Originality Assessment

Powered by https://plagiarismcheckerx.com

12%

Overall Similarity

Date: May 3, 2024
Matches: 526 / 4333 words
Sources: 29

Remarks: Moderate similarity detected, consider enhancing the document if necessary.

Verify Report:
Scan this QR Code

Antidiabetic of Activity of Diospyros mespiliformis Stembark on Alloxan-induced Diabetic Rats

Abstract

The rate of morbidity and mortality attributed to diabetes has become a concern and challenge for individuals and governments. The availability, affordability, and efficacy of plant-based drugs make them an attractive choice for diabetic management therapy in low-income countries and rural communities. Thus, their application in folkloric medicine for diabetic managementtherapy. This study investigated the antidiabetic activity of the crude ethanol extract (CRE), ethyl acetate (EAF), and aqueous (AQF) fractions Diospyros mespiliformis (DM) stembark on alloxan-induced diabetic rats to justify its acclaimed applications in folkloric medicine. The effect of the plant extract and its fractions was evaluated following 21 days of administration of the extracts. The serum levels of on the aspartate aminotransferase, glutamyl aminotransferase, albumin, urea, creatinine, electrolytes, and lipid profile profiles of the rats was were determined by biochemical assayvia spectrophotometric methods. The result showed a significant ($p < 0.05$) decrease in fasting blood glucose for all the extracts. Furthermore,while the aspartate aminotransferase significantly ($p < 0.05$) decreased in the CRE and EAF only while, gamma-glutamyl transferase significantly ($p < 0.05$) decreased for all the treatment groups. Moreover, and albumin were was significantly ($p < 0.05$) decreased in the EAF only. The urea and creatinine levels of the CRE and AQF were decreased significantly ($p < 0.05$) while the creatinine was significantly ($p < 0.05$) decreased for the AQF only. Additionally, the K^+ , Cl^-, and HCO_3^- levels decreased significantly ($p < 0.05$) for the treatment groups. A Furthermore, a significant ($p < 0.05$) decrease in total cholesterol was observed for all the treatment groups whileand triglyceride level wassignificantly ($p < 0.05$) decreased for the EAF and AQF only. Moreover, the high-density lipoprotein cholesterol significantly

increased for the CRE group only observed for the EAF. Conclusively, DM exhibited significant hypoglycemic and hypolipidemic potential with improved lipid profile and hepato-renal function. Thus, the observed antidiabetic activity of the plant might justify its acclaimed utilization in the management of diabetes and its related ailment.

Keywords: Alloxan; Antidiabetic activity; Antihyperglycemic; Antihyperlipidemic; Diospyros mespiliformis; Electrolytes

Introduction

Diabetes is a metabolic ailment composed of a collection of metabolic disorders associated with persistent hyperglycemia accompanied by acute and chronic complications including nephropathy, retinopathy, and neuropathy.1 It has been regarded to be among the leading causes of morbidity and mortality, yet treatment remains a challenge.2 The recommended treatment option is proper diet and exercise though drugs are used in necessary situations.3 Worldwide, the ailment continues to be a concern to individuals and governments, creating financial and welfare burdens on the concerned entity.2 A 2021 global report showed diabetic prevalence to be up to 10% in adults between the ages of 20 to 72 years and the expected projection to be 12% by 2045 irrespective of gender.2 Moreover, the global expenditure on diabetes and related ailments was estimated to rise to 1,054 billion USD by 2045 from the reported 966 billion USD in 2021.2 Thus, the cost and affordability of antidiabetic drugs are also a consideration, especially for low-income countries and rural communities.

Diabetes as a multifactorial metabolic disorder creates more challenges in treatment, often leading to combined therapy and multiple doses of antidiabetic agents.4 The continued use of antidiabetic drugs is often rendered undesirable to individuals leading to prospects for other treatment options. Moreover, these drugs were reported to possess undesirable

adverse effects, including hypoglycemia, bloating, nausea, and anorexia.4 Furthermore, for rural communities, in addition to poverty, access to proper healthcare is a challenge, often relying on herbal formulations for therapeutic purposes.5 Thus, they often indulge in the use of plant-based drugs as an alternative to achieve therapeutic goals. Medicinal plants in different preparations and formulations of varying efficacy are used in folkloric medicine for the treatment of ailments including diabetes.5 The antidiabetic activity of these plants is attributed to their secondary metabolite contents including flavonoids and saponins.6-10 Moreover, the diverse and synergistic effects of plant-based drugs make them an attractive choice of therapy, considering diabetes as a collection of multiple metabolic disorders.11 Previous reports showed the use of plants including Diospyros mespiliformis in the management of diabetic pathology, including inflammation and oxidative stress.7-10, 12-18

