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NATURAL ORIGIN OF ANTICANCER AGENTS: A REVIEW ON *CATHARANTHUS ROSEUS* AND ITS VINCA ALKALOIDS

Dr. Janavi G.*[1], Dr. Joeann Marylin Wilson[2], Dr. Shrusti A. C.[2], Dr. Dezney Remica Fernandes[2]

[1,2]Pharm D, Department of Pharmacy Practice, Krupanidhi College of Pharmacy, Rajiv Gandhi university of health sciences, Carmelaram- 560035, Karnataka, India.

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***Corresponding Author**

Dr. Janavi G.

Pharm D, Department of Pharmacy Practice, Krupanidhi College of Pharmacy, Rajiv Gandhi university of health sciences, Carmelaram-560035, Karnataka, India.

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ABSTRACT

India has a vast biodiversity of medicinal plants that have yet to be fully studied. Medicinal plants have long been used in traditional medicine. Cancer, the most dreaded six-letter word harming humanity in the worst imaginable manner. Despite significant advancements in recent decades, cancer treatment remains a mystery. Nature maintains equilibrium, and plants offer promise anti-cancer benefits. *Catharanthus roseus* alkaloids were proven to be effective in cancer chemotherapy. This plant is well-known in Ayurvedic medicine. It is a vital native, evergreen, legendary medicinal herb from Madagascar's Indian Ocean islands, belonging to the Apocynaceae family. The plant possesses a wide range of biological properties, including antibacterial, anticancer, antioxidant, antihyperglycemic, antidiabetic, and wound healing. The plant kingdom is still regarded as the primary source of medicine, with demonstrated efficacy in treating a variety of ailments such as diabetes, hypertension, asthma, painful ulcers, malaria, Hodgkin disease, leukaemia, and dysentery. Many ancient treatments were delivered without knowing the core mechanism; yet, their usefulness could be shown further with the application of modern technologies and instruments. This well-organised review shed light on the agrotechnological, biological, alkaloid toxicity, and pharmacological characteristics of Madagascar periwinkle, as well as potential pathways and modes of action.

KEYWORDS: *Catharanthus Roseus*; Vinca toxicity; Pharmacological Activity; Vinca alkaloids.

1. INTRODUCTION

Ayurveda is an Indian traditional practice of medicine that emphasises the medicinal properties of plants. *Catharanthus roseus (C. roseus)*, sometimes known as Madagascar periwinkle (MP), is a natural and indigenous to Madagascar.[1] *C. roseus* comes from the Greek word for pure flower, whilst roseus indicates red or blushing.[2] *C. roseus* is derived from Greek, meaning pure flower. Roseus means red, rose, or rosy.[3] Medicinal plants have played an important role in global health care.[4] Today, therapeutic plants are available in a variety of colours, including white, hot pink, and mauve, as well as the classic Pinkas.[5] Ethno-herbal data on therapeutic plants and their use by indigenous people is important for the preservation of traditional societies, biodiversity, network medicinal services, and medication development.[6] Periwinkle is also known as Nayantara or Sadabahar. Tropical countries are native to Madagascar and have expanded throughout the northern and southern highlands of India.[7] It is a ubiquitous ornamental plant in gardens and homes around the world, particularly in warmer areas.

Vinca alkaloids are the most widely used plant alkaloids for disease treatment.[8] Vinca plant includes the first generation (vincristine, vinblastine), the second generation (vindesine, vinorelbine), and the third generation (vinflunine).[9] Vinca alkaloids are a type of cell cycle phase M specific antitublin drug. Vinflunine was the first alkaloid utilised as an anticancer treatment, and the most recent fluorinated version is used to treat bladder cancer.[10] (G.) Don is a dicotyledonous angiosperm that contains two terpene indole alkaloids: vincristine and vinblastine, which are used to treat disease.[11] The hypoglycaemic and antibacterial properties have not been confirmed, while one of the alkaloids in ajmalicine has been shown to have transitory depressor activity on blood vessel pulse.[12] It contains secondary metabolites, including alkaloids, and has 70 known pharmacological characteristics, including oleanolic acid, cholinergic acid, and loganic acid.[13]

Regional herbal medicine has used all parts of the plant, including the dried root, leaves, stalks, and flowers.[14] Plant extracts contain important chemicals such as tannins, terpenoids, flavonoids, and alkaloids. The extracted plant leaves and flowers of oil have antibacterial and anti-yeast properties.[15]

One method for reducing the toxicity of microbial infections is to use plant extracts rich in antibacterial chemicals. *C. roseus* contains antifungal compounds such as diterpenes, which can inhibit C. albican by damaging the cell membrane via a lipoplic mode of action.[16] It includes a substantial number of volatile and phenolic chemicals, such as caffeoylquinic acids and flavanol glycosides, which function as antioxidants and contribute to the plant's defence system.[17] Antioxidants protect against free radicals, delaying the onset of CVD, cancer, and IBD.[1,18] It is an endangered species that needs to be protected by procedures like as micropropagation. CrTPT2, an ABC transporter that enhances catharanthine transit and accumulation on the leaf epidermal surface, was recently discovered.[13] Gene overexpression and RNAi-mediated silencing are commonly utilised in the investigation of metabolic pathways in plants, including *C. roseus*.[19] Medicinal plants are regarded as an effective and safe alternative to synthetic antibiotics. *C. roseus* has numerous medical and therapeutic benefits, making it a promising herb for future research.[20]

2. METHODOLOGY

This review gathered comprehensive information about the plant from peer-reviewed scholarly articles and online databases. Resources include Scopus, Pub Med, Med Line, Springer Link, Google Scholar, Research Gate, and Science Direct. The online search terms used were *Catharanthus roseus*, Apocynacea family, biology, distribution, diversity, ethnobotanical importance, pharmacological properties, bioactive constituents, antidiabetic, antioxidant, antimicrobial, adverse, and anticancer activities. *C. roseus* has been used for medicinal purposes in acute and chronic disorders for a long time, indicating its therapeutic safety for clinical usage.

3. HISTORY OF VINCA ROSEA

C. roseus is one of the few pharmaceutical plants with a lengthy history of therapeutic usage, reaching back to Mesopotamian folklore circa 2600 BCE and still playing an important role in herbal and traditional medicine for a variety of illnesses. In 1759, Carl von Linneanus, a Swedish naturalist, was given the name *Vinca rosea*, the first of his genus. In 1828, German botanist Heinrich Gottlieb Ludwig Reichenbach proposed the genus Lochnera. Medicinal plants provide therapeutic qualities for human illnesses (Krishnaraju et al., 2005).[21] In the 1950s, Canadian scientists Robert Noble and Charles Beer discovered vinca alkaloids for the first time. Vinflunine, a novel synthetic vinca alkaloid introduced in 2008, is currently licensed for medicinal use in Europe.[51]

In 1910, Peckolt recorded how the plant's leaves were utilised in Brazil to treat haemorrhage, scurvy, toothache, and wound healing.[7,21] In the 1950s, the US National Cancer Institute saw the potential of natural compounds as anticancer agents.[22] Since 1950, vinca alkaloids have been used in cancer treatment for both their toxic and therapeutic properties.[19] *C. roseus* is a genus that includes eight species, seven of which are native to Madagascar, and one other, pusillus. Zárate and Verpoorte discovered that *C. roseus* contains several terpenoids with antifungal effects.[23] The National Cancer Council of Malaysia uses the *C. roseus* dogo as a symbol of hope for cancer patients.[24] In the British West Indies, it has been used to treat diabetic ulcers, and in the Philippines, it is regarded as a successful oral hypoglycaemic agent. Chopra et al. found that the whole alkaloids have minimal antibacterial activity but exhibit considerable and prolonged hypotensive effects.[25]

4. MORPHOLOGY

The plant was 1m tall and commercially grown in India, Australia, Africa, and southern Europe. The blossoms range in colour from pink to purple, and the leaves are arranged in opposing pairs. (2) It blooms year-round with pink, purple, or white flowers (Hogan, 2003). The leaves are oval to oblong, 2.5-9.0 cm long, and 1-3.5 cm broad. They are glossy green and hairless, with a pale midrib and a short petiole of around 1- 1.8 centimetres long. C. roseus is classified into two varieties based on bloom colour: Rosea (pink) and Alba (white). The fruit is a pair of follicles about 2-4 cm long and 3 mm wide.[3,5,20,26]

