ejpmr, 2023, 10(1), 86-91

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

CATHARANTHUS ROSEUS LEAF ASSISTED GREEN SYNTHESIS OF METAL OXIDE NANOPARTICLE: A REVIEW

Dnyaneshwar Ansarwade* and Shriniwas Patil

Alard College of Pharmacy, Marunje, PCMC- 411 057, Pune.

Corresponding Author: Dnyaneshwar Ansarwade

Alard College of Pharmacy, Marunje, PCMC- 411 057, Pune.

Article Received on 03/11/2022 **Article Revised on 24/11/2022** **Article Accepted on 14/12/2022**

ABSTRACT

Numerous attempts have been made for green synthesis of metal oxide nanoparticles; revealing the significance of plant extracts in reducing metal sources to nanoparticles and applications in various scientific domains. *Catharanthus roseus* is an evergreen herbaceous plant, belonging to the family Apocynaceae. Its leaves are reported to contain several phytochemicals like indole alkaloids like vinblastine, vincristine, vindesine. This article focuses on applications of *Catharanthus roseus* leaves extract in the fabrication of nanoparticles of various metal oxides like copper oxide, zinc oxide, titanium dioxide, and nickel oxide. These metal oxide nanoparticles were evaluated in many research studies for a variety of uses, including antibacterial, and photocatalytic properties. The utilization of *Catharanthus roseus* leaf aqueous extract revealed that its phytocompounds were involved in lowering the metal oxides and stabilizing their nanoparticles. In conclusion, it could be noted that metal oxide nanoparticles have antimicrobial activity and photocatalytic potential.

KEYWORDS: *Catharanthus roseus*; metal oxide nanoparticles; Green synthesis; applications.

INTRODUCTION

An expanding discipline of research known as nanotechnology involves the creation and synthesis of different nanomaterials. The objects between 1-100 nm in size that may differ from the bulk material due to their size are considered nanoparticles.[1] Both top-down and bottom-up methods are widely used to create nanoparticles. The mechanical methods of size reduction, which involve gradually reducing bulk materials to nanosized structures, are the foundation of the top-down approach. Atoms or molecules are assembled to form molecular structures in the nanoscale range in bottom-up techniques.[2] The use of metallic nanoparticles is currently in demand because they appear to allow for the regulation of particle size and surface features as well as the release of therapeutic active elements to produce site-specific pharmacological effects at an ideal rate and dosing schedule.[3] Nanomaterials are utilized in biological and biomedical applications, including biological labels that glow in the dark, delivery of genes and drugs, pathogen-detection, protein detection, investigation of the DNA's structure, proliferative medicine, elimination of malignancies with heating (hyperthermia), MRI contrast enhancement, phagokinetic research, and cell and biochemical separation and purification.[4] Herb *Catharanthus roseus* is a member of the Apocynaceae family of plants. It is a herbaceous plant that can expand to a height of 80cm to 1 m. The leaves are oppositely oriented, oval to oblong, 2.5–9.0 cm long, 1–3.5 cm broad, glossy green, hairless, with a pale midrib, and a short petiole slightly 1.8–1.8 cm long. Madagascar's Indian Ocean Island is the home to the plant. For its therapeutic diagnostics, it is predominantly cultivated in Southern Europe, China, Africa, Australia, and the United States. Traditional and folkloric uses of a paste made from the leaves as a wound healer that also diminishes the suffering from anaphylactic reactions and halt bleeding, accelerating the healing process. Furthermore, many suggest that periwinkle might assist with depression, headaches, and lethargy.[5]

MORPHOLOGY

An evergreen sub-herb and herbaceous plant, Catharanthus roseus can reach a height of 1 m. The leaves are glossy green, hairless, oval to oblong, 2.5 – 9.0 cm long, and 1 -3.5 cm wide. They are oriented in opposite pairs and each has a pale midrib and a petiole that is only a few centimetres long. The flowers range in color from white to dark pink with a dark red center. The basal tube is about 2.5 – 3 cm long, and the corolla has 5 lobes that resemble petals. A Pair of follicles that are about 2 – 4 cm in length and 3 mm wide make up the fruit.[6]

Pharmacological activities

Due to the presence of different types of phytochemicals, *C.roseus* extracts have been reported to exhibit various pharmacological activities (Table 1).

