

## ETHNOPHARMACOLOGICAL UPDATE ON *CATHARANTHUS ROSEUS*.L

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### ABSTRACT

Natural products of plants origin have been used and are being used throughout the world for human and animal health care. Alternatively, global attention has been shifted towards hunting novel bio-molecules of plant origin for the development of new drugs. Since, the phytochemicals are more specific, biodegradable and are supposed to have fewer side effects. Phytochemicals offer unique platform for structural diversity and biological functionality which is indispensable for drug discovery. Based on the thrive search of a phytochemical, it is found *Catharanthus roseus* with potent medicinal plant with many pharmacological action and can be a drug of choice for many fatal

disease. In this review, an attempt has been made to summarize the pharmacological effect of the above plant against various disease starting from the antimicrobial to that of the antineoplastic diseases in a precise way to help the scientist and learners to understand the conversion of phytochemical as drug.

**KEYWORDS:** *Catharanthus roseus*, drug discovery, target, characteristics, medicinal value.

### INTRODUCTION

Emerging and re-emerging infectious diseases and spread of deadly drug resistant strains pose a challenge to public health care services. In particular, emergence of resistance to antibiotics has hampered the pace by which newer antibiotics are being introduced into the public domain(A. D. Russell,2002). However, because of inappropriate use of antibiotics in

human and veterinary medicines, certain strains of bacteria and fungi developed the ability to produce substances which block the action of antibiotic and change their target or ability to penetrate. This drives the discovery of novel antimicrobial therapeutic agents from the medicinal herbs (T. D. Gootz,1990). Despite ever increasing advancement in the field of medicine and molecular diagnosis, it is estimated that 80% of the world population is still dependent on the plant derived pharmaceuticals. WHO report depicts that plant based products or its derivatives accounts for nearly 28% of drugs available in the market (D.J. Newman, 2003). A large proportion of plant based compounds are used as lead molecules in drug discovery to produce synthetic molecular analogs that have similar skeletons yet intricate structures. This implicates that phytochemicals play a critical role in diversity oriented synthesis (DOS) of natural product-like pharma-compounds(L.A. Marcaurelle,2008) Green plants synthesize and preserve a variety of biochemical products, many of which are extractable and used as chemical feed stocks or as a raw material for various scientific investigation. Many secondary metabolites of plants are commercially found and used in a number of pharmaceutical compounds. Plant extracts contain many chemical compound which are biologically active in the human body. For centuries, human had used plants and plant extracts to treat various disease conditions and more recently to produce new drugs. Most of the plants can provide biologically active molecules that are inevitable for the sustenance of life. (Anju and Oommen, 2015)

### MEDICINAL PLANTS

Plants which have one or more of its organ containing substances that can be used for the therapeutic purpose, are called medicinal plants. Sofowara(1993). Several phytochemical surveys have been published, including the random sampling approach which involved some plant accessions collected from all parts of the world. The major chemical substances of interest in these surveys have been the alkaloids and steroidal sapogenins (saponins) however, other diverse groups of naturally occurring phytochemicals such as flavonoids, tannins, unsaturated sterols, triterpenoids, essential oils etc. also have been reported Farnsworth (1966). Phytochemical are very important in medicine and constitute most of the valuable drugs. Alkaloids are rich in medicine and constitute most of the valuable drugs. They have physiological effect on animals. Edeoga et al., (2001). Laily et.al. (2002) worked out a preliminary phytochemical survey of plants in crocker range ,Sabbah Malaysia.Choudhary et al., (2009) observed the studies on leaf epidermal micromorphology, wood element character and phytochemical screening of three medicinally important taxa of

the family *Convolvulaceae* Farhat Ali Khan *et.al*, (2011) observed the phytochemical screening of some Pakistanian Medicinal Plants. Sudipa *et al.*, (2013) observed the phytochemical analysis of methanolic extracts of leaves some medicinal plants and Chandrashekar *et al.*, (2012) observed the phytochemical analysis of ethanolic extracts of leaves of *Clerodendrum viscosum*.

