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CATHRANTHUS ROSEUS: AN ASSESSMENT OF ITS BOTANY, CONVENTIONAL UTILIZATION, PHYTOCHEMISTRY & PHARMACOLOGY

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ABSTRACT:
Ayurveda is the Indian traditional system of medicine which focuses on the medical potential of plants. Catharanthus roseus is one plant recognized well in Ayurveda. It is an evergreen plant first originated from islands of Madagascar. The flowers may vary in colour from pink to purple and leaves are arranged in opposite pairs. It produces nearly 130 alkaloids mainly ajmalicine, vincamine, reserpine, vincristine, vinblastine and raubasin. Vincristine and vinblastine are used for the treatment of various types of cancer such as Hodgkin's disease, breast cancer, skin cancer and lymphoblastic leukemia. It is an endangered species and need to be conserved using techniques like micropropagation. It has many pharmacological properties such as anti-oxidant, anti-microbial, anti-diabetic, wound healing, anti-ulcer, hypotensive, antidiarrhoeal, hypolipidemic and memory enhancement. The purpose of the current study is to document updated data about its traditional uses, isolated bioactive compounds and pharmacological activities reported.

keywords: Catharanthus roseus, phytochemicals, vincristine, vinblastine.

INTRODUCTION:

Therapeutic plants have a long history of utilization in customary medication. Ethno-herbal data on therapeutic plants and their utilization by indigenous societies is valuable in the preservation of conventional societies, biodiversity, network medicinal services and medication advancement. Catharanthus roseus. (G.) Don, is a significant therapeutic plant having a place with the Apocynaceae family; this plant is a dicotyledonous angiosperm and integrates two terpene indole alkaloids: vinblastine and vincristine that are utilized to battle disease [1]

Vinca alkaloids are a material of a class of natural mixes comprised of carbon, hydrogen, nitrogen and oxygen that is regularly gotten from plants is named alkaloid. Numerous alkaloids with having harmful qualities have physiological impacts excessively that make them helpful as medicines [2]

Medicinal plants have a long history of usage in traditional medicine. Ethno-botanical information on medicinal plants and their usage by indigenous cultures is useful in the conservation of traditional cultures, biodiversity, community health care and drug development. Catharanthus roseus, the plant contains about 130 alkaloids of the indole group out of which 25 are dimeric in nature. Two dimeric alkaloids vinblastine and vincristine mainly present in the aerial parts, that are

used to fight cancer. In the British West Indies, it has been used to treat diabetic ulcer and, in the Philippines, has been reported as being an effective oral hypoglycemic agent.[3]
Cathranthus roseas used in the treatment of human neoplasma. 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. More recently, Chopra et al. have reported that the total alkaloids possess a limited antibacterial activity as well as a significant and sustained hypotensive action. The hypoglycemic and antibacterial activities have not been confirmed, although one of the alkaloids isolated from this plant, ajmalicine, has been reported to possess transient depressor action on arterial blood pressure Periwinkle" or Catharanthus roseus, commonly known as "Nayantara" or "Sadabahar", the word Catharanthus derives from the Greek language meaning "pure flower." While, roseus means red, rose or rosy.[4]

