In vitro and *in vivo* Antidiabetic Activity of Ag Nanoparticles Mediated from Gymnemic Acid I and II

Navanita Sivaramakumar[1], Yedhunoori Ganesh Kumar[2], Bijo Mathew[3], Vinod Kumar Reddy Bondu[1], Madunuri Chandra Sekhar[4], Mohd Abdul Hadi[5], Bala Gurivi Reddy Vemireddy[6], Vijaya Babu Penke,[7] Kalakotla Shanker[1],*

[1]Department of Pharmacognosy, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Ooty, Nilgiris, Tamil Nadu, INDIA.
[2]Department of Pharmaceutics, KVK College of Pharmacy, Surmaiguda, Abdullapurmet, Rangareddy, Hyderabad, Telangana, INDIA.
[3]Department of Pharmaceutical Chemistry, Amrita School of Pharmacy, Amrita Vishwa Vidyapeetham, AIMS Health Sciences Campus, Kochi, Kerala, INDIA.
[4]Department of Physics, Chaitanya Bharathi Institute of Technology, Hyderabad, Telangana, INDIA.
[5]Department of Pharmaceutics, School of Pharmacy, College of Health Sciences and Medicine, Wolaita Sodo University, Wolaita Sodo Town, ETHIOPIA.
[6]Department of Physics, PGT, New Middle East International School, Riyadh, KINGDOM OF SAUDI ARABIA.
[7]Dr. Reddy's Institute of Life Sciences, University of Hyderabad Campus, INDIA.

ABSTRACT

Background: *Gymnema sylvestre* is traditionally used to treat diabetes in Asia. The triterpenoid glycosides Gymnemic acid-I (GA-I) and Gymnemic acid-II are the main biologically active components (GA-II). Glide has yet to be used to define the mechanisms of action of drugs, nevertheless. **Materials and methods:** To dock to the active site of protein tyrosine phosphate 1B, the GA-I and GA-II compounds were used. The identical nanoparticles were produced using the straightforward centrifugation green synthesis technique using silver nitrate at a predetermined temperature. The created nanoparticles have undergone XRD, UV, FESEM, TEM, DLS, and Zeta potential characterization. Using the PTP 1B assay and a diabetic animal model induced by streptozotocin, the anti-hyperglycemic activity of green-produced nanoparticles was determined *in vitro* and *in vivo*. The GA-I-induced AgNPs showed exceptional PTP 1B enzyme inhibitory effectiveness among other medicines. Rats with diabetes are administered 100 mg/kg and 200 mg/kg of GA-I mediated AgNPs, 100 mg/kg and 200 mg/kg of GA-II mediated AgNPs and 50 mg/kg of metformin. **Results:** Blood glucose levels were significantly decreased (p 0.001) at a dose of 200 mg/kg (b.wt. p.o.) of GA-I mediated AgNPs compared to the GA-II mediated AgNP treated group. **Conclusion:** Hence, it may indicate that GA-I mediated AgNPs be exploited as prospective nanomedicine for treating type-2 diabetes mellitus.

Keywords: Gymnemic Acid-I, Gymnemic Acid-II, *Gymnema sylvestre*, Molecular docking, PTP 1B, Antihyperglycemic activity.

INTRODUCTION

GA-I and II are triterpenoid glycosides segregated from the leaves of *Gymnema sylvestre* (GS) belonging to the family apocynaceae, which is known to have potent anti-diabetic activity. GA-I and GA-II are the main active phytoconstituents of the GS plant and were responsible for the potent inhibitory action of glucose uptake.[1] Protein Tyrosine Phosphatase 1B (PTP 1B) has sparked widespread attention as a new strategic target for the treatment of diabetes and obesity. PTPs are made up of a group of receptors similar to the cytoplasmic signal transducing enzymes that played

a part in suppressing the insulin signal transduction pathway.[2] These enzymes were categorized according to their cellular location and identified using the Protein Tyrosine Phosphatase signature concept, which refers to their shared 230–280 amino acid catalytic domains.[3] PTP 1B is mostly seen interacting with other PTPs in a variety of human tissues. Oxidation, nitrosylation, proteolytic cleavage, and phosphorylation are other post-translational modifications that have an impact on PTP 1B activities. This enzyme is a precise target for Type 2 diabetes and obesity due to its capacity to affect a variety of signaling pathways in a cell/tissue and stimulus-dependent manner.[4] At the same time, the molecular docking studies of the interaction between PTP 1B and its specific inhibitors were also evolving,[5] which laid a bottom line for screening specific PTP1B inhibitors. The current study focuses on targeting PTP 1B to find promising antidiabetic natural compounds by molecular docking studies, followed by

assessing the *in vitro* and *in vivo* therapeutic potential of PTP 1B silver nanoparticles.[6] These studies paved the way for PTP 1B inhibitory activity molecular docking studies. They helped gain insight into the pharmacological effects of GA-I, GA-II, and silver nanoparticles.

