Research Article

Comparative free radical scavenging and hypoglycemic activities of n-hexane, ethyl-acetate, and aqueous fractions of *Azanza garckeana* pulp

Abubakar A. Yusuf[1], Toheeb D. Yissa[2], Abdulhakeem R. Agboola[3], Sodiq M. Balogun[4], Peter O. Adeboye[5], Opeyemi N. Hassan[6], Iliyasu S. Raji[1]

[1]Department of Biochemistry, IBB University Lapai, Lapai, Niger State, Nigeria
[2]Department of Biochemistry, College of Medicine, University of Lagos, Lagos State, Nigeria.
[3]Department of Biochemistry, University of Calabar, Calabar Cross River State Nigeria
[4]Department of Biochemistry, Federal University of Technology Minna, Nigeria
[5]Department of Biochemistry, University of Ilorin, Ilorin, Nigeria
[6]Centre International Universitaire Des Meilleurs (C.I.U.M), Bestower International University Seme-Podji-Republique Du Benin.

Corresponding author* Abubakar A. Yusuf**;** awwaluinyass@gmail.com
Received: 05 June 2021, Revised: 12 August 2021, Published: 18 August 2021

Abstract

Background: The prevalence of diabetes mellitus is increasing on a global trend. The aim of the present study is to identify the most effective antioxidants and hypoglycemic fraction of *Azanza garckeana*. **Methods:** The fractions (n-hexane or ethyl-acetate or aqueous) of *A. garckeana* were administered to the alloxan-induced diabetic rats at doses of 100, 200, and 400 mg/kg for 15 days. Antioxidants activities were evaluated at concentrations of 62.5, 125, 250, and 500 µg/mL using the DPPH scavenging assay. **Results:** Results revealed that both the hexane, ethyl-acetate, and aqueous fractions exhibited hypoglycemic and antioxidants activities in a dose-dependent manner. The n-hexane fraction demonstrated highest percentage DPPH scavenging effect of 26.34±3.43, 38.44±4.35, 59.34±3.45, and 74.83±5.35 at 62.5, 125, 250, and 500 µg/mL respectively. The ethyl-acetate fraction demonstrated 19.33±2.98, 28.94±3.24, 47.34±2.90, and 57.82±4.54 respectively while the aqueous fraction exhibited the least activities of 12.45±23.45, 18.64±2.94, 27.94±3.89, and 39.43±3.89 at concentrations of 62.5, 125, 250, and 500 µg/mL respectively. In addition, the n-hexane fraction demonstrated the most significant hypoglycemic effect with the highest glucose reduction of 58.97 ±3.45 %, 63.86±5.35 %, and 66.51±4.35 %, ethyl acetate fraction demonstrated glucose reduction of 7.55±0.54%, 21.77±2.35 %, and 29.56±3.46 % while the aqueous fraction demonstrated the least hypoglycemic effect of 9.89±2.67 %, 18.09±3.45 %, and 18.87±3.24 at 100, 200 and 400 mg/kg bw respectively. **Conclusion:** The n-hexane fraction of *Azanza garckeana* extract could serve as a reservoir of bioactive agents that could be useful for the development of a new anti-diabetic agent

Keyword: *Azanza garckeana, hypoglycemic; antioxidative; free radical scavenging;*

Citations: Yusuf, A.A., Yissa, T.D., Agboola, A.R., Balogun, M.S., Adeboye, P.O., Hassan O.N. and Raji, I.S. (2021). Comparative free radical scavenging and hypoglycemic activities of n-hexane, ethyl-acetate, and aqueous fractions of *Azanza garckeana* pulp. AROC in Natural Products Research, 1(2);1-8, https://doi.org/10.53858/arocnpr01020108

1.0 Introduction

With more than 300 million cases, diabetes mellitus is a global burden. It is highly associated with impaired health-related poor life quality with a substantial socioeconomic burden [1,2]. The toxicity, in availability, in accessibility of synthetic hypoglycemic and antioxidants drugs is a serious medical concern [3].

The undesirable effect associated with this conventional drugs has led to the low quality of life and poor prognosis of patients [4]. Considering the probable adverse effects of these drugs, as well as their limited ability to provide long-term remission, there is therefore a need for the development of novel therapeutic agents, capable of providing more efficacious activities and less side effect compare to the conventional therapy [5].

