ORIGINAL ARTICLE

Antidiabetic potential and high synergistic antibacterial activity of silver nanoparticles synthesised with *Musa Paradisiaca* tepal extract

Chinnakrishnan Shanmuga Sundaram, PhD[1], Jayaprakash Sivakumar, PhD[2], Suresh Kumar Subbiah, PhD[3,4], Thant Zin, PhD[5], Mahadeva Rao Uttarkar Sathyanarayana Rao, PhD[5]

[1]PG & Research Department of Microbiology, Hindustan College of Arts & Science, Padur, Chennai, India, [2]PG & Research Department of Biotechnology, Hindustan College of Arts & Science, Padur, Chennai, India, [3]Department of Medical Microbiology and Parasitology, Universiti Putra Malaysia, Serdang, Selangor, Malaysia, [4]UPM MAKNA Cancer Research Laboratory, Institute of Bioscience, Universiti Putra Malaysia, Serdang, Selangor, Malaysia, [5]Faculty of Medicine, Universiti Sultan Zainal Abidin, Terengganu, Malaysia

ABSTRACT

This work investigates the *Musa Paradisiaca* plant and its tepal extracts. The research findings show that the tepal extracts of *M. Paradisiaca* contain high phytochemical activity. Hence we can conclude that these plants have a number of beneficial properties. Phytochemical analysis concludes that the plant is rich in flavonoids, phenolic compounds, tannins, terpenoids, and phytosterol. In the current work, silver nanoparticles (AgNPs) have revealed the antioxidant properties of *M. Paradisiaca*. The results show that the methanolic extracts of these tepals exhibit antioxidant potential and are also sources of natural antioxidant compounds, though comparatively, AgNPs have shown the best antioxidant activity. This work investigates the link between the ethnopharmacological statements and the bioactive constituents found in *M. Paradisiaca* toward all probable markers for cervical cancer via in vivo studies and molecular docking, to form a pharmacophore setting for the active target. However, most of the mechanisms of action of herbal medicines are not in total agreement, and the information collected from their traditional remedies over the years must not be neglected. Hence, it is sensible to investigate the options available in herbal medicine for cancer progression. Biosynthesised AgNPs are principally spherical and nanosized. It was also found that tepal-mediated AgNPs exhibit excellent antimicrobial efficacy against tested human pathogens. This green method can be used as a better alternative source than the chemical fabrication of nanomaterials and the biosynthesised nanoparticles can be used in antibacterial medicines. The methanolictepal extract of *M. Paradisiaca* with AgNPs displayed proficient antidiabetic properties in the diabetes rat model and so could have a possible development for medical use in the future.

KEYWORDS:
Musa Paradisiaca, diabetes, antioxidant, silver nanoparticles, flavonoids

INTRODUCTION

Nanotechnology is a rapidly growing field owing to its application in science and technology for engineering new materials at the nanoscale level. The term "'nano" specifies one billionth of a meter (10^{-9}) and particles of size less than 100 nm are stated as nanoparticles (NPs).[1,2] Currently, nanotechnology is one of the key compelling research areas in material science with the discovery of different plants for the use of NP synthesis. Nanotechnology can be administered in various fields including agriculture, medicine, healthcare, transport, textiles, water treatment, and cosmetics, which enhances the value of products. It is a characterisation, design, production, and application system by monitoring the shape and size on a certain nanometer scale.[3]

Diabetes mellitus (DM) is an endocrine metabolic disorder and it is quickly cumulating worldwide. People with DM are not able to secrete sufficient insulin, hence they have abnormal levels of blood glucose in their body. If this is not treated, it may lead to severe disease. The most common form of the disease is differentiated into two main types: Type-1 and Type-2 DM. Type-1 is responsible for at least 5%–10% of the total cases while Type-2 comprises more than 90%–95% of all cases. The risk factors of DM are undefined, however both genetic and environmental factors including obesity and lack of physical activity seem to play an important role.[5]

DM-associated complications include diabetic retinopathy, diabetic nephropathy, and arteriosclerosis, which are the principal causes of morbidity and mortality among diabetic patients. These complications are caused by low levels of cellular antioxidant enzymes which lead to oxidative stress. The World Health Organization (WHO) reports that patients with diabetes are predicted to grow to 300 million or even more by the year 2025.[6] Studies of diabetes has grown recently and its treatment options are therapies including use of insulin, medicinal plants, and numerous other oral antidiabetic drugs such as sulfonylureas, biguanides, alfa-glucosidase inhibitors, and glinides. It has been seen that entirely oral antidiabetic agents have adverse effects.