Table 1: Pharmacological activities of *C. roseus.*

Pharmacological Activity	Reference no.
Hypolipidemic effect	[7]
Hypotensive property	[8]
Anti-ulcer property	[9]
Anticancer property	[10]
Anti-diabetic property	[11]
Anti-oxidant property	[11]
Anti-microbial property	[12]
Anti-diarrheal property	[13]
Insecticidal property	[14]
Anthelminthic property	[15]
Phytoremediation property	[16]

Phytochemical constituents

So far, CR leaves have been reported to contain various indole alkaloids like vinblastine, vincristine, vindesine.[17] vindoline, vindolidine, vindolicine, vindolinine, perivine, serpentine, and vindogentianine.[18]

Metal oxide nanoparticles synthesized using *C. roseus* leaves

Copper Oxide Nanoparticles

S. Nazarath Begum et al. 2019 synthesized copper oxide nanoparticles using *Catharanthus roseus* leaf extract. They prepared an aqueous extract of *Catharanthus roseus* leaves using deionized water. They added the extract to 0.1M solutions of copper sulfate and stirred vigorously for 3 hours. Then, they heated the mixture for 12 hours in the oven and at 150°C calcinated at 400°C for 2 hours. Further, they characterized these copper oxideNPs by XRD, UV, and FTIR and tested for antimicrobial activity by standard disc diffusion method. The XRD pattern should peaks at 25.35, 35.46, 38.67 and 43.29 which revealed that copper oxide NPs are having monoclinic crystal system. The FTIR spectrum showed the peaks of 3406 (O-H stretching), 1184 (SO_2 absorbance), 1002 (-C-O-C- or -C-O-), 651 (C-H bend), 1384 (amine group), 2852 (asymmetric structure). The UV spectrum should have the absorption max of copper oxide NPs at 310 nm. Further, researchers evaluated the antimicrobial activity of copper oxide NPs using the disc diffusion method against *E. coli*. The zone of inhibition was found dose-dependent for doses 10-40 µl.[19]

Mari et. al in the year 2020 experimented to synthesize copper oxide NPs using *Catharanthus roseus* leaf extract. They prepared an aqueous extract of Catharanthus roseus leaves using 50 ml deionized water and boiled the mixture for 20 min changed the colour of the aqueous solution from colourless to light yellow. Further, they filtered the mixture using Whatman filter paper. They added 20 ml extract to 2 gm of copper nitrate and constantly stirred and the temperature attained 60°C. Dried precipitate further, they transferred to the crucible and calcinated at 400°C for 4 hours. Further, they characterized these CuO NPs by XRD, PL, FTIR, SEM, EDX, and HR-TEM and performed photocatalytic activity. The XRD diffraction plot confirmed the pattern of pure monoclinic structure NPs. The peaks had appeared at 32.44°, 35.52°, 38.66°, 48.64°, 53.37°, 58.17°, and 66.18°. In the PL analysis two emission peaks are observed at 410 nm (violet), 450 nm and 468 nm (blue) for CuO nanoparticles. The FTIR spectrum showed the peaks of 520 (Cu-O intense band), 3443 (O-H stretching), and IR bands ranged at 400-600 cm confirmed the formation of CuO nanoparticles from the green synthesis. The SEM image illustrated that nanorod-like morphology with homogenous distribution and slight agglomeration. EDX analysis confirmed the stochiometric proportion of Cu and O elements in the sample. On performing HR-TEM analysis for the CuO NPs they observed the nanorod-like structure and its size observed to be 23 nm. Further, researchers used photocatalytic activity changed in the absorption spectra of the rose Bengal exposed to UV light for various irradiation times (0, 15, 30, 45, 60, 75, 90, 105, and 120 min) at the presence of CuO nanoparticles.[20]

