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Comparative Anti-hyperglycemic Effects of Green Extracts of Cinnamon, Cumin and Coriander in Streptozotocin-Induced Diabetic Rats

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Abstract

DIABETES mellitus is a major global health challenge, characterized by chronic hyperglycemia resulting from insulin deficiency or resistance, and often leading to severe complications. The objective of this study was to evaluate the comparative beneficial potential of aqueous green extracts of cinnamon, cumin, and coriander on blood glucose regulation in streptozotocin (STZ)-induced diabetic rats. A chemical analysis was performed to determine total antioxidant capacity, phenolic content, total flavonoid content, DPPH (2,2-diphenyl-1-picryl-hydrazil) scavenging activity, the concentration providing 50% inhibition of DPPH (IC_{50})values, and specific phenolic compounds. Results exhibited cinnamon to have the highest antioxidant values (total antioxidant capacity 1230.4 mg ascorbic acid equivalent/100 g sample, total phenolics content 1111.523 mg Gallic acid equivalent/100g sample, and DPPH scavenging activity 80.14 %). The rat experiment involved twelve groups, with diabetes induced in groups 2–12. Following six weeks of treatment, all extract-treated groups demonstrated a statistically significant reduction in blood glucose levels, with cinnamon extract at 2 ml/kg body weight demonstrating the most pronounced hypoglycemic effect, comparable to the non-diabetic control group. These observations suggest that aqueous extracts of cinnamon, cumin, and coriander have promising potential as functional food ingredients for diabetes management, owing to their high antioxidant activity and rich content of phenolic compounds and flavonoids.

Keywords: Antioxidants; Spices; Glibenclamide; Physicochemical composition; Pancreatic Histopathology.

Introduction

Diabetes mellitus is a metabolic disorder of the endocrine system that has become a major global health challenge. In 2021, an estimated 537 million people worldwide were living with type 2 diabetes mellitus (T2DM), a number projected to increase by 46% to 783 million by 2045. Type 2 diabetes mellitus (T2DM) is characterized by persistent hyperglycemia resulting from inadequate insulin secretion or reduced insulin sensitivity [1]. Natural approaches to diabetes management, including the use of medicinal plants, are well established, and several commonly used culinary spices have also demonstrated therapeutic potential in improving diabetic conditions [2]. Cinnamon (*Cinnamomum verum*) belongs to the family Lauraceae, and is widely used as a culinary spice and traditional remedy, and is rich in polysaccharides, polyphenols, flavonoids, and saponins. Numerous studies show its ability to lower blood glucose in type 2 diabetes, supporting its potential as a complementary dietary strategy alongside standard treatments. [3]. Cumin (*Cuminum cyminum* L) is a multipurpose spice belonging to the family Apiaceae. It has long been used in ancient Ayurvedic medicine to treat gastrointestinal disorders, diarrhea, and jaundice. Oral administration of cumin significantly lowers blood glucose and glycosylated hemoglobin levels, while also preventing weight loss. Additionally, cumin has been shown to reduce phospholipid, cholesterol, free fatty acid, and triglyceride levels in the tissues and plasma of experimental rats [4]. Coriander (*Coriandrum Sativum* L.), belonging to

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the family Apiaceae, is one of the most ancient spices utilized not only for culinary purposes but also for its medicinal attributes, including diabetes. The potent antioxidant properties of *C. Sativum* provide a key mechanism to support its protective effects against neurodegenerative diseases, metabolic syndrome, and cancer. These nutritional and therapeutic values, along with their integration into daily uses, make the coriander a distinguished functional food of interest [5].

The concept of green extraction of natural products is a modern approach designed to address the challenges of the 21st century by safeguarding both the environment and consumers. It also aims to encourage industries to be more eco-friendly, cost-effective, and innovative. The growing interest in using water as a green solvent can be attributed to its widespread availability and affordability, as well as its eco-friendly characteristics, such as non-toxicity, renewability, safety, ease of handling, and simple treatment and degradation processes [6]

Coriander, cinnamon, and cumin have been individually studied for their antidiabetic properties. However, direct comparative studies evaluating these three spices under identical experimental conditions remain limited. The novelty of this study lies in its comparative approach, aiming to elucidate the relative efficacy and underlying mechanisms of these extracts in managing diabetes. This will be made through the comparative evaluation of the antioxidant and chemical composition of three aqueous "green" extracts of cumin, cinnamon, and coriander, and compare three different concentrations of aqueous extracts of each spice on the management of hyperglycemia and histopathology of pancreatic tissues in diabetic rats

Material and Methods

The following part describes the materials and methods used in the present study. The study was conducted during 2023-2024. All laboratory experiments were performed in the Regional Center for Food and Feed at the Agricultural Research Center, Giza, Egypt.

Plants

Three plants were used in the present study, namely (Cinnamon) *Cinnamomum verum* Park, (Cumin) *Cuminum cyminum* L, and (Coriander) *Coriandrum sativum* L seeds. They were purchased from a hypermarket, cleaned of solid materials and finely ground by an electric grinder, and stored in zipped plastic bags at 4ºC.

Animals

Seventy two adult male albino rats were used. The present study was conducted at the Experimental Animal House of the Food Technology Institute, Agricultural Research Centre in Giza, using Wistar rats weighing 200 ±10 g.

Chemicals

In this investigation, glibenclamide was purchased from the Sanofi Aventis company. Streptozotocin (STZ) was purchased from Sigma-Aldrich, and all chemicals were of analytical purity.

Kits

The blood analysis kits for this study (which included glucose) were acquired from Spectrum, Egyptian Company for Biotechnology (S.A.E.) in the Obour City Industrial Area of Cairo, Egypt.

Preparation of extracts

Each spice's green (aqueous) extract was made independently by mixing 100 g of powdered cumin, coriander, or cinnamon with one liter of distilled water. After 30 minutes of boiling in conical flasks, the mixtures were filtered. After being dried at 50°C, the resultant filtrates (aqueous extracts) were placed in airtight brown bottles and refrigerated at 4°C until they could be further examined. The extracts used in the rats' experiment were prepared freshly every week or on demand in the same manner (10 g of spice/100 ml of distilled water), and the filtrates (stock solutions) were stored in airtight brown bottles in a refrigerator at 4°C until use. The following doses were administered during the experiment: cinnamon extract (1, 2, and 3 ml/kg body weight), cumin extract (1.5, 2.5, and 3.5 ml/kg body weight), and coriander extract (2, 4, and 6 ml/kg body weight).

