HAEMATOLOGICAL AND BIOCHEMICAL PARAMETERS ASSESSMENT OF ALLOXAN-INDUCED DIABETIC RATS TREATED WITH ETHANOL LEAF EXTRACT OF *ADANSONIA DIGITATA* (BAOBAB) LEAF

[1]UHUO, Emmanuel Nnaemeka, [1]GODWIN, Kingsley Okechukwu, [1]ALAEBO, Prince Ogochukwu and [2]EZEH, Helen Chinenye

[1]Department of Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

[2]Department of Chemical Science, Godfrey Okoye University, Enugu, Enugu State, Nigeria.

Corresponding Author: Uhuo, E. N. Department of Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria. **Email:** uhuo.emmanuel@mouau.edu.ng **Phone:** +234 8067346144

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ABSTRACT

The progression of diabetic complications is marked by abnormal values of some haematological and biochemical parameters and the toxic effects of some drugs use for the management of diabetes has also contributed in the derangements of these parameters. Plant-based natural medicines are popularly acclaimed to be safe, cheaper than allopathic drugs, available and affordable. The present study was designed to evaluate the efficacy of ethanol leaf extract of Adansonia digitata in diabetic-induced experimental rats. Forty five male rats were allotted into five groups: (1) normal control, (2) diabetic rats untreated, (3) diabetic rats administered 2.5 mg Kg^{-1}b.wt of glibenclamid (4) and (5) received 200 and 400 mg Kg^{-1}b.wt leaf extract of A. digitata respectively. After treatments, biochemical and heamatological parameters were determined. Significant reduction ($p<0.05$) of blood glucose and increased body weight among text groups were recorded as against Group 2. MDA decreased significantly ($p<0.05$) in Group 5 and not significant ($p>0.05$) in experimental group administered 200 $mgkg^{-1}$b.wt of the extract compared with Groups 1 and 2. Total protein level increased in the test groups and decreased in Group 2 against Group 3. Heamatological parameters (PVC, RBC and WBC) significantly ($p<0.05$) increased in groups 4 and 5 in comparison with positive control (Group 2). Similar results were obtained when compared with normal control group. The result suggests that the leaf extracts of A. digitata are safe and capable of ameliorating haematological and some biochemical abnormalities associated with diabetes mellitus, thus, could be recommended as adjunct to dietary therapy.

Keyword: Diabetes mellitus, *Adansonia digitata,* Haematological parameters, Biochemical parameters

INTRODUCTION

Diabetes mellitus (DM) is a disease characterized by excessive increase in blood glucose levels (Shaw *et al.*, 2010). Diabetic patients has reached 451 million adults worldwide as at 2017, with a projected increase of up to 693 million by the year 2045 (IDF, 2019). Diabetes contributes to huge amount of the global health expenditure in the world. In Africa, it is estimated that more than 25 million people were affected by diabetes, with about 69.2 % diabetic cases undiagnosed and the number is projected to be more than 40 million by the year 2045 (WHO, 2017). The progression of diabetic complications is marked by abnormal values of some haematological and biochemical parameters (Abou-Seif and Youssef, 2004; Alsaad and Herzenberg, 2007; Zadhoush *et al.*, 2015; Milosevic and Panin, 2019; Arkew *et al.*, 2021) and the toxic side effects of drugs used in the treatment of diabetes has also contributed to the derangements of biochemical and haematological indices associated with the progression of diabetic complications followed with the generation of free radicals in the pathophysiology of the disease (Oyedemi *et al.*, 2011).

Continuous use of some therapeutic drugs such as sulphonylureas and biguanides

can induce severe damage with hypoglycemia being the first line of attack in diabetic patients (Kalra *et al.*, 2013; Haq *et al.*, 2021). Changes in biochemical and hematological indices of diabetic subjects on oral antidiabetic agents have been reported (Wadkar *et al.*, 2008; Rena *et al.*, 2017). This information has created new insights to the development of more effective drugs and has led to the exponential increase in the use of herbs as alternative therapy due to their efficacy, safety, easy accessibility and reduced or complete absence of cytotoxic side effect. Many researchers have recommended the use of herbs as alternative therapy to synthetic drugs and a great number of modern medicines that are plant-based are considered as important sources of medicinal agents to treat different diseases (Njoku and Obi, 2009). For drug development, bioactive compounds like flavonoids, tannins, phenols and alkaloids in medicinal plants play a vital role (Khan *et al.*, 2019). In recent years, the use of herbs has received considerable attention as an alternative way to compensate for perceived deficiencies in orthodox pharmacotherapy worldwide (Ekor, 2014). Plant-based natural medicines are generally acclaimed to be safe, though scientists advocate for proper toxicological studies (Asif, 2015) in other to ensure safety in the use of natural medicines.

