Irish Interdisciplinary Journal of Science & Research (IIJSR)
Volume 10, Issue 2, Pages 85-98, April-June 2026

Synergistic Effects of *Xylopia aethiopica* (Uda) and *Aframomum melegueta* (Alligator Pepper) Seed Extracts on Pancreatic β-Cells of Streptozotocin-Induced Diabetic Rats

ENYINDAH, Kingsley Chimene[1] & OWO, Gogo James[2*]

[1,2]*Department of Animal and Environmental Biology, Faculty of Natural and Applied Sciences, Ignatius Ajuru University of Education, Rumuolumeni, Port Harcourt, 500102, Rivers State, Nigeria.*
Corresponding Author Email: james.owo@iaue.edu.ng[*]

DOI: https://doi.org/10.46759/iijsr.2026.10210

Article Received: 27 April 2026 *Article Accepted: 28 June 2026* *Article Published: 30 June 2026*

ABSTRACT

This study aimed to evaluate the synergistic effects of *Xylopia aethiopica* (Uda) and *Aframomum melegueta* (Alligator Pepper) seed extracts on pancreatic β-cells of streptozotocin-induced diabetic rats. Diabetes was induced using streptozotocin (STZ), and the therapeutic effects of the combined leaf extracts were assessed over a 28-day period. Key biomarkers, including fasting blood glucose (FBG), serum insulin levels, and oxidative stress markers, were analysed. The combined extract demonstrated significant improvements in FBG levels, enhanced insulin secretion, and reduced oxidative stress compared to individual treatments. Both *X. aethiopica* and *A. melegueta* extracts have beneficial effects on managing diabetes by improving blood glucose regulation, enhancing insulin secretion, and reducing oxidative stress through β-cell protection and regeneration.

Keywords: *Xylopia aethiopica*; *Aframomum melegueta*; Pancreatic β-cells; Diabetes; Synergistic Effects; Oxidative Stress; Antidiabetic Activity; Antioxidant; Insulin; Fasting Blood Glucose.

1. Introduction

Diabetes mellitus is a group of metabolic disorders characterised by chronic hyperglycaemia due to inadequate insulin production, insulin resistance, or a combination of both. This condition affects the ability of the body to regulate blood glucose levels, leading to long-term damage to various organs and tissues [1, 2].

Diabetes is classified into several types, the most common being Type 1 diabetes, Type 2 diabetes, and gestational diabetes [3, 4]. Type 1 diabetes is an autoimmune disorder in which the immune system attacks and destroys the insulin-producing β-cells of the pancreas. This leads to an absolute deficiency in insulin, requiring lifelong insulin replacement therapy. It is commonly diagnosed in children and young adults, although it can occur at any age [4, 5]. Whereas, type 2 diabetes is the most prevalent form, accounting for approximately 90-95% of all diabetes cases. It is primarily characterised by insulin resistance, where the body's cells do not respond effectively to insulin. Over time, pancreatic β-cells may also fail, exacerbating hyperglycaemia. It is strongly associated with lifestyle factors such as obesity, physical inactivity, and poor dietary habits [6]. Gestational diabetes occurs during pregnancy and is marked by impaired glucose tolerance. While it usually resolves after delivery, women who experience gestational diabetes have an increased risk of developing Type 2 diabetes later in life [7]. The condition can also lead to complications for both the mother and the baby, such as preeclampsia and macrosomia [8].

The prevalence of diabetes has risen dramatically over the past few decades, driven by urbanisation, ageing populations, and the adoption of unhealthy lifestyles [6, 9]. According to the International Diabetes Federation (IDF), approximately 537 million adults were living with diabetes in 2021, and this number is projected to rise to 643 million by 2030 [4, 10]. The economic burden of diabetes is also substantial, with direct healthcare costs and lost productivity impacting individuals and healthcare systems globally [11, 12].

Medicinal plants have been relevant in the development of treatments for numerous ailments, including diabetes [13-15]. Plants contain a wide array of bioactive compounds such as alkaloids, flavonoids, tannins, and phenolic acids that have demonstrated anti-diabetic [16-18], antioxidant [19, 20], and anti-inflammatory properties [19, 21]. These compounds often act synergistically, offering a lot of benefits that synthetic drugs may not achieve [23].

Among these medicinal plants, *X. aethiopica* (commonly known as Uda) and *A. melegueta* (commonly referred to as Alligator Pepper) have garnered attention for their diverse pharmacological properties, including their potential anti-diabetic effects [24].

X. aethiopica is traditionally used in the treatment of various ailments, including diabetes, inflammation, and infections [25-27]. Its seeds are rich in essential oils, alkaloids, and flavonoids, which are believed to contribute to its therapeutic effects [28]. Similarly, *A. melegueta* is renowned for its aromatic seeds and seeds. It is traditionally employed in managing conditions such as hypertension, gastrointestinal disorders, and diabetes [29]. The seeds of *A. melegueta* are also known to contain potent bioactive compounds, including gingerols and paradols, which exhibit antioxidant and anti-inflammatory activities [30].

Emerging research focuses on novel therapeutic approaches, including β-cell regeneration, immunomodulation in Type 1 diabetes [31], and the development of non-invasive glucose monitoring devices [32]. Additionally, there is increasing interest in plant-based therapies due to their affordability and minimal side effects compared to synthetic drugs [33].

The concept of synergy, wherein the combination of two or more agents produces a therapeutic effect greater than the sum of their individual effects, is well established in pharmacology [34]. Exploring the synergistic potential of these plants could provide a novel and effective approach to diabetes management, particularly in addressing β-cell dysfunction and destruction.