The recent growth in knowledge of free radicals and reactive oxygen species (ROS) in biological systems is producing a medical revolution that promises a new age of health [6]. The implicative role of free radicals in many pathological conditions such as liver disease, diabetes, coronary heart diseases, carcinogenesis, drug toxicity and neurodegenerative disorders like Alzheimer and Parkinson diseases has been well established [7]. Redox reaction in body system sometimes leads to the generation of free radicals which initiate chain reactions that causes cellular

damage. However, antioxidants cease the reaction chain by removing the intermediates radicals and prevent further oxidation reaction [8].

with over 70 % of the world's population primarily on medicinal plants for their medical needs, medicinal plants still remain the most preferred primary health care system in many communities around the world [9-13]. This is due to it accessibility, affordability, efficacy, safety and low cost as opposed to most conventional therapies. Studies have confirmed the benefits of medicinal plants with hypoglycemic properties in the management of diabetes mellitus [14]. The effects of these plants may delay the development of diabetic complications and attenuate the diabetic induced metabolic abnormalities [15].

The *Azanza garckeana* (Goron Tula.) is an important medicinal plant commonly found in African countries including Nigeria, Botswana, Kenya, Malawi, South Africa, Mozambique, Sudan and some other part of Africa [16,17]. A numbers of phytochemicals including alkaloids, phenols, flavonoids, glucosides, a tannins and saponins have been identified from *A. garckeana* [17,18]. Traditionally, the plant has been reportedly used for the treatment of various diseases including convulsion, gastrointestinal disorders, malaria and anaemia [19,20]. The plant has also been reported for various pharmacological activities including anti-oxidants, antimicrobial, anti-inflammatory, analgesic, anti-arthritic and wound healing effect among others [16,17]. However, little attention has been placed on the antioxidants and antidiabetic potential of the plant.

2.0 Materials and Methods

2.1 Collection and identification of plant material

The pulp of *A. garckeana* were collected from a Local Government area, of Gombe State, Nigeria. The plant was authenticated at the Biological Science Department of Ibrahim Badamasi Babangida University Lapai, Niger State, Nigeria

2.2 Experimental animals

Apparently healthy Swiss albino male rats (126.98±6.90 g) were obtained from Department of Biochemistry, Federal University of Technology, Minna, Nigeria. They were housed under standard environmental conditions of temperature and relative humidity, 12 hrs day light/night cycle) with access to commercial feed pellets and water ad *libitum*. Animals were kept in compliance with internationally accepted principles for human handling and use of laboratory animals in the Canadian council on Animal Care Guidelines and Protocol Review.

2.3 Plant preparation, extraction, and fractionation

Extraction and fractionation of the *A. garckeana* pulp were carried out according to the method reported in our previous study [17], Briefly, the plant materials were air dried, pulverized. The crude extract was obtained through soxhlet extraction with methanol. The crude extract was concentrated using a rotary evaporator. The resulting extract was sequentially fractionated with n-hexane, ethyl acetate and distilled water to obtained n-hexane, ethyl-acetate and aqueous fractions respectively.

2.4 DPPH (2,2-Diphenyl-1-Picrylhydrazyl) radical Scavenging Assay

The antioxidant activity of the plant extracts was estimated using the DPPH radical scavenging assay as described by Oyaizu [21]. Briefly, different concentrations of extracts (62.5, 125, 250 and 500 µg/mL) were prepared from stock solutions (1000 µg/mL), prepared by weighing and dissolving 0.01g of the extracts and ascorbic acid, respectively in 10 mL of methanol. Thereafter, 2 mL of 0.004% DPPH in methanol added to 1 mL of various concentrations of plant extracts and ascorbic acid, respectively. The reaction mixtures were incubated at 25°C for 30 minutes. The absorbance of each test mixture was read against blank at 517 nm using double beam Shimadzu UV-1800 series spectrophotometer. The experiment was performed in triplicates. The percentage antioxidant activity was calculated using the formula below:

$$\% \text{ Inhibition} = \frac{\text{Ablank} - \text{Asample}}{\text{Ablank}} X100$$

2.5 Evaluation of antidiabetic effects of the extracts

Alloxan was dissolved in normal saline and injected intraperitoneally in overnight fasted

Wistar albino rats of body weight 110 ± 12 g at the dose of 120 mg/kg body weight [22]. The animals were distributed into 3 groups for each of the fractions and orally administered with doses of 100, 200 and 400 mg/kg body weight, respectively. Glibenclimide was used as standard antidiabetic drug at a dose of 5 mg/kg body weight. The animals were treated for a period of 15 days and the fasting blood glucose (FBG) was recorded on 3-day intervals for that period of time.