In the literature, there are 400 plant species mentioned that have hypoglycemic properties. However, the search for new antidiabetic agents from medicinal plants continues to be in demand because they contain novel substances that reveal safe and cost-effective impacts on DM. Most natural plants

This article was accepted: 29 November 2020
Corresponding Author: U.S. Mahadeva Rao
Email: raousm@gmail.com

have secondary metabolites such as flavonoids, alkaloids, glycosides, terpenoids, and carotenoids that are commonly associated with antidiabetic activity.[7] Ethnobotanical evidence recommends that about 800 plants may contain antidiabetic potential, and among them, *Momordica charantia, Pterocarpus marsupium,* and *Trigonella foenum greacum* seem to be most valuable for the treatment of Type 2 diabetes.[8]

Medicinal plants have an optimistic future as there are still half a million undiscovered plants in the world.[9] However, the application of the whole plant for research or treatment has many disadvantages, such as variations in the plant bioactive components based on the climate.[10] The different plant parts are the root, fruit, skin, leaf, seeds, and flowers. The bioactive materials in almost all medicinal plants have treatment properties that can serve as therapeutic agents.[11] There are over one-tenth of plant extracts (more than 50,000 species) that are incorporated into cosmetic and pharmaceutical products.[12,13] Plants with antioxidant properties have been reported to be valuable for atherosclerosis and cardiovascular disease prevention by halting lipids peroxidation.[14] Natural products have various mechanisms to cope with this issue, using antioxidant enzymes.[15]

NPs from plants are much stable and the synthesis is more rapid than NPs from microorganisms. The benefits of using medicinal plant and plant based compounds for the synthesis of metal NPs have been attentive to explore the mechanisms of metal ions uptake and bioreduction by the plants, and the likely mechanisms of metal NPs production in plants. The plant extracts may function as reducing and capping agents in NPs synthesis.[16] NPs can be used to monitor the oxidative status of tissues *in vivo* using conjugated biosensor.[17] NPs are reported to have antimicrobial activity.[18] They are used for cell tagging and drug delivery.[19] and can also be applied as a conjugated biosensor for reaction oxygen species in diabetes. Nanotechnology is concerned with the synthesis of NPs of various sizes and shapes and their potential applications.[17]

The use of medicinal remedies for the prevention and treatment for the disease is of increasing because the advantage and efficiency phytoconstituents activity in the herbs. Medicinal plants have a number of medicinal. One of such plant is *M. paradisiaca*. It has been reported to have biological activities such as antioxidant, antilithiatic, antimicrobial, antidiabetic, antidiarrheal, antiulcer, hepatoprotective, hypocholesterolaemic, anti-snake venom, wound healing and anti menorrhagic.[20] Banana is the commonly used term used for genus Musa, herbaceous plants for the fruit they produce. It is one of the oldest cultivated plants. All the parts in banana tree have medicinal uses: the flowers are used in dysentery and bronchitis and ulcers. Cooked flowers used in patients with diabetes. The astringent plant is used for patients such as hysteria, leprosy, fevers, epilepsy, haemorrhages, acute dysentery and diarrhea and also for hemorrhoids, insect bites, and stings.[21] In this study *M. paradisiaca* flowers (tepals) the edible part will be used for anti diabetic activity with the help of NPs. In previous studies antidiabetic drugs were discovered from different plant materials which will be used on human kind. The key objective of the study is to determine the ethno pharmacological knowledge of M. *paradisiaca* using green Technology.

MATERIALS AND METHODS

Collection of specimens

The *M. paradisiaca* flowers were collected from vegetable market of Koyambedu, Chennai. The plants were washed properly with tap water and air-dried. The drying of plant is necessary to eliminate the water remaining from the plants before storing. The air dried plants were powdered using conventional blender for future use.

Preparation of methanolic crude extract

Compound with limited solubility in solvent must be subjected to soxhlet extraction. This method uses only single batch of solvent instead of several portions of solvent being exposed to the compound. However, this method cannot be used for thermo labile compound as extended exposure to heating can lead to degradation of compounds.[22]

Qualitative analysis of phytochemicals

Phytochemical analysis was performed for the following components such as alkaloids, amino acids, carbohydrates, phenolic compounds, saponins, phytosterols, flavanoids, and terpenoids.

Synthesis of silver nanoparticles

An amount of 1 mM silver nitrate ($AgNO_3$) in aqueous solution was prepared in 250 mL. For reduction into Ag+ ions, tepal extract was added. The mixture was microwaved at 300 W for 4 min for complete bioreduction to avoid pressure increase. While the colour changed from light to yellowish brown and then to reddish brown and to colloidal brown, the variation was observed at room temperature for at least 30 min by UV-visible spectrophotometry (in dark to avoid photoactivation of $AgNO_3$). Experimental controls were sustained for the entire period. $AgNO_3$ was completely reduced to Ag^+ ions, established by the presence of colloidal brown colour changes. The solution was then cooled and left for about 24 h for comprehensive bioreduction. after which the mixture was stored in an airtight container for further analysis. The silver nanoparticle (AgNP) formation was confirmed by spectrophotometric analysis.[23]

Characterization of AgNPs

Analysis using scanning electron microscopy (SEM) was performed by fabrication of suspension onto clean electric stubs and permitting water for complete evaporation. For voltage acceleration to 15 kW, JEOL-5800-LV16 SEM was used with a sample current of 41 µA.