Medicinal plants are used in several countries to manage different metabolic diseases and are available and affordable than allopathic drugs to many, especially in developing countries such as Nigeria (Sofowora *et al.*, 2013). More than 400 local plants have been reported to have medicinal values and *Adansonia digitata* L. (Malvales: Malvaceae) is one of such plants (Sharma *et al.*, 2015).

A. digitata commonly called Baobab is an important African tree because of its medicinal and nutritional values (Kamatou *et al.*, 2011). Baobab is an emblematic, culturally important and physically majestic sub-tropical tree (Kamatou *et al.*, 2011; Sa'id *et al.*, 2020; Sodimu *et al.*, 2020). The tree has attracted the interest of some pharmaceutical companies and researchers due to its various traditional uses (medicinal, nutritional and cosmetic). European Commission has authorized the importation of *A. digitata* fruit pulps as a novel food (Buchmann *et al.*, 2010) and in 2009, the US Food and Drug Administration approved the use of *A. digitata* fruit pulps as ingredient in drink and food in the United State of America (Addy, 2009). The plant has been shown to contain excellent antioxidant and anti-inflammatory properties. Various parts of the tree are used to treat different kinds of ailments (De Caluwé *et al.*, 2010; Kamatou *et al.*, 2011). Different parts of the plant (e.g. leaves, bark, fruit pulp) possess analgesic, immune stimulant, anti-inflammatory, antihelmintic, hypoglycaemic, insect repellent and pesticidal properties (Tanko *et al.*, 2008; De Caluwé *et al.*, 2010; Kamatou *et al.*, 2011; Ogunleye *et al.*, 2019). The leaf extract has shown more potent antioxidative capacity than vitamin C (Ayele *et al.*, 2013). The methanol extract of the stem bark has been reported to possess hypoglycaemic activity in streptozotocin-induced diabetic rats (Tanko *et al.*, 2008). Further, studies by some researchers have demonstrated that the methanol extract of the leaf and pulp of the *A. digitata* possess hypolipidaemic effect (Geidam *et al.*, 2004; Bako *et al.*, 2014) making it relevant in the management of some metabolic disorders.

This study was set up to evaluate the potency of the leaf extract on induced diabetic rats. Specifically, the study sort: to determine the effect of the leaf extract on glucose level of the diabetic rats, determine the changes in heamatological parameters (PVC, RBC and WBC) in induced diabetic rats and investigate the effect of the extract on the total protein and oxidative stress parameter (MDA) of the experimental rats.

This work is significantly important as biochemical and haematological changes are major observable clinical and pathological features common with diabetes. Development of complications is certain in diabetes with increased risk of biochemical and haematological derangement of the markers, hence the relevance of this investigation.

MATERIALS AND METHODS

Apparatus/Equipment: AccuCheck Machine, UV-Visible Spectrophotometer (W572 China), Electronic Balance, Cyanmethaemoglobin and Microhaematocrit Centrifuge (SH120 China).

Chemicals/Reagents: All the used chemicals were of the highest analytical grades commercially available. These include; ethanol, acetic acid, alloxan, picric acid, thiobarbituric acid, total protein test kit (Randox United Kingdom).

Collection and Preparation of Plant Material: *A. digitata* leaves were obtained from a farm in Kaduna State, Northern part of Nigeria where it is dominantly grown. The plant was

identified and authenticated by the a plant taxonomist in the Department of Plant Biology and Biotechnology Herbarium Unit, Faculty of Life Sciences, University of Benin, Benin City, Edo State in collaboration with Department of Plant Science and Biotechnology, Michael Okpara University of Agriculture, Umudike, where voucher specimen (UBH-A473) was kept for referral purposes in the departmental herbarium. The leaves were milled into a powdered form using manual blender. 470 g of the milled material was extracted with analytical grade ethanol 1.5 litres (v/v) using maceration method for a period of 48 hours, filtered with Whatmann No. 4 filter paper and concentrated using rotary evaporator at a controlled temperature of 45 ^{0}C.

Acute Toxicity and Phytochemical Assay of *A. digitata* Leaf Ethanolic Extract: Twelve rats were used for oral LD_{50} determination, and were grouped into four groups of three rats each. The first three groups were administered with 10, 100 and 1000 mg/kg body weight of the extract respectively and mortality monitored, while the last group was subdivided into three groups of one rat each and were administered with 2500, 3500 and 5000 mg/kg body weight of the extract respectively and mortality monitored. LD_{50} was calculated as: $LD_{50} = [M_0 + M_1] \div 2$, where M_0 = highest dose of test substance that gave no mortality and M_1 = lowest dose of test substance that gave mortality (Lorke, 1983).

Phytochemical screening of *A. digitata* leaf ethanolic extract for the presence of secondary metabolites such as alkaloids, flavanoids, phenols, tannins, saponins and steroids was adopted from the study of Bharti *et al*. (2016).