MATERIALS AND METHODS

SR Life Science Pvt. Ltd., in Hyderabad, India, supplied chemicals such as pNPP, EDTA, DMSO, and Silver Nitrate ($AgNO_3$). Gymnemic acid was furnished by Sigma Aldrich. GSE was procured from local vendor. All of the other compounds in the technique were made with analytical-grade chemicals.

Green synthesis of silver nanoparticle

10 mL of gymnemic acid solution (1 mg/mL concentration) was added dropwise to 45 mL of 1 mM $AgNO_3$ solution in conical flasks, and the mixture was quickly agitated with a magnetic stirrer for 6, 12, and 24 hr. The conical flasks were incubated at room temperature for 12-24 hr. The solution combination's appearance changed from brilliant yellow to dark brown. In an 83-SR Thermo Fischer cooling microcentrifuge, the decreased solution was spun for 20 min at 5000 rpm. The supernatant was discarded, while the residue was kept and washed and dried with sterile distilled water.

Characterization of AgNPs

X-ray diffraction, Ultraviolet spectroscopy, Field Emission Scanning Electron Microscope, Transmission Electron Microscope, Zeta potential, and Dynamic Light Scattering analysis were used to successfully determine the amorphous or crystalline nature, surface morphology, and particle size analysis of the synthesized AgNPs.

Molecular docking methodology

The majority of active compounds were docked into the active site of protein tyrosine phosphate 1B inhibitor using Glide (version 5.7, Schrodinger, LLC, New York, NY, 2011),[7] from the three-dimensional structure of the enzyme complex (PDB ID: 1NL9) obtained from the protein data bank. To optimize and minimize the protein structure, the OPLS-2005 force field was applied. The docking process is also used in the previously disclosed approach.[8]

Oral Glucose Tolerance Test (OGTT)[9]

Assessment of glucose tolerance in normal healthy rats

The rats were divided into nine various groups of six animals each after being fasted (*n*=6). Animals in group I received 0.5 mL/kg of vehicle (0.9% w/v saline) as a control. Group II got metformin (50 mg/kg, p.o.) suspended in a vehicle as a reference medication. The animals in each group received doses of GSE (200 mg/kg), GA-I AgNPs (100 and 200 mg/kg), and GA-II AgNPs (100 and 200 mg/kg). Following the administration of the test medications, rats from all groups were then given glucose (2g/kg, p.o.) 30 min later. Blood samples were taken from the retro-orbital sinus under ether anesthesia at 0 min, 30 min, 60 min, 90 min, and 120 min for Accu Check's assessment of the glucose level.

In vitro PTP 1B assay

Protein tyrosine phosphatase inhibitory activity was carried out with slight modifications.[10] Protein tyrosine phosphatase 1B was obtained from the rat liver homogenate. Mice's livers were rapidly removed, and 100 mg of wet liver tissue was added to the ice-cold sucrose solutions. The wet liver was diluted with a sucrose solution after the mixture was homogenized at 4°C for 1 min. The homogenate was centrifuged for 30 min. at 4°C and 12,000 rpm. The fluid from the supernatant was gathered and frozen at -50°C for analysis. The test substances (5-50 M, 5 l) were pre-incubated for 30 min with liver homogenate (3 l) in HEPES buffer (4-(2-hydroxyethyl)-1-piperazine ethane sulfonic acid). The test combination contained 10 mM of p-nitrophenyl phosphate in a 50 mM HEPES buffer with a pH of 7.0, and the experiment was carried out in a final volume of 200μL. After 10 min of incubation at 37°C, the reaction was stopped by adding 50 l of 0.1 N Sodium hydroxide. Sodium orthovanadate served as the standard in this enzyme experiment.

Acute Oral Toxicity Studies: (OECD 2001)

According to OECD guidelines 423, acute toxicity experiments for the GSE, GA-I, and GA-II mediated silver nanoparticles were carried out. The goal of the study was to determine the best doses to test the antidiabetic and anti-hyperlipidemic effects. For the investigation, female albino mice weighing 20–30 g were utilized. Five groups of three animals each were created from the selected animals. Silver nanoparticles and regular distilled water (2 mL/kg) were given to the control group. The GSE, GA-I AgNPs, and GA-II AgNPs were administered in graduated amounts (2000 mg/kg body weight) to the other groups. Animals were observed for any behavioural abnormalities and deaths routinely, if any, intermittently for the following 6 hr after the medication dose, then once more at 24 hr later. After receiving the medication, they were monitored for up to 28 days to determine whether any of them had died. At 8 A.M. and 8 P.M. each day, the observations were made (OECD 2008-Guideline on Acute Oral Toxicity) (AOT).