Antioxidant assay (DPPH Assay)

The crude extracts and AgNP antioxidant effects were evaluated by DPPH assay according to the method described previously.[24] The free radical DPPH (2,2-diphenyl-2-picryl hydrazyl) changes to diphenyl–picryl hydrazine which is noticed by color changes from deep violet to light yellow when acted upon by an antioxidant. The changes can be measured using a spectrophotometer at 518 nm to determine

Table I: Phytochemical screening of Musa paradisiaca

S. No	Constituent	Test	Inference
1.	Alkaloids	Mayer's test	++
2.	Amino acid	Ninhydrin test	+
3.	Carbohydrate	Molish's test	+
4.	Phenolic Compounds	Ferric Chloride test	+
5.	Protein	Biuret test	+
6.	Saponin	Foam test	+
7.	Phytosterol	Libermann–Burchard's test	–
8.	Flavonoid	Alkaline reagent test++	
9.	Triterpenes	Terpenoid test	++

the DPPH scavenging activity of the antioxidant sample. Extracts measuring 25 µm and 0.48 ml of methanol were added to 0.5 ml of methanolic solution of DPPH. The mixed solution was allowed for reaction to take place at room temperature for at least 30 min. Methanol was used as blank and AgNPs served as the positive control. After incubation, the purple colored discolorisation was measured at 518 nm.

Antibacterial activity by disc diffusion method

Antibacterial activities of crude extracts and AgNPs were carried out using disc diffusion technique following the Kirby–Bauer technique.[25,26] The bacterial strain was culture in nutrient agar (NA). Pure culture was inoculated from the Petri plate to the MHA plate for subculture at 37ºC for 24 h. The aseptically prepared inoculum was prepared by inoculating the fresh culture into 2 ml of sterile 0.145 mol/L saline tube and the cell density (1.5×108 cfu/ml) was adjusted according to 0.5 McFarland turbidity standard. Then the inoculum was plated evenly on an MHA plate to yield a lawn culture. Sterile Whatman No. 1 filter paper discs 5 mm in diameter were placed and impregnated with plant extracts (100 µg/disc) on the inoculated MHA plates. The plates were allowed to incubate for 24 h at 4ºC and incubated at 37ºC. The following day, the plates were monitored for a clear zone around the disc, indicating inhibition of bacterial growth. The inhibition zone was measure in millimeters. A clear zone indicates no activity.[27] Experiments were done in triplicate and expressed as resistant (<7 mm), intermediate (8–10 mm), and sensitive (>11 mm).[28]

Antidiabetic activity

Chemicals and reagents

The following chemicals were purchased from invitrogen Sigma–Aldrich

MTT(3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide), acridine orange amphotericin B, and all other solvent chemicals, respectively.

Cell lines and culture

3T3 cells were purchased from the National Centre For Cell Science (NCCS, Pune), sustained in Rose well Park Memorial Institute medium (RPMI), supplemented with 10% fetal bovine serum, and penicillin/streptomycin (250 U/mL) at 37°C in a humidified atmosphere of 5% CO_2. Cells grown to log phase were used for analysis.

Cell viability assay

The cytotoxicity and cell viability were assessed by colorimetric assay (MTT). Cells were cultured (1X105 cells/mL) in culture plates (96 well) and pretreatment was done according to the assay requirements. In all, 10 µm of MTT (5 mg/mL) was supplemented to the cell containing well and subjected to incubation for another 4 h. The solution was decanted and the tetrazolium product was dissolved with 100 µL of DMSO per well. The absorbance reading was obtained (570 nm) using a spectrophotometer and the cell viability values were calculated.[29]

RESULTS

Methanolic crude extract of *M. Paradisiaca*

The methanolic crude extract was prepared from the powdered flowers of M. paradisiaca using soxhlet apparatus at 1.4 mg after yield. The extract was concentrated by vacuum and dried in a dessicator.

Phytochemical screening of methanolic extract of M. paradisiaca

Qualitative analysis of the *M. paradisiaca* methanolic extract revealed the existence of flavonoids, alkaloids, glycosides, polyphenols, tannins, proteins, saponins, sterols, and triterpenes in the tepal extract (Table I).

Synthesis of AgNPs

Noble metals are recognized to display exclusive optical activity as they have the property of surface plasmon resonance. The AgNPs formation was supervised with change of color. The color of the reaction mixture changed to yellowish brown in 10 min and to reddish brown after 1 h, signifying the production of AgNPs, because silver metal ions Ag+ reduced to AgNPs Ag through the active molecules.

Characterisation of crude extract and AgNPs by SEM analysis

SEM images of the crude extract and AgNPs are shown in Figure 1. It is observed that different shapes of AgNPs were taken from different tepal extracts and used as reducing and capping agents. *M. paradisiaca* tepal extracts produced are spherical, triangular, and cuboidal AgNPs. This might be affected by the different quantity and nature of capping agents in the different tepal extracts.

The morphology of the produced AgNPs using SEM magnified at 9400X and 10,000X are shown in Figure 2 for both the control and treated samples. The monodispersed spherical AgNPs were shaped on the surface of methanolic crude extract derived biological materials. The picture acquired from FESEM also presented spherical NPs, approving the result achieved by SEM.

Antioxidant activity

DPPH assay

The percentage inhibition of free radical generation by methanolic extracts was found to increase in a concentration-dependent manner, showing an IC50 value of 152.6 µg/ml (53.4% inhibition) and 118.2 µg/ml (59.36% inhibition), respectively, compared with the standard, ascorbic acid IC50 value (112.7 µg/ml). With regard to peroxide radical activity, MFF extract exhibited high inhibition (58.63% with IC_{50} value of 130.3 µg/ml) compared to TTF (53.26% inhibition with IC_{50} value of 190.4 µg/ml) when taking into account the IC50 value of standard, ascorbic acid (111.7 µg/ml) (Figure 2).