HABIT: A perennial herb.
STEM: Erect, cylindrical, branched, solid, reddish green, glabrous.
ROOT: Tap root; rarely branches.
LEAF: Cauline, simple, opposite, decussate, petiolate, extipulate, entire, mucronate apex, unicostate, reticulate veration.
INFLOROSENCE: Cymose, with flowers grouped in axxillary pairs.
FLOWER: Pedicellate, bractate, hermaphrodite, actinomorphic, complete, pink, hypogynous.
CALYX [K]: 5, polysepalous, glandular, green, inferior, quincunical, aestivate.
COROLLA [C] 5, gampetalous framed corolla tube, hairy throat producing a corona, distorted and aestivate.
ANDROCIUM [A]: 5, free, epipetalous, alternate to petals, nearly sessile, anthers dorsified, yellowish.
GYNOECIUM (G): The flower has two carpells that are bicarpellary and syncarpous. The carpels are connected above the style and stigma, the ovaries are absent, nectar glands are present, the flower is unilocular, and there is marginal plaventation.
FRUIT: consists of two elongated follicles.[26–28]
SEEDS: 1-2 mm, are numerous and grooved on one side.

4.1 CLIMATE, SOIL AND PROPAGATION

The plant demands regular moisture, but avoid over watering. The plant produces seeds between 12 and 16 weeks. Before the final frost. Plants reproduce naturally by seeds, which require complete darkness to germinate. The plants were cut in late summer and developed roots. High fertility soil does not promote flowering, and flowers typically drop off after blooming.[29] Flowering occurs throughout the year in equatorial conditions and from spring to late fall in warm temperate areas.

SOIL: Full-sun, well-drained soil is recommended. Flowering requires bright light, including three to four hours of direct sunlight per day.
TEMPERATURE: Normal room temperatures are appropriate at all times. It cannot tolerate temperatures below 10°C (50°F). Water the potting mixture thoroughly, but avoid submerging the pot in water.
FEEDING: Once flowering starts, apply liquid fertiliser every two weeks. Plants are not tolerant of excessive fertiliser.
IRRIGATION: They require frequent moisture, but avoid overhead watering. It requires moderate watering during the growing season but is drought-resistant once established. They will recover with a decent watering.
FERTILIZATION: The plants are not heavy breeders. Apply liquid fertiliser on a biweekly or monthly basis as needed. Excessive fertilisation might result in more foliage than blossoms.[5,8,28,29]

5. GEOGRAPHICAL DISTRIBUTION

C. roseus is indigenous to the Indian Ocean Island of Madagascar. This decorative plant has gained popularity in tropical and subtropical climates worldwide. It is commercially grown in Spain, the US, China, Africa, Australia, India, and Southern Europe for therapeutic purposes. This plant's medications are widely used in the USA, Hungary, West Germany, Italy, the Netherlands, and the United Kingdom. (Anonymous, 2011; Lata, 2007).[20] The plant is currently widespread in tropical and subtropical locations, including the Southern United States.[25,28] Germany, Italy, the Netherlands, and the United Kingdom.[26] MP is a drought and salinity-tolerant plant that thrives in several settings, including sandy soils, shrublands, grasslands, and inland rivers. Its resilience makes it suitable for a variety of environments, including banks, savanna dunes, dry wastelands, homes, roadsides, and limestone rocks. It thrives at altitudes ranging from 0 to 900 meters. MP thrives on soils with a pH range of 5.5-6.5, can tolerate up to 2000 ppm of salt, and is resistant to heat and drought. This plant thrives in dry, frost-free, humid settings with adequate rainfall. It prefers full sun or partial shade and well-drained soil. This plant produces blooms and fruits throughout the year in warm areas. MP cannot resist excessive water, damp soils, or cool springs.[11,26]

Fig 1: *Catharanthus roseus.*

6. PHARMACOGNOSTICAL STUDIES

Macroscopical features include opposite, simple, petiolate leaves; long, glabrous or softly pubescent petioles; lamina elliptic, obovate, or oblong-elliptic, obtuse or retuse, mucronulate, base cuneate or subcuneate, frequently oblique, slightly decurrent; and an entire margin that may or may not be hairy, membranous, or barely noticeable. Lower surface pubescent, dark brilliant green, upper surface pubescent or glabrescent.

6.1 Microscopic properties[30]

The leaf is dorsiventral. The top epidermal cells have somewhat curved or sinuous walls, while the lower epidermal cells have sinous walls. 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.

6.2 Powder characteristics

It displays patches of lower epidermis with sinuous anticlinal walls and the same types of stomata, as well as pieces of upper epidermis in surface view with straight anticlinal walls and anomocytic and anisocytic stomata.

6.3 Chemical constituents

Being a major Alkaloids range from 0.74 to 0.82%; vincristine, vinblastine, catharanthamine, and vincoline are significant. Deoxyvinblastine, leurosine, pleurosin, leurocristine, leurosidine, vincolinine, vinacardine, roseadine, vindolicine, rosicine, and other alkaloids are extracted. Vinca alkaloids have physiological effects in addition to their toxic properties, which makes them effective as medications. Every portion of the plant contains alkaloids. The highest is found in the bark of the roots, especially during blossoming. Antineoplastic dimeric alkaloids, such as vinblastine and vincristine in the aerial parts and ajmalicine and serpentine in the roots, are physiologically significant alkaloids. The anthocyanidin pigment rosinidin is present in C. roseus flowers.[25,28]

7. SCIENTIFIC CLASSIFICATION[14,24,30]

Table no 1: Scientific classification of *C. roseus*

Sl.no	Taxonomic Rank	Classification
1.	**Domain**	Eukarya
2.	**Kingdom**	Plantae
3.	**Subkingdom**	Tracheobionta
4.	**Super Division**	Spermatophyta
5.	**Division**	Magnoliophyta
6.	**Class**	Magnoliopsida
7.	**Subclass**	Asteridae
8.	**Superorder**	Gentiananae
9.	**Order**	Gentianales
10.	**Family**	Apocynaceae
11.	**Subfamily**	Rauvolfioideae
12.	**Tribe**	Vinceae
13.	**Genus**	*Catharanthus* G. Don
14.	**Specific Epithet**	*roseus* G. Don

8. VERNACULAR NAMES[22,26]

Table no 2: Local names of *C. roseus*

Sl.no	Language	Local Name(s)
1.	Tamil	Cutkattu malli, Cutukattu malli, Cutukattuppu, Sudukattu mallikai
2.	Telugu	Billaganneru
3.	Kannada	Batla hoo, Bili kaasi kanigalu, Ganeshana hoo, Kempu kassi kanigalu
4.	Bengali	Nayantara
5.	Gujarati	Barmasi
6.	Sanskrit	Ransa, Sadampuspa, Nitya Kalyani
7.	Marathi	Sadaphul, Sadaphuli
8.	Punjabi	Rattan jot
9.	Konkani	Sada Pushpa, Sadapushpa
10.	English	Cayenne jasmine, Bright-eyes, Cape periwinkle, Graveyard plant, Madagascar periwinkle, Old-maid, Rose periwinkle, Rosy periwinkle
11.	Ethiopia	Phlox
12.	Chinese	Chang Chun Hua
13.	Dutch	Roze maagdenpalm, Creole Bigalo
14.	French	Pervenche de Madagascar, Rose amere, Sorcerer's violet
15.	German	Zimmerimmergrün, Creole Kaka poule
16.	Hindi	Sadabahar, Baramassi, Ainskati, Ushamanjari
17.	Indonesian	Tapak dara, Kembang sari cina
18.	Malayalam	Nithyakalyani, Savakkottappacha, Ushamalari, Malay Kemunting cina
19.	Myanmarese	Thin-Baw-Ma-Hnyo
20.	Persian	Gul-e-Farang
21.	Portuguese	Boa-noite, Boa-tarde, Lavadeira, Pervinca-rosa, Vinca-de-gato, Vinca-de-Madagascar, Vina-rosea, Krio Ngyange
22.	Afrikaans	Kanniedood
23.	Spanish	Chatas, Chula, Pervinca de Madagascar, Vinca pervinca, Hierba doncella
24.	Swedish	Rosenskona

9. SYNONYMS OF *VINCA ROSEA*[25,27,31]

a. Ammocallis rosea (L.) Small (1903)
b. Lochnera rosea (L.) Rchb.(1838)
c. Lochnera rosea var. flava Tsiang
d. Pervinca rosea (L.) Moench (1794),
e. Vinca gulielmi-waldemarii Klotzsch
f. Vinca rosea L. (1759) (basionym)
g. Vinca rosea var. albiflora Bertol.
h. Vinca speciosa Salisb.