Experimental Animals

Male Wistar rats weighing 180–200 g were utilised in the investigation. According to document 1684/PO/a/13/CPCSEA, the Institutional Animal Ethical Committee (IAEC) has given its permission to the animal study protocol. The selected animals were housed in a controlled environment with 45-55% humidity, 25°C temperatures, and a light/dark cycle of 12 hr each day. The rats had free access to water and a standard lab diet.

Experimental design

Under a strict fasting regimen, the rats were split into six groups of six. The animals in Group I (the control group) were given an oral dose of 0.5 mL/kg of vehicle (0.9% w/v saline). A reference medicine, metformin (50 mg/kg, p.o.), was administered to Group II while it was suspended in the vehicle. Animals in groups IV and V were given GA-I+ AgNPs (100 and 200 mg/kg), whereas those in groups VI and VII were given GA-II+ AgNPs (100 and 200 mg/kg) as shown in Table 1. Under ether anaesthesia, blood was drawn from the retro-orbital sinus and analysed using a glucometer to assess blood glucose levels (Accu-Chek Active).[11]

Induction of diabetes

For this study, Wistar rats fasted overnight and received an intraperitoneal injection of Streptozotocin (STZ) (40 mg/kg in 0.1 M citrate buffer, pH 4.5). After STZ was given to the rats for 48 hr, hyperglycemia was induced.[12] The study relied on rats with blood glucose levels of 250 mg/dL or higher.

In vivo Estimation of serum glucose

After collecting blood through retro-orbital puncture, it was centrifuged at 5000 rpm in a fast centrifuge (REMI-CM12). On the 14th day, serum glucose was estimated at 0 hr, 1 hr, 2 hr, and 4 hr using a fully automated biochemistry analyzer (SPHEARA-ACCUREX455).

Histopathological studies

The selected rats from the relevant groups were dissected on the 15th day of the current suggested investigation. The pancreas was extracted and fixed in 10% neutral buffered formalin for 24 hr. The separated organs were processed and sectioned at 5 μm thickness and submitted to histological examinations.

RESULTS

Characterization

XRD analysis

X-ray diffraction (XRD) is used to determine and describe the crystal structure of the AgNPs. Figure 1A displays the XRD patterns obtained from the produced AgNPs. According to the same indexing scheme used by the Joint Committee on Powder Diffraction, the peaks at 38.23°, 44.37°, 64.63°, and 77.51° in a sample containing silver correspond to the (111), (200), (220), and (311) Bragg's reflections of the face centre cubic (fcc) structure of metallic silver.

UV analysis

Metal nanoparticles in the 2-100 nm size range are often characterised using light with wavelengths in the 200-800 nm range. The AgNPs are characterised by spectrophotometric absorption measurements in the 460 nm region. Surface Plasmon Resonance, an oscillation of Ag electrons in the conduction band, is responsible for this distinctive peak (SPR). The production and stability of AgNPs in an aqueous solution were evaluated using UV-visible spectroscopy. The region of wavelengths between 200 and 800 nm is where AgNPs' signature surface plasmon band is most prominent. The creation of silver nanoparticles is verified by the development of a surface plasmon peak at 420 nm (Figure 1B).

FESEM analysis

It's a FE-SEM picture of the surface morphology of NPs made via green synthesis. The FE-SEM picture clearly demonstrated the surface shape of the produced AgNPs (Figure 1C). The green-synthesized AgNPs were about spherical, and they were produced by the GA plant. Different classes of phytochemicals, such as GA-I and GA-II, may be responsible for this shape shift since they aid in the attenuation and stabilisation of AgNPs during their production. Since FE-SEM and DLS are based on distinct characterisation techniques and require entirely separate sample preparation procedures, the findings produced from the two approaches may differ.

TEM analysis

Figure 1D displays TEM images used to determine the shape and size of the produced AgNPs. The resulting particles were round, and it was shown that the AgNPs, which were also spherical, had a sizable surface area. AgNPs formed with sizes between 10 and 40 nm. There were not many particles of varying sizes; the particles were mostly monodispersing.