Disc diffusion method

The methanolic extract antibacterial activity against human pathogenic organisms by disc diffusion technique demonstrated a full zone of inhibition. The antibacterial activity of AgNPs was examined on *Bacillus, Pseudomonus, Staphylococcus*, and *E. coli colonies* in NA plates impregnated with AgNPs. The zones of inhibition show the maximum activity toward the test sample. In addition, crude extracts showed better inhibition when associated with AgNO3 and AgNPs. The data obtained from previous work showed similar results, which support the antibacterial activity of AgNPs. Less inhibition zone was seen in the controls (Figure 3).

Antimicrobial activity

In the present study, cytotoxicity of the methanolic crude extract *in vitro* and AgNPs was evaluated against 3T3 diabetic cell line at different concentrations. The samples indicated prominent cytotoxicity activity against the 3T3 cells. The data displayed that cell proliferation of 3T3 was inhibited significantly by methanolic crude extract: AgNPs with an IC_{5} value of 41.55 (*µ*g/ml) of the crude extract and 47.19 (*µ*g/ml) of the NPs. The percentage of toxicity increases with the concentration of AgNPs, proposing that synthesised AgNPs are important in medicine as antidiabetic agents. The percentage viability of the diabetic cells reduced with increased concentration of the samples, while cytotoxicity against 3T3 cell lines increased with the increased concentration of the samples (Figure 4). MTT assay of methanolic crude extract and AgNPs was performed. Of these, AgNPs showed better cytotoxicity results (Figure 5).

Antidiabetic activity

MTT Assay (3T3 cell line)

Comparative study of AgNPs and methanolic crude extract

DISCUSSION

Traditional medicine worldwide is redefined by research activities on various plants and their therapeutic values. Currently an epidemic expansion of DM has been reported worldwide. There are several therapeutic benefits of the different parts of the *M. paradisiaca*. However, most of the pharmacological properties of *M. paradisiaca* are based on anecdotal data and hence the present study was made to scientifically evaluate the antidiabetic property of *M. paradisiaca* tepal extract. Preliminary research showed the nontoxicity of the tepal extract on 3T3 cell lines.

The medicinal properties of the plant depend on the bioactive compounds that produce a certain physiological reaction on the human physiological process. Recently, some work has been done on phytochemistry, specifically on the banana flower of the *Musa species*. Preliminary screening phytochemical analysis of the air dried leaves and fruit peels from *M. paradisiaca* exposed the existence of glycosides, anthocyanin, tannins, flavonoids, and carbohydrate.[30] A quantitative study on saponin and flavonoid was reported by Bosha,[31] and later, the phenolic content by Mazumder.[32] The bark of *M. paradisiaca* was testified to comprise anthocyanins such as delphinidin, pelargonidin, peonidin, and malvidin.[33,34] The total phenolic content in bracts was reported to be the lowest compared with that in other plant parts such as the rhizome and fruit peels. Some bracts are almost bioactive compounds whose structure is identical to insulin and function as 'insulin-like elements,' aiding in the treatment of type I and type II diabetes.

Almost all plants with antidiabetic activity showed to have secondary metabolites like glycosides, alkaloids and flavonoids.[35] It has also been reported that numerous plants display effective antioxidant activity due to their phenolic compounds. Flavonoids and tannins are the phenolic compounds and plant phenolics are the main category of compounds that are primary antioxidant-free radical scavengers.[36] Various *in-vitro* studies have shown that certain flavonoids are potent inhibitors of the oxidative modification of LDL by macrophages.[37]

Flavonoids play a crucial part in the treatment of diabetes[38] as they can protect against hyperglycemic and alloxan-induced oxidative stress in experimental *in vivo* models.[39] Plant alkaloids have the tendency to release insulin from pancreatic beta cells and also have the possibility to protect it from alloxan-induced pancreatic damage in experimental animals.[40] Terpenoids as vitamins act as metabolism regulators and are protective antioxidants.[41] The results of the present study indicate that the tepal extract contains biologically active ingredients of known pharmacological actions.

Nanotechnology includes research and technology development at the atomic, molecular or macromolecular levels. The methanolic extract was used to synthesise silver nanoparticles and showed that the silver nanoparticles was successfully synthesised and identified by the colour change of the extract. The characterised silver nanoparticles were analysed by the displayed SEM images. So far many studies have investigated the antioxidant and antibacterial features of *M. paradiasiaca*.[42] A comparative study was also done between the methanolic crude extract and nanoparticles. The results also showed that the Silver nanoparticles have more stable and better zone of inhibition against bacteria. Therefore the silver nanoparticles have many applications such antibactericidal, antioxidant properties. Antidiabetic activity of *M. Paradisiaca* against 3T3 cell line was confirmed against methanolic crude extract and silver nanoparticles. From the results it showed that the percentage of cell viability decreases and for cytotoxcity it increases. Hence it proves that *M. Paradisiaca* AgNps has better antidiabetic activity.

