ATATÜRK ÜNİVERSİTESİ YAYINLARI
ATATURK UNIVERSITY PUBLICATIONS

Research Article *Araştırma Makalesi* DOI: 10.5152/VetSciPract.2023.23127

Hypoglycemic and Hypolipidemic Activities of Aqueous Root Extract of *Senna alata* in Alloxan-Induced Diabetic Wistar Rats

Senna alata'nın Aköz Kök Ekstraktının Alloksan ile İndüklenmiş Diyabetli Wistar Sıçanlarında Hipoglisemik ve Hipolipidemik Aktiviteleri

Samuel C. ATTAMA[1,2]
Ngozi OKWELUM[4]
Paul F. EGUNLETI[3]
Solomon C. DAVID[1]
Timothy U. OBETTA[1]
Michael J. AGUIYI[5]

[1]Department of Veterinary Physiology and Pharmacology, University of Nigeria, Nsukka, Nigeria
[2]Department of Veterinary Pharmacology and Toxicology, Federal University of Agriculture, Abeokuta, Nigeria
[3]Department of Veterinary Physiology and Biochemistry, Federal University of Agriculture, Abeokuta, Nigeria
[4]Institute of Food Security, Environmental Resources and Agricultural Research, Federal University of Agriculture, Abeokuta, Nigeria
[5]Department of Veterinary Surgery and Radiology, Universisty of Nigeria, Nsukka, Enugu State, Nigeria

Geliş Tarihi/Received: 27.04.2023
Kabul Tarihi/Accepted: 11.07.2023
Yayın Tarihi/Publication Date: 16.08.2023

Sorumlu Yazar/Corresponding Author: Samuel CHIJIOKE ATTAMA
E-mail: attamasc@funaab.edu.ng

Atıf: Attama SC, Okwelum N, Egunleti PF, David SC, Obetta TU, Aguiyi MJ. *Senna alata*'nın aköz kök ekstraktının alloksan ile indüklenmiş diyabetli Wistar sıçanlarında hipoglisemik ve hipolipidemik aktiviteleri. *Vet Sci Pract*. 2023;18(2):83-88.

Cite this article as: Attama SC, Okwelum N, Egunleti PF, David SC, Obetta TU, Aguiyi MJ. Hypoglycemic and hypolipidemic activities of aqueous root extract of *Senna alata* in alloxan-induced diabetic Wistar rats. *Vet Sci Pract*. 2023;18(2):83-88.

ABSTRACT

In this study, rats with alloxan-induced diabetes were used to examine the hypoglycemic and hypolipidemic effects of *Senna alata* aqueous root extract. Twenty male albino Wistar rats were selected for this study. They were randomly assigned into 4 groups (1-4) of 5 rats in each group. Alloxan monohydrate was administered intraperitoneally to groups 2-4 rats at 160 mg/kg. Forty-eight hours after administration and upon confirmation of diabetes mellitus (fasting blood glucose ≥ 126 mg/dL), group 3 rats were treated with *Senna alata* extract (400 mg/kg) while group 4 rats were treated with glibenclamide (2 mg/kg). Groups 1 and 2 rats received distilled water and were apportioned as normal and negative control groups, respectively. For 21 consecutive days, the treatments were given orally, once daily. Rats in all groups had their fasting blood glucose levels checked after 1 hour, 6 hours, 24 hours, 7 days, 14 days, and 21 days. On the 21 days post-treatment, serum samples were collected from all groups for lipid panel and kidney function examination while pancreases were freshly harvested for histomorphology. In comparison to the diabetic rats in the untreated (negative control) group, the *Senna alata* extract-treated rats had significantly reduced levels of fasting blood glucose, cholesterol, triglycerides, and low-density lipoprotein but higher levels of high-density lipoprotein. Histomorphology of the pancreas of rats treated with *Senna alata* extract revealed more populations of beta-cells compared to that of the diabetic untreated group. This study has demonstrated that aqueous root extract of *Senna alata* has hypoglycemic and hypolipidemic activities and restored pancreatic tissue from injury caused by the alloxan challenge in diabetic rats.

Keywords: Alloxan monohydrate, diabetes mellitus, hypoglycemic, hypolipidemic, *Senna alata*