2.6 Determination of Fasting Blood Sugar

The samples of blood were collected from the tail of the rat at an interval of 2 days. Blood glucose level was estimated using an Achu-check glucometer with its commercial test strips based on the glucose oxidase method.

2.7 Data analysis.

All analysis was conducted in triplicate and analyzed using statistical package for social science (SPSS) version 16 and presented as means ± standard error of the mean. One-way analysis of variance (ANOVA) at $p < 0.05$ were used for comparing the significant differences between treatment groups.

3.0 Results

3.1 Antioxidant activities of n--hexane, ethyl acetate and aqueous fractions of *Azanza garckeana*

The n-hexane, ethyl acetate and aqueous fractions of *A. garckeana* demonstrated dose dependent DPPH radical scavenging activities with percentage scavenging effect in the range of between 12.45±23.45 and 74.83±5.35 %. The n-hexane fraction demonstrated highest percentage DPPH scavenging effect of 26.34±3.43, 38.44±4.35, 59.34±3.45, and 74.83±5.35 at concentrations of 62.5, 125, 250 and 500 µg/mL respectively. The ethyl-acetate fraction demonstrated DPPH scavenging effect of 19.33±2.98, 28.94±3.24, 47.34±2.90, and 57.82±4.54 respectively while the aqueous fraction demonstrated the least DPPH scavenging effect of 12.45±23.45, 18.64±2.94, 27.94±3.89, and 39.43±3.89 at concentrations of 62.5, 125, 250 and 500 µg/mL respectively (Table 1).

3.2 Hypoglycemic activities of n-hexane, ethyl acetate and aqueous fractions of *Azanza garckeana*

The hypoglycemic effect of n-hexane, ethyl acetate and aqueous fractions of *A. garckeana* in alloxan induced diabetic rats is shown in figures 1-3 respectively. Interestingly both n-hexane (figure 1), ethyl acetate (figure 2), and aqueous (figure 3) fractions of *A. garckeana* demonstrated significant ($p<0.05$) hypoglycemic effect in alloxan induced diabetic rats. The n-hexane fractions demonstrated the most significant hypoglycemic effect when compared with the hypoglycemic effect demonstrated by the ethyl acetate and aqueous fractions of *A. garckeana.*

The n-hexane fraction demonstrated dose dependent hypoglycemic effect with percentage glucose reduction of 58.97 ±3.45 %, 63.86±5.35 %, and 66.51±4.35 % at 100, 200 and 400 mg/kg bw respectively. The ethyl acetate fraction also demonstrated dose dependent hypoglycemic effect with percentage glucose reduction of 7.55±0.54%, 21.77±2.35 %, and 29.56±3.46 % at 100, 200 and 400 mg/kg bw respectively, while the aqueous extract exhibited hypoglycemic effect of 9.89±2.67 %, 18.09±3.45 %, and 18.87±3.24 at 100, 200 and 400 mg/kg bw respectively (Table 2)

Table 1: DPPH radical scavenging activities of n-hexane, ethyl acetate and aqueous fractions of *Azanza garckeana*

	Conc. (µg/mL)			
Sample	500	250	125	62.5
n-hexane fraction	74.83±5.35 ^{d}	59.34±3.45 ^{c}	38.44±4.35 ^{b}	26.34±3.43^{a}
Ethyl acetate fraction	57.82±4.54 ^{d}	47.34±2.90 ^{c}	28.94±3.24 ^{b}	19.33±2.98 ^{a}
Aqueous fraction	39.43±3.89 ^{d}	27.94±3.89 ^{c}	18.64±2.94 ^{b}	12.45±23.45 ^{a}

Values are Mean ±SEM of triplicate determinations. Data followed by different superscript alphab*et al*ong the row were significantly different ($p<0.05$).