DLS, Zeta and EDAX analysis

The particle hydrodynamic size (Z-average diameter) produced from DLS analysis is the size at which particles behave hydrodynamically while suspended in a liquid. Figure 2A shows the hydrodynamic size of our produced AgNPs, 24nm. Once again, the surface zeta potential is an important metric for describing the stability of AgNPs in water. Figure 2B shows the surface zeta potential of our produced nanoparticles which were 2 mV, which suggests the particles have high stability. EDAX was

Table 1: Classification of animal groups for treatment.

Group	Treatment	Dose
I	Normal control	Saline
II	Diabetic control	STZ 40 mg/kg, p.o
III	Metformin	50 mg/kg, p.o
IV	*GA I* + AgNPs	100 mg/kg in, p.o
V	*GA I* + AgNPs	200 mg/kg in, p.o
VI	*GA II* + AgNPs	100 mg/kg, p.o
VII	*GA II* + AgNPs	200 mg/kg, p.o
VIII	GA I	200 mg/kg, p.o
IX	GSE	400 mg/kg, p.o

used to denote silver's optical absorption. Carbon and potassium were also detected, at 1.0 and 1.2 keV, respectively, in addition to silver, at 2.5 keV (Figure 2C).

Docking Results

Molecular docking experiments were used to determine the compound's putative binding mechanism in the enzyme's active site (Figures 3A-3D). The computational analyses found that among three compounds, Gymnemic Acid-I is predominantly stabilised by nine hydrogen bonding interactions, including Tyr 46, Lys 120, Ser 216, Ala 217, Gly 218, Ile 219, Gly 220, Arg 221, and Gln 216. The docking experiments demonstrated that GA-I exhibited docking score of -10.2 which was more effective than GA-II which exhibited docking score of -7.5. When compared to other drugs tested for *in vitro* antidiabetic action, those mediated by GA-I demonstrated the greatest PTP 1B enzyme inhibitory activity. This finding is consistent with findings from molecular docking experiments. *In vivo* results: GA-I mediated AgNps at the dosage level of 200 mg/kg b.wt demonstrated substantial suppression of ($p < 0.001$) blood glucose levels in diabetic rats as compared with *GA-I* (100mg/kg), GA-II (100 mg/kg and 200mg/kg) treated group. Based on these findings, GA-I mediated AgNPs are superior than GA-II mediated AgNPs with respect to their anti-hyperglycemic efficacy.

In vitro and *in vivo* antidiabetic activity

The PTP enzyme is strongly inhibited by the GA-I induced AgNPs, as shown in Figure 4A. Inhibition ranged from 84.21% with the conventional chemical sodium orthovanadate (concentration = 10 μM) to 82.16% with GA-I mediated AgNPs and 60.09% with GA-I mediated AgNPs, respectively. Extract from *GS* revealed some PTP enzyme inhibition (40.08%).

Our earlier research showed that herbal plant extract nanoparticles made in our lab had potent pharmacological antidiabetic effect.[13,14] Controlling blood glucose levels, GA-I mediated AgNPs showed remarkable efficacy in managing diabetes. The

indices were normalised in the diabetic rats treated with GA-I mediated AgNPs ($p < 0.001$), confirming the efficacy of these particles (Figure 4B).

Single doses of 100 and 200 mg/kg of GA -1, GA-II mediated AgNPs and GSE were used in hypoglycemic state glucose tolerance experiments, as shown in Table 2. Based on the findings of the glucose tolerance test, it was established that neither GA-1 nor GA-II mediated AgNPs nor GSE exhibited any hypoglycemic effect in healthy, normal rats.

Data on insulin regeneration are shown in Table 3. In comparison to diabetic control animals, insulin levels in rats treated with GA-I AgNPs returned to normal levels during the fasting state ($p < 0.001$). In the current study, hyperglycemia was considerably induced by STZ, and a 14-day oral administration of GA-I AgNPs resulted in a considerable reduction in hyperglycemia. As the fundamental improvement in the amount of insulin HM AgNPs treated animals produced was evident, the precise mechanism by which GA-I AgNPs interceded their hypoglycemic influence would be by enhancing pancreatic insulin emission from the existing -cells of islets.[15] As evidenced by the statistically significant increase in insulin levels seen in the GA-I AgNPs-treated animal groups, this hypothesis is supported.