Proximate Analysis

The amounts of moisture, protein, total fat, crude fibre, and ash [7]. Total carbohydrate, also known as non-nitrogen extract [7]. by difference = 100 - (protein + fat + fibre + moisture + ash).

Minerals Analysis

Mineral contents were determined by atomic absorption spectrophotometer (Agilent Technologies 4210 MP-AES) [8].

Total antioxidant capacity

The total antioxidant capacity of spices extracts was determined using the phosphomolybdenum method [9]. The antioxidant activity was expressed as mg ascorbic acid equivalent/100 g sample (mgAAE/100g).

Total phenols and flavonoids

Total phenolic content was determined using the Folin-Ciocalteau method [10] Gallic acid is used as standard and the results are expressed as mg Gallic acid equivalent/100g sample (mgGAE/100g). Total flavonoids were determined using the aluminium chloride method [11]. Quercetin is used as standard and the results are expressed as mg Quercetin equivalent/100g sample (mgQE/100g). The TPC of the extracts was determined using the Folin–Ciocalteu method. A mixture of 0.5 mL of extract,

2.5 mL of 10% Folin–Ciocalteu reagent, and 2 mL of 7.5% sodium carbonate was incubated at room temperature for 30 minutes. The absorbance was measured at 765 nm using a UV-Visible spectrophotometer (Shimadzu UV-1800, Japan). Gallic acid was used as the standard, and results were expressed as mg gallic acid equivalents (GAE) per gram of extract.

Determination of DPPH%

The free radical scavenging activity of different extracts were measured by the 2, 2- diphenyl-1 picryl- hydrazil (DPPH) method [12]., with minor modifications. Briefly, 1 mL of 0.1 mM DPPH solution in methanol was mixed with 1 mL of the extract at different concentrations. The mixture was incubated in the dark for 30 minutes at room temperature. The absorbance was measured at 517 nm using a UV-Visible spectrophotometer (Model: Shimadzu UV-1800, Japan). The concentration of spice extract providing 50% inhibition of DPPH (IC50) was calculated from the graph plotting inhibition percentage against extract concentration [13].

Determination of Phenolic Compounds

Phenolic compounds of dried spice extract powder were determined by high-performance liquid chromatography HPLC [14]. High-performance liquid chromatography (HPLC) was used to identify and quantify the phenolic compounds in the extracts. The analysis was performed on an Agilent 1260 Infinity HPLC system equipped with a diode-array detector (DAD). Separation was achieved using a C18 column (250 × 4.6 mm, 5 µm) at 25°C. The mobile phase consisted of solvent A (0.1% formic acid in water) and solvent B (methanol), with a flow rate of 1.0 mL/min using a gradient elution. Detection was carried out at 280 nm and 320 nm. Identification of compounds was done by comparing retention times and UV spectra with those of standards.

Biological Experimental Design

Seventy-two rats were housed in a controlled environment according to the guidelines for the care and use of laboratory animals. During the acclimatization (2 weeks) and experimental (6 weeks) periods, all rats were provided with tap water and a balanced basal diet ad libitum.

Type 2 diabetes mellitus was induced in rats of groups 2–12 by fasting them for 8–10 hours, followed by a single intraperitoneal injection of streptozotocin (STZ) at a dose of 50 mg/kg body weight [15]. STZ was freshly prepared in cold 0.1 M citrate buffer (pH 4.5). To prevent acute hypoglycaemia, rats were given a 10% glucose solution for 24 hours post-injection. After one-week, fasting blood glucose levels were measured, and rats with glucose levels ≥ 200 mg/dL were considered diabetic and included in the diabetic groups.

Diabetic rats in groups 3–11 received daily oral doses of one of the three aqueous plant extracts via stomach tube. Group 12 received glibenclamide (0.5 mg/kg body weight) daily as a standard antidiabetic drug [16].

The animals were randomly divided into 12 groups (n = 6 per group) as follows:

G1: Normal control
G2: Diabetic control
G3–G5: Diabetic + cinnamon extract (1, 2, and 3 mL/kg)
G6–G8: Diabetic + cumin extract (1.5, 2.5, and 3.5 mL/kg)
G9–G11: Diabetic + coriander extract (2, 4, and 6 mL/kg)
G12: Diabetic + Glibenclamide (0.5 mg/kg)

Treatments were administered orally for 6 consecutive weeks. Blood samples were collected at baseline and the end of the study for the assessment of glucose levels. Pancreatic tissues were also collected for histopathological examination.

All experimental procedures were conducted at the Food Technology Research Institute, Agricultural Research Center, Giza, Egypt.

Blood analysis

After blood centrifugation, serum was used for the following tests:

a. Serum glucose was measured using the technique described by [17].

Histopathological examination

Specimens from the pancreas were collected in 10% neutral formalin buffer and processed by the paraffin-embedding technique. Tissue sections (4µm thick) were stained using Hematoxylin and Eosin stain [18]. and examined using light microscopy.

Statistical analysis

Statistical analysis was performed with SPSS software. Results were expressed as means ± SE (standard error), and statistically analyzed using the least significant difference test (LSD) when calculated probability value $p \leq 0.05$, and one-way analysis of variance (ANOVA) by Duncan's method was used for statistical analysis of mean differences among groups. Tukey's Honestly Significant Difference test (Tukey HSD) was performed as a post hoc test to compare the means. The significant differences among treatments were expressed using different superscript letters. [19].

Results

Physicochemical composition

The results of proximate analysis showed a significant difference between coriander, cumin, and cinnamon extracts, as shown in Table 1. The three extracts have a comparable moisture content.