Diospyros mespiliformis is a tree of African origin, often referred to as African ebony which harbors fruits consumed as food.19 In folkloric medicine, the plant parts are employed in the management of diabetes20 and its related conditions, including inflammation21 and oxidative stress.19 Thus, in our study, we justified the antidiabetic application of the plant in folkloric medicine by investigating the antidiabetic activity of its crude ethanol extractCRE, ethyl acetateEAF, and aqueous AQF fractions in alloxan-induced diabetic rats, considering the effects in the liver, kidney, and lipid profile of the diabetic rats.

Methods

Plant sample and preparation

The plants' stem bark sample was obtained from the Mayo-belwa Aarea of Adamawa State, Nigeria. It was, and authenticated in the Forest Technology Department of Adamawa State Polytechnic where a voucher specimen (Nno. ASP/FT/091) was deposited. The stembark was air-dried and powdered with a blender.

Experimental animals

Male albino rats were obtained from Hema Farms Nigeria Ltd., Yola, Adamawa State. The rats weighing 150 ±20 g were kept under normal dark/light circles and acclimatized for 7 days with free access to feed (Finisher pellet, Chikun Feed, Crown Flour Mill Ltd, Lagos) and water. The Norwegian National Committee for Research Ethics in Science and Technology (NENT) 2018 ethical guideline was strictly followed for all the experimental procedures.22

Extraction and fractionation

Exactly 1 kg of the sample was macerated for 7 days in 70% ethanol (v/v) and filtered, followed by drying with a rotary evaporator (Buchi Rotavapor R-200) under reduced pressure at 40 °C, yielding with a rotary evaporator (Buchi Rotavapor R-200) yielding 95 g of the crude ethanol extract (CRE). Exactly 50 g of the CRE was suspended to complete dissolution in 200 ml of distilled water and continuously partitioned in a separating funnel by the addition of ethyl acetate until the formation of a clear ethyl acetate layer, yielding the ethyl acetate fraction (EAF). The remaining aqueous layer was regarded as the aqueous fraction (AQF). Both the EEF and AQF were subjected to the same drying condition as the CRE to yield 10.60 g and 36.80 g of the EEF and AQF, respectively.

Induction of diabetes

Alloxan monohydrate (Oxford Lab Fine Chem LLP, India) prepared in normal saline was used to induce diabetes at 150 mg/kg body weight intraperitoneally to overnight fasted diabetic rats. Diabetes was confirmed in rats exhibiting fasting blood glucose (FBG) above 200 mg/dl and treatment was initiated immediately.23

Experimental design

The animals were randomly grouped into 6 groups and treatment was administered by

intragastric tube daily for 21 days. Group I (non-diabetic) and II (diabetic) received 5 ml/kg body weight distilled water. Group III (diabetic) received 150 mg/kg metformin while IV (CRE), V (EAF), and VI (AQF) were all diabetic and received 300 mg/kg body weight CRE, EAF, and AQF, respectively.

The standard drug metformin [(Diabetmin®) Hovid Pharmaceuticals Ltd, Nigeria] was employed as a positive control. The fasting blood glucose (FBG) was read at the beginning and end of the experiment by tail vein puncture using a glucometer (SD CodeFree™, SD Biosensor, Inc., Korea) whereas the body weight was measured weekly for 3 weeks. The rats were pre-anesthetized with chloroform before blood collection into lithium-heparin tubes by cardiac puncture and centrifuged for 20 minutes at 3000 rpm, separating serum from the cells.

Biochemical assay

The following biochemical parameters were determined by previously described methods as follows:

Aspartate aminotransferase (AST) as described by Reitmann.24

Gamma-glutamyl transferase (GGT) as described by Szasz.25

Albumin concentration as described by Grant.26

Urea concentration as described by Chaney and Marbach.27

Creatinine concentration as described by Bartels.28

The estimation of electrolytes was according to the kit's manufacturer's instructions.