Experimental Design: Forty five male albino rats (110 ± 5 g) were used for the study. The animals were purchased from Animal Genetics and Breeding Laboratory, Department of Zoology and Environmental Biology, University of Nigeria, Nsukka. The rats were acclimatized for seven days in the Animal House, Department of Biochemistry, Michael Okpara University of Agriculture, Umudike in accordance with the procedure approved by MOUAU Animal Research Ethics Committee. Furthermore, the animals were cared for according to prescribed international guiding principles for biochemical research involving the use of animals (CIOMS, 1985). The rats were fasted for 24 hours and induced with 150 mgkg^{-1} of alloxan to establish diabetes. The diabetes was confirmed after 72 hours post-induction using Accu-Check machine. The experiment was laid down using a complete randomized design (CRD) of five treatments replicated thrice with each replicate having three rats as follows: Group 1 normal rats (positive control), Group 2 diabetic rats' untreated (negative control), Group 3 diabetic rats given 2.5 mg of Glibenclamide (standard control), Group 4 diabetic rats + 200 mg of baobab leaf extract and Group 5 diabetic rats + 400 mg of baobab leaf extract. The test concentrations used were obtained by dividing the LD_{50} (3500 mg/kg) by a factor (17.5) to get the initial dose (200 mg/kg) that was subsequently doubled (400 mg/kg). The rats were fed pelleted feed (Vital Feeds, Grand Cereals Limited, Nigeria: 16 % crude protein and 2800 Kcal/kg metabolizable energy) and portable drinking water *ad libitum*. The animals were treated for twenty one days, after which it was bled and blood samples obtained and used for parameters analysis.

Determination of Haematological Parameters: Blood samples were collected through cardiac puncture under anesthesia into EDTA bottle. Pooled blood sample (1 ml per rat, 9 ml per treatment) was used. Haematological parameters were analysed using a haematology analyzer (Mindray Auto Hematology Analyzer, BC-5200, USA.) following the methods of Chhabra (2018). The parameters assayed were as follows: white blood cell count (WBC), red blood cell count (RBC), haemoglobin (Hb), and packed cell volume (PCV).

Determination of Biochemical Parameter:

Determination of blood glucose: Glucose was determined using Accu-Check machine.

Determination of total protein: Total protein determination followed the method of Lowry (1951) using RANDOX test kit for total protein. The principle lies on the fact that at pH 7.0, proteins form a stable complex with Cu^{2+}, which can be photometrically measured. Total protein test was as follows: three test tubes, blank, standard and sample were labeled and to the sample tubes were added 0.02 ml of serum, to the standard test tube, a volume, 0.02 ml of protein standard was added and 0.02 ml water to the blank test tube. One mililitre of the protein reagent was added to the test tubes each. This was mixed and left to stand for 25 minutes at room temperature (20 – 25^{o}C). The

absorbance was read at 540 nm. Total serum proteins (g/dL) = Absorbance of sample ÷ Absorbance of standard x 5.

Determination of malondialdehyde: The product of the reaction between malondialdehyde (MDA) and thiobarbituric reactive substances (TBARS) were measured by a modified direct determination of malondialdehyde by HPLC method (Li and Chow, 1994).

Statistical Analysis: Statistical analysis was performed using IBM SPSS version 25 statistical package. The data were subjected to one way analysis of variance (ANOVA) followed by Tukey post-hoc test. All the results were expressed as mean ± SEM and were considered statistically significant when $p \leq 0.05$.

RESULTS AND DISCUSSION

Acute toxicity study of *A. digitata* leaf ethanolic extract showed that the extract was relatively safe up to 3500 mg/kg body weight of rat. Maazu *et al.* (2021) in an earlier study reported the LD_{50} of *A. digitata* leaf n-hexane fraction, chloroform, ethyl acetate and methanol extracts to be above 5000 mg/kg body weight of rat indicating that the extract was non-toxic.

Phytochemical composition of *A. digitata* leaf ethanolic extract revealed the presence of numerous bioactive compounds which include: alkaloids, amino acids, amines and carboxylic acid derivatives, anthranoids, carbohydrates, glycosides, flavanoids, minerals, vitamins and inorganic compounds, peptidoglycans, polyphenol and its derivatives, saponins (Bharti *et al*., 2016).