Cinnamon extract contains the largest value of fiber (2.34%), carbohydrate, and energy (83.77% and 351.76 kcal, respectively). Cumin extract had the greatest content of ash (18.26%), followed by coriander and cinnamon extracts (14.32% and 5.11%, respectively). Coriander extract contained the greatest content of protein (15.8%) and the highest amount of fat (4.34%). The results of some elements in the three extracts are presented in Table 1. The cinnamon extract showed the highest level of manganese (569.4 mg/kg) and selenium (8.19 mg/kg), while the cumin extract had the greatest zinc and copper concentration (76.2 and 58.1 mg/kg, respectively). The coriander extract contained the highest iron level (796.8 mg/kg), followed by cumin (230.1 mg/kg) and cinnamon (179.6 mg/kg).

Total antioxidant

As shown in Table 2, all three spice extracts demonstrated measurable antioxidant capacities. However, the total antioxidant capacity of the cinnamon extract (1230.4 mg AAE/100g) was significantly higher than that of the cumin (378.07 mg AAE/100g) and coriander (359.91 mg AAE/100g) extracts. This corresponds with the results of the total phenolic content (1111.52 mg GAE/100g) and DPPH radical scavenging activity (80.14%), which were also significantly the highest in cinnamon. In contrast, cumin extract showed significantly the highest total flavonoid content (110.22 mg QE/100g) and the best value of IC_{50}.

Polyphenol contents by HPLC

High-performance liquid chromatography (HPLC) was used to identify and quantify the polyphenolic compounds in the three aqueous extracts, as shown in Table 2. The cinnamon extract contained several polyphenols, with the highest concentrations of daidzein (11,019.26 µg/g), chlorogenic acid (CGA, 1,355.54 µg/g), cinnamic acid (1,147.07 µg/g), gallic acid (912.90 µg/g), and hesperetin (770.27 µg/g). In the cumin extract, the major compounds were chlorogenic acid (3828.35 µg/g), ferulic acid (1774.55 µg/g), coumaric acid (1007.67 µg/g), and rutin (7581.52 µg/g). The coriander extract contained lower amounts of polyphenols compared to the other extracts, with chlorogenic acid (299.76 µg/g), gallic acid (207.38 µg/g), syringic acid (191.30 µg/g), and caffeic acid (151.04 µg/g) being the most abundant. Daidzein (DDZ) was found at the highest concentration in cinnamon extract, followed by coriander and cumin extracts (11019.26, 96.17, and 77.12 µg/g, respectively). Chlorogenic acid (CGA) was highest in cumin extract, followed by cinnamon and coriander (3828.35, 1355.54, and 299.76 µg/g, respectively). Gallic acid (GA) was most abundant in cinnamon extract, then cumin and coriander (912.90, 713.45, and 207.38 µg/g, respectively). Ferulic acid (FA) showed the highest concentration in cumin extract, compared to coriander and cinnamon (1774.55, 129.24, and 15.83 µg/g, respectively).

Effect of the three extracts on Biochemical Parameters

The results of blood glucose levels, presented in Table 4, showed that after one week of STZ injection, the "initial" fasting blood glucose levels in diabetic rats (Groups 2–12) were significantly higher ($p \leq 0.05$) than those in the non-diabetic control group (G1). After six weeks of treatment (final), glucose levels in all groups administered various concentrations of the three spice extracts significantly decreased and approached normal glucose levels, except for Group 2 (positive control) and Group 12 (standard drug), which showed reductions but did not reach normal levels. Cinnamon extract at 2 ml/kg bwt. reduced glucose levels from 568 ± 13.04 mg/dL before treatment to 94.2 ± 23.82 mg/dL after 6 weeks. These reductions were statistically significant compared to the positive control group, indicating a potent hypoglycemic effect. The wide standard errors in some groups may be due to inter-individual differences, small subgroup sizes, and natural biological fluctuations.

Histopathological Changes of the Pancreas

In the present study, after six weeks of treatment, pancreatic histological examination of the negative control group revealed normal pancreatic architecture (Fig. 1- G1). In contrast, rats injected with STZ (positive control, G2) exhibited pancreatic damage characterized by necrosis, lysis of some pancreatic acini and islets, and infiltration of inflammatory cells in the perivascular regions and pancreatic islets (G2). All treated groups (G3–G11), which received various concentrations of spice extracts, demonstrated noticeable amelioration in pancreatic structure, as shown in Figures 3 to 11. Notably, groups G4 and G5, treated with cinnamon extract at 2 and 3 ml/kg bw.t, respectively, showed marked improvement. However, mild pathological changes were still observed in some groups, including slight atrophy of certain pancreatic islets in rats treated with cinnamon extract at 1 ml/kg bw.t. (G3), mild infiltration of inflammatory cells in the portal area in rats treated with cumin extract at 1.5 ml/kg bw.t. (G6)). The pancreas of rats treated with the standard drug (G12) showed severe acellular zones with lytic pancreatic tissue and necrosis.

Discussion

Physicochemical composition

Proximate analysis of plant extracts plays a critical role in determining their nutritional and functional value, particularly for medicinal and food applications. In the present study, the significant variation in the proximate composition of cinnamon, cumin, and coriander aqueous extracts highlights the biochemical diversity and functional specificity of

these spices. Cinnamon extract demonstrated the highest levels of fiber (2.34%), carbohydrates (83.77%), and energy (351.76 kcal/100g). This compositional profile supports cinnamon's role as a high-energy botanical with metabolic benefits, particularly in glycemic modulation and gut health, as dietary fiber has been associated with slowing glucose absorption, enhancing satiety, and modulating gut microbiota, all of which are relevant in diabetes management [20], which emphasize cinnamon's role as a nutritionally dense spice with metabolic regulatory properties. Cumin extract, on the other hand, contained the highest ash content (18.26%), suggesting a superior total mineral load. The high ash value implies a rich profile of inorganic nutrients, which may explain cumin's traditional use in enhancing digestive enzyme activity, supporting liver function, and improving mineral balance in the body. This interpretation is consistent with its ethnopharmacological use [21]. Coriander extract showed the highest protein (15.8%) and fat content (4.34%), indicating a robust macronutrient contribution, particularly in providing essential amino acids and unsaturated fatty acids, which are crucial for cellular repair, hormone synthesis, and energy metabolism.

