Antidiabetic Potential of *Azadirachta indica* Aqueous Stem-Bark Extract Streptozotocin-Induced Diabetic Wistar Rats

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Abstract
Diabetes mellitus is a dangerous chronic illness that develops over time when the body cannot correctly use the insulin it does make, cannot create enough insulin or both and this leads to elevated blood glucose levels. If not properly managed, it can lead to serious health complications such as cardiovascular diseases, kidney damage, nerve damage, visual loss, etc that can be life-threatening or cause disability, but if diabetes is well-managed, these serious complications can be delayed or avoided. This study was carried out to evaluate the antidiabetic potential of aqueous stem-bark extract of *Azadirachta indica* on streptozotocin (STZ)-induced diabetic Wistar rats. 60 mg/kg of STZ was administered intraperitoneally to Wistar rats which induced diabetes. Thirty male rats were randomly distributed into groups of 5 rats each. Normal and diabetic groups received distilled water; diabetic rats were orally treated with 100, 300 and 400 mg/kg *A. indica* stem-bark extract and 5 mg/kg glibenclamide for 4 weeks. Fasting blood glucose was monitored weekly. Administration of STZ significantly ($p<0.05$) increased fasting blood glucose, TC, TG, LDL, urea and creatinine levels. SOD, CAT, GSH, HDL levels were significantly reduced. However, treatment with the extract reversed the effect of STZ on above parameters. It is observed from the study that the extract is potent in the management of diabetes.

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Introduction

Diabetes Mellitus

Diabetes mellitus (DM) is a dangerous chronic illness that develops over time when the body cannot correctly use the insulin it does make, cannot create enough insulin, or both. This leads to elevated blood glucose levels (IDF, 2021). If diabetes is not properly managed, it can lead to serious health complications such as cardiovascular diseases (CVD), kidney damage (nephropathy), nerve damage (neuropathy), visual loss or blindness (retinopathy), etc. that can be life-threatening or cause disability. However, if diabetes is well-managed, these serious complications can be delayed or avoided (IDF, 2021). It is estimated that 537 million people worldwide suffer from diabetes; this figure is expected to rise to 643 million by 2030 and 783 million by 2045, according to the 10th edition of the International Diabetes Federation (IDF, 2021). It is anticipated that in 2021, diabetes-related causes of death claimed the lives of nearly 6.9 million people aged 20 to 79 (IDF, 2021). Every year, there is a growth in the number of children and adolescents (those under the age of 19) who have diabetes (IDF, 2021). More than 1.2 million kids and teenagers worldwide have type 1 diabetes in 2021 (IDF, 2021). Diabetes already results in direct medical costs that are around $1 trillion USD, and this number will surpass the 2030 estimate (IDF, 2021). However, it has been forecasted that by 2045, the highest prevalence of diabetes (94%), will be found in low- and middle-income nations due to anticipated faster population growth (IDF, 2021).

The plant kingdom represents a rich store of organic compounds, many of which have been used for medicinal purposes and could serve as a lead for the development of novel agents (Innocent *et al*., 2021) [17]. Nowadays, due high demand and side effects of conventional medicines, some parts of the world started to use plants for the treatment and prevention of diseases (Santosh *et al*., 2020) [25]. *Azardirachta indica* (neem), divine tree (Jose *et al*., 2020) [18]. has been declared the tree of the 21st century by the United Nations (Innocent *et al*., 2021) [17], is the most versatile and useful medicinal plant ever found (Subendu *et al*., 2021) [28].

Fig 1: Stem-bark of *Azadirachta indica*

Materials and Methods

Sample Collection and Identification

The sample was collected from the take-off Campus, Federal University Dutsin-Ma, Katsina State, Nigeria and was taken same day for identification.

Sample Identification

The sample was identified at the Herbarium of Botany Unit of the Department of Biological Sciences, Federal University Dutsin-Ma, Katsina State. Voucher number: FUDMA/PSB/00002 was issued.

Sample Preparation

The sample was sorted and air dried under shade at room temperature for two weeks, it was grounded to powder. Distilled water 1000 ml was added to each 150 g of the powdered sample and was soaked for 24 hours. It was filtered with muslin cloth followed by whatman filter paper number 1and the extract was collected and dried in oven at 60ºC which was used for the analyses.

