Trends in
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Hypoglycemic effects of seed extract of *Artocarpus heterophyllus*

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Abstract: Seed extract of *Artocarpus heterophyllus* is used in the management of diabetes in folkloric medicine, but its efficacy has not been scientifically validated. This study was carried out to evaluate the hypoglycemic effects of this seed extract. Dried and pulverized seeds of *A. heteropllus* were cold macerated in 80 % ethanol for 48 hours, filtered and the filtrate dried over water bath at 40ºC. Acute toxicity study and phytochemical screening were carried out. Hypoglycaemic effects of the extract (250 and 500 mg/kg) were tested on Alloxan induced hyperglycaemic model using a set of 20 diabetic albino rats of both sexes that were grouped into four (n=5). Groups I and II served as the negative and positive controls having received respectively distilled water (10 ml/ kg) and Metformin (100 mg/kg) orally.Groups III and IV received the extract (250 and 500 mg/kg) p.o. Histopathology analysis of rats' pancreas was carried out. Raw data were subjected to one-way analyses of variance (ANOVA) followed by post hoc turkey's test. $P < 0.05$ was considered to be statistically significant. The estimated oral median dose (LD_{50}) of the extract was higher than 5000 mg/kg. Secondary metabolites such as tannins and saponins were present. The two doses (250 and 500 mg/kg) of the extract conferred a dose-related significant ($p<0.05$) reduction in the fasting blood sugar (FBS) levels when compared to the control. The histopathology results also revealed the hypoglycemic effect of the extract.

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INTRODUCTION

Medicinal plants have continued to attract attention in the global search of plants for the treatment of various diseases affecting humans (Afrisham *et al.,* 2015). Ethnopharmacology is a major tool in the search for herbal remedy from medicinal plants in Africa (Howes *et al*., 2020) This is evident by the multiple ethnopharmacological surveys for medicinal plants used for the treatment of diabetes in West Africa (Karou *et al*., 2011). Plants and many of their derivatives have demonstrated anti-diabetic effect (Akah *et al.,* 2010). Some plants have also shown higher antidiabetic activity than some of the synthetic oral hypoglycaemic agents currently in use (Mahamed *et al.,* 2006). *Artocarpus heterophyllus* (Moraceae) is an evergreen fruit tree belonging to the *Artocarpus* genus (Figure 1). Its common name is Jackfruit tree. It is also known as Epa Oyibo (Yoruba), Jack'ya'yanitace (Hausa) and Ukwa Oyibo (Igbo) ethnic groups of Nigeria. It is found in tropical and subtropical regions (Saxena *et al*., 2011). Jack fruit trees are perennials and can produce fruit for 30 to 60 years. The tree itself can live up to 100 years. A fruit can contain 100 to 500 seeds which can be consumed roasted, boiled, steamed, or eaten as snack (Ibironke, 2008). Jack fruit is considered to be nutritious and has the ability to prevent excessive formation of bile as well as being able to increase virility. Renowned Ayurvedic and Unani practitioners have found that jackfruit is useful against various ailments including leprosy, ulcers, constipation, heart disease and rheumatism. Its potential benefits in strengthening the bones have also been suggested (https://www.paybima.com>blog). The seed are typically discarded despite their beneficial effects but some herbalist prescribe the seed extract for its hypoglycemic effect.

Diabetes mellitus (DM) is a syndrome of disturbed metabolism involving carbohydrate, protein, and fat which results from the degree of insulin deficiency (absolute or relative) and tissue sensitivity to its actions. This disease has shown a tremendous increase in prevalence with a demographic transition in its epidemiology in recent years. Prevalence figure published by the International Diabetes Federation (IDF) is 425 million persons living with DM worldwide, with nearly 50% of these undiagnosed (Int Diabetes Federation 2017). Management of DM employs modifications of diet, change of lifestyle, intake of oral hypoglycemic, administration of exogenous insulin and herbal remedies (Venkatesh *et al;* 2010). Studies have demonstrated that most diabetic patients had at least one DTP (Ogbonna *et al;* 2014). Patients with diabetes are subject to receive multiple drug therapies for the multiple co-morbidities associated with DM (Cipolle *et al*; 2013).