Collectively, these differences in macro- and micronutrient content reflect the unique nutritional and therapeutic potential of each extract. Their combined or targeted use in functional foods or dietary interventions may offer synergistic health benefits, especially in the context of metabolic disorders, oxidative stress management, and nutrient deficiencies.

Total antioxidant

The results indicated that cinnamon exhibited the highest antioxidant values, highlighting its potent antioxidant activity and confirming its role as a valuable natural source of antioxidants. Consistent with these findings, both water and ethanolic extracts of cinnamon have been reported to contain considerable levels of phenolic compounds and antioxidants [22]. Phenols and flavonoids are known for their various biological activities, including antiviral, antibacterial, and antihepatotoxic effects; thus, the antioxidant properties of the tested spices can be largely attributed to their phenolic acid and flavonoid content [23]. Cumin demonstrated the highest total flavonoid content, which may explain its ranking as the second most potent antioxidant among the tested spices. Similarly, aqueous extracts of cumin, prepared with a 1:40 solid–liquid ratio, have been reported to contain total phenolic compounds (14.7 mg GAE/g DM) and exhibit antioxidant activity (0.52 mg Trolox equivalents/mL) [24]. In contrast, coriander extract showed significantly lower antioxidant activity compared to cinnamon and cumin. Nevertheless, coriander's aqueous extract still possesses notable antioxidant properties, as confirmed by previous studies [25].

Polyphenol contents by HPLC

The polyphenolic profiles of the three spice extracts revealed distinct compositional differences. Cinnamon extract contained several polyphenols, ranked: daidzein, chlorogenic acid, cinnamic acid, gallic acid, and hesperetin. While in cumin extract, the major compounds were chlorogenic acid, ferulic acid, coumaric acid, and rutin, respectively. The coriander extract, while exhibiting a comparatively lower total polyphenol content than the other evaluated extracts, still contained notable amounts of chlorogenic acid, gallic acid, syringic acid, caffeic acid, and others. This composition suggests that, despite the lower concentration, coriander may exert significant bioactivity due to the presence of these bioactive compounds, which are well-documented for their antioxidant and therapeutic effects. Collectively, the three spices were found to contain a diverse array of phenolic compounds with a range of biological activities. An overview of these compounds and their properties is presented below. This is consistent with our experimental results, which demonstrated significant modulatory effects on blood glucose levels, and pancreatic tissue architecture. Daidzein (DDZ) was found at the highest concentration in cinnamon extract (11019.26 µg/g) followed by coriander (96.17 µg/g) and cumin extract (77.12 µg/g). Daidzein exhibits a diverse spectrum of pharmacological and health-promoting effects, encompassing cardiovascular health, cholesterol modulation, anticancer properties, antifibrotic effects, and antidiabetic actions, thereby rendering it advantageous for the management of numerous health conditions. Its molecular structure and functional mechanisms closely resemble those of human estrogens, which are crucial in mitigating the risks associated with osteoporosis, malignancies, and postmenopausal complications [26]. Chlorogenic acid (CGA) was highest in cumin extract (3828.35), followed by cinnamon and coriander (1355.54 and 299.76 µg/g, respectively). CGA has been recognized as a promising antioxidant [27], with reported anti-inflammatory, antihypertensive, and antiviral activities. It also exhibits antimicrobial efficacy against a wide variety of pathogens, including bacteria, yeasts, molds, viruses, and amoebas [28]. Cinnamic acid (CA), primarily found in cinnamon, has demonstrated the ability to reduce hyperglycemia-induced complications in HepG2 cells by downregulating the expression of inflammatory genes (e.g., IL-6 and NF-κB) and inhibiting DPP4 expression. Additionally, it limits oxidative stress, as demonstrated by reduced malondialdehyde (MDA) levels and increased levels of antioxidant enzymes like superoxide dismutase (SOD) and glutathione (GSH) [29]. Gallic acid (GA) was most abundant in cinnamon extract (912.90

µg/g), followed by cumin (713.45 µg/g) and coriander (207.38 µg/g). GA has been shown to reduce intracellular reactive oxygen species (ROS) production, particularly in lipopolysaccharides (LPS)-stimulated cells such as macrophages, neutrophils, and corneal epithelial cells, suggesting its protective role against oxidative stress [30]. Ferulic acid (FA) is found in the highest concentration in cumin extract (1774.55 µg/g), compared to coriander and cinnamon (129.24 and 15.83 µg/g, respectively). FA is a widely occurring phytochemical derived from the metabolism of phenylalanine and tyrosine, known for its strong antioxidant properties. It contributes to various biological effects, including anti-allergic, anti-inflammatory, antithrombotic, anticancer, and sperm viability-promoting activities [31]. Coumaric acid, predominantly found in cumin, displays diverse biological activities, such as antioxidant, antimicrobial, anticancer, antiviral, antiplatelet aggregation, anti-inflammatory, analgesic, anxiolytic, antipyretic, and anti-arthritic effects. Additionally, it has been reported to help in managing conditions such as diabetes, obesity, hyperlipidemia, and gout. [32].

Rutin, predominantly present in cumin, is a naturally occurring bioflavonoid widely acknowledged as one of the most effective antioxidants [33]. As a powerful antioxidant, Rutin has the potential to improve nitrergic and/or endothelial dysfunction in diabetic animal models [34]. Interestingly, chlorogenic acid emerged as the predominant phenolic acid in the present study, whereas caffeic acid had previously been reported as the major compound among four fractions isolated by column chromatography from an aqueous coriander extract [35].