Experimental Animals

A total of thirty (30) male Wistar rats with average weight 152.73g were used and were purchased from the Department of Pharmacology and Therapeutics, Faculty of Pharmaceutical Sciences, Ahmadu Bello University Zaria. They were maintained and housed in aluminum cages in the Animal house, Biochemistry section, Federal University Dutsin-Ma. They were allowed to acclimatize for two weeks. The animals were fed with standard diet and water *ad libitum* throughout the experiment.

Phytochemical Analysis of The Plant (*Azadirachta indica*)

Phytochemical tests were carried out on the aqueous extracts using standard phytochemical methods as described by Evans and Trease, (1999) [12], Sofowora (1984) [27], Harbone (1973) and El-Olemyl *et al.,* (1994) [11].

Induction of Diabetes

Diabetes was induced by[a]single intra-peritoneal injection of 60 mg/kg streptozotocin (Sigma St Louis, M.O., USA) dissolved in 0.9% normal saline to overnight fasted rats using insulin syringe. Diabetes mellitus was confirmed after the 7th day of streptozotocin treatment by the observation of fasting blood glucose (FBG)>300 mg/dl using glucometer (Accu-check) (Osibemhe *et al.,* 2018) [23].

Experimental Design

The animals were divided randomly into 6 groups of 5 rats each. The groups are: group 1: normal rats (control group), group 2: STZ-induced diabetic treated with standard drug (glibenclamide), group 3: STZ-induced diabetic untreated, group 4: STZ-induced diabetic treated with *Azadirachta indica* stem-bark extract 100 mg/kg, group 5: STZ-induced diabetic treated with *Azadirachta indica* stem-bark extract 300 mg/kg and group 6: STZ-induced diabetic treated with *Azadirachta indica* stem-bark extract 400 mg/kg. The dose of extract was selected on the basis of the acute oral toxicity reported on the plant from the previous studies carried out by (Tijjani & Asma'u, 2022). Blood glucose levels were measured weekly for the period of 8 weeks. Body weight of each animal was determined at the initiation and end of the study.

Collection of Blood Sample

The diabetic rats were kept for the period of 8 weeks after which diabetic nephropathy was confirmed and 4 weeks treatment was initiated. After the completion of the 4 week treatment, the rats were fasted overnight for eight hours, anaesthetized in using chloroform. Blood samples were collected from the animals through abdominal aorta into a sterile syringe and were put in heparinized containers and centrifuged at 5000 rpm for 10 minutes for separating blood plasma. The plasma obtained was pipette into labeled specimen test tubes for estimation of biochemical parameters.

Biochemical Analysis

Diagnostic kits were utilized for analyzing the biochemical parameters including blood glucose test, Randox for lipid profile, liver function test, kidney function test, colorimetric assay for antioxidant parameters, MDA assay kits and elisa kits for insulin and makers of nephropathy.

Statistical Analysis of Results

Data obtained from the experiments were analyzed using the Statistical Package for Social Sciences (SPSS) software for windows version 21 (SPSS Inc., Chicago, Illinois, USA). The results were reported as Mean ± SEM of the values and Duncan comparison was used to compare mean values. $P<0.05$ was considered significant.

Results

Phytochemical Constituents of Aqueous Extract of *Azadirachta indica* Stem-Bark

Table 1 represents the phytochemical constituents of *Azadirachta indica* stem-bark extract. The phytochemical analysis showed the presence of alkaloids, flavanoids, phenols, cardiac glycosides and saponins.

Table 1: Phytochemical constituents of aqueous extract of *Azadirachta indica* stem-bark

Compound	Presence in Leaves	Symbol
Alkaloids	Present	+
Tannins	Not Detected	ND
Flavonoids	Present	+
Terpenoids	Not Detected	ND
Phenols	Present	+
Cardiac Glycosides	Present	+
Saponins	Present	+

Key: (+): present and (ND): not detected.

Table 2 shows the changes in blood glucose concentrations of STZ-induced diabetic rats administered aqueous extract *A. indica* stem-bark during the 4 weeks treatment. The result indicated significant increase ($p<0.05$) in blood glucose concentrations in the diabetic group when compared with the normal control. However, administration of aqueous extract *A. indica* stem-bark resulted to significant decrease ($p<0.05$) in blood glucose concentrations in the treated groups when compared with the untreated. Treatment with glibenclamide 5 mg/kg and 400 mg/kg stem-bark extract showed the most effective decrease when compared with other treated groups.

