A review of the taxonomy, ethnobotany, chemistry and pharmacology of *Catharanthus roseus (Apocyanaceae*)

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ABSTRACT :

Periwinkle(nayantara) is the common name for a pair of perennial flowering shrubs belonging to the *Apocynaceae* family. It is cultivated as an ornamental plant almost throughout the tropical world. It is abundantly naturalised in many regions, particularly in arid coastal locations. The herb has been used for centuries to treat a variety of ailments and was a favourite ingredient of magical charms it was in the middle ages. The latin name for this herb is *Catharanthus roseus*, but it was classified as *Vinca rosea*, and is still called by that name in some of the herbal literature. The present review evaluates the antibacterial activity, antihyperglycemic activity, antihypertensive activity, cytotoxic activity, antitumour activity, antidiabetic activity, diabetic wound healing activity and phytochemical constituents of *Catharanthus roseus*. The highest diabetic wound healing activity was observed with ethanol extract is attributed due to the presence of alkaloids, tannins and tri-terpenoids. *Catharanthus roseus* leaves extract treated animals have show the hypotensive effects due to the presence of alkaloids and carbohydrates. The methanolic extracts of various parts of *Catharanthus roseus* was possessed high antioxidant activity due to the presence of flavonoids, coumarin, quinine and phenolic compounds. Herbal anticancer drug like *Catharanthus roseus* is wildly used because of their well defined mechanism of action as anticancer drug. Proper chemical and biological investigations, understanding of the mechanisms of action, development of the structure activity relationship and high yield production by plant tissue culture of these herbal drugs promote their use against cancer as such or there semi synthetic analogues.

Contents

1. Introduction

Vinca rosea (*C. roseus*) Linn. (*Apocynaceae*) is an herbaceous sub shrub also known as Madagascar periwinkle, *Vinca rosea*, or *Lchnera rosea* worldwide. It is cultivated mainly for its alkaloids, which are having anticancer activities(Jaleel et al., 2006). The two classes of active compounds in *Vinca* are alkaloids and tannins. *Catharanthus roseus* produces more than 100 monoterpenoids indole alkaloids (TIA) in different organs (Jordan et al., 1991). The leaves and stems are the sources of dimeric alkaloids,vinacristine and vinblastine that are indispensable cancer drugs, while roots have antihypertensive, ajmalicine and serpentine (Kulkarni et al., 1999). The leaves are used traditionally in various regions of the world including India, West Indies as well as Nigeria to control diabetes (Cowley and Bennett 1928). The leaves have been known to contain 150 useful alkaloids among other pharmacologically active compounds. Significant antihyperglycemic and hypotensive activity of the leaf extracts (hydroalcoholic or dichloromethane-methanol) have been reported in laboratory animals (Pillai et al., 1959). Fresh leaf juice of *C. roseus* has been reported to reduce blood glucose in normal and alloxan diabetic rabbits (Nammi et al., 2003). Leaves and twigs of *Catharanthus roseus* have been reported to have hypoglycaemic activity in streptozotocin induced diabetic rats (Singh et al., 2001). *Catharanthus roseus*(*Apocyanaceae*) also known as *Vinca rosea*, is native to the carribean basin and has historically been used assortment of diseases(Heijden et al., 2004). It has more than 400 alkaloids, some of which are approved as antineoplastic agents to treat leukemia, hodgkin's disesase, malignant lymphomas, neuroplastoma, wilm's tumour and other cancers(Taylor and Fransworth 1975).

Medicinal plants represent a rich source from which antimicrobial agents are obtained. They are a source of many potent and powerful drugs(Srivastava et al., 1996). The use of medicinal plants to treat human diseases has its pre-historical roots. Medicinal plants are used by 80% of the world population as the only available source of medicines especially in developing countries(Hashim et al., 2010) .

Most part of the medicinal plants including leaves, roots, stems, flowers, fruits and twigs are used for extract as raw drugs. While some of these raw drugs are collected in smaller quantities by the local communities and folk healers for local uses, many other raw drugs are collected in larger quantities and traded in the market as the raw material for many herbal industries(Uniyal et al., 2006). Plants used for traditional medicine contain a wide range of substances that can be used to treat chronically infectious diseases. Clinical microbiologists have great interest in screening of medicinal plants for antimicrobial activities and phytochemicals as potential new therapeutics. The active principles of many drugs found in plants are secondary metabolites(Ghani, 1990 and Dobelis, 1993) The antimicrobial activities of plant extracts may reside in a variety of different components, including aldehydes and phenolic(Lai and Roy, 2004). The beneficial medicinal effects of plant materials typically result from *the* combinations of secondary products present in the plant. In plants, these compounds are mostly secondary metabolites such as alkaloids, steroids, tannins, phenolics, flavonoids, steroids, resins, and fatty acids, which are capable of producing definite physiological action. The development of drug resistance in human pathogens against commonly used antibiotics has necessitated a search for new antimicrobial substances from other sources including plants. Screening of medicinal plants for antimicrobial activities and phytochemicals is important for finding potential new drugs for therapeutic use.

