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**Exploring the In-vitro antidiabetic efficacy of *Fagonia arabica linn.* leaf extract****Sujata V. Lambe<sup>1\*</sup>, Dr.Pradip B. Ghogare<sup>2</sup>, Manisha D. Sonawane<sup>3</sup>, Sonali T. Gade<sup>4</sup>**<sup>1</sup>Asst. Prof., Department of Pharmaceutical chemistry, S. M. B. T. College of Pharmacy, Dhamangaon. Tal. Igatpuri Dist., Nashik. (M.S)<sup>2</sup>Prof., Department of Pharmacognosy, S. M. B. T. College of Pharmacy, Dhamangaon Tal. Igatpuri Dist., Nashik. (M.S)<sup>3</sup>Asst. Prof., Department of Pharmaceutical chemistry, Pravara Rural College of Pharmacy, Loni. Tal-Rahata, Dist.- Ahilyanagar<sup>4</sup>Asst. Prof., Department of Pharmaceutical chemistry, MES's College of Pharmacy, Sonai. Tal-Newasa, Dist.- Ahilyanagar**Article Information**

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**Keywords***Silver nanoparticles, albino mice, Antihyperglycemic, Fagonia arabica***ABSTRACT**

Therapeutic components generated from medicinal plants and environmentally friendly plant-based technologies for producing silver nanoparticles have shown great promise in the treatment of type 2 diabetes mellitus (T2DM). The present study assessed the anti-diabetic potential of biogenic silver nanoparticles (Fa AgNPs) mediated by *Fagonia arabica* using both in-vitro and in-vivo techniques. Several techniques, including UV-VIS spectrophotometry and FTIR analysis, were used to describe the bio-synthesised (FaAgNPs). FaAgNPs' in vitro efficacy was assessed against the enzymes  $\alpha$ -glucosidase and  $\alpha$ -amylase. For in-vivo studies, twenty male Balb/C albino-mice were divided into four groups (n = 5) at random: the normal group, the sickness group (diabetes group without therapy), the control group, and the treatment group (diabetic group treated with FaAgNPs). At doses ranging from 62 to 1000  $\mu$ g/mL, the (FaAgNPs) showed a dose-dependent inhibition against  $\alpha$ -amylase and  $\alpha$ -glucosidase, with IC<sub>50</sub> values of 92 and 100  $\mu$ g/mL, respectively. Mice with STZ-induced diabetes showed a marked decrease in blood glucose levels after treatment with (Fa AgNPs). Compared to animals treated with a standard drug ( $128.6 \pm 2.73^{**}$  mg/dL), animals treated with Fa AgNPs demonstrated a strong anti-hyperglycemic impact ( $105 \pm 3.22^{**}$ ). Our results suggest that (Fa AgNPs) have a preliminary multi-target efficacy against type-2 diabetes, which calls for more thorough research.

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**1. INTRODUCTION:**

Insulin resistance, hyperglycemia, and inflammatory markers are the hallmarks of diabetes, a global health concern. It results in metabolic dysfunction, oxidative stress, and damage to the liver and kidneys. Organ insulin resistance is a common consequence of type 2 diabetes mellitus (T2DM). Diabetes affects 422 million people worldwide and ranks as the sixth leading cause of morbidity and mortality. There will be 640 million diabetics worldwide by 2040. Reducing the amount of glucose absorbed by the gastrointestinal tract is one way to manage type 2 diabetes. Dietary carbohydrates are converted into simple mono-saccharides by the enzyme  $\alpha$ -glucosidase, also known as  $\alpha$ -D-glucoside

glucohydrolase, which catalyzes the release of  $\alpha$ -glucose from the non-reducing end of the substrate. Furthermore, long-chain carbohydrates are biologically broken down by the  $\alpha$ -amylase enzyme, which makes them easier to absorb. The common diabetic drug metformin indirectly stimulates the AMPK signaling system, which reduces vitamin B12 absorption and causes symptoms like stomach pain, diarrhea, anorexia, and flatulence. By phosphorylating AMPK, AgNPs increase insulin sensitivity and alter the effects of insulin. AgNPs boost the expression of GLUT2 and IRS1, which decreases blood glucose and increases insulin production and release. Additionally, elevated IRS1 protein can mitigate the consequences of hyperglycemia.