Table 2: Changes in blood glucose concentrations of streptozotocin-induced diabetic rats administered aqueous extract *Azadirachta indica* stem-bark during the 4 weeks treatment

Group	1st Week (mg/dl)	2nd Week (mg/dl)	3rd Week (mg/dl)	4th Week (mg/dl)
1	80.00±0.70^{a}	76.80±1.06^{a}	85.80±0.86^{a}	81.00±0.70^{a}
2	398.20±1.68^{b}	383.80±0.86^{d}	260.80±1.15^{b}	94.60±1.43^{b}
3	460.60±1.20^{d}	450.60±1.16^{e}	405.60±2.13^{f}	401.20±0.86^{f}
4	410.00±0.70^{c}	369.00±1.58^{c}	310.40±0.87^{e}	280.40±0.67^{e}
5	399.40±1.50^{b}	362.20±5.06^{b}	297.40±0.74^{d}	199.20±0.58^{d}
6	398.60±0.92^{b}	339.00±1.00^{b}	277.00±1.00^{c}	148.60±0.67^{c}

Results are Mean ± SEM of 5 determinations. Values in the same column with different superscript are statistically different; values with same superscript in the same column are statistically not different at ($p<0.05$). Group 1: normal control, Group 2: glibenclamide control, Group 3: diabetic untreated, Group 4: 100 mg/kg stem-bark extract, Group 5: 300 mg/kg stem-bark extract and Group 6: 400 mg/kg stem-bark extract.

Liver Function Indices of Streptozotocin-Induced Diabetic Rats Administered Aqueous Extract *Azadirachta indica* Stem-Bark

Liver function indices of STZ-induced diabetic rats administered aqueous extract *A. indica* stem-bark is depicted in Table 3. The result showed significant increase ($p<0.05$) in the activities of ALT, AST, ALP and concentrations of TB and CB and also a significant decrease in TP, ALB and GLO concentrations in the diabetic untreated groups when compared with the normal control. However, administration of aqueous extract *A. indica* stem-bark resulted to[a] Significant decrease ($p<0.05$) in the activities of ALT, AST, ALP and concentrations of TB and CB and a significant increase ($p<0.05$) in the concentrations of TP, ALB and GLO respectively when compared with diabetic untreated. Treatment with glibenclamide 5 mg/kg and 400 mg/kg showed the most effective decrease in the activities of ALT, ALP and the concentrations of TB and CB whereas in 300 mg/kg in AST. The treated result also showed significant increase in the concentrations of TP, ALB and GLO in which glibenclamide 5 mg/kg and 400 mg/kg exerted the most effective increase in TP and ALB among the treated groups.

Table 3: Liver function indices of streptozotocin-induced diabetic rats administered aqueous extract *Azadirachta indica* stem-bark

Group	ALT (µ/l)	AST (µ/l)	ALP (µ/l)	TP (g/dl)	ALB (g/dl)	GLO (g/dl)	TB (mg/dl)	CB (mg/dl)
1	16.20±0.37^{a}	8.00±0.44^{a}	68.00±0.70^{a}	5.90±0.07^{a}	3.98±0.08^{a}	1.92±0.09^{a}	1.24±0.02^{a}	0.12±0.02^{a}
2	19.60±0.40^{b}	9.60±0.24^{b}	80.80±0.58^{b}	5.70±0.07^{e}	4.00±0.07^{a}	1.70±0.08$^{a, b, c}$	1.54±0.02^{b}	0.18±0.03^{a}
3	89.40±0.50^{f}	100.80±0.37^{f}	217.00±0.44^{f}	1.76±0.05^{f}	1.68±0.08^{e}	0.20±0.03^{d}	8.28±0.13^{f}	1.50±0.03^{c}
4	47.60±0.50^{e}	48.20±0.58^{e}	161.40±0.50^{e}	4.14±0.09^{b}	3.32±0.07^{b}	1.82±0.15$^{a, c}$	3.40±0.04^{e}	0.74±0.06^{d}
5	38.20±0.37^{d}	20.40±0.50^{c}	127.60±0.67^{d}	4.62±0.10^{c}	3.30±0.07^{c}	1.32±0.08^{b}	6.26±0.07^{d}	0.38±0.02^{b}
6	32.75±0.47^{c}	22.75±0.47^{d}	109.50±0.64^{c}	5.15±0.09^{d}	3.70±0.07^{d}	1.45±0.14$^{b, c}$	2.27±0.06^{c}	0.22±0.02^{a}