2.Taxonomy

2.1 Description

Catharanthus roseus

Family: *Apocynaceae*

- Kingdom : Plantae
- Order : Gentianales
- Family Name : *Apocynaceae*
- Genus : *Catharanthus*

- Species : *roseus*
- Binomial name: *Catharanthus roseus*
- Botanical Name: *Vinca rosea*

(Erdogrul, 2002)

This species was formerly known as *Vinca rosea.* This is a large Family with about 1500 species found mainly in tropical regions. It includes many of the most well-known tropical ornamental plants (Oleander, Frangipani, Allamanda, Mandevilla). Many are large trees with buttress roots found in rainforests, some are smaller, evergreen or deciduous trees, shrubs or climbers from other warm areas of the world, and one or two are found in temperate regions (*Vinca*). The sap of most plants is a milky latex, which is often of economic importance for medicinial use, or for the production of rubber. This sap is often toxic.

Leaves are simple and undivided, and are either opposite or in rings around the stem. There is a calyx with five parts, either separate or joined to form a tube. The flowers are in clusters and are often large and showy. They usually have five petals joined into a tube at the base. There are five stamens joined together. The seeds capsule has two parts and may be either inside the flower or not. Seeds are very variable, and may be small with a hairy tuft (Nerium) or large and woody (Allamanda). Members of this family usually have Simple leaves, Milky sap , Five part calyx, Clusters of flowers, five large petals joined at the base and five stamens. Most parts of many members of this plant family are poisonous. Each plant of this family (*Apocyanaceae)* posses different medicinal behaviour(Varuna et al., 2010).

Vernacular names:

Periwinkle, Nityakalyani(Tamil), Billaganneru(Kannadam), Ainskati(Sanskrit), Nayantara(Bengali), Rattanjot, Sadabahar, Sadaphul(Marathi), Ushamanjairi, Vinca branca(European), Vinca rosada(Spanish).

2.2 Origin and distribution

Native of Madagascar. Abundantly naturalised in many regions. Particularly in arid coastal locations. Grown commercially for its medicinal uses in Australia, Africa, India and southern Europe. Cultivated as an ornamental plant almost throughout the tropical and subtropical world.(Mohammad et el., 2009)

3.0 Medicinal properties

Catharanthus roseus (Apocynaceae) a perennial plant is commonly seen in tropical countries. It is more commonly known as Madagascar periwinkle. This plant produces beautiful flowers with a variety of colours such as purple, pink and white and commonly planted for decorative purposes(Padua et al., 1999). Historically, Madagascar periwinkle had been used for various treatments, e.g., diabetes mellitus, high blood pressure and infection. Leaf part of the plant contains 90 different alkaloids. The most abundant ones are the monomers like catharanthine and vindoline. Two derivative of vincamine widely used as medicine is known as ethyl-apovincaminate or vinpocetine. It has vasodilating, blood thinning, and memory-enhancing actions, antherosclerotic plaques(Basker et al., 1995). Extracts of *Vinca* have significant anticancer activity against numerous cell types.

The most abundant ones are the monomers like catharanthine and vindoline. Two of the common anti-cancer drugs which are derived from this plant are vincristine and vinblastine. Vincristine is used in the chemotherapeutic regimen for Hodgkin's lymphoma while vinblastine is used for childhood leukemia. *Catharanthus roseus* (*apocyanaceae*) also known as *Vinca rosea*, is native to the caribbean basin and has historically been used to treat a wide assortment of diseases. European herbalists used the plant for conditions as varied as headache to a folk remedy for diabetes. It has more than 400 known alkaloids, some of which are approved as antineoplastic agents to treat leukemia, hodghin's disease, malignant lymphomas, neuroblastoma, rhabdomyosarcoma, wilms' tumor, and other cancers(Brun et al.,1999). The two classes of active compounds in *Vinca* are alkaloids and tannins. The major alkaloid is vincamine and its closely related semi-synthetic derivative widely used as prophylactic agent in many of the diseases, which sometime are of the magnitude of an epidemic (Prajakta et al., 2010).

The extracts of *Vinca* have demonstrated significant anticancer activity against numerous cell types. Extracts from the dried or wet flowers and leaves of plants are applied as a paste on wounds in some rural area. The fresh juice from the flowers of *Cantharanthus roseus* made into a tea has been used by ayurvedic physicians in India for external use to treat skin problems, dermatitis, eczema and acne(Sayed and Cordell, 1981). *Vinca* has more alkaloids. Some are used by the pharmaceutical industry for the treatment of testicular cancer and cancerous tumors. Taken as a daily supplement, it improves the blood supply to the brain, increases oxygen and glucose for the brain to use, helps prevent abnormal coagulation of blood, and it raises brain levels of the neurotransmitter serotonin(Hisiger and Jolicoer 2007).