Acute toxicity and Histopathology studies

The absence of cytotoxicity proved the safe therapeutic uses of these nanoparticles, and the results provided clear justification that green produced NPs give a non-toxic coating of GA-I and GA-II and plant extracts (Table 4). An acute oral toxicity research was performed using green produced GA-I AgNPs, GA-I AgNPs, and GSE at 2000 mg/kg dosage levels in accordance with OECD guideline number 423. Furthermore, no changes in animal weight, aberrant development, skin inflammation, or the beginning of toxicities were seen following oral administration of green produced nanoparticles, indicating the biocompatibility and non-toxicity of the particles. Neither a microscopic nor a microscopic histological abnormality was detected.

Table 2: Effect of *GA-I* AgNPs, *GA-II* AgNPs and GSE on OGTT in Normal rats.

| Group	Treatment and dose	0 min	30 min	60 min	90 min	120 min
I	Normal	81±2.90	114±2.80	119±3.32	93±0.21	84±1.99
II	Metformin (50 mg/kg)	86±0.88	112±0.34	80±0.71	79±1.02	78±0.90
III	GSE (200 mg/kg)	85±1.50	113±0.99	117±0.32	94±0.45	90±0.55
III	GA-I AgNPs (100 mg/kg)	86±0.34	106±1.88	89±1.01	81±0.74	84±0.87
IV	GA-I AgNPs (200 mg/kg)	87±0.75	96±0.96	90±0.23	84±0.79	82±0.97
V	GA-II AgNPs (100 mg/kg)	90±0.98	107±0.67	91±0.76	85±0.98	84±0.65
VI	GA-II AgNPs (200 mg/kg)	88±0.99	98±0.19	85±0.74	80±0.70	81±0.89
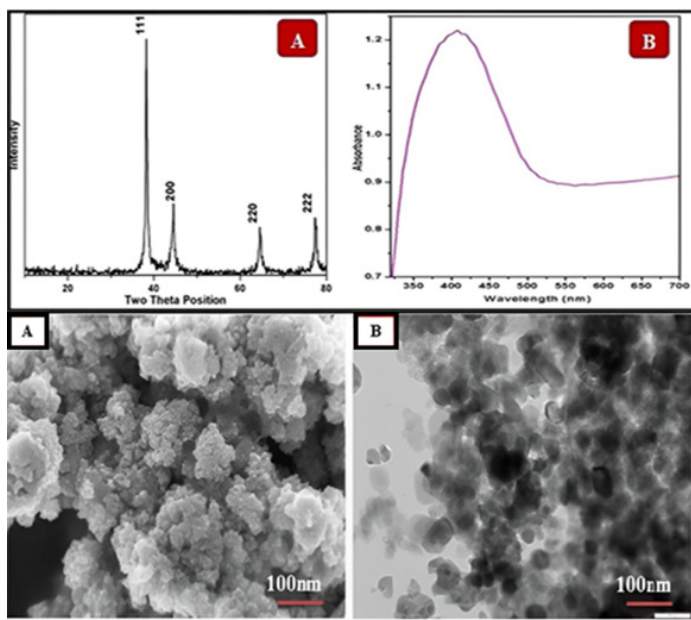
Figure 1: A: XRD graph obtained for GA-AgNPs, B: UV spectrum of GA-AgNPs, C: FESEM image of GA-AgNPs, D: TEM image of GA-AgNPs.

Figure 2: A: Particles diameter spectrum, B: Zeta sizer, C: EDAX of GA-AgNPs.
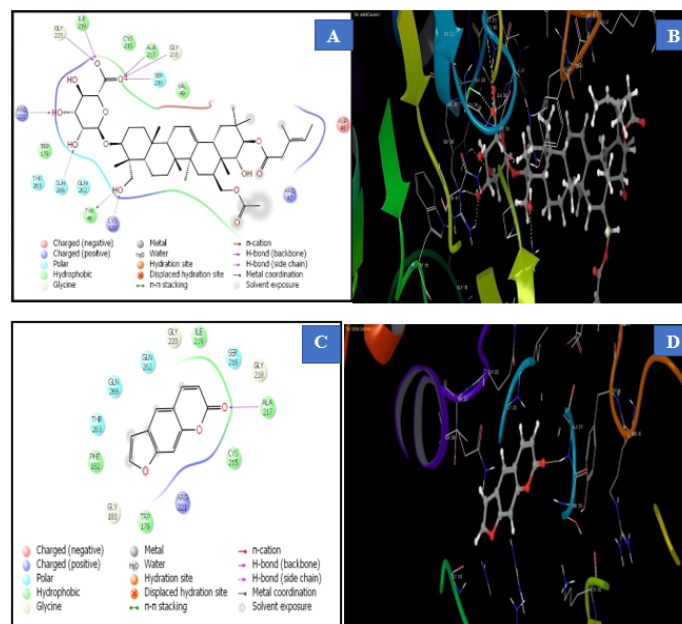

