Investigational
Medicinal Chemistry & Pharmacology

Research Article Open Access

# Antidiabetic effects of *Cassia abbreviata* Oliv. leaf fractions extracts in type 2 diabetic male adult Wistar rats

Emmanuel M. Musenge[1]*, Lavina Prashar[1], Sergio Muwowo[2], Isaac Mweemba[2], Victoria Mwiinga-Kalusopa[3], Marie-Claire Uwamahoro[4], Fastone M. Goma[1]

## Abstract

**Background:** Globally, type 2 diabetes mellitus, or diabetes, comprises over 96% of all diabetic cases. Therefore, we investigated the antidiabetic effects of *Cassia abbreviata* fractions of chloroform, ethyl acetate, and petroleum ether in type 2 diabetic male adult Wistar rats.
**Methods:** Type 2 diabetes was induced via a single intraperitoneal injection of streptozotocin (35 mg/kg body weight) following a high-fat, high-sucrose diet. Diabetic rats were treated with different fractions, semaglutide, or distilled water for four weeks. Blood glucose levels were monitored, and pancreatic islet tissues were examined. Data were analyzed using one-way ANOVA followed by Dunnett's post hoc test in SPSS.
**Results:** Phytochemical screening indicated the presence of cardiac glycosides, flavonoids, phenols, saponins, sterols, and terpenoids, with more observed in ethyl acetate than other fractions. At the conclusion of the study, semaglutide (0.23 mg/kg body weight) and ethyl acetate fraction (381 mg/kg body weight) exhibited statistically significantly improved oral glucose tolerance ($P < .001$) and reduced fasting blood glucose levels ($P < .001$) compared to the diabetic control. On the other hand, the normal control group had a statistically significant ($P < .05$) increase in the Lee index from diabetes induction to the end of treatment when compared with the diabetic control. Particularly, the treated groups revealed restored pancreatic islet structures, whereas the untreated diabetic group exhibited shrunken islets and cellular degeneration.
**Conclusion:** The observed effects are likely attributed to the phytochemicals present in the fractions, suggesting that *Cassia abbreviata* could be a potential therapeutic agent in type 2 diabetes management..

**Keywords:** *Cassia abbreviata;* ethyl acetate; oral glucose tolerance test; fasting blood glucose; Lee index; pancreatic islet β-cells.

*Correspondence: Tel.: +260 977 885979; E-mail address: emmanuel.musenge@unza.zm; ORCID: https://orcid.org/0000-0002-2982-5175 (Emmanuel M. Musenge)

[1]Department of Physiological Sciences, School of Medicine, University of Zambia, P. O. Box 50110, Lusaka, Zambia; [2]Department of Pathology and Microbiology, University Teaching Hospitals, PB RW1X, Nationalist Rd. Lusaka, Zambia; [3]Department of Basic and Clinical Nursing Sciences, School of Nursing Sciences, University of Zambia, P. O. Box 50110, Lusaka, Zambia; [4]Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, 3330 Hospital Drive NW, Calgary, Canada

Other authors

Email: lavina.prashar@unza.zm; ORCID: https://orcid.org/0000-0002-1438-1647 (Lavina Prashar), Email: sergiomuwowo@gmail.com; ORCID: https://orcid.org/0009-0001-2124-0228 (Sergio Muwowo), Email: imweemba70@gmail.com (Isaac Mweemba), Email: victoria.kalusopa@unza.zm; ORCID: https://orcid.org/0000-0002-9086-750X (Victoria Mwiinga-Kalusopa), Email: marieclaire.uwamahor@ucalgary.ca; ORCID: https://orcid.org/0000-0002-0750-3992 (Marie-Claire Uwamahoro), Email: gomafm@yahoo.co.uk; ORCID: https://orcid.org/0000-0002-9159-1621 (Fastone M. Goma)

Citation on this article: Musenge EM, Prashar L, Muwowo S, Mweemba I, Mwiinga-Kalusopa V, Uwamahoro M-C, Goma FM. Antidiabetic effects of Cassia abbreviata Oliv. leaf fractions extracts in type 2 diabetic male adult Wistar rats. Investigational Medicinal Chemistry and Pharmacology (2025) 8(2):110; Doi: https://dx.doi.org/10.31183/imcp.2025.00110

## Background

Globally, type 2 diabetes mellitus (T2DM) accounts for over 96% of diabetes cases [1], and approximately 95% of individuals diagnosed with T2DM are overweight or physically inactive [2]. T2DM is linked to genetic and lifestyle-related risk factors. In T2DM, obesity promotes insulin resistance through inflammatory pathways, including releasing free fatty acids and disrupting adipokine regulation. The development of T2DM typically involves insulin resistance in peripheral tissues, followed by a gradual decline in pancreatic islet function due to reduced β-cell mass or β-cell dedifferentiation. Progression of T2DM leads to hyperglycemia, oxidative stress, and potentially damaging the cardiovascular structures [1]. The economic burden is substantial, with global healthcare expenditures reaching $966 billion in 2021 [3]. Low- and middle-income countries face significant challenges in managing T2DM, with over 80% of patients residing in these regions [4].

The current treatments for T2DM are mostly palliative and fail to prevent long-term cardiovascular complications. Although conventional oral medications are effective, they can have side effects, and disparities in their access persist [4]. Eventually, over 30% of patients with T2DM require exogenous insulin therapy [5]. Due to these limitations, medicinal plants are being explored as an affordable alternative with minimal side effects [6]. *Cassia abbreviata* (*C. abbreviata*) Oliv. plant species belongs to the Fabaceae family and is native to the dry tropical areas of West, East, and Southern Africa [7]. It is a very common plant in Zambia and locally known as 'Umunsokansoka' in the Bemba language. Different parts of the plant contain a range of phytochemicals, namely alkaloids, cardiac glycosides, phenolics (phenols, flavonoids, tannins, anthraquinones), saponins, sterols, terpenes, and terpenoids [8,9]. Conversely, local traditional healers have been using *C. abbreviata* to treat various ailments such as fever, venereal diseases, barrenness in women, toothache, and diarrheal diseases. On the other hand, local scientific studies have characterized its phytochemical presence [8] and antidiarrheal properties [10].

Research has shown that chloroform (TCM), ethanol (EtOH), and methanol crude extracts of *C. abbreviata* may help improve hyperglycemia via modulation of intestinal *α*-glucosidase, hexokinase, and glucose-6-phosphatase enzyme activities in both normal and diabetic rats [9,11]. Studying potential antidiabetic effects of *C. abbreviata* fractions on pancreatic islet β-cells may potentially lead to new diabetes treatment avenues [12]. We investigated the antidiabetic effects of *C. abbreviata* fractions specifically TCM, ethyl acetate (EA), and petroleum ether (PE) in type 2 diabetic male Wistar rats.

