World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

Check for updates

Effect of ethanolic leaf extract of *Mucuna pruriens* (velvet bean) on the pancreas and pituitary gland of alloxan-induced diabetic rats

Johnson Ukwa Agbai [1], Njoku Oji Ifegwu [1, *], Nancy Pauline Igwe [3], Eberechukwu Lolly Mbanaso [2] and Chamberlin Jamike Elem [1]

[1] *Department of Anatomy, College of Medicine and Health Sciences, Abia State University Uturu, Abia State, Nigeria.*
[2] *Department of Physiology, College of Medicine and Health Sciences, Abia State, University Uturu, Abia State, Nigeria.*
[3] *Department of Anatomy, Faculty of Basic Medicine, Alex Ekwueme Federal University Ndufu Alike Ikwo, Nigeria.*

World Journal of Advanced Research and Reviews, 2023, 19(03), 283–294

Publication history: Received on 02 July 2023; revised on 28 August 2023; accepted on 31 August 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.19.3.1627

Abstract

Objective: This study was carried out to find out the effects of ethanolic leaf extract of *Mucuna pruriens* on the pancreas and pituitary gland alloxan-induced diabetic rats.

Methodology: Twenty-five (25) male rats weighing between 160 g - 200 g were purchased and acclimatized for two weeks, after which they were divided into 7 groups of 5 rats each and housed in cages. The groups were designated as groups A, B, C, D and E. Groups B - E were induced with diabetes using alloxan. Groups A and B served as control groups and received only distilled water; while groups C – D diabetic that served as test groups received Glucophage, 400 mg/kg of *M. pruriens* and 800 mg/kg of *M. pruriens* respectively for 21 days via oral route with the aid of oral intubation tube. On the 22nd day, the animals were sacrificed via chloroform inhalation, and testes were harvested for histological studies.

Result: There were poorly perfused pancreatic tissue with severe focal areas of Islets of Langerhans atrophy, and moderate to severe degeneration with necrosis of the anterior pituitary, severe scanty cytoplasm with either eosinophil or basophilic focal loss of tissues of the pancreas and pituitary gland respectively in group B when compared with the control group A and group C that received water and Glucophage respectively. These effects were ameliorated in Groups C - D that received variable doses of the ethanolic leaf extracts of *M. prurines*.

Conclusion: Leaf extracts of *M. pruriens* have ameliorating/antidiabetic effect on the histology of pancreas and pituitary gland of alloxan-induced rats.

Keywords: *Mucuna purines*; Pancreas; Pituitary gland; Alloxan; Glucophage.

1. Introduction

Diabetes refers to a chronic disease which occurs either when one of the body organs called pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces [1]. It is characterized by high blood glucose levels with increased thirst, increased urination and increased hunger [2]. Other symptoms include blurred vision, drowsiness, nausea and decreased endurance during exercise [2]. According to Erika [2], when the blood glucose level rises above 160 to 180 mg/dL (8.9 to 10.0 mmol/L), glucose spills into the urine. Also, when the level of glucose in the urine rises even higher, the kidneys excrete additional water to dilute the large amount of glucose [2]. Because the kidneys produce excessive urine, people with diabetes urinate large volumes frequently (polyuria), thus creating

* Corresponding author: Njoku Oji Ifegwu

abnormal thirst (polydipsia) [2]. Because excessive calories are lost in the urine, people may lose weight, and often feel excessively hungry to compensate for the lost calories [2]. DM has many subclassifications which include type 1, type 2, maturity-onset diabetes of the young (MODY), gestational diabetes, neonatal diabetes, and steroid-induced diabetes [3]. Type 1 and 2 DM are the main subtypes, each with different pathophysiology, presentation, and management, but both have a potential for hyperglycemia [3].

According to Global Burden of Disease Collaborative Network [4], diabetes is the direct cause of 1.5 million deaths in 2019, and 48 % of all deaths due to diabetes occurred before the age of 70 years. Also, another 460 000 kidney disease deaths were caused by diabetes, while raised blood glucose causes around 20 % of cardiovascular deaths [4]. It is a dangerous condition because it can exist undetected for years, during this time, many conditions can develop as a result of this underlying problem, and is also associated with long-term complications that affect almost every part of the body, such as blindness, heart and blood vessel disease, stroke, kidney failure, amputations and nerve damage [5]. The major long-term complications of diabetes, is to damage to blood vessels. This doubles the risk of cardiovascular disease [6] and about 75% of deaths in people with diabetes are due to coronary artery disease [7]. Other macrovascular diseases include stroke, and peripheral artery disease [8]. These complications are also a strong risk factor for severe COVID-19 illness [9]. The primary complications of diabetes due to damage in small blood vessels include damage to the eyes, kidneys, and nerves [10]. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and eventual blindness [10]. Diabetes also increases the risk of having glaucoma, cataracts, and other eye problems [11].

Pancreas is an elongated organ (approximately 15 cm) that lies obliquely across the posterior abdominal wall, at the level of the L1 and L2 vertebral bodies **[12]**. Its beta cell produces insulin and makes up approximately 75 percent of each islet. Elevated blood glucose levels stimulate the release of insulin [13]. The pancreas is supposed to automatically produces the right amount of insulin to move glucose from blood into the cells, but in people with diabetes, it either produces little or no insulin, or the cells do not respond to the insulin that is produced, thus, glucose builds up in the blood [14]. Insulin is the principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially liver, adipose tissue and muscle, except smooth muscle, in which insulin acts via the IGF-1 [11]. Therefore, deficiency of insulin or the insensitivity of its receptors play a central role in all forms of diabetes mellitus [15]. If the amount of insulin available is insufficient, or if cells respond poorly to the effects of insulin (insulin resistance), or if the insulin itself is defective, then glucose is not absorbed properly by the body cells that require it, and is not stored appropriately in the liver and muscles [13]. The net effect is persistently high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as metabolic acidosis in cases of complete insulin deficiency [16]. Diabetes aggravates acute pancreatitis and suppresses regeneration of the exocrine tissue [17]. On the other hand, the pituitary gland, or hypophysis, is the 'master gland' that secretes multiple hormones which regulate the functioning of other endocrine organs, such as the thyroid, adrenal cortex and gonads. Though none of the major pituitary hormones directly control the endocrine glandular components of the pancreas, there are multiple indirect interactions that alter glucose homeostasis [18].

Alloxan is a toxic glucose analogue, which selectively destroys insulin-producing cells (beta cells) in the pancreas when administered to rodents and many other animal species thereby causing an insulin-dependent diabetes mellitus (called "alloxan diabetes") in these animals, with characteristics similar to type 1 diabetes in humans [19]. Because alloxan selectively kills the insulin-producing beta-cells found in the pancreas, it is used to induce diabetes in laboratory animals [20, 21]. Its presence of in the intracellular thiols, generates reactive oxygen species (ROS) in a cyclic reaction with its reduction product, dialuric acid [19]. Thus, beta cell toxic action of alloxan is initiated by free radicals formed in this redox reaction [19]. Glucophage (*Metformin*) on the other hand, belongs to the class of medications called oral hypoglycemics, which are medications that lower blood sugar, and is used to control blood glucose (blood sugar) for people with type 2 diabetes [22].

