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Research Article

Effects of Silver Nanoparticle Modified *Corchorus olitorius* (Jute) Leaf Extract on Blood Sugar and Lipid Profile of Diabetic Wistar

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ABSTRACT

Diabetes, a high prevalent and non-infectious disease characterized with expensive management coupled with its complication exerts serious economic burden on patients and healthcare practitioners. This study aimed at evaluating the effects of silver nanoparticles modified *Corchorus olitorius* leaf extracts (AgNPs-COLE) on blood sugar and lipid profile of alloxan induced diabetic wistar rats. Phytochemical screening of *Corchorus olitorius* leaf extract (COLE) was carried out using gravimetric method. The energy dispersive x-ray fluorescence spectrometer was used to determine the elemental content of green synthesized silver nanoparticles. Thirty-five (35) Wistar rats of 184 – 201g were used and grouped into A-G of 5 per group. Group A were non-induced and not treated except feeding only, Groups B-G were induced with diabetes using 130mg/kg alloxan monohydrate, while Group B were not treated, group C were administered 10mg/kg glibenclamide (GLB), groups D and E were administered with aqueous leaf extracts of *Cochorus olitorius* of 200mg/kg and 400mg/kg, respectively, and groups F and G were administered with 200 mg/kg and 400mg/kg of AgNPs modified Jute leaf extract, respectively. The blood sugar level and lipids assay were determined. Data analysis was carried out using multivariate ANOVA of SPSS version 26 with inferior p-value of 0.05. Alkaloid, flavonoid, terpernoids, steroid and saponins were predominant phytochemicals with yields of 16.46, 11.42, 6.9, 3.58 and 2.42 %. Blood sugar levels of the rats were significantly reduced in all groups following treatment regime. Total cholesterol, TG, HDL-C and LDL-C levels of diabetic rats significantly reduced when administered with AgNPs-COLE compared to COLE and GLB, respectively. Thus, silver nanoparticles enhanced anti-diabetogenic potentials of *C. olitorius* leaf extract and performed better than glibenclamide in diabetes management.

Keywords: *Cochorus olitorius leaf, phytochemicals, silver nanoparticles, antidiabetic, blood lipids.*

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INTRODUCTION

Diabetes mellitus (DM), a major multietiological metabolic disorder associated with hyperglycemia and other plethora of complications such as obesity, retinopathy, nephropathy, neuropathy, fatty liver and atherosclerosis to mention a few (Ganesan and Xu, 2019). This causes decrease in secretion of insulin and leads to increase in blood sugar level. Diabetes mellitus may be type 1 which associated with failure of β-cells of pancreas to produce insulin or type 2 which associated with deficiency of insulin, thereby, caused cells resistance to utilize the glucose in the blood (Zeka *et al*., 2017; Wu & Yan, 2015; Lucchesi *et al*, 2015). The prevalence of diabetes mellitus increases yearly. The continuous hyperglycaemic condition induces oxidative stress, reactive oxygen species, toxic effect of intakes to the liver via increase auto-oxidation of glucose, activation of polyol path-way and non-enzymatic protein glycation (Pukas *et al*., 2004; Diniz *et al*., 2004 and Saravanan and Ponmurugan, 2013).

Green plants like *Corchorus olitorius* plant have been reported to reduce the incidence of chronic diseases because of their rich in anti-oxidant compounds (Lu and Foo, 2000), affordable, relatively available and source of all classes of food with low calorie content (Nath *et al*., 2013; Muhammad and Shinkafi,, 2014). Plant bioactive molecules like vitamin, phenolic compounds and some phytochemical contents plays an important role in breaking the chain reaction formed by the reactive oxygen-species (Ramadan *et al*., 2008; Hefnaway and Ramadan, 2013). This prevents alteration in proteins, lipids, DNA denaturation and chronic disease onset (Neffati *et al*., 2017). *C. olitorius* plant contains active phytochemicals that boost the immune-system with anti-inflammatory, anti-pyretic, anti-neoplastic, anti-diabetic, anti-hypertensive and cytotoxic effects (Ahmed and Sarkar, 2022). Although the quest for a more potent drug delivery system with improved bioavailability, stability, site target release and biodegradation have been linked to nanoparticles drug enhancement therapy (Lu and Foo, 2000).