The pathophysiology of diabetes involves oxidative stress, chronic inflammation, and apoptosis of pancreatic β-cells [35]. Preliminary studies have shown that the bioactive compounds exhibit antioxidative and anti-inflammatory properties [22, 24, 36], which are critical in mitigating β-cell damage [37].

Despite extensive research on the individual anti-diabetic properties of *X. aethiopica* and *A. melegueta*, limited studies have explored their combined effects. However, the potential synergistic effects of combining these plants on pancreatic β-cells have not been thoroughly investigated. This study aims to fill this gap by evaluating the impact of their combined leaf extracts on β-cell function, insulin secretion, and glycaemic control in STZ-induced diabetic rats.

1.1. Study Objectives

The main objective of this study was to evaluate the synergistic effects of *Xylopia aethiopica* (Uda) and *Aframomum melegueta* (Alligator Pepper) seed extracts on pancreatic β-cells in streptozotocin-induced diabetic rats. The specific objectives were to:

1. Determine the effect of the individual and combined seed extracts of *Xylopia aethiopica* and *Aframomum melegueta* on fasting blood glucose levels in streptozotocin-induced diabetic rats.

2. Evaluate the influence of the individual and combined seed extracts on serum insulin concentration as an indicator of pancreatic β-cell functional activity.

3. Assess the antioxidant effects of the individual and combined seed extracts by determining selected oxidative stress biomarkers in streptozotocin-induced diabetic rats.

2. Materials and Methods

2.1. Plant Materials

Fresh seeds of *X. aethiopica* (Uda) and *A. melegueta* (Alligator Pepper) (Fig. 1a and b respectively) were collected from a local market in Southern Nigeria. The plants were authenticated by a botanist at the Department of Plant Science and Biotechnology, University of Port Harcourt, Port Harcourt, Rivers State, Nigeria, where voucher specimens were deposited for future reference.

Figure 1a. Seeds of *X. aethiopica* (Uda); **1b.** Seeds of *A. melegueta* (Alligator Pepper).

2.2. Experimental Animals

Male Wistar rats weighing 150–200 g were obtained from the animal house of the University of Port Harcourt. The rats were housed under standard laboratory conditions (12-hour light/dark cycle, temperature of 22 ± 2°C) with free access to standard pellet feed and water. The study adhered to the ethical guidelines for animal care and use, approved by the research ethics committee of the University of Port Harcourt, Rivers State, Nigeria.

2.3. Chemicals and Reagents

Streptozotocin (STZ) was procured from Sigma-Aldrich, Inc., (St. Louis, MO, USA). All other chemicals, ELISA kits, and reagents were of the highest analytical grade commercially available.

2.4. Preparation of Plant Extracts

The collected seeds were thoroughly washed with distilled water to remove debris and air-dried at room temperature for 10 days. The dried seeds were then pulverised into fine powder using an electric blender. The powdered seeds of *X. aethiopica* and *A. melegueta* were extracted separately using methanol. A 200 g portion of each powder was soaked in 1 L of methanol for 72 hours with intermittent shaking. The mixtures were filtered

using Whatman No. 1 filter paper, and the filtrates were concentrated using a rotary evaporator at 40°C. Equal portions of the concentrated extracts of *X. aethiopica* and *A. melegueta* were mixed to prepare the synergistic extract. The combined extract was stored in an airtight container at 4°C until use.

2.5. Induction of Diabetes

Experimental diabetes was induced in the rats using streptozotocin (STZ). A single intraperitoneal injection of STZ (50 mg/kg body weight) dissolved in freshly prepared citrate buffer (0.1 M, pH 4.5) was administered. After 72 hours, fasting blood glucose levels were measured using a glucometer. Rats with fasting blood glucose levels ≥200 mg/dL were considered diabetic and included in the study.

2.6. Experimental Design

The diabetic rats were randomly divided into six groups of six animals each (n = 6):

Group 1 (Normal Control): Non-diabetic rats receiving distilled water.

Group 2 (Diabetic Control): Diabetic rats receiving distilled water.

Group 3 (Standard Control): Diabetic rats treated with insulin (5 U/kg).

Group 4: Diabetic rats treated with *X. aethiopica* extract (200 mg/kg body weight).

Group 5: Diabetic rats treated with *A. melegueta* extract (200 mg/kg body weight).

Group 6: Diabetic rats treated with the combined extract of *X. aethiopica* and *A. melegueta* (200 mg/kg body weight).

All treatments were administered orally once daily for 28 days.

2.7. Assessment of Biochemical Parameters

Blood Glucose Levels: Fasting blood glucose levels were measured weekly using a glucometer (Accu-Chek Blood Glucose Meter; Roche Diabetes Care). Blood samples were collected from the tail vein.

Serum Insulin Levels: Serum insulin levels were measured using an enzyme-linked immunosorbent assay (ELISA) kit (Elabscience Biotechnology Inc., Wuhan, China) following the manufacturer's instructions.

Oxidative Stress Markers: Biochemical assays for oxidative stress markers such as malondialdehyde (MDA), superoxide dismutase (SOD), and catalase (CAT) were performed to evaluate the antioxidant potential of the extracts using the procedures described by Okari et al. [38].

2.8. Statistical Analysis

Data were expressed as mean ± standard error of the mean (SEM). Statistical comparisons were made using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test. A p-value < 0.05 was considered statistically significant. Analyses were performed using SPSS software (version 25.0).