The pituitary gland, or hypophysis, is the 'master gland' that secretes multiple hormones which regulate the functioning of other endocrine organs, such as the thyroid, adrenal cortex and gonads [18]. Though none of the major pituitary hormones directly control the endocrine glandular components of the pancreas, there are multiple indirect interactions that alter glucose homeostasis [18]. Pituitary tumors are often accompanied by impaired glucose tolerance or diabetes mellitus, which is often an early manifestation of these tumors. The presence of glucose metabolism disorders further increases the risk of cardiovascular disease-associated morbidity and mortality in patients with pituitary tumors [23]. Also, diabetes mellitus may affect the treatment plan for patients with pituitary tumors because the therapeutic agents for pituitary tumors may affect glucose metabolism [24].

Medicinal plants according to Ahn [25] and Smith-Hall *et al* [26] are used with the intention of maintaining health, to be administered for a specific condition, or both, whether in modern medicine or in traditional medicine. They may provide

health benefits to the people who consume them as medicines; financial benefits to people who harvest, process, and distribute them for sale; and society-wide benefits, such as job opportunities, taxation income, and a healthier labour force [26]. One of such medicinal plants is the *Mucuna pruriens.*

Mucuna prurins (MP), also referred to as the velvet bean, is a legume that grows in tropical and subtropical areas across the world including Africa, Asia, the Caribbean and the Pacific Islands [27]. It is an annual climbing shrub with long vines that can reach over 15 metres (50 feet) in length [28]. Its English common names are monkey tamarind, velvet bean, Bengal velvet bean, Florida velvet bean, Mauritius velvet bean, Yokohama velvet bean, cowage, cowitch, lacuna bean, and Lyon bean [29]. The plant is notorious for the extreme itchiness it produces on contact [30], particularly with the young foliage and the seed pods. It also produces many medium-sized red swollen bumps along with the itching. It has agricultural and horticultural value and is used in herbalism [27].

The plant and its extracts have long been used in tribal communities as an antidote for snakebite. More recently, its effects against bites by *Naja* (cobra) [31], *Echis* (saw-scaled viper) [32], *Calloselasma* (Malayan pit viper), and *Bungarus* (krait) species have been studied. It has been investigated as a treatment for Parkinson's disease [33] due to its high L-DOPA content [34, 35], while the seeds have been recognized for their ability to significantly alleviate neurotoxicity associated with the condition [36]. Research has shown that leaf extracts of *M. pruriens* have ameliorative effect on the hormonal levels [37] and the testes [38] of alloxan-induced Wistar rats.

Thus, this study will help to create an awareness on the effects of ethanolic leaf extract of *Mucuna pruriens* on the pancreas and pituitary gland alloxan-induced diabetic rats.

2. Material and methods

2.1. Animal procurement, care, and treatment

Twenty-five (25) male rats which weighed between 160 g - 200 g were procured and housed at the Animal house of Anatomy Department, Abia State University, Uturu with wire gauze cages in a well-ventilated area. They were fed with standard commercial pellet diet and water *ad libitum*. There were acclimatized for two weeks before the experiment and their health statuses were closely monitored before and during the experiment. All procedures were carried out in strict accordance with the Institutional guidelines on the care and use of experimental animals.

2.2. Collection, identification, and preparation of plant material

M. pruriens fresh leaves were plucked from a local farm settlement in Uturu, Isuikwuato Local Government Area of Abia state. The leaves were washed properly with water to remove sand and other impurities. They leaves were authenticated at the herbarium of the of Physiology and Pharmacology, Department of Forestry, College of Natural Resources and Environmental Management, Micheal Okpara University of Agriculture, Umudike. The voucher number assigned to the identified plant was MOUAU/VPP/17/017 [37, 38]. The leaves were air dried and crushed using laboratory blender and its extract was obtained using ethanol extraction. The crude ethanol extracts were filtered into a stainless basin with the aid of a white cloth, and were placed in a water bath so as to dry up the ethanol. 250 mg of these extracts/kg body weights were dissolved in 10 mls of distilled water and administered to the animals [38]. Department

2.3. Induction of lead and Vitamin C administration

The rats were divided into non-diabetic control group and experimental groups. The baseline blood glucose level of the experimental group to be inducted was determined before the induction of diabetes. The rats were allowed to fast over-night prior to injection of alloxan and diabetes was induced by intra-peritoneal administration of 150 mg of alloxan per kg body weight of rat (150 mg/kg body weight) [38]. After the induction, the rats were allowed to have free access to the same feed and water. After 72 hours, blood samples obtained through tail tip puncture of the rats were used to confirm diabetes in the rats by testing for hyperglycemia using Glucometer. Diabetes was confirmed at fasting blood glucose levels greater than 200 mg/dl (Adenowo *et al,* [39].

2.4. Experimental protocol

The animals were grouped into five (5) groups of five (5) rats each. Different doses of the leaf extracts were administered via oral route with the aid of oral gastric tube as shown below:

- **Group A** (The Control group) distilled water.
- **Group B** (Diabetic group) distilled water.

- **Group C** Diabetic + Glucophage
- **Group D** Diabetic + 400 mg/kg of *M. pruriens* leaf extract.
- **Group E** Diabetic + 800 mg/kg of *M. pruriens* leaf extract [37. 38].

2.5. Sample collection and analysis

The extracts were administered for twenty-one (21) days. On the 22nd day, the animals were sacrificed by anaesthetizing under chloroform vapour and dissected. Testes organs were harvested from the animals, and were fixed in 10 % formal saline for four hours. This was followed by histological and histochemical methods of tissue processing [38].

3. Results

3.1. Histopathological findings

Results of the histopathological findings of the effects of ethanolic leaf extract of *Mucuna pruriens* on the pancreas and pituitary gland alloxan-induced diabetic rats are as shown below:

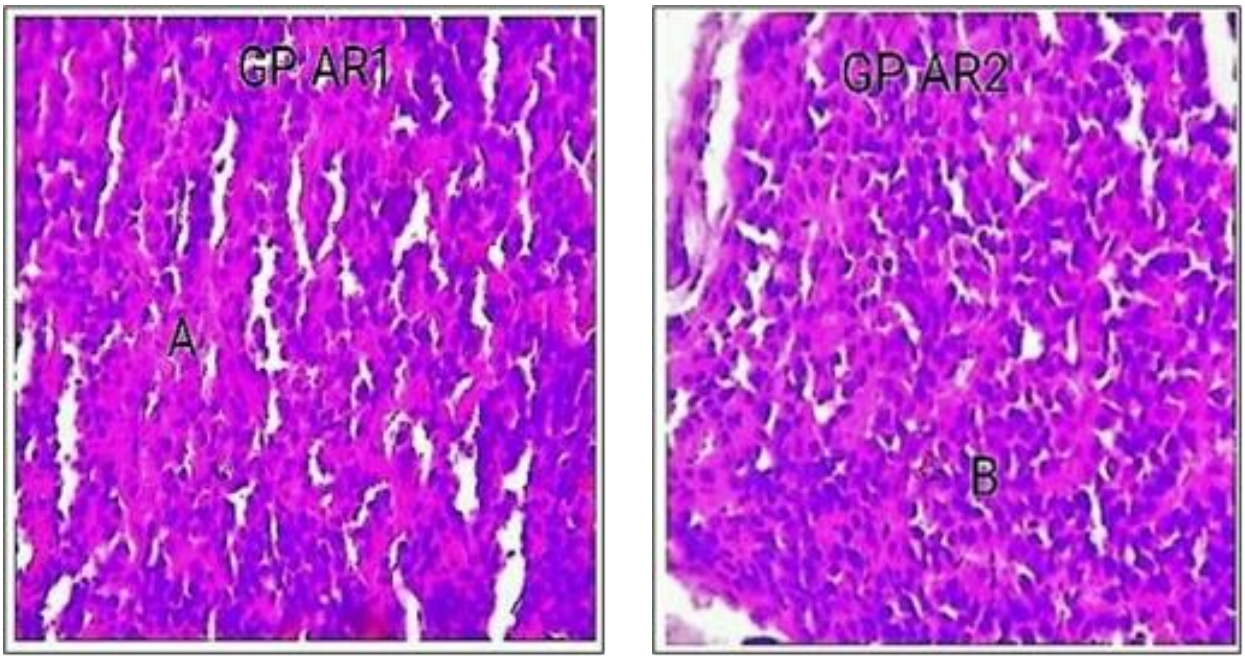

Figure 1 This is a photomicrograph of group A (R1R2) control section of pituitary gland (x400) (H/E) showing normal histoarchitecture of the pituitary gland with acidophils (A) and basophils (B). Each cell type seen presents distinct cell outline and prominent nuclei.

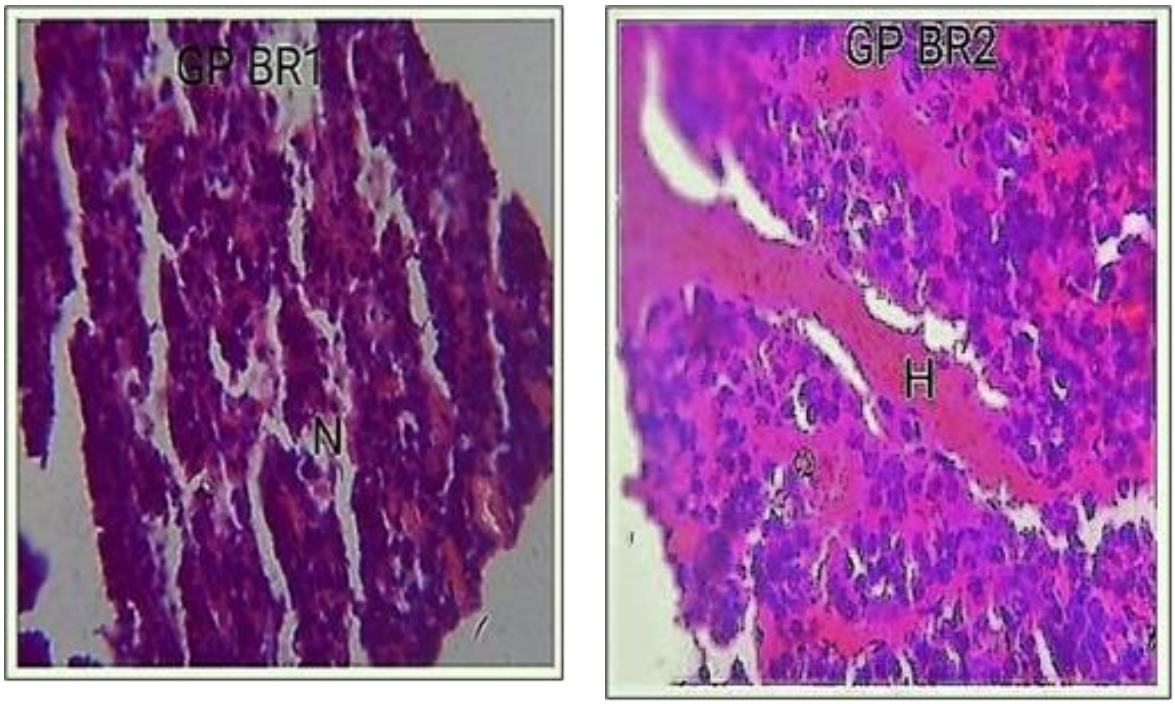

Figure 2 This is a photomicrograph of group B (R1R2) section of pituitary gland (x400) (H/E) induced with alloxan only showing moderate to severe degeneration with necrotic acidophil (N) and focal area of hemorrhage (H).

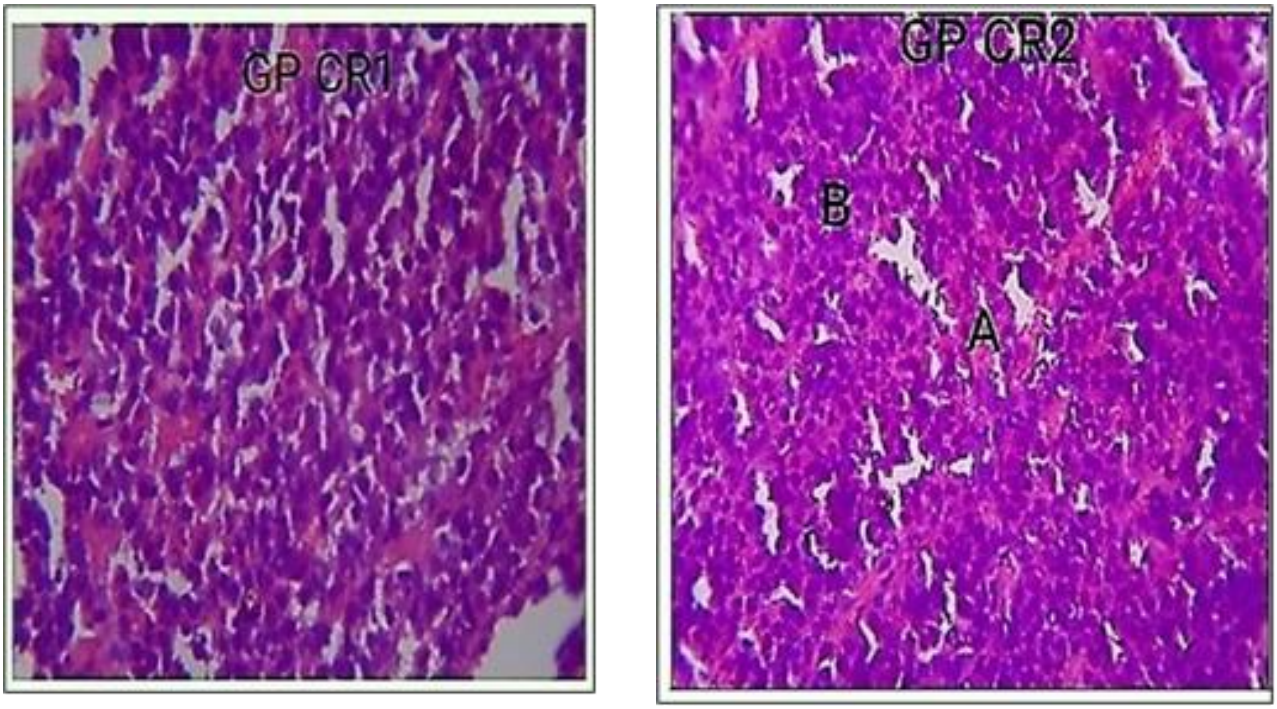

Figure 3 This is a photomicrograph of group C (R1R2) section of pituitary gland administered with alloxan and treated with Glucophage (x400) (H/E) showing well regenerated pituitary gland with active acidophil (A) and basophile (B) well outlined.