Total Cholesterol (TC) as described by Stein.29

Triglyceride Concentration (TG) as described by McGowan.30

High-density Lipoprotein-Cholesterol (HDL-C) as described by Warnick and Albers.31

Low-density Lipoprotein Cholesterol (LDL-C) as described by Friedewald.32

Statistics

The data obtained was statistically evaluated with Statistical Package for Social Sciences

(SPSS) software version 22 and expressed as mean ± standard mean error (± SEM). One-way analysis of variance was employed to evaluate the difference among the groups and subsequently evaluated by Turkey's multiple comparison tests at $p < 0.05$ significant level.

Results and discussion

FBG and body weight

The effect of the CRE, EAF, and AQF on the FBG and body weight of the diabetic rats is presented in Figure 18. The diabetic groups demonstrated a significant ($p < 0.05$) rise in initial FBG than the naïve control. However, at the end of the experiment, the negative control exhibited significantly ($p < 0.05$) higher FBG than the treatment groups with no significant ($p > 0.05$) difference among the treatment groupsm. The AQF exhibited a significant ($p < 0.05$) increase in body weight than the EAF at weeks 1 and 2 while the naïve control was at week 3. However, the negative control demonstrated a significant ($p < 0.05$) decrease in body weight than all the groups at week 3. The administration of alloxan to the rats led to a rise in FBG that was persistent to the end of the experiment for the negative control. This was due to the necrotic action of alloxan on the β-cells, inhibiting insulin secretion and causing apoptosis to β-cells apoptosis via the generation of free radicals.23 The observed decreased hyperglycemia for the treatment groups might be attributed to the reversal of the alloxan-induced damage to the β-cells via the antioxidant activity of the extracts. The improvement in β-cell function might further be attributed t be responsible foro the improved body weight observed in the treated groups as opposed to the negative control with decreased body weight due to muscle wasting.33

Figure 1. Effects of DM on the; a) FBG and b) Body weights. Values with a and c superscripts are significantly ($p < 0.05$) higher than naïve and negative control, respectively

while values with b superscripts are significantly ($p < 0.05$) lower than negative control. Values with e superscripts are significantly ($p < 0.05$) higher than EAF

AST, GGT, and albumin

The effect of the CRE, EAF, and AQF on the levels of serum AST, GGT, and albumin is presented in Table 14. A significant ($p < 0.05$) rise in AST level was observed for the negative control (150.00 ± 2.88 IU/L) compared to the naïve control (116.40 ± 8.64 IU/L), CRE (102.80 ± 0.97 IU/L), and EAF (82.20 ± 4.92 IU/L). Furthermore, a significant ($p < 0.05$) decrease in the AST level was observed for the CRE and EAF compared to the AQF (144.00 ± 1.05 IU/L) and Metformin (135.60 ± 5.96 IU/L) with the latter significantly ($p < 0.05$) decreased than the naïve control. The GGT level of the negative control (12.00 ± 0.28 IU/L) was significantly ($p < 0.05$) increased compared to the other groups.

Table 1. Effects of CRE, EAF, and AQF of DM on the serum levels of AST, GGT, and albumin

Groups

AST (IU/L)

GGT (IU/L)

Albumin (g/L)

Naïve control

116.40 ± 8.64d

8.32 ± 0.42b

25.40 ± 0.93b

Negative control

150.00 ± 2.88a

12.00 ± 0.28

31.00 ± 1.05

Metformin

135.60 ± 5.96a

9.08 ± 0.40b

26.40 ± 0.98b

CRE

102.80 ± 0.97bcd

7.80 ± 0.70b

33.20 ± 0.37ad

EAF

82.20 ± 4.92bc

7.00 ± 0.55bc

25.00 ± 1.30b

AQF

144.00 ± 1.05ade

6.6 ± 0.68bc

28.20 ± 0.37d

Values are expressed as mean ± SEM: n = 5

Values in the same column with b and c superscripts were significantly ($p < 0.05$) lower than the negative control and Metformin group, respectively while those with a, d, and e were higher than naïve control, EAF, and CRE groups, respectively.