Blood glucose

This study provides a comprehensive evaluation of the antidiabetic effects of cinnamon, cumin, and coriander in STZ-induced diabetic rats. Among all tested treatments, cinnamon extract at a dose of 2 ml/kg, exhibited the most significant reduction in serum glucose levels, restoring them to near-normoglycemic values (94.2 mg/dl), closely comparable to those observed in the non-diabetic control group. These results were further confirmed by longitudinal monitoring, where cinnamon consistently outperformed other treatments in lowering blood glucose. In agreement, Garg [4] reported a significant reduction in blood glucose in diabetic rats treated with cinnamon extract over eight weeks (210 ± 29.9 vs. 449 ± 48.4 mg/dL; $P \leq 0.001$), underscoring its sustained hypoglycemic potential. This remarkable effect can be largely attributed to cinnamon's rich phytochemical profile, particularly its high concentration of phenolic compounds such as cinnamic acid, gallic acid, daidzein, and hesperetin. Importantly, recent findings suggest that cinnamon polyphenols may also regulate gene expression related to insulin signaling. For instance, they may upregulate insulin-regulating genes, including INS, PDX1, and MAFA, which are commonly downregulated in diabetic conditions due to hyperglycemia-induced glucotoxicity. In addition, compounds such as chlorogenic acid (CGA), cinnamic acid, gallic acid, and hesperetin found in cinnamon are known for their anti-inflammatory, antioxidant, and insulin-sensitizing properties. Alongside cinnamon, both cumin and coriander extracts produced statistically significant reductions in blood glucose levels across all tested doses, though to a lesser degree. This moderate but notable hypoglycemic activity is consistent with previous findings: cumin has been shown to enhance insulin secretion, promote glycogen synthesis, and protect pancreatic β-cells, while also exerting anti-inflammatory effects and modulating oxidative biomarkers [36]. Similarly, coriander has demonstrated time-dependent hypoglycemic effects, where plasma glucose levels decreased steadily from Day 7 and reached normoglycemia by Day 21, although the cessation of treatment reversed the effect, suggesting the need for continued administration [37]. The hypoglycemic effects of cumin and coriander can be attributed to compounds such as chlorogenic acid, ferulic acid, rutin, and gallic acid, which are known to inhibit α-amylase and α-glucosidase enzymes, suppress hepatic gluconeogenesis, and enhance peripheral glucose utilization. Furthermore, specific signature bioactive compounds in each extract may play unique roles: Cinnamaldehyde (from cinnamon) has been shown to enhance insulin receptor sensitivity, reduce inflammatory signaling, and inhibit gluconeogenic pathways. Cinnamaldehyde (from cumin) modulates key metabolic enzymes and improves hepatic insulin sensitivity. Linalool (from coriander) has demonstrated activity in reducing oxidative damage and improving insulin action. Taken together, these findings suggest that the glucose-lowering effects observed in this study result from a multi-targeted mechanism involving antioxidant defense, insulin signaling enhancement, β-cell preservation, and gene expression modulation. The data strongly support the use of cinnamon as a particularly potent functional food for glycemic control in diabetic conditions, while also highlighting the therapeutic contributions of cumin and coriander in a complementary or supportive role [38].

Histopathological Changes of the Pancreas

Histological analysis of the pancreatic tissue in the STZ-induced diabetic group (Fig.1) G2) revealed extensive structural deterioration, including widespread necrosis, lysis of both acinar and islet cells, and dense infiltration of inflammatory cells. These histopathological alterations align with the well-documented β-cell cytotoxicity of

streptozotocin, which induces DNA alkylation and oxidative stress, leading to impaired insulin synthesis and persistent hyperglycemia. In stark contrast, the groups treated with aqueous extracts of cinnamon, cumin, and coriander (G3–G11) exhibited varying degrees of histological restoration and regeneration of pancreatic architecture. The most profound improvement was noted in groups G4 and G5, which received cinnamon extract at 2 and 3 ml/kg bw.t, respectively. These groups demonstrated restored islet architecture, reduced inflammatory cell infiltration, and intact acinar structures, indicating substantial tissue regeneration. This structural recovery strongly correlates with the glycemic normalization observed in G4 (94.2 mg/dL, Table 4). Moderate histological improvements were also observed in G3 (1 ml/kg cinnamon) and G6 (1.5 ml/kg cumin), consistent with their intermediate glucose-lowering and antioxidant activities. While cumin displayed less glycemic potency, its presence of chlorogenic acid, rutin, and rosmarinic acid (Table 3) provides a mechanistic basis for its anti-inflammatory and cytoprotective effects on pancreatic tissue. Coriander-treated groups (G9–G11) exhibited partial restoration of pancreatic histoarchitecture, with mild inflammatory persistence, especially at moderate doses (G10: 4 ml/kg). Nevertheless, coriander's high iron content (796.8 mg/kg, Table 1) and presence of caffeic acid, ferulic acid, and quercetin (Table 3) may contribute to its ability to attenuate oxidative damage and preserve islet structure to a certain extent. of particular interest, the standard drug-treated group (G12) displayed significant necrotic and lytic changes in pancreatic tissue, despite modest improvements in serum glucose levels. This paradox highlights the possibility of non-antioxidant mechanisms and potential cytotoxicity of the pharmacological agent used, thereby underscoring the superior safety and tissue-protective profile of the natural extracts. Taken together, the histological outcomes strongly reinforce the biochemical and antioxidant data, indicating that cinnamon, cumin, and coriander possess multimodal protective properties. These include: Glycemic regulation, Oxidative stress reduction, Anti-inflammatory action, Islet cell preservation The strong correlation between histopathological recovery and biochemical markers (Tables 1–4) further supports the potential of these extracts as promising complementary therapies for diabetes, targeting both metabolic control and organ protection. At the end of treatments, histological examination of pancreatic tissues revealed that all treated groups (Groups 3–11), which received various concentrations of spice extracts, exhibited notable amelioration in pancreatic architecture compared to the diabetic control. Notably, cinnamon extracts at 2 and 3 mL/kg showed marked improvement in islet cell morphology, indicating a protective or regenerative effect on β-cells. However, mild pathological changes were still observed in some treated groups. For instance: a slight atrophy of some pancreatic islets was noticed in rats treated with cinnamon extract 1 ml/kg (G3), slight infiltration of inflammatory cells in portal area as in rats treated with cumin extract 1.5 mg/kg (G6). These mild alterations suggest partial protection at lower or moderate doses, potentially reflecting a threshold-dependent effect of the bioactive compounds within the extracts. The protective effects observed may be linked to the presence of phenolic compounds with their antioxidant and anti-inflammatory properties, which likely play a key role in preserving cellular and tissue integrity, thereby mitigating damage and supporting pancreatic recovery. For example, chlorogenic acid (CGA), found in all three spices, has been reported to mitigate inflammation and oxidative stress-induced damage in various organs. CGA has demonstrated efficacy in reducing colon inflammation and renal injury by suppressing inflammatory mediators and oxidative pathways [39]. Consistent with our observations, previous research has shown that cinnamon aqueous extract contributes to both qualitative and quantitative improvements in pancreatic β-cell morphology, along with an increase in total antioxidant status, emphasizing its potent antioxidant capacity [40]]. Similarly, ethanolic cumin seed extract has shown promise as an anti-diabetic agent, these histological findings are consistent with the blood glucose results observed in this study, where all spice-treated groups showed a significant reduction in glucose levels compared to both the diabetic control and the standard drug group. This hypoglycemic effect can likely be attributed to the phenolic and flavonoid content of the spice extracts, which exert antioxidant, anti-inflammatory, and insulin-sensitizing activities, as discussed earlier.