Extracts of *Vinca* have significant anticancer activity against numerous cell types(Baskar et al., 1995) Over 130 constituents with an indole or dihydroindole structure; including the principal component vindoline; vincaleukoblastine (vinblastine), 22-oxovincaleukoblastine (vineristine), reserpine, vincamine, alstonine, leurocristine, ajmalicine, vinine, vinomine, vinoxine, vintsine, leurosine (Heijden et al., 2004). The hypoglycemic activity of alkaloids isolated from *Catharanthus roseus* have been studied pharmacologically and a remedy derived from the plant has been marketed under the proprietary name vinculin as a treatment for diabetes(Chattapadhyay, 1999 and Fischhof et al., 1996). Madagascar periwinkle's most potent constituent is the reserpine. Reserpine is recommended for the treatment of hypertension, mild anxiety states and chronic psychoses. (Siddiqui and Khan, 1968; Kirtikar and Basu, 1984). It works by vessels so that blood can flow more easily through the vessels.

4. Phytochemistry

Cantharanthus roseus is rich in alkaloids, carbohydrates, flavonoids, triterpenoids, tannins, coumarin, quinone and phenolic compounds (Uniyal et al., 2001).

The leaves of *Cantharanthus roseus* rich alkaloids and carbohydrates. It has demonstrated antibacterial and antidiabetic effects and is able to reduce the blood sugar (Singh et al., 2001). The flowers of *Catharanthus roseus* was rich in tannins, triterpenoids and alkaloids were responsible for diabetic wound healing activity(Zhoe et al., 2009). *Catharanthus roseus* has antioxidant properrties attributed to polyphenols found in its leaves. The stem and root of *C.roseus* contains considerable amount of coumarin, quinones and it has antibacterial activities (Ferrers 2008). The rootbark contains the alkaloid alstonine which has been used traditionally for its calming drug namely vincristine and vinblastine are produced from *Catharanthus roseus (Bhadra et al., 1993).* Besides alkaloids Catharanthus roseus produces a wide spectrum of phenolic compounds, this includes C6C1 compounds such as 2,3-dihydoxybenzoic acid, as well as phenylpropanoids such as cinnamic acid derivatives, flavonoids and anthocyanins(Harborne and William 2009). The occurrence of these compounds in C. roseus is reviewed as well as their biosynthesis and the regulation of the pathways. Both types of compounds compete with the indole alkaloid biosynthesis for chorismate, an important intermediate in plant metabolism(Hall et al., 1986).

Catharanthus roseus produces more than 100 monoterpenoids indole alkaloids (TIA) in different organs (Barnett et al., 1978). The leaves and stems are the sources of dimeric alkaloids, vinacristine and vinblastine that are indispensable cancer drugs, while roots have antihypertensive, ajmalicine and serpentine (Berrier et al., 1987) The leaves are used traditionally in various regions of the world including India, West Indies as well as Nigeria to control diabetes (Pearce 1990). The leaves have been known to contain 150 useful alkaloids among other pharmacologically active compounds. Significant antihyperglycemic and or dichloromethane-methanol) have been reported in laboratory animals (Mohammed Ibrahim et al., 2011). Fresh leaf juice of *C. roseus* has been reported to reduce blood glucose in normal and alloxan diabetic rabbits (Sumana and Suryawashi 2001). Leaves and twigs of *Catharanthus roseus* have been reported to have hypoglycaemic activity in streptozotocin induced diabetic rats.