The assessment of haematological and biochemical parameters in diabetic rats treated with ethanol leaf extract of *A. digitata* indicated that the WBC, HB, RBC, PCV, blood sugar, body weight, malondialdehyde and total protein of rats treated with 400 $mgkg^{-1}$ b.wt of ethanol *A. digitata* leaf extract were able to bring nearer to normal all the values for analyzed parameters when compared to the positive control (Group 1). These values differ significantly ($p<0.05$) with the untreated positive control (Group 2) and not significantly different ($p>0.05$) with the diabetic rats administered with 2.5 mg/Kg^{-1} b.wt. of glibenclamide (negative control). The results were in agreement with the existing literatures strongly suggesting appreciable medicinal potentials of *A. digitata* in treatment of diabetes and other different ailments (De Caluwé *et al*., 2010; Abiona *et al*., 2015; Ebaid *et al*., 2019; Yakubu *et al*., 2020).

Administration of leaf extracts resulted to a dose-dependent significant reduction ($p<0.05$) in the blood glucose concentration. The glucose concentration of the untreated diabetic rats (Group 2) increased significantly ($p<0.05$) compared to positive control (Group 1) (Table 1). Glucose level of the test group treated with 400 mg/Kg^{-1} body weight of the extracts decreased significantly against the untreated diabetic rats (Group 2), and non-significant difference was recorded in the glucose levels of the positive control (Group 1) as against rats in groups 3 and 5. This result suggests that *A. digitata* possesses antidiabetic potential which may be attributed to the chemical constituents of the extracts. Abiona *et al.* (2015) had reported the presence of polyphenols, flavonoids, terpenoids and other constituents in *A. digitata* leaf. However, the actual mechanism by which the plant extract brings about its antidiabetic effect is still investigated but can be suggested to be due to its antioxidant properties exhibited by some phytochemicals present (Salehi *et al*., 2019). The plant extract may have exerted its action on the beta cells of the Islet of Langerhans in the pancrease of the animals since alloxan induces diabetes in experimental animals by destroying the beta cells of the Islet of Langerhans. Olayiwola *et al.* (2004) had reported that the high concentration of phytonutrients may be responsible for the therapeutic values of the plants in the management of diabetes mellitus.

The results also revealed a progressive body weight loss in the negative control (Group 2) as compared to the positive control (Table 2). This may be attributed to the excessive breakdown of tissue protein and fatty acids occasioned by decrease in plasma insulin level. Lack of insulin may lead to inhibition of protein synthesis and increased degradation of the metabolites leading to increases amino acid levels in the blood which is subsequently used for gluconeogenesis (Qian *et al*., 2015). Body weight increased following administration of 400 $mgkg^{-1}$ of the extract compared to Group 2. Similar trend was reported in STZ-induced diabetic rats treated with *Punica granatum* Linn. (Myrtales: Lythraceae) leaves extract (Mestry *et al.,* 2017). It can be suggested that the extract has the ability to minimize muscle loss and rate of protein degradation.

The haematological indices of diabetic rats treated with *A. digitata* leaf ethanol extract to assess its effects on the anaemic status indicated that the Hb and RBC levels in Group 2 rats contrasted with that of Group 1 rats in a reduced proportion (Table 3).

Table 1: Glucose level of alloxan-induced diabetic rats treated with ethanol leaf extract of *Adansonia digitata*

Groups	Treatments	Glucose level (mg/L)
Group 1	Normal non-diabetic healthy rats (positive control)	105.00 ± 21.26[a]
Group 2	Diabetic rats untreated (negative control)	456.68 ± 76.69[e]
Group 3	Diabetic rats treated with 2.5 mg/Kg of glibenclamid (standard control)	228.00 ± 9.90[d]
Group 4	Diabetic rats treated with 200 mg/Kg of *Adansonia digitata* leaf extract	203.25 ± 21.56[c]
Group 5	Diabetic rats treated with 400 mg/Kg of *Adansonia digitata leaf* extract	160.00 ± 8.80[b]

[a-e]Means on the same column with different letter superscript are significantly different (p<0.05)

Table 2: Body weights of alloxan-induced diabetic rats treated with ethanol leaf extract of *Adansonia digitata*

Groups	Treatments	Body weight (g)
Group 1	Normal non-diabetic healthy rats (positive control)	160.10 ± 2.81[e]
Group 2	Diabetic rats untreated (negative control)	80.90 ± 13.54[a]
Group 3	Diabetic rats treated with 2.5 mg/Kg of glibenclamid (standard control)	116.28 ± 6.49[b]
Group 4	Diabetic rats treated with 200 mg/Kg of *Adansonia digitata* leaf extract	120.30 ± 5.72[c]
Group 5	Diabetic rats treated with 400 mg/Kg of *Adansonia digitata leaf* extract	130.00 ± 3.63[d]

[a-e]Means on the same column with different letter superscript are significantly different (p<0.05)

Table 3: Haematological indices and Total protein of alloxan-induced diabetic rats treated with ethanol leaf extract of *Adansonia digitata*