Limitations of the study

There are several limitations to this study. First, the small sample size per group may limit the generalizability of the findings. this is to comply with ethical guideline for the use of animals in scientific research, However, appropriate statistical methods were applied to mitigate this issue. Second, this research was conducted using a single animal model because the rat offers many advantages as a model of human disease, the physiology is easier to monitor and the size of the animal enhances its laboratory use. Third, no long-term toxicity evaluation was conducted in this study, which is an important aspect for safety assessment. Further research including long-term toxicity analysis is therefore warranted. Despite these limitations, the study provides valuable preliminary insights into the investigated topic

Conclusion

This study shows that water-based extracts of cinnamon, cumin, and coriander have strong

potential in lowering blood sugar and improving pancreatic health in diabetic rats. Their benefits come from being rich in antioxidants, phenols, flavonoids, and dietary fiber.

Among the three, cinnamon extract at 2 ml/kg body weight showed the strongest effect even better than the diabetes drug glibenclamide.

The study recommends further research into using these spices alone or combined as natural, safe alternatives for managing and preventing diabetes. Adding them to diabetic-friendly foods could offer real health benefits and reduce the need for synthetic additives.

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Declaration of Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper

Ethical Approval

All animal experimental procedures were approved by the Institutional Animal Care and Use Committee (IACUC) of the Agricultural Research Center, and were conducted by their ethical guidelines (Approval No ARC RCFF 89 23).

Credit authorship contribution statement

Amany A. Fares: Writing – original draft, Resources, Methodology, Investigation. Eman S. Ramis: Resources, review & editing, Methodology. Mohamed S. Abbas – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors have no conflict of interest to declare. There are no known conflicts of interest associated with this publication, and significant financial support for this work that could have influenced its outcome.

Data availability

Data will be made available on request.

Abbreviation list

(T2DM:) Type 2 diabetes mellitus
(STZ): Streptozotocin
(DPPH): 2,2-diphenyl-1-picryl-hydrazil
(IC_{50}): The concentration providing 50% inhibition of DPPH
(mgAAE/100g): milligrams of Ascorbic acid equivalents per 100 grams
(mgGAE/100g): mg gallic acid equivalent per 100grams
(mgQE/100g): mg quercetin equivalent per 100grams
(HPLC): High-performance liquid chromatography
(CGA): chlorogenic acid
(DDZ) Daidzein
(SOD): superoxide dismutase
(GSH): glutathione
(ROS): Reactive oxygen species
(LPS): lipopolysaccharides
(GA)Gallic acid
(FA) Ferulic acid

TABLE 1. Physicochemical composition of cinnamon, cumin and coriander aqueous extract.

Items %	Sample name		
	Cinnamon extract	**Cumin extract**	**Coriander extract**
Moisture	14.9^{a} ±0.057	14.2^{c}±0.11	14.5^{b}±0.11
Protein	1.7^{c} ±0.11	6.69^{b} ±0.17	15.8^{a} ±0.28
Ash	5.13^{c} ±0.01	18.62^{a} ±0.17	14.32^{b} ±0.01
Fat	4.18^{b}±0.04	2.47^{c}±0.05	4.34^{a}±0.03
Fiber	2.34^{a} ±0.03	0.29^{c} ±0.005	0.46^{b} ±0.01
Carbohydrates	83.77^{a} ±0.33	62.3^{b}±0.17	60.03^{c}±0.05
Energy value(kcl)	351.76	306.4	320.76
Minerals (mg/100g)			
Mn	569.4^{a} ±1.03	0.53^{b} ±0.02	0.867^{b} ±0.006
Cu	8.81^{c} ±0.01	58.1^{a} ±1.8	16.78^{b} ±0.04
Zn	27.5^{c} ±0.017	76.2^{a} ±0.4	46.95^{b} ±1.8
Fe	179.6^{c} ±1.15	230.1^{b} ±1.8	796.8^{a} ±2
Se	8.19^{a} ±0.08	2.43^{b} ±1.8	2.43^{b} ±2

The superscript letters indicate statistically significant differences, with $P \leq 0.05$. within the same rows ± SE. Stander Error

TABLE 2. Antioxidant profile of cinnamon, cumin and coriander aqueous extracts.

