Review Article

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Review on Anti-diabetic Research on Two Important Spices: *Trachyspermum ammi* and *Pimpinella anisum*

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Abstract

Diabetes mellitus (DM) arises from a cascade of factors, primarily stemming from defective insulin secretion by the pancreas and emergence of insulin resistance. These alterations disrupt lipid and protein metabolism, which may lay the foundation for hyperglycemia. The efficacy and safety of spice herbs from traditional medicine have long been regarded for the potential to treat this condition. Remarkably, many of the drugs we rely on today have origins, either directly or indirectly, in the realm of plant sources. The exploration of hypoglycemic potential extends beyond the boundaries of herbs and spices, embracing a diverse tapestry of food extracts. Among the spices, *Trachyspermum ammi* and *Pimpinella anisum* are plants in the *Umbelliferae* family, and their fruits are used traditionally as carminatives, aromatics, disinfectants, and galactogogues. In this comprehensive review the published scientific articles related to antidiabetic properties of both seeds are discussed.

Keywords

Diabetes, insulin, *Pimpinella anisum;* phytoconstituents, *Trachyspermum ammi*.

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Introduction

Diabetes mellitus (DM) is a chronic endocrine disorder that affects a variety of metabolic pathways. The exact aetiology of DM is unknown; however, obesity along with a lack of exercise appear to have a crucial influence in both environmental and hereditary variables [1]. This complex ailment is characterized by impaired insulin activity arising from insufficient insulin secretion and compromised tissue responsiveness along the intricate avenues of hormonal interactions. Chromic hyperglycemia has a detrimental effect in individuals with DM and eventually leads to organ failure. Critical organs, such as the eyes, heart, nerves, kidneys, blood vessels, and liver bear the brunt of this ongoing assault. The consequences of such organ compromise reverberates as micro- and macro-vascular disorders induce a cascade of pathologic changes, including neuropathy, nephropathy, cardiovascular disease, and cerebrovascular alterations [2, 3]. Pre-diabetes is a precursor stage of DM wherein individuals exhibit elevated blood glucose levels that do not yet meet the threshold for a DM diagnosis. Individuals with pre-diabetes are more likely to acquire type 2 diabetes and heart disease [4].

According to the International Diabetes Federation (IDF), the diabetic population will likely reach 642 million people or more by 2040, with 75% of diabetics residing in low- and middle-income developing countries [5]. DM is rapidly expanding in developing countries around the world and it is now recognised that the incidence and prevalence of DM in young people, particularly obese children, is increasing at an alarming rate [6].

The American Diabetes Association (ADA) diagnoses DM by observing symptoms, such as polyuria, polydipsia, and weight loss, along with a plasma blood glucose level of 11.11 mmol/L. Diabetic complications include myocardial infarction, stroke, and peripheral vascular disease. Diabetic complications are divided into micro- and macro-vascular diseases. Glycation of glucose leads to the formation of glycosylated haemoglobin, also known as HbA1c. DM is defined as an HbA1c ≤ 6.5%, while pre-diabetes or individuals at-risk for diabetes is defined as an HbA1c between 6.0% and 6.5% [7, 8].

DM is traditionally divided into four types: type I DM (insulin-dependent DM);

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type II DM (non-insulin-dependent DM [NIDDM]); gestational DM (GDM); and other specific types of DM due to other causes, (e.g., genetic defects of insulin action, β-cell function, diseases of the exocrine pancreas, and chemically-induced) [7].

Present drugs and the mechanism of action in DM

DM is managed by reducing and maintaining a normal plasma glucose level. Both Western and traditional medicine approaches to treating DM are based on the following mechanisms [1]: 1. pancreatic islet cells are stimulated; 2. hormones that elevate blood glucose levels are inhibited; 3. increasing the number of insulin receptors and their sensitivity; 4. decreased glycogen-to-blood-glucose conversion; and 5. facilitate glucose absorption by organs and tissues.

Plant-based medication for treatment of DM

Insulin and a variety of oral antidiabetic medicines, such as sulfonylureas, biguanides, thiazolidinediones, glucosidase inhibitors, and glinides are currently available as effective treatments for DM. Hepatotoxicity, abdominal pain, flatulence, diarrhea, and hypoglycemia are a few of the major side effects of these medication. Drug effectiveness of these treatments is frequently manifested after long-term use [9]. As a result, research into obtaining anti-hyperglycemic/hypoglycemic medications from therapeutic plants has gained traction in recent years. Metformin was discovered and synthesized from the medicinal plant, *Galega officinalis* L. (Fabaceae) [10]. Laboratories worldwide are conducting technological studies on these curative plants to advance alternative medications and progressive management approached of DM [11].