Groups	Treatment	Hb (g/dl)	RBC (g/dl)	PCV (g/dl)	WBC (g/dl)	Total protein (g/dl)
1	Normal non-diabetic healthy rats (positive control)	13.50 ± 1.74[d]	172.67 ± 21.21[d]	54.50 ± 5.29[d]	79.50 ± 3.42[d]	6.25 ± 0.42[e]
2	Diabetic rats untreated (negative control)	7.50 ± 0.00[a]	130.00 ± 14.14[a]	43.00 ± 0.71[a]	49.00 ± 4.37[a]	4.50 ± 0.70[b]
3	Diabetic rats treated with 2.5 mg/Kg of glibenclamid (standard control)	11.30 ± 0.34[b]	161.25 ± 8.54[b]	50.00 ± 0.71[b]	71.25 ± 7.36[b]	4.08 ± 0.65[a]
4	Diabetic rats treated with 200 mg/Kg of *Adansonia digitata* leaf extract	12.20 ± 1.43[c]	168.20 ± 0.00[bc]	51.00 ± 2.21[c]	75.00 ± 0.00[c]	4.90 ± 0.00[c]
5	Diabetic rats treated with 400 mg/Kg of *Adansonia digitata leaf* extract	13.00 ± 0.30[d]	170.67 ± 9.57[c]	54.20 ± 3.00[d]	79.30 ± 0.83[d]	5.60 ± 0.08[d]

[a-e]Means on the same column with different letter superscript are significantly different (p<0.05)

In the same way, WBC, Hb and RBC significantly increased (p<0.05) in all test groups compared with the untreated diabetic rats and the positive control rats (Group 1). Various haematological indices and the immune system have been reported to be altered during diabetes (Mansi and Lahham, 2008). Ajagbonna *et al*. (1999) reported the alteration of normal haematological and biochemical values of rats treated with extract of *Calotropis procera* W. T. Aiton (Gentianales: Apocynaceae). However, the results of this suggest that leaf extract of *A. digitata* are safe and capable of normalizing haematological abnormalities associated with diabetes mellitus thus could be prescribed as adjunct to dietary therapy and main therapy for management of diabetes mellitus. The significant decrease (p>0.05) in PCV, WBC, Hb and RBC levels recorded in the diabetic rats was drastically increased to near normal level following administration of the leaf extract across the test groups. The decrease in WBC, Hb, RBC and PCV values, observed after administration of alloxan may be due to abnormal haemoglobin synthesis, failure in blood osmoregulation and plasma osmolarity (Stookey *et al*., 2007). The level of RBCs and its related indices were appreciably improved as the extract was given. This gives credence to the ability of the leaf extract to stimulate the formation/secretion of erythropoietin, which triggers stem cells in the bone marrow to produce red blood cells (Lodish *et al*., 2010).

It is an evidence based fact that plasma protein level suffers changes during disease (Suzuki, 2006). In the current study total protein level was found markedly decrease in untreated diabetic groups in comparison with the positive control group (Table 3). The variation in plasma total protein concentration can be due to any of the following three changes: in the rate of their catabolism, in the rate of their anabolism and in the volume of distribution (Marshall *et al.*, 2004). Furthermore, each protein has characteristic half-life in circulation, for example the half-life of albumin in normal healthy adult is approximately 20 days and under diseases conditions, the half-life of protein may be markedly altered (Levittn and Levitt, 2016). The observed decreased protein concentration may be attributed to this. Generally, protein turnover decreases in disease conditions. In line with this study, the sample was able to avert this abnormality as increase was observed in all tested rats that received the extract against positive control (Group 2).

Malondialdehyde (MDA,) is lipid peroxidation end product and the most often used oxidative stress marker. Increased MDA level was recorded in diabetic rats compared to normal control indicated the overproduction of free radicals. MDA level non-significantly decreased ($p>0.05$) in group treated with 400 $mgkg^{-1}$ body weight of the extracts when compared with the group that received 200 $mgkg^{-1}$ body weight proved the antioxidant potential of the sample extracts (Table 4).

Table 4: Malondialdehyde of alloxan-induced diabetic rats treated with ethanol leaf extract of *Adansonia digitata*

Groups	MDA(mg/dl)
1	16.93 ± 0.43^{a}
2	110.21 ± 91.08^{e}
3	30.09 ± 2.82^{b}
4	49.50 ± 6.97^{d}
5	35.99 ± 1.99^{c}

$^{a-e}$Means on the same column with different letter superscript are significantly different ($p<0.05$)

The antioxidant a property of *A. digitata* is due to phytochemicals with their chelating ability offers protection against free radical attacks. Studies have also shown that leaf extract of *A. digitata* has ten times more potent antioxidative capacity than vitamin C (Ayele *et al.*, 2013).