ÖZ

Bu çalışmada, alloksan ile diyabet oluşturulan sıçanlar kullanılarak *Senna alata*'nın sulu kök özütünün hipoglisemik ve hipolipidemik etkileri incelenmiştir. Bu çalışma için yirmi erkek albino Wistar sıçan seçilmiştir. Sıçanlar rastgele olarak 4 gruba (1-4) ayrılmıştır, her bir grup içinde 5 sıçan bulunmaktadır. Alloksan monohidrat, 2-4 grup sıçanlarına 160 mg/kg dozda intraperitoneal olarak uygulanmıştır. Uygulamanın 48 saat sonrasında ve diabetes mellitus'un teyidi üzerine (açlık kan şekeri ≥ 126 mg/dl), 3. gruptaki sıçanlara Senna alata özütü (400 mg/kg) ile 4. gruptaki sıçanlara glibenklamid (2 mg/kg) tedavisi uygulanmıştır. 1. ve 2. grup sıçanlar ise sırasıyla normal kontrol ve negatif kontrol grupları olarak belirlenmiş olup, distile su verilmiştir. Ardışık 21 gün boyunca tedaviler günde bir kez oral yolla uygulanmıştır. Tüm gruplardaki sıçanların açlık kan şekeri düzeyleri 1 saat, 6 saat, 24 saat, 7 gün, 14 gün ve 21 gün sonra kontrol edilmiştir. Tedavinin 21. gününde, tüm gruplardan serum örnekleri lipid paneli ve böbrek fonksiyonu incelemesi için toplanmış, pankreaslar ise taze olarak histomorfoloji için alınmıştır. *Senna alata* özütü ile tedavi edilen sıçanlar, tedavi edilmemiş (negatif kontrol) grup içindeki diyabetik sıçanlara kıyasla açlık kan şekeri, kolesterol, trigliserit ve düşük yoğunluklu lipoprotein düzeylerinde belirgin bir şekilde azalma göstermiş, aynı zamanda yüksek yoğunluklu lipoprotein düzeylerinde artış gözlenmiştir. Senna alata özütü ile tedavi edilen sıçanların pankreas histomorfolojisi, tedavi edilmemiş diyabetik gruba kıyasla daha fazla beta hücresi popülasyonunu göstermiştir. Bu çalışma, *Senna alata*'nın sulu kök özütünün hipoglisemik ve hipolipidemik etkilere sahip olduğunu ve diyabetik sıçanlarda alloksanın neden olduğu pankreas dokusundaki hasarı onardığını göstermiştir.

Anahtar Kelimeler: Alloksan monohidrat, diabetes mellitus, hipoglisemik, hipolipidemik, *Senna alata*

INTRODUCTION

Diabetes mellitus (DM) is an endocrine and metabolic disorder which manifests as impaired carbohydrate, fat, and protein metabolism.[1] These disorders could be due to a lack of insulin secretion or reduced sensitivity of tissues to insulin.[2] Etiologically, DM is divided into insulin-dependent DM or juvenile-onset DM and non-insulin-dependent DM or adult-onset DM.[3]

Alloxan monohydrate and streptozotocin are the commonest chemicals used in the induction of experimental DM, and both drugs exert their diabetogenic actions when they are administered parenterally.[4] These agents are known to generate free radicals that selectively destroy the insulin-producing pancreatic islets, which are responsible for insulin production.[5] Hyperglycemia usually manifests due to lack of insulin production since insulin is saddled with metabolizing glucose and maintenance of its optimal serum level.[6]

Hyperlipidemia is one of the common long-term complications associated with DM. It's known to occasion various lipid abnormalities including high levels of tryglicerides, low-density lipoproteins (LDL), total cholesterols, and reduced levels of high-density lipoproteins (HDL). These abnormalities predispose to atherosclerosis and cardiovascular diseases. When blood sugar levels are properly maintained, these problems are less frequent and less severe.[7] Pharmacological glycemic control involves using insulin and oral hypoglycemic drugs. There is poor compliance with the use of these agents, especially in developing countries due to their high cost, unavailability, and associated health risks.[8] This has therefore necessitated the search for alternative natural therapeutic agents. Plant sources of drugs are known to possess various advantages over orthodox drugs with regards to their readily availability, low cost, and side effects.[9] The use of herbal medicines in the treatment of ailments is a common practice, especially in developing countries.[10] World Health Organization over the years has advocated the need to explore antidiabetic drugs from natural sources. Therefore, the screening of medicinal plants in each other to identify new and potent hypoglycemic agents is increasing by day among scientific researchers.

Senna alata (SA) is a perennial plant of the Leguminosae family. It is widely dispersed in Africa including Nigeria. It has various common names which include ringworm bush, candle bush, and craw-craw plant, among others. It has been thoroughly screened for biological activities by scientific researchers and has been reported to possess various chemical constituents such as terpenoids, flavonoids, phenols, anthraquinones, and steroids.[11,12] These phytochemicals are known to possess biological activities.[13] Various organs of SA have been investigated for antidiabetic activity.[14,15] However, little is known regarding the hypoglycemic and hypolipidemic properties of SA's aqueous root extract. So, the aim of this study is to determine whether SA's aqueous root extract has any potential hypoglycemic and hypolipidemic effects on alloxan-induced diabetic rats.

