

# A Study on Potential Phytopharmaceuticals Assets in *Catharanthus roseus* L. (Alba)

Priyanka Tolambiya and Sujata Mathur

Department of Botany, University of Rajasthan, Jaipur, India

Email: ptolambiya@gmail.com

**Abstract**— Herbal medicinal plants are boon for human being as treatment of existing and new diseases are being developed either direct or indirect usage of plants. But availability of such plants and their properties also play an important role. *Catharanthus roseus* is a very important medicinal herb in this direction as availability and its property both are fortunate thing for humankind. This plant is used in treatment of several diseases like diabetes, cancer, high blood pressure, asthma, inflammation, dysentery, brain imbalance, angiogenesis, malaria and other diseases that occur due to potent micro organisms. Though it's a native of Madagascar but it is found most parts of the world. It is also appreciated for its long flowering period throughout the year. Its roots, plant stems and flowers having active constituents to inhibit the growth of disease and other micro organism. Extracts from the dried or wet flowers and leaves of plants are applied as a paste on wounds in some rural communities. The substances vinblastine and vincristine extracted from the plant are used in the treatment of leukemia and Hodgkin's lymphoma. The fresh juice from the flowers of *C. roseus* is used to treat various skin problems e.g. dermatitis, eczema and acne. Therefore, the main active constituents present in this plant are alkaloids, flavonoids, steroids and phenolic acid. As *C. roseus* has mammoth potential to heal many syndrome due to its phytopharmaceuticals assets and it's intact fractions i.e. root, leaf, stem and flower are drug complaint. Still further research is required to find main utility in healing of diseases arises due to deadly viruses.

**Index Terms**— Medicinal plants, *Catharanthus roseus*, Alkaloids, Anti-diabetic, Anti-oxidant, Anti-fungal, Anti-bacterial.

## I. INTRODUCTION

*Catharanthus roseus*, commonly known as the Madagascar periwinkle, is a species of apocynaceae family and endemic to Madagascar. Other English names occasionally used include *Vinca rosea*, *Lochnera rosea*, *Ammocallis rosea*, Cape periwinkle, rose periwinkle, rosy periwinkle and "old-maid".

*Catharanthus* is a genus of flowering plants in the dogbane family, Apocynaceae. Like genus *Vinca*, they are known commonly as periwinkles. There are eight known species. Out of eight, seven are endemic to Madagascar[1]. Though one, *C. roseus*, is widely naturalized around the world[2]. The eighth species, *C. pusillus* is native to India and Sri Lanka. The name

*catharanthus* comes from the Greek for "pure flower" and *roseus* means red, rose, rosy. It rejoices in sun or rain, or the seaside, in good or indifferent soil and often grows wild. It is known as 'Sadabahar' meaning 'always in bloom' and is used for worship. These are perennial herbs (small shrub) with oppositely decussate or almost oppositely arranged leaves. Flowers are usually solitary in the leaf axils. Each has a calyx with five long, narrow lobes and a corolla with a tubular throat and five lobes. It grows to 20-80 cm high and blooms with pink, purple, or white flowers[3]. There are over 100 cultivars of *C. roseus* known [4].

The main active constituents in plants are phenolic acids, flavonoids and alkaloids. These active substances perform a number of protective functions in the human organism and are involved in important anti-oxidative, anti-allergic, antibiotic, hypoglycaemic and anti-carcinogen activities [5] [6] [7]. *Catharanthus roseus* is formerly known as *Vinca rosea* and main source of vinca alkaloids, now sometimes called *catharanthus* alkaloids. These are more than 130 alkaloids[8] including about 100 monoterpenoid indole alkaloids[9]. Vinblastine and vincristine are the dimers, formed by the coupling of Monoindole alkaloids such as catharanthine and vindoline[10] mainly present in aerial part of plants used to treat cancer. Vincristine and vinblastine require both aerial and root parts of a plant to be synthesized [11]. *Catharanthus roseus* as a source of valuable alkaloids resembling those from *Rauwolfia* species. Roots of *Catharanthus* have more ajmalicine (vasodilating) and serpentine (hypertensive) than even *Rauwolfia serpentina*. They also possess reserpine[12][13]. The alkaloids possess hypotensive, sedative and tranquillising properties. The root bark contains the alkaloid Alstonine which has been used traditionally for its calming effect and its ability to reduce blood pressure. Yohimbine (Procomil) is an alkaloid with stimulant and aphrodisiac effects found naturally in *Pausinystalia yohimbine*[14]. *C. roseus* also shows the presence of this compound along with another flavonoid hirsutidin[15]. Prepare decoction of *C. roseus* leaves and drink early in the morning for 7 days its beneficial to diabetes patients.