Moreover, the GGT levels of EAF (7.00 ± 0.55 IU/L) and AQF (6.6 ± 0.68 IU/L) were significantly ($p < 0.05$) decreased compared to the Metformin (9.08 ± 0.40 IU/L). Additionally, the albumin level of the negative control (31.00 ± 1.05 IU/L) was significantly ($p < 0.05$) increased than the naïve control (25.40 ± 0.93 IU/L), Metformin (26.40 ± 0.98 IU/L), and EAF (25.00 ± 1.30 IU/L). The albumin level of the EAF was significantly ($p < 0.05$) decreased compared to the CRE (33.20 ± 0.37 IU/L) and AQF (28.20 ± 0.37 IU/L). The observed increased levels of AST, GGT, and albumin are indicators of liver injury or

dysfunction34 observed in the negative control which might be attributed to the hyperglycemia.35 Thus, the decreased level observed for the treatment groups might be due to improved 27 β-cell function and glycemic control.

Urea, creatinine, electrolytes

Table 25 reveals the effect of the CRE, EAF, and AQF on the serum urea, and creatinine, and electrolyte levels. A significantly ($p < 0.05$) higher urea level (14.66 ± 1.29 mM/L) was demonstrated by the EAF compared to the other groups. The urea level of the naïve control (6.94 ± 0.09 mM/L) and CRE (6.72 ± 0.45 mM/L) was significantly ($p < 0.05$) decreased compared to the negative control (9.70 ± 0.19 mM/L). The naïve control (50.00 ± 2.39 µM/L), Metformin (58.60 ± 3.42 µM/L), and AQF (71.40 ± 1.17 µM/L) exhibited a significant ($p < 0.05$) decrease in creatinine levels than the negative control (94.60 ± 10.22 µM/L). Additionally, the creatinine level of the EAF (99.60 ± 2.36 µM/L) exhibited a significant ($p < 0.05$) increase compared to Metformin. The Na+ level of all the groups wasn't significantly ($p > 0.05$) different. However, a significant ($p < 0.05$) increase decrease in K+ level was exhibited by the treatment groups compared to the naïve (9.54 ± 0.58 mEq/L) and negative (8.68 ± 0.27 mEq/L) control. Furthermore, all the diabetic groups showed a significant ($p < 0.05$) decrease in Cl- levels compared to the naïve control (102.8 ± 1.83 mM/L). The negative control (17.20 ± 0.49 mM/L) showed a significant ($p < 0.05$) rise increase in HCO3- level than the other groups with all the extract treatments showing a significant ($p < 0.05$) decrease compared to the naïve control (28.60 ± 0.25 mM/L).

Table 2. Effects of CRE, EAF, and AQF of DM on the serum levels of urea, creatinine, and electrolytes

Groups

Urea (mM/L)

Creatinine (µM/L)

Na+ (mEq/L)

K+ (mEq/L)

Cl- (mM/L)

HCO3- (mM/L)

Naïve control

6.94 ± 0.09

50.00 ± 2.39

141.40 ± 1.08

9.54 ± 0.58

102.8 ± 1.83

28.60 ± 0.25

Negative control

9.70 ± 0.19a

94.60 ± 10.22a

142.00 ± 0.55

8.68 ± 0.27

96.80 ± 0.80f

17.20 ± 0.49f

Metformin

7.82 ± 0.44

58.60 ± 3.42e

141.60 ± 0.40

6.44 ± 0.14df

98.00 ± 0.45f

25.20 ± 1.69b

CRE

6.72 ± 0.45de

91.2 ± 4.13ac

141.20 ± 1.66

6.04 ± 0.33df

95.60 ± 1.21f

21.80 ± 0.37bf

EAF

14.66 ± 1.29abc

99.60 ± 2.36ac

140.40 ± 0.93

7.24 ± 0.13df

97.00 ± 0.89f

22.20 ± 0.20bf

AQF

8.10 ± 0.07e

71.40 ± 1.17ef

141.00 ± 0.71

7.06 ± 0.19df

97.40 ± 0.40f

24.40 ± 0.75bf

Values [22] are expressed as mean ± SEM: n = 5

Values in the same column with a, b, and c superscripts were significantly ($p < 0.05$) higher than naïve control, negative control groups, and Metformin, respectively while those with d, e, and f superscripts were significantly ($p < 0.05$) lower than negative control, EAF, and naïve control groups, respectively.

Kidney dysfunction can be marked by increased urea and creatinine levels, and metabolic waste filtered from blood by the kidney.36 In our study, a significant decrease in the urea

level might indicate an improved renal function for the CRE and Metformin groups with a decreased creatinine level for the AQF. In diabetes, increased plasma osmolarity and impaired renal function associated with hyperglycemia create electrolyte imbalance.37 All the treatment groups presented hypokalemia which might be induced by the treatments.38 Furthermore, the diabetic groups exhibited hypochloremia which might be due to ketoacidosis-induced alkalosis.39 Moreover, all the treatment groups presented improved decreased bicarbonate due to ketoacidosis39 observed in the negative control group.