Several methods have been used for synthesis of nanoparticles, especially, the silver nanoparticles as presented in Figure 1 (Xu *et al*., 2020). Of all synthetic methods, plant mediated AgNPs have been reported to be a promising techniques due to its availability, good stabilizing materials, biocompatibility, easy, cost-effectiveness and high reducing potential (Khorrami *et al*., 2018; Meena *et al*, 2020), and the cytotoxicity of many organs by biosynthesized AgNPs like kidney, reproductive system, immune system have been reported at high concentration but effective at low concentration (Meena *et al*, 2020). The deployment of nanoparticles in drug delivery as carriers for small and large molecules have been reported to improve the pharmaco-dynamic properties of various types of drug molecules, protect the drug entity in the systemic circulation, deliver the drug at a controlled and sustained rate to the site of action, and minimizing side effects (Vila *et al*., 2002; Mu and Feng, 2003; Mohanraj and Chen, 2006). Expensive nature of of synthetic drugs for diabetes therapy, drug resistance couple with side effects remains a great challenge. So, the sources for biocompatible with local available green or alternative drug has been promising means for researchers. In this study, effects of silver nanoparticles modified *C. olitorius* leaf extracts (AgNPs-COLE) on blood sugar and lipid profile of alloxan induced diabetic Wistar rats was aimed to be investigated.

MATERIALS AND METHODS

Preparation of plant material: *Cochorus olitorius* (*C. olitorius*) leaves were collected from Botanical garden of Federal University of Technology, Owerri, Nigeria and identified by a botanist from the Crop Science Department. The leaves were properly washed, air-dried at ambient temperature for a period of two weeks, then powdered using an electric lab blender and stored in a labeled bottle K.

Extraction of phytochemicals: The method described by Ahmed *et al*. (2001) and modified by Ogbonna *et al*. (2023) was used to extract, identify and quantify the phytochemicals of *C. olitorius* leaf. Twenty five grams (25 g) of powdered *C. olitorius* measured and added to 250mL of distilled water in a conical flask. The mixture was heated at 800C for 3 hours using magnetic heat stirrer, filtered using Whatman filter paper no. 1 and the filtrate was stored at 40C further use. The phytochemical analysis of the aqueous extracts of C.olitorius leaf was determined.

Synthesis and characterization of silver nanoparticles: The procedure used by Ahmed *et al*. (2016) and modified by Xu *et al* (2020) was employed to biosynthesis and characterize the silver nanoparticles, respectively. Aqueous neem extract of ten (10) mL was added to 90 mL of aqueous silver nitrate solution (1 mM), and heated to about 800C for 3 hours using magnetic stirrer. AgNPs was primarily detected based on color change from yellow to brown. The biosynthesized nanoparticles was centrifuged at 15,000 × g for 20 min and washed several times. The elemental characterization was achieved using energy dispersive x-ray fluorescence spectrometer (EDXRF) of EDX3600B model.