*Catharanthus roseus* contains significant amounts of volatile and phenolic compounds including caffeoylquinic acids and flavonal glycosides which are known to antioxidant activity. It has a important role in the body defense system that is acts as a antioxidants

against reactive oxygen species (ROS)[16]. *Catharanthus roseus* also possess good antibacterial, antifungal, anti-oxidant, anti-diabetic and antiviral potential [13][17][18].

## II. TAXONOMY

### A. Description

*Catharanthus roseus* is a long-lived (perennial) sub-shrub or herb, usually erect, 30-100 cm high and at least somewhat woody at the base, sometimes sprawling. White latex is present.

Stems are cylindrical (terete), longitudinally ridged or narrowly winged, green or dark red, pubescent at least when young. Leaves opposite, borne on short petioles, 2.5-9.0 cm long, usually elliptical to obovate (egg-shaped in outline but with the narrower end at the base), green with paler veins. The leaf tip is rounded to acute with a tiny point extending from the midrib. Stems and leaves usually with hairs (pubescent), sometimes hairless.

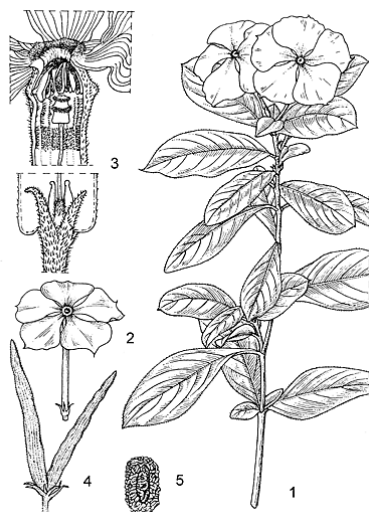


Figure 1. 1, flowering twig; 2, flower; 3, base and top of corolla tube in longitudinal section; 4, fruit; 5, seed.(Source: PROSEA)

Flowers borne in leaf axils; either singly or paired on very short stalks (pedicels). Sepals 5, 2-6 mm long, narrow, usually with hairs (pubescent). Corolla with a long narrow tube and lobes that spread perpendicular to the tube and almost flat.; corolla tube greenish, usually at least 2.2 cm long, with the inside of the mouth often dark pink or sometimes yellow, pubescent inside the throat with rings of stiff hairs below the mouth and anthers; corolla lobes 5, pink to white or pinkish purple, 1.0-2.8 cm long, obovate. Anthers 5, attached to the inside of the corolla tube in the upper portion and concealed within it

The fruit is a follicle, 2.0-4.7 cm long, with numerous small black seeds.

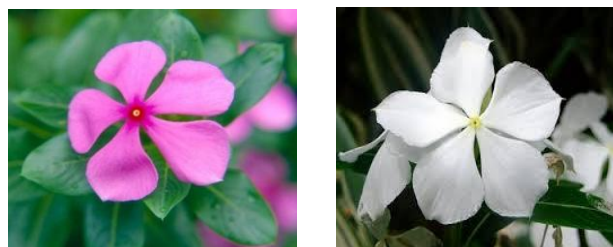
### B. Classification

|                |                            |
|----------------|----------------------------|
| Kingdom        | Plantae                    |
| Phylum         | Magnoliopsida              |
| Class          | Annonidae                  |
| Order          | Gentianales                |
| Family         | Apocynaceae                |
| Genus          | <i>Catharanthus</i>        |
| Species        | <i>roseus</i>              |
| Botanical Name | <i>Catharanthus roseus</i> |