MATERIALS AND METHODS

Reagents and Chemicals

Chemicals and reagents used in this study were procured as follows: alloxan monohydrate (Sigma Aldrich, Gallingham, Dorset, UK); glibenclamide (Hovid, Shek Tong Tsui, Hong Kong); creatinine assay kit (Sigma Aldrich); urea assay kit (Sigma Aldrich); total cholesterol assay kit (Cell Biolabs Inc., San Diego, California, USA); triacylglycerides assay kit (Sigma Aldrich); HDL cholesterol assay kit (Elabscience, Houston, Texas, USA). All chemicals used in this study are of optimum analytical grade.

Plant Collection and Preparation of Extract

Senna alata roots were freshly collected at the peak of raining season (July 2022) from the Botanical Garden belonging to Plant Science and Biotechnology Department, University of Nigeria, Nsukka, and were authenticated in the same Department by a botanist. The voucher specimen (*Senna alata*: INTERCEED/2852) was kept at the herbarium. The roots of the plant were washed, sliced into smaller sizes with a clean sharp knife, and dried in a shade room for 28 days. The sliced roots were pulverized into powder using an electric blender. A cold maceration technique with distilled water was used. Two hundred grams of the powdered plant roots were taken and soaked in 400 mL distilled water and allowed for 48 hours with 2 hourly intermittent shaking. To secure the aqueous extract, they were then sieved using No. 1 Whatman filter paper. The aqueous extract was freeze-dried and kept in a rubber screw-cap bottle and preserved in the refrigerator at a temperature of 4°C until needed.

The aqueous root extract of SA produced a yield of 14.5 g (7.25% w/w).

Experimental Animals

Male albino Wistar rats (120-140 g) were procured from a reputable source. The animals were allowed for 2 weeks of acclimatization in a clean wire mesh cage in a controlled environment (temperature 25 ± 2°C 12-hour dark/light cycles) and fed with standard laboratory animal diet ad libitum before the commencement of the study.

The study was carried out after obtaining Institutional Animal Ethical Committee's clearance (Date: 12.08.2022, Number: FVM-UNN-IACUC-2022-0334).

Experimental Protocol

For this study, 20 male Albino Wistar rats were used. They were divided into 4 groups at random (n = 5). Alloxan monohydrate (160 mg/kg) was reconstituted in distilled water and then administered intraperitoneally once to groups 2-4 to induce DM. The remaining 5 rats were normoglycemic (un-induced) rats that formed group 1, 48 hours following alloxan monohydrate administration and upon confirmation of DM (fasting blood glucose (FBG) level ≥ 126 mg/dL), the animals in groups 2-4 (n = 5 per group) were sorted to ensure there were no significant differences in FBG levels among the groups. The treatment agents (SA and glibenclamide) used in this study were reconstituted in distilled water, and all animals were treated as follows:

1 (group 1): uninduced normoglycemic rats in group 1 were given 10 mg/kg of distilled water (normal control); 2 (group 2): negative control group of induced diabetic rats were given 10 mL/kg of distilled water; 3 (group 3): induced-diabetic rats in group 3 were given a 400 mg/kg aqueous extract of SA; 4 (group 4): rats with induced diabetes were placed in group 4 and given 2 mg/kg glibenclamide (standard control). For a total of 21 days, the treatments were given orally once daily. Fasting blood glucose levels were measured using a one-touch ultra-easy glucometer that automatically displays the FBG levels on the screen at intervals of 1 hour, 6 hours, 24 hours, 7 days, 14 days, and

then 21 days. The 400 mg/kg of SA was chosen with respect to the effects observed with its use as reported by previous researchers.[16,17]

Sample Collection

Whole blood was collected for glucose estimation using the tail snip technique during which 1 drop of whole blood from the snipped tail was allowed to fall directly into a glucometer strip. On the last day of the study (day 21), blood samples for serum lipid panels and kidney function tests (triglycerides, total cholesterol, HDL, creatinine, and urea) were collected into heparin-coated bottles through the medial canthus of the rat eye. Thereafter, the animals were humanely sacrificed by inhalation anesthesia using chloroform followed by cervical dislocation. The animals were cut open via the midline of the thoracic and abdominal regions and pancreases were freshly detached for a histopathology examination.

Determination of Serum Biochemical Parameters and Histopathology

The blood samples collected after 21 days of the study were spun in a centrifuge at 10 000 *g* for 10 minutes and the resulting sera were decanted. Triacylglyceride (TAG) value was assayed by quantitative enzymatic method.[18] The cholesterol value was assayed by the enzymatic method.[19] High-density lipoprotein was assayed by using the dextran sulfate-magnesium II precipitation technique.[20] Friedwald formula was applied in calculating the values of LDL and triglycerol values were divided by 5 to get the very-LDL values. The creatinine assay was determined by Jaffe reaction method.[21] Serum urea was assayed according to the Urease-Berthelot method.[22] The histopathological studies of the freshly harvested pancreas were done according to Carlleton's histological technique.[23] The processed slides were viewed with a light microscope at 400× magnification.