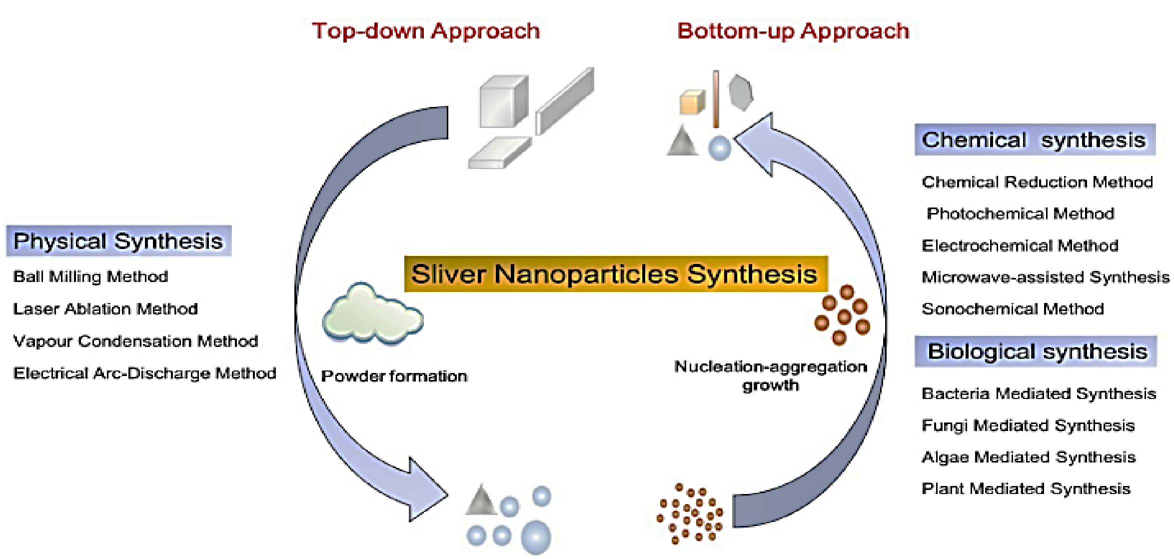

Figure 1: Synthesis of silver nanoparticles (Xu *et al*., 2020)

Table 1:
Experimental design of wistar rats

Group	Description
A	Rats were fed with normal rats chow and water only (normal control).
B	Rats were induced with diabetes (alloxan) without treatment.
C	Rats were induced with diabetes (alloxan) treated with 10mg of Glibenclamide (positive control) /kg bodyweight.
D	Rats were induced with diabetes (alloxan) and treated with 200mg of aqueous leaf extract of *C. olitorius* /kg bodyweight.
E	Rats were induced with diabetes (alloxan) treated with 400mg of aqueous leaf extract of *C. olitorius*/kg bodyweight.
F	Rats were induced with diabetes (alloxan) treated with 200mg of AgNPs modified modified *C. olitorius* leaves extract/kg bodyweight.
G	Rats were induced with diabetes (alloxan) treated with 400mg of AgNPs modified *C. olitorius* leaves extract/kg bodyweight.

Conjugation of biosynthesized nanoparticles and *C. olitorus* leaf extract: The concentrated leaf extracts of *C. olitorus* and synthesized nanoparticles was prepared in ratio 1:1, then dispersed in distilled water and stirred using a mechanical shaker for 1 hour at room temperature to ensure thorough conjugation and functionalization of the nanoparticles. The resulting mixture was then sealed in an airtight glass container and stored at 40C.

Induction of diabetes and experimental therapy of wistar rats models: Thirty-five adult albino wistar rats weighing between 184 -201g were sourced from an animal farm in Umuahia and acclimatized for 15 days. All 35 rats were fasted for 12 hours with free access to water. Freshly prepared alloxan monohydrate (130mg/kg;i.p.) in ice-cold normal saline was injected intra-peritoneally. Blood glucose levels of the animals were checked 48hrs later, the animals showing blood glucose value more than 200 mg/dl were considered diabetic as reported by Oboh *et al* (2015). All drug and extracts at varying therapeutic doses were administered daily for three weeks (21days) as presented in Table 1.

Blood glucose estimation: Blood sample was collected by pricking the tail vein of the rats using tail snipping technique from all the overnight fasted (16-20hr) animals. Blood was gently milked, dropped on a glucose strip and measured using glucometer. This was done at baseline, after induction of diabetes, 5 and 10 days after onset of experiment and last day of experiment.

Determination of lipid serum parameters: Total serum cholesterol (CHOL), high density lipoprotein cholesterol (HDL-C) and triglyceride (TG) levels were determined by enzymatic colorimetric techniques at standards of 5.18, 1.34 and 2.26mmol/L, respectively. The spectrophotometer was zeroed with the reagent blank at 500 nm and the absorbance was measured and CHOL, HDL-C and TG were evaluated using equation (1) as given by Naito (1984) and Fossati *et al* (1982). Low density lipoprotein cholesterol (LDL-C) was evaluated using Friedwald's model as given by equation (2) (Friedwald *et al*, 1972).

$$L_p = \frac{A_{serum} x C_{std}}{A_{std}} \quad \text{.....(1)}$$

L_p, A_{serum}, C_{std} and A_{std} represent the lipid serum parameter (CHOL, HDL-C and TG) measured in mmol/L, absorbance of serum, concentration of standard and absorbance of standard, respectively.

$$LDL - C(mmol/L) = Total\ C - (HDL - C + TG/2.2) \quad \text{.....(2)}$$

Statistical Analysis: Data were analyzed using Statistical Package for Social Science (SPSS) version 26 and expressed as Mean ± SD (Standard Deviation) and inferior p-value of 0.05 was considered significant.