### C. Vernacular names

|             |                        |
|-------------|------------------------|
| Common name | Periwinkle, Vinca      |
| Hindi       | Sadabahar              |
| Malyalam    | ShayamNaari, Usamalari |
| Marathi     | Sadaphuli              |
| Bengali     | Nayantara              |
| Oriya       | Visayan                |
| Punjabi     | Rattanjot              |
| Sanskrit    | Nityakalyani           |
| Tamil       | Sudukattumallikai      |
| Telugu      | Billaganneru.          |
| Kannada     | Kempukesi, Kanigalu    |
| European    | Vinca branca           |
| Spanish     | Vinca rosada           |

There are two major cultivars of *Catharanthus roseus* L., which are distinguishable on the basis of their flower colors, namely 'rosea' (Pink) and 'alba' (White) shown in Fig. 2, are commonly found in India.



(a) rosea (b) alba

Figure 2. Major cultivars of *Catharanthus roseus*

## III. PROPERTIES

### A. Alkaloids

*Catharanthus roseus* has been found to contain as many as 130 constituents with an indole or dihydroindole structure. The principal component is vindoline ( up to

0.5%); other compounds are serpentine, catharanthine, ajmalicine, akuammine, lochnerine, lochnerine and tetrahydroalstonine. Alkaloids present in various part of *Catharanthus roseus* are summarized below:

- **Leaf-** Catharanthine, Vindoline, Vindolidine, Vindolicine, Vindolinine, ibogaine, yohimbine, raubasine, Vinblastine, Vincristine, Leurosine, Lochnerine.
- **Stem-** Leurosine, Lochnerine, Catharanthine, Vindoline.
- **Root-** Ajmalicine, Serpentine, Catharanthine, Vindoline, Leurosine, Lochnerine, Reserpine, Alstonine, Tabersonine, Horhammericine, Lochnericine, echitovenine [19].
- **Flower-** Catharanthine, Vindoline, Leurosine, Lochnerine, Tricin (Flavones).
- **Seeds -** Vingramine, Methylvingramine [20].

The physiologically important and antineoplastic alkaloids, vincristine and vinblastine (Fig. 2), are mainly present in the leaves and antihypertensive alkaloids are found in roots such as ajmalicine, serpentine, and reserpine (2 ref). Vincristine and vinblastine alkaloids are used in the treatment of various types of lymphoma and leukemia (3,4 ref). These *Catharanthus* alkaloids are also used for the treatment of both malignant and non-malignant diseases and in platelet and platelet associated disorders.

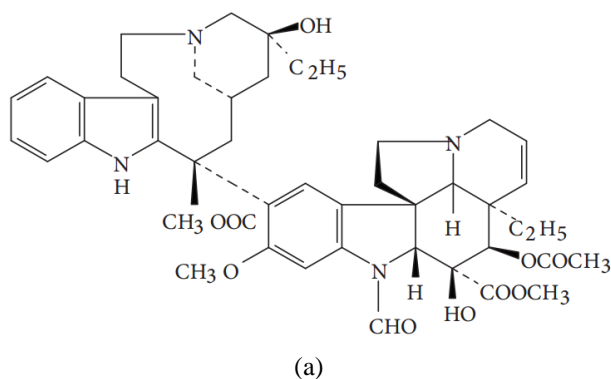


Figure 3. Structure formulae of vincristine (a) and vinblastine (b) in *Catharanthus roseus* L.

#### IV. USES

A decoction of all parts of *Catharanthus roseus* is well known is well known as an oral hypoglycaemic agent. The decoction is also taken to treat

#### B. Traditional

In traditional medicine, *Catharanthus roseus* has been used to treat a variety of ailments in Madagascar as well as in other parts of the world where the plant has naturalized. Folk Remedies and Traditional Uses of *Catharanthus roseus* are summarized below:

- In India, the juice from the leaves is used to treat wasp sting with [21]
- In Hawai'i extract of boiled plant is used to arrest bleeding[21]
- In Cuba and Jamaica- Flower extract is used for eye wash in infants<sup>[21]</sup>.
- In Africa- Leaves are used for menorrhagia and rheumatism. (Dobelis, 1997; Walts, 2004)[21]
- In Philippines-Decoction of leaves is used in diabetes and decoction of young leaves is used in stomach cramps, root decoction is used for intestinal parasitism. Infusion of leaves is used for treating menorrhagia. Crude leaf extracts and root has anti cancer activity. Roots used for dysentery[22].
- In Madagascar- The bitter and astringent leaves are used as vomitive, roots used as purgative, vermifugl, depurative, hemostatic and toothache remedies[22].
- In Mauritius- The juice of leaves is used for indigestion and dyspepsia[22].
- In West Indies and Nigeria- The plant is used in diabetes[22].
- In Bahamas- Decoction of flower is used in asthma, tuberculosis and flautlence[22].
- In Malaysia- The plant is used in diabetes, hypertension, insomnia and cancer[22].
- In America- Gargle of plant is used to ease soarthroats, chest ailments and laryngitis[22].

#### C. Modern

Whilst researching the anti-diabetic properties of the plant in the 1950s, scientists discovered the presence of several highly toxic alkaloids in its tissues.

These alkaloids are now used in the treatment of a number of different types of cancer, with one derived compound, called vincristine, having been credited with raising the survival rate in childhood leukaemia from less than 10% in 1960 to over 90% today. Brief summary of *Catharanthus roseus*'s therapeutic properties are presented in Table I.

TABLE I. THERAPEUTIC PROPERTIES *CATHARANTHUS ROSEUS*

| S. No. | Therapeutic Properties | Plant parts and methods used  | Doses               | Organism   | References |
|--------|------------------------|---|---------------------|--|------------|
| 1.     | Anti-diabetic activity | Dichloromethane: methanol extract (1:1) of leaves and twigs                             | 500mg/kg            | streptozotocin (STZ) induced diabetic rat model. | 23,24,25   |
| 2.     | Anti-oxidant activity  | Methanolic leaf extract , Dichloromethane extract (DE), Ethanolic extracts of the roots | 12.5and 25.0 µg/mL. | β-TC6 cells                                      | 6,26       |
| 3.     | Hypolipidemic Activity | Leaf juice of <i>Catharanthus roseus</i> , Aqueous extract of leaves.                   | -                   | Guinea Pigs, Alloxan induced diabetic rats.      | 22,27      |

|     |                             |  |                             |  |              |
|-----|-----------------------------|--|-----------------------------|--|--------------|
| 4.  | Wound Healing Activity      | Methanolic extract of <i>C. roseus</i> leaf  | 200 and 400 mg/kg           | Streptozotocin-induced diabetic Mice   | 28,29        |
| 5.  | Cytotoxic activity          | Methanolic extract   | -                           | HCT-116 colorectal carcinoma cell  | 30           |
| 6.  | Antifungal activity         | Different extract (acetone, methanol, ethanol), Ethanol leaf extract                                   | -                           | <i>Aspergillus niger</i> , <i>Candida albicans</i> , <i>Penicillium chrysogenum</i>  | 31,32, 33    |
| 7.  | Antibacterial activity      | Different extract (acetone, methanol, ethanol), Ethanol leaf extract                                   | -                           | <i>Staphylococcus aureus</i> , <i>E.coli</i> , <i>Klebsiella oxytoca</i> , <i>Klebsiella pneumonia</i> , <i>Pseudomonas aeruginosa</i> , | 31,32,33     |
| 8.  | Antidiarrheal activity      | Ethanol leaf extract   | 200 and 500 mg/kg           | Wistar rat   | 17,32        |
| 9.  | Hypoglycemic activity       | Aqueous extract of flowers, leaves, roots, and stems   | 250 mg/kg                   | Healthy and alloxan diabetic mice  | 34           |
| 10. | Anti-hyperglycemic activity | Leaf powder, leaf dichloromethane: methanol (1:1) Extracts   | 55mg/kg, 500 mg/body weight | Streptozotocin-induced diabetic rats, normal and Alloxan induced diabetic rats.  | 23,27,35,    |
| 11. | Anticancer activity         | Ethanol, Methanol and Aqueous Extract of leaves, stem, root, aerial part of <i>Catharanthus roseus</i> | 50 and 100 mg/kg            | MCF (breast cancer) cell lines, Jurkat, HCT-116, 9KB,P-338 cell lines  | 36,37, 38,39 |
| 12. | Anti-helminthic activity    | Ethanol extract of <i>Catharanthus roseus</i> (Whole plant)  | 250 mg/ml                   | <i>Pheretima posthuma</i>  | 16,40        |
| 13. | Antiviral activity          | Selected <i>Catharanthus</i> alkaloids.  | -                           | vaccinia and polio type III viruses.   | 41           |