Statistical Analysis

One-way analysis of variance was used to analyze the data generated from this study (The Statistical Package for Social Sciences version 23.0 software, IBM Corp.; Armonk, NY, USA). Variable means were separated using Duncan's multiple range test, and differences were deemed significant at $P = .05$. In tables, results were shown as mean and standard error of means.

RESULTS

Effects of Aqueous Root Extract of Senna alata on Fasting Blood Glucose Levels Observed from Preinduction to 21 Days of Treatment in Alloxan-Induced Diabetic Wistar Rats

Findings showed that on day 21 post-treatment, rats treated with SA extract and glibenclamide had FBG levels that were statistically equivalent ($P = .05$), but rats in the untreated (negative control) group had FBG levels that were considerably ($P = .05$) lower (Table 1).

The Percentage Reduction in Fasting Blood Glucose Levels of Alloxan-Induced Diabetic Rats Treated with Aqueous Root Extract of Senna alata

The results also revealed that rats given SA experienced a progressive decline in FBG levels from the first hour to the final 21 days after treatment, while the FBG levels of rats of the diabetic untreated group remained high even with day 21 post-treatment. However, SA and glibenclamide-treated groups recorded 65.25% and 66.36%, respectively, on 21 days post-treatment (Figure 1).

The Effects of Aqueous Root Extract of Senna alata on Lipid Panel of Alloxan-Induced Diabetic Rats

According to the results of the lipid profile, the rats treated with SA had cholesterol levels that were statistically equal ($P < .05$) to those of the rats treated with glibenclamide but significantly ($P < .05$) lower than those of the rats in the diabetic-untreated group. Triglycerol levels were statistically comparable in all groups except for those of the diabetic-untreated group, which were significantly ($P < .05$) higher. High-density lipoprotein values were statistically comparable ($P < .05$) in all groups except those of the diabetic-untreated group, which were significantly ($P < .05$) lower. Rats in the SA and glibenclamide-treated groups had LDL values that were statistically equivalent ($P = 0.05$) but were considerably ($P = 0.05$) lower than rats in the diabetic-untreated group (Table 2).

The Effects of Aqueous Root Extract of Senna alata on Kidney Function of Alloxan-Induced Diabetic Rats

According to Table 3, the urea and creatinine levels of the rats treated with SA and glibenclamide were statistically equivalent ($P = .05$), but they were significantly ($P = .05$) lower than the rats in the untreated diabetic group.

The Photomicrograph of Diabetic Rat Pancreas Treated with Senna alata Extract

Results of the photomicrograph showed that the population of islet cells in both SA-treated rats and those of normal control and glibencamide-treated groups were comparable. However, islet cells were scanty and atrophic in congested pancreatic ducts in rats of the diabetic untreated group (Figure 2).

DISCUSSION

This study investigated the potential hypolipidemic and hypoglycemic effects of SA aqueous root extract in alloxan-induced diabetic rats. Diabetes mellitus, a known chronic disease, is characterized by FBG levels and often associated with certain complications like atherosclerosis, hepatotoxicity, nephrotoxicity, cardiovascular diseases, etc. Alloxan monohydrate is a diabetogenic agent known to induce hyperglycemia by generation of free radicals that damage the beta cells of islets of Langerhans, which in turn occasions low production of insulin.

Table 1. Effects of Aqueous Root Extract of *Senna alata* on Fasting Blood Glucose Levels Observed from Preinduction to 21 Days of Treatment in Alloxan-Induced Diabetic Wistar Rats

	Fasting Blood Glucose Levels (mg/dL)							
Groups	Pre-Induction	48-Hour Pre-Induction	1-Hour Post-Treatment	6-Hour Post-Treatment	24-Hour Post-Treatment	7 Days Post-Treatment	14 Days Post-Treatment	21 Days Post-Treatment
1	81.25 ± 0.56^{a}	81.90 ± 0.35^{a}	82.20 ± 0.80^{a}	80.40 ± 0.55^{a}	78.70 ± 0.07^{a}	78.25 ± 0.15^{a}	79.50 ± 0.55^{a}	76.82 ± 0.72^{a}
2	80.90 ± 0.75^{a}	242.20 ± 1.25^{d}	242.35 ± 1.00^{d}	240.20 ± 1.80^{d}	218.00 ± 1.06^{d}	212.15 ± 1.08^{d}	201.35 ± 1.14^{d}	186.34 ± 1.06^{c}
3	80.40 ± 0.65^{a}	243.00 ± 1.50^{d}	220.50 ± 1.30^{c}	180.45 ± 1.25^{c}	142.70 ± 1.08^{c}	120.55 ± 1.06^{c}	85.70 ± 1.08^{ab}	84.45 ± 1.12^{b}
4	81.30 ± 0.42^{a}	243.75 ± 1.00^{d}	140.66 ± 1.45^{b}	121.60 ± 1.05^{b}	85.40 ± 1.04^{b}	83.68 ± 1.02^{ab}	83.10 ± 1.00^{a}	82.00 ± 1.02^{ab}

Significant differences between groups are denoted by the superscripted letters a, b, c, and d ($P = .05$).