10. ALKALOIDS AND OTHER SECONDARY METABOLITES

Vinca alkaloids belong to a class of organic compounds known as alkaloids, which are nitrogen-containing secondary metabolites composed primarily of carbon, hydrogen, nitrogen, and oxygen. These compounds are typically derived from plants and occur in various tissues such as leaves, bark, roots, and seeds. The total alkaloid content in Vinca species ranges between 0.74% and 0.82%, with major constituents including vincristine,

vinblastine, catharanthamine, and vincoline.[28] Vinca alkaloids represent one of the oldest classes of plant-derived anticancer agents.[50]

10.1Primary and Secondary Metabolites

Plants produce two main categories of metabolites: primary and secondary.

- Primary metabolites, such as proteins, lipids, and carbohydrates, are essential for fundamental biological processes like photosynthesis, respiration, and growth.
- Secondary metabolites, derived from these primary compounds, include phenolics, terpenes, and nitrogen-containing alkaloids that contribute to the plant's defense, reproduction, and adaptation.[23]

10.2Major Vinca Alkaloid Constituents

C. roseus produces a variety of alkaloids including anhydro vinblastine, vindoline, catharanthine, ajmalicine, and serpentine. Kisakürek and Hesse classified these alkaloids into several subclasses such as vincosan, corynanthean, vallesiachotaman, strychnan, aspidospermatan, plumeran, ibogan, eburnan, and bisindole alkaloids.[20] Vinca alkaloids, originally sourced from Madagascar, have become globally significant pharmaceutical agents. In the plant kingdom, there are nearly one thousand known alkaloids, particularly abundant in dicot families such as Rutaceae, Apocynaceae, Papaveraceae, and Solanaceae.[32]

10.3Pharmacological Importance

Commonly referred to as Sadafuli or Sadabahar, Vinca plants contain antimicrotubular and antimitotic alkaloids that disrupt cell division. Clinically, vinblastine is used in the treatment of Hodgkin's lymphoma, while vincristine is widely used in paediatric Leukemia therapy.[33]

Although the active compounds are extractable from the leaves, the living plant does not contain them in significant amounts. Instead, it produces precursor alkaloids notably vindoline and catharanthine that combine through biosynthetic pathways to form pharmacologically active molecules.[20]

10.4Biosynthetic and Chemical Properties

C. roseus produces over 400 alkaloids, many of which serve diverse applications such as insecticides, flavoring agents, agrochemicals, and medicines.[21] The milky sap of the stem alone contains approximately 70 indole alkaloids[28], and the plant's organs collectively yield about 90 monoterpenoid indole alkaloids.[5] Among these, around 130 oncolytic alkaloids exhibit anticancer activity, including vinblastine, vincristine, ajmalicine, reserpine, flavonoids, and phenolic acids.[5,28]

10.5General Characteristics of Alkaloids

1. Composed of carbon, hydrogen, and nitrogen, usually forming salts with acids.
2. Mostly colourless crystalline substances.
3. Free alkaloids are insoluble in water but soluble in organic solvents such as ether and chloroform.
4. Most alkaloids are laevorotatory, except for conine and papaverine.

10.6Biological Functions of Alkaloids

1. Regulation of growth and development.
2. Nitrogen storage within plant tissues.
3. Acting as pollination aids by attracting insects through coloration or scent.
4. Functioning as chemical deterrents against herbivores and pathogens.[53][19,34]

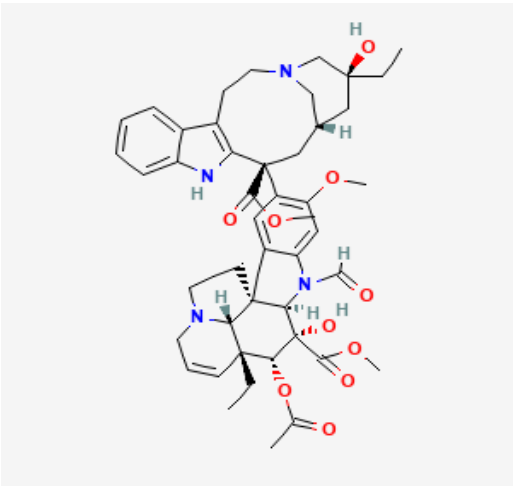

Fig 2: VINBLASTINE

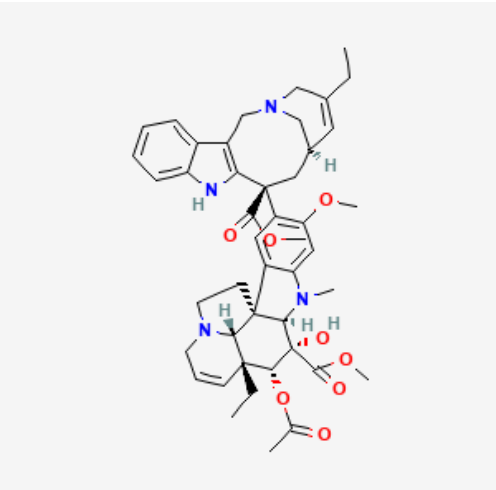

Fig 3: VINORELBINE

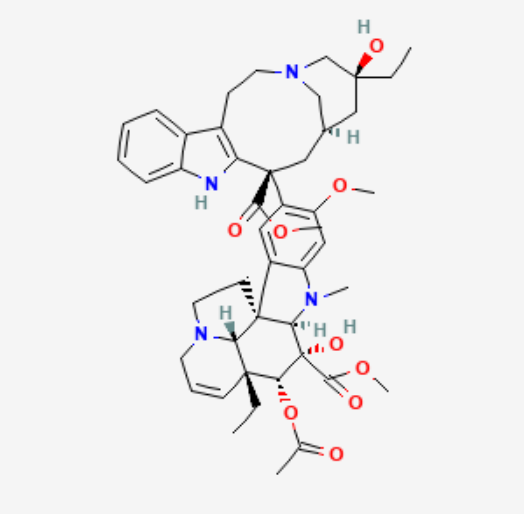

Fig 4: VINCRISTINE

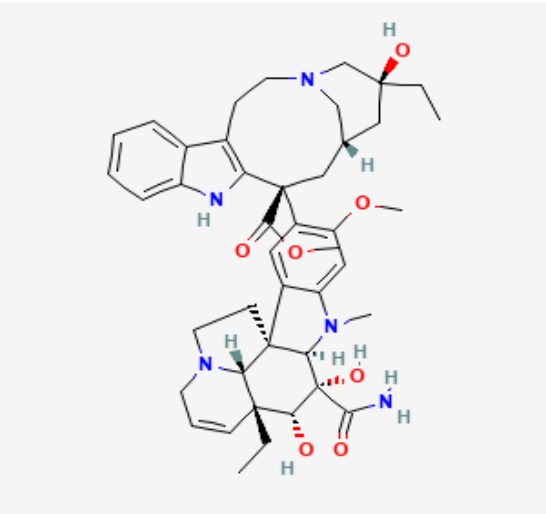

Fig 5: VINDESINE

11. MECHANISM OF ACTION

Alkaloids primarily cause metaphase arrest through their interactions with tubulin and disruption of microtubule function, especially that of the microtubules that make up the mitotic spindle machinery. They can, however, engage in a wide range of other metabolic processes that may or may not be connected to how they affect microtubules. Many of the effects that do not involve microtubule disruption only occur when cells are treated with vinca alkaloids at levels that are clinically insignificant. However, because microtubules are involved in numerous non-mitotic processes, vinca alkaloids and other anti-microtubule drugs also affect malignant and non-malignant cells in the non-mitotic cell cycle. The alkaloids bind to tubulin binding sites that are distinct from those of the taxanes, guanosine-5'-triphosphate, colchicine, and podophyllotoxin.