#### V. CATHARANTHUS ROSEUS IN DIABETIC TREATMENTS

Diabetes mellitus is a disease common in all parts of the world. The use of insulin and control achieved over the disease are of comparatively recent origin when one takes into account the long history of this disease. The problem of drug intolerance, hypersensitivity and resistance to insulin makes it all the more important to search for safe, effective and cheaper remedies. Even before the advent of modern medicine, man has been using various forms of plant therapy to fight this disease. *C. roseus* has been traditionally used for diabetes. Recent studies have shown that *C. roseus* has significant anti-diabetic activity. Leaf extract of *C. roseus* reportedly lowered blood sugar in STZ-diabetic rats[42]. Hypoglycemic activity has also been reported for dichloromethane-methanol extract of stems and twigs of the plant in STZ-diabetic rats[24]. The extract reportedly improved enzymic activities of glycogen synthase, glucose 6-phosphate dehydrogenase, succinate dehydrogenase and malate dehydrogenase in liver of diabetic animals. Juice of fresh leaves of the plant was observed to reduce blood glucose in normal and alloxan diabetic rabbit[43]. Extract of the plant also stimulated glucose utilization in hepatocytes[44]. Ethanol extract of the plant lowered blood glucose levels in oral glucose tolerance tests in glucose induced hyperglycemic rats[45]. Antihyperglycemic activity has been reported following administration of leaf powder in STZ-diabetic rats[46]. Inhibition of aldose reductase (a key enzyme in cataractogenesis) as well as free radical scavenging activity was reported for the plant extract, suggesting that administration of the extract can delay diabetes-induced cataract formation[47]. Also some studies have shown that *C. roseus* is effective in both insulin dependent and non-insulin dependent diabetes (Table II).

TABLE II. CATHARANTHUS ROSEUS IN DIABETES

| Type of use                             | Symptoms  | Plant part used and method  |
|---|---|---|
| Insulin dependent Diabetes mellitus     | Disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action or both | Aqueous Extracts from <i>Catharanthus roseus</i> leaf, stem, root, flower / Whole plant |
| Non-insulin dependent Diabetes mellitus | Insulin resistance (Gita Bisla <i>et al.</i> ,2013)[13]   | Aqueous Extracts from <i>Catharanthus roseus</i> leaf                                   |

#### VI. CONCLUSION AND FUTURE WORK

The leaf juice or water decoction of *Catharanthus roseus* L. (Apocyanaceae) is used as a folk medicine for the treatment of diabetes all over the world. In continuation to this its other parts like root, stem & flower have active components like alkaloid, flavonoids, steroids and phenolic acids which effectively make it in usage as antimicrobial, anti diabetic, anti- syndrome, anti-oxidant. The above study reveals that *C. roseus* has a potential Phytopharmaceuticals assets and further more research is required to find out its actual responsible component, so that its main utility can be used in healing of diseases arising due to death.

#### REFERENCES

- [1] G. Brun, J.M. Bessière, M.G. Dijoux-Franca, A.M. David and B. Mariotte, "Volatile Components of *Catharanthus roseus* (L.) G. Don (Apocynaceae)," *Flavour Fragr. J.* vol. 16(2):116-119, 2001.
- [2] S. Rahmatzadeh & S. K. Kazemitabar, "Biochemical and antioxidant changes in regenerated periwinkle plantlets due to mycorrhizal colonization during acclimatization," *JACS*, vol. 5, no 14, pp.1535-1540, 2013.
- [3] A. Swanberg & W. Dai, "Plant Regeneration of Periwinkle (*Catharanthus roseus*) via Organogenesis," *HortScience*. vol.43( 3):832-836, 2008.
- [4] C. Ku, W.C. Chung, L.L. Chen & C.H. Kuo, "The Complete Plastid Genome Sequence of Madagascar Periwinkle *Catharanthus roseus* (L.) G. Don: Plastid Genome Evolution,