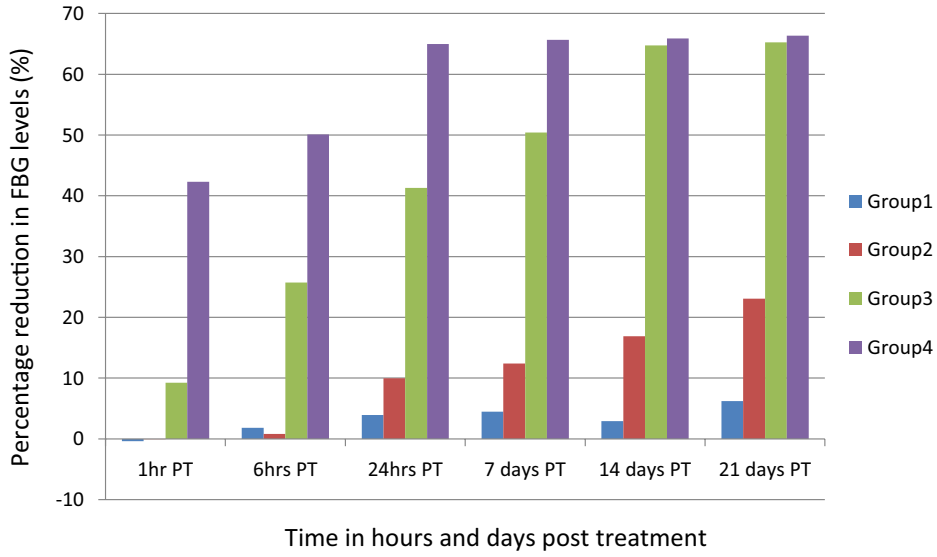

Figure 1. Percentage reduction in fasting blood glucose levels of alloxan-induced diabetic rats treated with aqueous root extract of SA. hr, hour(s); PT, post-treatment; SA, *Senna alata*.

Table 2. Effects of Aqueous Root Extract of *Senna alata* on Lipid Panel of Alloxan-Iinduced Diabetic Rats

	Lipid Panels (mmol/L)				
Groups	Cholesterol	Triglycerol	High-Density Lipoprotein	Low-Density Lipoprotein	Very-Low-Density Lipoprotein
1	4.28 ± 0.01^{a}	1.58 ± 0.02^{a}	2.54 ± 0.04^{b}	1.02 ± 0.07^{a}	0.32 ± 0.01^{a}
2	5.52 ± 0.43^{c}	1.93 ± 0.12^{b}	1.75 ± 0.05^{a}	2.86 ± 0.02^{c}	0.39 ± 0.00^{a}
3	4.61 ± 0.10^{b}	1.64 ± 0.01^{a}	2.36 ± 0.13^{b}	1.50 ± 0.05^{b}	0.33 ± 0.02^{a}
4	4.55 ± 0.06^{b}	1.62 ± 0.03^{a}	2.41 ± 0.08^{b}	1.40 ± 0.08^{b}	0.32 ± 0.12^{a}

The letters a, b, and c in superscripts denote significant differences ($P = .05$) between groups.

Studies showed a significant increase in FBG levels in rats challenged with alloxan monohydrate compared to rats of normal control. However, after 21 days of treatment, animals given the SA root extract had significantly lower FBG levels than rats in the negative control group. This finding corroborates with the work of other researchers [14,15] who reported the hypoglycemic activity of leaf and bark extract of SA in rats.

Dyslipidemia is a complication often associated with diabetes.[24] Findings of this study showed remarkably high concentrations of serum cholesterol, TAG, LDL, and low HDL in untreated diabetic rats, which is consistent with reports from previous studies[25,26] which reported that induction of DM leads to an increase in blood glucose level which also resulted in a commensurate increase in serum lipids. The liver, an organ that depends on insulin and is crucial for maintaining blood sugar and lipid levels, is severely affected by diabetes.[27] Diabetes often leads to lipoprotein abnormalities which are characterized by abnormally high levels of cholesterol, TAG, LDL, and low HDL.[24,28] It is generally known that high serum lipid levels in diabetic patients originate from the enhanced mobilization of free fatty acids from accessory fat depots as a result of insulin's inhibition of hormone-sensitive lipase.[29] It could also be due to certain hormones that enhance lipolysis such as glucagon and catecholamines. The surplus fatty acids produced owing to these effects are usually converted to cholesterol and phospholipids that combine with the excess triglycerols produced simultaneously in the liver and are distributed into the circulation as lipoproteins. Therefore, significant hyperlipidemias ($P > .05$) recorded in diabetic untreated rats could be regarded as an effect of the uninterrupted activity of lipolytic hormones in the fat depots.[30] Treatment of diabetic rats with the SA extract resulted in the alleviation of all dyslipidemia, thereby justifying its antihyperlipidemic potency. These effects, however, could be ascribed to the presence of phytochemicals composed of the SA extract, which may have hindered cholesterol or bile acid absorption. This finding is consistent with the reports of previous researchers.[15,31]