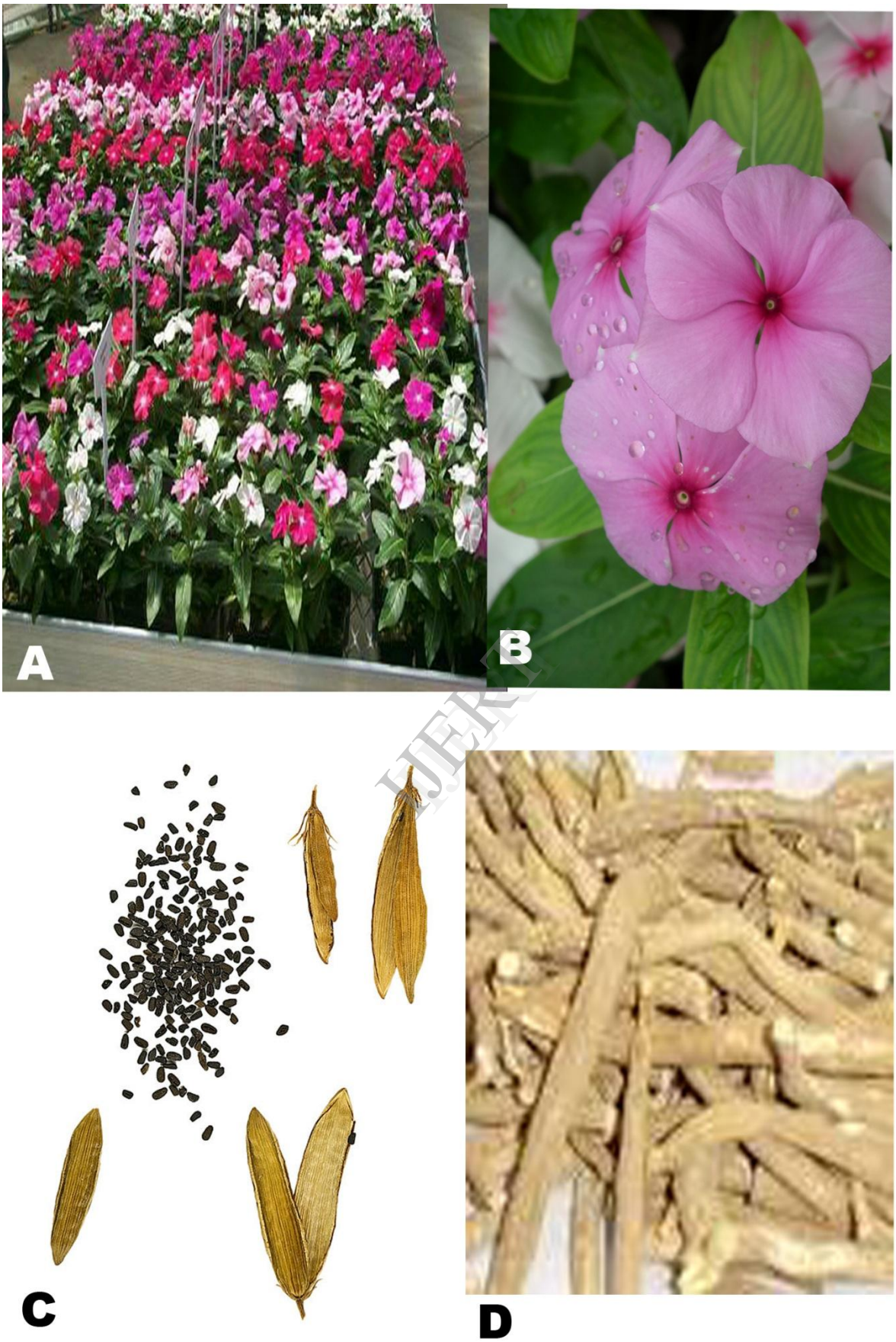


Figure 1. *Catharanthus roseus* (A) Commercial plantation (B) flowers of *Catharanthus roseus* (C) fruit and Seeds of *Catharanthus roseus* (D) dried roots of *Catharanthus roseus.*

5. Pharmocognosy

5.1 Microbial activity

Catharanthus roseus is an important medicinal plant for novel pharmaceuticals since most of the bacterial pathogens are developing resistance against many of the currently available antimicrobial drugs. Plants have proved to be significant natural resources for effective chemotherapeutic agents and offering a broad spectrum of activity.

The anticancer properties of *Catharanthus roseus* has been the major interest in all investigations. The antimicrobial activity has been checked against microorganisms like, *Pseudomonas aeruginosa* NCIM 2036 , *Salmonella typhimurium* NCIM 2501, *Staphylococcus aureus* NCIM 5021. The findings show that the extracts from the leaves of this plant can be used probably increased glycogenesis, decreased gluconeogenesis or decreased absorption of glucose from intestine(Patil and Ghosh 2010).s

The antibacterial activity of crude extracts from different parts of *Catharanthus roseus* against several bacterial species of clinical significance. Extraction of each plant part in appropriate solvent followed by evaluation of antibacterial activity by agar well diffusion assay against a total of six bacterial stains. Further, minimum inhibitory concentration(s) was evaluated for active crude extracts. Data indicated that the pattern of inhibition depends largely upon the extraction procedure, the plant part used for extraction, state of plant part (fresh or dry), solvent used for extraction and the microorganism tested. Dry powder extracts of all plant parts demonstrated more antibacterial activity than extracts prepared from fresh parts. Furthermore, extracts prepared from leaves were shown to have better efficacy than stem, root, and flower extracts. Organic extracts provided more potent antibacterial activity as compared to aqueous extracts. Among all the extracts, the ethanolic extract was found to be most active against almost all the bacterial species tested.

Hot water and cold water extracts were completely inactive. Gram-positive bacteria were found more sensitive than Gram-negative bacteria. *(Siddiqui et al., 2010)*[5].

5.2 Hypotensive and hypolipidemic effects

The leaves extract of C*atharanthus roseus* was investigated for hypotensive and hypolipidemic effects in adrenaline-induced hypertensive rats (AIHR) and compared with those of Atenolol in a crossover design. The pharmacologically active components responsible for hypotensive activities were isolated from plant using bioassay guided purification approach and the structure of the compounds was proposed by spectroscopic methods C*atharanthus roseus* leaves extract and commercial drug Atenolol were administered through intraperitoneal (i.p) route for one week. Different biochemical parameters such as heart weight, blood glucose level, serum cholesterol level, serum triglyceride level, body weight and the relationships between them were measured. C*atharanthus roseus* leaves extract at a dose of 30 mg/155±15 gm of body weight was injected in rat at every morning during the treatment period. The dose of Atenolol was determined according to its pharmacokinetic parameters. Clinically effective plasma concentration as a hypotensive drug was obtained after the injection of 0.1 mg/155±15 gm of body weight of the drug. The *Catharanthus roseus* leaves extract madesignificant changes in each cardiovascular parameter after investigation. C*atharanthus roseus* leaves extract treated animals have shown the hypotensive effects. Hypotensive effects were also shown by Atenolol.(Naznin et al., 2009).