3. Results

3.1. Effects of Extracts on Fasting Blood Glucose Levels

Table 1 demonstrates the changes in fasting blood glucose (FBG) levels over a 4-week period in various treatment groups. The normal control group (Group 1) maintained stable glucose levels around 92–95 mg/dL, reflecting normal glucose regulation. The diabetic control group (Group 2) showed a steady increase in glucose levels, from 260 ± 10 mg/dL at baseline to 275 ± 14 mg/dL at Week 4, confirming hyperglycemia due to diabetes. The standard control group treated with insulin (Group 3) experienced a significant reduction in glucose levels, achieving near-normal levels (100 ± 6 mg/dL) by Week 4.

Both the diabetic rats treated with *X. aethiopica* extract (Group 4) and *A. melegueta* extract (Group 5) exhibited progressive glucose reductions, though neither achieved normoglycemia. By Week 4, FBG levels were 145 ± 7 mg/dL and 148 ± 6 mg/dL, respectively.

The synergistic extract group (Group 6) showed the most notable improvement among the treatment groups, reducing glucose levels to 120 ± 5 mg/dL by Week 4, demonstrating a pronounced hypoglycemic effect when the extracts were combined.

Table 1. Effects of Extracts on Fasting Blood Glucose Levels (mg/dL).

Group	Week 0 (Baseline)	Week 1	Week 2	Week 3	Week 4
Normal Control	95 ± 5	95 ± 4	94 ± 6	93 ± 5	92 ± 6
Diabetic Control	260 ± 10	258 ± 12	265 ± 15	270 ± 13	275 ± 14
Standard Control	261 ± 9	170 ± 8	125 ± 6	110 ± 5	100 ± 6
Xylopia Extract	259 ± 11	220 ± 10	180 ± 9	150 ± 8	145 ± 7
Aframomum Extract	258 ± 10	225 ± 9	190 ± 10	160 ± 7	148 ± 6
Synergistic Extract	260 ± 10	190 ± 9	140 ± 7	125 ± 6	120 ± 5

3.2. Effect of Extracts on Serum Insulin Levels

The impact of different treatments on serum insulin levels in diabetic and control groups are presented in Table 2. The normal control group (Group 1) exhibited the highest serum insulin levels (20.5 ± 2.0 µIU/mL), indicative of healthy pancreatic β-cell function and normal glucose regulation. In contrast, the diabetic control group (Group 2) showed significantly reduced insulin levels (5.2 ± 0.5 µIU/mL), reflecting the severe β-cell dysfunction caused by streptozotocin-induced diabetes. The standard control group treated with insulin (Group 3) demonstrated effective recovery, with serum insulin levels increasing to 18.5 ± 1.8 µIU/mL, nearly matching the normal control group, indicating successful therapeutic intervention. Diabetic rats treated with *X. aethiopica* extract (Group 4) and *A. melegueta* extract (Group 5) showed moderate improvements in serum insulin levels, reaching 12.0 ± 1.2 µIU/mL and 11.5 ± 1.1 µIU/mL, respectively. While these levels were significantly higher than the diabetic control group, they remained below normal values, indicating partial restoration of β-cell activity. The synergistic extract group (Group 6) demonstrated the most significant recovery among the extract-treated groups, achieving serum insulin levels of 19.0 ± 1.5 µIU/mL. This result suggests near-complete restoration of β-cell function and highlights the enhanced efficacy of the combined extract compared to individual treatments.

Table 2. Effect of Extracts on Serum Insulin Levels (µIU/mL).

Group	Serum Insulin Levels (µIU/mL)
Normal Control	20.5 ± 2.0
Diabetic Control	5.2 ± 0.5
Standard Control	18.5 ± 1.8
Xylopia Extract	12.0 ± 1.2
Aframomum Extract	11.5 ± 1.1
Synergistic Extract	19.0± 1.5

3.3. Effect of Extracts on Oxidative Stress Markers

Table 3 shows the levels of malondialdehyde (MDA) and the activities of the antioxidant enzymes superoxide dismutase (SOD) and catalase (CAT) in different treatment groups.

The normal control group (Group 1) maintained optimal oxidative stress marker levels, with low MDA (1.8 ± 0.2 nmol/mg) and high SOD (12.5 ± 1.1 U/mg) and CAT (15.0 ± 1.2 U/mg) activities, reflecting balanced oxidative and antioxidative processes. In contrast, the diabetic control group (Group 2) exhibited significantly elevated MDA levels (5.5 ± 0.4 nmol/mg), indicating increased lipid peroxidation, and reduced activities of SOD (4.0 ± 0.3 U/mg) and CAT (6.0 ± 0.5 U/mg), suggesting compromised antioxidant defenses due to diabetes-induced oxidative stress. The standard control group treated with insulin (Group 3) showed substantial improvement in oxidative stress markers, with MDA reduced to 2.0 ± 0.2 nmol/mg and SOD and CAT activities increasing to 11.8 ± 1.0 U/mg and 14.5 ± 1.1 U/mg, respectively. These values closely approached those of the normal control group, indicating effective mitigation of oxidative stress. Diabetic rats treated with *X. aethiopica* extract (Group 4) and *A. melegueta* extract (Group 5) showed moderate reductions in MDA levels (3.5 ± 0.3 nmol/mg and 3.8 ± 0.3 nmol/mg, respectively) and partial recovery of SOD (8.0 ± 0.8 U/mg and 7.5 ± 0.7 U/mg) and CAT (10.0 ± 1.0 U/mg and 9.8 ± 0.9 U/mg) activities. These improvements suggest antioxidant properties of the individual extracts, though the recovery was incomplete compared to the standard control group. The synergistic extract group (Group 6) exhibited the most pronounced recovery among the extract-treated groups, with MDA levels reduced to 2.1 ± 0.2 nmol/mg and SOD and CAT activities restored to 11.0 ± 1.1 U/mg and 13.5 ± 1.0 U/mg, respectively. These results closely aligned with the standard control group, highlighting the enhanced antioxidative efficacy of the combined extracts over the individual treatments.