Table 3. Effects of Aqueous Root Extract of *Senna alata* on Kidney Function of Alloxan-Induced Diabetic Rats

Groups	Urea (mg/dL)	Creatinine (mg/dL)
1	61.32 ± 3.11^{a}	2.05 ± 0.04^{a}
2	85.55 ± 0.17^{c}	3.28 ± 0.16^{c}
3	71.20 ± 2.10^{b}	2.65 ± 0.01^{b}
4	69.85 ± 1.00^{b}	2.60 ± 0.02^{b}

The superscript letters a, b, and c indicate significant differences across the groups.

This study observed abnormally high levels of serum urea and creatinine in rats of the diabetic untreated group compared to normal and treated groups. This finding is consistent with the work of a previous researcher[16] who reported a significant reduction to normal levels of serum creatinine, urea, and uric acid in diabetic rats after treatment with SA leaf extract. Renal dysfunction is a common complication associated with diabetes, which increases significantly in diabetic conditions.[32] Due to the kidney's diminished capacity to filter these waste products from the

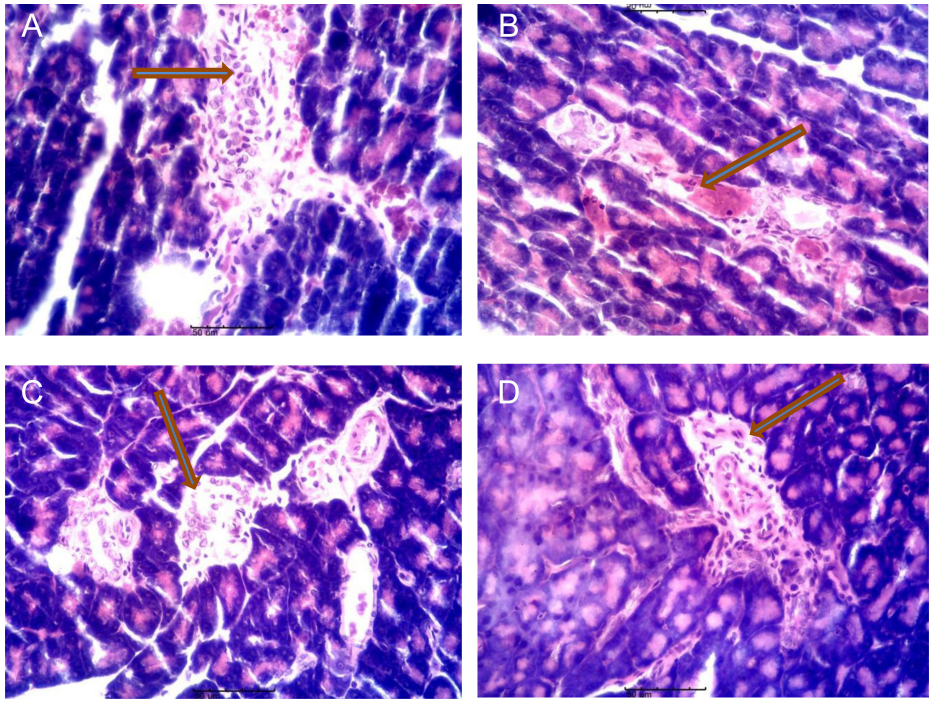

Figure 2. Photomicrograph of the pancreas of rats. (A) Group 1 rats showing well-populated islet cells. (B) Group 2 rats showing severely depleted and atrophic islet cells. (C) Group 3 rats showing relatively moderate islet cell population. (D) Group 4 rats showing well-populated islet cells (arrows) H&E 400×.

blood and ensure that they are excreted into the urine, the significantly increased serum levels of urea and creatinine found in the diabetic untreated group may be explained. Treatment with the SA extract, however, significantly ($P = .05$) decreased serum levels of urea and creatinine in a way that was similar to the standard drug (glibenclamide). This finding implies that SA extract can either directly improve the structural and functional integrity of blood, kidney, and liver cells or may be able to give a protective impact on the kidney.

The findings of this study revealed that induction of DM with alloxan monohydrate caused significant histopathological changes in the pancreas of rats compared to the control group. Previous reports[33] showed that administration of alloxan to experimental rats caused a selective pancreatic beta-cell membrane disruption and intracellular accumulation which resulted in cytotoxicity. Histomorphological observation of the pancreas in the present work confirmed an improvement in rats of the treatment groups compared with the rats of the negative control group. Treatment with SA extract restored the pancreas to normal architecture evident in the regeneration and increased the number of islet cells. This finding is consistent with the reports of previous researchers[34,35] that the plant extract increases the number of beta-cells by reduction of blood glucose.