Results are Mean ± SEM of 5 determinations. Values in the same column with different superscript are statistically different and values with same superscript in the same column are not statistically different at (p<0.05). Key: ALT: Alanine amino transferase, AST: Aspatate amino transferase, ALP: Alkaline phospatase, TP: Total protein, ALB: Albumin, GLO: Globulin, TB: Total bilirubin, CB: Conjugated bilirubin. Group 1: normal control, Group 2: glibenclamide control, Group 3: diabetic untreated, Group 4: 100 mg/kg stem-bark extract, Group 5: 300 mg/kg stem-bark extract and Group 6: 400 mg/kg stem-bark extract.

Urea and Creatinine Concentrations of Streptozotocin-Induced Diabetic Rats Administered Aqueous Extract *Azadirachta indica* Stem-Bark

Table 4 represents urea and creatinine concentrations of STZ-induced diabetic rats administered aqueous extract *A. indica* stem-bark. The result showed significant increase ($p<0.05$) in urea and creatinine concentrations in the diabetic groups when compared with the normal control. However, administration aqueous extract of *A. indica* stem-bark resulted to significant decrease ($p<0.05$) in the urea and creatinine concentrations in the treated groups when compared with the diabetic untreated. Treatment with glibenclamide 5 mg/kg and 400 mg/kg stem-bark extract exhibited the most effective decrease in urea and creatinine concentrations among the treated groups.

Table 4: Urea and creatinine concentrations of streptozotocin-induced diabetic rats administered aqueous extract *Azadirachta indica* stem-bark

Group	Urea (mmol/l)	Creatinine (µmol/l)
1	4.52±0.05[a]	51.40±0.50[a]
2	4.96±0.09[b]	57.80±0.37[b]
3	11.94±0.07[f]	279.00±0.70[f]
4	9.06±0.06[e]	174.20±0.37[e]
5	7.50±0.03[d]	139.80±0.37[d]
6	6.65±0.06[c]	97.25±0.47[c]

Results are Mean ± SEM of 5 determinations. Values in the same column with different same superscript are statistically different and values in the same column with same superscript are not statistically different at ($p<0.05$). Group 1: normal control, Group 2: glibenclamide control, Group 3: diabetic untreated, Group 4: 100 mg/kg stem-bark extract, Group 5: 300 mg/kg stem-bark extract and Group 6: 400 mg/kg stem-bark extract.

Antioxidant Parameters of Streptozotocin-Induced Diabetic Rats Administered Aqueous Extract *Azadirachta indica* Stem-Bark

Table 5 shows antioxidant parameters of STZ-induced diabetic rats administered aqueous extract *A. indica* stem-bark. The result indicated significant decrease ($p<0.05$) in the activities of antioxidant enzymes and GSH and a significant increase in MDA concentration in diabetic untreated when compared with the normal control. Administration of aqueous extract *A. indica* stem-bark resulted to significant increase ($p<0.05$) in the activities of SOD, CAT and the concentration of GSH in the treated groups when compared with the diabetic untreated. Treatment with glibenclamide 5 mg/kg, 300 mg/kg and 400 mg/kg stem-bark extract exhibited the most effective increase in the activities of SOD and CAT whereas 300 mg/kg and 400 mg/kg stem-bark extract showed most effective increase in the concentration of GSH and also the most effective decrease in the concentration of MDA among treated groups.