Dayana KS et al. in the year 2021 experimented to synthesize copper oxide NPs using *Catharanthus roseus* leaf extract. The CuO NPs were combined by the co-precipitation method. The extract was prepared using grinded washed leaves of Catharanthus roseus with the help of a mixer grinder. Then refined and employed grinded paste for the synthesis process. Then prepared 0.2M Copper sulfate ($CuSO_45H_2O$) solution by using double distilled water. They added dropwise *Catharanthus roseus* extract to copper sulfate solution separately until the precipitated forms. The colour changed declares the reduction of copper ions and so this confirmed the formation of oxide NPs. The obtained precipitate was collected in a petri dish and dried in a hot air oven at 100°C by the calcinated process with resulted yield of about 3.7gm. The thus synthesized CuO NPs were further characterized by analytical methods like XRD, FTIR, UV-DRS, SEM, EDX, and Zeta potential. XRD analysis was confirmed with various diffraction angles. Peaks revealed the existence of orthorhombic crystal structure with planes at (020), (103), (212), (220), (123), (222), (133), (321), (026), and (404) respectively. FTIR analysis was carried out to confirmed possible biomolecules and responded to the formation of the functional group of CuO NPs. The FTIR showed the peaks of 1618 (C=O group), 1107 (amides), 400-600 region (Cu–O vibration) confirmed formation of CuO NPs, 608 (Cu-O Functional group), 3376 (hydroxyl functional group). When UV-DRS was used, the sample included strong and distinct radiation peaks at 607 nm. SEM characterization helped in the analysis of the study of the Surface morphology and elemental organization of the CuO NPs. The SEM analysis depicted that the spherical agglomeration green synthesized CuO NPs whose size was found to be around 43 nm. EDX analysis showed that the peak S usually indicates the presence of plant extract. Further, the EDX spectra for CuO NPs corroborated the presence of oxygen and copper within the NPs without impurity. EDX Spectrum confirmed the presence of CuO NPs in the sample. NPs founded that the narrow and strong diffraction peaks indicate particles

are purely crystalline in nature. The zeta potential was determined. The zeta potential of oxide NPs prepared used an extract of *Catharanthus roseus* leaf well dispersed in water was found to have been -1.88 mV. Negative charged on NPs resulted in the high stability of the oxide NPs. The high negative zeta potential indicated that a very strong repulsion force between the particles indicated quality and stability.[21]

Zinc Oxide Nanoparticles

Khan K.A et al. in 2022 synthesized zinc oxide NPs using *Catharanthus roseus* leaf extract. They prepared an aqueous extract of *Catharanthus roseus* leaf using distilled water. They added the extract to 0.3M zinc acetate dihydrate (Zn $(CH_3COO)_2$-$2H_2O$) and dried at 80°C. Then, they grinded the dried sample and centrifuged it at 4000 rpm about 15 times. Further, they dried at 100°C with mortar and utilized to create ZnO NPs. Further, they evaluated Zinc oxide NPs by GC-MS, XRD, FESEM, FTIR, EDX, and VSM and tested for antibacterial activity. The GS-MS showed more than 65 prominent peaks in the retention time range 5–59 and analysed the *Catharanthus roseus* reveals the presence of poly-alcohols, carboxylic acids, ketones, sterols, terpenoids, carotenoid, etc. The XRD pattern should peaks at 31.92, 34.60, 36.33, 47.77, 56.62, 63.00, 68.07 for 400ºC. Further, they calcinated at 500ºC peaks showed at 31.89, 34.59, 36.34, 47.68, 56.73, 63.01, 68.10 again calcinated at 600ºC peaks observed at 31.82, 34.43, 36.42, 47.63, 56.73, 62.96, 66.53, 68.07, 69.30. XRD analysis indicated that the reflection peaks become sharper and the intensity of diffraction peaks increased with increasing calcination temperature. The FESEM analysis conducted showed particles are nanosized at 400°C and 500°C further they formed nanoparticles with a homogeneous and spherical shape at 600°C.The FTIR spectrum showed the peaks of 3848 (N-H stretch amide), 3430 (O-H stretch phenolic compound), 2932 (C=O stretching vibration), and 2391(C-H stretch). EDX analysis showed no coercivity. VSM analysis showed that the saturation magnetization of the ZnO NPs was 0.00182 emu/g.[22]