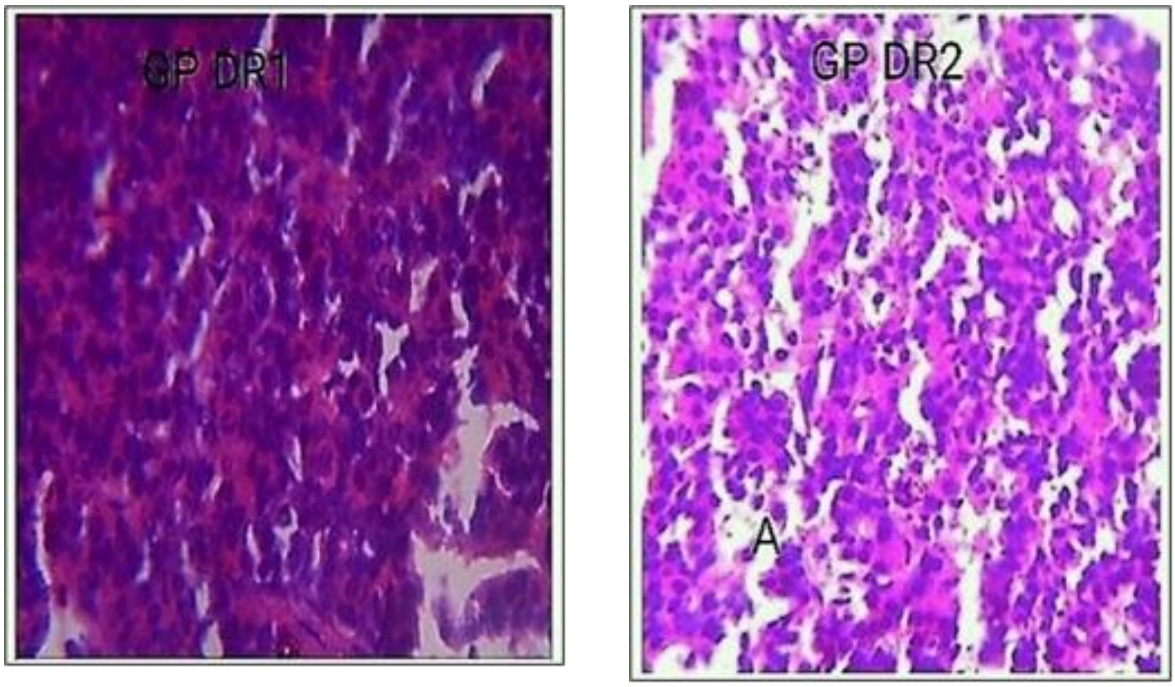

Figure 4 This is a photomicrograph of group D (R1R2) section of pituitary gland (x400) (H/E) alloxan and treated with 400 mg/kg of *M. pruriens* leaf extract showing moderate regeneration with mild basophil outnumbering the acidophil in R1 and moderate atrophy (A) of basophilic cells.

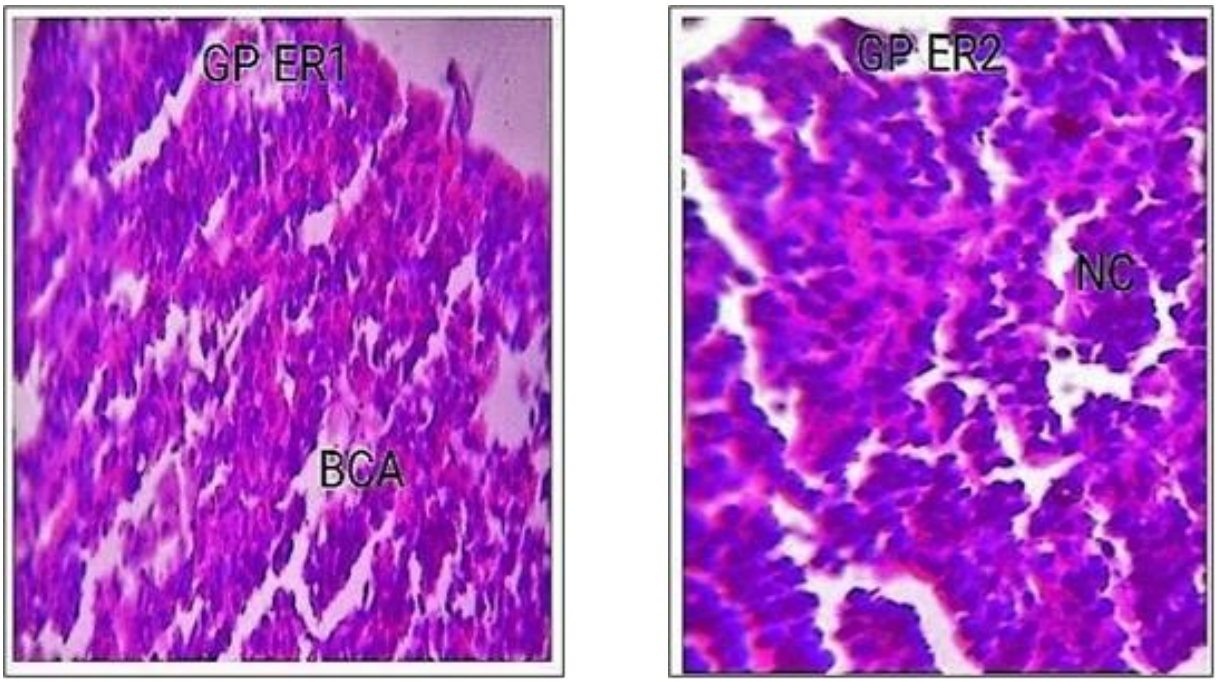

Figure 5 This is a photomicrograph of group E (R1R2) section of pituitary gland (x400) (H/E) induced with alloxan and treated with 800 mg/kg *M. pruriens* leaf extract showing mild regeneration with moderate basophilic cell atrophy (BCA) and necrotic cells (NC) with non-distinct cellular outline.