### *Catharanthus roseus*

*Catharanthus roseus* natively called as 'Periwinkle' in English is a common ornamental plant grown in the gardens of residential and official compounds. *Catharanthus roseus* native of South-eastern and eastern Madagascar found growing as wild plant species in rain forest. (Dr. Arvind Singh). There are eight known species. Out of eight, seven are endemic to Madagascar (Brun *et al.*, 2001). Though one, *C. roseus*, is widely naturalized around the world (Pandey-Rai *et al.*, 2006, Rahmatzadeh & Kazemitabar, 2013). 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 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 (Swanberg & Dai 2008). There are over 100 cultivars of *C. roseus* known (Ku *et al.*, 2013).

### GEOGRAPHICAL DISTRIBUTION

*Catharanthus roseus* is native to the Indian Ocean Island of Madagascar. In the wild, it is found to be an endangered plant and the main cause of their decline is the habitat destruction by the slash and burn agriculture however, it is now common in many tropical and subtropical regions worldwide, including the Southern United states. (Santhosh *et al.*, 2015)

### SCIENTIFIC CLASSIFICATION

Botanical Name(s): *Vinca Rosea* (*Catharanthus roseus*)

Family Name: Apocynaceae

Kingdom: Plantae

Division: Magnoliophyta (Flowering plants)

Class: Magnoliopsida (Dicotyledons)

Order: Gentianales

Family: Apocynaceae

Genus: Catharanthus

Species: C. roseus

### VERNACULAR NAMES

English	- cayenne jasmine, old maid, periwinkle
Hindi	-sada bahar, sada bahar
Kannada	-batlahoo, bilikaasi kanigalu, ganeshana hoo, kempu kaasi kanigalu
Malayalam	-banappuvu, nityakalyani, shavanari, usamalari
Marathi	-sadaphool, sadaphul, sadaphuli
Sanskrit	-nityakalyani, rasna, sadampuspa, sadapushpi
Tamil	-cutkattumalli, cutukattumalli, cutukattuppu
Telugu	-billaganneru
Gujarati	-Barmasi
Bengali	-noyontara

### MORPHOLOGY

*Catharanthus roseus* roseus is an evergreen subherb or herbaceous plant growing to 1 m. tall. The leaves are oval to oblong, 2.5- 9.0 cm. long and 1- 3.5 cm. broad glossy green hairless with a pale midrib and a short petiole about 1- 1.8 cm. long and they are arranged in the opposite pairs. The flowers are white to dark pink with a dark red centre, with a basal tube about 2.5- 3 cm. long and a corolla about 2-5 cm. diameter with five petal like lobes. The fruit is a pair of follicles about 2-4 cm. long and 3 mm broad. (Santhosh et al., 2015)

### CHARACTERISTICS

Plant tissues are composed of various cell types with unique sizes, shapes, and biological functions that play different roles in normal plant growth, development, and reproduction. Each of these different roles calls for a different complement of proteins produced in each cell type. Among these cell types, the epidermis, composed of epidermal cells, trichomes, and guard cells, constitutes the surface layer of the plant that is directly exposed to the outside environment. The leaf epidermis usually constitutes a single layer of cells that serves as a protective barrier to environmental factors (i.e., UV light, water loss, herbivory, and pathogen attack). Similarly, the leaf epidermis also has specialized cells, such as glandular trichomes, that possess highly specialized systems for biosynthesis, secretion, and/or accumulation of toxic phytochemicals to defend plants against insects and pathogens. By contrast, guard cells

are the important physical openings that control gas exchange between the plant tissue and the atmosphere. In underground plant parts, the root epidermis is involved in water uptake from soil, where these cells also encounter a variety of microorganisms in the rhizosphere. (Jun Murata *et al.*, 2008)

### CULTIVATION

*C. roseus* is best grown as an annual bedding plant in well drained sandy loams in full sun to part shade. Needs regular moisture, but avoid overhead watering. Superior soil drainage is the key to growing this annual well. Starts seeds indoors 12-16 weeks before last frost date. Thrives in hot and humid summer weather. Cutting may be taken from plants in late summer for overwintering so as to provide a stock the following spring. Container plants may be overwintered indoors. May self-seed in optimum growing conditions. Numerous cultivators have been selected for variation in flower colour (white, mauve, peach, scarlet and reddish orange) and also for tolerance of cooler growing condition in temperate regions. (Monika, Vandana, 2013)