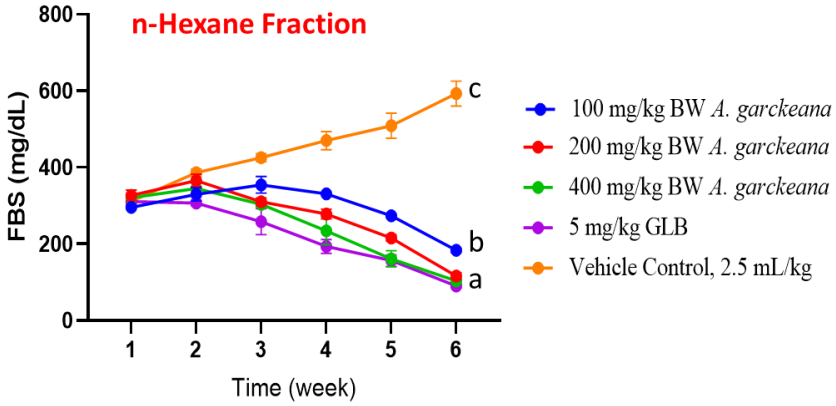

Figure 1: Hypoglycemic effect of n-hexane fraction of *Azanza garckeana* in alloxan induced diabetic rats**.** Each bars represents MEAN±SEM of triplicate determinations. Bars with different superscript alphabets were significantly different ($p<0.05$)

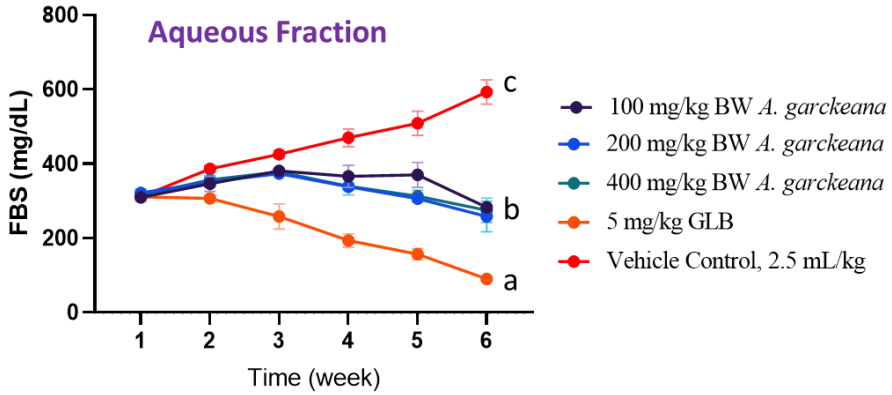

Figure 2: Hypoglycemic effect of aqueous fraction of *Azanza garckeana* in alloxan induced diabetic rats. Each bars represents MEAN±SEM of triplicate determinations. Bars with different superscript alphabets were significantly different ($p<0.05$)

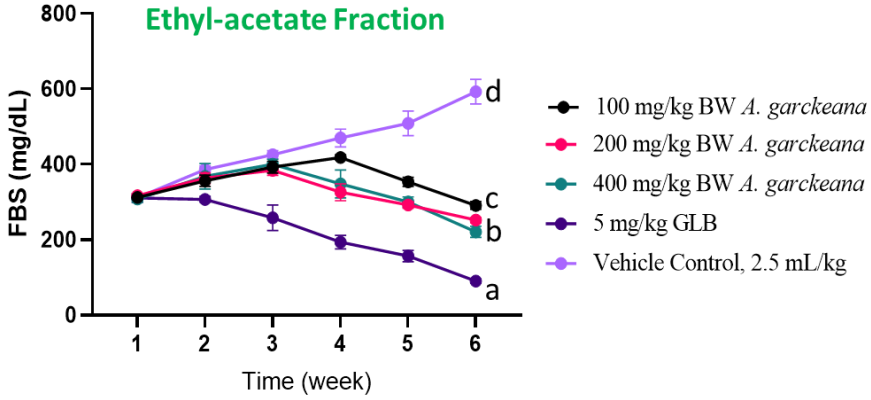

Figure 3: Hypoglycemic effect of ethyl acetate fraction of *Azanza garckeana* in alloxan induced diabetic rats. Each bars represents MEAN±SEM of triplicate determinations. Bars with different superscript alphabets were significantly different ($p<0.05$).