TC, TG, HDL-C, and LDL-C

Table 36 reveals the effects of the CRE, EAF, and AQF on the serum TC, TG, HDL-C, and LDL-C levels. A significantly ($p < 0.05$) higher TC level was exhibited by the negative control (85.02 ± 3.78 mg/dl) than the other groups without a significant ($p > 0.05$) difference among the treatment groups. Moreover, the TG level of the negative control (275.90 ± 6.29 mg/dl) was significantly ($p < 0.05$) increased compared to the other groups except for the CRE (201.14 ± 31.14 mg/dl) with a significant ($p < 0.05$) rise than EAF (110.36 ± 7.23 mg/dl) and AQF (90.78 ± 17.21 mg/dl). The CRE and Metformin (28.08 ± 4.34 mg/dl) exhibited a significantly ($p < 0.05$) decreased HDL-C level than the naïve (101.4 ± 7.99 mg/dl) and negative (99.06 ± 7.04 mg/dl) control (99.06 ± 7.04 mg/dl) while the EAF (94.38 ± 6.09 mg/dl) and AQF (82.68 ± 2.887 mg/dl) were higher than Metformin only. The LDL-C level of Metformin (28.08 ± 4.34 mg/dl) was significantly ($p < 0.05$) decreased compared to the naïve control (64.74 ± 13.93 mg/dl), (53.04 ± 6.36 mg/dl), and EAF (63.96 ± 10.58 mg/dl).

Table 3. Effects of CRE, EAF, and AQF of DM on the serum levels of TC, TG, HDL-C, and LDL-C

Groups

TC (mg/dl)

TG (mg/dl)

HDL-C (mg/dl)

LDL-C (mg/dl)

Naïve control

52.26 ± 2.65b

131.72 ± 15.26b

101.4 ± 7.99c

64.74 ± 13.93c

Negative control

85.02 ± 3.78

275.90 ± 6.29

99.06 ± 7.04

49.92 ± 2.87

Metformin

52.26 ± 3.40b

131.72 ± 10.30bd

41.34 ± 5.02b

28.08 ± 4.34

CRE

60.06 ± 3.65b

201.14 ± 31.14

67.08 ± 5.43bf

49.14 ± 4.71

EAF

49.92 ± 4.51b

110.36 ± 7.23bd

94.38 ± 6.09ce

63.96 ± 10.58c

AQF

47.58 ± 0.78b

90.78 ± 17.21bd

82.68 ± 2.887c

53.04 ± 6.36c

Values [22] are expressed as mean ± SEM: n = 5

Values in the same column with a, c, and e superscripts were significantly ($p < 0.05$) higher than naïve control, Metformin, and CRE groups, respectively while those with b, d, and f were significantly ($p < 0.05$) lower than negative control, CRE, and naïve control groups, respectively.

The loss of glycemic control in diabetes can lead to dyslipidemia with a rise in TC, TG, LDL-C, and decreased HDL-C levels, however, the LDL-C might remain unchanged.40 An increased TC and TG level might indicate dyslipidemia., However, all the treatment groups demonstrated improved levels, thus improved renal functions. In the present study, the antidiabetic potential of DM was explored in vivo, revealing its effect on glucose level, hepato-renal function, and lipid profile. However, the specific compounds exhibiting the reported effects were not identified. Thus, further studies profiling the compounds present in DM and their specific antidiabetic mechanism of action are warranted.

Conclusion

DM exhibited significant hypoglycemic and hypolipidemic potential with improved lipid

profile and hepato-renal function. Thus, the observed antidiabetic activity of the plant might justify its acclaimed utilization in the treatment/management of diabetes and its related ailment.

Acknowledgment

The authors acknowledge the immense contribution of the Tertiary Education Fund of Nigeria for sponsoring this research through the Institution-Based Research Fund. Special gratitude also goes to the Pharmaceutical Technology Department of Adamawa State Polytechnic Yola for institutional support.

Conflict of interest

All authors declare that there is no potential conflict of interest with the research, authorship, and/or an article publication.