Vinca alkaloids and other microtubule disrupting agents have the ability to inhibit malignant angiogenesis in vitro. The evidence that is currently available supports the existence of two vinca alkaloid binding sites per mole of tubulin dimer. We can observe approximately 16–17 high-affinity binding sites in each microtubule that are located at the ends of each microtubule. Binding of the vinca alkaloids to these sites disrupts microtubule congregation, but one of the most significant effects of low drug concentrations can cause a "kinetic cap and suppress function. For instance, when combined with antibodies against vascular endothelial growth factor, low doses of VBL significantly increased the antitumor response, even in tumours resistant to the drug's direct cytotoxic effects. Vinca alkaloids inhibit cell proliferation by binding to microtubules, which can cause a mitotic block and apoptosis; VCR and related compounds produce destabilisation of microtubules by binding to tubulin and blocking the polymerisation.[50][26]

12. ACTION AGANIST P-1584

The detection of activity against the P-1584 Leukemia was considered particularly significant, owing to the fact that this tumour system has detected other clinically useful antitumor agents and has been sensitive enough to study structure-activity relationships of active compounds which correlated with the clinical activity. Additionally, VLB has been clinically verified.[35] Vinca leucoblastin: VLB's leukopenic effect in normal rats, which was utilised for its bioassay, was its most notable biological action. Later, it was shown in the Collip and Lilly Laboratories that Additionally, VLB significantly suppressed P-1584 leukaemia. Leurosine: Among the alkaloids examined, leurosine, an isomeric with VLB, has likewise demonstrated a discernible slowdown of the P-1534 leukaemia. It has typically been less consistent and of a lower order of activity than VLB.[35]

13. TRADITIONAL USE OF *CATHARANTHUS ROSEUS*

Historically, the herb has been used to treat a variety of illnesses. For ages, people in Europe utilised it as a traditional treatment for diabetes. This has long been used to treat a number of regional illnesses in both Traditional Chinese treatment (TCM) and Ayurvedic treatment.[23] Significant clinical activity has been observed mostly in the treatment of non-small cell lung cancer, breast cancer, and transitional cell carcinoma of the urothelial tract. Vinflunine has also been evaluated in individuals with first-line advanced breast cancer and TCCU.[50]The infusion of leaves is used to cure rheumatism and menorrhagia.[12] The leaf portion contained about 90 alkaloids, with catharanthine and vindoline being the most prevalent ones. Ethyl-apovincaminate, also known as vinpocetine, is a derivative of vincamine that has been used extensively in medicine for atherosclerotic plaques, blood thinning, vaso-dilating, and memory-enhancing effects.[12,36] One of the best and most effective herbs for treating dermatitis, psoriasis, sores, ringworm, abscesses, eczema, epilepsy, malaria, and heart tonics.

LEAVES: Used to alleviate stomach pains, diabetes mellitus, and as an emetic. The vinca plant's leaves are

used to induce vomiting. Because it increases insulin secretion, it is used to treat diabetes. Young leaves for cramping in the stomach.
ROOT: used to treat diarrhoea and as an antibacterial and antifungal agent. It also possesses antifungal and antibacterial qualities. Haemostatic, vermifuge, purgative, and depurative.[20]
FLOWERS: used to treat asthma and clean adults' eyes. Infants use flower extract as an eye wipe, asthma.[37]

14. FOLK MEDICINAL USES

Periwinkle has numerous traditional and folkloric uses that have been tried and proven and validated by people's beliefs.[5] The paste made from the leaves is a great way to cure wounds and ease the discomfort of wasp stings. It can halt bleeding, accelerating the healing process. Periwinkle is also said to be helpful in relieving fatigue, headaches, and depression.[20]

Table no 3: Medicinal uses of *C. roseus.*

Sl.no	Region	Traditional Use
1.	**India**	Leaf juice used for wasp stings; hot water extract of dried whole plant taken orally for cancer and Hodgkin's disease; root extract used orally for menorrhagia.
2.	**Hawaii**	Boiled herb used as a poultice to stop bleeding.
3.	**China**	Used as a cough remedy, diuretic, and astringent.
4.	**Central & South America**	Used as a homemade cold cure to reduce lung inflammation and congestion.
5.	**France**	Hot water extract of entire plant used as a galactagogue.
6.	**French Guiana**	Hot water extract of entire plant consumed orally as a cholagogue.
7.	**Jamaica**	Hot water extract of dried leaves taken orally for diabetes.
8.	**Kenya**	Hot water extract of dried leaves taken orally for diabetes.
9.	**Mexico**	Infusion of whole plant taken orally for stomach trouble.
10.	**Malaysia**	Hot water extract of dried leaves taken orally for diabetes.
11.	**Mozambique**	Root extract taken orally as a hypotensive and febrifuge; leaf extract used for diabetes and rheumatism.
12.	**North Vietnam**	Hot water extract of aerial parts administered orally to control menstruation.
13.	**Pakistan**	Hot water extract of dried ovules taken orally for diabetes.
14.	**Africa**	Leaves used to treat menorrhagia and rheumatism.
15.	**Mauritius**	Leaf juice used to treat dyspepsia and indigestion.
16.	**Nigeria & West Indies**	Herb used to treat diabetes.[20,26,36]

15. IDENTIFICATION BY TLC:

By using TLC to identify standard and sample, vinblastine is generated in the mobile phase. -Butanol: Acetic acid: 5:1:1 water with a modified Dragondroff's reagent spray. Vinblastine is represented by an Rf value of 0.24 in both the standard and sample solution tracks. The analytical procedure is comparable to TLC identification; however, precoated Silica gel 60 F254 plates are utilised, and the plate is densitometrically scanned at 560 nm following development. The peak area under the curve can be used to determine the percentage of vinblastine.

Quantitative standards.[28]
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%

ECONOMIC VALUES

The global market consumed 5–10 kg of vincristine and vinblastine in 1990, totalling US$4.5–7.5 million in 1991, and it was estimated that the global market was worth US$150–300 million in 2005.[11,14,26]

16. PHARMACOLOGICAL ACTIVITIES

16.1 ANTI OXIDANT PROPERTY

In recent years, diseases and disorders linked to oxidative stress have received special attention. Metabolic, neurological, cardiovascular, mitochondrial, and even cancer diseases are among the most prevalent. It has been demonstrated that both synthetic and natural antioxidants are highly effective in lowering the production of free radicals, limiting their harmful effects, and supporting the body's detoxification and antioxidant systems. The study of the antioxidant potential of phenolic extracts from plant species is one of the most popular topics in the scientific community; nonetheless, in vitro research is the most common. *C. roseus* contains significant amounts of volatile and phenolic compounds that are known to have antioxidant properties, such as flavonol glycosides and caffeoylquinic acids.