5.3 Diabetic activity

The antidiabetic and hypolipidemic effects of petroleum-ether, ethyl acetate and chloroform fractions from ethanolic extract of the leaves of *Catharanthus roseus* were investigated in normal and streptozotocin-induced diabetic rats (SIDRs).

Single doses (150 mg/kg, i.p.) of *C. roseus* extracts in the fasting blood glucose (FBG) levels were determined in normal and SIDRs on 0, 1, 2, 3, 6, 10, 16, and 24th hours and serum triglyceride (TG) and serum total cholesterol (TC) levels were determined after 24th hour. In normoglycemic rats and in SIDRs, petroleum-ether and ethyl acetate fraction of *C. roseus* reduced blood glucose level significantly. In case of hypolipidemic effects, all fractions reduced serum total cholesterol but the ethyl acetate fraction of *C. roseus* was the most effective. All fractions of *C. roseus* reduced serum triglyceride level but the ethyl acetate fractio reduced triglyceride level at the highest. The antidiabetic and hypolipidemic activities were compared to metformin HCl (150 mg/kg). Of all the three fractions, ethyl acetate fractions were the best in activity.(Islam et al 2009)

5.4 Anthelmintic activity

The leaves extract of show potent anthelmintic activity. The pharmacologically active components responsible for hypotensive activities were isolated from plant using bioassay guided purification approach and the structure of the compounds was proposed by spectroscopic methods. C*atharanthus roseus* leaves extract and commercial drug Atenolol were administered through intraperitoneal (i.p) route for one week. Different biochemical parameters such as heart weight, blood glucose level, serum cholesterol level, serum triglyceride level, body weight and the relationships between them were measured. C*atharanthus roseus* leaves extract at a dose of 30 mg/155±15 gm of body weight was injected in rat at every morning during the treatment aqueous, methanol, ethyl acetate and ethanol extract of *Catharanthus roseus* was found to be least active. Piperazine citrate diluted with water, about 50mg/ml concentration of piperazine citrate was served as standard and poured into Petri dishes. The synthesized compounds (aqueous, methanol, ethyl acetate and ethanol) were prepared in minimal quantity of water and diluted to prepare two concentrations i.e. 100mg per ml and 150 mg per ml, up to 25ml of compound solution with water for each compound is prepared. Normal saline serve as control. Three earthworms of nearly equal size about 3-5 cm in length and 0.1-0.2 cm in width are taken for each concentration andplaced in Petri dishes at room temperature. The time taken for complete paralysis and death are recorded. The mean paralysis time and mean death time for each sample was calculated (each reading taken in triplicate). The time taken for worms to become motionless was noted as paralysis time and to ascertain death, each worm was frequently applied with external stimuli,which stimulates and induce movement in the earthworms(Akash jain and Akhilesh Rawal, 2011). It is concluded that the aqueous, methanol, ethyl acetate and ethanol extract of *Cathranthus roseus* showed anthelmintic activity.

5.5 Hypoglycemic effects

The effect of the aqueous extracts of *Catharanthus roseus* and chlorpropamide (Diabenese) on the levels of serum cholesterol, total protein, lipid peroxidation, blood glucose and liver enzymes were compared in alloxan-induced diabetic rats. Four groups namely A, B, C and D comprising of nine rats each were used. A and B were administered with chlorpropamide and *C. roseus* extracts respectively, while C and D served as diabetic and non-diabetic controls respectively.The results showed comparatively significant reductions (P_0.05) in the levels of glucose,protein, cholesterol, lipid peroxidation and liver enzymes in the groups administered *C. roseus* extracts and chlorpropamide relative to the controls. The reductions were higher in the groups treated with *C. roseus* extract than in the groups treated with diabenese(Iweala and Okeke, 2005).