Figure 3: A and B: *GA-I*: Different interactions with amino acids target molecule and Different bond formations, C and D: *GA-II*: Different interactions with amino acids target molecule and Different bond formations.
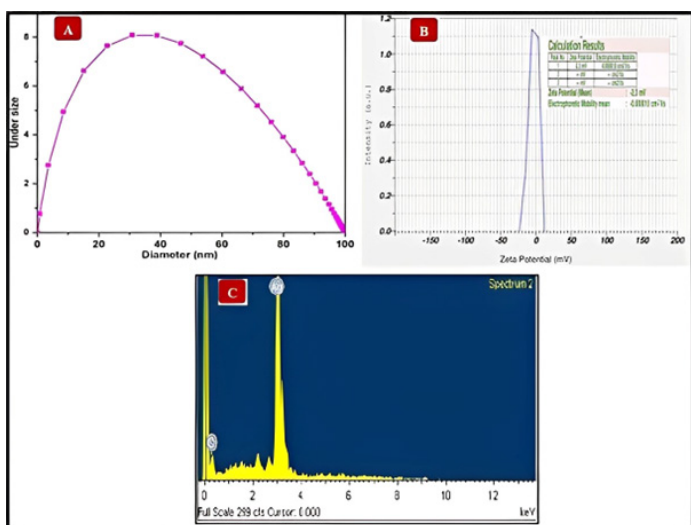

Figure 4: A: *In vitro* PTP 1B enzyme inhibitory activity of GA-I AgNPs, GA-I AgNPs and GSE, B: *In vivo* antidiabetic activity of GA-I AgNPs, GA-I AgNPs and GSE.

Histopathology of pancreatic tissue samples taken from healthy control animals (Group-I). Widespread β cells may be seen in the islet. Islets of Langerhans showed that β cells in group V and VII were not different from those in the normal control group, either in terms of quantity or distribution. In comparison to the normal group of animals, a lower number of cells was seen in the diabetes group. A and B in Figure 5. Streptozotocin was able to kill off the beta cells, which is how diabetes is triggered.

Animals given metformin are depicted in Figure 5C; their β cells appear to be on par with the normative sample. The arrows in Figures 5D, 5E, and 5F represent the fractional recovery of islets cells in GA-I, GA-II, and GSE-treated rats. In addition, treatment with GA-I and GA-II AgNPs did not result in the damaged β cells
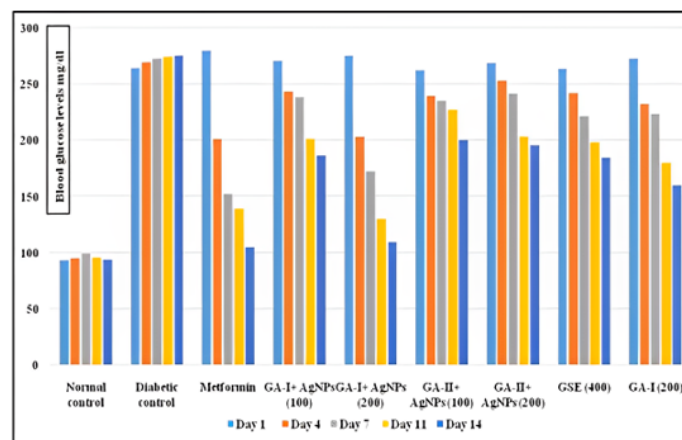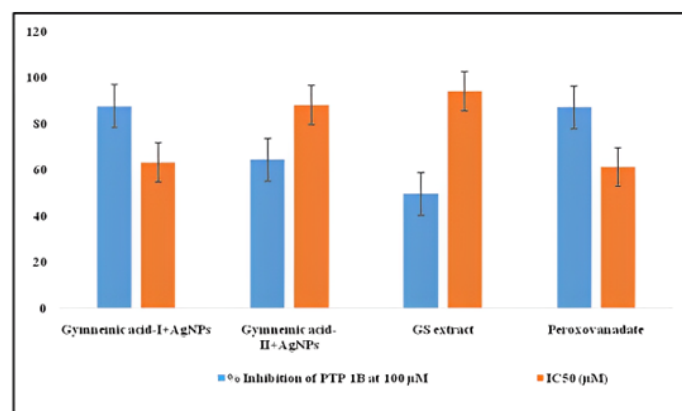
often found in the onset of diabetes. Recovery of necrotic β cells was especially well-articulated following treatment with 200 mg/kg of GA-I-AgNPS, in contrast to the group given GS extract.