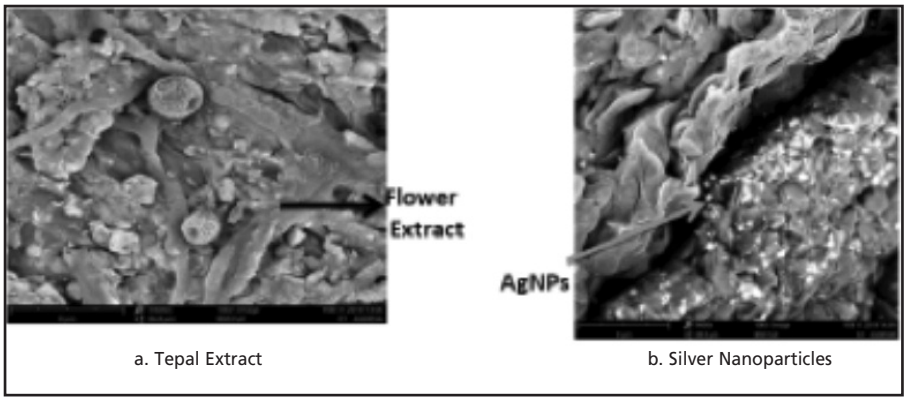


Fig. 1: Comparative SEM image of Tepal Extract and Silver Nanoparticles at 10,000X.

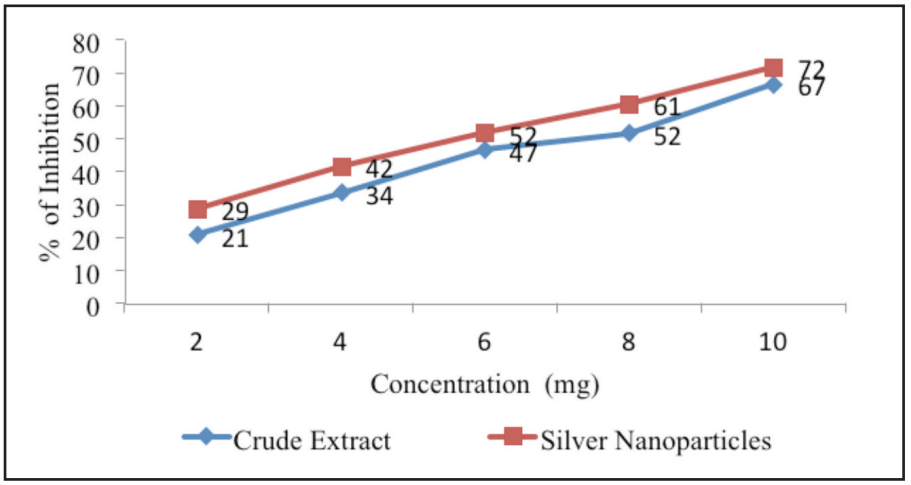
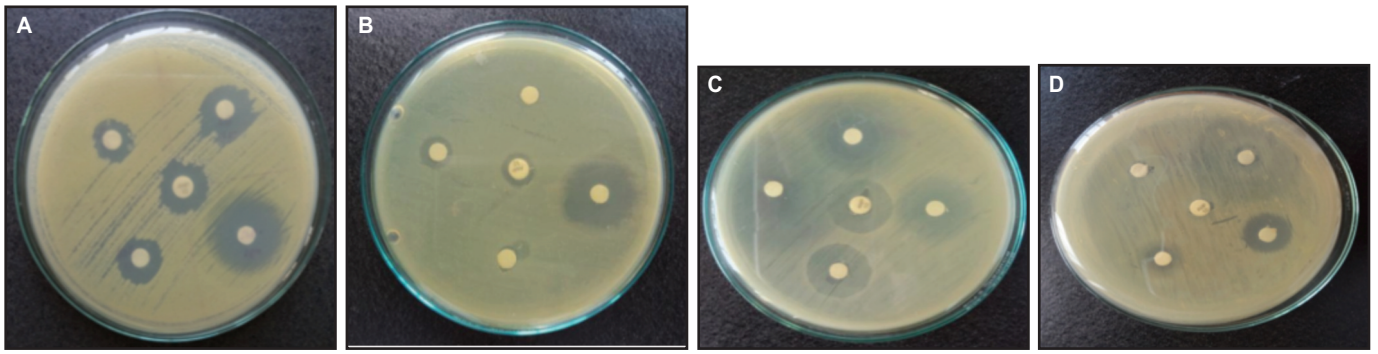


Fig. 2: Antioxidant activity in different concentrations.



25 µl crude extract – 9 mm
50 µl crude extract – 15 mm
25 µl silver nanoparticles – 16 mm
50 µl silver nanoparticles – 25 mm
Ampicillin – 10 mm

25 µl crude extract – no zone
50 µl crude extract – no zone
25 µl silver nanoparticles – 16 mm
50 µl silver nanoparticles – 25 mm
Ampicillin – 10 mm

25 µl crude extract – 19 mm
50 µl crude extract – 24 mm
25 µl silver nanoparticles – 16 mm
50 µl silver nanoparticles – 21 mm
Ampicillin – 12 mm

25 µl crude extract – no zone
50 µl crude extract – 4 mm
25 µl silver nanoparticles – 1\6 mm
50 µl silver nanoparticles – 24 mm
Ampicillin – 2 mm

Fig. 3: Antimicrobial activity of crude extract and Silver nanoparticles against A) Escherichia coli, B) Pseudomonas aeruginosa, C) Staphylococcus aureus and D) Candida albicans.