5.6 Wound healing activity

5.6.1 Flower

Catharanthus roseus L (*C. roseus*) has been used to treat a wide assortment of diseases including diabetes. The antimicrobial and wound healing activity of the flower extract of *Catharanthus* in rat was detected. Wound healing activity was determined in rats,

after administration (100 mg kg^{-1} day^{-1}) of the ethanol extract of *C. roseus* flower, using excision, incision and dead space wounds models. The animals were divided into two groups of 6 each in all the models. In the excision model, group 1 animals were topically treated with carboxymethyl cellulose as placebo control and group 2 received topical application of the ethanol extract of *C. roseus* at a dose of 100 mg/kg body weight/day. In an incision and dead space model group 1 animals were given normal saline and group 2 received the extract orally at a dose of 100 mg kg^{-1} day^{-1}. Healing was assessed by the rate of wound contraction, period of epithelization, tensile strength (skin breaking strength), granulation tissue weight, and hydoxyproline content. Antimicrobial activity of the flower extract against four microorganisms was also assessed The extract of *C. roseus* significantly increased the wound breaking strength in the incision wound model compared with controls ($P < 0.001$). The extract-treated wounds were found to epithelialize faster, and the rate of wound contraction was significantly increased in comparison to control wounds ($P < 0.001$), Wet and dry granulation tissue weights, and hydroxyproline content in a dead space wound model increased significantly ($p < 0.05$). *Pseudomonas aeruginosa* and *Staphylococcus aureus* demonstrated sensitivity to *C. roseus.* Increased wound contraction and tensile strength, augmented hydroxyproline content along with antimicrobial activity support the use of *C. roseus* in the topical management of wound healing(Nayak and Pinto Pereira, 2006).

5.6.2 Leaves

Vinca rosea has historically been used to treat a wide assortment of diseases. European herbalists used the plant for conditions as varied as headache to a folk remedy for diabetes. The diabetic wound healing activity of *Vinca rosea* using the excision wound model in a streptozotocin induced diabetic rats.

The diabetic wound healing activity of *Vinca rosea* using the excision wound model in a streptozotocin induced diabetic rats. The animals were weight matched and placed into five groups (n=6 per group). Animals in groups 1 and 2 were normal control (Vaseline) and normal experimental (extract treated) respectively; those in groups 3 and 4 were the diabetic control and diabetic experimental batches. Diabetic animals in a reference group 5 were treated with topical mupirocin ointment. All animals were experimentally wounded on the posterior surface. The ethanol extract of (100 mg kg-1 body weight) was applied to animals of group 2 and 4 for ten days. Wounds were measured on days 1, 5 and 11. granulation tissue formed on the wound was excised on the 11th day and used for the histology and biochemical work up. The wound size in animals of the *Vinca rosea* treated group were significantly reduced ($P<0.001$) when compared with the diabetic control and mupirocin treated animals. Significant increases in the weight of the granulation tissue ($P<0.001$) and the hydroxyproline content ($P<0.001$) were also observed in extract treated animals. Our previous study showed that the ethanol extract of *Vinca rosea* promotes significant wound healing and closure in diabetic rats compared with mupirocin and further evaluation of this activity in humans is suggested(Shivananda Nayak, 2006).

5.7 Radical scavenging activity

The different parts of *Vinca rosea* are studied for their antioxidant and antimicrobial activities against selected bacterial strains. The flower of *Vinca rosea* showed the highest antioxidant activity of 97.44% at 800 µg which was higher than the standard L-ascorbic acid (94%). The view, supports that the medicinal plant might be useful as antioxidant and antimicrobial agents. Experiments were carried out in triplicate, according to the method of Blois (1958) with the slight modification in Briefly, 25 mg/l solution of DPPH radical (Aldrich) in methanol was prepared and then 2 ml of this solution was mixed with different concentration (400, 600 & 800 µg) of sample solution to achieve the final volume of 3 ml.

After 30 min the absorbance was measured at 517 nm. Decrease in the absorbance of the DPPH solution indicates an increase of the DPPH antioxidant activity. It have been reported that all the sparts of *Vinca rosea* showed better radical scavenging activity. ***(Jayakumar et al., 2010)***.

5.8 Antibiogram activity

The antibiogram of different extracts of two varieties of *Catharanthus roseus* (L.) G. Don. "rosea" and "alba". The plant parts, leaves, stems, roots and flowers were separately tested for their antibiogram by using different solvents (methanol, acetone and ethyl acetate). Among the three solvents used for antibiogram, ethyl acetate extracts of different plant parts were found to induce best antibiogram followed by methanol and acetone extracts. Of the two varieties tested, "rosea" had better antibiogram than "alba". Extracts of all parts of both varieties of *C. roseus* like root, stem, leaf and flower found to cause the largest antibiogram towards Bacillus subtilis followed by *Klebsiella sp.* while least antibiogram was observed against Streptococcus sp. The *Staphylococcus aureus* was moderately sensitive to different solvent extracts of the plant The best antibiogram of ethyl acetate could be attributed to high solubility of the active compounds of *Catharanthus* in this solvent compared to other solvents(Sathiya et al., 2008).