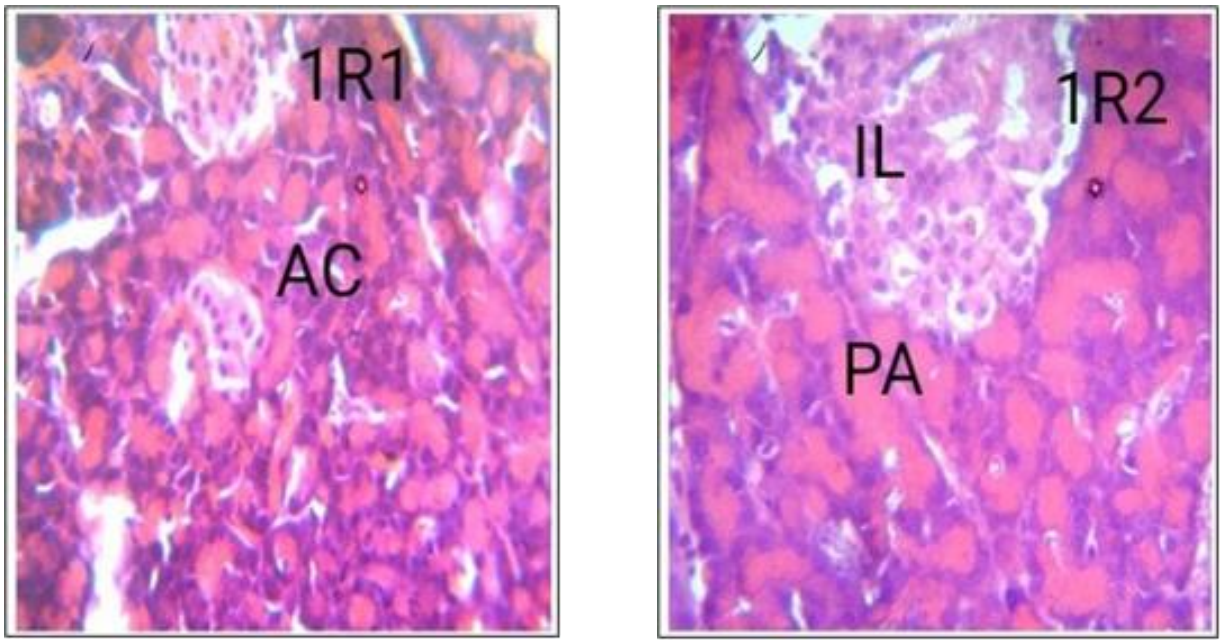

Figure 6 This is a photomicrograph of group A (1R1R2) control section of pancreas (x400) (H/E) showing normal Well perfused pancreatic tissue with islets of Langerhans (IL), pancreatic acini (PA) and well outlined acini cell (AC).

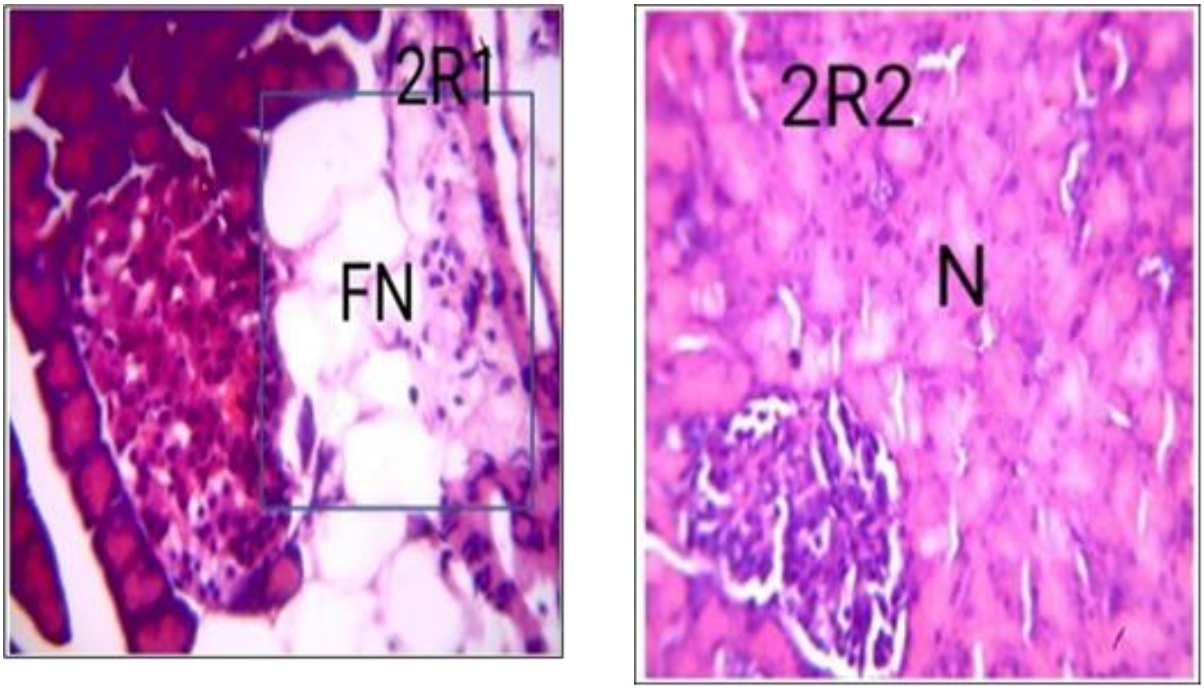

Figure 7 Photomicrograph of group B (2R1R2) section of pancreas induced alloxan only (x400) (H/E) showing severe degeneration with focal area of fatty necrosis (FN) and severe necrotic(N) pancreatic acini with non-acini cell outline.