## Methods

*Plant Material, Preparation of the Fractions Extracts and Phytochemical Screening*

*C. abbreviata* leaves were harvested in August 2022 from bushes in Kamaila Village, Chisamba District, Zambia (15°05'02.1"S, 28°17'59.9"E), at an elevation of around 1,228 m above sea level. The plant species was identified and authenticated, and a voucher specimen with accession number UZL 22418 was deposited in the Herbarium of the Department of Biological Sciences (DBS), University of Zambia (UNZA) [9]. The powdered leaves were macerated in EtOH (50 g/250 mL) at room temperature (18-25°C) for 48 hours, repeating the extraction three times. The infusion was filtered with Ahlstrom filter paper grade 1 and concentrated to dryness under reduced pressure at 40ºC using Büchi® Rotavapor® RII evaporator (Büchi Labortechnik AG), yielding the leaf ethanol crude extract (LECE). To obtain the fractions, the LECE was partitioned using the solvent extraction method [13]. Distilled water was added to the LECE in a glass flask (1 g/10 mL) and shaken until complete dissolution. The LECE was transferred into the separatory funnel, equilibrated, and successfully partitioned thrice until the mixture was clear using PE (least polar), TCM, and EA (most polar; [1:1; v/v]). The fractions were concentrated as explained above and stored in dry, airtight and waterproof containers in a refrigerator at 4ºC until required for further analysis [9]. Several qualitative tests were performed to detect various phytochemicals, including alkaloids (Dragendorff's test), cardiac glycosides (Keller-Kiliani test), flavonoids (alkaline test), phenols (ferric chloride test), saponins (foam test), and sterols and terpenoids (Liebermann-Burchard test) in the fractions. These tests rely on observing color or mixture changes to determine the presence or absence of these compounds [14,15].

*Chemicals*

The 50% dextrose and semaglutide (Reybelsus) tablets; EtOH, TCM, EA, dimethyl sulfoxide ([DMSO]; >95%); and PE 40-60 ºC were locally purchased from Link Pharmacy, Kansma Investments Limited and Chemsol Scientific Limited Zambia respectively. Other chemicals included hematoxylin and eosin staining solutions (Merck, South Africa), streptozotocin ([STZ]; AdipoGen Life Sciences, Switzerland), citrate buffer (Boster Biological Technology Company, Limited, United States of America [USA]), and sucrose (HiMedia Laboratories Private Limited, India). All the chemical substances were of AR grade. Aseel Vegetable Ghee (United Foods Company, United Arab Emirates) and coconut oil (Nuts About Cooking, South Africa) were purchased from a local shop, Melissa Supermarket, Zambia.

*Experimental Animals*

The experiments were conducted on healthy adult male Wistar albino rats aged, weighing, and length of between eight to twelve weeks, 160 - 210 g, and 18 – 22 cm respectively. This study utilised male rats due to their documented stable hormonal status and tendency to develop more pronounced insulin resistance compared to female rats [16]. They were obtained from the DBS, School of Natural and Applied Sciences (SNAS), UNZA. The animals were housed in colony cages of 6 rats per cage at ambient temperature and humidity of 25 ± 2ºC and 55 ± 10%, correspondingly. They were housed in a standard 12 h light and 12 h dark cycle environment and fed fresh NAMFEED™ standard pellets (National Milling Corporation Limited, Zambia) and water *ad libitum* (*ad lib*). The animals were allowed to acclimatize to the laboratory environment for seven days before commencement of the experiments [9,17].

This study adhered to the Animal Research: Reporting *In Vivo* Experiments guidelines and received approval from the Institution Animal Care and Use Committee of the UNZA Biomedical Research Ethics Committee (Ref. No. 1396-2020) and the National Health Research Authority (NHRA; Ref. No. NHRA00005/15/03/2021) in February 2021.

*Determination of Fasting Blood Glucose and Oral Glucose Tolerance*

A day before the procedures, the rats were fasted overnight for 14–16 h. On the morning of the tests, they were weighed, and the dose of glucose to be administered calculated for each rat. The baseline blood glucose levels (BGLs) were measured and 2 g/kg body weight (bw) of glucose solution was administered immediately using 16 g oral gavage needle. During the oral glucose tolerance test (OGTT), blood was collected by tail tip bleeding at baseline (0 min), 30 min, 60 min, 120 min, and 180 min of glucose administration. The daily blood samples collected from each rat constituted less than 1.0% of their total blood volume, which is approximately 64 mL/kg bw [18]. The baseline BGLs were taken as the fasting blood glucose levels (FBGLs). The FBGLs and OGTT were performed weekly during the study period using Accu-Chek glucometer (Roche Diagnostics GmbH, Germany).

*Anthropometric Measurements*

The bw and length were measured in all rats weekly for seven weeks using the measuring tape and Taconic rat scale (Pelouze Scale Company, USA). The bw and length were used to determine the Lee index, a measure of obesity in rats [19]. Lee index = $\sqrt[3]{\text{wt (g)}}$/length (cm) × 1000. Rats with a Lee index of more than 310 and around 300 are considered obese and overweight, respectively. This was extrapolated to estimate body fat percentage and to account for differences in body size changes of the rats during the experimental period. Additionally, an approximate 20% increase in weight after two weeks of a high-fat, high-sucrose diet (HFHSD) was taken as evidence of overweight to signify insulin resistance [11].

*Induction of Experimental Type 2 Diabetes Mellitus*

T2DM was induced in the diabetic rats by first feeding them HFHSD, which constituted ghee and coconut oil [20], along with 20% sucrose [21], which was added to drinking water. HFHSD was prepared by mixing ghee and coconut oil in the ratio of 3:1 (v/v) and was administered to the rats at a dose of 3 mL/kg bw every day using a 16 g gavage needle. The diabetic rats were fed on standard pellet diet, HFHSD and 20% sucrose for two weeks, while the normal control group was fed on a standard pellet diet only. Thereafter, a single intraperitoneal (IP) injection dose of STZ (35 mg/kg bw) was administered after an overnight fast of 14–16 h [11,22]. STZ was freshly dissolved in 0.1 M citrate buffer solution (pH 4.5) and administered immediately. Normal control group were injected citrate buffer 0.25 mL/kg bw IP [23]. Animals were allowed free access to standard pellet diet and 5% glucose solution as drinking water ad lib for 48 hours to prevent STZ-induced hypoglycemia. T2DM was confirmed three days after STZ injection and allowed to be established by day five. HFHSD and 20% sucrose were discontinued after induction of T2DM, and animals were reverted to a standard pellet diet and water ad lib. The animals were continuously monitored for any unusual behavioral, neurological, and autonomic activities. Animals with FBGL > 7.8 mmol/L twice after an overnight fast were considered diabetic and used in the study [24].