India, which has long been recognised as a source of spices and aromatic plants, is still one of the major producers of medicinal plants and spices globally. Medicinal plants and spices have high medicinal value and have long been used in home medicines [12, 13]. Traditional herbal treatments based on plants aid in the management of DM [14]. Herbal medicines are given because herbal medicines are thought to be more effective, have fewer adverse effects, and are less expensive [15].

Spices

Spice is a culinary phrase rather than a botanical classification. Spice does not refer to a specific plant or plant part. A spice is a natural substance derived from the seeds, fruits, flowers, or stem (skin, roots, and leaves) of a variety of plants and used to enhance the taste, smell, or flavour of food. Spices are widely utilised as essential nutritional supplements worldwide, most commonly in tropical oriental and Indian cuisines [16]. Each spice has its own distinct flavour and fragrance, which are generated from phytochemicals or secondary compounds [17].

Spices and herbs, which have long been used in home remedies, have enormous medicinal potential [13]. The *Umbelliferae* plant family has a special role in home-based remedies for a variety of digestive and intestinal diseases. There are approximately 275 genera and 2850 species in the *Umbelliferae* family, which is divided into three subfamilies (*Hydrocotyloideae*, *Saniculoideae*, and *Apioideae*) [18].

For readers interested in DM, the implications, and management, this review serves as a comprehensive and informative resource. Indeed, this review provides a clear explanation of the origin of DM, the impact on vital organs, and the complexities of treatment. The inclusion of plant-based medicines as a potential resource for managing DM gives readers insight into alternative approaches beyond traditional pharmaceutical interventions. This review aims to give a synthesis of the current state of research on the anti-diabetic properties of two samples (*Trachyspermum ammi* and *Pimpinella anisum*). This review seeks to underscore the role of plant-based medicines in the management of DM, highlighting the potential to offer novel therapeutic approaches. By presenting a well-researched synthesis of current knowledge and ongoing research, the review serves as a valuable resource for healthcare professionals, researchers, and individuals affected by or interested in DM.

Trachyspermum ammi

The taxonomic classification of *T. ammi* [19] is as follows: kingdom, Plantae; subkingdom, Tracheobionta (vascular plant); superdivision, Spermatophyta (seed plants); division, Magnoliophyta and Angiospermae; class, Magnoliopsida and Dicotyledonae; order, Apiales; family, *Apiaceae* and *Umbelliferae*; genus, *Trachyspermum*; species, *Trachyspermum ammi* (L.) (**Figure 1**); and common

Figure 1 *Trachyspermum ammi.*

names, Bishop's weed, Ajma, Ajowain, Ajwain, Omam, and Yaviniki.

T. ammi is known by various scientific names in different parts of the world, including *Carum copticum* and Sprague. *T. ammi* is also termed *Carum copticum* Benth, and in some documents Aromaticum has been used by various herbalists [20].

Ajwain has been used to treat stomach problems, and a hot, dry fomentation of the fruits has been used to treat asthma when lathered on the chest [21, 22]. To treat worm infections, many Ayurvedic medicines containing ajwain are used. Ajwain is also used to treat flatulence, dyspepsia, spasmodic diseases, the common cold, acute pharyngitis, and painful and congested throats [23].

In vitro anti-diabetic activity

A study investigated the anti-diabetic properties of fractions and subfractions from the ethyl acetate extract of *T. ammi* seeds. The crude extract was analyzed using thin layer chromatography (TLC), followed by column chromatography to isolate the fractions. Primary screening was performed using the starch-agar gel diffusion assay, followed by secondary screening using the glucose-uptake assay in yeast cells. The results of the starch-agar gel diffusion assay showed that *T. ammi* had anti-diabetic activity by inhibiting the α-amylase enzyme (fraction 8) and facilitating glucose utilization in adipose tissues and skeletal muscles (subfraction-I). The hypoglycemic activity of the *T. ammi* ethyl acetate extract was confirmed in 3T3-L1 cell lines by comparing the *T. ammi* crude and subfraction-I. The glucose uptake activity was shown to be the highest in the *T. ammi* subfraction-I extract at a concentration of 100 μg/mL [24].