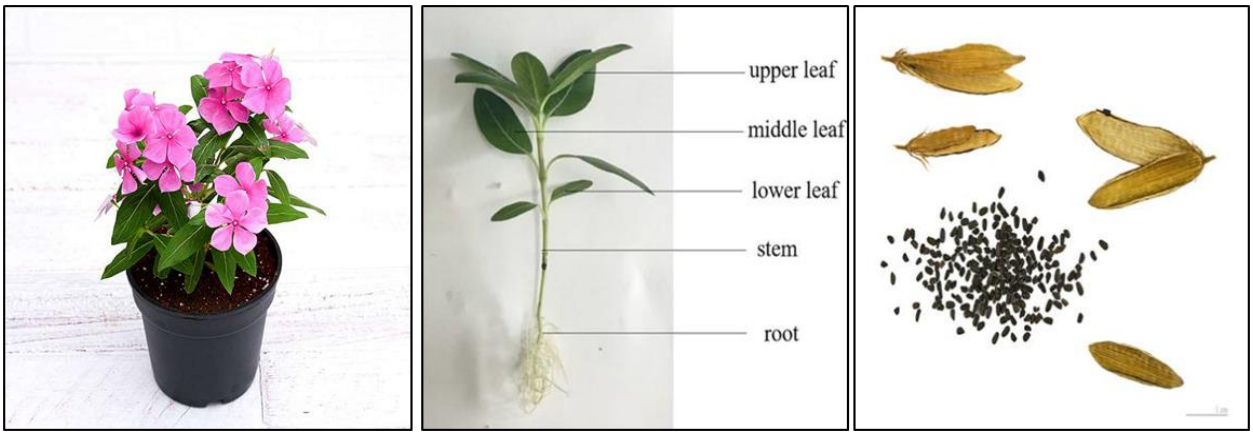

Figure-1; Cathranthus roseus (Annual vinca,Madagascar Periwinkle;

Vernacular names:
English: cayenne jasmine, old maid, periwinkle
Hindi : sada bahar, sadabahar
Kannada : batla hoo, bili kaasi kanigalu, ganeshana hoo, kempu kaasi kanigalu
Malayalam : banappuvu, nityakalyani, savanari, usamalari
Marathi : sadaphool, sadaphul, sadaphuli
Sanskrit : nityakalyani, rasna, sadampuspa, sadapushpi
Tamil : cutkattu malli, cutukattu malli, cutukattuppu
Telugu : billaganneru
Gujarati : Barmasi
Bengali : noyontar
Scientific classification [5]
Botanical Name(s): Vinca Rosea (Catharanthus roseus)
Family Name: Apocynaceae
Kingdom: Plantae
Division: Magnoliophyta (Flowering plants)
Class: Magnoliopsida (Dicotyledons)
Order: Gentianales
Family: Apocynaceae
Genus: Catharanthus
Species: C. roseus

Potentially Active Chemical Constituents:
In excess of 400 alkaloids are available in the plant, which are utilized as pharmaceuticals, agrochemicals, flavor and aroma, fixings, food and specialists researching its therapeutic properties

found that it contained a gathering of alkaloids that, however amazingly harmful, had expected utilizations in disease treatment. Plants can blend a wide assortment of synthetic aggravates that are utilized to perform significant natural capacities, and to protect against assault from predators, for example, creepy crawlies, parasites and herbivorous well evolved creatures. C. roseus force's starch, flavinoid, saponin and alkaloids. Alkaloids are the most possibly dynaded substances and pesticides. The alkaloids like actineo plastidemeric, Vinblastine, Vincristine, Vindesine, Vindeline Tabersonine and so on are primarily present in airborne parts though ajmalicine, vinceine, vincamine, raubasin, reserpine, catharanthine and so on are available in roots and basal stem. Rosindin is an anthocyanin color found in the bloom of C. roseus [6].

Botanical Description:

It is an herbaceous plant on 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 withma purple "eye" in their centres. Erect or accumbent suffrage, 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 fertilizer 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.

Fertilizing: 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 [7,8 ,9,].

Geographical Distribution:

Catharanthus roseus is originated from the Indian OceanIsland 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 .

Table: 1: Traditional Medicinal Uses of Catharanthus roseus in various developed and developing countries.[10-25]

Countries	Uses
Australia	Hot water extract of dried leaves is taken orally for menorrhagia, diabetes, and extract of root bark is taken orally as febrifuge.
Brazil	The hot water e9xtract of dried whole plant is taken orally by a human for diabetes mellitus.
China	Hot water extract of the areal parts is taken orally as a menstrual regulator.
Cook-Island	Decoction of dried leves used orally to treat Diabetes, Hypertension and Cancer.
Dominica	Hot water extract of leaves is taken orally by pregnant women to combat primary inertia in childbirth and the boiled leaves are used to treat diabetes.
England	Hot water extract of dried whole plant is taken orally for the curing of diabetes.
Europe	Decoction of dried leaves is taken orally fir Diabetes mellitus.
India	The hot water extract of dried entire plant is taken orally by human for cancer. Hot water extract of dried leaves arouses orally to Hodgkin`s disease. The root the extract is taken orally for menorrhagia.
Mexico	Infusion of whole plant is taken orally for stomach problem.
Malaysia	Hot water extract of dried leaves is taken orally for Diabetes.
Kenya	Hot water extract of dried leaves is taken orally for diabetes.
Pakistan	Hot water extract of dried ovules is utilized orally for diabetes.