*Experimental Design*

A completely randomised design was used, and animals were randomly divided into seven groups of six animals each (n=6). Groups 1 (normal control) and 2 (diabetic control) received only the vehicle, 2.5 mL/kg bw of 0.5-1% DMSO. Groups 3 diabetic groups, received 0.23 mg/kg bw of semaglutide [25,26], the standard antidiabetic drug. Groups 4, 5, and group 6 diabetic groups received fractions of TCM 381 mg/kg bw, EA 381 mg/kg bw, and PE 381 mg/kg bw, respectively. The doses of the fractions were selected based on their efficacy in previous screening experiments for hypoglycemic effects [9]. Animals were dosed using a 16 g oral gavage needle every day from the 5$^{th}$ day after T2DM induction for four weeks. Before the commencement of treatments, animals in all the groups were fasted overnight for 14–16 h but still allowed free access to water *ad lib* throughout.

*Histopathology*

At the end of the experimental period, rats were fasted overnight for 14–16 h, weighed, and euthanized under ether anesthesia using the open drop jar method followed by cervical dislocation. Pancreatic tissue samples were dissected and immediately fixed in 10% Neutral Buffered Formalin for 48 hours. The tissues were then dehydrated through increasing concentrations of ethanol, cleared with xylene, and embedded in paraffin wax. Sections of 5 µm thickness were cut using a LEICA Microtome, deparaffinated with xylene, and hydrated with decreasing concentrations of ethanol followed by water before being stained with hematoxylin and eosin. Stained sections were again dehydrated, cleared with xylene, and mounted with a coverslip. The sections were then examined under an Olympus CX 23 Microscope and Microscope Digital Camera Olympus EP 50 to assess pancreatic islet tissue morphology and histopathological changes.

*Statistical Analysis*

One-way ANOVA followed by Dunnett's post hoc multiple comparison test was performed in IBM SPSS Statistics (Version 26). The statistical significance level was set at 5%. The data were expressed as mean ± standard error of the mean (SEM).

## Results

*Phytochemical Screening*

Phytochemical analysis confirmed the presence of cardiac glycosides, flavonoids, phenols, saponins, sterols, and terpenoids except for the alkaloids. More phytochemicals were observed in EA fraction than TCM and PE fractions (Table 1).

*Oral Glucose Tolerance Test*

At induction of T2DM, the OGTT results revealed that there was a statistically significant reduction of BGLs for all groups at times 0 to 180 min ($P < .001$) compared to the normal control group (Figure 1). On the other hand, at the end of four weeks of treatment, all the five groups, namely normal control, semaglutide 0.23 mg/kg bw, EA 381 mg/kg bw, TCM 381 mg/kg bw and PE 381 mg/kg bw, had BGLs statistically significantly reduced at times 0 min to 180 min ($P < .001$) compared to the diabetic control group (Figure 2). However, semaglutide 0.23 mg/kg bw and EA 381 mg/kg bw reduced the BGLs the most, while PE 381 mg/kg bw reduced the blood glucose levels the least.

*Fasting Blood Glucose Levels*

Our data showed that at induction of diabetes, there was a statistically significantly reduced FBGLs in the normal control group ($P < .001$) compared to the diabetic control group. At week zero (commencement of treatments), there was a statistically significant difference in FBGLs in the normal control group ($P < .001$) and TCM 381 mg/kg bw group ($P = .027$), respectively, compared to the diabetic control group. Generally, all five groups, namely normal control, semaglutide 0.23 mg/kg bw, EA 381 mg/kg bw, TCM 381 mg/kg bw and PE 381 mg/kg bw, had FBGLs statistically significantly reduced at week zero, week two, week three and week four of treatment compared to the diabetic control group ($P < .001$; [Figure 3]).

*Lee Index*

The obtained data showed that the normal control group had a statistically significant increase in the Lee index ($P < .05$) from induction of T2DM to the end of treatment compared with the diabetic control (Table 2).

*Effects of Cassia abbreviata Leaf Fractions on Pancreatic Islets*

The results showed that the normal control group had well-defined boundaries of islets, while the diabetic control group showed a reduction in size and degeneration of cellular components. The diabetic treatment groups, specifically semaglutide 0.23 mg/kg bw, EA 381 mg/kg bw, TCM 381 mg/kg bw and PE 381 mg/kg bw exhibited varying degrees of islet cell recovery and restoration at the end of the experiments (Figure 4).

## Discussion

The antidiabetic effects of *C. abbreviata* fractions in STZ-induced type 2 diabetic rats were evaluated via OGTT, FBGLs, and hematoxylin and eosin staining. The effect of *C. abbreviata* fractions on the Lee index in type 2 diabetic rats was also assessed.

Our study showed that the EA fraction contained a wide range of phytochemicals, including cardiac glycosides, flavonoids, phenols, saponins, sterols, and terpenoids, compared to the TCM and PE fractions. Phytochemicals such as flavonoids, phenols, terpenoids and sterols improve insulin sensitivity and protect pancreatic islet β-cells, whereas saponins improve lipid profiles [27,28]. These phytochemicals may play a role in managing diabetes and mitigating related complications [29-31]. The use of fractions decreases their unwanted effects and increases their therapeutic effectiveness [31,32].

Additionally, at induction of T2DM during OGTT, the normal control group had statistically significantly reduced BGLs at times 0 min to 180 min ($P < .001$) compared to the diabetic control group. There was a statistically significant difference in BGLs of the EA 381 mg/kg bw group at time 30 min ($P = .008$) compared to the normal control group. Comparable results were obtained in previous studies [33]. In insulin resistance, there is reduced sensitivity of muscles, fat, and liver cells to physiological levels of insulin, potentially giving rise to prediabetes [34]. Thus, diabetic groups had statistically significantly impaired glucose clearance compared to the normal control group. At the end of four weeks of treatment, semaglutide 0.23 mg/kg and EA 381 mg/kg bw statistically significantly reduced BGLs at times 0 min to 180 min ($P < .001$) compared to the diabetic control group. This corroborates previous studies where the treated groups had better glucose clearance compared to the diabetic control group [11,35].