By functioning as an antioxidant against Reactive Oxygen Species (ROS), which are hazardous because they are created by regular cell aerobic respiration, it

plays a critical role in the body's defence mechanism. The petals, seeds, and other parts of *C. roseus* have antioxidant properties.[12] Chronic conditions like cancer, atherosclerosis, inflammatory bowel syndrome, cardiovascular disease (CVD), and Alzheimer's disease are regularly delayed by these antioxidants.[38] Bozin and associates, 2006 The plant's vindolicine showed the strongest antioxidant capability in ORAC and DPPH assays. Furthermore, it was shown that *C. roseus* was a good source of antioxidants, both enzymatic and non-enzymatic. (Jaleel and others, 2006; 2007).[20] It has several applications in the culinary, cosmetics, and pharmaceutical industries. In addition to their antioxidant activity, these compounds have antiallergic, anti-inflammatory, antibacterial, anti-thrombotic, cardioprotective, and vasodilatory qualities. The ethanolic extract of the roots of periwinkle varieties showed an adequate scavenging effect throughout the assay in a concentration-dependent manner, despite the fact that *C. roseus* was found to have higher antioxidant activity than *C. Alba*.[12,39]

16.2 ANTI CANCER ACTIVITY

Vinblastine and vincristine are anticancer alkaloids derived from the stem and leaves of *C. roseus*. Vinblastine is used in experiments to treat neoplasms and is recommended for Hodgkin's disease and choriocarcinoma. Vincristine is another alkaloid used to treat leukaemia in children. Vinblastine is sold under the brand name Velban, and vincristine under the brand name Oncovin.[12] It was shown that different percentages of Catharanthus methanolic crude extracts demonstrated strong anticancer activity against a range of cell types in vitro (Ueda et al., 2002)[11], with multidrug resistant tumour forms showing the strongest activity (Wang et al., 2004).[20] Vinca alkaloids, sometimes referred to as mitotic spindle poisons, effectively inhibit the growth of cancer cells by blocking the formation of spindle forms from microtubules, which stops the cell cycle's mitosis. Every Vinca alkaloid has unique characteristics of its own.[28] In vitro, it was discovered that C. roseus demonstrated significant anticancer activity against a variety of cell types, with the multidrug-safe tumour forms showing the strongest effect.[8]

16.3 ANTI DIABETIC ACTIVITY

In a streptozotocin-induced diabetic rat model, the dichloromethane: methanol extract (1:1) of the leaves and twigs of the *C. roseus* plant was administered orally for seven and fifteen days at a concentration of 500 mg/kg to determine hypoglycemic activity. Hypoglycemic activity of 48.6 and 57.6% was observed, and further treatment for 30 days provided complete protection against the STZ challenge (75 mg/kg/i.p.[28] Ethanolic extracts of *C. roseus* leaves and flowers showed a dose-dependent drop in blood sugar when compared to the popular drug glibenclamide. The aqueous extract was found to lower blood glucose levels in diabetic rats to about 20%, whilst the dichloromethane and methanol extracts reduced blood glucose levels to 49–58%. The hypoglycemic effects of alkaloids derived from *C. roseus* have been studied pharmacologically, and Vinculin, a plant-based drug, is marketed as a diabetes treatment. Additionally, vindolinine, vindolicine, and vindolidine had strong inhibitory effect against protein tyrosine phosphatase-1B (PTP-1B), indicating its potential as a treatment for type 2 diabetes.[20]The popular medication glibenclamide is about equal to the reduction of glucose. Hypoglycaemic activity has risen as a result of the liver consuming more glucose(8,28). Numerous traditional medicinal plants are reported to have hypoglycemic properties, such as Allium sativum (garlic), Azadirachta indica (neem), Vinca rosea (Nayantara), Trigonella foenum (fenugreek), Momordica charantia (bitter ground), and Ocimum santum (tulsi). Some of these are less effective at lowering blood glucose levels in people with severe diabetes.[35]

16.4 ANTI MICROBIAL AND ANTI-ULCER ACTIVITY

C. roseus has been discovered to be a helpful medicinal plant for the creation of novel pharmaceuticals because the majority of bacterial infections were growing more resistant to many of the known antimicrobial drugs. Plants have been shown to be significant natural sources of active chemotherapeutic medications, indicating a broad range of activity with an emphasis on prevention.[28] Few studies, however, demonstrate the antiviral and antibacterial capabilities of a single alkaloid produced from *C. roseus*. According to Özçelik et al., yohimbine, which is found naturally in C. roseus and Pausinystalia yohimbine, has an antiviral effect on the type 1 herpes simplex virus with a cytopathogenic effect at 0.8 µg/mL.[52] Crude extracts from different plant sections were tested for their antibacterial activities. The antibacterial qualities of the plant's leaf extract were tested against germs like *Pseudomonas aeruginosa*, *Salmonella typhimurium, and Staphylococcus aureus*, and it was used as a prophylactic strategy to treat a variety of ailments. (Prajakta and Ghosh, 2010).[12,19] Because the mutagen causes genomic changes that impact the quantity and combination of bio-dynamic mixes like vincristine, vinblastine, and vindoline in tissue, the variation in antibacterial movement between freak and control plant leaves may be expected. This could be a commitment to the previously reported antibacterial properties of periwinkle leaves.[8]

The alkaloids vincamine and vindoline from the plant showed antiulcer effects.[1] The leaves of the *C. roseus* plant have been demonstrated to have anti-ulcer qualities in test animals with ulcers, according to Babulova et al. (2003).[10]

16.5 HYPOTENSIVE AND ANTI DIARRHOEAL PROPERTY

Blood pressure was considerably lowered by the plant's leaf extract. The leaf extracts (hydroalcoholic or dichloromethane-methanol) have demonstrated notable

antihyperglycemic and hypotensive effects in experimental animals. Alkaloids are among the chemicals that have pharmacological activity. Leaf extracts (hydroalcoholic or dichloromethane-methanol) have demonstrated notable antihyperglycemic and hypotensive effects in laboratory animals (Pillay et al., 1959).[20] Using castor oil as an experimental diarrhoea-inducing agent in addition to the extract's pretreatment, the in vivo anti-diarrheal effect of *C. roseus* ethanolic leaf extract was evaluated in Wistar rats; the standard medications were loperamide and atropine sulphate. At dosages of 200 and 500 mg/kg, the ethanolic extract of *C. roseus* showed a dose-dependent suppression of the diarrhoea caused by castor oil.[40,41]

16.6 HYPOLIPIDIMIC AND WOUND HEALING EFFECT

By reducing serum levels of total cholesterol, triglycerides, LDL-c, and VLDL, vinca leaf juice has an anti-atherosclerotic action. As a result, vinca leaf juice contains a flavonoid that resembles vinpocetine and has antioxidant properties.[27,37] According to a study, the leaf juice of Catharanthus roseus (Linn.) dramatically lowered serum levels of triglycerides, LDL-c, VLDL, total cholesterol, and the histology of the kidney, liver, and aorta.

To see if *C. roseus* ethanol extract could heal wounds, rats were given 100 mg/kg/day.[8] In comparison to the controls, a high rate of wound contraction was noted, along with a notable increase in the dry weight and hydroxyproline content of the granulation tissue and a considerable decrease in the epithelization period.[28] G. Donn the application of *C. roseus* in the treatment of wound healing is supported by wound contraction as well as enhanced tensile strength and hydroxyproline content.[12]

16.7 ANTIHELMINTHIC PROPERTY

Both humans and cattle can develop chronic illnesses as a result of Helminthes infections.(28)The chronic sickness that affects both humans and cattle is helminthes infections. It was discovered that *C. roseus* has been utilised as an anti-helminthic agent since ancient times. Using Pherithema postuma as an experimental model and piperazine citrate as the standard reference, the anti-helminthic properties of *C. roseus* have been assessed. The anthelminthic property of *C. roseus* has been assessed using Piperazine citrate as the standard reference and Pherithema posthuma as an experimental model.[20] The ethnomedical claims of *C. roseus* as an anthelminthic herb are supported by our work.[28]

16.8 PHYTOREMEDIATION PROPERTY

Pollutants are eliminated from environmental components using phytoremediation. The effects of lead and cadmium on *C. roseus* were noted by Pandey et al. (2007). beneficial for reclaiming and cleaning up soil and land contaminated by chromium. Subhashini and Swamy (2013) employed Catharanthus roseus for phytoremediation of lead and nickel.[20]

16.9 MEMORY ENHANCEMENT ACTIVITY:

According to reports, vinpocetine has a number of activities that could potentially help with Alzheimer's disease (AD). There was no benefit identified in the one research that looked at this medication in a specific group of AD patients. There is now not enough data to justify the clinical use of vinpocetine, according to a meta-analysis of earlier research on the drug in poorly defined dementia groups. In clinical trials for dementia and stroke, vinpocetine has been well tolerated at doses up to 60 mg/d with no notable side effects.[8,42]

16.10 BIOPESTICIDAL PROPERTY

The gramme pod borer Helicoverpa armigera larvae (Lepidoptera: Noctuidae) were used to test the biological activity of solvent extracts of Catharanthus roseus. It was discovered that ethyl acetate fractions of *C. roseus* leaf extract were a powerful biopesticide (Ramya et al., 2008). Deshmukhe et al. (2010)[8,20] have also reported the insecticidal activities of *C. roseus*.