PHARMACOLOGICAL ACTIVITIES:

Antioxidant activity:

In the last years, oxidative stress-related diseases/disorders have gained a special attention. Metabolic, neurodegenerative, cardiovascular, mitochondrial diseases and even cancer, are among the most frequent [26] &[27].Numerous studies have been investigating the underlying triggering factors, in order to understand the mechanisms of action of free radicals, as well as to discover effective substances towards preventing and even reversing the occurrence of oxidative damages [28] & [29]. Antioxidants, both from natural and synthetic sources, have proved to be highly effective to control the magnitude of free radicals production, to prevent its undesirable effects, as well as to support the organism's antioxidant and detoxifying mechanisms [30], [31] & [32]. Phenolic compounds have shown promising antioxidant properties, with its potentia being directly related to the type of solvent used in the extraction, but also with plant origin, growing conditions, harvesting time, and storage conditions [33] & [34]. The study of the antioxidant potential of phenolic extracts derived from plant species is one of the hot topics among the scientific community; however, in vitro studies are the most common [35], [36] & [37].

Antihelminthic activity:

Helminthes infections are the chronic illnesses affecting human beings and cattle. Catharanthus roseus was found to be used from the traditional period as an anthelminthic agent. The anthelminthic property of Catharanthus roseus has been evaluated by using Pherithema posthuma as an experimental model and with Piperazine citrate as the standard reference. The ethanolic extract of the concentration of 250 mg/ml was found to show the significant anthelminthic activity with death time of 46.33 min whereas the standard drug at 50 mg/ml was found to show the death time of 40.67 min This investigation supported the ethnomedical claims of Catharanthus roseus as an anthelminthic plant[38]. Helminthes contaminations causes constant infections in individuals and

steers. The assessment of anthelminthic property of C. roseus was completed by utilizing Pherithema posthuma as an exploratory model and with Piperazine citrate as the standard reference. Critical anthelminthic action was seen in the ethanolic separate in the convergence of 250 mg/ml with death season of 46.33 min and the standard medication at 50 mg/ml was found to show the passing season of 40.67 min This examination bears help to the ethnomedical cases of C. roseus as an anthelminthic plant [39].

Anti hyperglycemic effect:

The effect of the daily oral administration of Catharanthus roseus (CR) leaf dichloromethane: methanol (1:1) extracts (500 mg/ body weight) for 20 days was tested on the blood glucose and hepatic enzymes in the normal and Alloxan induced diabetic rats. The extract showed significant increase in the body weight and decrease in the blood glucose, urea, cholesterol levels of the test animals. The activity of the hepatic enzymes such as hexokinase was increased whereas glucose 6-phosphatase and fructose 1, 6- bisphosphatase were found to be decreased significantly [40].

Anti-cancer activity:

C. roseus was found to show the noteworthy anticancer movement against various cell types in vitro condition and particularly most prominent action was found against the multidrug safe tumor types. Vinca alkaloids likewise called as mitotic axle harms, they restrain get together of the axle structures from microtubules, there by hinderingmitosis in cell cycle. Vinca alkaloids subsequently effectively keep disease cells from partitioning. Distinctive Vinca alkaloids have their own special properties [41]. Vinca alkaloids square cells in mitosis since they are cell cycle explicit specialists. The vinca alkaloids tie explicitly to btubulin and obstruct its capacity to polymerize with a-tubulin into microtubules. Without a flawless mitotic axle, copied chromosomes can't adjust along the division plate and cell division is captured in metaphase. Cells obstructed in mitosis go through changes normal for apoptosis. They are additionally utilized for therapy of leukemias, lymphomas, and testicular disease (Retna et al., 2013) [42]. The anticancer alkaloids Vinblastine and Vincristine are derived from stem and leaf of Catharanthus roseus. These alkaloids have growth inhibition effect to some human tumors. Vinblastine is used experimentally for treatment of neoplasmas and is recommended for Hodgkins disease, chorio carcinoma. Vincristine another alkaloids is used for leukemia in children. Different percentage of the methanolic crude extracts of Catharanthus was found to show the significant anticancer activity against numerous cell types in the in vitro condition and especially greatest activity was found against the multidrug resistant tumor types. Vinblastine is sold as Velban or Vincristine as oncovin [43,44]

Anti-diabetic activity:

The ethanolic extracts of the leaves and flower of C. roseus showed a dose dependent lowering of blood sugar in comparable to the standard drug. Lowering of blood sugar in comparable to the standard drug glibenclamide.[45]. The Hypoglycemic effect has appeared due to the result of the increase glucose utilization in the liver. The aqueous extract was found to lower the blood glucose of about 20% in diabetic rats when compared to that of the dichloromethane and methanol extracts which lowered the blood glucose level to 49-58%. The hypoglycemic effect has appeared due to the result of the increased glucose utilization in the liver.[46] The hypoglycemic activity of alkaloids isolated from C. roseus have been studied pharmacologically and a remedy derived from the plant has been marketed under the propritery name Vinculin as a treatment for diabetes [47,48]

Anti-microbial activity:

C. roseus has been found to be a significant restorative plant for the making of the novel pharmaceuticals as the greater part of the bacterial microorganisms were improving obstruction against a considerable lot of the accessible enemy of microbial medications. Plants have been supported to be important regular assets for the dynamic chemotherapeutic operators and recommend a wide range of activity with the more prominent accentuation on the preventive

activity [49]. It is exhibited that freak leaf extricates had great antibacterial potential against S. aureus, S. citreus, and E. coli and P. aeruginosa microscopic organisms while B. subtilis was notinfluenced. The vacillation in antibacterial movement among freak and control plant leaves may be expected to the genomic changes, stirred by the mutagen correspondingly affecting the combination and level of bio-dynamic mixes like vincristine, Vinblastine, vindoline in tissue, which may be commitment for antibacterial property of periwinkle leaves as additionally detailed before [50]

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 [51]. The compound vinpocetine has remarkable action on Alzheimer's disease. Scientific studies reported that vinpocetine will improve our memory and brain functions [52,53]. The required amount of vinpocetine for the treatment is 60mg/d for stroke and dementia [54].

Anti-ulcer property :
Vincamine and Vindoline alkaloids of the plant showed antiulcer property. The alkaloid vincamine, present in the plant leaves shows cerebrovasodilatory and neuroprotective activity. The plant leaves proved for anti-ulcer activity against experimentally induced gastric damage in rats [55]

Hypotensive property :
Extract of leaves of the plant made significant change in hypotensive. The leaves have been known to contain 150 useful alkaloids among other pharmacologically active compounds. Significant anti hyperglycemic and hypotensive activity of the leaf extracts (hydroalcoholic or dichloromethane-methanol) have been reported in laboratory animals [56]

Anti-diarrheal property:
The anti-diarrheal activity of the plant ethanolic leaf extracts as tested in the wistar rats with castor oil as an experimental diarrhea inducing agent in addition to the pretreatment of the extract. The anti-diarrheal effect of ethanolic extracts C. roseus showed the dose dependant inhibition of the castor oil induced diarrhea [57]

Wound healing property:
treated with 100 mg /kg/day of the Catharanthus roseus ethanol extract had high rate of wound contraction significantly decreased epithelization period, significant increase in dry weight and hydroxyproline content of the granulation tissue when compared with the controls. Wound contraction together with increased tensile strength and hydroxyproline content support the use of C. roseus in the management of wound healing [58]

Memory enhancement activity:
Vinpocetine has been reported to have a variety of actions that would hypothetically be beneficial in Alzheimer's disease (AD). The only study investigating this agent in a well-defined cohort of AD patients found no benefit. Metaanalysis of older studies of vinpocetine in poorly-defined dementia populations concluded that there is insufficient evidence to support its clinical use at this time. Vinpocetine has been well tolerated at doses up to 60 mg/d in clinical trials of dementia and stroke, and no significant adverse events [59]

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 [60].

Conclusion:
Current progress in pharmacological studies and traditional used of C. roseus have proved the significant medicinal properties of the plant, which continuously being utilized to cure various diseases. Enormous number of phytochemicals especially alkaloids have been identified with their medicinal properties such as anti-cancer, anti-diabetic, anti-helminthic, anti-malarial, antimicrobial and so on. The commercial production of alkaloids containing in this plant need to be urged since most monomers were successfully identified in the culture media with intense yield. A thorough research need to be done to optimized the cultural conditions at various levels and consider the synthesis of the novel life-saving drug with a powerful combination of existing bioactive compounds from natural resource.

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Conflict of interest
The authors declare no conflict of interest.

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Ethical approvals
This study does not involve experiments on animals or human subjects

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