With applications in public health, medicine, food additives, cosmetics, agriculture, and environmental preservation, nanotechnology is a significant discipline that involves designing, generating, and altering particle structures. The electrical, optical, and magnetic properties of noble metal nanoparticles, or AgNPs, make them useful for a variety of applications. The physical, chemical, and biological processes that result in them include chemical reduction and green synthesis. Green synthesis is more flexible, cost-effective, and environmentally safe than physical and chemical procedures.

AgNPs and other plant extracts are used in electrical batteries, medical equipment, and pigments to treat diseases like cancer, diabetes, malaria, and tuberculosis. Anti-cancer, antibacterial, and antidiabetic properties have been proven by AgNPs; their antidiabetic impact is linked to enzymes that break down carbs. Diabetes is an oxidative stress-based disease that results in apoptosis and  $\beta$ -cell maturation due to high reactive oxygen species production. AgNPs provide a multitude of antioxidants and are efficient free radical scavengers. STZ causes diabetes because it is preferentially employed to degenerate insulin-producing  $\beta$ -cells, which ultimately leads to necrosis. Blood glucose and insulin levels are altered by the drug STZ. Scientists are particularly interested in *F. arabica*, a plant with significant therapeutic potential, due to its bitter and sour taste. Found in the arid calcareous rocks of Saudi Arabia, Egypt, Morocco, Tunisia, Algeria, Pakistan, and western India, it treats conditions of the liver, blood, brain, and inflammation.

There are several medicinal applications for extracts from the *Fagonia* genus. A unique plant extract known as *F. arabica* has been identified as a reducing and stabilizing agent for the manufacture of AgNPs due to its availability and low cost. The

study examines biosynthesis and characterization using UV-Vis, FT-IR spectroscopy, and scanning electron microscopy. The anti-diabetic effects of *F. arabica* AgNPs will be assessed in vitro and in vivo using diabetic mice.

## **2. MATERIALS AND METHODS:**

### **2.1 Plant collection:**

*F. arabica* leaves were gathered from the areas surrounding Ahmednagar, Maharashtra. Through letter no. 35/2021-2022 dated July 14, 2021, Prof. Dr. P.E. Jagdale, Head of the Department of Botany at Arts, Science & Commerce College, Rahuri, Dist. Ahmednagar, identified and verified the leaves of *F. arabica* with the help of the local flora. Water and deionized water were used to properly wash the *F. arabica* leaves. After being thinly sliced into tiny pieces, the leaves were allowed to dry at room temperature in the shade.

### **2.2 Preparation of *F. arabica* leaves extract**

The fresh *F. arabica* leaves were cleansed with water to remove dust and other impurities, and then they were air dried to remove any remaining moisture or wetness before being ground into a powder. The plant extract was made by mixing 160 mg of *F. arabica* with 10 mL of distilled water in a 250 mL conical flask, and it was then boiled for 10 to 15 minutes. Whatman filter paper was then used to filter the resulting solution. In order to convert silver ions ( $\text{Ag}^+$ ) into AgNPs later on, the solution was then stored at 4°C. (Ali et al. 2016)

### **2.3 Silver nitrate ( $\text{AgNO}_3$ ) salt synthesis**

To create 5 mM of  $\text{AgNO}_3$ , 100 mL of distilled water was mixed with 85 mg of  $\text{AgNO}_3$  (Sigma-Aldrich, St. Louis, MO, USA) and vigorously stirred for approximately half an hour at room temperature. (Kwon et al., 2005).

### **2.4 The synthesis of AgNPs**

To raise the pH of the silver nitrate solution to 11, one millimole of NaOH was added very gently. The silver nitrate solution was then added while the extract was still being shaken. Under a microscope, a change in the solution's hue indicates the creation of AgNPs. The nanoparticles were created, centrifuged at 20,000 RPM, and then rinsed again to remove them from the aqueous phase. A pH of 7 was obtained by centrifuging and cleaning the nanoparticles. Finally, a vacuum oven was used to dry the generated AgNPs at 80°C. (Jacob et al., 2012; Nikbakht and Pourali, 2015).

### **2.5 Characterization of AgNPs**

### 2.5.1 UV-visible spectroscopy analysis of AgNPs

AgNPs were produced using *F. arabica* leaf extract as a reducing agent, and the AgNO<sub>3</sub> solution was confirmed by UV-vis spectroscopy. The absorbency of the generated AgNPs was evaluated using pure water as a control (blank). To investigate the synthesis of AgNPs, UV-vis spectroscopy was performed using a UV-2600 double beam UV-vis spectrometer (Shimadzu thermal scientific UV spectrophotometer 2600) with a resolution of 1 nm. At wavelengths ranging from 200 to 800 nm, the spectrum absorbency of AgNPs produced from the reaction mixture was investigated.