### PHYTOCONSTITUENTS

The solvent extracts of different plants were subjected to preliminary phytochemical screening to identify the chemical constituents (Singh, Thalwal, 2013)

**Potentially Active Chemical Constituents-** *C. roseus* possess carbohydrate, flavonoid, saponin and alkaloids. Alkaloids are the most potentially active chemical constituents of *Catharanthus roseus*. More than 400 alkaloids are present in the plant, which are used as pharmaceuticals, agrochemicals, flavor and fragrance, ingredients, food additives and pesticides. The alkaloids like actineo plastidemic, Vinblastine, Vincristine, Vindesine, Vindeline Tabersonine etc. are mainly present in aerial parts whereas ajmalicine, vinceine, vineamine, raubasin, reserpine, catharanthine, etc. are present in roots and basal stem. Rosindin is an anthocyanin pigment found in the flower of *C. roseus* (Monika, Vandana, 2013)

### MEDICINAL IMPORTANCE OF *Catharanthus roseus*

*Catharanthus roseus* is a tropical plant used for medicinal purpose. The plant contains 2 types of active compound such as alkaloid and tannins. The plant contains reserpine. The plant has a long history of use as medicine in Ayurveda and Unani. The whole plant possesses medicinal properties. Followings are some medicinal properties of *Catharanthus*:

- It decreases blood pressure and reduces excitement.
- It is also proved anti-diabetic.
- It is used as an anticancer agent. It is most effective for the treatment of lung cancer.
- It is used for the treatment of Leukaemia.
- It has antibacterial and antiviral property.
- The plant extract is useful for the treatment of dysentery and diarrhoea.
- It is also anti-inflammatory in nature.
- The medicine prepared from the alkaloid of this plant is used for the treatment of Hodgkin's lymphoma in children.
- The flower petals and seeds have antioxidant property.
- It cures various skin diseases such as acne, eczema and dermatitis.
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(ANOOP, 2015)

### **Antimicrobial**

*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 anti-microbial drugs. Plants have proved to be significant natural resources for effective chemotherapeutic agents and offering a broad spectrum of activity with greater emphasis on preventive action. This study aims to investigate some of the anti-microbial properties of this plant. 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, and *Staphylococcus aureus* NCIM 5021. The findings show that the extracts from the leaves of

this plant can be used as prophylactic agent in many of the diseases, which sometime are of the magnitude of an epidemic. (Prajakta, 2010)

### **Antidiabetic**

Most reports on antidiabetic activity of this plant have been conducted using crude extracts rather than the pure bioactive compounds. Chattopadhyay and Singh *et al.* concluded that the extract of this plant exhibited hypoglycemic activity in a streptozotocin induced diabetic rat model. Ferreres *et al.* reported the scavenging ability for the aqueous leaves extract of this plant against DPPH (IC<sub>50</sub> at 447 µg/mL), superoxide and nitric oxide radicals.

The ethanolic extracts of the leaves and flower of *C. roseus* showed a dose dependent lowering of blood sugar in comparable to the standard drug. Lowering of blood sugar in comparable to the standard drug gliben clamide. The Hypo glycemic effect has appeared due to the result of the increase glucose utilization in the liver.

### **Anti-oxidant property**

The anti oxidant potential of the ethanolic extract of the roots of the two varieties of *C.roseus* namely rosea (pink flower) and alba (white flower) was obtained by using different system of assay such as Hydroxyl radical scavenging activity, superoxide radical-scavenging activity, DPPH radical- scavenging activity and nitric oxide radical inhibition method. The result obtained proved that the ethanolic extract of the roots of Periwinkle varieties has exhibited the satisfactory scavenging effect in the entire assay in a concentration dependent manner but *C.roseus* was found to possess more antioxidant activity than that of *C.alba*. (Alba, 2011)

### **Anticancerous**

The anticancer alkaloids Vinblastine and Vincristine are derived from stem and leaf of *Catharanthus roseus*. These alkaloids have growth inhibition effect to some human tumors. Vinblastine is used experimentally for treatment of neoplasmas and is recommended for Hodgkin's disease, chorio carcinoma. Vincristine another alkaloids is used for leukemia in children. Vinblastine is sold as Velban or Vincristine as oncovin.