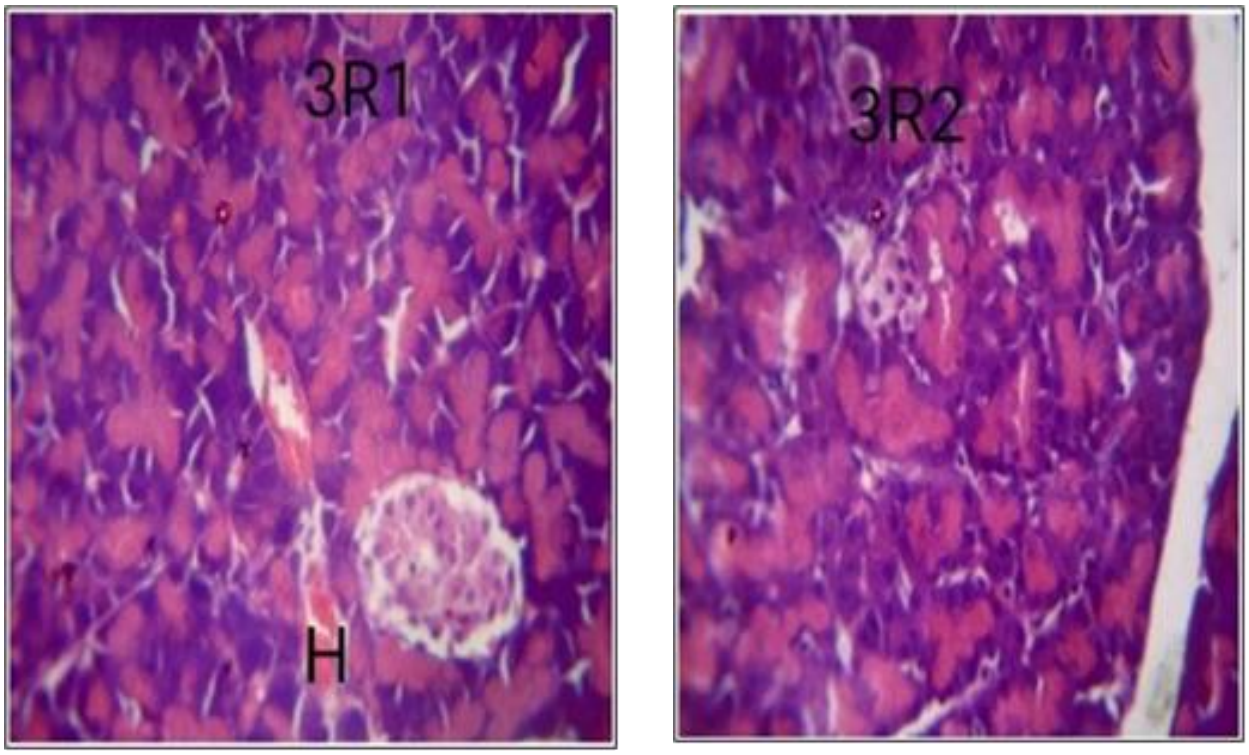

Figure 8 This is a photomicrograph of group C (3R1R2) section of pancreas induced and treated with Glucophage (x400) (H/E) showing moderate regeneration with mild focal area of hemorrhage (H) otherwise normal.

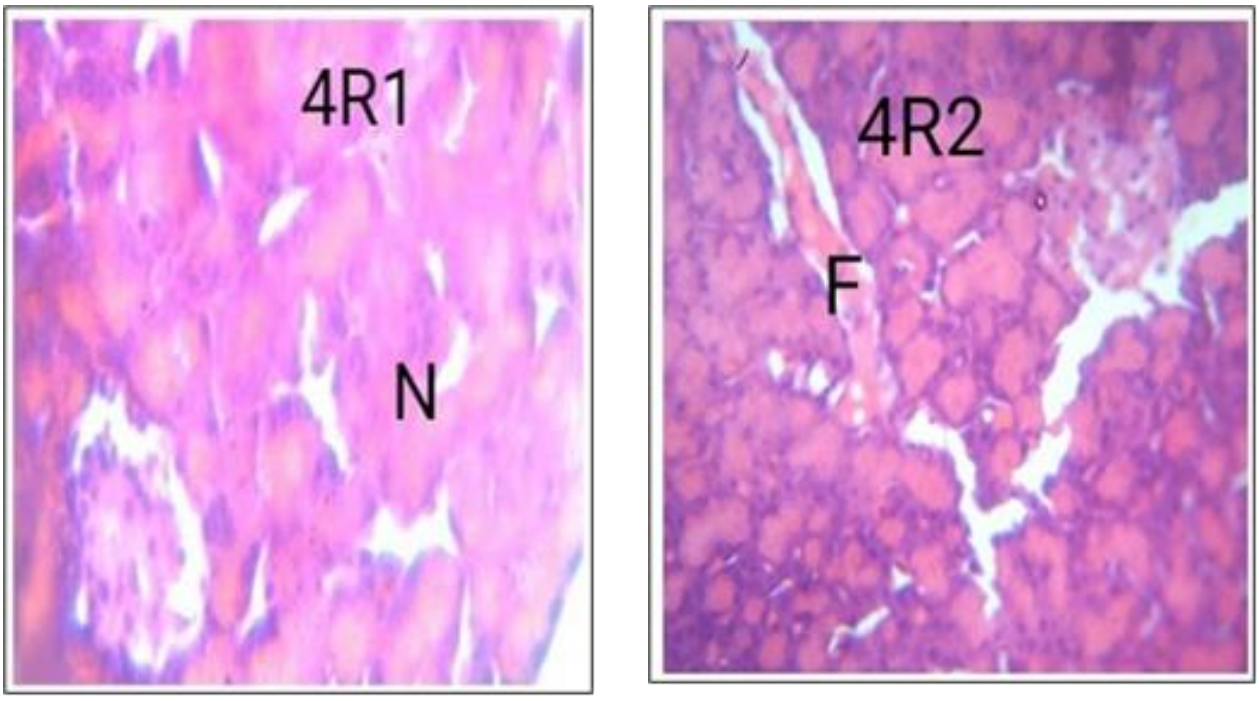

Figure 9 This is a photomicrograph of group D (4R1R2) section of pancreas induced with alloxan and treated with 400 mg/kg of *M. pruriens* leaf extract (x400) (H/E) showing moderate regeneration with mild necrotic (N) pancreatic acini in R1 with non-distinct pancreatic cell outline and fibrosis (F).

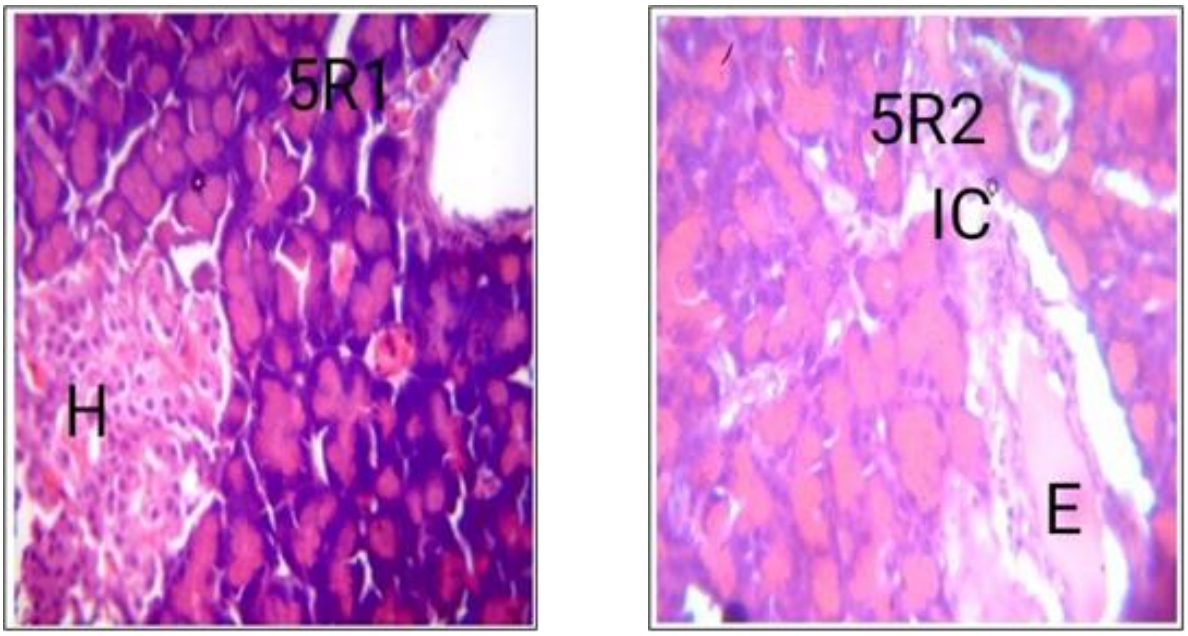

Figure 10 This is a photomicrograph of group E (5R1R2) section of pancreas induced with alloxan and treated with 800 mg /kg of *M. pruriens* leaf extract (x400) (H/E) showing mild regeneration with mild hemorrhagic islet (H) in R1 and moderate focal area of edema (E) surrounded by inflammatory cell (IC) in R2.