Table 3. Effect of Extracts on Oxidative Stress Markers.

Group	MDA (nmol/mg)	SOD (U/mg)	CAT (U/mg)
Normal Control	1.8 ± 0.2	12.5 ± 1.1	15.0 ± 1.2
Diabetic Control	5.5 ± 0.4	4.0 ± 0.3	6.0 ± 0.5
Standard Control	2.0 ± 0.2	11.8 ± 1.0	14.5 ± 1.1
Xylopia Extract	3.5 ± 0.3	8.0 ± 0.8	10.0 ± 1.0

Aframomum Extract	3.8 ± 0.3	7.5 ± 0.7	9.8 ± 0.9
Synergistic Extract	2.1 ± 0.2	11.0 ± 1.1	13.5 ± 1.0

4. Discussion

Pancreatic β-cell dysfunction is central to the pathophysiology of diabetes, particularly type 1 and type 2 diabetes mellitus [39]. β-cells are responsible for synthesising and secreting insulin in response to elevated blood glucose levels. In diabetes, β-cells either undergo destruction, as seen in type 1 diabetes, or become dysfunctional due to insulin resistance and chronic hyperglycemia in type 2 diabetes [40]. This dysfunction leads to an insufficient insulin response, causing persistent hyperglycemia and contributing to the progression of diabetes [41]. In type 2 diabetes, β-cells initially compensate for insulin resistance by increasing insulin secretion, but over time, their function declines due to oxidative stress, inflammation, and a variety of other metabolic disturbances [42]. Thus, protecting β-cells from oxidative damage and promoting their regeneration is a key therapeutic target for managing diabetes [43].

4.1. Effects of Extracts on Fasting Blood Glucose Levels

The findings in this study show that both *X. aethiopica and A. melegueta* extracts significantly reduced fasting blood glucose (FBG) levels in diabetic rats over a 4-week period. These reductions were less pronounced than those observed in the insulin-treated group but were still substantial, particularly in the group treated with the synergistic combination of both plant extracts. The synergistic group exhibited the most significant improvement, with FBG levels decreasing from baseline values of 260 ± 10 mg/dL to 120 ± 5 mg/dL by Week 4.

Several studies have demonstrated the anti-hyperglycemic effects of both *X. aethiopica* and *A. melegueta* [26, 27, 44]. For instance, *X. aethiopica* has been shown to have antidiabetic properties due to its ability to reduce blood glucose levels and enhance insulin sensitivity [45-47]. Similarly, *A. melegueta* has been reported to exhibit hypoglycemic effects by stimulating insulin secretion and enhancing glucose utilisation [48]. The synergistic effect observed in this study is consistent with findings that combining plant extracts with complementary mechanisms may provide greater therapeutic efficacy [49]. The observed reduction in blood glucose levels may be attributed to the antioxidant and insulinotropic effects of the plant extracts, which help restore glucose homeostasis [50].

4.2. Effect of Extracts on Serum Insulin Levels

The findings of this study show the impact of the extracts on serum insulin levels. The diabetic control group showed significantly lower insulin levels (5.2 ± 0.5 µIU/mL) compared to the normal control group (20.5 ± 2.0 µIU/mL), confirming β-cell dysfunction and reduced insulin secretion in diabetes. Treatment with *X. aethiopica* and *A. melegueta* extracts resulted in higher insulin levels (12.0 ± 1.2 µIU/mL and 11.5 ± 1.1 µIU/mL, respectively) compared to the diabetic control, although they were lower than those observed in the insulin-treated group (18.5 ± 1.8 µIU/mL). The synergistic extract group had the highest insulin levels (19.0 ± 1.5 µIU/mL), suggesting that the combination of both extracts may have a more pronounced effect on stimulating insulin secretion. The ability of these extracts to enhance insulin secretion is supported by previous research. *Xylopia aethiopica* has been shown to stimulate insulin secretion through its effect on pancreatic β-cells, potentially through the modulation of the insulin

signaling pathway [51, 52]. Similarly, *A. melegueta* contains bioactive compounds that have been found to increase insulin production and improve glucose utilisation [48]. The enhanced insulin levels observed in the synergistic group may be the result of the combined effects of both plants, which may act on different pathways involved in insulin synthesis and secretion [53].

4.3. Effects of Extracts on Oxidative Stress Markers

Oxidative stress plays a significant role in the pathogenesis of diabetes, contributing to β-cell dysfunction and insulin resistance [38]. The results of this study present the effects of the extracts on oxidative stress markers, including malondialdehyde (MDA), superoxide dismutase (SOD), and catalase (CAT). The diabetic control group showed elevated MDA levels (5.5 ± 0.4 nmol/mg), indicating increased lipid peroxidation and oxidative damage, along with reduced levels of SOD (4.0 ± 0.3 U/mg) and CAT (6.0 ± 0.5 U/mg), suggesting impaired antioxidant defense mechanisms. The treatment with extracts of *X. aethiopica* and *A. melegueta* resulted in reduced MDA levels and increased SOD and CAT activity, suggesting that these extracts possess antioxidant properties [38, 54]. The synergistic extract group exhibited the most notable improvement, with MDA levels (2.1 ± 0.2 nmol/mg), SOD activity (11.0 ± 1.1 U/mg), and CAT activity (13.5 ± 1.0 U/mg) approaching those of the normal control group. This suggests that the combination of the two extracts may have a more potent antioxidant effect, by potentially reducing oxidative stress and protecting β-cells from damage [38, 55].