16.11 ANTINEOPLASTIC ACTIVITY

Alkaloids with anti-tumour and anti-cancer effects are found in the leaves and stems.

It suppresses the tumours. Vinblastine is used to treat chorio carcinoma and Hodgkins's disease tumours.[27,37] The activity of roseus bisindole alkaloids is explained by their capacity to upset microtubules, which results in the disintegration of mitotic spindles and metaphase arrest in split cells. In vitro, various percentages of the methanolic extracts found in rosea were found to exhibit significant anti-cancer properties against a variety of cell types.[5] Vinorelbine and vinflunine bind to tubulin to produce their anticancer effects. The alkaloids, commonly known as mitotic spindle poisons, prevent microtubule metaphase, which prevents cell cycle mitosis. Thus, alkaloida aids in stopping the cancer from spreading.[27]

16.12 ANTIMALARIAL ACTIVITY

When *Vinca rosea* root chloroform extract was administered orally to chickens at a dose of 400 mg/kg and water extract at a dose of 4.42 gm/kg, Plasmodium gallinaceum showed limited activity.[5]

16.13 ALZHEIMER'S DISEASE

Vinca rosea contains Vinpocetine alkaloids, which have a number of effects to enhance memory and brain function and are generally helpful in the case of Alzheimer's disease. In clinical trials for dementia and stroke, vinpocetine at well-tolerated doses up to 60 mg/day showed no significant side effects.[5,28]

16.14 OTHER ACTIVITIES

Any blood thinners, including aspirin and warfarin, as well as certain dietary supplements including ginkgo, vitamin E, and garlic, should not be used with vinpocetine.[28]

17. VINCA ALKALOID TOXICITY

When taken orally, Madagascar periwinkles might be harmful. It produces hallucinogens and is mentioned in the Louisiana State Act 159 (under *Vinca rosea*).[5] Despite the use of several antidotes, such as thiamine, vitamin B12, folinic acid, pyridoxine, and neuroactive drugs, their efficacy has not been clearly demonstrated. Any prescription medications taken in conjunction with chemotherapy, as well as any other illnesses like chickenpox, herpes zoster infection, gout, kidney stones, infections, liver disease, nerve or muscle disease, should be reported by patients to their clinician.[51] Peripheral, symmetric, variable sensory motor and autonomic polyneuropathy is the primary indicator of neurotoxicity. Effects on the central nervous system, including disorientation, mental status changes, depression, hallucinations, agitation, sleeplessness, seizures, coma, syndrome abnormal production of antidiuretic hormone, and visual problems, are rare because to the poor absorption of VCR into the brain. Bloating, constipation, ileus, and abdominal pain are symptoms of gastrointestinal autonomic dysfunction that are most frequently associated with VCR or high dosages of the other vinca alkaloids.[50]

17.1VINCRISTINE

In chemotherapy, vincristine is also known as leurocristine and is sold under the brand name Oncovin, among other names.[5] The most frequent adverse effect of vincristine is neurotoxicity. It is estimated that 1.36 percent of children have vincristine-induced neuropathy. An increased chance of developing sensory polyneuropathy is associated with pre-existing diabetic neuropathy and Charcot-Marie-Tooth disease type I. When vincristine is used, the incidence of peripheral neuropathy is close to 30%.[44]

17.2 VINBLASTINE

Vinblastine is a medication that is sold under various brands, including Velban.[5] Research indicates that paralytic ileus occurs in 2 to 4 percent of patients receiving vinblastine, despite the fact that it is known to be more common with the administration of vincristine. Studies on animals have shown that vinblastine is poisonous, mutagenic, carcinogenic, and should not be administered to pregnant women.[5]

17.3 VINORELBINE

Constipation and neuropathy are mild to moderate. A third of vinorelbine users have been reported to experience mild to moderate nausea and vomiting, although stomatitis and diarrhoea are less common. According to the national comprehensive cancer network guidelines, the risk of febrile neutropenia in patients following treatment with ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) for Hodgkin lymphoma is less than 10%.[5,10]

17.4 PERIPHERAL NERVOUS SYSTEM

It is known that vincristine-induced neurotoxicity manifests as autonomic, motor, and sensory symptoms. Vincristine's dose-limiting toxicity is mostly sensory and manifests as painful dysesthesias, ataxia, foot drop, and cranial nerve palsy. In order to avoid neurotoxicity, guidelines recommend that a single dose of vincristine not exceed 2 mg.[1,22,43] Vincristine has also been linked to a severe peripheral neuropathy that manifests as quadriparesis in Guillain-Barre syndrome patients. Thirty percent of individuals experience "coasting" a worsening of neuropathy symptoms after stopping chemotherapy. Preventive laxatives may be necessary for autonomic neuropathy, which manifests as constipation, ileus, cramping in the abdomen, urine retention, polyuria, and dysuria. Orthostatic hypotension and arterial hypertension or hypotension are two manifestations of autonomic influences on the cardiovascular system. Even nine years after stopping vincristine treatment, long-term neuropathy consequences have been seen in patients, and a detrimental effect on quality of life contributes to the long-term morbidity linked to its use.[44]

17.5 CENTRAL NERVOUS SYATEM

These medications may cause acute or subacute encephalopathy, convulsions, and blindness. Other less common adverse effects include parkinsonism, ataxia, visual hallucinations, tremors, unilateral or bilateral optic neuropathy, transient cortical blindness with posterior reversible encephalopathy syndrome, and syndrome of inappropriate antidiuretic hormone secretion.[21,45,46] Vincristine has been used to treat neuropathic jaw pain that does not respond to conventional painkillers. There have also been reports in the literature of vincristine-induced vocal cord palsy, which is a possibly reversible condition that goes away when the medication is stopped. Vocal cord palsy has also been linked to higher dosages, preexisting hepatic dysfunction, neuropathic illness, a history of drug hypersensitivity, and co-administration of other cancer chemotherapy agents and non-chemotherapy medications like mitomycin-C, allopurinol, azathioprine, phenytoin, isoniazid, and itraconazole.[44]

17.6 HEMATOTOGICAL, RENAL AND PULMONARY TOXICITY

Typically, vincristine is a medication that spares bone marrow. Thrombocytopenia is less prevalent than leucopenia. Bone marrow toxicity has also been linked to vindesine and vinorelbine.[44] Renal excretion of vinblastine and its active metabolites, desacetylvinblastine, vincristine, and vindesine, is minimal (between 10 and 15%). Due to a higher risk of side effects, patients receiving haemodialysis have a 50% reduction in vinorelbine dosage. When vincristine and vinblastine are used concurrently with mitomycin-C, acute dyspnoea and bronchospasm may result.[44]

17.7 HEPATIC AND CARDIOVASCULAR TOXICITY

Since the liver is where vincristine is mostly metabolised, dose modifications are advised when hepatic dysfunction and hyperbilirubinemia occur, especially when the direct bilirubin percentage is elevated. Hepatic sinusoidal obstruction syndrome (hepatic veno-occlusive disease) is known to be caused by both vincristine and vinblastine in predisposed individuals, including youngsters, those with greater radiation doses, and concurrent use of dactinomycin and cyclophosphamide.[44] These medications have also been linked to myocardial infarction and heart ischaemic discomfort that manifests as ECG anomalies.[19]

17.8 LOCAL AND RARE ADVERSE EFFECTS

Erythema, discomfort, and discolouration are examples of injection-related local responses. One uncommon side effect of these medications is alopecia.[44]

18. EVALUATION

The National Cancer Institute's "Common Terminology Criteria for Adverse Events" (CTCAE), the "European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire C30" (EORTC QLQ-C30), and the "Chemotherapy-Induced Peripheral Neuropathy-20 Questionnaire" (CIPN20) are some of the instruments used to assess chemotherapy-induced peripheral neuropathy. Although electromyography and nerve conduction investigations are expected to show signs of an axonopathy, they are not frequently carried out because of the expense. Urine and plasma osmolarity measurements may be necessary for the diagnosis of SIADH, which is known to be associated with hypovolemic hyponatraemia symptoms. Hepatic Veno-occlusive disease can be diagnosed with both the Seattle and Baltimore criteria.[13,20,47,48]