The seed extract of jack fruit can be of great relief to diabetic patients considering the fact that the cooked seeds are already eaten as snacks. Most of the aforementioned challenges in the management of diabetes could be addressed through development of a naturally occurring strong hypoglycemic agent that could easily be assessed locally like jack fruit seeds, hence the desire for this study.

Figure 1: **The seeds and fruits of *Artocarpus heterophyllus* (Jackfruit) (Moke *et al*., 2017)**

MATERIALS AND METHODS

Collection and identification of Plant materials

The seed of plant *Artocarpus heterophylla* was collected from Nkwelle Ezunaka in Anambra State, Nigeria and authenticated by a Taxonomist at the Department of Botany, Nnamdi Azikiwe University, Awka, Nigeria and a herbarium specimen, *Artocarpus heterophylla* NAUH-19^{A} was kept in the herbarium. The seeds were removed and shade-dried for 7 days.

Chemicals, reagents and drugs

Alloxan monohydrate (Sigma LTD USA), Metformin (NGC, Nigeria), Ethanol (JHD, Guangdong Guanghua Schi-Tech. Ltd China), Formaldehyde 40 %w/v.

Animals

Twenty albino rats of both sexes, (weighting between 100-150g) were purchased from Animal House of Chukwuemeka Odumegwu Ojukwu University, Igbariam, Nigeria. They were housed in clean metal cages, supplied portable water and fed with commercial pelleted feed (Guniea Feed®, Nigeria). Animals were handled in compliance with the National Institute of Health Guidelines for care and use of laboratory animals and approved by the Faculty of Pharmaceutical Sciences Animal

Research Ethics Committee with approval number: PHACOOU/AREC/2023/011

Preparation of the extract

The dry seeds were grounded coarsely to enable separation of the seeds from the outer portion. The seeds were further pulverized with electrical blender to fine powder. The powdered seed (98g) was cold macerated with 80% ethanol for 48 hours. This was first filtered by passing it through a cotton plug and further filtered with filter paper (Whatman filter paper, No 1). The seed extract *was* dried to a constant weight using water bath at 40ºC and stored at 4°C in an amber-colored bottle until required for experiment.

Qualitative phytochemical analysis

Screening for the presence of secondary metabolites was carried out following the standard phytochemical tests as demonstrated by Vishnu *et al* (2019). The secondary metabolites tested were: tannins, saponins, alkaloids, flavonoids, cardiac glycosides, reducing sugars, proteins, terpenoids and anthraquinones.

Acute toxicity study

The acute toxicity test of the extract was conducted using the Up and Down Procedure (UDP) adopted by Lorgue *et al*; (1996) and revised by Saganuwan, (2014). Using this method, the animals were dosed one at a time and the doses were dependent on the response of the first animal to the initial dose. The second animal receives a lower dose if the first animal dies (the initial dose is decreased by a factor of 3.2) or the second animal receives a higher dose if the first animal survives (the initial dose is increased by a factor of 3.2). Three rats weighing 150-200 g were used as starting point. Two rats served as negative control having received 10 ml/kg of distilled water orally while the test animal received a default oral dose of 5000 mg/kg of the extract. The animals were then observed continuously for 4 hours for changes in behavior or any other obvious signs of toxicity and subsequently daily for a total of 14 days for delayed toxicity.

Induction of experimental diabetes

Using the method described by Kannur *et al.;* (2006), alloxan monohydrate was used to induce experimental diabetes in rats. After starving the animals for 24 hours with free access to water, diabetes was induced by injecting (i.p) single dose of alloxan monohydrate (150 mg/kg). After the administration of alloxan monohydrate, the animals were allowed access to feed and water for 3 days, allowing for development of hyperglycaemia. Baseline fasting blood sugar (FBS) levels were determined using One Touch Glucometer (Life scan, USA). Rats with glucose levels above 200 mg/kg were recruited for the study.