Bhumi G and Savithramma N. 2014 synthesized the zinc oxide NPs using *Catharanthus roseus* leaf extract. They added the aqueous extract to 0.025 M aqueous Zinc acetate and adjusted the pH 12. The generated light-coloured precipitate was rinsed with water and ethanol without even being vacuum-dried. Further characterization was done by then using SEM, EDX, XRD, and FT-Raman Spectroscopy analysis and tested antibacterial activity by standard disc diffusion method. SEM characterization helped in the analysis of the study of the morphology of biosynthesized and chemical synthesis of the ZnO NPs. SEM image illustrated the spherical shape nanoparticles formed with a diameter range of 23 to 57 nm. It also showed the aggregated molecule formed in the range of 20 nm. EDX spectrum analysis identified the other element along with Zn. EDX analysis showed element OK with an atomic percentage of 25.21 and element ZnK with an atomic percentage of 74.79. The XRD pattern should peaks at 20, 32, 35 and 40 degrees which revealed that the ZnO NPs are having hexagonal wurtezite structure. The FT-Raman spectroscopy showed the peaks of strong and sharp bands 1340 (Zn- N and Zn-O bonds), 1351 (amino (or) carboxylate group (or) both the broad ones),1523 (carboxylate group stretching vibrations with symmetric and asymmetric C = 0). Further, explored the antibacterial activity of ZnO NPs using the disc diffusion method of two-gram negative *E. coli* and *pseudomonas aeruginosa* and two-gram positive bacteria *Staphylococcus aureus* and *Bacillus thuringiensis*. *Pseudomonas* (13 mm), *Staphylococcus* (12 mm), *E. coli* (10 mm), and *Bacillus* (12 mm) were found to reside within the inhibitory zone.[23]

Kalaiselvi A et. al 2016 attempted zinc oxide NPs using *Catharanthus roseus* leaf extract. For this, they used washed, dried and grounded leaves into small pieces by the motor. Further, they extracted by using the Soxhlet extraction process used to remove hydrocarbons from the plant material with petroleum ether followed by methanol and distilled using water baths. About 100 ml of 1 mM zinc acetate solution was prepared by adding double-distilled water. Then 80 ml zinc acetate was added to a methanolic extract of 20 ml and stirred at 60°C. Formed ZnO NPs were examined every 1 hour with the help of UV-Visible spectroscopy. Further, they characterized by FTIR, XRD, AFM, DLS, Zeta potential, SEM, EDAX, TEM, and SAED. FTIR analysis is preferred to confirm the presence of the various functional group. The FTIR spectrum showed the peaks around 1091 and 3458 are due to O–H stretching and deformation and peaks at 1639 and 621 corresponded to Zn–O stretching and deformation vibration. The XRD pattern should peaks at (100), (002), (101), (102), (103), (200), (112), (201), and (202) which revealed that ZnO NPs are having crystalline form. AFM analysis showed the morphological analysis of green synthesized ZnO NPs. The average size of biosynthesized ZnO NPs 21.97 nm was analysed by AFM measurement. DLS is used for determined the average mean particle size called z-average diameter. The hydrodynamic size distribution of synthesized ZnO NPs was determined to be 287.00 nm. The zeta potential obtained from methanolic synthesized metal oxide nanoparticles was – 50.5 mV. They performed SEM to determine the size range which was observed at around 98-110 nm. EDAX showed peaks with elemental composition as 84.75% of the zinc and 15.25% of the oxides. TEM analysis with ZnO NPs resulted in a size of 10-50 nm. SAED showed the uniform distribution of the particle. Further, the researcher evaluated the dye degradation process that was carried out using optimized ZnO NPs with phenol red dye. One milliliter of phenol red dye was mixed with 0.25 mg of synthesized ZnO NP dispersions with different aliquots at various time intervals and kept under UV irradiation light source 365 nm wavelength. The absorbance range was taken from 200 to 800 nm.