### **Anti helminthic property**

Helminthes infections are the chronic illness, affecting human beings and cattle. *Catharanthus roseus* was found to be used from the traditional period as an anti-helminthic agent. (Vandana Sharma *et al.*, 2013) ethanolic extract of the concentration of 250 mg/ml was

found to show the significant anti helminthic activity. *Pherithemapostuma* as an experimental model and with Piperazine citrate as the standard reference.

#### **Anti-ulcer property**

Vincamine and Vindoline alkaloids of the plant showed anti-ulcer property.

#### **Hypotensive property**

Extract of leaves of the plant made significant change in hypotensive.

#### **Anti-diarrheal property**

The anti-diarrheal activity of the plant ethanolic leaf extracts was tested in the wistar rats with castor oil as a experimental diarrhea inducing agent in addition to the pre-treatment of the extract. The anti-diarrheal effect of ethanolic extracts *C.roseus* showed the dose dependant inhibition of the castor oil induced diarrhea.

#### **Phyto remediation**

Exposed *C. roseus* bio-accumulates heavy metal like cd etc., so it is used in phyto remediation.

#### **Folkloric uses**

In India- The juice of leaves is used as application to bee sting/ wasp sting.

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.

In Madagascar- The bitter and astringent leaves are used as vomitive, roots used as purgative, vermifugl, depurative, hemostatic and toothache remedies.

In Mauritius- The juice of leaves is used for indigestion and dyspepsia.

In West Indies and Nigeria- The plant is used in diabetes.

In Cuba and Jamaica- Flower extract is used for eye wash in infants.

In Bahamas- Decoction of flower is used in asthma, tuberculosis and flautlence.

In Malaysia- The plant is used in diabetes, hypertension, insomnia and cancer.

In Hawaii - Extract of boiled plant is used to arrest bleeding.

In America- Gargle of plant is used to ease soarthroats, chest ailments and laryngitis.

In Africa- Leaves are used for menorrhagia and rheumatism.

**(Priyanka Tolambiya and Sujata Mathur)**

*Catharanthus roseus* is used in plant pathology as experiment host for phytoplasmas. This is because it is easy to infect with a large majority of phytoplasmas and also often has very distinctive symptoms such as phyllody and significantly reduced leaf size. **(Santhosh et al., 2015)**

#### **AYURVEDIC USES OF THE PLANT**

The pink and the white varieties are grown for its medicinal value. The leaves are around 3cm, oval and oblong. The fruit is 3-4cm long and a pair follicle. The species is cultivated as herbal medicine. In Ayurveda, the plant root and shoot are poisonous, yet used as medicine against several diseases. **(Anoop, 2015)**

#### **GAS CHROMATOGRAPHY-MASS SPECTROMETRY (GC-MS) ANALYSIS**

The column used for GC programme was elite-1 (100% Dimethyl poly siloxane), 30 x 0.25 mm x 1  $\mu$ mdf. The equipment was GC Clarus 500 Perkin Elmer. The carrier gas used in GC-MS programme was helium 1 ml/minute (split: 10:1). The detector used was mass detector (turbo mass gold-perkin Elmer), the software was turbomass 5.4.2. 2  $\mu$ l of the sample was injected into the GC-MS. The initial oven temperature was 110°C and it was kept hold for 2 mins, and it was raised upto 200°C at the rate of 10°C per min without holding. Further it was raised upto 280°C at the rate of 5°C per minute and kept hold for 9 minutes. The injector temperature was 250°C. The total GC running time was 36 minutes. The library used in the MS was NIST Version-Year 2005. The inlet line temperature of MS program was 200°C and the source temperature was 200°C. The electron energy used was 70 eV, the mass scan (m/z) was 45-450. The total MS running time was 36 minutes. **(Chandra Mohan., 2015)**