Hypoglycemic study of the extract

The method described by Salim and Dikko (2016) was employed for this study while the dose of extract to be administered was determined using the method described by Neharkar and Gaikad, (2011). Group of 20 diabetic albino rats of both sexes were used. The rats were randomly divided into four groups (n=5); groups 1 and 2 served as the negative (10 ml/kgbw distilled water,) and the positive (Metformin 100 mg/kg) controls respectively. Groups 3 and 4 received the extract; 250 and 500 mg/kg respectively. After recording the baseline blood glucose level (zero hour) of animals, blood glucose level was measured at 2, 4, 6, 8 and 10 hours respectively on that first day (acute study). This was followed by daily administration (p.o) of Metformin (100 mg/kg) and extract (250 and 500 mg/kg) for a period of 14 days. Fasting blood sugar level was subsequently measured on days 2, 4, 6, 8, 10, 12 and 14. At the end of 2 weeks, the animals were starved overnight and final blood glucose level taken after which the rats were sacrificed using excess chloroform and their pancreas removed for histology study.

Histological study of the pancreas

Histological examination of the pancreas was carried out using the method described by Drury and Wallington (1980). The harvested pancreas preserved in 10% formaldehyde solution were dehydrated in ascending grades of ethanol, cleared in xylene and embedded in paraffin wax. Sections (6mm in thickness) of the tissues were prepared and stained with Haematoxylin and Eosin and subsequently examined under microscope

Statistical analysis

The data were analyzed using Statistical Package for Social Sciences (SPSS version 20) using one way ANOVA, followed by post-hoc turkey's test for multiple comparisons. The data were expressed as mean ± standard error of mean (SEM). Graphical representation was done using Microsoft Excel 2010. The difference between the mean were considered significant at $p < 0.05$.

RESULTS

Acute toxicity study (LD_{50})

Oral administration of the extract up to 5000 mg/kg dose produced no change in behavior, neither was there any mortality in any of the groups. Therefore,

the LD_{50} of ethanol seed extract of *X. aethiopeca* is above 5000 mg/kg.

Phytochemical study

The results of the phytochemical screening of the extract revealed the presence of tannins, saponins, alkaloids, flavonoids, glycosides, reducing sugar, proteins and fats and oil (Table 1)

Table 1: Qualitative phytochemical result

Tan	Sap.	Alk	Flav	Gly	Red	Prot	Fats/oil	Terp	Anth
++	+++	+++	+++	++	+	+	+	++	++

Key: Absent= -, traces=+, moderately present =++, abundance=+++. Tan=tannins, Sap=saponins, Alk=alkaloids, Flav= flavonoids, Gly=cardiac glycosides, Red= reducing sugars, Prot =proteins, Terp= terpenoids, Anth= anthraquinones

Effect of extract on blood sugar level (acute or hourly study).

The reduction in blood sugar level by the extract (250 and 500 mg//kg) became significant ($P < 0.05$) from the 4th hour after administration. By the 10th hour the standard drug (Metformin 100 mg/kg), the extract (250 mg/kg) and (500 mg/kg), caused percentage reduction of 17%, 19.9% and 23.68 % respectively (Table 2)

Effect of extract on blood sugar level (daily study)

The extract caused significant ($p < 0.05$) reduction in the FBS level from 4th day. This significant ($p < 0.05$) reduction continued to the 14th day of treatment. However, on the 14th day, the percentage reduction on FBS caused by extract 500 mg/kg (82.19%) was higher than that for reference drug Metformin 100 mg/kg (80.51%) (Table 3).

Effect of extract on body weight

Induction of diabetics caused reduction in the initial weight of the albino rats. The seed extract of *A. heterophyllus* caused a dose-related and significant ($p < 0.05$) increase in the weight of the diabetic albino rats when compared to the negative control (Table 4).

Effect of the extract on pancreas histology

The negative control group (Figure 2A) revealed deeply affected histoarchitecture of the pancreas. Treatment with the extract protected the pancreas of the diabetic rats (Figure 2C and 2D) resulting in moderate damage to the histoarchitecture of the pancreas. Likewise, similar to the effect of Metformin (Figure 2B).