The anti-diabetic activity of methanol (Me) extracts of *T. copticum*, *Trigonella foenum*, and *Nigella sativum* were combined at a 1:1:1 ratio in polyherbal therapy. This polyherbal formulation was given at 2 oral doses (100 and 200 mg/kg) for 15 d to treat streptozotocin (STZ)-induced diabetic Sprague-Dawley male and female rats. The parameters studied included the oral glucose tolerance test (OGTT) results, the normal blood glucose level, the fasting blood glucose (FBG) level, the serum lipid profile, the serum insulin level, the atherogenic index, and other tests, including glucose uptake, liver glycogen content, and glycogenolytic activity. Also, the extent of pancreatic damage was determined by histopathologic evaluation in each group. Both doses showed significant hypoglycemic activity and improved the serum insulin levels. High serum lipid levels were reversed to normal. A noticeable increase in glucose uptake and liver glycogen content was observed along with a decrease in glycogenolytic activity. The combination therapy reduced hyperlipidemia and hyperglycemia. The herbs in combination exhibited synergistic activity in surmounting DM and associated complications [25].

The α-glucosidase inhibitory potential of the essential oil and ethanolic extract of *T. ammi* (L.) Sprague, as well as the seeds and bark of *Cinnamomum zeylanicum*, were evaluated using gas chromatography (GC)/mass spectrometry (MS). The essential oil of *C. zeylanicum* bark yielded 14 constituents with a 99.92% purity, whereas the essential oil of *T. ammi* seeds yielded 22 compounds with a 99.18% purity. The IC_{50} values for *T. ammi* seeds oil and extract were 160±1.27 μg/ml and 220±2.03 μg/ml, respectively, whereas the IC_{50} values for *C. zeylanicum* bark oil and extract were 90±0.85 μg/ml and 180±2.61 μg/ml, respectively. *T. ammi* seeds were shown to lower postprandial hyperglycemia by blocking the enzyme, α-glucosidase [26].

T. ammi oil from solvent extract was tested for *in vitro* α-amylase and α-glucosidase inhibitory activity. Furthermore, L6 cell lines were cultured and the 3-(4,5 dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay was performed to assess cytotoxicity of the extracted oil. Then, the 6-(N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl) amino)-2-deoxyglucose assay was performed to determine the anti-diabetic activity of extracted oil using differentiated L6 myotubes. The results showed inhibition of α-amylase (IC_{50} = 0.47 μL/ml) and α-glucosidase (IC_{50} = 0.37 μL/ml) without a cytotoxic effect, thereby reducing the postprandial hyperglycemia. Moreover, the *T. ammi* oil had proved its ability to promote glucose uptake in the L6 cell line myotubes in a dose-dependent manner [27].

Similarly, inhibition of amylase and glucosidase activity along with antioxidant activity against glucose and protein oxidation, lipid peroxidation (LPO), and protein glycation of *T. ammi*, *Thymus kotschyanus*, *Oliveria decumbens*, and *Zataria multiflora* essential oils was reported in a study by Siahbalaei *et al.* in 2020. The essential oils were prepared in gelatin-pectin composite nanoparticles with rheologic properties that resulted in a size range of 500–700 nm. Then, Fourier-transform infrared (FTIR) spectroscopy of nanoparticles were performed to identify the spectrum and interaction among pectin, gelatin, and essential oils. Also, GC-MS analysis revealed that thymol, cavacrol, gamma-terpinene, para-cymene, geraniol, and spathulenol were the main components of all essential oils. The antioxidant nature of essential oils reduced glucose oxidation (130–150 μg/ml) and protein glycation (145–170 μg/ml), and inhibited lipid peroxidation (120–130 μg/ml) and protein oxidation (150–168 μg/ml). All essential oils inhibited alpha-amylase (210–230 μg/ml) similar to acarbose. In addition, the oils inhibited alpha-glucosidase (210–240 μg/ml) similar to acarbose. Because both alpha-amylase and alpha-glucosidase are responsible for the breakdown of carbohydrates to starch and disaccharides during digestive process, inhibition of these enzymes reduces postprandial hyperglycemia [28].