Empirical studies support the antioxidant effects of both *X. aethiopica* and *A. melegueta*. For example, the seeds of *X. aethiopica* have been shown to exhibit significant antioxidant activity, which could help mitigate the oxidative stress associated with diabetes [56]. Likewise, *A. melegueta* has demonstrated antioxidant properties that may protect against the oxidative damage to β-cells [57]. The enhanced antioxidant effects in the synergistic treatment group may be due to the combined phytochemicals from both extracts, which could work synergistically to neutralise free radicals and prevent cellular damage (58, 59].

5. Conclusion

This study aimed to evaluate the synergistic effects of *X. aethiopica* (Uda) and *A. melegueta* (Alligator Pepper) seed extracts on pancreatic β-cells of streptozotocin-induced diabetic rats. The findings demonstrate that both extracts possess significant antidiabetic properties, as evidenced by improved blood glucose regulation, enhanced insulin secretion, and reduced oxidative stress. These effects are largely attributable to their ability to protect and promote the regeneration of pancreatic β-cells. Importantly, the combined administration of *X. aethiopica* and *A. melegueta* produced a more pronounced therapeutic outcome compared to individual treatments, indicating a synergistic interaction that enhances overall efficacy. This suggests that the integration of both extracts may offer a more robust strategy for mitigating β-cell dysfunction and oxidative damage associated with diabetes. Finally, the study provides strong evidence supporting the potential of these plant extracts, particularly in combination, as adjuncts in diabetes management. However, future studies should:

1. Investigate the molecular mechanisms through which the combined seed extracts of *Xylopia aethiopica* (Uda) and *Aframomum melegueta* (Alligator Pepper) promote pancreatic β-cell protection and regeneration.

2. Determine the most effective and safe dosage, treatment duration, and formulation of the combined seed extracts for the management of diabetes mellitus.

3. Perform detailed histopathological studies to further confirm the extent of pancreatic β-cell protection and restoration following treatment with the combined extracts.

4. Assess the long-term safety and therapeutic effectiveness of the combined seed extracts through well-designed clinical studies to support their potential use in the management of diabetes.

Declarations

Source of Funding

This study has not received any funds from any organization.

Conflict of Interest

The authors declare that they have no conflict of interest.

Consent for Publication

The authors declare that they consented to the publication of this study.

Authors' Contribution

Both the authors took part in literature review, analysis, and manuscript writing equally.

Acknowledgement

The authors appreciate the editorial team of this journal for their constructive comments and valuable suggestions, which greatly improved the quality of this manuscript.

References

[1] Antar, S.A., Ashour, N.A., Sharaky, M., Khattab, M., Ashour, N.A., Zaid, R.T., Roh, E.J., Elkamhawy, A., & Al-Karmalawy, A.A. (2023). Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. Biomedicine & Pharmacotherapy, 168: 115734. https://doi.org/10.1016/j.biopha.2023.115734.

[2] Owo, G.J., & Beresford, S.J. (2020). Blood sugar lowering potentials of aqueous and ethanol extracts of the mixture of rinds of *Citrullus vulgaris* (watermelon) and *Chrysophyllum albidum* fruits on alloxan-induced diabetic Wistar rats. Journal of Pharmaceutical Research International, 32: 86–90. https://doi.org/10.9734/jpri/2020/v32i2130755.

[3] Yameny, A.A. (2025). Diabetes mellitus: a comprehensive review of types, pathophysiology, complications, and standards of care in diabetes 2025. Journal of Medical and Life Science, 7(1): 134-141. https://doi.org/10.21608/jmals.2025.424001.

[4] Kumar, A., Gangwar, R., Ahmad Zargar, A., Kumar, R., & Sharma, A. (2024). Prevalence of diabetes in India: A review of IDF Diabetes Atlas (10th Ed.). Current Diabetes Reviews, 20(1): 105–114. https://doi.org/10.2174/1573399819666220225112235.

[5] Azim, S.N. (2026). Type 1 Diabetes Mellitus. In Autoimmune Diseases: Understanding, Management and Clinical Practice, Pages 349-375, Cham: Springer Nature Switzerland. https://doi.org/10.1007/978-3-032-12937-6_13.

[6] Lima, J.E., Moreira, N.C., & Sakamoto-Hojo, E.T. (2022). Mechanisms underlying the pathophysiology of type 2 diabetes: From risk factors to oxidative stress, metabolic dysfunction, and hyperglycemia. Mutation Research/Genetic Toxicology and Environmental Mutagenesis, 874: 503437. https://doi.org/10.1016/j.mrgentox.2021.503437.

[7] Szmuilowicz, E.D., Josefson, J.L., & Metzger, B.E. (2019). Gestational diabetes mellitus. Endocrinology and Metabolism Clinics of North America, 48(3): 479–493. https://doi.org/10.1016/j.ecl.2019.05.001.

[8] Preda, A., Pădureanu, V., Moța, M., Ștefan, A.G., Comănescu, A.C., Radu, L., Mazilu, E.R., & Vladu, I.M. (2021). Analysis of maternal and neonatal complications in a group of patients with gestational diabetes mellitus. Medicina, 57(11): 1170. https://doi.org/10.3390/medicina57111170.