Table 3: Effect of GA-I AgNPs, GA-II AgNPs and GSE on insulin levels in Streptozotocin induced diabetic rats.

Groups	Treatment	Dose	Insulin levels (µIU/mL)
I	Normal	NA	7.84±0.76
II	Diabetic control (STZ)	40 mg/kg	4.45±0.84
III	Standard (Metformin)	50 mg/kg	7.25±0.76
IV	AgNPs	200 mg/kg	3.25±0.28
V	GSE	200 mg/kg	4.11±0.82
VI	GA-I AgNPs	100 mg/kg	4.99±0.11[a]
VII	GA-I AgNPs	200 mg/kg	5.43±0.32[a]
VIII	GA-II AgNPs	100 mg/kg	6.02±0.76
IX	GA-II AgNPs	200 mg/kg	6.90±0.98

The data is expressed as mean ± S.E.M.; n = 6 in each group. [a] $p < 0.001$, significant when compared to normal control.

Table 4: Effect of Acute toxicity studies of GA-I AgNPs, GA-II AgNPs and GSE.

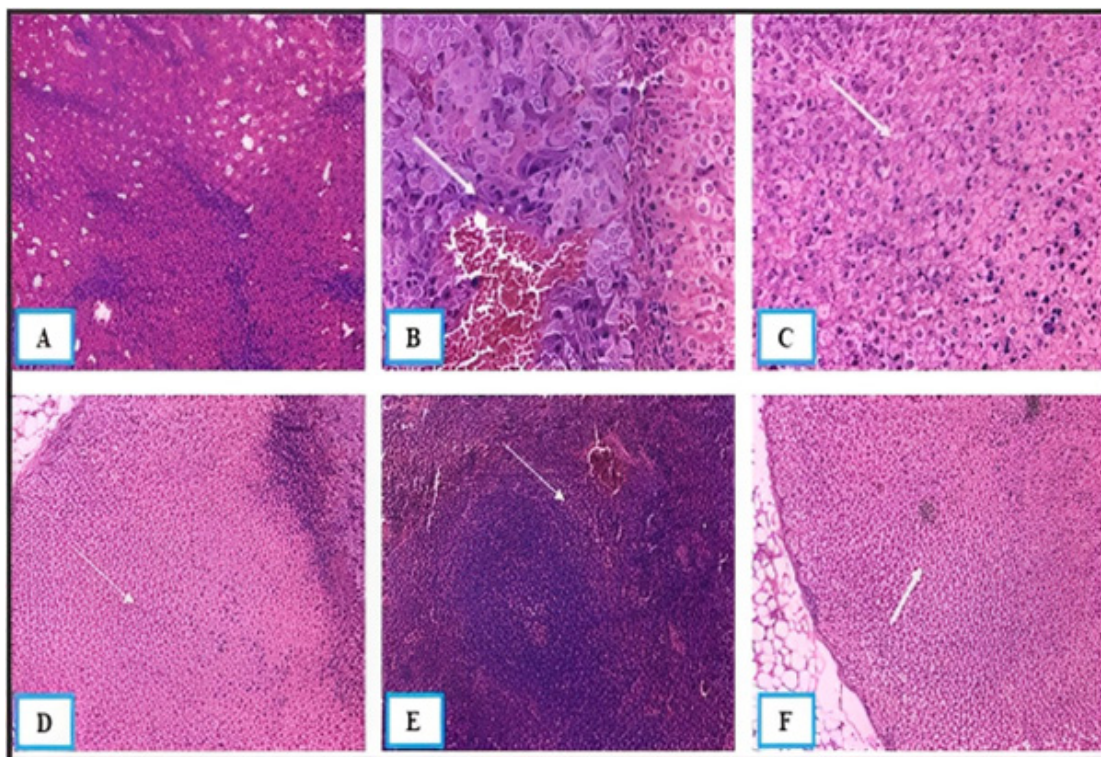| Groups	Treatment Dose	Weight of animal		Sign of Toxicity	Onset of Toxicity	Reversible/ Irreversible
		Day 1	Day 28			
G I	Control (0.9% Nacl)	25±2.32	28±1.94	NO	NO	Nil
G II	AgNPs (2000 mg/kg)	24±2.08	29±1.09	NO	NO	Nil
G III	GSE (2000 mg/kg)	25±3.44	30±2.25	NO	NO	Nil
G IV	GA-I AgNPs (2000 mg/kg)	26±3.20	31±2.32	NO	NO	Nil
G V	GA-II AgNPs (2000 mg/kg)	24±2.01	28±2.92	NO	NO	Nil

Figure 5: A: Histopathology of normal control group, B: Diabetic control group, C: Standard group, D: GA-I AgNPs, E: GA-II AgNPs group, F: GSE group.