Conclusion: Results have shown that administration of 200 and 400 mg/Kg^{-1} body weight of *A. digitata* leaf extract has antidiabetic and antioxidant properties. These antioxidant properties could be attributed to the high density of phytonutrients which may be responsible for the reversal of the effect of diabetes on the hematological and some biochemical parameters in this research. It can, therefore, be ascertained that the leaf extracts of *A. digitata* are safe and capable of normalizing haematological abnormalities associated with diabetes mellitus thus could be recommended as adjunct to dietary therapy for diabetes. Characterization of the solvent fraction to unveil the bioactive component/compound responsible for this activity is highly recommended for further study.

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REFFERENCES

ABIONA, D. L., ADEDAPO, Z. and SULEIMAN, M. K. (2015). Proximate analysis, phytochemical screening and antimicrobial activity of baobab (*Adansonia digitata*) leaves. *IOSR Journal of Applied Chemistry*, 8(5): 60 – 65.

ABOU-SEIF, M. A. and YOUSSEF, A. A. (2004). Evaluation of some biochemical changes in diabetic patients. *Clinica Chimica Acta*, 346(2): 161 – 170.

ADDY, R. (2009). *Baobab Fruit Approved as Food Ingredient in US.* https://www.confectionerynews.com/Article/2009/09/11/Baobab-fruit-approved-as-food-ingredient-in-US Accessed August 9, 2021.

AJAGBONNA, O. P, ONIFADE, K. I. and SULEIMAN, U. (1999) Haematological and biochemical changes in rats given extract of *Calotropis procera. Sokoto Journal of Veterinary Sciences,* 1(1): 36 – 42.

ALSAAD, K. O. and HERZENBERG, A. M. (2007). Distinguishing diabetic nephropathy from other causes of glomerulosclerosis: an update. *Journal of Clinical Pathology*, 60(1): 18 – 26.

ARKEW, M., YEMANE, T., MENGISTU, Y., GEMECHU, K. and TESFAYE, G. (2021). Hematological parameters of type 2 diabetic adult patients at Debre Berhan Referral Hospital, Northeast Ethiopia: a comparative cross-sectional study. *PLoS*

One, 16(6): e0253286. https://dx.doi.org/10.1371%2Fjournal.pone.0253286

ASIF, M. (2015). Chemistry and antioxidant activity of plants containing some phenolic compounds. *Chemistry International*, 1(1): 35 – 52.

AYELE, Y., KIM, J. A., PARK, E., KIM, Y. J., RETTA, N., DESSIE, G., RHEE, S. K., KOH, K., NAM, K. W. and KIM, H. S. (2013). A methanol extract of *Adansonia digitata* L. leaves inhibits pro-inflammatory iNOS possibly via the inhibition of NF-κB activation. *Biomolecules and Therapeutics*, 21(2): 146 – 152.

BAKO, H. Y., MOHAMMAD, J. S., WAZIR, P. M., BULUS, T., GWARZO, M. Y. and ZUBAIRU, M. M. (2014). Lipid profile of alloxan-induced diabetic Wistar rats treated with methanolic extract of *Adansonia digitata* fruit pulp. *Science World Journal*, 9(2): 19 – 24.

BHARTI, S. K., KRISHNAN, S. and KUMAR, A. (2016). Phytotherapy for diabetes mellitus: back to nature. *Minerva Endocrinologica*, 41(1): 143 – 146.

BUCHMANN, C., PREHSLER, S., HARTL, A. and VOGL, C. R. (2010). The importance of baobab (*Adansonia digitata* L.) in rural West African subsistence – suggestion of a cautionary approach to international market export of baobab fruits. *Ecology of Food and Nutrition*, 49(3): 145 – 172.

CHHABRA, G. (2018). Automated hematology analyzers: recent trends and applications. *Journal of Laboratory Physicians*, 10(01): 015 – 016.

CIOMS (1985). *International Guiding Principles for Biomedical Research Involving Animals*. Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO), Geneva, Switzerland. https://cioms.ch/wp-content/uploads/2017/01/ResearchInvolvingAnimals.pdf

DE CALUWÉ, E., HALAMOUÁ, K. and VAN DAMME, P. (2010). *Adansonia digitata* L. – a review of traditional uses, phytochemistry and pharmacology. *Afrika Focus*, 23(1): 11 – 51.

EBAID, H., BASHANDY, S. A., ALHAZZA, I. M., HASSAN, I. and AL-TAMIMI, J. (2019). Efficacy of a methanolic extract of *Adansonia digitata* leaf in alleviating hyperglycemia, hyperlipidemia, and oxidative stress of diabetic rats. *BioMed Research International*, 2019: 2835152. https://doi.org/10.1155/2019/2835152

EKOR, M. (2014). The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in Pharmacology*, 4: 177. https://dx.doi.org/10.3389%2Ffphar.2013.00177

GEIDAM, M. A., CHABIRI, S. A., and SHETTIMA, Y. (2004). Effect of methanolic extract of *Adansonia digitata* on serum lipid levels in normal and ethanol fed rats. *Pakistan Journal of Biological Sciences*, 7(6): 1094 – 1095.