RESULTS

The phytochemicals of aqueous extract of *C. olitorius* leaf is presented in Table 2. The phytochemical analysis of *Corchorus olitorius* plant extract revealed the presence of alkaloids, phenols, flavonoids, steroids, cardiac glycosides, saponins, tannins and, terpenoids with high content of alkaloids and flavonoids. Figure 2 depict elemental composition of synthesized AgNPs with neem leaf extract using EDXRF analysis. The existence of AgNPs as a minor constituent was obtained. The major constituents, calcium (Ca), arsenic (As), and lead (Pb) may be originated from the plant extract used. The change in fasting blood sugar level (FBSL) models of both non-diabetes and diabetes, groups A-G, of wistar rats at increased therapy time are presented in Figure 3. The high fasting blood sugar level was obtained for all groups B-G after induction but low for group A. The serum profile comprises of the total cholesterol (CHOL), high and low density lipoproteins (LDL-C) and triglyceride (TG) of wistar rats is presented in Table 3 based on therapeutic drugs. The induction of alloxan significantly increased the CHOL, LDL-C and TG levels but reduced the HDL-C of the diabetes wistar rats as observed in Table 3.

Table 2:
Phytochemicals of the crude aqueous extract of *C. olitorius*.

Phytochemicals	Percentage (%)	Quantification
Alkaloid	16.46	+++
Flavonoid	11.42	+++
Phenols	0.36	+
Saponin	2.42	+
Steroid	3.58	++
Terpernoids	6.90	++
Tannin	0.3	+
Cardiac glycoside	0.02	++

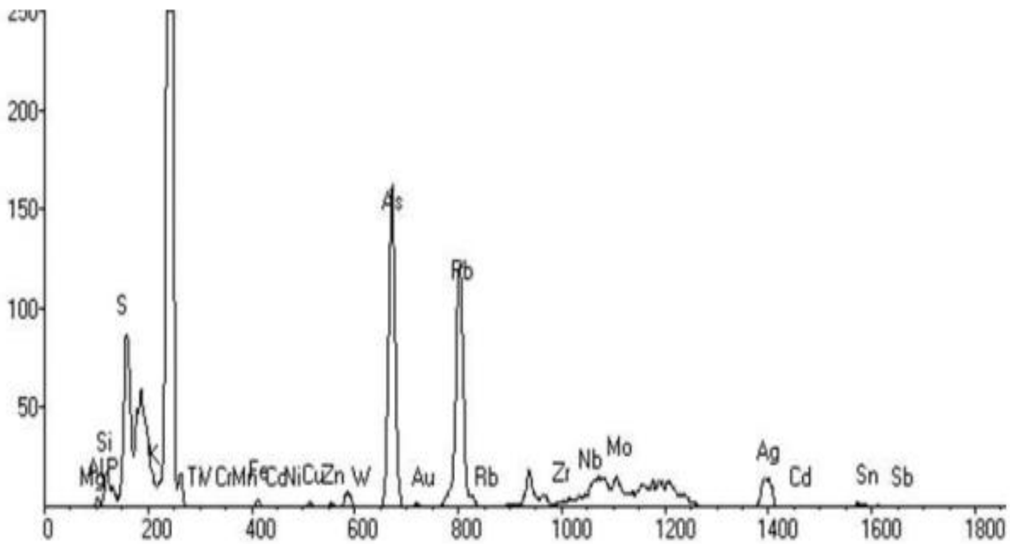

Figure 2:
Elemental composition of colloidal sample of AgNPs-aqueous neem extract