Table 2. Effect of extract on blood sugar level and percentage reduction (hourly study)

Treatment	Dose/kg	FBS (mg/dl)					
		0 hr	2hr	4hr	6hr	8hr	**10hr**
Negative control	10ml, D.H2O	459.98±8.00	466.13 ± 1.11 (-1.34%)	479.38±0.33 (-4.22%)	482.21 ±1.45 (-4.83%)	483.22±0.28 (-5.05%)	483.45±1.36 (-5.10%)
Positive control	100 mg	468.00±0.43	457.40±0.99 (2.26%)	440.30±0.61* (5.92%)	418.60 ±1.69* (10.56%)	395.30 ±1.44* (13.58%)	384.84±2.65* (17.77%)
ESEAH	250 mg	493.40±9.87	458.00±14.94 (7.17%)	440.00±06.65* (10.82%)	425.90 ±24.00* (13.68%)	410.00 ±2.00* (16.90%)	394.77±1.67* (19.99%)
	500 mg	505.69±0.59	468.20±1.11 (7.41%)	429.30±0.66* (15.11%)	408.00 ±1.63* (19.32%)	392.13 ±0.88* (22.46%)	386.22±1.55* (23.63%)

Key: FBS=fasting blood sugar, negative control= Distilled water (D.H2O), Positive control =Metformin, ESEAH=ethanol seed extract of *Artocarpus heterophyllus*. Values are represented as mean ± standard error of mean (n=5). *p<0.05: Statistically significantly different from the control

Table 3: Effect of extract on blood sugar level and percentage reduction (daily study)

	Day 1	**Day 2**	**Day 4**	**Day 6**	**Day 8**	**Day 10**	**Day 12**	**Day14**
Negative control	459.98±08.00	487.67±0.87 (-6.02%)	492.44±2.03 (-7.06%)	499.57±1.00 (-8.61%)	511.47±0.9 (-11.19%)	531.88±3.05 (-15.63%)	537.77±0.7 (-16.91%)	541.69±0.56 (-17.76%)
Positive control	468.00 ± .43	370.10±0.97* (20.92%)	351.45±0.78* (24.90%)	240.45±0.64* (48.62%)	234.78±1.0 (49.83%)	198.78±0.76* (57.53%)	109.56±2.6 (76.59%)	91.22±1.98* (80.51%)
ESEAH	493.40±9.87	345.98±0.98*	325.33±1.09*	320.34±0.87*	256.76±1.98*	233.45±1.00*	200.87±21*	110.77±0.98*
250 mg/kg		(29.88%)	(34.06%)	(35.07%)	(47.96%)	(52.69%)	(59.29%)	(77.55%)
ESEAH	505.69±0.59	351.29±0.77*	321.47±0.37*	290.99±1.99*	245.60±2.00*	221.11±2.00*	176.75±1.00*	90.05±2.00*
500 mg/kg		(30.53)	(36.43%)	(42.46%)	(51.43%)	(56.28%)	(65.05%)	(82.19%)

Key: FBS=fasting blood sugar, negative control= distilled water, Positive control=Metformin, ESEAH=ethanol seed extract of *A. heterophyllus*. Values are shown as the mean ± Standard error of the mean, with n =5. *p<0.05: Statistically significantly different from the control group.

Table 4. Effect of extract on body weight

Treatment	Dose	Weight before Treatment	Weight after alloxan induced	Weight After treatment
Negative control	10 mg/ml	129.44±1.64	117.77±1.05	95.08 ±1.07
Positive control	100 mg/kg	150.12±0.45	121.36±1.14	155.05±0.59*
ESEAH	250 mg/kg	134.45±1.87	120.76±0.73	135.41±0.63*

Negative control= distilled water, positive control =Metformin: ESEAH=ethanol seed extract of *A. heterophyllus*. Values are shown as the mean ± Standard error of the mean, with n =5, *p < 0.05: Statistically significantly different from the control group.