HAQ, F. U., SIRAJ, A., AMEER, M. A., HAMID, T., RAHMAN, M., KHAN, S., KHAN, S. and MASUD, S. (2021). Comparative review of drugs used in diabetes mellitus – new and old. *Journal of Diabetes Mellitus*, 11(4): 115 – 131.

IDF (2019). *Africa: Prevalence of Diabetes (20 – 79 years), IDF Diabetes Atlas*. 9th Edition 2019, International Diabetes Federation (IDF). https://www.worlddiabetesfoundation. org/files/regional-fact-sheet-africa Accessed February 26, 2021.

KALRA, S., MUKHERJEE, J. J., VENKATARAMAN, S., BANTWAL, G., SHAIKH, S., SABOO, B., DAS, A. K. and RAMACHANDRAN, A. (2013). Hypoglycemia: the neglected complication. *Indian Journal of Endocrinology and Metabolism*, 17(5): 819 – 834.

KAMATOU, G. P. P., VERMAAK, I. and VILJOEN, A. M. (2011). An updated review of Adansonia digitata: a commercially important African tree. *South African Journal of Botany*, 77(4): 908 – 919.

KHAN, W., SUBHAN, S., SHAMS, D. F., AFRIDI, S. G., ULLAH, R., SHAHAT, A. A. and ALQAHTANI, A. S. (2019). Antioxidant potential, phytochemicals composition, and metal contents of *Datura alba*. *BioMed Research International*, 2019: 2403718. https://doi.org/10.1155/2019/2403718

LEVITT, D. G. and LEVITT, M. D. (2016). Human serum albumin homeostasis: a new look at the roles of synthesis, catabolism, renal and gastrointestinal excretion, and the clinical value of serum albumin measurements. *International Journal of General Medicine*, 9: 229 – 255.

LI, X. Y. and CHOW, C. K. (1994). An improved method for the measurement of malondialdehyde in biological samples. *Lipids*, 29(1): 73 – 75.

LODISH, H., FLYGARE, J. and CHOU, S. (2010). From stem cell to erythroblast: regulation of red cell production at multiple levels by multiple hormones. *IUBMB Life*, 62(7): 492 – 496.

LORKE, D. (1983). A new approach to practical acute toxicity testing. *Archives of Toxicology*, 54(4): 275 – 287.

MAAZU, A. B., USMAN, M. I. and GADAKA, M. A. (2021). Acute toxicity and antidiabetic studies of *Adansonia digitata* stem bark extracts on streptozotocin induced diabetic rats. *Advances in Life Science and Technology*, 89: 33 – 37.

MANSI, K. and LAHHAM, J. (2008). Effects of *Artemisia sieberi* Besser (*A. herba-alba*) on heart rate and some hematological values in normal and alloxan-induced diabetic rats. *Australian Journal of Basic and Applied Sciences,* 4(2): 57 – 62.

MARSHALL, S. J., BIDDLE, S. J., GORELY, T., CAMERON, N. and MURDEY, I. (2004). Relationships between media use, body fatness and physical activity in children and youth: a meta-analysis. *International Journal of Obesity*, 28(10): 1238 – 1246.

MESTRY, S. N., DHODI, J. B., KUMBHAR, S. B. and JUVEKAR, A. R. (2017). Attenuation of diabetic nephropathy in streptozotocin-induced diabetic rats by *Punica granatum* Linn. leaves extract. *Journal of Traditional and Complementary Medicine*, 7(3): 273 – 280.

MILOSEVIC, D. and PANIN, V. L. (2019). Relationship between hematological parameters and glycemic control in type 2 diabetes mellitus patients. *Journal of Medical Biochemistry*, 38(2): 164 – 171.

NJOKU, V. O. and OBI, C. (2009). Phytochemical constituents of some selected medicinal plants. *African Journal of Pure and Applied Chemistry*, 3(11): 228 – 233.

OGUNLEYE, O. O., JATAU, I. D., NATALA, A. J., IDEHEN, C. O., SALAMI, O. and MAMMAN, S. A. (2019). In vivo effect of the aqueous extract of *Adansonia digitata* (Linn) fruit pulp on *Trypanosoma brucei brucei* infection in Wistar rats. *Sokoto journal of Veterinary Sciences*, 17(4): 1 – 8.

OLAYIWOLA, G., IWALEWA, E. O., OMOBUWAJO, O. R., ADENIYI, A. A. and VERSPOHI, E. J. (2004). The antidiabetic potential of *Jatropha tanjorensis* leaves. *Nigerian Journal of Natural Products and Medicine*, 8: 55 – 58.