Table 5: Antioxidant parameters of streptozotocin-induced diabetic rats administered aqueous extract *Azadirachta indica* stem-bark

Group	SOD (U/ml)	CAT (U/ml)	GSH (U/ml)	MDA (nmol/ml)
1	26.84±0.60[a]	15.04±0.27[a]	17.76±0.38[a]	99.10±0.12[a]
2	21.90±0.57[e]	11.96±0.20[d]	14.84±0.22[b]	117.96±0.23[d]
3	18.00±0.72[b]	7.64±0.16[f]	8.60±0.29[d]	140.26±0.16[f]
4	19.96±0.66[c]	9.32±0.08[b]	14.18±0.16[b]	120.28±0.13[e]
5	24.46±0.11[f]	11.06±0.82[c]	16.72±0.60[c]	100.52±0.96[c]
6	20.70±0.07[d]	13.15±0.22[e]	16.47±0.51[c]	98.70±0.41[b]

Results are Mean ± SEM of 5 determinations. Values in the same column with different same superscript are statistically different and values in the same column with same superscript are not statistically different at ($p<0.05$). Key: SOD: Superoxide dismutase, CAT: Catalase, GSH: Reduced glutathion and MDA: Malondialdehyde. Group 1: normal control, Group 2: glibenclamide control, Group 3: diabetic untreated, Group 4: 100 mg/kg stem-bark extract, Group 5: 300 mg/kg stem-bark extract and Group 6: 400 mg/kg stem-bark extract.

Lipid Profile of Streptozotocin-Induced Diabetic Rats Administered Aqueous Extract *Azadirachta indica* Stem-Bark

Table 6 shows TC, TG, HDL, LDL and AI concentrations of STZ-induced diabetic rats administered aqueous extract *A. indica* stem-bark. The result indicated significant increase ($p<0.05$) in TC, TG, LDL and AI concentrations and[a]significant decrease in HDL concentration in diabetic untreated when compared with the normal control. Administration of aqueous extract *A. indica* stem-bark resulted to significant decrease ($p<0.05$) in TC, TG, LDL and AI and[a]significant increase in HDL concentration in the treated groups when compared with the diabetic untreated. Treatment with 300 mg/kg and 400 mg/kg stem-bark extract showed the most significant decrease in TC. Similarly, treatment with glibenclamide 5 mg/kg and 400 mg/kg stem-bark extract was observed to have the most effective decrease in TG, LDL and AI respectively and most sufficient increase in HDL concentration among the treated groups.

Table 6: Lipid profile of streptozotocin-induced diabetic rats administered aqueous extract *Azadirachta indica* stem-bark

Group	TC (mmol/l)	TG (mmol/l)	HDL (mmol/l)	LDL (mmol/l)	AI
1	3.72±0.05[a]	1.84±0.04[a]	1.20±0.03[a]	2.28±0.03[a]	1.90±0.02[a]
2	5.34±0.02[c]	1.78±0.03[a]	2.52±0.02[f]	2.26±0.03[b]	1.03±0.01[a]
3	8.18±0.03[e]	6.40±0.03[e]	0.36±0.02[e]	7.46±0.02[f]	21.13±1.51[e]
4	6.10±0.05[d]	3.44±0.04[d]	0.66±0.02[b]	5.10±0.07[e]	7.77±0.31[d]
5	5.10±0.04[b]	3.08±0.03[c]	0.90±0.03[c]	4.00±0.03[d]	4.46±0.14[c]
6	4.84±0.05[b]	2.80±0.04[b]	1.05±0.02[d]	3.52±0.02[c]	3.36±0.14[b, c]

Results are Mean±SEM of 5 determinations. Values in the same column with different same superscript are statistically different and values in the same column with same superscript are not statistically different at ($p<0.050$. Key: TC: Total cholesterol, TG: triglycerides, HDL: High density lipoprotein, LDL: Low density lipoprotein and AI: Artherogenic index. Group 1: normal control, Group 2: glibenclamide control, Group 3: diabetic untreated, Group 4: 100 mg/kg stem-bark extract, Group 5: 300 mg/kg stem-bark extract and Group 6: 400 mg/kg stem-bark extract.