#### **Impact of cadmium and lead on *Catharanthus roseus*--a phytoremediation study.**

**(Pandey S.et al.,)**

*Catharanthus roseus* (a valued medicinal plant) was exposed to different concentrations of heavy metals like, CdCl<sub>2</sub> and PbCl<sub>2</sub>, with a view to observe their bioaccumulation efficiency. Germination was inhibited by both the heavy metals in the seeds previously imbibed in GA, and KNO<sub>3</sub>, for 24 hr. EC50 (the effective concentration which inhibits root length by 50%) was recorded as 180 microM for CdCl<sub>2</sub>, and 50 microM for PbCl<sub>2</sub>. Both alpha-amylase and

protease activity were reduced substantially on treatment of seeds with increasing concentrations of CdCl<sub>2</sub>, and PbCl<sub>2</sub>. Malondialdehyde (MDA) a product of lipoxigenase (LOX) activity also increased due to the treatment of both CdCl<sub>2</sub> and PbCl<sub>2</sub>. When two-months-old plants grown in normal soil were transferred to soils containing increasing amounts of these two heavy metals, senescence of lower leaves and extensive chlorosis were noticed after four days of transfer. However, plants gradually acclimatized and after 20 days the chlorophyll content was almost comparable to normal. Plants receiving CdCl<sub>2</sub> treatment (250 microg g<sup>-1</sup>) and less became acclimatized after two weeks and started normal growth. But PbCl<sub>2</sub> of 432 microg g<sup>-1</sup> and less could not affect the plant growth throughout, after a preliminary shock was erased. In case of CdCl<sub>2</sub> treatment, a stunted growth with reduced leaf area, reduced biomass and sterility were recorded after six months, while plants show normal growth and flowering in case of PbCl<sub>2</sub> treatment. Total alkaloid was also found to be decreased in the roots of CdCl<sub>2</sub> treated plants. No change was observed in case of PbCl<sub>2</sub>. GA<sub>3</sub> treatments to the CdCl<sub>2</sub> treated plants show internode elongation and increase in leaf area with relatively elongated leaves and thinning of stem diameter. AAS analyses of leaves of treated plants exhibited 5-10% accumulation of cadmium, but there was no accumulation of lead at all.

*Catharanthus roseus* is unsafe when taken by mouth due to the presence of poisonous chemicals known as Vinca alkaloids.

## CONCLUSION

Thus, this review indicates that *Catharanthus roseus* leaves, has properties that render and it is capable of promoting accelerated wound healing, antidiabetic, antioxidant, antihelminthic, phytoremediation activity and many more. These support further evaluation of *Catharanthus roseus* in the improvement as drug of choice in many therapeutic areas.

## Bibliography

1. Alba Bhutkar, M. A and Bhise, S. B. (2011). Comparative Studies on Antioxidant Properties of *Catharanthus roseus* and *Catharanthus*. International Journal of Pharmaceutical Techniques, 3(3): 1551-1556.
2. Anju Chandran and Oommen. P. Saj Phytochemical studies on the medicinal herb, *Catharanthus pusillus* World Journal of Pharmaceutical Research Volume 5, Issue 01, 152-171.