19. TREATMENT

Early detection of neurological symptomatic adverse events requires routine surveillance and patient education techniques.[21] The best ways to manage the side effects appear to be changing the dosage, using an alternative treatment (in patients with Charcot-Marie-Tooth disease, substituting vindesine for vincristine is advised), and stopping chemotherapy in the event of severe, potentially fatal toxicities. While pre-clinical research has examined the role of glutamic acid in the therapy of vincristine-induced peripheral neuropathy, both pyridostigmine and pyridoxine have demonstrated an improvement in the pace of recovery.[44]According to reports, a double-blind, randomised control experiment to evaluate glutamic acid's effectiveness in preventing vincristine-induced neurotoxicity had a poor result.[49]

Due to the possibility of neurotoxicity, which has been documented to manifest as seizures, clinicians should refrain from using these medications concurrently with azole antifungals. To reduce irritation following injection, it is recommended to flush the veins. To reduce irritation following injection, it is recommended to flush the veins. The usage of vincristine should be thoroughly taught to chemists and cancer care nurses. Vincristine administration expertise and training must be readily available in every unit offering chemotherapy services. In addition to preventing risk factors that increase the likelihood of a neurological injury, patient and carer education, lifestyle modifications, physical treatment, and occupational therapy techniques can further enhance results.[44]

20. CONCLUSION

Catharanthus roseus is among the 21,000 important medicinal herbs. The plant also has a number of other properties, including anti-cancer, anti-diabetic, anti-helminthic, anti-diarrheal, and antimicrobial. Therefore, there is a lot of room for research on the aforementioned plant to unravel its mysteries and meet the needs of the modern pharmaceutical industry. Vinca alkaloids will continue to be one of the first cancer treatments and are currently the second most popular family of cancer medications. Extensive study is required to optimise the culture conditions at different levels and take into account the manufacture of the revolutionary life-saving medication using a potent blend of naturally occurring bioactive components.

REFERENCES

1. Van Der Heijden R, Jacobs DI, Snoeijer W, Hallard D, Verpoorte R. The Catharanthus Alkaloids: Pharmacognosy and Biotechnology. Vol. 11, Current Medicinal Chemistry. 2004.
2. Noble' RL. The discovery of the vinca alkaloids-chemotherapeutic agents against cancer1 [Internet]. Available from: www.nrcresearchpress.com
3. Wang LY, Gu YH, Zhou QZ, Ma GH, Wan YH, Su ZG. Preparation and characterization of uniform-sized chitosan microspheres containing insulin by membrane emulsification and a two-step solidification process. Colloids Surf B Biointerfaces. 2006 Jul 1; 50(2): 126–35.
4. Cragg GM, Grothaus PG, Newman DJ. Impact of natural products on developing new anti-cancer agents. Chem Rev. 2009 Jul 8; 109(7): 3012–43.
5. Kumar G, Kumar R, Gautam GK, Rana H. The phytochemical and pharmacological properties of Catharanthus roseus (Vinca). Science Progress and Research. 2022 Jan 10; 2(1): 472–7.
6. Manivannan P, Jaleel CA, Sankar B, Kishorekumar A, Somasundaram R, Lakshmanan GMA, et al. Growth, biochemical modifications and proline metabolism in Helianthus annuus L. as induced by drought stress. Colloids Surf B Biointerfaces. 2007 Oct 1; 59(2): 141–9.
7. Setzer WN. The Phytochemistry of Cherokee Aromatic Medicinal Plants. Medicines. 2018 Nov 12; 5(4): 121.
8. Dubey A, Tiwari D, Srivastava K, Prakash O, Kushwaha R. A discussion on vinca plant. ~ 27 ~ Journal of Pharmacognosy and Phytochemistry

[Internet]. 2020; 9(5). Available from: www.phytojournal.com
9. Jaleel CA, Manivannan P, Wahid A, Farooq M, Somasundaram R, Panneerselvam R. Drought stress in plants: a review on morphological characteristics and pigments composition. Int J Agric Biol [Internet]. 2009; 11: 100–5. Available from: http: //www.fspublishers.org
10. Salama M, Mohammed Ezzat S, salem M. Bioactive lead compounds and molecular targets for the treatment of heart disease.Phytochemicals as Lead Compounds for New Drug Discoverys [Internet]. Available from: https: //buescholar.bue.edu.eg/pharmacy/488
11. Banyal A, Tiwari S, Sharma A, Chanana I, Patel SKS, Kulshrestha S, et al. Vinca alkaloids as a potential cancer therapeutics: recent update and future challenges. Vol. 13, 3 Biotech. Springer Science and Business Media Deutschland GmbH; 2023.
12. Nisar A, Soh Mamat A, Irfan Hatim Mohamed Dzahir M, Syarhabil Ahmad M. AN UPDATED REVIEW ON CATHARANTHUS ROSEUS: PHYTOCHEMICAL AND PHARMACOLOGICAL ANALYSIS [Internet]. Vol. 57, Article in Indian Research Journal of Pharmacy and Science. 2016. Available from: https: //www.irjps.in
13. Mosissa D. Invasive Alien Plant Species in the Northwestern & Western Provenance of Ethiopia and Linking Its' Phonological Implication to Management and Control. 2019; 74. Available from: www.iiste.org
14. Jain N, Kumar A, Singh N, Kumar D, Dayal R, Singh S, et al. CATHARANTHUS ROSEUS: TRADITIONAL USES, PHYTOCHEMISTRY, AND MODERN PHARMACOLOGY. International Journal of Medical Science. 2025 Oct 5; 5(1): 41–70.
15. Khani S, Barar J, Movafeghi A, Omidi Y. Production of Anticancer Secondary Metabolites: Impacts of Bioprocess Engineering. In: Biotechnological Production of Plant Secondary Metabolites. Bentham Science Publishers Ltd.; 2012. p. 215–40.
16. Okaiyeto K, Gigliobianco MR, Di Martino P. Biogenic Zinc Oxide Nanoparticles as a Promising Antibacterial Agent: Synthesis and Characterization. Vol. 25, International Journal of Molecular Sciences. Multidisciplinary Digital Publishing Institute (MDPI); 2024.
17. Kulkarni RN, Baskaran K, Jhang T. Breeding medicinal plant, periwinkle [Catharanthus roseus (L) G. Don]: A review. Vol. 14, Plant Genetic Resources: Characterisation and Utilisation. Cambridge University Press; 2016. p. 283–302.
18. Baskaran K, Jhang T. Breeding medicinal plant, periwinkle [Internet]. Available from: www.ijtsrd.com
19. El-Sayed M, Verpoorte R. Catharanthus terpenoid indole alkaloids: Biosynthesis and regulation. Vol. 6, Phytochemistry Reviews. 2007; p. 277–305.
20. Das S, Krishi Viswavidyalaya C, Sharangi AB. Madagascar periwinkle (Catharanthus roseus L.): Diverse medicinal and therapeutic benefits to humankind. ~ 1695 ~ Journal of Pharmacognosy and Phytochemistry. 2017; 6(5): 1695–701.
21. Kumar Verma N, Narayan Mishra J. A brief study on Catharanthus Roseus: A review Formulation and evaluation of herbal tablets containing Agaricus bisporus powder View project A brief study on Catharanthus Roseus: A review [Internet]. Vol. 2, International Journal of Research in Pharmacy and Pharmaceutical Sciences. 2017. Available from: https: //www.researchgate.net/publication/319007421
22. Aslam J, Hamdard J, Siddiqui ZH, Zohra F, Khan SH, Fatima Z, et al. Mehpara Maqsood PHARMACIE GLOBALE INTERNATIONAL JOURNAL OF COMPREHENSIVE PHARMACY Catharanthus roseus (L.) G. Don. AN IMPORTANT DRUG: IT'S APPLICATIONS AND PRODUCTION [Internet]. Vol. 01. 2010. Available from: https: //www.researchgate.net/publication/49596279
23. Gomaa S, Yahayu M, Dailin DJ, Gomaa SE, Nurjayadi M, Enshasy H El. Antimicrobial Compounds from Catharanthus roseus-A review Purification and characterization of laccase produced from Cerrena sp. View project Pullulan production View project Antimicrobial Compounds from Catharanthus roseus-A review. Article in International Journal of Scientific & Technology Research [Internet]. 2019; 8(10). Available from: www.ijstr.org
24. Palombo EA. Traditional medicinal plant extracts and natural products with activity against oral bacteria: Potential application in the prevention and treatment of oral diseases. Vol. 2011, Evidence-based Complementary and Alternative Medicine. 2011.
25. Santhosh Aruna M, Surya Prabha M, Santhi Priya N, Nadendla R. CATHARANTHUS ROSEUS: ORNAMENTAL PLANT IS NOW MEDICINAL BOUTIQUE. Journal of Drug Delivery & Therapeutics [Internet]. 2015; 5(3): 1–4. Available from: http: //jddtonline.info
26. Nejat N, Valdiani A, Cahill D, Tan YH, Maziah M, Abiri R. Ornamental exterior versus therapeutic interior of Madagascar periwinkle (Catharanthus roseus): The two faces of a versatile herb. Vol. 2015, Scientific World Journal. Hindawi Publishing Corporation, 2015.
27. Allamsetty J, Pedada SP, Pedada N, Dhanunjayarao K. A BASIC REVIEW ON VINCA ROSEA *Corresponding Author. Vol. 1, International Journal of Pharmacognosy and Chemistry. 2020.
28. Padmaa Paarakh M, Swathi S, Taj T, Tejashwini V, Tejashwini B. Catharanthus Roseus Linn—A