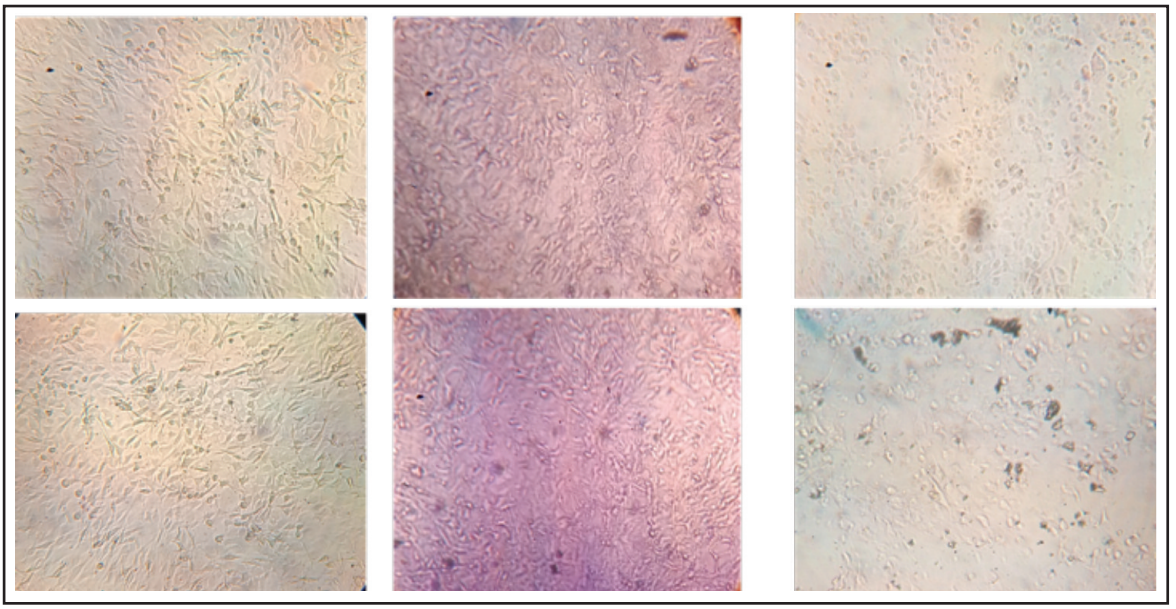


Fig. 4: Antidiabetic activity of Silver nanoparticles and crude extract against 3T3 cell line.

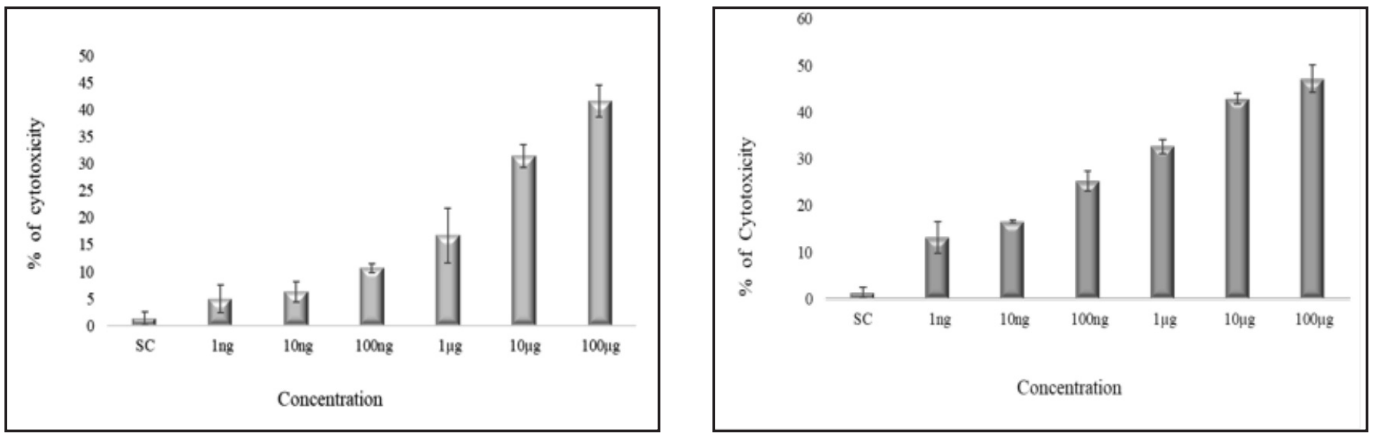


Fig. 5: MTT assay of methanolic crude extract and silver nanoparticles.