### 2.5.2 Fourier-transform infrared (FT-IR) spectroscopy

The AgNPs were dried, combined with KBr, and then compressed in a hydraulic pellet press to create the sample pellet. The "Bruker Alpha II FTIR Spectrometer" was used to perform FT-IR spectroscopy on the sample at the "Department of pharmaceutical Chemistry, SMBT College of pharmacy, Nashik" with a resolution of 4 cm<sup>-1</sup> in the range of 4,000 cm<sup>-1</sup>–0 cm<sup>-1</sup>.

## 2.6 In vitro anti-diabetic studies

### 2.6.1 Assay for $\alpha$ -glucosidase inhibition

The samples were analyzed for  $\alpha$ -glucosidase inhibition (Mccue et al., 2005). In summary, 0.5 units/mL of the  $\alpha$ -glucosidase enzyme were dissolved in 0.1 M phosphate buffer to produce a solution (pH 6.9). The final enzyme mixture consists of 120  $\mu$ L of 0.1 M phosphate buffer and 20  $\mu$ L of  $\alpha$ -glucosidase (0.5 units/mL). In the same buffer (pH 6.9), a 5 mM substrate solution of p-nitrophenyl-D-glucopyranoside was made. Test samples were mixed with an enzyme solution at doses ranging from 31.25  $\mu$ g/mL to 1,000  $\mu$ g/mL. The samples were thereafter incubated at 37°C for 15 minutes. The enzyme mixture was re-incubated for 15 minutes at 37°C after 20  $\mu$ L of substrate solution was added. After 80  $\mu$ L of a 0.2 M sodium carbonate solution was added, the reaction was finished. Using a UV visible spectrophotometer (Thermo electron corporation, United States), absorbance at 405 nm was determined.  $\alpha$ -glucosidase-free system was used as a blank, and acarbose was used as a positive control. Each experiment was run three times, and the % inhibition was calculated using a formula.

$$\% \text{ Inhibition} = \frac{\text{Absorbance of Control} - \text{Absorbance of Sample}}{\text{Absorbance of Control}} \times 100$$

### 2.6.1 Assay for $\alpha$ -amylase inhibition

The similar methodology was used in the  $\alpha$ -amylase inhibitory experiments (Nair et al., 2013). To summarize, 20  $\mu$ L of enzyme was mixed with 200  $\mu$ L of 0.02 M sodium phosphate buffer containing plant extracts (test substances) in doses ranging from 31.25  $\mu$ g/mL to 1,000  $\mu$ g/mL. 200  $\mu$ L of starch was added to the assay mixes after 10 minutes at 25°C  $\pm$  3°C. To halt the reaction, 400  $\mu$ L of DNS reagent (dinitro salicylic acid) was added to the mixture. The resultant solution was chilled after five minutes in a bath of hot water. After cooling, 15 mL of distilled water was added to further dilute the liquid, and the absorbance at 540 nm was measured. The usual medication was acarbose, and the amount of enzyme inhibition was determined using formula.

$$\% \text{inhibition} = [1 - (A/B)] \times 100$$

Where A = absorbance of test and B = absorbance of enzyme control.

## 2.7 In vivo anti-diabetic activity

### 2.7.1 Experimental animals

Male Balb/C albino mice that were 6 weeks old and weighed between 25 and 35 g were kept in separate cages at 22°C–26°C with a 12-h light/dark cycle and free access to standard lab food.

### 2.7.2 Acute toxicity study

An acute toxicity test was conducted in accordance with the Organization for Economic Cooperation and Development's (OECD) standards (Leist et al., 2012). Four groups of five Balb/C albino mice each were created from the experiment's twenty animals. The mice in each group received a single dosage of silver nanoparticles (AgNPs). For groups 1–4, the concentrations were 5, 10, 15, and 20 mg/kg body weight. After the AgNPs were administered, the mice were watched for 30 minutes to look for any immediate impacts, such behavioral abnormalities or mortality. After that, the mice were regularly checked for any further behavioral or symptom changes at 4 and 24 hours.