Table 2: The percentage dose dependent hypoglycemic effect of n-hexane, ethyl acetate and aqueous fractions of *Azanza garckeana* in alloxan induced diabetic rats

Sample	Conc. (mg/kg bw)	Initial FBS	Final FBS	Hypoglycemic (%)
n-hexane fraction	100	298.40±5.90	122.43±2.43	58.97 ±3.45 [d]
	200	327.20±8.04	118.23±3.68	63.86±5.35 [d]
	400	320.96±5.34	103.33±3.09	66.51±4.35 [e]
Ethyl acetate fraction	100	312.40±4.59	288.80±4.80	7.55±0.54[a]
	200	316.66±3.26	247.7±5.17	21.77±2.35 [b]
	400	308.50±5.25	217.30±7.05	29.56±3.46 [c]
Aqueous fraction	100	309.43±5.54	278.80±5.02	9.89±2.67 [a]
	200	321.36±5.77	263.20±17.44	18.09±3.45 [b]
	400	321.40±4.47	260.73±19.60	18.87±3.24 [b]
Glibenclimide	5	310.86±6.77	90.33±2.97	70.94±4.56 [f]
Control	5mL/kg bw	311.90±4.59	592.97±18.85	-90.15±6.57

Values are Mean ±SEM of triplicate determinations. Data followed by different superscript alphab*et al*ong the column were significantly different ($p<0.05$). FBS: fasting blood sugar

4.0 Discussion

The effect of free radicals in the pathogenesis of diseases has been documented [23]. The balance homeostasis between the free radicals and antioxidants are vital in the defense mechanisms of the body against these diseases [24]. However, negative shift in favor of the free radicals may result in oxidative stress that catalyzes the proliferation of diseases.

Literatures indicated that natural antioxidants can prevent or reverse abnormal health effect associated with antioxidants and oxidative stress [25]. With such a scenario, shifting to natural antioxidants is inevitable. In this study, the n-hexane, ethyl acetate and aqueous fractions of *A. garckeana* demonstrated dose dependent DPPH radical scavenging activities with percentage scavenging ranging between 12.45±23.45 and 74.83±5.35 %, thus providing scientific validation for their uses in treatments of various human diseases in traditional medicine [26].

The n-hexane fraction demonstrated highest percentage DPPH scavenging effect of 26.34±3.43, 38.44±4.35, 59.34±3.45, and 74.83±5.35 at concentrations of 62.5, 125, 250 and 500 µg/mL respectively. The ethyl-acetate fraction demonstrated DPPH scavenging effect of 19.33±2.98, 28.94±3.24, 47.34±2.90, and 57.82±4.54 respectively while the aqueous fraction demonstrated the least DPPH scavenging effect of 12.45±23.45, 18.64±2.94, 27.94±3.89, and 39.43±3.89 at concentrations of 62.5, 125, 250 and 500 µg/mL respectively.

The results of the present study are indication that the n-hexane and ethyl-acetate fractions of *A. garckeana* possess higher ability to scavenge the free radical and thus could be used as primary antioxidants since the antioxidant effect of extracts on DPPH is speculated to be due to their ability to donate hydrogen to free radicals.

Results of the present study is in agreement with the findings from previous studies [23] which reported that the DPPH scavenging activity from different solvent extracts of medicinal plants was concentration-dependent. Mshelia *et al*. [27] also reported that petroleum ether, methanol, acetone and ethyl acetate stem bark extracts of *A. garckeana* exhibited significant DPPH radical scavenging activity with methanol stem bark exhibiting the most potent effect (IC_{50} < 100 µg/mL).

Alloxan used to induced diabetes in the present study are well known to target Beta-cells [28]. Alloxan-induced diabetes has been proved by a significant elevation of the FBG level observed in the diabetic non treated rats [29]. Due to the low level of insulin, the glucose cannot metabolize in the cells and the FBG level increased drastically in diabetic rats.

Interestingly, both n-hexane, ethyl acetate and aqueous fractions of *A. garckeana* demonstrated significant ($p<0.05$) hypoglycemic effect in alloxan induced diabetic rats. The n-hexane fractions demonstrated the most significant hypoglycemic effect when compared with the hypoglycemic effect

demonstrated by the ethyl acetate and aqueous fractions of *A. garckeana*. In this experiment, the increased FBG level is recovered maximally toward vehicle-treated control after treatment with n-hexane fraction of *A. garckeana*. This activity may be due to stimulatory effect of above said fraction on pancreatic β-cells or enhance the generation of these cells to release insulin [30].