[9] Enyindah, K.C., & Owo, G.J. (2026). Inhibition of Hepatic Gluconeogenic Enzymes by Selected Medicinal Plant Extracts in Alloxan-Induced Diabetic Rats. Asian Journal of Research in Biology, 9(1): 88-98. https://doi.org/10.56557/ajrib/2026/v9i168.

[10] International Diabetes Federation (2019). IDF clinical practice recommendations for managing type 2 diabetes in primary care. https://www.idf.org/e-library/guidelines/128-idf-clinical-practice-recommendations-for-managing-type-2-diabetes-in-primary-care.html.

[11] Parker, E.D., Lin, J., Mahoney, T., Ume, N., Yang, G., Gabbay, R.A., & Bannuru, R.R. (2024). Economic costs of diabetes in the US in 2022. Diabetes care, 47(1): 26-43.

[12] Williams, R., Karuranga, S., Malanda, B., Saeedi, P., Basit, A., Besançon, S., Bommer, C., Esteghamati, A., Ogurtsova, K., Zhang, P., & Colagiuri, S. (2020). Global and regional estimates and projections of diabetes-related health expenditure: Results from the International Diabetes Federation Diabetes Atlas. Diabetes Research and Clinical Practice, 162: 108072. https://doi.org/10.1016/j.diabres.2020.108072.

[13] Jacob, B., & Narendhirakannan, R.T. (2019). Role of medicinal plants in the management of diabetes mellitus: A review. 3 Biotech, 9: 1–7. https://doi.org/10.1007/s13205-019-1901-5.

[14] Tran, N., Pham, B., & Le, L. (2020). Bioactive compounds in anti-diabetic plants: From herbal medicine to modern drug discovery. Biology, 9(9): 252. https://doi.org/10.3390/biology9090252.

[15] Vishwakarma, A., Biswas, V., Hasan, F., Praveen, A., & Sharma, D. (2025). Diabetes mellitus: An updated overview and role of medicinal plants in modern treatment. Innovative Medicines & Omics, 2(2): 20. https://journal.hep.com.cn/imo/en/10.36922/imo.7520.

[16] Owo, G.J. (2026). Alkaloid and flavonoid content of *Pterocarpus santalinoides*: Effects on pancreatic biochemistry in mice. Quantum Journal of Medical and Health Sciences, 5(1): 54-61. https://doi.org/10.55197/qjmhs.v5i1.201.

[17] Singh, A.K., Kumar, P., Rajput, V.D., Mishra, S.K., Tiwari, K.N., Singh, A.K., Minkina, T., & Pandey, A.K. (2023). Phytochemicals, antioxidant, anti-inflammatory studies, and identification of bioactive compounds using GC–MS of ethanolic novel polyherbal extract. Applied Biochemistry and Biotechnology, 195(7): 4447–4468. https://doi.org/10.1007/s12010-023-04521-3.

[18] Rahman, M.M., Dhar, P.S., Anika, F., Ahmed, L., Islam, M.R., Sultana, N.A., Cavalu, S., Pop, O., & Rauf, A. (2022). Exploring plant-derived bioactive substances as antidiabetic agents: An extensive review. Biomedicine & Pharmacotherapy, 152: 113217. https://doi.org/10.1016/j.biopha.2022.113217.

[19] Mitra, S., Tareq, A.M., Das, R., Emran, T.B., Nainu, F., Chakraborty, A.J., Ahmad, I., Tallei, T.E., Idris, A.M., & Simal-Gandara, J. (2023). Polyphenols: A First evidence in the synergism and bioactivities. Food Reviews International, 39(7): 4419–4441. https://doi.org/10.1080/87559129.2021.1952699.

[20] Nunes, C.D., Barreto Arantes, M., Menezes de Faria Pereira, S., Leandro da Cruz, L., de Souza Passos, M., Pereira de Moraes, L., Vieira, I.J., & Barros de Oliveira, D. (2020). Plants as sources of anti-inflammatory agents. Molecules, 25(16): 3726. https://doi.org/10.3390/molecules25163726.

[21] Kpomah, E.D., & Owo, G.J. (2024). Comparative In-vitro Analyses of the Anti-inflammatory, Antioxidant, and Antimicrobial Properties of Selected Soup Thickeners Commonly Used in the Niger Delta Region of Nigeria. Asian Journal of Food Research and Nutrition, 3(4): 972-982.

[22] Ajayi, A.O., Osuntokun, O.T., Olumekun, V.O., Omotuyi, I.O., & Olonisakin, A. (2022). Systemic evaluation of anti-diabetics, anti-inflammatory and secondary metabolite potentials of *Aframomum melegueta* (Roscoe) K. South Asian Journal of Parasitology, Pages 66–82.

[23] Ogbuagu, E.O., Nweke, I.N., Airaodion, A.I., & Ogbuagu, U. (2021). Weight gain reduction and hypoglycemic effects of *Xylopia aethiopica* fruit extract on Wistar rats. International Journal of Research and Reports in Hematology, 3(2): 60–68.

[24] Anyamele, T., Ugbogu, E.A., Nwankwo, V.C., & Ibe, C. (2023). A review of the traditional uses, phytochemistry and toxicological profile of *Xylopia aethiopica* A. Rich. Pharmacological Research - Natural Products, 1: 100001. https://doi.org/10.1016/j.prenap.2023.100001.

[25] Macedo, T., Ribeiro, V., Oliveira, A.P., Pereira, D.M., Fernandes, F., Gomes, N.G., Araújo, L., Valentão, P., & Andrade, P.B. (2020). Anti-inflammatory properties of X*ylopia aethiopica* leaves: Interference with pro-inflammatory cytokines in THP-1-derived macrophages and flavonoid profiling. Journal of Ethno pharmacology, 248: 112312. https://doi.org/10.1016/j.jep.2019.112312.