Items %	Sample name		
	Cinnamon extract	**Cumin extract**	**Coriander extract**
Total antioxidant capacity (TAC mgAAE/100g	1230.4±8.25 [a]	378.0667±0.89 [b]	359.9067±0.76 [c]
Total phenolics content (TPC) mgGAE/100g	1111.523±30.14 [a]	639.36±1.50 [b]	307.98±0.52 [c]
Total flavonoids Content (TFC mgQE/100g	22.662±0.91 [b]	110.22±3.1 [a]	10.176±0.40 [c]
Radical scavenging activity (DPPH, %)	80.14±0.52 [a]	30.13±0.40 [c]	50.14±0.46 [b]
IC_{50} (µg/g)	2.51±0.04 [b]	1.10±0.23 [c]	8.16±0.13 [a]

The superscript letters indicated statistically significant differences within the same rows ± SE (P ≤0.05)**.** (mgAAE/100g): milligrams of Ascorbic acid equivalents per 100 grams, (mgGAE/100g): mg gallic acid equivalent per 100g, (mgQE/100g): mg quercetin equivalent per 100g

TABLE 3. **Phenolic compounds in Cinnamon, Coriander, and Cumin extracts (µg/g).**

Polyphenol's components	Cinnamon	Cumin	Coriander	SEM
Caffeic acid	66.90c	193.01[a]	151.28[b]	1.836
Catechin	ND	550.20[a]	23.22[b]	0.793
Chlorogenic acid	1355.54[b]	3828.35[a]	299.59[c]	1.305
Cinnamic acid	1147.40[a]	26.59[c]	40.9[b]	2.082
Coumaric acid	11.07[c]	1007.67[a]	67.32[b]	1.811
Daidzein	11019.26[a]	77.12[c]	96.17[b]	1.068
Ellagic acid	ND	ND	24.65	-
Ferulic acid	15.83[c]	1774.55[a]	129.24[b]	1.107
Gallic acid	912.90[a]	713.45[b]	207.38[c]	2.505
Hesperetin	770.27	ND	ND	-
Kaempferol	ND	331.67	ND	-
Methyl gallate	118.43[b]	139.49[a]	21.36[c]	1.138
Naringenin	27.89[b]	86.33[a]	89.22[a]	2.952
Quercetin	52.16[b]	236.82[a]	22.85[c]	2.480
Rosmarinic acid	15.50[c]	356.87[a]	77.03[b]	1.950
Rutin	151.69[b]	7581.52[a]	ND	1.209
Syringic acid	38.09[c]	394.97[a]	191.30[b]	1.474
Vanillin	83.04[b]	26.57[c]	93.15[a]	2.189

SEM: standard error of the mean. ND: not detected. Different letters are significantly different within the same row (P≤0.05).

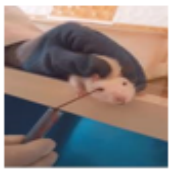
TABLE 4. Effect of the three extracts on serum Glucose (mg/dl) of rats.

Code	Treatments	Initial	Final
G1	Negative Control	91.6 [i] ±0.79	93.8 [i] ±0.20
G2	Positive Control	593.4 [a] ±3.34	568 [abc] ±3.94
G3	Cinnamon extract (1 ml/kg)	585.2 [ab] ±4.75	120.4 [hi] ±35.04
G4	Cinnamon extract (2 ml/kg)	568 [abc] ±13.04	94.2 [i] ±23.82
G5	Cinnamon extract (3 ml/kg)	556.6 [bc] ±9.97	114 [hi] ±29.25
G6	Cumin extract (1.5 ml/kg)	493.2 [e] ±23.67	131.2 [h] ±7.71
G7	Cumin extract (2.5 ml/kg)	540 [ed] ±13.03	136 [h] ±15.03
G8	Cumin extract (3.5 ml/kg)	515.6 [de] ±21.89	132.8 [h] ±15.07
G9	Coriander extract (2 ml/kg)	540 [cd] ±20.52	133.8 [h] ±14.05
G10	Coriander extract (4 ml/kg)	499.6 [e] ±3.32	137.4 [h] ±15.25
G11	Coriander extract (6 ml/kg)	440.2 [f] ±20.45	132.4 [h] ±11.49
G12	Standard Drug	537.8 [cd] ±29	360.6 [g] ±95.32

The superscript letters indicate significant differences (P ≤0.05) within the two columns± SE.

ANIMAL MODEL 72 male albino rats
HOUSING CONDITIONS, 12 h light /12 h dark, 22±2 °C, 50% ±5 humidity

DIABETES INDUCTION: Acclimation (2 weeks)
Injection by streptozotocin STZ 50 mg/kg



SAMPLE COLLECTION – AFTER–TREATMENT
Blood glucose, Total cholesterol, Kidney function tests, liver function tests, Triglyceride

Cumin extract dose (1.5-2.5-3.5ml/kg)

Cinnamon extract dose (1-2-3ml/kg)

Glibenclamide 0.5 mg/kg

Coriander extract dose(26ml/kg)

SAMPLE COLLECTION – AFTER–TREATMENT
Blood glucose, Total cholesterol, Kidney function tests, liver function tests, Triglyceride

END OF EXPERIMENT
Sample collection from the retroorbital plexus vein. Rats were **sacrificed,** and **pancreatic tissues** were collected and fixed in 10% formalin for histopathological examination .All biochemical data were statistically analyzed. Comparison between groups was carried out to evaluate the significance of treatment effects.