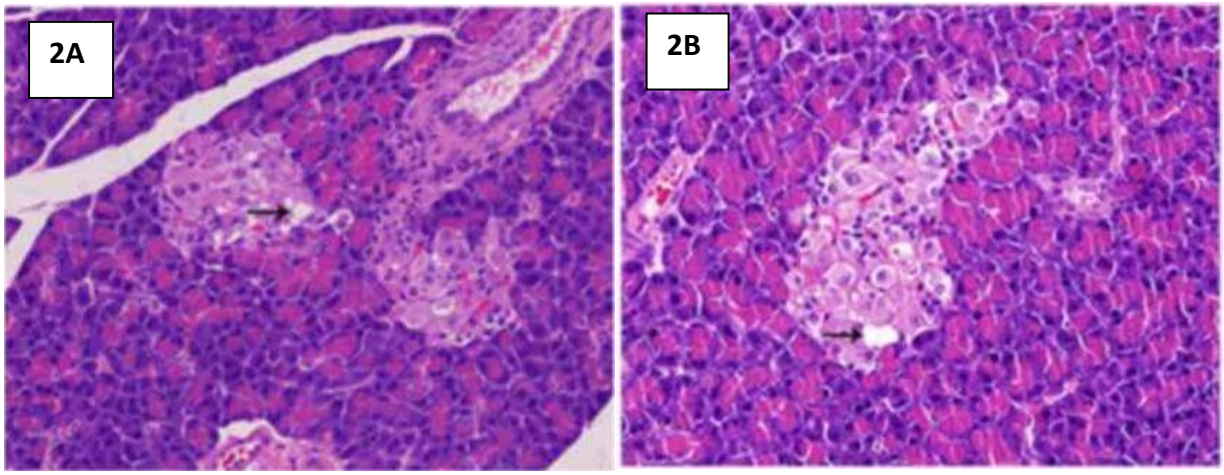

Figure 2A: Negative control: Diabetic pancreas features showed some acinar cells with islet-cells showing congested pyknotic nuclei with visible Lymphocytic infiltrates. Histoarchitecture deeply Affected.

Figure 2B: Positive control: Diabetic pancreas revealed acinar pattern structure with pyknotic nuclei of some acinar cells. The acinar cells which stained strongly are arranged in lobules with prominent nulei. The islet cells are seen embedded within the acinar cells and surrounded by a fine capsule. Histoarchitecture not affected.

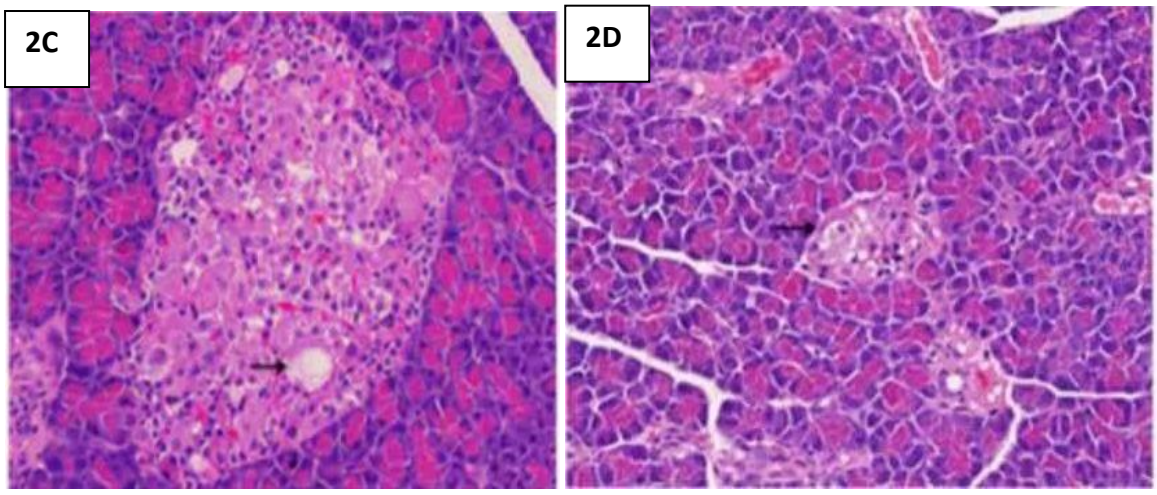

Figure 2C: 250 mg /kg seed extract: Pancreas features showed some acinar cells with islet-cells showing visible Lymphocytic infiltrates. Histoarchitecture moderately affected.
Figure 2D: 500 mg/kg seed extract: Pancreas features showing some acinar cells with islet-cells showing mildly despaired pyknotic nuclei with mildly lymphocytic infiltrates. Histoarchitecture slightly affected