### 2.7.3 Induction of T2DM

In order to induce diabetes in the test animals, the mice were given a single intraperitoneal (i.p.) dosage of freshly produced STZ (45 mg/kg body weight) in citrate buffer (0.05 M) after an overnight fast. After that, a 5% glucose solution was given by gavage. The control group simply received injections of citrate buffer, whereas the other groups received injections of STZ. Diabetes was experimentally produced and verified by measuring the blood glucose level 72 hours after receiving a STZ injection. Mice with blood glucose levels more than 180 mg/dL were used in subsequent diabetic research experiments. Metformin (200

mg/kg) was used as a routine medicine. The anti-diabetic activity was assessed using body weight, fasting blood glucose levels, and random-fed blood glucose levels. The mice were split up into the following four groups.

### Experimental groups

Male Balb/C albino mice were randomized into four groups. The control group, i.e., first group received water daily for 21 days 15 mice in the second group were injected with 45 mg/kg STZ i. p. to induce diabetes for 5 days. They were then divided into three more groups: diabetics who received no treatment, diabetics who received AgNPs from the *F. arabica* plant, and diabetics who received metformin. All groups received 21-day treatment. Five mice per group were evenly distributed.

- Group I: (Normal control group) Water was injected i. p. into the control group's (n = 5) mice.
- Group II: (STZ-treated Control group): For 21 days, distilled water was given to diabetic mice.
- Group III: AgNPs treated group: Diabetic mice were administered an i. p. injection of AgNPs.
- Group IV: Mice with diabetes were given daily doses of metformin (200 mg/kg body weight) for 21 days.

A weighing balance was used to determine the body weight of all of the experimental mice. From the beginning to the end of the study, the weight of the animals was regularly monitored (1st and 21st day). Blood glucose levels were measured using the "Rupturing tail vein technique" using the "EASYGLUCO" metre on the first, seventh, 14th, and twenty-first days of treatment.

### 2.8 Statistical analysis

Every in-vitro test was run three times, and the results were displayed as Mean  $\pm$  Standard Error of the Mean (SEM). Dunnett's test was used in conjunction with one-way ANOVA and multiple comparison to statistically compare test samples to control groups. The Origin v19 program was used to analyze the in-vivo data. A one-way analysis of variance (ANOVA) and the Tukey's HSD post hoc test for multiple comparisons were then employed. For intergroup comparisons, post hoc analysis utilizing the least significant difference test was carried out. Statistical significance was defined as p-values below 0.05.

## RESULTS:

### 2.1 Plant extract preparation

After the *F. arabica* extract solution was manufactured, 5 mM silver nitrate salt was dissolved in 100 mL of distilled water to form the silver nitrate salt solution. This plant is well known for its medicinal qualities. It was discovered that the herb in question could help with fever, toothaches, scabies, stomach issues, tumors, and urine discharges. (Saleh et al., 2011). It was also noted to have antibacterial, anti-inflammatory, anti-hemorrhagic, thrombolytic, and antioxidant characteristics (Sajid et al., 2011) and anti-diabetic actions (Kamran et al., 2017).

### 2.2 Green synthesis of AgNPs

Following the creation of solutions with silver nitrate salt and *F. arabica* plant extract, both solutions were mixed in the appropriate ratios. After properly mixing 45 mL of 5 mM AgNO<sub>3</sub> with 5 mL of aqueous *F. arabica* extract, the mixture was let to stand until the color of the solution changed from yellow to blackish brown. Gradual color changes from yellow to reddish yellow and from reddish yellow to dark brown were seen for an aqueous solution mixture containing 5 mM silver nitrate. The complete conversion of the aqueous solution from yellowish brown to blackish brown (AgNPs) indicates the full generation of AgNPs. Metal nanoparticles are responsible for these unique colour shifts (Johnson et al., 2014). After the AgNPs were produced, they were separated from the prepared solution using centrifugation. The AgNPs solution was centrifuged at a maximum speed of 6,000 rpm for around 40 minutes. The AgNPs were shaped into a pellet and then washed three times with distilled water. The extracted pellet was dried in an oven at 60°C to create AgNPs powder. AgNPs powder was produced following a 24-hour drying period. The color shift results from reducing Ag<sup>1+</sup> to Ag<sup>0</sup>. (Yasmin et al., 2020). Free silver atoms (Ag<sup>0</sup>) formed AgNPs by nucleation and growth (Raza et al., 2016). Electron oscillations in the conduction band are the source of surface plasmon resonance, or SPR. The color shift was tracked by UV-visible absorption. AgNPs are clinically useful due to their chemical stability and therapeutic applications. Chemical or physical methods are used to create AgNPs. Because of their ease of use, affordability, and safety, biosynthesis techniques—which employ plant extracts to lower NP metal salts—are widely used. (Souha et al., 2021).