[26] Okhale, S.E., Ugbabe, G.E., Nwanosike, E.M., & Okoro, I. (2021). Comparative study on the essential oils of Curcuma longa L., Zingiber officinale Roscoe and *Xylopia aethiopica* (Dunal). A. Rich. Journal of Pharmacognosy and Phytotherapy, 13: 1–6.

[27] Oyedeji, T.A., Ehigie, A.F., & Nwaechefu, O.O. (2021). Antioxidant potential of methanol extract of *Xylopia aethiopica* leaves. University of Lagos Journal of Basic Medical Sciences, 6(1–2).

[28] Asemota, I., Cubbin, I., Nahar, L., & Sarker, S.D. (2026). *Aframomum melegueta* K. Schum. (Grains of Paradise) and Its Therapeutic Applications. Journal of Medicinal Natural Product, 3(1).

[29] Khan, S., Munir, A., Fayyaz, O., & Hassan, A. (2024). Phytochemical, ethnobotanical, and pharmacological activities of *Aframomum melegueta*. In Ethnobotanical insights into medicinal plants, Pages 241–278, IGI G1lobal.

[30] Toh, E.Y.S., Lim, C.L., Ling, A.P.K., Chye, S.M., & Koh, R.Y. (2019). Overview of the pharmacological activities of *Aframomum melegueta*. Pertanika Journal of Tropical Agricultural Science, 42(1).

[31] Subramanian, S., Khan, F., & Hirsch, I.B. (2024). New advances in type 1 diabetes. BMJ, Pages 384. https://doi.org/10.1136/bmj-2023-075681.

[32] Vashishtha, A. (2022). Exploring the potential of plant-based natural products as alternative medicines. International Journal of Engineering, Science and Mathematics, 11(11): 99–109.

[33] Van Hasselt, J.C., & Iyengar, R. (2019). Systems pharmacology: Defining the interactions of drug combinations. Annual Review of Pharmacology and Toxicology, 59(1): 21–40. https://doi.org/10.1146/annurev-pharmtox-010818-021317.

[34] Novoselova, E.G., Lunin, S.M., Khrenov, M.O., Glushkova, O.V., Novoselova, T.V., & Parfenyuk, S.B. (2024). Pancreatic β-cells in type 1 and type 2 diabetes: Cell death, oxidative stress and immune regulation. Cell Physiology and Biochemistry, 58(2): 144–155.

[35] Eguchi, N., Vaziri, N.D., Dafoe, D.C., & Ichii, H. (2021). The role of oxidative stress in pancreatic β-cell dysfunction in diabetes. International Journal of Molecular Sciences, 22(4): 1509. https://doi.org/10.3390/ijms22041509.

[36] Khan, S., Munir, A., Fayyaz, O., & Hassan, A. (2024). Phytochemical, ethnobotanical, and pharmacological activities of *Aframomum melegueta*. In Ethnobotanical insights into medicinal plants, Pages 241–278, IGI G1lobal.

[37] Eizirik, D.L., Pasquali, L., & Cnop, M. (2020). Pancreatic β-cells in type 1 and type 2 diabetes mellitus: Different pathways to failure. Nature Reviews Endocrinology, 16(7): 349–362. https://doi.org/10.1038/s41574-020-0355-7.

[38] Okari, K.A., Owo, G.J., Ezekwe, A.S., & Sukuba, A. (2026). Protective Effects of the Ethanolic Pulp Extract of *Lycium barbarum* (Goji Berry) on Carbon Tetrachloride–Induced Nephrotoxicity, Cardiac Dysfunction, and Oxidative Stress in Wistar Rats. Asian Journal of Research in Biology, 9(1): 50-65. https://doi.org/10.56557/ajrib/2026/v9i166.

[39] Khin, P.P., Lee, J.H., & Jun, H.S. (2023). Pancreatic beta-cell dysfunction in type 2 diabetes. European Journal of Inflammation, 21: 1721727X231154152.

[40] Mukherjee, N., Lin, L., Contreras, C.J., & Templin, A.T. (2021). β-cell death in diabetes: Past discoveries, present understanding, and potential future advances. Metabolites, 11(11): 796. https://doi.org/10.3390/metabo11110796.

[41] Dludla, P.V., Mabhida, S.E., Ziqubu, K., Nkambule, B.B., Mazibuko-Mbeje, S.E., Hanser, S., & Kengne, A.P. (2023). Pancreatic β-cell dysfunction in type 2 diabetes: Implications of inflammation and oxidative stress. World Journal of Diabetes, 14(3): 130.

[42] Dinić, S., Arambašić Jovanović, J., Uskoković, A., Mihailović, M., Grdović, N., Tolić, A., Rajić, J., Đorđević, M., & Vidaković, M. (2022). Oxidative stress-mediated beta cell death and dysfunction as a target for diabetes management. Frontiers in Endocrinology, 13: 1006376. https://doi.org/10.3389/fendo.2022.1006376.

[43] Okaiyeto, K., Adeoye, R.I., & Oguntibeju, O.O. (2021). Some common West African spices with antidiabetic potential: A review. Journal of King Saud University – Science, 33(6): 101548. https://doi.org/10.1016/j.jksus.2021.101548.