DISCUSSION

The basic effect of insulin lacks or insulin resistance is to prevent the efficient uptake and utilization of glucose by most cells of the body, except those of the brain (Guyton and Hall, 2006). Insulin deficiency and sensitivity to its actions are most conveniently monitored by the degree of hyperglycemia. The ability of therapeutic compounds including medicinal plants to restore glycemic balance or homeostasis in hyperglycaemic condition is an index of their antidiabetic function and relevance (htts: //medlineplus.gov>article). Plants are one of the most attractive sources of new drugs and some have shown promise for the treatment of diabetes in-vivo (Haselgrübler *et al;* 2018) and in-vitro (Zao *et al;* 2018) while exhibiting multiple mechanisms of their actions.
The preliminary phytochemical analysis of the seed extract of *Artocarpus heterophyllus* revealed the presence of tannins, saponins, alkaloids, flavonoids, glycosides, reducing sugar, proteins and fats and oil. Alkaloids, saponins, flavonoids and tannins were found to be in abundance whereas terpenoid and anthraquinones were present in moderate amount. Natural products such as plants and herbs ameliorate and reduce blood glucose due to the presence of phytochemicals such as flavonoids, saponins, alkaloids, tannins, glycosides, terpenes (Dewanjee *et al.;* 2009). Absence of toxic signs and deaths in acute toxicity study are signs of the extract's relative safety. This result agrees with report by Lígia *et al* (2019). The higher hypoglycemic effect of the extract, when compared to Metformin agrees with the report by Melese *et al*. (2011) and Umeh *et al* (2020) where the plant extracts exhibited higher pharmacological activities than the reference drugs. Insulin is a hormone produced in the pancreas by special cells called beta cells. It is needed to move blood sugar (glucose) into the cells, where they are stored and later used for energy (htts: //medlineplus. gov>article). Alloxan is a popular diabetogenic agent used for assessing the antidiabetic or hypoglycemic capacity of test compounds. Alloxan monohydrate diabetic model employs two distinct pathological effects which include selective inhibition of glucose-stimulated insulin secretion, and induced formation of reactive oxygen species (ROS) which promotes selective necrosis of beta cells of the pancreas (Macdonald and Mohammed 2018). It could therefore be that the extract was able to revive these partially degraded beta cells leading to subsequent reduction in fasting blood sugar. Another possible mechanism of action for the extract is the anti-oxidant effects of its secondary metabolites. The anti-diabetic properties of flavonoids are attributed partly to their antioxidant potentials and partly due to their ability to modulate some cell signalling (Ramachandran and Baojun 2015). The radical scavenging activities of natural anthraquinones and phenol have been reported (Nguyen *et al.;* 2021). The anti-diabetic properties of *Anabasis articulate* are attributed to saponin present in it (Metwally *et al*; 2012). According to Kunyanga *et al.;* (2011), condensed tannins extracted from a-amaranth grain, finger millet, field bean, sunflower seed exhibited anti-diabetic effects mainly by inhibiting the activation of a-amylase and a-glucosidase activities. Hence, pharmacological activities which are associated with these phytochemicals may have contributed to the blood sugar-lowering effects of the seed extract. The result of the histology suggests

the possibility of the seed extract of *Artocarpus heterophyllus* exhibiting healing effect on the damaged diabetic pancreas. Pancreatitis is a condition in which pancreas becomes inflamed, which can lead to secondary diabetes. Alcohol and gall stones are main risk factors for pancreatitis but diabetes and some diabetic medications may increase the risk of pancreatitis (https://www.diabetes.co.uk>pancre...). Therefore, this extract could play a role in the protection of the pancreas as well as in the treatment of pancreatitis. Since management of diabetes involves modification of lifestyle, diet and use of anti-diabetic drugs, this seed extract could therefore play dual role; as diet for diabetic patients (inform of beverage) and as anti-diabetic drug that is affordable with little or no side effect.
In conclusion, seed extract of *Artocarpus heterophyllus* use in the management of diabetes could therefore be justified.

Conflict of Interest:

There was no conflict of interest in the execution and reporting of this study.