CONCLUSION

M. paradisiaca has been studied and the results of the present research findings show that the tepal extract was found to contain high phytochemical activity. Hence we can conclude that these plants are highly nutritious in nature. Phytochemical analysis concludes that it is rich in flavonoids, phenolic compounds, tannins, terpenoids, and phytosterol. In the present study, AgNPs showed the antioxidant activity of *M. paradisiaca*. The results showed that the methanolic extracts of these tepals also exhibit antioxidant potential and they are sources of natural antioxidant compounds. Comparatively, AgNPs showed the best antioxidant activity. This study aimed to find the link between ethnopharmacological claims and bioactive components in *M. paradisiaca* against all possible targets for cervical cancer through in vivo studies and molecular docking to develop a pharmacophore model for the active target. The biosynthesized AgNPs are predominantly spherical and nanosized. It is also found that tepal-mediated AgNPs exhibit excellent antimicrobial efficacy against tested human pathogens. This green method can be used as a better alternative source than chemical fabrication of nanomaterials and the biosynthesized NPs can be used in antibacterial medicines. The methanolictepal extract of M. paradisiaca of AgNPs exhibited efficient antidiabetic activity in the diabetic rat model, so they may have potential for developing medical use.

REFERENCES

1. Deepa K, Panda T. Synthesis of gold nanoparticles from different cellular fractions of Fusarium oxysporum. J Nanosci Nanotechnol 2014; 14: 3455.
2. Shi C, Zhu N, Cao Y, Wu P. Biosynthesis of gold nanoparticles assisted by the intracellular protein extract of Pycnoporus sanguine and its catalysis in degradation of 4-nitroaniline. Nanoscale Res Lett 2015; 10: 147.
3. Tidke PR, Gupta I, Gade AK, Rai M. Fungus-mediated synthesis of gold Nanoparticles and standardization of parameters for its biosynthesis. IEEE Trans Nanobiosicence 2014; 13: 397.
4. Tina N, Tapan KD. Photocatalytic activity of Aspergillus foetidus mediated biosynthesized CdS Nanoparticles on methylene blue dye. Ind J Biochemistry & Biophysics 2016; 53: 44-50.
5. Ramachandran V, Baojun X. Antidiabetic properties of dietary flavonoids: a cellular mechanism review. Nutr Metabol 2015; 12: 60.