Discussion

Herbal therapy remains the safest, accessible and affordable which people relied for the treatment of various ailments and such plants include *Azadirachta indica* (Ezeigwe *et al*., 2019) [13]. For decades, people have used *A. indica* extensively due to its numerous health advantages. Tiwari *et al*. (2014) reported, every portion of this plant has significance in traditional medicine. Stem-bark extract of *A. indica* is used in the treatment of various diseases, among which is diabetes mellitus. The phytochemical screening revealed the presence

of alkaloids, flavonoids, phenols, cardiac glycosides and saponins. These phytochemicals were believed to be responsible for the antidiabetic property of the extract. The results of the phytochemical study are consistent with the n-hexane and methanolic extracts found by Anarado *et al*. (2022). It also supports the results of Feyisara *et al*. (2023), who found anthraquinones, flavanoids, phenols, cardiac glycosides, phytosterols, saponins, and tannins. The stem-bark phytochemical results conforms with the findings of Idoko *et al*. (2018), who found that the aqueous stem-bark extract contained alkaloids, flavonoids, saponins, tannins, phenols, and glycosides. Additionally, it is consistent with the results of Aguoro *et al*. (2015) [2], who found that the stem-bark extract contained alkaloids, phenol, terpenoids, quinines, reducing sugar, and saponins.

Treatment of STZ-induced diabetic rats with aqueous extract of *A. indica* stem-bark significantly ($p<0.05$) decreased the concentration of fasting blood glucose to a level similar to the conventional drug used for the treatment of diabetes. The decreased concentration of blood glucose in the treated rats could be due to the presence of the phytochemicals; alkaloids, tannins, flavanoids, terpenoids, phenols, cardiac glycosides and saponins. Alkaloids were reported to inhibit the enzyme α-glucosidase (Rania *et al*., 2023). Furthermore, the antidiabetic effect of flavonoids is evident as they inhibit the enzyme aldose reductase that catalyzes the conversion of glucose to sorbitol, which contributes to complications of diabetes (Rania *et al*., 2023). Furthermore, the effect of extract may also be attributed to the possible enhancement of protein synthesis in the liver resulting in an increase in insulin secretion, and increase hepatic absorption of glucogenic amino acids (Arika *et al*., 2016; Rawi *et al*., 2011) [9, 24]. Saponins have been reported to cause hypoglycemia (Ezeigwe *et al*., 2020) [14]. The outcome this study agrees with a study by Shailey & Basir (2012), which showed that treatment with an aqueous extract of *A. indica* stem-bark significantly reduced blood glucose levels in rats with alloxan-induced diabetes. This study was also supported by the findings of Anarado *et al*. (2022), who found that methanolic extract is effective against hyperglycemia by inhibiting alpha amylase activity. Feyisara *et al*. (2023) revealed that the ethanolic extract of the stem-bark of *A. indica* had antidiabetic properties. *A. indica* stem-bark extract suppressed α-amylase and α-glucosidase, according to studies by Oyenike *et al*. (2022) and Mukherjee & Sengupta (2013). It was reported that the *A. indica* is very effective in maintenance of blood glucose concentration and also good in preventing and delaying the onset of diabetes (Rania *et al*., 2023). Oyenike *et al*. (2022) reported that stem-bark extract of *A. indica* inhibited α-amylase and α-glucosidase.

Moreover, the result from this work shows increase in the activities of antioxidant enzymes (SOD and CAT) and GSH concentration to almost normalcy. This suggests that STZ-induced oxidative stress could be inhibited by the action of the extracts. The result of the stem-bark aligns with a study by Muhammad (2016) [5] that found *A. indica* stem-bark extract had significant antioxidant capability. The study also conforms to a research by Shailey & Basir (2012), which showed that treatment with an aqueous extract of *A. indica* stem-bark significantly increased the concentration of GSH and the activities of SOD and CAT in alloxan-induced diabetic rats. It is also consistent with another study conducted by Olakunle *et al*. (2019), which reported antioxidant potential of *A. indica* stem-bark extract and was believed to avert oxidative stress generated due to hyperglycemia through electron transfer. The result of this study is also consistent with a study conducted by Ajibade *et al*. (2019) [4], which showed that treatment with an aqueous extract of *A. indica* significantly increased the concentration of GSH and the activity of SOD in STZ-induced diabetic rats. According to Feyisara *et al*. (2023), *A. indica* aqueous stem-bark has antioxidant potentials on DPPH, which makes it useful for managing oxidative stress. It is also in line with the results of Hafiz *et al*. (2022), who found that aqueous stem-bark extract of *A. indica* significantly increased the level of GSH and the activities of antioxidant enzymes, SOD and CAT. The stem-bark extract of *A. indica* exhibits significant antioxidant activity due to its complex phenolic content (Mohd *et al*., 2021).