References

Afrisham R, Aberomand M, Ghaffari M, Siahpoosh A and Jamalan M (2015). Inhibitory effect of *Heracleum persicum* and *Ziziphus jujube* on activity of alpha amylase. *Botany*,20(15): 82.

Akah, PA, Okoli CO, Ibiam AF, Ezike AC and Okoye TC (2010). Evaluation of antidiabetic potentials of *Phyllanthus niruri* in alloxan diabetic rats. *Africa Journal of Biotechnology, 9:*248-259.

Cipolle R, Strand L, Frakes M (2013). Diabetes: co-morbidities and drug therapy problems in patients with diabetes. Medication Management Systems, Inc: 1–10.

Dewanjee S, Das AK, Sahu R and Gangopadhyay M (2009). Antidiabetic activity of Diospyros peregrina fruit: effect on hyperglycemia, hyperlipidemia and augmented oxidative stress in experimental type 2 diabetes", *Food Chemical Toxicology*, 47, 2679–2685.

Drury RA and Wallington EA (1980). *Carleton's Histology Technique* (4th Edition), Oxford University Press London.

Guyton AC and Hall JE (2006). Textbook of Medical physiology. 11th Edition. Elsevier Inc, New Delhi.

Haselgrübler R, Stadlbauer V, Stübl F, Schwarzinger B, Rudzionyte I, Himmelsbach M, Iken M, Weghuber J (2018). Insulin mimetic properties of extracts prepared from bellis perennis. *Molecules.* ;23:2605.doi: 10.3390/molecules 23102605.

Howes MJR, Quave CL, Collemare J, Tatsis EC, Twilley D, Lulekal E, Farlow, A. Li L, Cazar ME, Leaman DJ, Prescott TAK., Milliken W, Martin C, Nic Lughadha A. (2020). Molecules from nature: reconciling biodiversity conservation and global healthcare imperatives for sustainable use of medicinal plants and fungi Plants. People Planet, 2 (5)(pp. 463-481, 10.1002/ppp3.10138.

Ibironke AA. (2008). Comparative study of the chemical composition and mineral element content of Artocarpus *heterophyllus* and *Treculia africana* seeds and seed oils. *Bioresources Technology, 99:* 5125-5129.

International Diabetes Federation (2017). Diabetes atlas. 8th ed. Brussels: International Diabetes Federation.

Kannur ST, Babu PV, Liu D, Gilbert ER (2006), Antidiabetic potential of methanolic leaf extracts of *Icacina trichantha* in alloxan - induced diabetic mice. *International Journal of Diabetes in Developing Countries* · DOI: 10.4103/0973 3930.66511

Karou S.D, Tchacondo T, Djikpo TMA, Abdoul-Rahaman S, Anani K, Koudouvo K, Batawila . AKA, Simpore JSC (2011). Ethnobotanical study of medicinal plants used in the management of diabetes mellitus and hypertension in the Central Region of Togo. *Pharmaceutical Biology*., 49 (12)pp. 12861297, 10.3109/13880209.2011.62195 9

Kunyanga CN, Imungi JK, Okoth M, Momanyi C, Biesalski HK, *et al*., (2011). Antioxidant and anti-diabetic properties of condensed tannins in acetonic extract of selected raw and processed indigenous food ingredients from Kenya, *Journal of Food Sciences,* 76(4),560-567.

Lígia B, Cristiane BS, Josimara NR, Luisa MS, Sérgio FA, Obdulio GM, Josiane FGD, Marilis DM (2019). Acute and subacute (28 days) toxicity, hemolytic and cytotoxic effect of Artocarpus heterophyllus seed extracts. Toxicology Reports Volume 6, Pages 1304-1308 https://doi.org/10.1016/j.toxrep.2018.02.006

Lorgue G, Lechenet J & Riviere A (1996). Lead. In: *Clinical Veterinary Toxicology (MJ Chapman, editor)*. Blackwell Science Ltd., London; 123-125.