Furthermore, this study revealed that, in the normal control group, semaglutide 0.23 mg/kg, EA 381 mg/kg bw, TCM 381 mg/kg bw and PE 381 mg/kg bw had FBGLs statistically significantly reduced from week zero to week four ($P < .001$) of treatment compared to the diabetic control group. The normalization of FBGLs by *C. abbreviata* fractions may be due to inhibition of α-amylase and α-glucosidase enzymes by phytochemicals. The α-amylase enzyme, which is found in saliva and pancreatic juice, is essential in converting carbohydrates into absorbable molecules. On the other hand, α-glucosidase in the mucosal brush border of the small intestine facilitates the last stages of starch and disaccharide breakdown. The inhibition of these enzymes by phytochemicals delays carbohydrate breakdown, therefore reducing the postprandial rise in blood glucose levels [28]. Also, glucose transporter type 4 (GLUT4) is the principal glucose transporter in skeletal muscle and adipose tissue. Phytochemicals can facilitate the translocation of GLUT4 to the cell membrane from intracellular vesicles to facilitate glucose uptake. This potential improvement of glucose uptake due to expression of GLUT-4 in skeletal muscle cells may contribute to effects observed [36,37]. On the other hand, semaglutide improves the efficiency of glucagon-like peptide 1 (GLP-1) function by activating GLP-1 receptors. This augments glucose-dependent insulin secretion from pancreatic islet β-cells, inhibits glucagon release from pancreatic α-cells, suppresses hepatic gluconeogenesis with consequent reduction in both fasting as well as postprandial glucose, and slows down the rate of nutrient absorption into the bloodstream [38].

With regard to the Lee index, this study showed that the normal control group had a statistically significant increase in the Lee index from induction of T2DM to the end of treatment compared with the diabetic control group ($P < .05$). In a similar study, the diabetic control group had a decreased Lee index compared to the normal control group [39]. The reduced Lee index may be influenced by weight loss as well. In diabetes, cells are unable to metabolize glucose, leading to starvation of cells despite adequate food intake. As a result, the body breaks down fat and muscle for energy, causing weight loss [40]. In our study, the reduced Lee index despite improvements in BGLs can be attributed to the treatments that were administered. Specifically, semaglutide has the ability to induce weight loss in a dose-dependent manner and with chronic administration [41]. However, another study reported improvement in weight in rats that were treated with *C. abbreviata* [11].

The histopathological evidence of the present study revealed that the normal control group had normal islets of Langerhans with well-defined boundaries interspaced among the acini. On the other hand, semaglutide 0.23 mg/kg, EA 381 mg/kg bw, TCM 381 mg/kg bw, and PE 381 mg/kg bw treated groups showed variations in recovery of islets of Langerhans cells following destruction by diabetes. Nonetheless, the diabetic control group showed shrinkage of islets of Langerhans with degeneration and necrosis of cellular components. However, previous studies on *C. abbreviata* antidiabetic properties did not investigate its effects on pancreatic islets [11,36]. *C. abbreviata's* pancreatic islet regenerative properties observed may be due to flavonoids, phenols and sterols, as these phytochemicals among other properties are believed to support the regeneration of pancreatic islet β-cells [29,30]. Although alkaloids and tannins have been shown to potentially facilitate the regeneration of damaged pancreatic islet β-cells [42], this study did not detect any presence. Other studies have shown that semaglutide can reduce β-cell

apoptosis, improve the proliferation of pancreatic islet cells, and restore islet size [43,44], corroborating with the results of our study. Phytochemicals have demonstrated the ability to improve the regeneration of pancreatic islet β-cells. A primary mechanism facilitating this regeneration is the direct stimulation of existing pancreatic islet β-cells to undergo division and replication. This process is regulated by cell cycle proteins, which can be altered by particular phytochemicals to promote pancreatic β-cell proliferation. Furthermore, phytochemicals can stimulate progenitor cells within or external to the islets of Langerhans to undergo neogenesis, leading to the generation of new β-cells. This process is essential for restoring pancreatic islet β-cell mass, especially in instances of β-cell injury or depletion, as seen in diabetes [45,46].

While this study showed that *C. abbreviata* has antidiabetic effects in type 2 diabetic male Wistar rats, it had some limitations. The study used fractions rather than isolated pure compounds, which might influence the observed effects. Furthermore, the four-week treatment duration may not be sufficient to determine the long-term efficacy of these fractions. However, in similar studies where the treatment duration was beyond four weeks, there was a significant and sustained reduction in the FBGLs to levels comparable to those of the normal control rats [47]. Despite these limitations, the findings suggest potential therapeutic benefits of *C. abbreviata* leaf fractions.

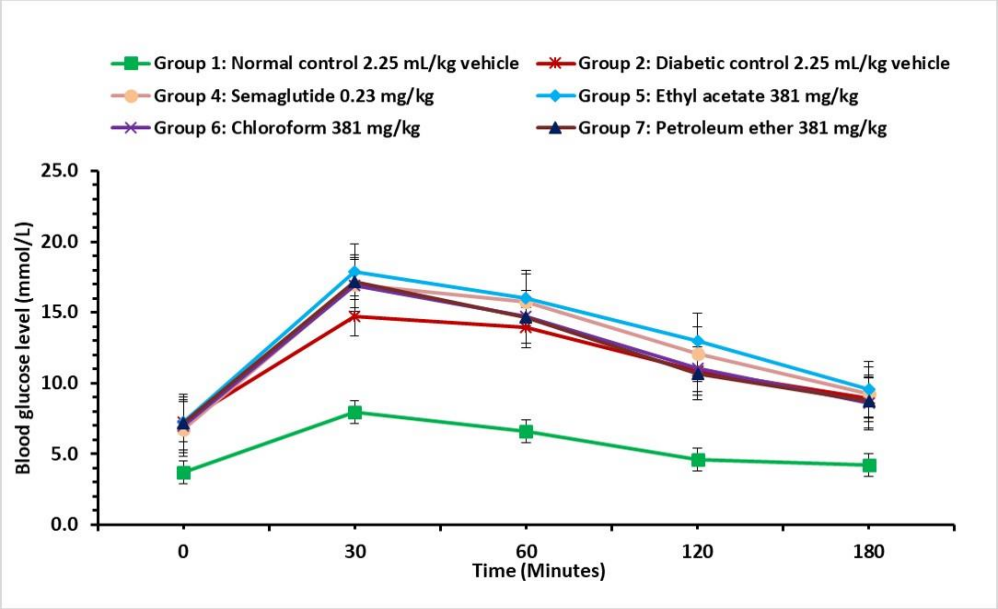


**Figure 1.** Changes in BGLs during OGTT at T2DM Induction. Peaks and troughs represent mean values ± SEM (n = 6). *P* value: < .05 as compared with normal control.