DISCUSSION

Docking experiments are now being conducted to compare the antidiabetic effectiveness of GA-I and GA-I mediated AgNPs. The present experimental results obtained demonstrated that the GA-I mediated AgNPs significantly inhibited ($p < 0.001$) blood glucose levels in diabetic rats when compared to GSE and GA-I compounds were administered at a dosage level of 200 mg/kg b.wt. Without the addition of silver nanoparticles, both GA-I (200mg/kg) and GSE (400mg/kg) failed to significantly lower glucose levels on day 14 of the experimental methodology. Gymnemic acid-I and gymnemic acid-II from the *G. sylvestre* plant were used in the synthesis of the AgNPs, which were then characterised by XRD, FE-SEM, TEM, EDAX, and PSA. GA-I induced AgNPs demonstrated strong PTP 1B and α-amylase enzyme inhibitory activity, among other drugs substantiated by molecular docking investigations. In addition, the hypothesis for the synthesis of AgNPs was to increase the surface area of the drug to achieve more significant and potent pharmacological activity, even in *in vivo* STZ induced animal model studies, by associating (enhanced biological properties) with a natural Gymnemic acid (non-toxic and chemically inert) (enhanced insulin levels). Hence, it may indicate that GA-I mediated AgNPs be exploited as prospective nanomedicine for treating type-2 diabetes mellitus. More research is needed to validate the precise mechanism of action of the green nanoparticle formulation used in the current study.

CONCLUSION

The docking experiments comparing the antidiabetic effectiveness of GA-I (Gymnemic acid-I) and GA-I mediated silver nanoparticles (AgNPs) have provided promising results. The experimental findings clearly demonstrated that GA-I mediated AgNPs significantly inhibited blood glucose levels in diabetic rats, surpassing the effects of GSE (Gymnema sylvestre extract) and GA-I compounds alone. The synthesis of AgNPs using GA-I and GA-II from the Gymnema sylvestre plant was characterized by various techniques, including XRD, FE-SEM, TEM, EDAX, and PSA. The GA-I induced AgNPs exhibited strong inhibitory activity against PTP 1B and α-amylase enzymes, as confirmed by molecular docking investigations. The hypothesis behind the synthesis of AgNPs was to enhance the surface area of the drug, leading to increased pharmacological activity, especially in in vivo studies using STZ induced animal models of diabetes. The association of enhanced biological properties with a natural Gymnemic acid, known for its non-toxic and chemically inert nature, aimed to elevate insulin levels and achieve more significant therapeutic effects. Therefore, GA-I mediated AgNPs hold great potential as prospective nanomedicine for the treatment of type-2 diabetes mellitus. However, further research is necessary to elucidate the precise mechanism of action of this green nanoparticle formulation used in the current study. Understanding the underlying molecular pathways and confirming the therapeutic efficacy through additional studies will be crucial in validating the use of GA-I mediated AgNPs as a viable and effective approach for managing diabetes.

ACKNOWLEDGEMENT

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

GSE: *Gymnema sylvestre* Extract; **GA-I:** *Gymnemic acid-I;* **GA-II:** *Gymnemic acid-II;* **AgNPs:** Silver NanoParticles; **XRD:** X-ray diffraction; **UV:** Ultraviolet spectroscopy; **FESEM:** Field Emission Scanning Electron Microscope; **TEM:** Transmission Electron Microscope; **DLS:** Dynamic Light Scattering analysis; **EDTA:** Ethylenediamine tetra acetic acid; **DMSO:** Dimethyl sulfoxide; **PTB:** Protein tyrosine phosphatase; **STZ:** Streptozotocin; **EDAX:** Energy Dispersive X-ray Analysis; **SPR:** Surface plasmon resonance.

SUMMARY

Gymnema sylvestre is an indigenous plant commonly used in treating diabetes mellitus in the traditional system of medicine. GS Plant has some special characteristics such as the blood-glucose-lowering effect, and this therapeutic activity is mainly attributed to GA-I and GA-II. The current study involves the green synthesis, characterization, *in vivo* antidiabetic activity, and *in vitro* PTP 1B inhibiting potential of green synthesized AgNPs via enzyme kinetic and molecular docking studies. From the results it is evident that *GA-I* mediated AgNPs be exploited as prospective nanomedicine for treating type-2 diabetes mellitus.

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