4. Discussion

Diabetes occurs when glucose builds up in the blood due to the pancreas not producing enough insulin (a hormone that the body's cells need to absorb glucose), or not using it correctly, thus, resulting in low energy levels [40]. About 422 million people worldwide have diabetes, the majority living in low-and middle-income countries, and 1.5 million deaths are directly attributed to diabetes each year [41]. Both the number of cases and the prevalence of diabetes have been steadily increasing over the past few decades [41]. According to Ryo [42], diabetes can affect the pituitary gland by altering the production and release of Growth Hormone (GH), which plays a critical role in regulating metabolism and growth. In people with uncontrolled diabetes, GH levels may be elevated, leading to increased insulin resistance and worsening of glucose control [42].

Figures 1 and 6 of the histopathological finding of this present study of groups A (R1R2) and (1R1R2) control sections of pituitary gland and pancreas (x400) (H/E) showed normal histoarchitecture of the pituitary gland with acidophils (A) and basophils (B) with each cell type seen presents distinct cell outline and prominent nuclei; and normal Well perfused pancreatic tissue with islets of Langerhans (IL), pancreatic acini (PA) and well outlined acini cell (AC) respectively.

In figures 2 and 7, the photomicrographs of groups B (R1R2) and B (2R1R2) sections of pituitary gland and pancreas (x400) (H/E) induced with alloxan only showed moderate to severe degeneration with necrotic acidophil (N) and focal area of hemorrhage (H); and severe degeneration with focal area of fatty necrosis (FN) and severe necrotic(N) pancreatic acini with non-acini cell outline respectively. These effects could be due to diabetes mellitus caused by the induced alloxan to the beta cells of the pancreas of the rats. Research has shown that alloxan selectively destroys insulin-producing cells (beta cells) in the pancreas when administered to rodents and many other animal species [19] thereby causing an insulin-dependent diabetes mellitus (called "alloxan diabetes") in these animals, with characteristics similar to type 1 diabetes in humans [19]. Thus, alloxan is used to induce diabetes in laboratory animals as it selectively kills the insulin-producing beta-cells found in the pancreas [20, 21].

Also, in figures 3 and 8 of the photomicrograph of groups C (R1R2) and (3R1R2) sections of pituitary gland and pancreas induced with alloxan and treated with Glucophage (x400) (H/E) showed well regenerated pituitary gland with active acidophil (A) and basophile (B) well outlined; and moderate regeneration with mild focal area of hemorrhage (H) otherwise normal respectively. These effects could be due to the ameliorating effect of Glucophage which is an oral hypoglycemics. Research has equally shown that Glucophage is used to control blood glucose (blood sugar) for people with type 2 diabetes [22].

Likewise, figures 4 and 9 of the photomicrograph of groups D (R1R2) and (4R1R2) sections of pituitary gland and pancreas (x400) (H/E) induced with alloxan and treated with 400 mg/kg of *M. pruriens* leaf extract showed moderate regeneration with mild basophil out-numbering the acidophil in R1 and moderate atrophy (A) of basophilic cells; and moderate regeneration with mild necrotic (N) pancreatic acini in R1 with non-distinct pancreatic cell outline and fibrosis (F). These effects could be due to the ameliorating/antidiabetic property of the *M. pruriens* leaf extract. Research has shown that leaf extracts of *M. pruriens* have ameliorative effect on the hormonal levels [37] and the testes [38] of alloxan-induced Wistar rats.

Lastly, in figures 5 and 10, the photomicrograph of groups E (R1R2) and (5R1R2) sections of pituitary gland and pancreas (x400) (H/E) induced with alloxan and treated with 800 mg/kg *M. pruriens* leaf extract showed mild regeneration with moderate basophilic cell atrophy (BCA) and necrotic cells (NC) with non-distinct cellular outline; and mild regeneration with mild hemorrhagic islet (H) in R1 and moderate focal area of edema (E) surrounded by inflammatory cell (IC) in R2 respectively. These effects could also be due to the ameliorating/antidiabetic property of the leaf extract *M. pruriens.* Research has shown that leaf extracts of *M. pruriens* have ameliorating/antidiabetic effect on the hormonal levels [37] and the testes [38] of alloxan-induced Wistar rats. Better results were obtained at 800 mg/kg of *M. pruriens* leaf extract showing the result is dose-dependent with better result at higher dosage.

5. Conclusion

Leaf extract of *Mucuna pruriens* has ameliorating/antidiabetic effect on the histology of pituitary gland and pancreas of alloxan-induced rats, and its ameliorating/antidiabetic effect is dose-dependent, and improves better with increase in dosages of the leaf extract.

Compliance with ethical standards

Acknowledgments

We wish to thank the Department of Anatomy, College of Medicine and Health Sciences, Abia State University Uturu, for the support and assistance provided during the entire study.

Disclosure of conflict of interest

No conflict of interest.

Statement of ethical approval

Approved by Ethical approval Committee, Human Anatomy Department, Abia State University, Uturu.

References

[1] WHO. Diabetes. April, 2023. https://www.who.int/news-room/fact-sheets/detail/diabetes

[2] Erika F. Brutsaert. Diabetes Mellitus (DM). MSD Manual Consumer Version, 2022. https://www.msdmanuals.com/home/hormonal-and-metabolic-disorders/diabetes-mellitus-dm-and-disorders-of-blood-sugar-metabolism/diabetes-mellitus-dm

[3] Sapra Am and Bhandari P. Diabetes. (Updated 2023 May 29). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551501/

[4] Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019. Results. Institute for Health Metrics and Evaluation. 2020 (https://vizhub.healthdata.org/gbd-results/).

[5] https://muschealth.org/medical-services/ddc/patients/digestive-diseases/pancreas/diabetes#:~:text=The%20pancreas%20is%20supposed%20to,builds%20up%20in%20th

[6] Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. June 2010; 375 (9733): 2215–2222.

[7] O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, de Lemos JA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology

Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. January, 2013; 127 (4): e362–e425.

[8] Papatheodorou K, Banach M, Bekiari E, Rizzo M, Edmonds M. Complications of Diabetes 2017. *Journal of Diabetes Research. 2018: 3086167.*

[9] Kompaniyets L, Pennington AF, Goodman AB, Rosenblum HG, Belay B, Ko JY, et al. Underlying Medical Conditions and Severe Illness Among 540,667 Adults Hospitalized With COVID-19, March 2020-March 2021. Preventing Chronic Disease. Centers for Disease Control and Prevention. July, 2021; 18: E66.