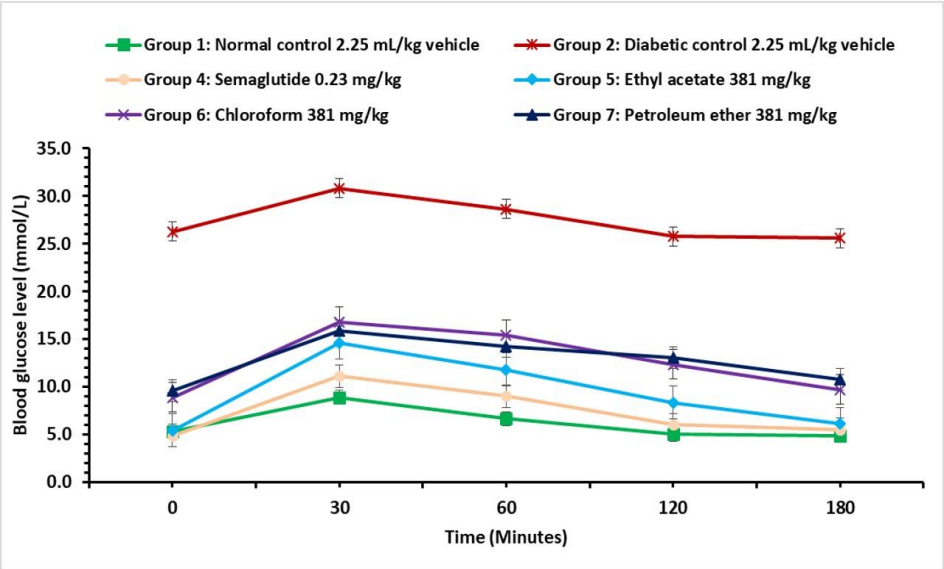


**Figure 2.** Effects of *C. abbreviata* Fractions on OGTT after four weeks of treatment.
Peaks and troughs represent mean values ± SEM (n = 6). *P* value: < .05 as compared with diabetic control.

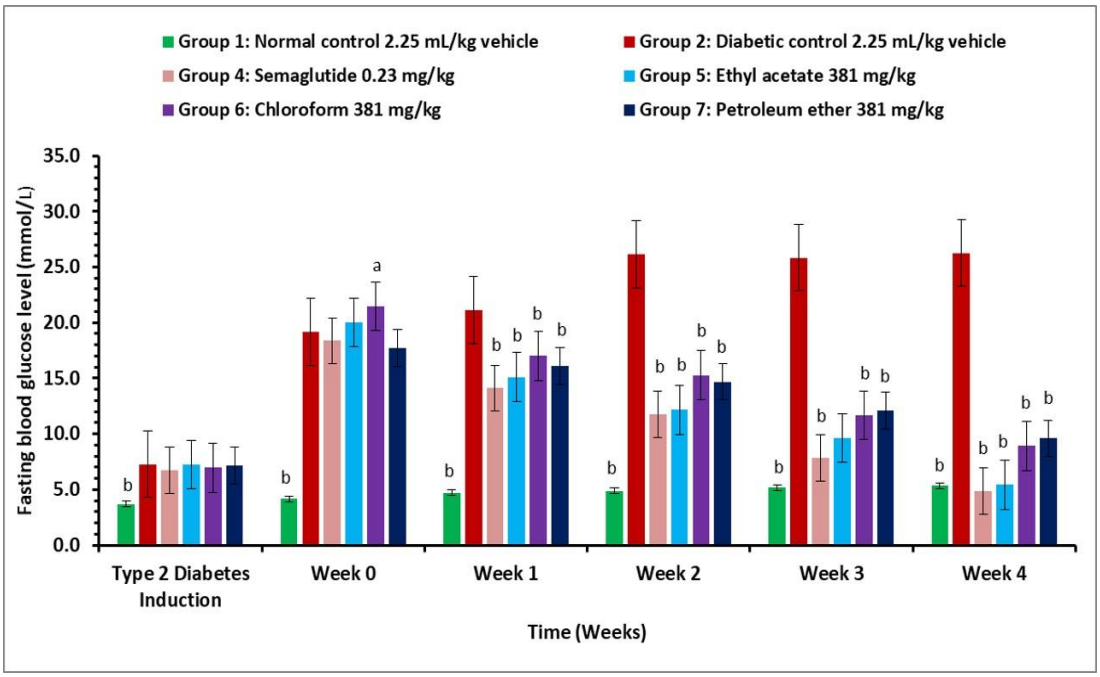


**Figure 3.** Effect of *C. abbreviata* Fractions on FBGLs.
Bars represent mean values ± SEM (n = 6). *P* values: a < 0.05, b < 0.001, as compared with diabetic control.