Macdonald O and Mohammed A (2018). Alloxan – induced diabetes, a common model for evaluating

the glycemic - control potential of therapeutic compounds and plants extract in experimental studies ScienceDirect Alloxan - induced diabetes, a common model for evaluating the glycemic-control potency. *Medicina*, *53* (6), 365–374. https: //doi. org/10.1016/j. medici.2018.02.001

Mahamed B, Abderrahrim Z, Hassane M, Abdelhafid T and Abdelkhaleq L (2006). Medicinal plants with potential antidiabetic activity-A review of ten years of herbal medicine research (1990-2000). *International Journal Diabetes* and *Metabolism. 14: 1-25*

Melese E, Asres K, Asad M and Engidawork E (2011). Evaluation of the antipeptic ulcer activity of the leaf extract of *Plantago lanceolata* L. in rodents. *Phytotherapeutics Research;* 25(8):1174–1180.

Metwally NS, Mohamed AM and ELSharabasy FS, (2012). Chemical constituents of the Egyptian plant Anabasis articulata (Forssk) Moq and its anti-diabetic effects on rats with streptozotocin-induced diabetic hepatopathy, *Journal of Applied Pharmaceutical Science*, 2, 54-65

Moke LE, Ngbolua K, Bongo GN, Messi LM, Noté OP, Mbing JN, and Mpiana PT (2017). Artocarpus heterophyllus Lam. (Moraceae): Phytochemistry, Pharmacology and Future Directions a mini-review. *Journal of Advanced Botany and Zoology, 5(3),* 1–8

Neharkar VS and Gaikad KG (2011). Hepatoprotective activity of *Cassia alata (linn*) leaves against paracetamol induced hepatic injury in rats. *Research Journal of Pharmaceutical, Biological and Chemical Sciences.2 (1): 783 - 788.*

Nguyen QT, Nguyen MT, Dao HC, Tran DM, Loc PH, Nguyen KH, Pham CN, Duong TQ, Adam M, and Quan V (2021). ACS Omega, 6, 20, 13391–13397

Zhao P, Ming Q, Qiu J, Tian D, Liu J, Shen J, Liu QH, Yang X. (2018). Ethanolic extract of *folium sennae* mediates the glucose uptake of l6 cells by glut4 and ca(2) Molecules. ;23:2934. doi: 10.3390/molecules23112934.

Ogbonna B, Ezenduka C, Opara C, Ahara L (2014). Drug Therapy Problems in Patients with Type-2 Diabetes in a Tertiary Hospital in Nigeria. International Journal of Innovative Research and Development|| ISSN 2278–0211 3.

Ramachandran V and Baojun X, (2015). Antidiabetic properties of dietary flavonoids: A cellular mechanism review, Nutrition and Metabolism, 12, 60.

Saganuwan SA (2014). Arithmetic method of rough estimation of median lethal dose (LD50) using Upand-Down Procedure. *Toxicology Letters*, 10.1016/j.toxlet.06.454, 2014

Salim MA, Imam AA, Dikko AAU, Tanko Y and Mohammed A (2016). Effect of Aqueous Garlic(Ag) Extract of vitexsumplicifolia on blood Glucose Level, liver Glycogen content, Lipid profile and Antioxidant Vitamins in Alloxan induced Diabetic wistar rats. *Bayero Journal Biomedical Sciences, 1(1):* 179-157

Saxena A, Bawa AS, and Raju PS (2011). Jackfruit (*Artocarpus heterophyllus* Lam.). In Postharvest Biology and Technology of Tropical and Subtropical Fruits: Cocona to Mango. Woodhead Publishing Limited. https://doi.org/10.1533/9780857092885.275

Umeh VN, Akah PA and Oforkansi MN (2020). Potentials of *Persea americana* Mill (Avocado) (Lauraceae) Seeds as Ulcer Protective Agent. *Research. Journal of Pharmacology., 14 (1): 1-11.*

Venkatesh S, Madhava RB, Dayanand RG, Mullangi R and Lakshman M (2010). Antihyperglycemic and hypolipidemic effects of *Helicteres isora* roots in alloxan induced diabetic rats: A possible mechanism of action, *Journal of Natural Medicine*,64, 295–304.@ NISCAIR

Vishnu B, Sheerin FMA, Sreenithi V (2019). A guide to phytochemical analysis. *IJARIIE-ISSN (O)-2395-4396:240-243.*

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