3. Brun, G., Bessie`re, J. M., Dijoux-Franca, M. G., David, B. and Mariotte, A. M. (2001). Volatile Components of *Catharanthus roseus* (L.) G. Don (Apocynaceae). Flavour Fragr. J. vol. 16(2): 116-119.
4. S. Chandra Mohan, T. Anand, G. S. Priyadharshini, V. Balamurugan. (2015). GC-MS Analysis of Phytochemicals and Hypoglycemic Effect of *Catharanthus roseus* in Alloxan-Induced Diabetic Rats. IndiaInt. J. Pharm. Sci. Rev. Res., Article No. 25, Pages: 123-128
5. Chandrashekar, R and Rao, S.N. (2012). "Phytochemical analysis of Ethanolic extract of leaves of *Clerodendrum viscosum* (EELCV)". World Journal of Pharmacy and Pharmaceutical Sciences. 1: 1092-1099.
6. Chattopadhyay, R. R., Banerjee, R. N., Sarkar, S. K., Ganguly, S., Basu, T. K. (1992). Indian J PhysiolPharmacol; 36(4): 291-2.
7. Choudhury, S., Rahaman, C. H. and Mandal, S. (2009). Studies on leaf epidermal micromorphology, wood element characters and phytochemical screening of three medicinally important taxa of the family Convolvulaceae. Journal of Environment and Sociobiology. 6: 2, 105-118.
8. Edeoga, H.O. and D.O. Eriata, (2001). Alkaloid, tannin and saponin contents of some Nigeria medicinal plants. J. Med. Aromatic Plant Sci., 23: 344-349.
9. Erdogru. (2002) Antibacterial activities of some plant extract used in folk medicine. Pharm. Biol, 40: 269-273.
10. Farnsworth, N. R., L. K. Henry, G. H. Svoboda, R. N. Blomster, M. J. Yates and K. L. Euler, (1966). Biological and phytochemical evaluation of plants. I. biological test procedures and results from two hundred accessions. Lloydia, 29: 01- 122.
11. Ghosh, R. K., Gupta, I. (1980). Effect of *Vincarosea* and *Ficusracemososus* on hyperglycemia in rats. Indian J. Animal Health.; 19: 145–148.
12. T. D. Gootz. (1990). Discovery and development of new antimicrobial agents, Clin. Microbiol. Rev., 313-31.
13. V. Govindaraji, (2007) PGR mediated in vitro metabolic engineering of alkaloid production in somatic explants of *Catharanthus roseus* (L.) G. Don., from google.
14. P. Goyal, A. Khanna, A. Chauhan, G. Goyal, (2008) In vitro evaluation of crude extract of *Catharanthus roseus* for potential antibacterial activity, IJGP, 2176-181.
15. J. B. Harborne, (1978) Phytochemical Methods: A guide to modern Techniques of Plant analysis, Chapman and Hall, London, pp.: 75.

16. Jun Murata, Jonathon Roepke, Heather Gordon and Vincenzo De Lucaa (2013). The Leaf Epidermome of *Catharanthus roseus* Reveals Its Biochemical Specialization. International Journal of Research in Pure and Applied Microbiology; concepts and application, 3(3): 77-82 pp. 967-972.
17. Khan, F.A., Hussain, I., Farooq, S., Ahmad, M., Arif, M. and Rehman, I.U. (2011). Phytochemical Screening of some Pakistanian Medicinal plants. Middle – East Journal of Scientific Research, 8(3): 575-578.
18. Ku, C., Chung, W. C., Chen, L. L. & Kuo, C. H. (2013). ‘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.
19. Laily, B., N. I. Yusoff., M. W. Samsudin., U. S. Salleh, A. Z. Ibrahim., A. Latiff and M. Said (2002). A preliminary phytochemical survey of plants in Crocker range Sabah, Malaysia. ASEAN Review of Biodiversity and Environmental Conservation (ARBEC). 1-5.
20. L. A. Marcaurelle, C. W. Johannes, (2008) Application of natural product-inspired-diversity -oriented synthesis of drug discovery, Prog. Drug Res., 66: 89-216.
21. Monika Sain and Vandana Sharma (2013) *Catharanthus roseus* (An anti-cancerous drug yielding plant) - A Review of Potential Therapeutic Properties Department of Botany, International Journal of Pure & Applied Bioscience 1(6): 139-142.
22. Nag, S., Paul, A. and Dutta, R. (2013). Phytochemical Analysis of Methanolic extracts of leaves of some medicinal plants. International Journal of Scientific and Research Publication, 3(4): 1-5.
23. Nammi, S., Boini M. K., Lodagala, S. D. and Behara, R. B. (2003). BMC Complement Altern Med.; 3: 4. [PubMed]
24. D. J. Newman, G. M. Cragg and K. M. Snader, (2003) Natural products as a source of new drug over the period, J. Nat. Prod., 6: 1022-37.
25. R. N. Okigbo, C. S. Bajiuka and C. O. Njoku. (2005). Antimicrobial potential of (UDA) *Xylopiasaeothopica* and *Ocimumgratissimum* L. on some pathogen of Man. Int. J. Mole. Medi. Adu. Sci., 1: 392-397.
26. Pandey Rai, S., Mallavarapu, G. R., Naqvi, A. A., Yadav, A., Rai, S. K., Srivastava, S., Singh, D., Mishra, R and Kumar, S. (2006). ‘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.