- Molecular Marker Identification and Phylogenetic Implications in Asterids," *PLOS ONE*, vol. 8, no. 6, pp. 1-11, 2013.
- [5] S.M. Stanković, M. Topuzović, S. Solujić and V. Mihailović, "Antioxidant activity and concentration of phenols and flavonoids in the whole plant and plant parts of *Teucrium chamaedrys* L. var. *glanduliferum* Haussk.," *J Med Plant Res* 4:2092-2098, 2010.
- [6] S.M. Stanković, G.M. Ćurčić, B.J. Žižić, D.M. Topuzović, R.S. Solujić and D.S. Marković, "Teucrium plant species as natural sources of novel anticancer compounds: antiproliferative, proapoptotic and antioxidant properties," *Int J Mol Sci* 12:4190-4205, 2011.
- [7] S.M. Stanković, N. Nićiforović, V. Mihailović, M. Topuzović and S. Solujić, "Antioxidant activity, total phenolic content and flavonoid concentrations of different plant parts of *Teucrium polium* L. subsp. *Polium*," *Acta Soc Bot Pol* 81:117-122, 2012.
- [8] R. Van Der Heijden, D.I. Jacobs, W. Snoeijer, D. Hallard and R. Verpoorte, "The *Catharanthus* alkaloids: pharmacognosy and biotechnology," *Curr Med Chem*.11(5): 607-28, 2004.
- [9] N. Rasool, K. Rizwan, M. Zubair, K. Naveed and V. Ahmed, "Antioxidant potential of different extracts and fractions of *Catharanthus roseus* shoots," *International Journal of Phytomedicine* vol 3:108-114, 2011.
- [10] K. Meenakshi, S. L. Neha., C. amesh and C. Sheela, "Catharanthus roseus and Prospects of its Endophytes: A New Avenue for Production of Bioactive Metabolites," *IJPSR*. Vol. 4(7): 2705-2716, 2013.
- [11] V. De Luca, P. Laflamme, "The expanding universe of alkaloid biosynthesis," *Curr Opin Plant Biol* 4 :225-233, 2001.
- [12] P. Mishra, G.C. Uniyal & S. Sharma, "Pattern of diversity for morphological and alkaloid yield related trades among the periwinkle *Catharanthus roseus* accessions collected from in and around Indian Subcontinent," *Genetic Research in Crop Evolutio*.vol. 48:273-286, 2001.
- [13] S Pandey-Rai, GR Mallavarapu, AA Naqvi, A Yadav, SK Rai, S Srivastava, et al., "Volatile components of leaves and flowers of periwinkle *Catharanthus roseus* (L.) G. Don from New Delhi," *Flavour Fragr.*,vol.21,no. 3,pp. 427-430, 2001.
- [14] M. J. Millon, T.A. Newman, V. Audinot, D. Cussac, F. Lejeune, J.P. Nicolas, et al. "Agonist and antagonist actions of Yohimbine as compared to fluparoxan at alpha (2)-adrenergic receptors (AR)," *Synapse*, 35:79-95, 2002.
- [15] A. Piovan, and R. Fillipini, "Anthocyanins in *Catharanthus roseus* in vivo and in vitro: A review," *Phytochem. Rev.* 6: 235-242, 2007.
- [16] K. Kabesh, P. Senthilkumar, R. Ragunathan and R. Raj Kumar, "Phytochemical analysis of *Catharanthus roseus* Plant Extract and its Antimicrobial Activity," *Int. J. Pure App. Biosci.* 3(2): 162-172, 2015.
- [17] S. Gajalakshmi, S. Vijayalakshmi & R.V. Devi, "Pharmacological activities of *Catharanthus roseus*: A perspective review," *Int J Pharma Sci.* 4(2): 431 - 439, 2013.
- [18] A. Marcone, E. Ragozzino & E. Seemuller, "Dodder transmission of alder yellows phytoplasma to the experimental host *Catharanthus roseus* (periwinkle)," *Forest Pathology*.vol. 27(6):347-350, 1997.
- [19] J.V. Shanks, R. Bhadra, J. Morgan, S. Rijhwani, S. Vani, "Quantification of metabolites in the indole alkaloid pathways of *Catharanthus roseus*: implications for metabolic engineering," *Biotechnol Bioeng.*58:333-338, 1998.
- [20] A. Jossang, P. Fodor, B. Bodo, "A new structural class of bisindole alkaloids from the seeds of *Catharanthus roseus*: vingarimine and methylvingarimine," *J Org Chem* 63:7162-7167,1998.
- [21] V. De Luca, P. Laflamme, "The expanding universe of alkaloid biosynthesis," *Curr Opin Plant Biol* 4 :225-233, 2001.
- [22] L. Muralidharan, "Catharanthus roseus Leaves as Antidiabetic and Hypolipidemic Agents in Alloxan- Induced Diabetic Rats," *American Journal of Phytomedicine and Clinical Therapeutics*, [2][12]:1393-1396, 2014.
- [23] G. Bisla, S. Choudhary, E. Singh and V. Chaudhary, "Hyperglycemia and hyperlipidemia mitigating impact of *Catharanthus roseus* (Sadabahar) leaves aqueous extract on type2 diabetes mellitus subjects," *Asian Journal of Plant Science and Research*. vol.3(4):170-174, 2013.