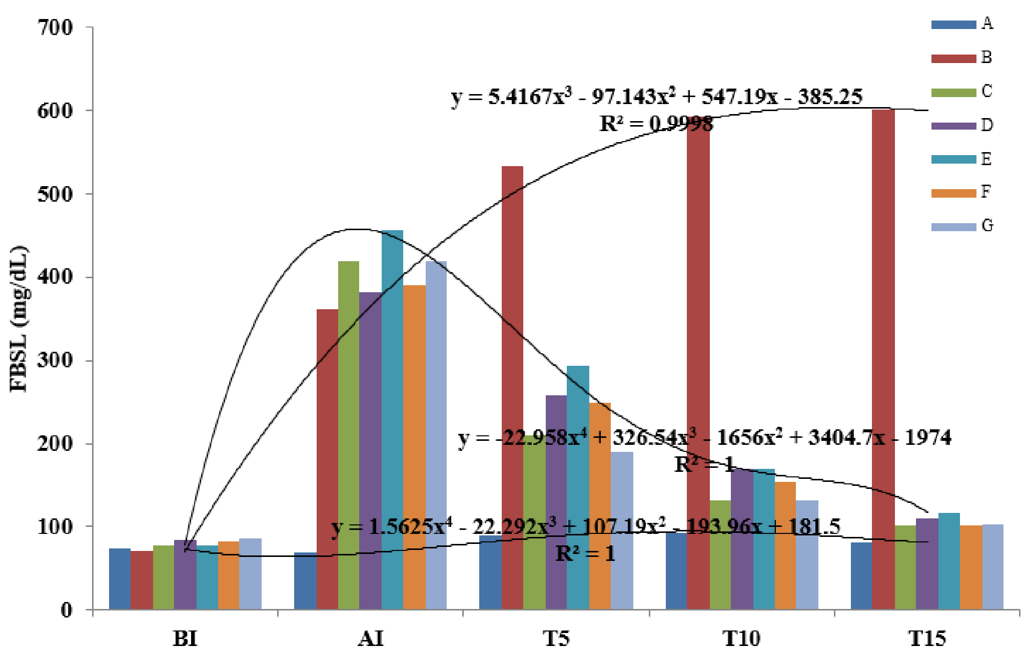

Figure 3:
Fasting blood sugar level of alloxan induced Wistar rats

Table 3:
Effects of therapies on the blood lipid profiles of the wistar rats

GROUP	CHOL	HDL-C	LDL-C	TG
A	94.60 ± 2.19^{b}	83.60 ± 8.14^{b}	$18.20 \pm 2.49^{b,c}$	107.00 ± 3.46^{b}
B	137.00 ± 3.32^{a}	14.40 ± 4.16	$65.60 \pm 2.61^{a,c}$	130.40 ± 2.51^{c}
C	$107.20 \pm 3.03^{a,b}$	87.20 ± 5.22^{b}	$24.40 \pm 2.61^{a,b}$	$108.80 \pm 4.7^{6,b}$
D	$99.00 \pm 1.87^{b,c}$	80.00 ± 2.92^{b}	$27.80 \pm 1.79^{a,b}$	$96.20 \pm 6.65^{a,b,c}$
E	$88.40 \pm 3.58^{b,c}$	84.20 ± 3.35^{b}	$26.60 \pm 2.70^{a,b}$	101.80 ± 2.49^{b}
F	$88.20 \pm 1.79^{b,c}$	84.80 ± 2.95^{b}	24.80 ± 1.79^{b}	$104.80 \pm 3.9^{6,b}$
G	$88.60 \pm 5.81^{b,c}$	83.20 ± 5.59^{b}	$27.80 \pm 2.68^{a,b}$	$92.80 \pm 2.68^{a,b,c}$

Subscripts a, b and c represent the mean value is significant at 0.05 level compared to groups A, B and C, respectively. CHOL, HDL, LDL and TG are total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol and triglyceride levels, respectively.

DISCUSSION

Results from this study show that aqueous extract of *C. olitorius* leaf possess phytochemical contents in decreasing order as follows: alkaloids > flavonoids > steroids > saponins > phenols > Tannins > cardiac glycosides. The high content of alkaloids in *C. olitorius* leaf similar to the report of (Parvin *et al*., 2015; Sadat *et al*., 2017), but saponins and tannins were found lower compared to the report of Mohammed *et al*., (2019). The variation in the phytochemical composition as reported, however, could be attributed to the source of *C. olitorius* plant, maturity, extraction techniques and variation in the growth conditions of the plant. The major constituents of alkaloids, flavonoids, saponins, tanmins and terpernoids exhibit good anti-diabetic and anti-oxidant potentials that inhibit α-glucosidase activity (Kazeem *et al*., 2013; Zeka *et al*., 2017; Hassan *et al*., 2018).

The elemental composition of synthesized AgNPs presence in the aqueous neem leaf extract was obtained. The high content of Ca, As, and Pb was observed which may be originated from the plant extract used. The formation of colloidal Ag metal nanoparticles resulted from the simultaneous mixing of silver nitrate and neem leaf extract solution. The colour change observed shows the formation of colloidal AgNPs (Ahmed *et al*, 2016). However, it can be pointed out that slight colour changes occurred which might be due to the variation in the size, shape and nanoparticle's surface plasmon resonances (SPRs) of nanoparticles.