6. Onakpa MM, Asuzu IU. Histological changes and antidiabetic activities of Icacinatrichanta tuber extract in beta cells of alloxan-induced diabetic rats. Asian J Trop Biomed 2015: 3: 628.
7. Erbas O, Pala HG, Pala EE, Artunc U, Akman L, Akman T, et al. Therapeutic effect of sunitinib on diabetes mellitus related ovarian injury: an experimental rat model study. Gynecol Endocrinol 2015; 31: 388.
8. Ponnusamy S, Ravindran R, Zinjarde S, Bhargava S, Kumar AR. Evaluation of traditional Indian antidiabetic medicinal plants for human pancreatic amylase inhibitory effect in vitro. Evid Based Complement. Alternat Med 2011: 515.
9. Singh R. Medicinal plants: A review. J Plant Sci 2015; 3: 50.
10. Zhang H. Bioactive Natural products: detection, isolation, and structural determination. Phytomedicine 2011; 18: 902.
11. Negahdari S, Galehdari H, Kesmati M, Rezaie A, Shariati G. Wound healing activity of extracts and formulations of Aloe vera, Henna, Adiantum capillus-veneris, and Myrrh on mouse dermal fibroblast cells. Int J Prev Med 2017; 8: 18.
12. Huang H. Plant diversity and conservation in China: planning a strategic bioresource for a sustainable future. Bot J Linn Soc 2011; 166: 282.
13. Rafieian-Kopaei M. Medicinal plants and the human needs. J Herb Med Pharmacol 2012; 1: 2.
14. Estampador AC, Franks PW. Precision Medicine in Obesity and Type 2 Diabetes: The Relevance of Early-Life Exposures. Clin Chem 2018; 64: 130.
15. Jasmine R, Ganesh Kumar A, Rajaram R. Probing the mechanism of the anti-diabetic of a terpenoid from Elephantopus scaber L., an Indian ethnomedicinal palnt in STZ diabetic rats- In vivo and in silico analysis. Ind J Biochemistry & Biophysics 2018; 55: 384-88.
16. Iravani, S. Green synthesis of metal nanoparticles using plants. Green Chem 2011; 13: 2638.
17. Kirthika P, Deeba B, Sivakumar R, Sheikh A. Int. J. Pharm & Pharmaceutical Science 2014; 6: 304.
18. Meena K, Muthu K, Meenatchi V, Rajasekar M, Bhagavannarayana G, Meenakshisundaram SP. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 2014; 124: 663-669.
19. Akgul A, Senol SG, Yildirim H, Secmen O, Dogan Y. An ethnobotanical study in Midyat (Turkey), a city on the silk road where cultures meet. J Ethnobiol Ethnomed 2018; 14: 1.
20. Nuri Y, Semir K, Alkim GSY, Cagdas S, Gurkan Y, Altug Y, et al. Silymarian ameliorates and ovarian damage in streptozotocin induced diabetic rat model. Ind J Biochemistry & Biophysics 2018; 55: 137.
21. Kumar KS, Bhowmik D, Duraivel S, Umadevi M. Traditional and medicinal uses of banana. Journal of Pharmacognosy and Phytochemistry 2012; 1: 1.
22. Nikhal SB, Dambe PA, Ghongade DB, Goupale DC. Hydroalcoholic extraction of Mangifera indica (leaves) by Soxhletion. International Journal of Pharmaceutical Sciences 2010; 2: 30.
23. Priya B, Leaf Extract Mediated Green Synthesis of Silver Nanoparticles from widely available Indian plants: synthesis, characterization, antimicrobial property and toxicity analysis. Bioresources and Bioprocessing 2014; 1: 3.
24. Kumar MP, Suba V, Reddy BR. Wound healing activity of Celtisti morensis Span. (Cannabaceae) leaf extract in wistar albino rats. Indian J Exp Biol 2017; 55: 688.
25. Aili SR, Touchard A, Escoubas P, Padula MP, Orivel J, Dejean A, et al. Diversity of peptide toxins from stinging ant venoms. Toxicon 2014; 92: 166.
26. Konrad M, Vyleta ML, Theis FJ, Stock M, Tragust S, Klatt M, et al. Social transfer of pathogenic fungus promotes active immunisation in ant colonies. PLoS Biol 2012; 10: 1001.
27. Torres AFC, Quinet YP, Havt A, Radis-Baptista G, Martins AMC. Molecular pharmacology and toxicology of venom from ants (Chapter 8), in integrated view of the molecular recognition and toxicology. Analytical procedures to biomedical applications 2013; 10: 5772.
28. Shukla RK, Painuly D, Shukla A, Kumar V, Singh J, Porval A, et al. Physical evaluation, proximate analysis and antimicrobial activity of Morus nigra seeds original article. Int J Pharm Pharm Sci 2015; 7: 191.
29. Tofighi Z, Moradi-Afrapoli F, Ebrahimi SN, Goodarzi S, Hadjiakhoondi A, Neuburger M et al. Securigenin glycosides as hypoglycaemic principles of Sercurigera securidaca seeds. J Nat Med 2016; 71: 272.
30. Kasali FM, Wendo FM, Muysia SK, Kadima JN, Comparative hypoglycemic activities of flavonoids and tannins fractions of Stachytar phetaindica (L) Vahl leaves extracts in guinea pigs and rabbits, Int J Pharm Pharm Res 2016; 5: 48.
31. Bosha A, Anaga AO, Asuzu IU. Bioassay-guided isolation and structural elucidation of anti-diabetic principle of methanol leaf extract of Newbouldia laevis (P. Beauv), J Pharm Pharmacol 2015; 3: 516.
32. Mazumder M, Ponnan P, Das U, Gourinath S, Khan HA, Yang J, et al. Investigations on binding pattern of kinase inhibitors with PPARγ: molecular docking, molecular dynamic simulations, and free energy calculation studies. PPAR Research 2017:1.
33. Aba PE, Asuzu IU. H-Proton NMR spectra of antihyperglycemic treterpenoid isolated from Cussonia arborea. J Nat Prod 2016; 9: 1.
34. Al-Numair KS, Chandramohan G, Veeramani C, Alsaif MA, Ameliorative effect of kaempferol, a flavonoid, on oxidative stress in streptotocin-induced diabetic rats, Redox Rep 2015; 20: 198.
35. Patrick EA, Issac UA. Mechanisms of actions of some bioactive anti-diabetic principles from phytochemicals of medicinal plants: A review, Indian J Nat Prod and Res 2018; 9: 85.
36. Abd El-Ghffar EA. Ameliorective effect of glabridin, a main component of Glycyrrhiza glabra L. roots in streptozotocin induced Type 1 diabetes in male albino rats, Indian J Tradti Knowle 2016; 15: 570.
37. El-Kashak WA, Hamed AR, El-Raey M, Elshamy AI, Abd-Ellatef GEF. Antiproliferative, antioxidant and antimicrobial activities of phenolic compounds from Acrocarpus fraxinifolius. J Chem Pharmaceut Res 2016; 8: 520.
38. Abd El-Ghffar EA, El-Nashar HAS, Eldahshan OA, Singab ANB. GC-MS analysis and hepatoprotective activity of the n-hexane extract of Acrocorpus fraxinifolius leaves against paracetamol-induced hepatotoxicity in male albino rats. Pharmaceut Biol 2016; 55: 441.
39. Alofi MT, Zaki AA, Abdel-Rahman HA, El Tigani EA. Antioxidant and anti-stress biomarkers of some nutraceuticals in alloxan-induced diabetic rats. Int J Basic Appl Med Sci 2016; 6: 68.
40. Eman Ali AEG, Safia MS. Antioxidant and anti-inflammatory effects of Acrocarpus fraxinifloius on hyperglycemia, hyperlipidemia and liver/kidney dysfunctions against alloxan induced Type 1 diabetes in rats, Ind J Trad Knowle 2018; 17: 223.
41. Ibrahim AA, Madkour NK. Insulin augmentation and glucagon inhibition in cinnamon treated diabetic rats. Int J Adv Res 2016; 4: 1227.
42. Kumas M, Esrefoglu M, Guler EM. Protective effects of silymarian against isotretinoin induced liver and kidney injury in mice. Indian J Exp Biol 2018; 56: 158.