Reference

1. American Diabetes Association Professional Practice Committee. 2022. 2 Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2022. Diabetes Care. 45(Supplement_1):S17-S38.

2. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al., 2022. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 183:109119.

3. American Diabetes Association. 2020. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2020. Diabetes Care. 43(Supplement_1):S98-S110.

4. Dahiru MM, Nadro SM. 2022. A review of the Mechanisms of Action and Side Effects of

Anti-diabetic Agents. Trends in Pharmaceutical Sciences. 8(3):195-210.

5. Sani S, Aliyu B, Haruna M, Yahya SM, Yakasai MA, Hayatu LW, et al., 2019. Local plants and diabetes management; folkloric practices in Metropolitan Kano, Nigeria. Bayero Journal of Pure and Applied Sciences. 12(1):268-273.

6. Dahiru MM. 2023. Recent advances in the therapeutic potential phytochemicals in managing diabetes. Journal of Clinical and Basic Research. 7(1):13-20.

7. Dahiru MM, Alfa MB, Abubakar MA, Abdulllahi AP. 2024. Assessment of in silico antioxidant, anti-inflammatory, and antidiabetic activites of Ximenia americana L. Olacaceae. Advances in Medical, Pharmaceutical and Dental Research. 4(1):1-13.

8. Dahiru MM, Musa N. 2024. Phytochemical Profiling, Antioxidant, Antidiabetic, and ADMET Study of Diospyros mespiliformis Leaf, Hochst Ex A. Dc Ebenaceae. J Fac Pharm Ankara/Ankara Ecz Fak Derg. 48(2):3-3.

9. Dahiru MM, Musa N, Abaka AM, Abubakar MA. 2023. Potential Antidiabetic Compounds from Anogeissus leiocarpus: Molecular Docking, Molecular Dynamic Simulation, and ADMET Studies. Borneo Journal of Pharmacy. 6(3):249-277.

10. Dahiru MM, Nadro MS. 2022. Anti-diabetic potential of Hyphaene thebaica fruit in streptozotocin-induced diabetic rats. Journal of Experimental and Molecular Biology. 23(1):29-36.

11. Gurumallu SC, AlRamadneh TN, Sarjan HN, Bhaskar A, Pereira CMF, Javaraiah R. 2022. Synergistic hypoglycemic and hypolipidemic effects of ω-3 and ω-6 fatty acids from Indian flax and sesame seed oils in streptozotocin-induced diabetic rats. Phytomedicine Plus. 2(3):100284.

12. Bindu J, Narendhirakannan RT. 2018. Role of medicinal plants in the management of diabetes mellitus: a review. 3 Biotech. 9(1):4.

13. Deyno S, Eneyew K, Seyfe S, Wondim E. 2021. Efficacy, safety and phytochemistry of medicinal plants used for the management of diabetes mellitus in Ethiopia: a systematic review. Clinical Phytoscience. 7(1):16.

14. Mohammed A, Tajuddeen N. 2022. Antidiabetic compounds from medicinal plants

traditionally used for the treatment of diabetes in Africa: A review update (2015–2020). S Afr J Bot. 146:585-602.

15. Dahiru MM, Ahmadi H, Faruk MU, Aminu H, Hamman AGC. 2023. Phytochemical Analysis and Antioxidant Potential of Ethylacetate Extract of Tamarindus Indica (Tamarind) Leaves by Frap Assay. Journal of Fundamental and Applied Pharmaceutical Science. 3(2):45-53.

16. Dahiru MM, Nadro MS. 2022. Phytochemical Composition and Antioxidant Potential of Hyphaene thebaica Fruit. Borneo Journal of Pharmacy. 5(4):325-333.

17. Dahiru MM, Nadro SM. 2022. Hypolipidemic Potential of Ethyl acetate Extract of Hyphaene thebaica Fruit in Streptozotocin-induced Diabetic Rats. Majalah Obat Tradisional. 27(2):159-164.

18. Dahiru MM, Umar AS, Muhammad M, Fari II, Musa ZY. 2024. Phytoconstituents, Fourier-Transform Infrared Characterization, and Antioxidant Potential of Ethyl Acetate Extract of Corchorus olitorius (Malvaceae). Sciences of Phytochemistry. 3(1):1-10.

19. Aminu SA, Ibrahim Y, Ismail HA, Ibrahim IO. 2021. Medicinal and Traditional Utilization of African Ebony (Diospyros mespiliformi): A Review. Int J Curr Microbiol App Sci. 10(06):811-817.