Review. Acta Scientific Pharmaceutical Sciences. 2019 Sep 6; 3(10): 19–24.

a. 29. Prabha Lahare Rajeshwari, Yadav HS, Dashahre AK, Kumar Bisen Y. An Updated Review on Phytochemical and Pharmacological Properties of Catharanthus rosea. Saudi Journal of Medical and Pharmaceutical Sciences. 2020 Dec 4; 6(12): 759–66.

29. Jaiswal R, Singh AK, Verma K, Mall C, Yadav V. CATHARANTHUS ROSEUS: CHEMICAL CONSTITUENTS AND PHARMACOLOGICAL ACTIVITIES-A REVIEW [Internet]. Available from: www.wjpls.org

30. Patzelt A, Pyšek P, Pergl J, van Kleunen M. Alien flora of Oman: invasion status, taxonomic composition, habitats, origin, and pathways of introduction. Biol Invasions. 2022 Apr 1; 24(4): 955–70.

31. Van Der Heijden R, Jacobs DI, Snoeijer W, Hallard D, Verpoorte R. The Catharanthus Alkaloids: Pharmacognosy and Biotechnology. Vol. 11, Current Medicinal Chemistry. 2004.

32. Biswas D, Chakraborty A, Mukherjee S, Ghosh B. Hairy root culture: a potent method for improved secondary metabolite production of Solanaceous plants. Vol. 14, Frontiers in Plant Science. Frontiers Media SA; 2023.

33. Thawabteh A, Juma S, Bader M, Karaman D, Scrano L, Bufo SA, et al. The biological activity of natural alkaloids against herbivores, cancerous cells and pathogens. Vol. 11, Toxins. MDPI AG; 2019.

34. Balaji H. Versatile Therapeutic effects of Vinca rosea Linn. Vol. 4, International Journal of Pharmaceutical Science and Health Care Issue, 2014.

35. Nisar A, Soh Mamat A, Irfan Hatim Mohamed Dzahir M, Syarhabil Ahmad M. AN UPDATED REVIEW ON CATHARANTHUS ROSEUS: PHYTOCHEMICAL AND PHARMACOLOGICAL ANALYSIS [Internet]. Vol. 14, Article in Indian Research Journal of Pharmacy and Science. 2016. Available from: https: //www.irjps.in

36. Allamsetty J, Pedada SP, Pedada N, Dhanunjayarao K. A BASIC REVIEW ON VINCA ROSEA International Journal of Pharmacognosy and Chemistry *Corresponding Author CASE REPORT ON HYPOGLYCEMIA INDUCED SEIZURES View project A BASIC REVIEW ON VINCA ROSEA *Corresponding Author [Internet]. Vol. 1, International Journal of Pharmacognosy and Chemistry. 2020. Available from: https: //www.researchgate.net/publication/349456872

37. Patharajan S, Bala Abirami S. ANTIOXIDANT ACTIVITY AND PHYTOCHEMICAL ANALYSIS OF FRACTIONATED LEAF EXTRACTS OF CATHARANTHUS ROSEUS. International Journal of Pharmacognosy [Internet]. 2014; 1(2): 138–81. Available from: http: //dx.doi.org/10.13040/IJPSR.0975-8232.IJP.1

38. LEAF EXTRACTS OF CATHARANTHUS ROSEUS. International Journal of Pharmacognosy.

39. INTERNATIONAL JOURNAL OF ADVANCES IN PHARMACY, BIOLOGY AND CHEMISTRY Research Article [Internet]. Available from: www.ijapbc.com

40. Tonal L, Kambu' K, Mesial K, Cimanga K, Apers-S, De Bruyne- T, et al. Biological screening of traditional preparations from some medicinal plants used as antidiarrhoeal in Kinshasa, Congo [Internet]. Vol. 6, Phytomedicine. 1999. Available from: http: //www.urbanfischer.de/journals/phytomed

41. Kumar Verma N, Narayan Mishra J. A brief study on Catharanthus Roseus: A review Formulation and evaluation of herbal tablets containing Agaricus bisporus powder View project A brief study on Catharanthus Roseus: A review [Internet]. Vol. 2, International Journal of Research in Pharmacy and Pharmaceutical Sciences. 2017. Available from: https: //www.researchgate.net/publication/319007421

42. Ganie IB, Ahmad Z, Shahzad A, Zaushintsena A, Neverova O, Ivanova S, et al. Biotechnological Intervention and Secondary Metabolite Production in Centella asiatica L. Vol. 11, Plants. MDPI; 2022.

43. Rahul D. Arora; Ritesh G. Menezes et al. Vinca Alkaloid Toxicity, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia. December 4, 2021.

44. Tangredi J. Ishihara Sangyo Kaisha, LTD. Petition for Determination of Nonregulated Status for Moth Orchid (Phalaenopsis spp. Hybrid) Containing the Flavonoid 3'5'-Hydroxylase Gene of Asiatic Dayflower (Commelina communis) Event ISK311NR-4 Draft Plant Pest Risk Assessment. 2025.

45. Dhandapani R, Sabna B. Phytochemical constituents of some Indian medicinal plants.

46. Ahsan M, Rana ZA, Ali M, Anwer K. Assessment of Knowledge, Concerns and Support of Physicians towards Bio banks in Pakistan, and their Willingness to Donate. Science Progress and Research. 2021 Oct 5; 1(4): 382–90.

47. Moudi M, Yong C, Nazre M. Toxicovigilance-Objectives of WHO vis-a-vis Implementation in developing world View project Development of novel microsatellite markers for the Malayan tapir View project [Internet]. Vinca Alkaloids Article in International Journal of Preventive Medicine. 2013. Available from: https: //www.researchgate.net/publication/259632262

48. For Non-Commercial Use. Multidisciplinary Digital Publishing Institute (MDPI); 2024.

49. Yong C, Nazre M. 149 PUBLICATIONS 1,484 CITATIONS SEE PROFILE. Int J Prev Med. 2013; 4(11).

50. Maryam Moudi, Rusea Go, Christina Yong Seok Yien, et al. Vinca Alkaloids. Int J Prev Med. 2013 Nov; 4(11): 1231–1235

51. Lorena Almagro, Francisco Fernández-Pérez ,Maria Angeles Pedreño et al. Indole Alkaloids from *Catharanthus roseus*: Bioproduction and Their Effect on Human Health. 12 February 2015, Available from: https: //doi.org/10.3390/molecules20022973
52. Ingalwad P, Veer V, Bhosale DA. 173 Overview on a Vinca Alkaloid & Its Medicinal, Therapeutic Properties.