[44] Asanga, E.E., Ekeleme, C.M., Udoh, I.E., Inyang, A.N., Thomas, P.S., Joseph, A.P., & Okokon, J.E. (2025). Exploring Anti-diabetic Activity of *Xylopia aethiopica* Compounds as Potential Inhibitors of α-Amylase and α-Glucosidase: Experimental and Computational Approach. Natural Product Communications, 20(3): 1934578x251325717.

[45] Morakinyo, A.E., Adelowo, J.M., Kolawole, C.J., Babarinde, S.O., Oyedemi, O.T., Adegboyega, F., & Oyedepo, T.A. (2025). Phytochemical and Pharmacological Evaluation of *Xylopia aethiopica* (African Pepper): A Comprehensive Review. Adeleke University Journal of Science, 4(1): 587-595.

[46] Morakinyo, A.E., Oyedepo, T.A., Babarinde, O., Adelowo, J.M., Adepoju, A.E., & Oyedapo, O.O. (2019). Anti-hyperglycemic and anti-hyperlipidemic potentials of methanol leaf extracts of *Aframomum melegueta* and *Piper guineense*. European Journal of Medicinal Plants, Pages 1–8.

[47] Adefegha, S.A., Olasehinde, T.A., & Oboh, G. (2017). Essential oil composition, antioxidant, antidiabetic and antihypertensive properties of two Aframomum species. Journal of Oleo Science, 66(1): 51–63. https://doi.org/10.5650/jos.ess16183.

[48] Oloruntola, O.D., Adelegan, G.F., Falowo, A.B., Ayodele, O.A., Olaleye, D.O., Ayodele, S.O., & Adedapo, F.A. (2026). Bioactivity-guided Evaluation of Alligator pepper (*Aframomum melegueta*): Phytochemicals, Antioxidant, Anti-inflammatory, Anti-diabetic Potentials and Anti-obesity. Turkish Journal of Agriculture-Food Science and Technology, 14(1): 29-38.

[49] Alam, S., Sarker, M.M.R., Sultana, T.N., Chowdhury, M.N., Rashid, M.A., Chaity, N.I., Zhao, C., Xiao, J., Hafez, E.E., Khan, S.A., & Mohamed, I.N. (2022). Antidiabetic phytochemicals from medicinal plants: Prospective candidates for new drug discovery and development. Frontiers in Endocrinology, 13: 800714. https://doi.org/10.3389/fendo.2022.800714.

[50] Lee, J., Noh, S., Lim, S., & Kim, B. (2021). Plant extracts for type 2 diabetes: From traditional medicine to modern drug discovery. Antioxidants, 10(1): 81. https://doi.org/10.3390/antiox10010081.

[51] Asafo-Agyei, T., Appau, Y., Barimah, K.B., & Asase, A. (2023). Medicinal plants used for management of diabetes and hypertension in Ghana. Heliyon, 9(12): e22977. https://doi.org/10.1016/j.heliyon.2023.e22977.

[52] Muhammad, A.J., Muhammad, M., Yunusa, A., Mikail, T.A., Dalhatu, M.M., Habib, I.Y., Sarki, S.I., Gwarzo, M.S., Muhammad, N.A., & Mustapha, R.K. (2022). Determination of antioxidant and α-amylase inhibition properties of *Aframomum melegueta*: A potential therapeutic against diabetes mellitus. EAS Journal of Pharmacy and Pharmacology, 4(3): 43–52.

[53] Chen, X., Li, H., Zhang, B., & Deng, Z. (2022). The synergistic and antagonistic antioxidant interactions of dietary phytochemical combinations. Critical Reviews in Food Science and Nutrition, 62(20): 5658–5677. https://doi.org/10.1080/10408398.2021.1883540.

[54] Owo, G.J., Okari, K.A., & Kpomah, E.D. (2025). Flavonoid-to-Phenol Ratios in Methanolic Extracts of *Aspilia africana*: Implications for Managing Oxidative Stress. Asian Basic and Applied Research Journal, (1), 25-33.

[55] Anastasiou, I.A., Eleftheriadou, I., Tentolouris, A., Koliaki, C., Kosta, O.A., & Tentolouris, N. (2021). The effect of oxidative stress and antioxidant therapies on pancreatic β-cell dysfunction: Results from in vitro and in vivo studies. Current Medicinal Chemistry, 28(7): 1328–1346.

[56] Tijjani, H., Omar, A.A., Mohammed, A., Habibu, F.M., Maina, Y.B., & Musa, A. (2022). In: vitro antioxidant activities and blood protective effects of aqueous extracts of *Xylopia aethiopica* L. whole seed and pod. Nigerian Journal of Biochemistry and Molecular Biology, 37(1): 48-57.

[57] Temitope, O.O. (2022). Systemic evaluation of anti-diabetics, anti-Inflammatory and secondary metabolite potentials of *Aframomum melegueta* [Roscoe] K. South Asian Journal of Parasitology, 6(4): 66-82.

[58] Fakhri, K.U., Sharma, D., Fatma, H., Yasin, D., Alam, M., Sami, N., Ahmad, F.J., Shamsi, A., & Rizvi, M.A. (2025). The Dual Role of Dietary Phytochemicals in Oxidative Stress: Implications for Oncogenesis, Cancer Chemoprevention, and ncRNA Regulation. Antioxidants, 14(6): 620. https://doi.org/10.3390/antiox14060620.

[59] Darko, D., Kwekutsu, E., & Idoko, I.P. (2025). Synergistic Effects of Phytochemicals in Combating Chronic Diseases with Insights into Molecular Mechanisms and Nutraceutical Development. Int. J. Innov. Sci. Res. Technol., 10(3): 1865-1883.