c, VLDL c as well as the histology of aorta, liver and kidney [30].

Alzheimer's disease

Vinpocetine has been reported to have a variety of actions to improve brain function and memory, particularly beneficial in the case of Alzheimer's disease. Vinpocetine when subjected to a well-tolerated dose up to 60 mg/d in clinical trials of dementia and stroke proved no significant adverse events [31].

Other activities

Vinpocetine is contra-indicated with any blood thinning agents such as warfarin, aspirin as well as some dietary supplements like ginkgo, vitamin E and garlic.

Safety aspects

The drug used traditionally in prescribed doses may be considered safe. The LD50 for vinblastine in mice is 17 mg/kg iv and for vincristine in mice is 5.2 mg/kg ip.

Dosage

Expressed juice: 10 to 20 ml; Paste: 10 g [32].

Conclusion

Most of the cancer are detected only at the later stage of development. The failure in treatment is attributed to late diagnosis. The complete cure for cancer is possible once the cancer forming cells are identified in the body. In this review, we emphasis the astounding facts of the plant *Catharanthus roseus*. Likewise, there are billions of medicinal anti cancerous plants waiting to be invaded and explored. With rapid advancement in treatment and prolonged research the complete cure for cancer has hope after all and the days of curing cancer are not very far.

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