Cleared surface plasmon resonance (SPR) was seen at the ninth hour. Therefore, 8 hours is the ideal amount of time for optimal dye breakdown.[24]

Monika Gupta et. al 2018 synthesized zinc oxide NPs using *Catharanthus roseus* leaf extract. They added 6g of dried powder mixed in 50 ml of distilled water and incubated it at room temperature for 24 hours. The extract followed filtering and a 30-minute, 4000 rpm centrifugation. They added 1 ml leaf extract to 0.01M zinc acetate dehydrate and constantly stirred till the formed white suspension. The pH was adjusted to 12.0 using 2M NaOH and kept on stirring until the ZnO NPs precipitate was completely dissolved. Further, they characterized these Zno NPs by UV-Visible spectroscopy, FTIR, XRD, TEM, SEM, EDX, and DLS and tested antimicrobial activity by standard disc diffusion method. The UV – vis spectroscopy showed the absorption max of ZnO NPs 366 nm. The FTIR spectra showed the peaks at 3233 (C-H stretch of alkenyl), 2104 (-C≡C- stretching), 1640 (C = O stretching), 1556 (C = C/amine – NH stretching), 1399 (C-H stretching), 1086 (stretching amine), 929 (C-N stretching amine), 773 (C-N stretching amine), 849 (C-N stretching amine), 715 (C-N stretching amine) and 1035 (C-O), C-F, alkyl halide strong. The XRD pattern should peaks at 34.88, 36.72, 47.99, 56.56, 63.68, 67.90, and 69.36 which revealed that ZnO NPs are having hexagonal crystal system. The Average particle size of Zinc oxide was 36.83 nm at (101) through Debye Sherrer's formula. TEM result indicated that ZnO NPs were hexagonal wurtzite shapes with an average diameter ranging from 50 to 92 nm. The SEM analysis conducted showed the spherical shape of ZnO NPs. It also gave an idea about the range of particle size which was approximately 62 and 94 nm and also investigated the morphology of the nanoparticles. EDAX studies showed higher counts at 10 keV due to zinc oxide ions, which confirmed the formation of ZnO NPs. DLS suggested that the particle size of ZnO NPs showed the average size distribution in the range of 50.73 nm along with a polydispersity index of 0.780. Further, explored the antimicrobial activity of ZnO NPs using the disc diffusion method against *S. aureus, S. pyogenes, P. mirabilis, E. coli, P. aeruginosa, B. cereus* for dose 1500 µg/ml displayed good antibacterial activity against all the six pathogenic bacteria.[25]

Titanium dioxide nanoparticles

Velayutham et al. 2012 researched the biosynthesis of titanium dioxide NPs using *Catharanthus roseus* leaf extract against *Hippobosca maculata* and *Bovicolaovis.* About 10gm of the thoroughly washed and finely cut leaves added in a 250 mL Erlenmeyer flask along with 100 mL of sterilized double distilled water and then boiled the mixture for 10 min before finally decanted it. This was then filtered the extract using Whatman filter paper no.01 and stored at -15°C and should be used within 1 week. They filtrate was treated with 20 ml of aqueous leaf extract added in 80 ml of 5 mM (39.94 mg of TiO_2 powder in 100 mL Milli-Q water) solution in an Erlenmeyer flask under stirring at 50°C. Upon the completion of 4 hours of continuous stirring, then formed light green colour change indicated the formation of TiO_2NPs. The characterization process was done with help of XRD, FTIR, SEM, and AFM. The XRD peaks were observed at three distinct diffraction peaks which can be assigned to the plane of (110), (101), (211) respectively indicating the Titanium dioxide NPs are cubic face-centred and crystalline in nature. Scherrer's formula was used to estimate the average grain size of the biosynthesized nanoparticle. FTIR analysis was carried out to identify biomolecules responsible for the capping of the bio-reduced TiO_2 NPs synthesized using plant extract. The FTIR spectrum showed peaks of 714 (TiO–O bond), 1076 (C–N stretch aliphatic amines), 1172 (C–O stretching vibrations in alcoholic groups), 1642 (N–H bend bond), and 3426 (O–H stretching due to alcoholic group). The SEM images illustrate clustered and irregular shapes. It also showed an average size of 25nm to 110 nm with interparticle distance. They performed AFM to determine a topological map of the surface of the synthesized nanoparticles.[26]