5.0 Conclusion

The results of the present study revealed that hexane, ethyl-acetate and aqueous fractions of *Azanza garckeana* exhibited hypoglycemic and antioxidants activities. However, from the comparative analysis of effective fraction solvents, it may be concluded that the maximum hypoglycemic and antioxidants effect of *Azanza garckeana* was noted in hexane fraction of *Azanza garckeana*. So, this study demonstrated that the n-hexane fraction of *Azanza garckeana* extract could serve as a reservoir of bioactive agent that could be useful for the development of new anti-diabetic agent

Author Contributions: The work was conducted in collaboration with all authors. All authors read and approved the final version of the manuscript.

Conflict of interest: The authors declare no conflict of interest

Funding: This research received no funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Acknowledgments: Not applicable.

Reference

1. Janssen, L.M.M.; Hiligsmann, M.; Elissen, A.M.J.; Joore, M.A.; Schaper, N.C.; Bosma, J.H.A.; Stehouwer, C.D.A.; Sep, S.J.S.; Koster, A.; Schram, M.T., et al. Burden of disease of type 2 diabetes mellitus: cost of illness and quality of life estimated using the Maastricht Study. *Diabet Med* **2020**, *37*, 1759-1765, doi:10.1111/dme.14285.

2. Ali, M.A.; Wahed, M.I.; Khatune, N.A.; Rahman, B.M.; Barman, R.K.; Islam, M.R. Antidiabetic and antioxidant activities of ethanolic extract of Semecarpus anacardium (Linn.) bark. *BMC Complement Altern Med* **2015**, *15*, 138, doi:10.1186/s12906-015-0662-z.

3. Soetan, K.; Aiyelaagbe, O. The need for bioactivity-safety evaluation and conservation of medicinal plants-A review. *Journal of medicinal plants research* **2009**, *3*, 324-328.

4. Skovgaard, L.; Pedersen, I.K.; Verhoef, M. Use of bodily sensations as a risk assessment tool: exploring people with Multiple Sclerosis' views on risks of negative interactions between herbal medicine and conventional drug therapies. *BMC complementary and alternative medicine* **2014**, *14*, 1-8.

5. Schmelzer, G.H.; Gurib-Fakim, A. *Medicinal plants*; Prota: 2008; Vol. 11.

6. El Omari, N.; Sayah, K.; Fettach, S.; El Blidi, O.; Bouyahya, A.; Faouzi, M.E.A.; Kamal, R.; Barkiyou, M. Evaluation of In Vitro Antioxidant and Antidiabetic Activities of Aristolochia longa Extracts. *Evidence-Based Complementary and Alternative Medicine* **2019**, *2019*, 7384735, doi:10.1155/2019/7384735.

7. Vaos, G.; Zavras, N. Antioxidants in experimental ischemia-reperfusion injury of the testis: Where are we heading towards? *World journal of methodology* **2017**, *7*, 37.

8. Tsado, N.; Lawal, B.; Ossa, P.; Jagaba, A.; Kontagora, G.N.; Gboke,

J.A.; Umar, A.; Oladunjoye, J. Antioxidants and antimicrobial activities of methanol extract of Newbouldia laevis and Crateva adansonii. *Journal of Pharmacy and Allied Health Sciences* **2016**, *6*, 14-19.

9. Bashir, L.; Shittu, O.; Sani, S.; Busari, M.; Adeniyi, K. African natural products with potential antitrypanosoma properties: A review. *Int J Biochem Res Rev* **2015**, *7*, 45-79.

10. Lawal, B.; Shittu, O.K.; Oibiokpa, F.I.; Berinyuy, E.B.; Mohammed, H. African natural products with potential antioxidants and hepatoprotectives properties: a review. *Clinical Phytoscience* **2017**, *2*, 1-66.

11. Lawal, B.; Shittu, O.K.; Kabiru, A.Y.; Jigam, A.A.; Umar, M.B.; Berinyuy, E.B.; Alozieuwa, B.U. Potential antimalarials from African natural products: A reviw. *Journal of intercultural ethnopharmacology* **2015**, *4*, 318.

12. Hostettmann, K.; Marston, A.; Ndjoko, K.; Wolfender, J.-L. The potential of African plants as a source of drugs. *Current Organic Chemistry* **2000**, *4*, 973-1010.

13. Afolayan, A.J.; Sunmonu, T.O. In vivo studies on antidiabetic plants used in South African herbal medicine. *Journal of clinical biochemistry and nutrition* **2010**, *47*, 98-106.