In a similar study by same author (Siahbalaei & Kavoosi, 2021), the anti-diabetic and anti-oxidative action of essential oil extracts of medicinal plants (*Zataria multiflora, T. ammi, Oliveria decumbens*, and *Thymus kotschyanus*) were studied by simulated *in vitro* digestion. Oils have a moderate potential of inhibiting protein, glucose, protein glycation, and lipid oxidation. Oils concentrate on the inhibition of amylase and glucosidase, implying that the oil extracts of these plants reduce oxidative stress caused by free radicals and exhibit anti-diabetic activity by inhibiting digestive enzymes. Based on this study, *T. ammi* demonstrated the strongest inhibitory action against α-amylase and α-glucosidase with IC_{50} values of 150 μg/ml and 180 μg/ml, respectively. Overall, the findings indicate that oil extracts from the studied plants may have health benefits and can be used as medicinal or functional food additives. Based on this study the main components in the GC-MS analysis of oil extracts from *Z. multiflora, T. ammi, O. decumbens*, and *T. kotschyanus* were shown to be thymol, linolenic acid, carvacrol, linoleic acid, oleic acid, and palmitic acid [29].

The study by Siahbalaei and Kavoosi (2020) investigated the anti-diabetic activities and amino acid composition of four medicinal plants. The free and protein amino acid extracts were shown to be mainly composed of amino acids with lower levels of monosaccharides, flavonoids, phenols, fatty acids, and tannins. The free amino acids exhibited moderate anti-lipid, anti-protein, and anti-glucose oxidation. The anti-diabetes activity of free amino acid (FAA) and protein amino acid (PAA) extracts from *T. ammi* among the four samples was shown to be glucose oxidation (IC_{50} = 117 µg/ml and 236 µg/ml, respectively), protein oxidation (IC_{50} = 168 µg/ml and 189 µg/ml, respectively), lipid oxidation (IC_{50} = 126 µg/ml and 277 µg/ml, respectively), protein glycation (IC_{50} = 143 µg/ml and 206 µg/ml, respectively), amylase inhibition (IC_{50} = 207 µg/ml and 299 µg/ml, respectively), and glucosidase inhibition (IC_{50} = 200 µg/ml and 348 µg/ml, respectively) [30].

Dutta et al. (2022) evaluated the chemical composition of *T. ammi* L. seed essential oils using GC/MS, 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) [ABTS] radical scavenging, antioxidant activity utilizing 2,2-diphenyl-1-picrylhydrazyl (DPPH), anti-diabetic activity using the α-amylase inhibitory and antimicrobial assays, and anti-inflammatory activity using protein denaturation assays. The presence of thymol (50.43%) as the predominant constituent was discovered by GC/MS analysis of Ajwain essential oil, followed by several minor and trace chemicals. The DPPH radical scavenging assay demonstrated that Ajwain essential oil has superior antioxidant activity compared to the standard, with an IC_{50} of 3.09 µL/mL, which was better than the ascorbic acid IC_{50} of 8.87 µL/mL. According to the ABTS assay, Ajwain essential oil has an IC_{50} value of 21.38 µL/mL, followed by ascorbic acid with a value of 79.13 µL/mL. Significant α-amylase enzyme inhibitory action was also observed, with an IC_{50} of 22.02 µL/mL, which was significantly higher than the conventional acarbose IC_{50} of 22.46 µL/mL. The presence of the polyphenolic compound thymol (50.43 %) resulted in strong antioxidant, anti-inflammatory, and anti-diabetic activities of Ajwain essential oil, which suggests that thymol can be used as a natural, cost-effective, and potential antioxidant with inflammation inhibition and anti-diabetic precursors for drug formulation in the future [31].

A study focused on anti-diabetic and anti-obesity activities using ethanol and chloroform extracts from fenugreek, green coffee beans, cumin seed, and *T. ammi*. The extracts were evaluated for *in vitro* α-amylase inhibitory activity against porcine pancreatic amylase. A colour comparative study was conducted for α-amylase inhibitory assay using starch as a substrate. *T. ammi* had α-amylase inhibitory action values between 20 and 22 µg/ml individually and 70–97.5 µg/ml when used in a mixture of drug containing *T. ammi, Trigonella foenum-graecum*, *Coffea arabica* and *Bunium bulbocastanum* [32].