[10] World Health Organization. Diabetes Programme. Archived from the original on 26 April 2014. Retrieved 22 April 2014.

[11] https://en.wikipedia.org/wiki/Diabetes

[12] https://www.kenhub.com/en/library/anatomy/the-pancreas

[13] https://open.oregonstate.education/aandp/chapter/17-9-the-pancreas/

[14] https://muschealth.org/medical-services/ddc/patients/digestive-diseases/pancreas/diabetes#:~:text=The%20pancreas%20is%20supposed%20to,builds%20up%20in%20the

[15] American Diabetes Association. Insulin Basics. Archived from the original on 21 June 2023. Retrieved 25 June 2023.

[16] Shoback DG, and Gardner D, eds. Greenspan's basic & clinical endocrinology (9th ed.). McGraw-Hill Medical, 2011. ISBN 978-0-07-162243-1.

[17] Zechner D, Spitzner M, Bobrowski A, Knapp N, Kuhla A, Vollmar B. Diabetes aggravates acute pancreatitis and inhibits pancreas regeneration in mice. Diabetologia. May, 2012; 55(5):1526-34.

[18] Bhattacharya S, Kalra S, Dutta D, Khandelwal D, Singla R. The Interplay Between Pituitary Health and Diabetes Mellitus - The Need for 'Hypophyseo-Vigilance'. Eur Endocrinol. April, 2020; 16(1):25-31.

[19] https://en.wikipedia.org/wiki/Alloxan

[20] Danilova I.G., Sarapultsev P.A., Medvedeva S.U., Gette I.F., Bulavintceva T.S., Sarapultsev A.P. Morphological Restructuring of Myocardium During the Early Phase of Experimental Diabetes Mellitus. Anat. Rec. 2014; 298 (2): 396–407,

[21] Loreto D, and Elina V. Experimental surgical models in the laboratory rat. Boca Raton: CRC Press, 2009.

[22] https://www.medbroadcast.com/drug/getdrug/glucophage

[23] Osorio RC, Oh JY, Choudhary N, Lad M, Savastano L, Aghi MK. Pituitary adenomas and cerebrovascular disease: a review on pathophysiology, prevalence, and treatment. Front Endocrinol. 2022;13.

[24] Frara S, Maffezzoni F, Mazziotti G, Giustina A. Current and emerging aspects of diabetes mellitus in acromegaly. Trends Endocrinol Metab. 2016; 27(7):470–483.

[25] Ahn, K. The worldwide trend of using botanical drugs and strategies for developing global drugs. BMB Reports. 2017; 50 (3): 111–116.

[26] Smith-Hall, C; Larsen, H.O.; Pouliot, M. People, plants and health: a conceptual framework for assessing changes in medicinal plant consumption. J Ethnobiol Ethnomed. 2012; 8: 43.

[27] https://www.apdaparkinson.org/article/mucuna-pruriens-for-parkinsons-disease/

[28] https://en.wikipedia.org/wiki/Mucuna_pruriens

[29] *Mucuna pruriens*. Germplasm Resources Information Network. Agricultural Research Service, United States Department of Agriculture. Retrieved 8 March 2015.

[30] Andersen HH, Elberling J, Arendt-Nielsen L. Human surrogate models of histaminergic and non-histaminergic itch (PDF). Acta Dermato-Venereologica. September, 2015; 95 (7): 771–7.

[31] Tan NH, Fung SY, Sim SM, Marinello E, Guerranti R, Aguiyi JC. The protective effect of *Mucuna pruriens* seeds against snake venom poisoning. Journal of Ethnopharmacology. June, 2009; 123 (2): 356–8.

[32] Characterization of the factor responsible for the antisnake activity of *Mucuna pruriens*' seeds (PDF). Journal of Preventive Medicine and Hygiene. 40: 25–28. 1999. Archived from the original (PDF) on 2010-09-23. Retrieved 2011-03-23.

[33] Katzenschlager R, Evans A, Manson A, Patsalos PN, Ratnaraj N, Watt H, Timmermann L, Van der Giessen R, Lees AJ. *Mucuna pruriens* in Parkinson's disease: a double blind clinical and pharmacological study. Journal of Neurology, Neurosurgery, and Psychiatry. December, 2004; 75 (12): 1672–7.

[34] Cassani E, Cilia R, Laguna J, Barichella M, Contin M, Cereda E, Isaias IU, Sparvoli F, Akpalu A, Budu KO, Scarpa MT, Pezzoli G. *Mucuna pruriens* for Parkinson's disease: Low-cost preparation method, laboratory measures and pharmacokinetics profile. Journal of the Neurological Sciences. June, 2016; 365: 175–80.

[35] Cohen, Pieter A.; Avula, Bharathi; Katragunta, Kumar; Khan, Ikhlas. Levodopa Content of *Mucuna pruriens* Supplements in the NIH Dietary Supplement Label Database. JAMA Neurology. October, 2022; 79 (10): 1085.

[36] Singh, Surya P.; Gedda, Mallikarjuna R.; Jadhav, Jyoti P.; Patil, Ravishankar R.; Zahra, Walia; Singh, Saumitra S.; Birla, Hareram; Rai, Sachchida N. (2017). *Mucuna pruriens* Protects against MPTP Intoxicated Neuroinflammation in Parkinson's Disease through NF-κB/pAKT Signaling Pathways. Frontiers in Aging Neuroscience. 2017; 9: 421.

[37] Agbai JU, Ifegwu NO, Njoku-Oji NN, Uchefuna RC, Okwuonu IF, Okonudo PO. Effect of ethanolic leaf extracts of *Mucuna pruriens* on serum hormonal level in alloxan-induced diabetic male wistar rat. Global Scientific Journals, September, 2012; 9 (9): 1008 – 1017.

[38] Ifegwu NO, Agbai JU, Njoku-Oji NN, Uchefuna RC, Okwuonu IF, Umezulike AJ. Effect of ethanolic leaf extract of *Mucuna pruriens* on the testes of alloxan-induced diabetic male wistar rat, Global Scientific Journals, September, 2021; 9 (9): 1978 – 1989.

[39] Adenowo A. F, Ilori M. F, Balogun F. O, Kazeem M. I. Protective effect of ethanol leaf extract of Carica papaya linn (Caricaceae) in alloxan-induced diabetic rats. Tropical Journal of Pharmaceutical Research. 2014; 13(11): 1877-1882

[40] https://muschealth.org/medical-services/ddc/patients/digestive-diseases/pancreas/diabetes#:~:text=Diabetes%20occurs%20when%20glucose%20builds,glucose%20passes%20into%20the%20bloodstream.

[41] https://www.who.int/health-topics/diabetes#tab=tab_1

[42] Ryo Matsuura. Diabetes and its impact on the endocrine system: Diabetes endocrinology. Diabetes Manag, 2023; 13 (1): 436–437.