20. Negbenebor H, Shehu K, Mukhtar Mairami F, Adeiza Z, Salisu N, Fagwalawa L. 2017. Ethnobotanical Survey of Medicinal Plants Used by Hausa People in the Management of Diabetes Mellitus in Kano Metropolis, Northern Nigeria. European Journal of Medicinal Plants. 18:1-10.

21. Abba A, Dogara AM. 2021. Ethnomedicinal survey of plants used for management of inflammatory diseases in Ringim local government, Jigawa state, Nigeria. Ethnobotany Research and Applications. 22:1-27.

22. Norwegian National Research Ethics Committees. Ethical Guidelines for the Use of Animals in Research. Oslo, Norway: The Norwegian National Committee for Research Ethics in Science and Technology; 2018. Available from: https://www.forskningsetikk.no/en/guidelines/science-and-technology/ethical-guidelines-for-

the-use-of-animals-in-research/.

23. Ighodaro OM, Adeosun AM, Akinloye OA. 2017. Alloxan-induced diabetes, a common model for evaluating the glycemic-control potential of therapeutic compounds and plants extracts in experimental studies. Medicina. 53(6):365-374.

24. Reitmann S. 1957. Colorimetric method for the determination of serum glutamic pyruvate and glutamic oxaaloacetate transaminase. Amer J Clin Path. 28:56.

25. Szasz G. 1969. A kinetic photometric method for serum γ-glutamyl transpeptidase. Clin Chem. 15(2):124-136.

26. Grant GH. 1987. Amino acids and proteins (Fundamentals of clinical chemistry). 3th edition ed. Philadelphia, USA: WB Saunders Company. 104-134 p.

27. Chaney AL, Marbach EP. 1962. Modified reagents for determination of urea and ammonia. Clin Chem. 8(2):130-132.

28. Bartels H, Böhmer M, Heierli C. 1972. Serum creatinine determination without protein precipitation. Clinica chimica acta; international journal of clinical chemistry. 37:193-197.

29. Stein EA. 1987. Lipids, lipoproteins and apolipoproteins. 3rd Edn. ed. Philadelphia, USA: W.B Sauders 809-861 p.

30. McGowan MW, Artiss JD, Strandbergh DR, Zak B. 1983. A peroxidase-coupled method for the colorimetric determination of serum triglycerides. Clin Chem. 29(3):538-542.

31. Warnick GR, Albers J. 1978. A comprehensive evaluation of the heparin–manganese precipitation procedure for estimating high density lipoprotein cholesterol. J Lipid Res. 19(1):65-76.

32. Friedewald WT, Levy RI, Fredrickson DS. 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 18(6):499-502.

33. Perry BD, Caldow MK, Brennan-Speranza TC, Sbaraglia M, Jerums G, Garnham A, et al., 2016. Muscle atrophy in patients with Type 2 Diabetes Mellitus: roles of inflammatory pathways, physical activity and exercise. Exerc Immunol Rev. 22:94.

34. De Silva NMG, Borges MC, Hingorani AD, Engmann J, Shah T, Zhang X, et al., 2019. Liver function and risk of type 2 diabetes: bidirectional Mendelian randomization study. Diabetes. 68(8):1681-1691.

35. Wan J-Y, Yang L-Z. 2022. Liver enzymes are associated with hyperglycemia in diabetes: A three-year retrospective study. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy.545-555.

36. Higgins C. 2016. Urea and the clinical value of measuring blood urea concentration. Acutecaretesting Org.1-6.

37. Eshetu B, Worede A, Fentie A, Chane E, Fetene G, Wondifraw H, et al., 2023. Assessment of Electrolyte Imbalance and Associated Factors Among Adult Diabetic Patients Attending the University of Gondar Comprehensive Specialized Hospital, Ethiopia: A Comparative Cross-Sectional Study. Diabetes Metab Syndr Obes.1207-1220.

38. Veltri K, Mason C. 2015. Medication-Induced Hypokalemia. P & T : a peer-reviewed journal for formulary management. 40:185-190.

39. Yasuda K, Hayashi M, Murayama M, Yamakita N. 2016. Acidosis-Induced Hypochloremic Alkalosis in Diabetic Ketoacidosis Confirmed by The Modified Base Excess Method. The Journal of Clinical Endocrinology & Metabolism. 101(6):2390-2395.