### 2.3 Characterization of AgNPs

Prior to examining the anti-diabetic activities of AgNPs, synthesized AgNPs were characterized. In a nutshell, this study used *F. arabica* leaf extract to green synthesize AgNPs at room temperature. The mixture turned brown as the plant extract and

silver nitrate solution reacted, signifying the production of AgNPs. Biosynthesized AgNPs were characterized using FT-IR and UV-Vis spectroscopy. The UV-visible spectra showed a significant broad absorbance peak at 205.5, 206.5, and 211.5 nm, indicating that AgNPs were produced. (Figure 1).

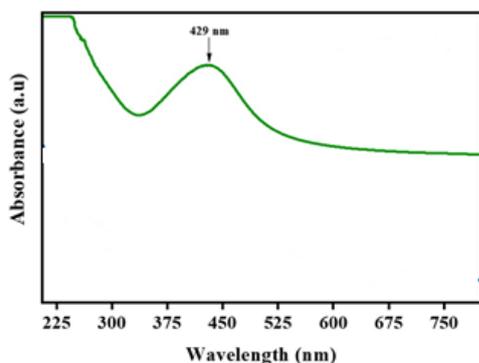


Figure 1: UV-Vis spectral patterns of *F. arabica* synthesized AgNPs

To examine the function of the functional groups in the plant extract as a capping agent and bio-reduction agent, FT-IR analysis was done (Kumar et al., 2018). Figure 4 shows the FT-IR absorption spectra of green AgNPs. The FT-IR analysis's measured spectra were compared to Coates's previously reported reference value (Coates, 2000). The leaf extract of *F. arabica* showed C-H bending at the peak values of 611.01 and 623.73, indicating the presence of carbohydrates. The aromatic C-H bending caused by glycosides was revealed by the absorption peak at 721.87. Peak at 978.33 suggested a C=C stretch, which may have been caused by the plant's coumarin, tannins, and terpenoids. The C-O stretch was shown by the absorption peaks at 1,000 to 1,295. The H-C-H bend at 1,448.94 suggested the presence of unsaturated alcohols or alkanes in the plant. The absorption peak 1,528.65 suggested an N-H bend caused by steroid amines. The presence of proteins, steroids, lactones, and flavonoids was indicated by the existence of an amide stretch C=O peak at 1,662.44. C=C alkynyl stretch was indicated by the peak at 2126.54. Peaks at 2975.81, 2890.30, and 2834.71 indicated Alkyl C-H stretch caused by glycosides. Peaks at 3620.38, 3779.5, 3829.87, 3874.93, 3892.63, 3908.35, 3925.58, and 3954 revealed that aliphatic compounds exhibit C-H stretching. That could be related to the fatty acid esters present in the plant extracts. The peak at 3779.57 suggested amide N-H stretch, which may have been caused by the plant's alkaloids (Bibi et al., 2019).

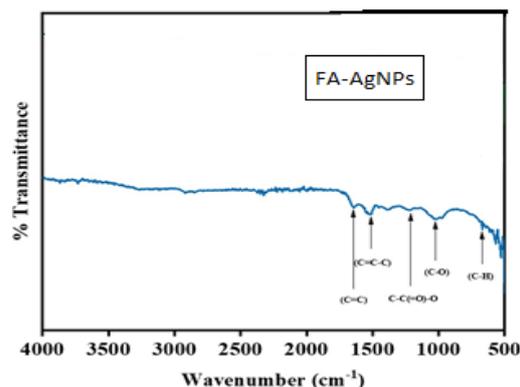


Figure 2: FTIR spectra of *F. arabica* synthesized AgNPs

## 2.4 In vitro study

### 2.4.1 $\alpha$ -Glucosidase inhibition study

The results of  $\alpha$ -glucosidase inhibition investigations are summarised in Table 1. AgNPs derived from *F. arabica* exhibited concentration-dependent inhibition of the  $\alpha$ -glucosidase enzyme. At 1,000  $\mu\text{g/mL}$ , AgNPs were the most efficient, inhibiting enzymes by  $81.74\% \pm 0.77\%$ . The IC<sub>50</sub> value for AgNPs was 250  $\mu\text{g/mL}$ . The inhibitory effects of AgNPs were similar to those of the positive control group. At the same dose, acarbose had an inhibitory action of  $91.45\% \pm 1.50\%$  (IC<sub>50</sub>s = 42  $\mu\text{g/mL}$ ). At the same quantities, Ag-NPs' inhibitory activity was equivalent to that of acarbose, the common medication.