Diagrammatic abstract

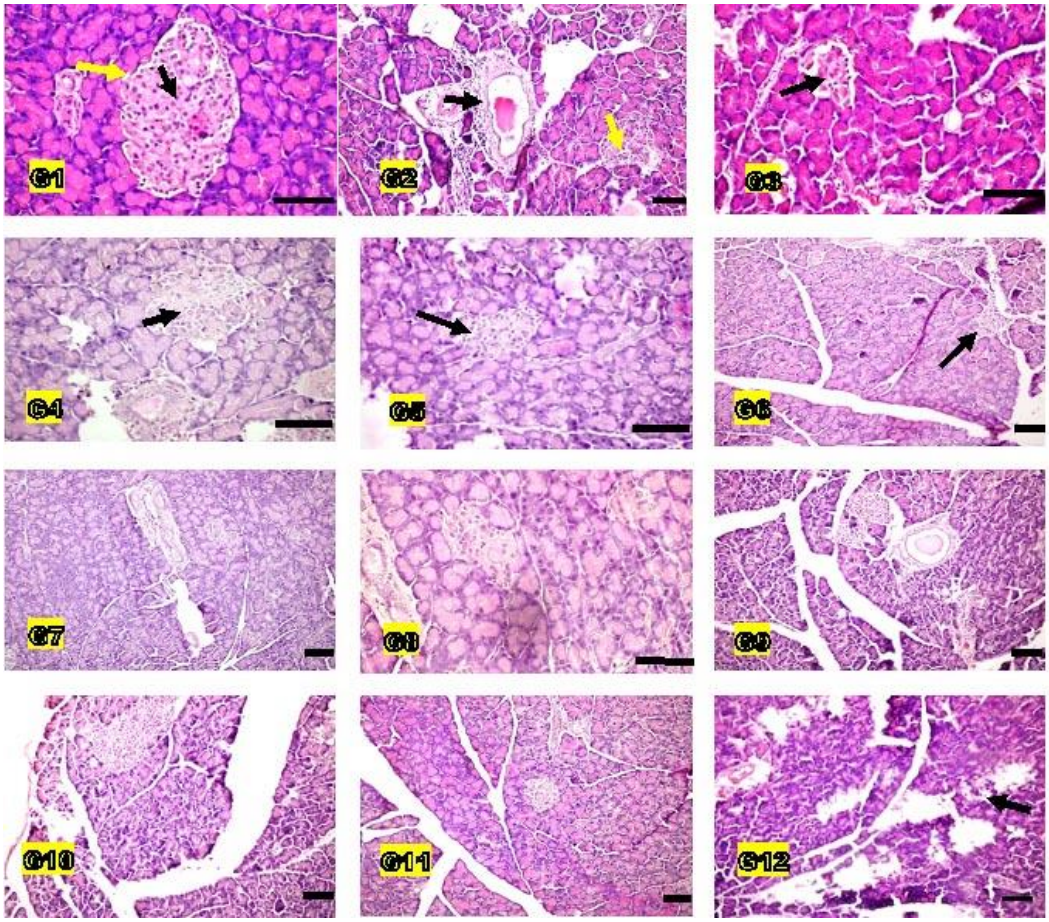


Fig. 1. G1 Normal pancreas showing control rat pancreas showing normal islets of Langerhans (yellow arrow), with pale, rounded, and ovoid β-cells in the center (black arrow), embedded in the exocrine portion of the pancreas (H&E stain; X400) (scale bars 100 µm)
G2 pancreas showing necrosis, lysis of a few pancreatic acini and islets (yellow arrow), accompanied by a huge accumulation of inflammatory cells in the perivascular area (black arrow) and in the pancreatic islets (H&E stain; X200) (scale bars 100 µm)
G3 pancreas showing slight atrophy of some pancreatic islets (StainHandEX400) (scale bars 100 µm)
G4 Pancreas showing marked regeneration of pancreatic islets (black arrow) and pancreatic acini (H&E stain; X400) (scale bars 100 µm)
G5 moderate amelioration of pancreatic islets (black arrow) and pancreatic acini (H&E stain; X400) (scale bars 100 µm)
G6 mild regeneration of pancreatic tissues with accumulation of an abundant number of inflammatory cells (black arrow) (HandEX200) (scale bars 100 µm)
G7 pancreas showing moderate recovery of pancreatic islets and acini (H&E stain; X200) (scale bars 100 µm)
G8 pancreas with moderate amelioration of pancreatic islets and pancreatic acini (H&E stain; X400) (scale bars 100 µm)
G9 Pancreas showing regeneration of pancreatic islets (H&E stain; X200) (scale bars 100 µm)
G10 Pancreas showing marked improvement of pancreatic islets and pancreatic acini (H&E stain; X200) (scale bars 100 µm)
G11 Pancreas showing moderate recovery of pancreatic islets and pancreatic acini (H&E stain; X200) (scale bars 100 µm)
G12 Pancreas showing severe pancreatic necrosis (black arrow) (H&E stain; X200) (scale bars 100 µm)

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المستخلصات الخضراء للقرفة والكمون والكزبرة: التأثيرات المقارنة على فرط سكر الدم في الجرذان المصابة بداء السكري

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الملخص

يُعَدّ داء السكري أحد أبرز التحديات الصحية العالمية، ويتميز بفرط سكر الدم المزمن الناتج عن عجز في إفراز الإنسولين أو مقاومة له، مما يؤدي غالبًا إلى مضاعفات خطيرة. هدفت هذه الدراسة إلى تقييم الأثر المقارن للمستخلصات المائية الخضراء لكل من القرفة والكمون والكزبرة على تنظيم مستويات سكر الدم في الجرذان المصابة بداء السكري المستحث بواسطة الستربتوزوتوسين (STZ). أُجري تحليل كيميائي لتقدير السعة الكلية لمضادات الأكسدة، ومحتوى الفينولات الكلية، ومحتوى الفلافونويدات الكلية، ونشاط اصطياد جذر(DPPH 12,2- picryl- hydrazil) diphenyl- وقيمة IC50% بالإضافة إلى تحديد المركبات الفينولية النوعية. أظهرت النتائج أن القرفة امتلكت أعلى القيم المضادة للأكسدة (السعة الكلية لمضادات الأكسدة 1230.4 ملغ مكافئ حمض الأسكوربيك/100 غ من العينة، محتوى الفينولات الكلية 1111.523 ملغ مكافئ حمض الجاليك/100 غ من العينة، ونشاط اصطياد DPPH بنسبة 80.14 %) شملت التجربة على الجرذان اثني عشرة مجموعة، حُفِّز داء السكري في المجموعات من 2–12. وبعد ستة أسابيع من المعالجة، أظهرت جميع المجموعات المعاملة بالمستخلصات انخفاضًا معنويًا في مستويات سكر الدم، حيث حقق مستخلص القرفة بجرعة 2 مل/كغ من وزن الجسم التأثير الخافض للسكر الأكثر وضوحًا، وكان مقارنًا بالمجموعة الضابطة غير المصابة بالسكري. وتشير هذه الملاحظات إلى أن المستخلصات المائية للقرفة والكمون والكزبرة تحمل وعودًا واعدة كمكونات غذائية وظيفية لإدارة داء السكري، نظرًا لامتلاكها نشاطًا عاليًا لمضادات الأكسدة وغناها بمركبات الفينولات والفلافونويدات.

الكلمات المفتاحية: مضادات الأكسدة؛ التوابل؛ جليبينكلامايد؛ ستربتوزوتوسين؛ علم النسج المرضي للبنكرياس.