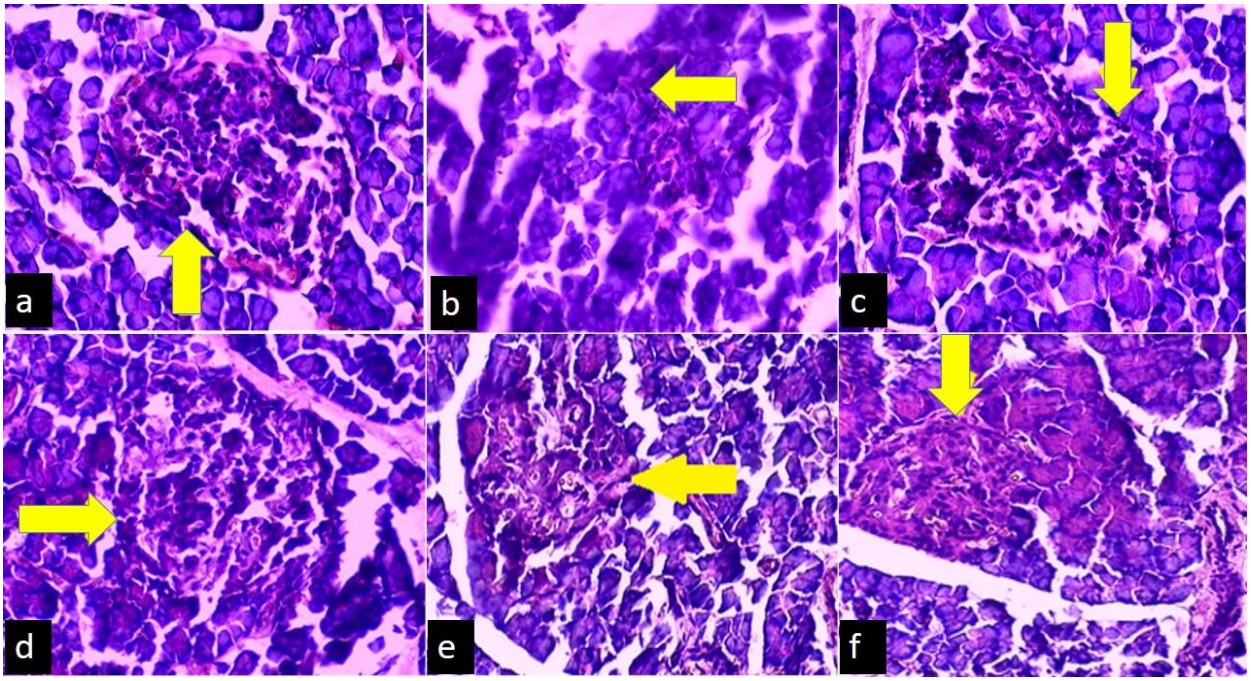


**Figure 4:** Photomicrograph of the Pancreatic Section after Four Weeks of Treatment (hematoxylin and eosin, x40 magnification).
Yellow arrows show the islet of Langerhans. a. Normal control group reveals normal islet of Langerhans with well-defined boundary interspaced among acini; b. Diabetic control group indicates shrinkage of islet of Langerhans with degeneration and necrosis of cellular components; c. Semaglutide 0.23 mg/kg bw group shows recovered and normal islet of Langerhans with well-defined boundary following destruction by diabetes; d. EA 381 mg/kg bw group reveals recovered islet of Langerhans cells with well-defined boundaries following destruction by diabetes; e. TCM 381 mg/kg bw group shows improvement in cellular density of islet of Langerhans after destruction by diabetes; and f. PE 381 mg/kg bw group reveals improvement of islet of Langerhans cells after destruction by diabetes.

**Table 1.** Phytochemical composition of *C. abbreviata* leaf fractions

| Phytochemical | Fraction | | |
|---|---|---|---|
| | **Chloroform** | **Ethyl acetate** | **Petroleum ether** |
| Saponins | - | + | - |
| Phenols | - | + | - |
| Flavanoids | - | + | - |
| Cardiac glycosides | + | + | + |
| Sterols | + | + | - |
| Terpenoids | + | + | + |
| Alkaloids | - | - | - |

Phytochemical screening results: (+) indicates presence, and (−) indicates absence.

**Table 2.** Effects of *C. abbreviata* fractions on Lee index of rats

| Group | Initial Lee index | Final Lee index | Change (%) |
|---|---|---|---|
| Diabetic control 2.5 mL/kg vehicle | 300.18 ± 3.401 | 274.13 ± 4.827 | -8.678 (Ref) |
| Normal control 2.5 mL/kg vehicle | 279.42 ± 1.153 | 292.07 ± 3.162 | 4.527 (*P* = .001)[a] |
| Semaglutide 0.23 mg/kg | 304.40 ± 8.688 | 291.33 ± 3.887 | -4.292 (*P* = .497) |
| Ethyl acetate 381 mg/kg | 300.25 ± 5.070 | 292.78 ± 4.009 | -2.488 (*P* = 244) |
| Chloroform 381 mg/kg | 303.17 ± 4.375 | 290.61 ± 4.161 | -4.145 (*P* = 517) |
| Petroleum ether 381 mg/kg | 302.20 ± 4.250 | 282.57 ± 4.037 | -6.496 (*P* = 958) |

The results are expressed as mean ± SEM (n = 6). *P* value: [a]< .05 as compared with diabetic control group.
A negative value (with minus {–} in front) indicates a percentage decrease in the Lee index, while a positive value (without any sign) indicates a percentage increase in the Lee index.

## Conclusion

The results of this study indicate that *C. abbreviata* fractions possess antidiabetic activities. The antidiabetic effects observed may be due to bioactive compounds in the fractions acting through various mechanisms. Consequently, *C. abbreviata* may hold therapeutic value in T2DM management. Future research should focus on further purification and structural characterization of bioactive compounds in these fractions, as well as investigation into the specific mechanisms of action of the bioactive compounds. Alternatively, formulating *C. abbreviata* fractions as supplements may need to be considered.

### Abbreviations

BGL Blood Glucose Level
DBS Department of Biological Sciences
DMSO Dimethyl sulfoxide
EA Ethyl acetate
EtOH Ethanol
FBGL Fasting Blood Glucose Level
GLP-1 Glucagon like peptide – 1
GLUT4 Glucose Transporter 4
HFHSD High-Fat, High-Sucrose Diet
LECE Leaf Ethanolic Crude Extract
NHRA National Health Research Authority
OGTT Oral Glucose Tolerance Test
PE Petroleum ether
SEM Standard error of the mean
SNAS School of Natural and Applied Sciences
STZ Streptozotocin
T2DM Type 2 diabetes mellitus
TCM Chloroform
UNZA University of Zambia
USA United States of America

### Authors' Contribution

We declare that this work was completed by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. EMM, LP, FMG conceived and designed the study. EMM, SM, IM, VMK, and MCU contributed to the conduct of the study. EMM and SM analyzed the data. LP and FMG supervised the whole study process. All the authors wrote and approved the final version of the manuscript for publication.

### Acknowledgments

The authors would like to appreciate the Departments of Physiological Sciences, Chemistry, and Pathology and Microbiology in the Schools of Medicine and Natural Sciences of UNZA and the University Teaching Hospital, Lusaka, Zambia respectively for granting us access to the laboratory facilities. Additionally, we would like to extend our special thanks to the staff at the animal and laboratory facilities for their valuable support and guidance. Finally, our gratitude goes to the Training and Development Office of UNZA for the special research fellowship award and support.