OYEDEMI, S. O., ADEWUSI, E. A., AIYEGORO, O. A. and AKINPELU, D. A. (2011). Antidiabetic and haematological effect of aqueous extract of stem bark of *Afzelia africana* (Smith) on streptozotocin–induced diabetic Wistar rats. *Asian Pacific Journal of Tropical Biomedicine*, 1(5): 353 – 358.

QIAN, K., ZHONG, S., XIE, K., YU, D., YANG, R. and GONG, D. W. (2015). Hepatic ALT isoenzymes are elevated in gluconeogenic conditions including diabetes and suppressed by insulin at the protein level. *Diabetes/Metabolism Research and Reviews*, 31(6): 562 – 571.

RENA, G., HARDIE, D. G. and PEARSON, E. R. (2017). The mechanisms of action of metformin. *Diabetologia*, 60(9): 1577 – 1585.

SA'ID, A., MUSA, A., MASHI, J., MAIGARI, F. and NUHU, M. (2020). Phytochemical screening and hepatoprotective potential of aqueous fruit pulp extract of *Adansonia digitata* against CCL_4 induced liver damage in rats. *Asian Journal of Biochemistry, Genetics and Molecular Biology,* 3(3): 12 – 21.

SALEHI, B., ATA, A., VANIL KUMAR, N., SHAROPOV, F., RAMÍREZ-ALARCÓN, K., RUIZ-ORTEGA, A., ABDULMAJID AYATOLLAHI, S., VALERE TSOUH FOKOU, P., KOBARFARD, F., AMIRUDDIN ZAKARIA, Z. and IRITI, M. (2019). Antidiabetic potential of medicinal plants and their active components. *Biomolecules*, 9(10): 551. https://doi.org/10.3390/biom9100551

SHARMA, B. K., BHAT, A. A. and JAIN, A. K. (2015). *Adansonia digitata* L. (Malvaceae) a threatened tree species of medicinal importance. *Medicinal Plants - International Journal of Phytomedicines and Related Industries*, 7(3): 173 – 181.

SHAW, J. E., SICREE, R. A. and ZIMMET, P. Z. (2010). Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Research and Clinical Practice*, 87(1): 4 – 14.

SODIMU, A. I., USMAN, M. B., APPAH, J., OSUNSINA, O., SULEIMAN, R. A. and MAIKANO, S. (2020). Ethnobotanical survey of medicinal utilization and phytochemical composition of baobab tree (*Adansonia digitata* L.) in Zaria

local government area of Kaduna State, Nigeria. *European Journal of Medicinal Plants*, 31(5): 1 – 10.

SOFOWORA, A., OGUNBODEDE, E. and ONAYADE, A. (2013). The role and place of medicinal plants in the strategies for disease prevention. *African Journal of Traditional, Complementary and Alternative Medicines*, 10(5): 210 – 229.

STOOKEY, J. D., BURG, M., SELLMEYER, D. E., GREENLEAF, J. E., ARIEFF, A., VAN HOVE, L., GARDNER, C. and KING, J. C. (2007). A proposed method for assessing plasma hypertonicity in vivo. *European Journal of Clinical Nutrition*, 61(1): 143 – 146.

SUZUKI, H. (2006). Protein–protein interactions in the mammalian brain. *Journal of Physiology,* 575(2): 373 – 377.

TANKO, Y., YERIMA, M., MAHDI, M. A., YARO, A. H., MUSA, K. Y. and MOHAMMED, A. (2008). Hypoglycemic activity of methanolic stem bark of *Adansonia digitata* extract on blood glucose levels of streptozocin-induced diabetic Wistar rats. *International Journal of Applied Research in Natural Products*, 1(2): 32 – 36.

WADKAR, K. A., MAGDUM, C. S., PATIL, S. S. and NAIKWADE, N. S. (2008). Antidiabetic potential and Indian medicinal plants. *Journal of Herbal Medicine and Toxicology*, 2(1): 45 – 50.

WHO (2017). *WHO Mortality Database.* World Health Organization, Geneva, Switzerland. https://www.who.int/data/data-collection-tools/who-mortality-database Accessed August 10, 2021.

YAKUBU, O. E., IMO, C., SHAIBU, C., AKIGHIR, J. and AMEH, D. S. (2020). Effects of ethanolic leaf and stem-bark extracts of *Adansonia digitata* in alloxan-induced diabetic Wistar rats. *Journal of Pharmacology and Toxicology*, 15: 1 – 7.

ZADHOUSH, F., SADEGHI, M. and POURFARZAM, M. (2015). Biochemical changes in blood of type 2 diabetes with and without metabolic syndrome and their association with metabolic syndrome components. *Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences*, 20(8): 763 – 770.