Nickel oxide NPs

Aarthi J et. al 2022 synthesized nickel oxide NPs using *Catharanthus roseus* leaf extract. The researchers characterized the NPs by analysing XRD, FTIR, UV-Visible spectroscopy, and SEM. On obtaining the result of XRD pattern analysis the synthesized NPs revealed a cubic structure pattern. The UV-vis spectroscopy showed the strong absorption of NiO NPs at 365 nm. SEM characterization helped in the analysis of the study of the morphology of biosynthesized and chemical synthesis of the NiO NPs. The biosynthesized ones were in spherical shape with a particle size range of 50-60 nm. Antioxidant activity was analyzed by DPPH assay in a dose-dependent manner. By increased concentration of the sample, photo chemically reduced NPs showed increased bactericidal action against gram-positive *staphylococcus aureus* and gram-negative *E. coli.*[27]

CONCLUSION

Metal oxide nanoparticles have several scientifically verified applications in a variety of disciplines. An environmentally friendly method involving the use of plant extracts for the green synthesis of different nanoparticles has been formulated to improve the environmental issues presented by chemical methods (which use hazardous chemicals) and the requirement of large, expensive machinery in physical methods of nanoparticle fabrication. The leaves of *Catharanthus roseus* (Apocynaceae) include a variety of phytochemicals that are made available for the reduction of donor compounds to corresponding nanoparticles by solvent extraction. Based on this review, it can be concluded that *C. roseus* extracts can be used for the green synthesis of nanoparticles of various metal oxides, including copper oxide, zinc oxide, titanium dioxide, and nickel oxide due to the presence of a limited percentage

of polar phytoconstituents. These nanoparticles have a wide range of applications in various scientific domains, including antimicrobial and photocatalytic activity activities.

ACKNOWLEDGEMENT

We, the authors of this review article are thankful to Managerial Board, Alard Charitable Trust's Alard College of Pharmacy, Marunje for providing internet and library facilities for carrying out literature survey.