### Conflict of interest

The authors declare no conflict of interest

**Article history:**

Received: 10 August 2025
Received in revised form: 23 September 2025
Accepted: 28 September 2025
Available online: 28 September 2025

## References


1. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. 2020. Pathophysiology of Type 2 Diabetes Mellitus. *Int J Mol Sci*. 21(17):6275.
2. GBD 2021 Diabetes Collaborators. 2023. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: A systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 402(10397):203–234.
3. International Diabetes Federation (IDF), 2021. *IDF Diabetes Atlas.* 10th edn. Brussels, Belgium.
4. Chan JCN, Lim L-L, Wareham NJ, Shaw JE, Orchard TJ, Zhang P, Lau ESH, Eliasson B, Kong APS, Ezzati M, Aguilar-Salinas CA, McGill M, Levitt NS, Ning G, So W-Y, Adams J, Bracco P, Forouhi NG, Gregory GA, Guo J, Hua X, Klatman EL, Magliano DJ, Ng B-P, Ogilvie D, Panter J, Pavkov M, Shao H, Unwin N, White M, Wou C, Ma RCW, Schmidt MI, Ramachandran A, Seino Y, Bennett PH, Oldenburg B, Gagliardino JJ, Luk AOY, Clarke PM, Ogle GD, Davies MJ, Holman RR, Gregg EW. 2021. The Lancet Commission on diabetes: using data to transform diabetes care and patient lives. *Lancet.* 396(10267):2019–2082.
5. Wu J, Li T, Guo M, Ji J, Meng X, Fu T, Nie T, Wei T, Zhou Y, Dong W, Zhang M, Shi Y, Cheng X, Yin H, Mou X, Feng Y, Xu X, Dong J, He D, Zhao Y, Zhou X, Wang X, Shen F, Wang Y, Ding G, Fu Z, Clinical Group. 2024. Treating a type 2 diabetic patient with impaired pancreatic islet function by personalized endoderm stem cell-derived islet tissue. *Cell Discov*. 10(1):45.
6. Alshehri MA, Ali Seyed M, Alasmari A, Panneerselvam C, Hajad Alboqami H, Ahmed Alkeridis L, Almalki DA, Sayed SM, Shukry M, Aioub AA. 2024. *Retama raetam* extract for testicular health in type 2 diabetic rats: insight view on the steroidogenesis, antioxidants, and molecular docking scores of bioactive compounds against bax. *J Food Biochem.* 2024:1–16.
7. Viol DI. 2009. Screening of traditional medicinal plants from Zimbabwe for photochemistry, antioxidant, antimicrobial, antiviral and toxicological activities. MPhil Dissertation, University of Zimbabwe, Harare, p. 41.
8. Kabuka R, Mudenda S, Kampamba M, Chulu M, Chimombe T, Hikaambo CN. 2022. Phytochemical analysis of leaf, stem bark, and root extracts of *Cassia abbreviata* grown in Zambia. *Pharm Pharm*. 13(5):119–128.
9. Musenge EM, Prashar L, Ezeala CC, Goma FM. 2024. Phytochemical screening, median lethal dose and effects of *Cassia abbreviata* Oliv. crude extracts and fractions on oral glucose tolerance in non-diabetic male Wistar rats. *Med J Zambia.* 50(3):202–216.
10. Chitoti J, Kaonga P, Prasha L. 2021. Anti-diarrhoeal properties of stem bark of *Cassia abbreviata* against castor oil-induced diarrhoea in Swiss albino mice. *Med J Zambia.* 47(4):252–260.
11. Bati K, Kwape TE, Chaturvedi P. 2017. Anti-diabetic effects of an ethanol extract of *Cassia abbreviata* stem bark on diabetic rats and possible mechanism of its action: - Anti-diabetic properties of *Cassia abbreviata. J. Pharmacopunct*. 20(1):45–51.
12. Banerjee, J., Dey, B.K., Khanal, H., Dahal, B., 2015. Phytochemical screening and evaluation of antioxidant activities of different parts of *Dendrobium ochreatum. World J Pharmacol Res.* 4(8):1824-1834.
13. Truong D-H, Ta NTA, Pham TV, Huynh TD, Do QTG, Dinh NCG, Dang CD, Nguyen TKC, Bui AV. 2021. Effects of solvent—solvent fractionation on the total terpenoid content and *in vitro* anti-inflammatory activity of *Serevenia buxifolia* bark extract. *Food Sci Nutr.* 9(3):1720-1735.
14. Alamzeb M, Khan MR, Ali S, Shah SQ, Rashid M-U. 2013. Antimicrobial properties of extracts and compounds isolated from *Berberis jaeschkeana*. *Bangladesh J Pharmacol.* 8(2):107–109.
15. Tyagi T, Agarwal M. 2017. Phytochemical screening and GC-MS analysis of bioactive constituents in the ethanolic extract of *Pistia stratiotes* L. and *Eichhornia crassipes* (Mart.) solms. *J Pharmacogn Phytochem.* 6(1):195–206.
16. Vital P, Larrieta E, Hiriart M. 2006. Sexual dimorphism in insulin sensitivity and susceptibility to develop diabetes in rats. *J Endocrinol.* 190(2):425-32.
17. Jere E, Ezeala CC, Prashar L. 2021. Phytochemical studies and blood glucose lowering effect of Zambian cultivars of *Piliostigma thonningii* in alloxan - induced diabetic rats. *Med J Zambia.* 48(2):70–77.
18. Guidelines for Survival Bleeding of Mice and Rats. NIH-ARAC Guidelines [online] 2005. Jan 12. Available from: http://oacu.od.nih.gov/ARAC/Bleeding.pdf [accessed on 2025 Sept 18].
19. Bracco EF, Yang MU, Segal K, Hashim SA, Van Itallie TB. 1983. A new method for estimation of body composition in the live rat. *Proc Soc Exp Biol Med.* 174(2):143–146.
20. Munshi, R.P., Joshi, S.G., Rane, B.N., 2014. Development of an experimental diet model in rats to study hyperlipidemia and insulin resistance, markers for coronary heart disease. *Indian J Pharmacol.* 46(3):270–276.
21. Magalhães DAD, Kume WT, Correia FS, Queiroz TS, Allebrandt Neto EW, Santos MPD, Kawashita NH, França SAD. 2019. High-fat diet and streptozotocin in the induction of type 2 diabetes mellitus: a new proposal. *An. Acad. Bras. Ciênc.* 91(1):e20180314.
22. Kennard MR, Nandi M, Chapple S, King AJ. 2022. The glucose tolerance test in mice: Sex, drugs and protocol. *Diabetes Obes Metab*. 24(11):2241–2252.
23. Qian C, Zhu C, Yu W, Jiang X, Zhang F. 2015. High-fat diet/low-dose streptozotocin-induced type 2 diabetes in rats impacts osteogenesis and wnt signaling in bone marrow stromal cells. *PLOS One*. 10(8):e0136390.