- [24] S.N. Singh, P. Vats, S. Suri, R. Shyam, M.M.Kumria, S. Ranganathan, et al., "Effect of an anti-diabetic extract of *Catharanthus roseus* on enzymic activities in streptozotocin induced diabetic rats," *J Ethnopharmacol.*76(3) : 269-77, 2001.
- [25] S.N. Singh, P. Vats, S. Suri, R. Shyam, M.M.L. Kumria, S. Ranganathan and K. Sridharan, "Effect of an antidiabetic extract of *Catharanthus roseus* on enzymic activities in streptozotocin induced diabetic rats," *Journal of Ethnopharmacology*. 76: 269-277, 2007.
- [26] M.A.Bhutkar, S.B. Bhise, "Comparative Studies on Antioxidant Properties of *Catharanthus rosea* and *Catharanthus alba*," *International Journal of PharmTech Research*.vol.3(3):1551-1556, 2011.
- [27] M. Jayanthi, N. Sowbala, G. Rajalakshmi, U. Kanagavalli and V.Sivakumar, "Study of Anti- hyperglycemic effect of *Catharanthus roseus* in Alloxan induced Diabetic Rats," *International Journal of Pharmacy and Pharmaceutical Sciences*. vol. 2(4):114-116, 2010.
- [28] A. Singh, P.K. Singh and R.K. Singh, "Antidiabetic and Wound Healing Activity of *Catharanthus roseus* L. in Streptozotocin - Induced Diabetic Mice," *American Journal of Phytomedicine and Clinical Therapeutics*. 2(6):686-692, 2014.
- [29] M. Favali, R. Muestti, S. Benvenuti, A. Bianchi & L. Pressacco, "Catharanthus roseus L. plants and explants infected with phytoplasmas: Alkaloid production and structural observations," *Protoplasma*, vol. 223, no. 1 pp.45-51, 2014.
- [30] M. Siddiqui, Z. Ismail, A. Aisha, A. Majid, "Cytotoxic activity of *Catharanthus roseus* (Apocynaceae) crude extracts and pure compounds against Human Colorectal Carcinoma Cell Line," *International Journal of Pharmacology*. 6(1):43-47, 2010.
- [31] A. Khalil, "Antimicrobial Activity of Ethanol Leaf Extracts of *Catharanthus roseus* from Saudi Arabia. 2nd International Conference on Environment Science and Biotechnology," *IPCBE*. V48. 2, 2012.
- [32] K. Hassan, A. Brenda, V. Patrick and O. Patrick, "In vivo antidiarrheal activity of the ethanolic leaf extract of *Catharanthus roseus* Linn. (Apocyanaceae) in Wistar rats," *African Journal of Pharmacy and Pharmacology* Vol 5(15) : 1797-1800, 2011.
- [33] S. Balaabirami and S. Patharajan, "In vitro antimicrobial and antifungal activity of *Catharanthus roseus* leaves extract against important pathogenic organisms," *International Journal of Pharmacy and Pharmaceutical Sciences*.vol 4(3) : 487-490, 2012.
- [34] E. Vega-Ávila, J.L. Cano-Velasco, F.J. Alarcón-Aguilar, M.C. Fajardo Ortíz, J.C. Almanza-Pérez and R. Román-Ramos, "Hypoglycemic Activity of Aqueous Extracts from *Catharanthus roseus*. Evidence-Based Complementary and Alternative Medicine," Article ID 934258,7 pages doi:10.1155/2012/934258, 2012.
- [35] K. Rasineni, R. Bellamkonda, S. Reddy, S. Desireddy, "Antihyperglycemic activity of *Catharanthus roseus* leaf powder in streptozotocin-induced diabetic rats," *Pharmacognosy Res.* 2(3): 195-201, 2010.
- [36] N.H. Ahmad, R.A. Rahim and I. Mat, "Catharanthus roseus aqueous extract is cytotoxic to Jurkat leukemic T-cells but induces the proliferation of normal peripheral blood mononuclear cells" *Tropical Life Sciences Research*, 21(2):101 - 113, 2010.
- [37] S. Mukhapadhyay and G.A. Cordell, "Catharanthus alkaloid XXXVI isolation of vinca leukoblastine (VLB) and performyline from *Catharanthus trichophyllus* and pericyclivine from *Catharanthus roseus*," *J Nat Prod.*44: 335-339, 1981.
- [38] R.S. Ruskin, S.R. Aruna., "In-vitro and In-vivo Antitumor Activity of *Catharanthus roseus*," *Int. Res J Pharm. App Sci.* 4(6):1-4, 2014.
- [39] W. Widowati, T. Mozef, C. Risdian and Y. Yellinaty, "Anticancer and free radical scavenging potency of *Catharanthus roseus*, *Dentrophloe petandra*, *Piper betle* and *Curcuma mangga* extracts in breast cancer cell lines," *Oxid Antioxid Med Sci.* 2(2):137-140, 2013.
- [40] H. Hoskeri, S. Agarwal, S. Jacob, N. Chettri, S. Bisoyi, A. Tazeen, et al., "In-vitro Antihelminthic Activity of *Catharanthus roseus* Extract," *International Journal of Pharmaceutical Sciences and Drug Research*. 3(3) : 211-213, 2011.
- [41] N.R. Farnsworth, G.H. Svoboda and R.N. Blomster, "Antiviral activity of selected *Catharanthus* alkaloids," *J.Pharmacol. Sci.* 57(12) : 2174-2175.