In conclusion, this study has revealed that the aqueous root extract of SA has hypoglycemic and hypolipidemic activities and restored pancreatic tissue injury caused by the alloxan challenge in diabetic rats. Therefore, aqueous root extract of SA has the potential in the management of DM and its associated complications. Further study to determine the mechanism of action of the SA extract that produced these effects is therefore recommended.

Ethics Committee Approval: This study was approved by the University of Nigeria, Nsukka, Faculty of Veterinary Medicine, Institutional Animal Care and Use Committee (Date: 12.08.2022, Number: FVM-UNN-IACUC-2022-0334).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.S.C.; Design – A.S.C., D.S.C., Supervision – A.S.C., D.S.C.; Resources – A.S.C., O.N.; Materials – O.N., A.M.J., E.P.F.; Data collection and/processing – A.S.C., O.T.U., AM.J.; Analysis and/or interpretation – A.S.C., O.N., D.S.C.; Literature search – A.S.C., E.P.F., O.T.U.; Writing Manuscript – A.S.C., O.N.; Critical Review – A.S.C., O.N., D.S.C.

Declaration of Interests: The authors declare that they have no competing interest.

Funding: The authors declared that this study has received no financial support.

Etik Komite Onayı: Bu çalışma için etik komite onayı Nijerya Üniversitesi, Nsukka, Veteriner Fakültesi, Kurumsal Hayvan Sağlığı ve Kullanımı Komitesi'nden (Tarih: 12.08.2022, Sayı: FVM-UNNIACUC-2022-0334) alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir – A.S.C.; Tasarım – A.S.C., D.S.C.; Denetleme – A.S.C., D.S.C.; Kaynaklar – A.S.C., O.N.; Malzemeler – O.N., A.M.J., E.P.F.; Veri Toplanması ve/veya İşlemesi – A.S.C., O.T.U., A.M.J.; Analiz ve/veya Yorum – A.S.C., O.N., D.S.C.; Literatür Taraması – A.S.C., E.P.F., O.T.U.; Yazıyı Yazan – A.S.C., O.N.; Eleştirel İnceleme – A.S.C., O.N., .D.S.C.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