### 2.4.2 Study of $\alpha$ -amylase inhibition

In amylase inhibition tests, AgNPs demonstrated enzyme inhibitory potentials that were contrasted with those of the reference medication, acarbose. All fractions exhibited concentration-dependent inhibition in studies on the inhibition of the enzyme  $\alpha$ -amylase, with AgNPs exhibiting the highest % inhibitions. AgNPs showed enzyme inhibitions of  $83.53 \pm 1.55$ ,  $72.97 \pm 0.50$ ,  $65.84 \pm 0.33$ ,  $56.75 \pm 0.66$ , and  $51.10\% \pm 1.00\%$  at the doses of 1,000, 500, 250, 125, and 62  $\mu\text{g/mL}$ . Table 1 shows that the IC<sub>50</sub>s for AgNPs were 118  $\mu\text{g/mL}$ . The positive control had an IC<sub>50</sub> of 40  $\mu\text{g/mL}$  and an enzyme inhibition of  $87.72\% \pm 0.70\%$ . Inhibiting  $\alpha$ -glucosidase and  $\alpha$ -amylase is one of the best ways to treat T2DM patients who have postprandial hyperglycemia. It has been demonstrated that one of the most significant sources for creating medications to treat DM is natural ingredients.

Numerous plants have been shown to have antihyperglycemic properties, either by themselves or in conjunction with conventional diabetic therapies. Among the medicinal plants and their fruits and seeds that have attracted increased attention due to their potential for scientific study are cinnamon, aloe, bitter melon, coffee, guava, cocoa, green tea, nettle, garlic, soybeans, turmeric,

and walnuts. For the treatment of type 2 diabetes, isolated natural substances such as phenomenal, galegine, pycnogenol, miglitol, voglibose, and

acarbose are utilized. (Ayaz et al., 2022).

**Table 1: Results of  $\alpha$ -amylase inhibition &  $\alpha$ -glucosidase inhibition**

<b><math>\alpha</math>-amylase inhibition results</b>			
Sample	Concentration	%Inhibition	IC <sub>50</sub>
AgNPs from <i>F. arabica</i> Sample	1,000	83.53 ± 1.55 <sup>ns</sup>	118
	500	72.97 ± 0.50 <sup>ns</sup>	
	250	65.84 ± 0.33 <sup>ns</sup>	
	125	56.75 ± 0.66 <sup>ns</sup>	
	62	51.10 ± 1.00 <sup>ns</sup>	
Positive Control	1,000	87.72 ± 0.70	40
	500	78.55 ± 0.55	
	250	71.90 ± 1.00	
	125	65.33 ± 1.40	
	62	59.80 ± 0.56	
<b><math>\alpha</math>-glucosidase inhibition results</b>			
Sample	Concentration ( $\mu$ g/mL)	%Inhibition	IC <sub>50</sub> ( $\mu$ g/mL)
AgNPs from <i>F. arabica</i> Sample	1,000	81.74 ± 0.77**	250
	500	73.84 ± 0.50*	
	250	60.49 ± 1.60*	
	125	51.49 ± 1.90**	
	62	39.50 ± 0.33***	
Positive Control	1,000	91.45 ± 1.50	42
	500	78.85 ± 0.69	
	250	71.33 ± 1.20	
	125	64.89 ± 1.33	
	62	55.90 ± 0.88	

## 2.5 In-Vivo studies

### 2.5.1 Acute toxicity

AgNPs were safe up to a dose of 20 mg/kg body weight, according to an acute toxicity research, since no fatality was observed till then. The mice were monitored for four hours following the administration of different doses to look for behavioral abnormalities such writhing, sleepiness, photosensitivity, and convulsions. When different dosages were administered to mice, AgNPs were found to be safe up to 20 mg/kg body weight, and no deaths or morbidities were seen over the course of 24 hours.

### 2.5.2 Effect of *F. arabica* plant AgNPs on body weight

Table 2 shows the effects of metformin and AgNPs on body weight. The final body weight of diabetic control mice was significantly lower than that of normal control mice. The body weight of diabetic mice treated with nanoparticles increased dramatically. When compared to the positive control group, the AgNPs treatment group showed a moderate increase in weight. However, after receiving AgNPs, diabetic mice's body weight significantly increased in comparison to diabetic control (DC) animals, indicating that the nanoparticles may have a preventive impact against the condition.