27. S. Pandey, K. Gupta and A. K. Mukherjee. (2007). Journal of Environmental Biology, 28(3) 655-662 (2007)
28. M. J. Pelezar, E. C. S. Chan, N. R. Knieg, Microbiology
29. C. Perez, M. Pauli and P. Bazerque. (1993). An Antibiotic assay by Agar Well Diffusion method, Acta Biologica Medecine Experimentalis, 15: 113-115.
30. Prajakta J. Patil and Jai S. Ghosh. 2010. Antimicrobial Activity of *Catharanthus roseus* – A Detailed Study. British Journal of Pharmacology and Toxicology, 1(1): 40-44.
31. Priyanka Tolambiya and Sujata Mathur. A Review on Potential Therapeutic property of *Catharanthus roseus* Alba variety: An Anti-diabetic drug yielding plant
32. Rahmatzadeh, S and Kazemitabar, S. K. (2013). 'Biochemical and antioxidant changes in regenerated periwinkle plantlets due to mycorrhizal colonization during acclimatization'. IJACS, vol. 5, no 14, pp.1535-1540
33. S. Ramya, R. Govindaraji, K. Navaneetha, R. J. Kannan, (2008) In vitro evaluation of antibacterial activity using crude extracts of *Catharanthus roseus*. L.(G) Don. Eth. Leaflets, 12: 1067-72.
34. D. Russell, (2002) Antibiotic and Biocide resistance in bacteria: Introduction, J. Appl. Microbiol. Symp. Supply 2: 176-181.
35. M. Santhosh Aruna, M. Surya Prabha, N. Santhi Priya, Ramarao Nadendla. (2015). *Catharanthus roseus*: ornamental plant is now medicinal boutique. Journal of Drug Delivery and Therapeutics
36. S. Satish, D. C. Mohana, M. P. Ranhavendra and K. A. Raveesha. (2009). Antifungal activity of some plant extracts against important seed borne pathogens of *Aspergillus*. sp., J. of Agricultural Technology, 3: 109-119.
37. H. Shanmugam, R. Rathinam, A. Chinnathambi and T. Venkatesan. (2009). Antimicrobial and mutagenic properties of the root tubers of *Gloriosa superba*, Pak. J. Bot. 41:293-299.
38. Singh Jagdeep and Thalwal Shweta Sen. Comparative analysis of Medicinal Plants for their Antimicrobial Potential and Phytoconstituents Screening International Journal of Pure & Applied Bioscience Related article at PubMed, Scholar Google
39. Singh, S. N., Vats, P., Suri, S., Shyam, R., Kumria, M. M., Ranganathan, S and Sridharan, K. (2001) J Ethnopharmacol; 76(3): 269-77.
40. Sofowora, A., (1993). Medicinal Plants and Traditional in Africa. Chichester John Wiley and Sons New York, pp.: 97-145.
41. Swanberg, A & Dai, W. (2008). 'Plant Regeneration of Periwinkle (*Catharanthus roseus*) via Organogenesis. HortScience. vol.43(3): 832-836

42. Van Wyk, B.E., Van Oudtshoorn, B and Gericke, N. (1997). Medicinal Plants of South Africa. Briza Publications; Pretoria.
43. Van Wyk B.E., Van Oudtshoorn B., Gericke N. (2002). Medicinal Plants of South Africa (2<sup>nd</sup> Ed.) Briza Publications; Pretoria: pp. 156–157.