REFERENCES

1. World Health Organization. *Global Health Report on Diabetes*. Geneva: WHO; 2016.
2. Guyton AC, Hall JE. *Textbook of Medical Physiology*. 10th ed. Philadelphia: W.B. Sanders Co; 2000:915-928.
3. James A, Luke B. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2009;32(1):62-69. [CrossRef]
4. Baramurugan AN, Miyamoto WW, Inoue K, Tabata Y. Streptozotocin (STZ) was used to induce diabetes in animal models. *J Ethnopharmacol*. 2013;26:102-103.
5. Masiello P. Animal models of type II diabetes with reduced pancreatic beta cell mass. *Int J Biochem Cell Biol*. 2006;38(5-6):873-893. [CrossRef]
6. Cynthia MK. *The Merck Veterinary Mannual*. 9th ed, Whitehouse Station, New Jersey, USA: Merck and Co. Inc.; 2004:168.
7. Nathan DM, Cleary PA, Backlund JY, et al. Intensive Diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med*. 2005;353(25):2643-2653. [CrossRef]
8. Adeneye AA, Agbaje EO. Pharmacological evaluation of oral Hypoglycemic and antidiabetic effects of fresh leaves of ethanol extract of Moringa lucidia Benth in normal andAlloxan-induced Diabetic Rats. *Afr J Biomed Res*. 2008;11(1):65-71.
9. De Ameida I, Alviano DS, Vieira DP, Alves PB, Blank AF, Lopes AH. Anti-giardia activity of Occimium Basilicum essential oil. *Parasitological research*. 2007;101(4):43-52.
10. Chaughule RS, Barve RS. Role of herbal medicines in the treatment of infectious diseases. *Vegetos*. 2023:1-11. [CrossRef]
11. Liu A, Xu L, Zou Z, Yang S. Studies on chemical constituents from leaves of Cassia alata. *Zhongguo Zhong Yao Za Zhi*. 2009;34(7): 861-863.
12. Fatmawati S, Yuliana PAS, Bakar MFA. Chemical constituents, usage and Pharmacological activity of Cassia alata. *Helyion*. 2020;6(7): 43-53.
13. Oladeji OS, Adelowo FE, Oluyori AP, Bankole DT. Ethnobotanical description and biological activities of *Senna alata*. *Evid Based Complement Alternat Med*. 2020;2020:2580259. [CrossRef]
14. Varghese GK, Bose LV, Habtemariam S. Antidiabetic components of *Cassia alata* leaves: identification through α-glucosidase inhibition studies. *Pharm Biol*. 2013;51(3):345-349. [CrossRef]
15. Onyegeme-Okerenta B, Anacletus F. Hypoglycemic and hypolipidemic potentials of Senna alata and its effect on the pancreas of alloxan-diabetic induced Albino rats. *J Appl Life Sci Int*. 2017;11(1):1-10. [CrossRef]
16. Sugumar M, Doss DVA, Maddisetty PNP. Hepato-renal protective effects of hydroethanolic extract of *Senna alata* on enzymatic and nonenzymatic antioxidant systems in streptozotocin induced diabetic rats. *Integr Med Res*. 2016;5(4):276-283. [CrossRef]
17. Uwazie JN, Yakubu MT, Ashafa AOT, Ajiboye TO. Identification and characterization of antidiabetic principle in *Senna alata* (Linn.) flower in alloxan-induced diabetic male rats. *J Ethnopharmacol*. 2020;261: 10-16.
18. Bucolo G, David H. Quantitative determination of serum triglycerides by the use of enzymes. *Clin Phytosci*. 1973;19(5):476-482. [CrossRef]
19. Allain CC, Poon LS, Chan CSG, Richmond W, Fu PC. Enzymatic determination of serum total cholesterol. *Clin Chem*. 1976;20(4):470-475.
20. Albers JJ, Warnick GR, Chenng MC. Quantification of high-density lipoproteins. *Lipids*. 1978;13(12):926-932. [CrossRef]
21. Blass KG, Thibert RJ, Lam LK. A study of the mechanism of the Jaffe reaction. *Clin Biochem*. 1974;12(7):336-343. [CrossRef]
22. Fawcett JK, Scott JE. A rapid and precise method for the determination of urea. *J Clin Pathol*. 1960;13(2):156-159. [CrossRef]
23. Drury RA. Wallington A and Cameroun SR. In: *Carlleton's Histological Techniques*. New York: Oxford University press; 1967:1-420.
24. Ayinla MT, Dada SO, Shittu ST, Olayaki LA, Akiode AO, Ojulari SL. Antihyperlipidemic effect of aqueous leaf extract of *Ocimum gratissimum* in alloxan- induced diabetic rats. *Int J Med Sci*. 2011;3: 360-363.
25. Soliman AM. Potential impact of Paracentrotus lividus extract on diabetic rat models induced by high fat/stretozotocin. *J Basic Sci Appl Res*. 2016;77:8-20.
26. Reuben Okoduwa S, Umar IA, James DB, Inuwa HM. Validation of the antidiabetic effects of *Vernonia amygdalina* delile leaf fractions in fortified diet-fed streptozotocin-treated rat model of type-2 Diabetes. *J Diabetol*. 2017;8(3):74-85. [CrossRef]
27. Ozkurk SA, Aytekin I, Ozsoy HO, Ozkurk AN, Yttmaz N. Effects of caffeic acid phenethyl ester on oxidative stress, histhopathology and some biochemical parameters in streptozotocin- induced diabetic rats. *Turk J Biochem*. 2015;40(2):149-156.
28. Kane JP, Pullinger CR, Goldfine ID, Malloy MJ. Dislipidemia and Diabetes: role of lipoprotein species and interrelated pathways in lipid metabolism in diabetes mellitus. *Curr Opin Pharmacol*. 2021;61: 21-27. [CrossRef]
29. Sharma SB, Gupta S, Ac R, Singh UR, Rajpoot R, Shukla SK. Antidiabetogenic action of Morus rubra L. leaf extract in streptozotocin-induced diabetic rats. *J Pharm Pharmacol* 2010; 62: 247-255.
30. Omran LMS, Alourfi Z, Barakat YA. The role of lipoprotein (a) and dislipidemia in diabetic retinopathy in a sample of Syrian Patients with type 2 diabetes mellitus. *Arab Board Med J*. 2022;23(1):28-34.
31. Nanna RS, Pamulaparthi A, Prathap V, Banala M. Experimental evaluation of antidiabetic activity and antihyperlipidemic evaluation of leaf extracts of *Senna alata* in alloxan induced diabetic rats. *Eur J Pharm Med Res*. 2015;2:227-237.
32. Farah RI, Al-Sabbagh MQ, Momani MS, et al. Diabetic kidney disease in patients with type 2 diabetes mellitus: a cross-sectional study. *BMC Nephrol*. 2021;22(1):223. [CrossRef]
33. Martha T, Zainab MA, Khaled KA, Lenia HS, Mushim A. Antidiabetic and hypolipidemic properties of garlic (*Allium sativum*) in streptozotocin-induced diabetic rats. *Int J Diabetes Metab*. 2007;15:108-115.
34. Eliakim-Ikechukwu CF, Obri AI. Histological changes in the pancreas following administration of ethanolic extract of *Alchornea cordifolia* leaf in alloxan-induced diabetic Wistar rats. *Nig J Phys Sci*. 2012;24(2):153-155. [CrossRef]