**Table 2: Comparison of initial and final body weights of the mice of different groups.**

Body weights	Group-I (normal-control)	Group-II (diabetic- control-STZ)	Group-III (silver- treated)	Group-V (metformin-treated)
Initial body weights	27.8 ± 1.60	19.2 ± 1.40	37.2 ± 0.8	28.02 ± 0.50
Final body weights	32.2 ± 1.12	15.3 ± 0.50	42 ± 0.7	33.4 ± 1.29

(n = 5 mice per group) The data are presented as Mean ± SEM. For the statistical analysis of the data, one-way ANOVA was used. As compared to the groups, all of the results were significantly different ( $p < 0.05$ ). All weights are in gram (g).

### 2.5.3 Effect of *F. arabica* AgNPs on blood glucose

On the first, seventh, fourteenth, and twenty-first

days of treatment, blood glucose levels were measured in both the experimental and normal mouse groups. Blood glucose levels increased significantly ( $p < 0.05$ ) after STZ treatment when compared to the normal control group. Blood glucose levels significantly decreased following 21 days of AgNP administration, demonstrating the hypoglycemic potential of AgNPs.

**Table 3 The Effect of AgNPs of *F. arabica* plant and standard drug Metformin on Pancreas panel: glucose, amylase; Liver function panel, Renal function panel and lipid profile in STZ-induced diabetic mice.**

Biochemical parameters (Units)	Group-I (normal control)	Group-II (diabetic control (STZ-Induced mice))	Group-III (silver-treated)	Group-V (metformin-treated)
Blood sugar (mg/dL)	108.6 ± 2.52	190.5 ± 5.0*	109.8 ± 3.39**	124.2 ± 2.20**
S. amylase (U/L)	1949.2 ± 1.51	3440.3 ± 40.04*	1945 ± 2.3**	195.6 ± 0.88**
Serum bilirubin (mg/dL)	0.78 ± 0.06	2.1 ± 0.08*	0.64 ± 0.102**	0.81 ± 0.12**
SGPT (ALT) (U/L)	33.7 ± 0.61	109.3 ± 2.9*	29 ± 0.7**	32.5 ± 1.30**
ALK-Phosphatase (U/L)	167 ± 7.2	287.7 ± 1.73*	153.8 ± 2.51**	163 ± 1.53**
S. albumin (g/dL)	4.5 ± 0.06	2.46 ± 0.04*	3.9 ± 0.05**	4.41 ± 0.05**
Blood urea (mg/dL)	22.3 ± 0.4	48.8 ± 0.3*	25.2 ± 0.5**	32.61 ± 0.5**
S. creatinine (mg/dL)	0.63 ± 0.03	1.81 ± 0.03*	0.574 ± 0.03**	0.75 ± 0.04**
Uric acid (mg/dL)	3.201 ± 0.06	78.011 ± 0.2*	3.764 ± 0.05**	3.001 ± 0.02**
S. cholestrol (mg/dL)	123 ± 1.42	141.5 ± 1.07*	71.6 ± 5.5**	99.8 ± 4.9**
S. triglyceride (mg/dL)	68.9 ± 2.7	75.3 ± 2.4*	64 ± 4.03**	65.5 ± 1.7**
HDL (mg/dL)	37.05 ± 0.49	79.6 ± 0.6*	36.2 ± 0.37**	36.9 ± 0.29**
LDL (mg/dL)	84.2 ± 4.09	127.7 ± 3.90*	69 ± 2.6**	76.3 ± 2.6**

Values are mean ± standard error of the mean (n = 5). \* $P < 0.05$ , significantly different with respect to control group; \*\* $P < 0.05$ , significantly different with respect to diabetic group (STZ group) for *post hoc* Tukey's test.

## DISCUSSION:

Researchers are paying a lot of attention to the synthesis of functional nanomaterials because of their many potential uses in fields like biomedicine, cancer treatment, bio-imaging, drug delivery, molecular-based detection, *etc.* However, the physical and chemical methods used to synthesize nanomaterials produce massive quantities of hazardous chemicals and toxic by-products, which have serious consequences for both the environment and human health. The development of non-toxic, safe, effective, non-lethal, environmentally friendly, and economically viable biological methods for the synthesis of NPs is therefore of increasing importance.

The *F. arabica* is well known as a medicine. The subject plant was found to be effective against fever, toothache, asthma, scabies, stomach problems, tumors, and urinary discharges. It was also said to have antimicrobial, anti-inflammatory, anti-bleeding, thrombolytic, and antioxidant properties (Kiani et al., 2022). Very little is known about how *F. arabica* plant extracts can be used to make AgNPs.