- [42] R.R. Chattopadhyay, "A comparative evaluation of some blood sugar lowering agents of plant origin," *Journal of Ethnopharmacology* 67:367–372, 1999.
- [43] S. Nammi, M.K. Boini, S.D. Lodagala, and R.S. Behara, "The juice of fresh leaves of *Catharanthus roseus* Linn. reduces blood glucose in normal and alloxan diabetic rabbits," *BMC Complementary and Alternative Medicine*. 3(4):-6882-6884.
- [44] M.V. Venter, S. Roux, L.C. Bungu, J. Louw, N.R. Crouch, O.M. Grace, et al., "Antidiabetic screening and scoring of 11 plants traditionally used in South Africa," *Journal of Ethnopharmacology*, 119:81–86, 2008.
- [45] M.A. Islam, M.A. Akhtar, M.R. Khan, M.S. Hossain, A.H. Alam, M.I. Ibne-Wahed, et al., "Oral glucose tolerance test (OGTT) in normal control and glucose induced hyperglycemic rats with *Coccinia cordifolia* L. and *Catharanthus roseus* L.," *Pakistan Journal of Pharmaceutical Sciences*. 22:402–404, 2009.
- [46] K. Rasineni, R. Bellamkonda, S.R. Singareddy, S. Desireddy, "Antihyperglycemic activity of *Catharanthus roseus* leaf powder in streptozotocin-induced diabetic rats," *Pharmacognosy Research*.;2:195–201, 2010.
- [47] R.N. Gacche, N.A. Dhole, "Profile of aldose reductase inhibition, anti-cataract and free radical scavenging activity of selected medicinal plants: an attempt to standardize the botanicals for amelioration of diabetes complications," *Food and Chemical Toxicology*. 49:1806–1813, 2011.