40. Bhowmik B, Siddiquee T, Mujumder A, Afsana F, Ahmed T, Mdala IA, et al., 2018. Serum lipid profile and its association with diabetes and prediabetes in a rural Bangladeshi population. International journal of environmental research and public health. 15(9):1944.

Original Research Article Template

Journal of Fundamental and Applied Pharmaceutical Science

Sources

1	https://scholar.google.com/citations?user=Xndfd3sAAAAJ INTERNET 2%
2	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10372355/ INTERNET 1%
3	https://www.mdpi.com/1648-9144/53/6/365 INTERNET 1%
4	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9288615/ INTERNET 1%
5	https://www.sciencedirect.com/science/article/pii/S2667031322000677 INTERNET 1%
6	https://www.nejm.org/doi/full/10.1056/NEJMra1503102 INTERNET <1%
7	https://doaj.org/article/fade1343b8b44156b4d24777d6037ea6 INTERNET <1%
8	https://www.researchgate.net/publication/314484871_Ethnobotanical_Survey_of_Medicinal_Plants_Used_by_Hausa_People_in_the_Management_of_Diabetes_Mellitus_in_Kano_Metropolis_Northern_Nigeria INTERNET <1%
9	https://link.springer.com/article/10.1007/s00580-008-0782-7 INTERNET <1%
10	https://apc.aast.edu/ojs/index.php/AMPDR/article/view/AMPDR.2024.04.1.735 INTERNET <1%
11	https://www.researchgate.net/publication/356942672_Antidiabetic_compounds_from_medicinal_plants_traditionally_used_for_the_treatment_of_diabetes_in_Africa_A_review_update_2015-2020 INTERNET <1%
12	https://www.acc.org/latest-in-cardiology/articles/2019/04/02/13/21/understanding-strengths-and-limitations-of-different-methods-of-ldl-c-estimation INTERNET <1%
13	https://pubmed.ncbi.nlm.nih.gov/31088856/ INTERNET <1%

14	https://www.researchgate.net/publication/357057679_Ethnomedicinal_Survey_of_Plants_used_for_Management_of_Inflammatory_Diseases_in_Ringim_Local_Government_Jigawa_State_Nigeria INTERNET	<1%
15	https://www.forskningsetikk.no/en/guidelines/science-and-technology/guidelines-for-research-ethics-in-science-and-technology/ INTERNET	<1%
16	https://www.researchgate.net/publication/293797077_Muscle_atrophy_in_patients_with_Type_2_Diabetes_Mellitus_Roles_of_inflammatory_pathways_physical_activity_and_exercise INTERNET	<1%
17	https://www.researchgate.net/publication/379084389_Assessment_Of_In_Silico_Antioxidant_Anti-Inflammatory_And_Antidiabetic_Activites_Of_Ximenia_Americana_L_Olacaceae INTERNET	<1%
18	https://dergipark.org.tr/en/pub/jfpanu/issue/83110/1354293 INTERNET	<1%
19	https://www.sciencedirect.com/science/article/pii/S0022227520415779 INTERNET	<1%
20	https://pubmed.ncbi.nlm.nih.gov/27050945/ INTERNET	<1%
21	https://pubmed.ncbi.nlm.nih.gov/30555770/ INTERNET	<1%
22	https://www.nature.com/articles/s41467-024-46829-0 INTERNET	<1%
23	https://www.scirp.org/reference/referencespapers?referenceid=169546 INTERNET	<1%
24	https://ijcmas.com/abstractview.php?ID=22283 INTERNET	<1%
25	https://pubmed.ncbi.nlm.nih.gov/13458125/ INTERNET	<1%
26	https://www.semanticscholar.org/paper/Diabetes,-Metabolic-Syndrome-and-Obesity:-Targets-Durán-Salto/04e0f7117d7aaf5a3b3628602284a4734a159bd2 INTERNET	<1%
27	https://www.sciencedirect.com/science/article/pii/S2090123223003120 INTERNET	<1%

28	https://embassy.science/wiki/Resource:B10af9a6-1eef-4aa9-afec-e4e19d36e897 INTERNET <1%
29	https://www.academia.edu/93495456/Medication_induced_hypokalemia INTERNET <1%

EXCLUDE CUSTOM MATCHES	OFF
EXCLUDE QUOTES	OFF
EXCLUDE BIBLIOGRAPHY	ON