*F. arabica* bioreducing agents used to synthesize AgNPs are of great interest due to the NPs' novel properties. As a result of the excitation of the NP surface plasmons, the reduction of  $\text{AgNO}_3$  by the *F. arabica* extract results in a change in color from light orange to dark red, indicating a significant absorption of visible light. The Ag NPs' size, shape, and concentration all affect how the color changes (Wang and Joseph, 1999). Moreover, UV-vis spectra were taken to confirm the reduction of Ag ions to metallic AgNPs, and the maximum absorbance was seen at 205.5, 206.5, and 211.5 nm

(Figure 1). Bogle et al. (Bogle et al., 2006), reported the UV-spectra of AgNPs around 455 nm, Banala reported at 470 nm (Banala et al., 2015), Ali et al., reported (Ali et al., 2023) UV-spectra at 420 nm. The size of NPs is a major concern, especially for their use in biology, because the size of NPs has a big effect on how fast they move through biological membranes. For specific biological applications, it is preferable that NPs be of a certain size; Nevertheless, it has been noted in the past that smaller NPs have greater penetrating capability; yet, the problem with having a size that is too small is that it brings the issue of higher toxicity in comparison to bigger size NPs (Hasan et al., 2013).

FT-IR spectrum was 4, 000–500  $\text{cm}^{-1}$ . Alkane C-H stretching vibration mode is at 2977  $\text{cm}^{-1}$ . PGE primary amines (proteins) are at 1,582  $\text{cm}^{-1}$ . Phenols' O-H bond is the peak at 1,388  $\text{cm}^{-1}$ . FT-IR measurements of the plant extract showed active biomolecules that capped and reduced  $\text{Ag}^+$  to  $\text{Ag}^0$  (Khan et al., 2020). Diabetes Mellitus (DM) often causes dyslipidemia, which raises cholesterol and triglycerides. Hormone-sensitive enzymes like lipase may cause this rise (Soni et al., 2018). Hypertriglyceridemia and hypercholesterolemia (Ayaz et al., 2022) are the most prevalent lipid disorders in diabetics. In our work, STZ-induced diabetic mice had greater levels of cholesterol and triglyceride than AgNPs and Metformin-treated mice. Nagaraja (Nagaraja et al., 2022) found that PGE and *Psidium guajava* (PG) AgNPs significantly lowered blood glucose in diabetic rats, avoiding weight loss and improving lipid profile markers. Ul Haq (Haq et al., 2022) stated there was a dramatic decrease in blood glucose levels, a rise in body weight, and a marked enhancement in lipid, liver, and kidney profiles. Fluctuating blood lipid levels are definitely caused by extended cyclic adenosine monophosphate, which is responsible for lipid formation. AgNPs significantly decreased cholesterol, triglyceride, and LDL levels while increasing HDL levels in diabetic rats. There was a notable correction of anomalies in body weight,

urine, and serum levels after administration of the biosynthesized AgNPs, suggesting the drug has great potential as an anti-diabetic treatment.

Wahab (Wahab et al., 2022) reported that the goal of the study is to shed light on the therapeutic potential of AgNPs as an antidiabetic drug in STZ-induced diabetic BALB/C mice by reporting an unique synthesis of these nanoparticles utilizing aqueous extract of *Thymus serpyllum*. The  $\alpha$ -amylase inhibition and antioxidant activity were checked through  $\alpha$ -amylase respectively. According to our previous study, the SeNPs of *F.arabica* exhibited good anti- diabetic, antioxidant activities as well as anti-hyperlipidemic via both *in-vitro* and *in-vivo* approaches (Khan et al., 2023). So, our results of AgNPs correlate well with the literature surveys.

### CONCLUSION:

According to the findings of the current research, the AgNPs that were derived from the leaf extract of *F. arabica* demonstrated properties that were anti- diabetic. The findings of the study were evaluated *in-vitro* and *in-vivo* using methods that are intended to treat diabetes. It was discovered that the AgNPs that were generated from the leaf extract might have qualities that could help treat diabetes. AgNPs, which are obtained from leaf extract, might 1 day be manufactured on a commercial scale and put to use in the treatment of diabetes. AgNPs of the *F. arabica* have been shown to have anti-diabetic properties and may be further investigated as a useful and less expensive treatment option for T2DM.

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