14. Osadebe, P.O.; Odoh, E.U.; Uzor, P.F. Natural products as potential sources of antidiabetic drugs. *Journal of Pharmaceutical Research International* **2014**, 2075-2095.

15. Yatoo, M.I.; Saxena, A.; Gopalakris, A.; Alagawany, M.; Dhama, K. Promising antidiabetic drugs, medicinal plants and herbs: An update. *International Journal of Pharmacology* **2017**, *13*, 732-745.

16. Mojeremane, W.; Tshwenyane, S. Azanza garckeana: A valuable edible indigenous fruit tree of Botswana. **2004**.

17. Yusuf, A.A.; Lawal, B.; Sani, S.; Garba, R.; Mohammed, B.A.; Oshevire, D.B.; Adesina, D.A. Pharmacological activities of Azanza garckeana (Goron Tula) grown in Nigeria. *Clinical Phytoscience* **2020**, *6*, 1-8.

18. Michael, K.; Onyia, L.; Jidauna, S. Evaluation of Phytochemicals in Azanza garckeana (Gorontula) Seed. *Journal of Agriculture and Veterinary Science* **2015**, *8*, 71-74.

19. Akoroda, M. Ethnobotany of Telfairia occidentalis (cucurbitaceae) among Igbos of Nigeria. *Economic botany* **1990**, *44*, 29-39.

20. Eseyin, O.A.; Sattar, M.A.; Rathore, H.A. A review of the pharmacological and biological activities of the aerial parts of Telfairia occidentalis Hook. f.(Cucurbitaceae). *Tropical Journal of Pharmaceutical Research* **2014**, *13*, 1761-1769.

21. Oyaizu, M. Studies on products of browning reaction antioxidative activities of products of browning reaction prepared from glucosamine. *The Japanese journal of nutrition and dietetics* **1986**, *44*, 307-315.

22. Etuk, E. Animals models for studying diabetes mellitus. *Agric Biol JN Am* **2010**, *1*, 130-134.

23. Krishna-Kumar, H.; Navyashree, S.; Rakshitha, H.; Chauhan, J. Studies on the free radical scavenging

activity of Syagrus romanzoffiana. *Int. J. Pharm. Biomed. Res* **2012**, *3*, 81-84.

24. Lawal, B.; Shittu, O.K.; Ossai, P.C.; Abubakar, A.N.; Ibrahim, A.M. Evaluation of antioxidant activity of giant African snail (Achachatina maginata) haemolymph in CCl4-induced hepatotoxixity in albino rats. *Journal of Pharmaceutical Research International* **2015**, 141-154.

25. Sakha, H.; Hora, R.; Shrestha, S.; Acharya, S.; Dhakal, D.; Thapaliya, S.; Prajapati, K. Antimicrobial activity of ethanolic extract of medicinal plants against human pathogenic bacteria. *Tribhuvan University Journal of Microbiology* **2018**, *5*, 1-6.

26. Maroyi, A. Azanza garckeana fruit tree: phytochemistry, pharmacology, nutritional and primary healthcare applications as herbal medicine: a review. *Research Journal of Medicinal Plants* **2017**, *11*, 115-123.

27. Mshelia, E.; Watirahyel, E.; Maigari, A.; Yohanna, C.; Ismail, F. Cytotoxicity and antioxidant activity of stem bark extracts of Azanza garckeana (kola of Tula). *European Journal of Pure and Applied Chemistry* **2016**, *3*, 2398-1385.

28. Cooperstein, S.; Watkins, D. The islets of Langerhans. *New York: Academic* **1981**, 387-425.

29. Ali, K.; Chatterjee, K.; De D, B.T.; Ghosh, D. Efficacy of aqueous extract of seed of Holarrhena antidysenterica for the management of diabetes in experimental model rat: A correlative study with antihyperlipidemic activity. *Int J Appl Res Nat Prod* **2009**, *2*, 13-21.

30. Bera, T.K.; De, D.; Chatterjee, K.; Ali, K.M.; Ghosh, D. Effect of Diashis, a polyherbal formulation, in streptozotocin-induced diabetic male albino rats. *International Journal of Ayurveda Research* **2010**, *1*, 18.

Author's Research Profile

Yusuf AA: https://orcid.org/0000-0001-7780-8487

Yissa TD: http://orchid.org/0000-0002-7984-5879

Agboola AR: https://orcid.org/0000-0003-3364-8121

Balogun MS: https://orcid.org/0000-0002-7984-5879