5.9 Antihyperglycemic activity

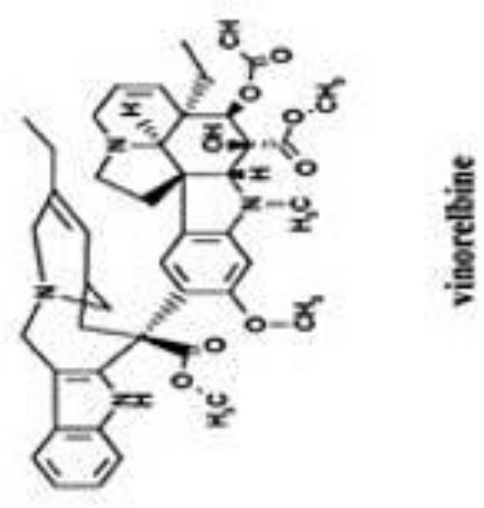
Catharanthus roseus Linn (*Apocynaceae)*, is a traditional medicinal plant used to control diabetes, in various regions of the world. The possible antidiabetic and hypolipidemic effect of *C. roseus* (*Catharanthus roseus*) leaf powder in diabetic rats were evaluated. Diabetes was induced by intraperitoneal injection of streptozotocin (STZ, 55 mg/kg body wt) to male Wistar rats. The animals were divided into four groups: Control, control-treated, diabetic, and diabetic-treated group. Diabetic-treated and control-treated rats were treated with *C. roseus* leaf powder suspension in 2 ml distilled water, orally (100 mg/kg body weight/day/60 days). In diabetic rats (D-group) the plasma glucose was increased and the plasma insulin was decreased gradually. In the diabetic-treated group lowering of plasma glucose and an increase in plasma insulin were observed after 15 days and by the end of the experimental period the plasma glucose had almost reached the normal level, but insulin had not. The significant enhancement in plasma total cholesterol, triglycerides, LDL and VLDL-cholesterol, and the atherogenic index of diabetic rats were normalized in diabetic-treated rats. Decreased hepatic and muscle glycogen content and alterations in the activities of enzymes of glucose metabolism (glycogen phosphorylase, hexokinase, phosphofructokinase, pyruvate kinase, and glucose-6-phosphate dehydrogenase), as observed in the diabetic control rats, were prevented with *C. roseus* administration. *C. roseus* with its antidiabetic and hypolipidemic properties could be a potential herbal medicine in treating diabetes(Karuna Rasineni et al., 2010).

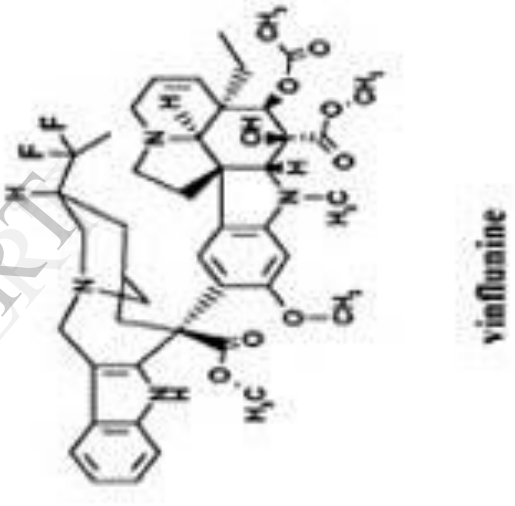
5.10 Cytotoxic activity

Catharanthus roseus well known for being rich in alkaloids was investigated for its cytotoxic activity by using MTT assay against Human Colorectal Carcinoma Cell Line (HCT 116). The preliminary cytotoxicity study demonstrated dose independent cytotoxic activity of the methanol extract of *C. roseus* when screened against HCT-116 colorectal carcinoma cell line. n-hexane, chloroform and methanol fractions also showed dose independent cytotoxic activity with chloroform fraction showing the highest activity. Water fraction showed a minor cytotoxic activity, vindoline also showed some cytotoxic activity at 200 µg mL^{-1}. Catharanthine showed the most promising activity while dose dependent cytotoxic activity of its IC_{50} value was found to be at 60 µg mL^{-1}. Simple and facile method has been developed for the isolation of compounds catharanthine and vindoline from this plant(Pankay Goyal et al., 2008).

5.11 Antitumor activity

Vinflunine, or 20',20'-difluoro-3',4'-dihydrovinorelbine, is a novel *Vinca* alkaloid obtained by hemisyn-thesis using superacidic chemistry. The most impressive structural modification of this vinorelbine derivative was the selective introduction of two fluorine atoms at the 20' position, a part of the molecule previously inaccessible by classic chemistry.
The antitumor activity of vinflunine was evaluated against a range of transplantable murine and human tumors.





Vinflunine exhibited marked activity against murine P388 grafted i.v. when given i.p. in single or multiple doses according to various schedules or in single i.v. or p.o. doses. Increases in life span achieved with vinflunine, as assessed by T/C ratios, ranged from 200% to 457% and proved markedly superior to those of 129±186% obtained with the other *Vinca* alkaloids tested. Against s.c.-implante B16 melanoma, multiple i.p. administration of vinflunine proved active in terms of both survival prolonga- tion and tumor growth inhibition, with optimal T/C values and relative areas under the tumor growth curves (rAUC) being 24% and 36%, respectively. The extent of this activity was superior to that noted for vinorelbine under the same experimental conditions.Drug namely vincristine and vinblastine are produced from *Catharanthus roseus*. More recently extracts from *Catharanthus roseus* have been shown to be effective in the treatment of various kinds of leukemia, skin cancer, lympcancer, breast cancer and Hodgkins disease.