REFERENCES

1. Hasan S. A review on nanoparticles: their synthesis and types. Res. J. Recent Sci, 2015; 2277: 2502.
2. Khandel P, Yadaw RK, Soni DK, Kanwar L, Shahi SK. Biogenesis of metal nanoparticles and their pharmacological applications: present status and application prospects. Journal of Nanostructure in Chemistry, 2018; 8(3): 217-54.
3. Mohanraj VJ, Chen Y. Nanoparticles-a review. Tropical journal of pharmaceutical research, 2006; 5(1): 561-73.
4. Salata OV. Applications of nanoparticles in biology and medicine. Journal of nanobiotechnology, 2004; 2(1): 1-6.
5. Das S, Sharangi AB. Madagascar periwinkle (Catharanthus roseus L.): Diverse medicinal and therapeutic benefits to humankind. Journal of Pharmacognosy and Phytochemistry, 2017; 6(5): 1695-701.
6. Mishra JN, Verma NK. A brief study on Catharanthus roseus: A review. Intern J Res Pharmacy Pharmaceut Sci, 2017; 2(2): 20-3.
7. Patel Y. Evaluation of hypolipidemic activity of leaf juice of Catharanthus roseus (Linn.). ActaPoloniae Pharmaceutica - Drug Research, 2011; 68(6): 927-935.
8. Pillay PP, Nair CPM, Santi Kumari TN. Lochnera rosea as a potential source of hypotensive and other remedies. Bulletin of Research Institute of the University of Kerala, Ser A6, 1959; 1: 51-54.
9. Sain M, Sharma V. Catharanthus roseus (An anticancerous drug yielding plant) - A Review of Potential Therapeutic Properties. International Journal of Pure and Applied Bioscience, 2013; 1: 139-142.
10. Banskota AH. Antiproliferative activity of Vietnamese medicinal plants. Biological Pharmaceutical Bulletin, 2002; 25(6): 753- 60.
11. Tiong SH, Looi CY, Hazni H, Arya A, Paydar M, Wong et al. Antidiabetic and Antioxidant Properties of Alkaloids from Catharanthus roseus (L.) G. Don. Molecules, 2013; 18: 9770-9784.
12. Prajakta JP, Ghosh JS Antimicrobial Activity of Catharanthus roseus A Detailed Study. British Journal of Pharmacology and Toxicology, 2010; 1(1): 40-44.
13. Rajput M, Nair V. Akansha Chauhan. Evaluation of Antidiarrheal Activity of Aerial Parts of Vinca major in Experimental Animals. Middle-East Journal of Scientific Research, 2011; 7(5): 784-788.
14. Deshmukhe PV, Hooli AA, Holihosur SN. Bioinsecticidal potential of Vinca rosea against the tobacco caterpillar, Spodoptera litura (Fabricius) (Lepidoptera: Noctuidae). Recent Research Science and Technology, 2010; 2(1): 01- 05.
15. Rawat Sand Gupta. A Development and study of wound healing activity of an Ayurvedic formulation. Asian Journal of Research in Pharmaceutical Sciences, 2011; 1(1): 26-28.
16. Pandey S, Gupta K, Mukherjee AK. Impact of cadmium and lead on Catharanthus roseus - A phytoremediation study. Journal of Environmental Biology, 2007; 28(3): 655-662.
17. Sunil Kumar, Bikarma Singh, Ramesh Singh Catharanthus roseus (L.) G. Don: A review of its ethnobotany, phytochemistry, ethnopharmacology and toxicities. Journal of Ethnopharmacology, 2022; 284: 114647.
18. Tiong SH, Looi CY, Arya A, Wong WF, Hazni H, Mustafa MR, Awang K. Vindogentianine, a hypoglycemic alkaloid from Catharanthus roseus (L.) G. Don (Apocynaceae). Fitoterapia, 2015 Apr 1; 102: 182-8.
19. Begum SN, Esakkiraja A, Asan SM, Muthumari M, Raj GV. Green Synthesis of Copper Oxide Nanoparticles Using Catharanthus Roseus Leaf Extract and Their Antibacterial Activity. Int. J. Sci. Res. in Multidisciplinary Studies, 2019; 5: 8.
20. Mari A, Vincent MV, Mookkaiah R, Subramani R. Catharanthus roseus leaf extract mediated facile green synthesis of copper oxide nanoparticles and its photocatalytic activity. Chemical Methodologies, 2020; 4(4): 424-36.
21. Dayana KS, Jothimani R, Durai SV. Green Synthesis of Copper Oxide Nanoparticles from Catharanthus Roseus Plant Leaf Extract and Its Investigation. Journal of Nano-and Electronic Physics, 2021; 13(1).
22. Khan KA, Islam MS, Khan MI, Bhattacharyya S. Synthesis and Characterization of Zinc Oxide Nanoparticles Using Catharanthus Roseus Leaf Extract. InTopical Drifts in Intelligent Computing: Proceedings of International Conference on Computational Techniques and Applications (ICCTA 2021) 2022 (426, p. 357). Springer Nature.
23. Bhumi G, Savithramma N. Biological synthesis of zinc oxide nanoparticles from Catharanthus roseus (L.) G. Don. Leaf extract and validation for antibacterial activity. International Journal of Drug Development and Research, 2014; 6(1): 0.
24. Kalaiselvi A, Roopan SM, Madhumitha G, Ramalingam C, Al-Dhabi NA, Arasu MV. Catharanthus roseus-mediated zinc oxide nanoparticles against photocatalytic application of phenol red under UV@ 365 nm. Current Science, 2016; 1811-5.
25. Gupta M, Tomar RS, Kaushik S, Mishra RK, Sharma D. Effective antimicrobial activity of green

ZnO nano particles of Catharanthus roseus. Frontiers in microbiology, 2018; 9: 2030.
26. Velayutham K, Rahuman AA, Rajakumar G, Santhoshkumar T, Marimuthu S, Jayaseelan C, Bagavan A, Kirthi AV, Kamaraj C, Zahir AA, Elango G. Evaluation of Catharanthus roseus leaf extract-mediated biosynthesis of titanium dioxide nanoparticles against Hippobosca maculata and Bovicolaovis. Parasitology research, 2012; 111(6): 2329-37.
27. Aarthi J, Sanjana S, Sornambal S, Chandrasekaran K, Sharmila S, Suba R, Akshaya P, KaviyaPriya S, Gowri S. Green Synthesis and Characterization of NiO Nanoparticles using Catharanthus Roseus Leaf Extract. Materials Today: Proceedings, 2022; 69: 1455-61.