24. Chis IC, Coseriu A, Simedrea R, Oros A, Nagy AL, Clichici S. 2015. In vivo effects of quercetin in association with moderate exercise training in improving streptozotocin-induced aortic tissue injuries. *Molecules.* 20(12):21770–21786.
25. Mathur N. 2023. Oral diabetes drug semaglutide fights obesity in mice: A game-changer for human treatment? *News-Medical.* Available: https://www.news-medical.net/news/20230903/Oral-diabetes-drug-semaglutide-fights-obesity-in-mice-A-game-changer-for-human-treatment.aspx (Accessed January 24).
26. Rakhat Y, Wang L, Han W, Rustemova A, Kulzhanova N, Yamada Y, Yabe D, Seino Y, Yada T. 2023. Oral semaglutide under human protocols and doses regulates food intake, body weight, and glycaemia in diet-induced obese mice. *Nutrients.* 15(17):3765.
27. Singh S, Bansal A, Singh V, Chopra T, Poddar J. 2022. Flavonoids, alkaloids and terpenoids: a new hope for the treatment of diabetes mellitus. *J Diabetes Metab Disord.* 21(1):941–950.
28. Tanveer S, Masood A, Ali S, Arshad A. 2023. Analysis of phytochemical potential and investigation of hypoglycemic effect of *Cassia fistula* L. fruit wall extracts by alpha-amylase assay and streptozotocin-induced diabetic rat model. *Thai J Pharm Sci*. 47(1).
29. De Paulo Farias D, De Araújo FF, Neri-Numa IA, Pastore GM. 2021. Antidiabetic potential of dietary polyphenols: A mechanistic review. *Food Res Int.* 145:110383.
30. Jayaraman S, Roy A, Vengadassalapathy S, Sekar R, Veeraraghavan VP, Rajagopal P, Rengasamy G, Mukherjee R, Sekar D, Manjunathan R. 2021. An overview on the therapeutic function of foods enriched with plant sterols in diabetes management. *Antioxidants.* 10(12):1903.
31. Haleem MA, ul-Ain Q, Saadiq M, Iqbal M, Gulab H, Ali S, Khan S. 2022. Probing the chemical constituents of *Cassia javanica* and its *in vitro* analyses as a potent drug. *R Soc Open Sci.* 9(1):211626.
32. Xavier F, Hanafi M, Desmiaty Y, Lotulung PDN, Minarti M, Meilawati L, Artanti N. 2025. Phytoconstituents and bioactivities of *Cassia fistula* leaf and stem bark: Antioxidant capacity and α-glucosidase inhibition via molecular docking and *in vitro* approaches. *Biocatal Agric Biotechnol.* 66:103589.
33. Holmes A, Coppey LJ, Davidson EP, Yorek MA. 2015. Rat models of diet-induced obesity and high fat/low dose streptozotocin type 2 diabetes: Effect of reversal of high fat diet compared to treatment with enalapril or menhaden oil on glucose utilization and neuropathic endpoints. *J Diabetes Res.* 2015:1–8.
34. Lee S-H, Park S-Y, Choi CS. 2022. Insulin resistance: from mechanisms to therapeutic strategies. *Diabetes Metab J.* 46(1):15–37.
35. Jangir R, Jain G, Jain G, Jain G. 2018. Evaluation of protective effects of hydroalcoholic extract of *Cassia fistula* Linn. pod on pancreas in streptozotocin-induced diabetic rats. *Pharmacogn Res.* 10(2):212.
36. Kamga-Simo FDY, Kamatou GP, Ssemakalu C, Shai LJ. 2021. *Cassia abbreviata* enhances glucose uptake and glucose transporter 4 translocation in c2c12 mouse skeletal muscle cells. *J Evid-Based Integr Med.* 26:1-11.
37. Wang T, Wang J, Hu X, Huang X, Chen G-X. 2020. Current understanding of glucose transporter 4 expression and functional mechanisms. *World J Biol Chem.* 11(3):76–98.
38. Knudsen LB, Lau J. 2019. The discovery and development of liraglutide and semaglutide. *Front Endocrinol.* 10:155.
39. Cruz PL, Moraes-Silva IC, Ribeiro AA, Machi JF, De Melo MDT, Dos Santos F, Da Silva MB, Strunz CMC, Caldini EG, Irigoyen M-C. 2021. Nicotinamide attenuates streptozotocin-induced diabetes complications and increases survival rate in rats: Role of the autonomic nervous system. *BMC Endocr Disord.* 21(1):133.
40. Chen H. 2022. Reasons for unexplainable weight loss among diabetics. *Afr J Diabetes Med.* 30(11).
41. Cawthon CR, Blonde GD, Nisi AV, Bloomston HM, Krubitski B, Le Roux CW, Spector AC. 2023. Chronic semaglutide treatment in rats leads to daily excessive concentration-dependent sucrose intake. *J Endocr Soc.* 7(7):1-17.
42. Eliakim-Ikechukwu CF, Asukwo AE, Uduak MW, Stephen OO, Churchill JI. 2013. Phytochemical composition of *Cassia alata* leaf extract and its effect on the histology of the pancreas of diabetic Wistar rats. *IOSR-JPBS.* 5(5):7–13.
43. Marinho TDS, Martins FF, Cardoso LEDM, Aguila MB, Mandarim-de-Lacerda CA. 2022. Pancreatic islet cells disarray, apoptosis, and proliferation in obese mice. The role of semaglutide treatment. *Biochimie.* 193:126–136.
44. Luo Y, Li J-E, Zeng H, Zhang Y, Yang S, Liu J. 2025. Semaglutide alleviates the pancreatic β cell function via the METTL14 signaling and modulating gut microbiota in type 2 diabetes mellitus mice. *Life Sci.* 361:123328.
45. Kimani CN, Reuter H, Kotzé SH, Muller CJF. 2023. Regeneration of pancreatic beta cells by modulation of molecular targets using plant-derived compounds: pharmacological mechanisms and clinical potential. *Curr Issues Mol Biol.* 45(8):6216–6245.
46. Chernysheva MB, Ruchko ES, Karimova MV, Vorotelyak EA, Vasiliev AV. 2024. Development, regeneration, and physiological expansion of functional β-cells: Cellular sources and regulators. *Front Cell Dev Biol.* 12:1424278.
47. Indu S, Vijayalakshmi P, Selvaraj J, Rajalakshmi M. 2021. Novel triterpenoids from *Cassia fistula* stem bark depreciates STZ-induced detrimental changes in IRS-1/Akt-mediated insulin signaling mechanisms in type-1 diabetic rats. *Molecules.* 26(22):6812.