The significant decrease in MDA levels could be the ability of the polyphenols present in the extracts to prevent lipid peroxidation; another reason could be the ability of polyphenols to form adducts with aldehydes like between polyphenols and methyl glyoxal. Constituents of *A. indica* such as flavonoids, phenols and tannins have antioxidant activity. These phytochemicals might be responsible for the lipid peroxidation inhibition by scavenging free radicals (Doaa *et al*., 2011). Findings from this research correspond with the report by Olakunle *et al*. (2019) who revealed significant decrease in the concentration of MDA in diabetic rats after treatment with *A. indica* stem-bark extract in a dose dependent manner. The findings from this study also conforms with a study by Ajibade *et al*. (2019) [4] who reported significant decrease in the concentration of MDA after treatment with aqueous extract of *A. indica* in STZ-induced diabetic rats.

The extract significantly decreased lipid profile (TC, TG and LDL) and significantly increased HDL level. This might be because of the presence of phytochemicals, such as saponins, which are known to reduce TG levels because of their lytic role. It is also known that VLDL cholesterol is the primary transporter of TG in the serum and that it can precipitate the anterohepatic circulation of bile acid, which prevents it from being absorbed by the intestinal tract and lowers cholesterol levels (Dosofunjo *et al*., 2013). The results of the study are consistent with those of Arnarado *et al*. (2022), who found that diabetic rats fed with *A. indica* stem-bark methanolic extract had significantly higher HDL and significantly lower TC, TG, and LDL. According to research by Sanni *et al*. (2019), ethanolic stem-bark extract of *A. indica* inhibits lipid peroxidation, which in turn lowers the amount of TG, TC, and VLDL produced. The outcome also agrees with a study by Ahmed *et al*. (2023) [3], which showed a large increase in HDL and a significant drop in TC, TG, and LDL in alloxan-induced diabetic Wistar rats given stem-bark extract from *Khaya senegalensis*.

The activities of AST, ALT, and ALP were significantly ($p<0.05$) reduced and the levels of total protein and albumin increased after treatment with *A. indica* stem-bark extract. Study by Ajibade *et al*. (2019) [4], which found a substantial decrease in AST, ALT, and ALP activities in STZ-induced diabetic rats treated with *A. indica* aqueous extract, is consistent with the stem-bark extract results obtained from this investigation. According to a study by Mohammad (2016) [21], the aqueous extract of *A. indica* stem-bark has strong antioxidant potentials, which is consistent with the results of this study. This study also supports the finding of Olakunle *et al*. (2019), who found that the stem-bark of *A.*

indica contains bioactive components that reduced hyperglycemia by increasing glucose absorption, inhibiting important enzymes connected to diabetes, and relieving oxidative stress.

Urea and creatinine serve as biomarkers for renal function and their rise in blood indicate renal impairment. Treatment with *A. indica* extracts significantly ($p<0.05$) decreased their concentrations. The significant reduction in urea and creatinine concentrations can be attributed to the presence of flavonoids and phenols, which possess the capacity to counteract inflammation, enhance hepatocyte lipid metabolism, or control glucose levels by impeding the effects of epinephrine on glycogenolysis and peripheral glucose utilization (Arabshomali *et al*., 2023; Parveen *et al*., 2018) [8]. This outcome is consistent with research by Ahmed *et al*. (2023) [3], which found that treating alloxan-induced diabetic Wistar rats with stem-bark extract from *Khaya senegalensis* significantly reduced urea and creatinine levels. Additionally, it is consistent with a study by Alhassan *et al*. (2017) [5] that showed urea and creatinine levels in alloxan-diabetic rats treated with *K. senegalensis* stem-bark extract significantly decreased. It also agrees with the results of Adel *et al*. (2020) [1], who found that administration of *K. senegalensis* stem-bark extract to alloxan-induced diabetic had lowered the levels of urea and creatinine.

Conclusion

The study revealed that aqueous stem-bark extract of *A. indica* at varied doses is potent in the management of diabetes. This indicated that *A. indica* is a store of phytochemicals that can serve as a good source of diabetic drug discovery.

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Conflict of Interest

Authors have declared no conflicting interests regarding the publication of this article.

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