Growth inhibition of human tumor xenografts LX-1 (lung) and MX-1 (breast) was also observed following four weekly i.p.injections of vinflunine as rejected by optimal T/C values of 23% and 26%, respectively, and significant differences in the rAUCs noted for treated versus control animals.

It was also noticeable that vinflunine induced considerably more prolonged inhibitory effects on tumor growth than did vinorelbine. These results demonstrate hat vinflunine is well tolerated and is definitively active against a range of experimental animal tumor models. . Vinflunine activity has been documented in terms of both survival prolongation and tumor growth inhibition, with definite superiority over vinorelbine being shown in each tumor model evaluated(Anna kruczynski et al., 1998).

5.12 Antioxidant activity

The anticancer activity was determined with TS(3-(4,5-dimethylthiazol -2-yl)-5-(3-carboxymethoxyphenyl)-2(4sulfopheyl)-2H-tetrazolium) assay. The antioxidant activity was determined by using *in vitro* assay of 2,diphenyl-1-picrylhydrazyl (DPPH) scavenging activity. *C. roseus* extracts was able to inhibit T47D cell proliferation with IC50 55.2 µg/ml, 26.22 µg/ml. *C.roseus* extracts showed potent antioxidant activity(Wahya widowati et al., 2011).

6. Conclusion

Catharanthus roseus (periwinkle) is an important medicinal plant, mentioned in Ayurveda, an ancient Indian Sanskrit literature. Breast cancer is the most common cancer among women. The betel leaves of madagascar prewinkle (*Catharanthus roseus* [L] G.Don), has been reported to exhibit antioxidant, and antimutation that suggested the chemopreventive potential against various cancer including breast cancer.

The *Catharanthus roseus* have shown a more potent antidiabetic activity, anticancer activity, antioxidant activity and cytotoxic activity. Ethanol extracts of leaves and flowers show highest diabetic wound healing activity. The phytochemical and antimicrobial studies made on *Catharanthus roseus* have shown that it has very important antimicrobial components alkaloids, flavonoids, steroids, phenolics, tannins and saponins.. The methnol, ethanol, acetone and chloroform extracts of these plants have shown antibacterial activity against commonhuman pathogens *Escherichia coli*, *Vibrio cholerae*, *Styphylococcus aureus* and *Streptococcus faecalis*. This review, therefore, has provided some biochemical basis for the ethnomedical use of extracts from *Catharanthus roseus* in the treatment of various diseases and prevention of infections. A rich source of phytochemical in *Catharanthus roseus* can be potential source of useful drugs. The discovery of a potent remedy from plant origin will be a great advancement in bacterial infection therapies.

Out of large number of indole alkaloids of *Catharanthus roseus*, about 20 dimeric indole-dihydroindole alkaloids possess oncolytic activity and among them *Vincristine* and *Vinblastine* are most significant. Other alkaloids reported are vincoside, isovincoside (strictosidine), catharanthine, vindolinine, lochrovicine, vincolidine, ajmalicine (raubasine), reserpine, serpentine, leurosine, lochnerine, tetrahydroalstonine, vindoline, pericalline, perivine, periformyline, perividine, carosine, leurosivine, leurosidine and rovidine. *Vinblastine* contains indole alkaloid part called catharanthine and dihydroindole alkaloid part called vindoline.

The alkaloid contents in different parts show large variations as roots 0.14-1.34%, stem 0.074-0.48%, leaves 0.32-1.16%, flowers 0.005-0.84%, fruits 0.40%, seeds 0.18% and pericarp 1.14%. [11] Dry leaves contain *Vinblastine* (vincaleucoblastine or VLB) 0.00013-0.00063%, and *Vincristine* (leurocristine or LC) 0.0000003-0.0000153% which have anti-cancerous activity. The *Vinca* alkaloids are cell cycle–specific agents, and block cells in mitosis. The vinca alkaloids bind specifically to b-tubulin and block its ability to polymerize with a-tubulin into microtubules. In the absence of an intact mitotic spindle, duplicated chromosomes cannot align along the division plate and cell division is arrested in metaphase. Cells blocked in mitosis undergo changes characteristic of apoptosis. They are used for treatment of leukemias, lymphomas, and testicular cancer. **T**hese results suggest that the plant extracts possess compounds with antimicrobial properties that can be further explored for antimicrobial activity. The antibacterials study of the plant extracts demonstrated that folk medicine can be as effective as modern medicine. The millenarian use of this plant in folk medicine suggests that they represent an economic and safe alternative to treat diseases. This plant could serve as useful sources for new antimicrobial agents. Further studies is needed to isolate the active principle from the plant extracts and to carry out pharmaceutical studies.

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