The rise in FBSL beyond the normal for all groups B-G with exception of group A was deduced. This indicated hyperglycemia of the wistar rats. With increased time, the fasting blood sugar level fall drastically for groups C-G while that of group B increases. Further increase in FBSL may be due to uncontrolled condition, non-improvement in diabetes conditions as well as inability of pancreas to produce insulin as observed in group B. The drastic decrease in FBSL of groups C-G may be attributed to therapeutic effect of GLB, extract and AgNPs modified *C. olitorius* extract. The presence of alkaloids induced glucose uptake by β-cells pancreatic (Tiong *et al*., 2013), exerting an insulin like effect on peripheral tissues either by promoting glucose uptake and metabolism or inhibiting hepatic gluconeogenesis. This may have led to the decrease in the blood glucose level of the diabetic wistar rats of groups C-G except the control group. The treatment trends of diabetes wistar rats using GLB, *C. olitorius* leaf extract and AgNPs modified *C. olitorius* leaf extract were found to be polynomial models of order four while that of untreated wistar rats exhibits order three. This means, decrease in FBSL for therapy of diabetes animals is at a slow rate while the increase in FBSL for untreated wistar rats is at higher rate. The performance of drugs used was determined using percentage reduction of FBSL. The higher the dosage of extract gave higher the percentage reduction of FBSL of Wistar rats. It can also be deduced that the percentage reduction of FBSL for AgNPs modified *C. olitorius* extracts of 200 and 400 mg/kg of rats (74.09 and 75.21%), respectively, higher that of *C. olitorius* extracts of 200 and 400mg/kg of rats (71.03 and 74.3%), but less than that of 10mg of GLB/kg of rats. This indicated AgNPs enhanced the performance of extract in FBSL in wistar rats, thereby, improved the anti-diabetogenic potentials of extract of *C. olitorius* leaf.

The administration of GLB of diabetic wistar rats significantly reduced the CHOL, LDL-C and TG levels, but increased the HDL-C. The increase in dosage of extract from 200-400mg of *C. olitorius*/kg of rats significant decreases the CHOL and LDL-C levels, but reduced the HDL-C and TG levels. More so, AgNPs modified *C. olitorius* extract lowered the CHOL and LDL-C level when compared with administered *C. olitorius* extract, but raised the HDL-C and TG at 200mg/kg of rats, vice-versa at higher dosage of 400mg/kg of rats. It can also be seen that CHOL, HDL-C, LDL-C and TG levels lowered when *C. olitorius* extract and AgNPs modified *C. olitorius* extract were administered compared with GLB. The reduction and increase in the lipid profile of wistar rats may be attributed to the phytochemicals of alkanoids, flavonoids, tannins and saponins as reported by researches (Nwodo *et al*, 2013; Ogunka-Nnoka *et al*, 2018). The mechanism of phytochemicals reduced the fatty acid, enhanced LDL receptors and activates lipase as well as of acetyl-CoA carboxylase, thereby, reduced the HMG-CoA reductase at mRNA and protein levels (Elekofehintimi *et al*., 2012). Endogenous cholesterol reduced and mobilized from extra-hepatic tissues to the liver for bile acid biosynthesis (Adeli *et al*., 2002; Chao *et al*., 2002; Borradaile *et al*., 2003) and increased in HDL-C level. The lipid profile obtained was found to be within the standard range.

In conclusion, aqueous extract of *Corchorus olitorius* leaf contains high content of alkaloids, flavonoids, saponins and tannins with potentials of fasting blood sugar reduction, thereby, serves as anti-diabetogenic effect. Modification of aqueous extract of *C. olitorius* leaf by biosynthesized silver nanoparticles enhanced the reduction of the total cholesterol, low density lipoprotein and triglyceride, but increased high density lipoprotein cholesterol in the blood. More so, the biosynthesized silver nanoparticles enhanced the performance of aqueous *C. olitorius* leaf extract on fasting blood sugar level and lipid profile more than glibenclamide drug. Thus, silver nanoparticles modified aqueous *Corchorus olitorius* leaf extract is a good anti-diabetogenic agent and it could be used as an alternate to diabetes therapy

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