In vivo anti-diabetic activity

A study was conducted to isolate the active constituent of *T. ammi* and evaluate the anti-diabetic and neuroprotective activities in STZ Wistar rats. The study showed that thymol, an isolated compound, was anti-diabetic and neuroprotective, yielding controlled glucose levels and defensive nerve damage in STZ-treated Wistar rats. In addition, the study detected significant differences in endogenous biomarkers (superoxide dismutase [SOD], lipid peroxidation, nitric oxide [NO], TNF-α, and Na^+K^+ATPase), FBG levels, lipid profile levels, behavioural studies (thermal algesia, cold hyperalgesia, mechanical hyperalgesia, grip strength, spontaneous locomotor testing, writhing responses, and neuromuscular coordination) and histopathologic studies between the treated and diabetic groups. Thymol (10 and 20 mg/kg) from *T. ammi* showed improvement in the glucose levels of the treated groups (treated group 1, 129.01±3.45 mg/dl; treated group 2, 117.12±1.35 mg/dl) compared to the diabetic control group (308.27±0.37 mg/dl) on day 28 of the experiment [33].

Zolfaghari et al. (2023) investigated the effect of *T. ammi* on the liver of STZ-induced diabetic rats. The methanol composition of *T. ammi* was identified, with three compounds prevalent compounds (thymol, γ-terpinene, and p-cymene). The rats were treated with *T. ammi* (200 and 500 mg/kg) or losartan (20 mg/kg) daily for 60 days. There was a significant ($p < 0.01$) decline in the FBG level in the treated groups compared to the diabetic group. In the losartan group, the glucose level was similar to the diabetic control group ($p > 0.05$). *T. ammi* significantly restored antioxidant balance in the liver and reduced hepatic indicators, LPO markers, and pro-inflammatory mediators. The extract also increased antioxidant enzyme levels and reduced pathologic changes in liver tissue samples. It was concluded that *T. ammi* significantly restored liver inflammation and the antioxidant balance caused by hyperglycemia [34].

A study on diabetic nephropathy in STZ-diabetic rats treated with Me extracts of *T. ammi* seeds (300-400 mg/kg) for 8 weeks showed that *T. ammi* seeds reduce blood glucose levels, oxidative stress, renal function biomarkers, and inflammatory cytokines caused by STZ. The study also showed that *T. ammi* seeds increased the serotonin level, decreased the malondialdehyde (MDA) level, and inhibited IL-18 and TNF-α expression. Therefore, *T. ammi* seeds could be a potential new treatment for diabetic nephropathy [35].

Pimpinella anisum

The taxonomic classification of *P. anisum* [36] is as follows: kingdom, Plantae; subkingdom, Tracheobionta (vascular plants); superdivision, Spermatophyta (seed plants); division, Magnoliophyta and Angiospermae; class, Magnoliopsida and Dicotyledonae; order, Apiales; family, *Apiaceae* and *Umbelliferae;* genus, *Pimpinella* L.; species, *Pimpinella anisum* L. (**Figure 2**); and common names, anise seeds, Shetapusapa, Vilayati Saunf, and sowa.

P. anisum L. (Synan, *Anisum vulgare*, Geetner, *Anisum officianlis*, and Moed) is a fragrant annual plant with white

Figure 2 *Pimpinella anisum.*

blooms and little yellow–green seeds that grow in Egypt, Mexico, Spain, the eastern Mediterranean region, the Middle East, and West Asia [37].

In vitro anti-diabetic activity

Aniseed Me extract and its fractions were tested for anti-diabetic and anti-peroxidative effects utilizing α-amylase and α-glucosidase, as well as a linoleic acid model system and a liver homogenate model, respectively. Although the anti-peroxidative and anti-diabetic activities of the Me extract and all fractions of aniseeds were dose-dependent, the ethyl acetate fraction of aniseed exhibited the highest anti-diabetic activities with respect to α-amylase and α-glucosidase (IC_{50} = 0.12 mg/ml and 0.15 mg/ml, respectively) inhibitory activities, the liver homogenate model (IC_{50} = 199 µg/ml), and the highest anti-peroxidative effect (IC_{50} = 185 µg/ml) [38].

Barabadi et al. (2023) used *P. anisum* aqueous seed extract to synthesize silver nanoparticles (AgNPs) with an average hydrodynamic diameter of 65.4 nm as smart nanomedicine platforms for diagnosing and treating various disorders, including infectious diseases and cancer. The NPs have a spherical morphology and exhibit significant antibacterial activity against reference stains of *Escherichia coli* and pathogenic *E. coli* isolates. The NPs also inhibited biofilm formation and had genotoxic effects, with 82.44±1.43% DPPH inhibition, 67.65±4.78% glucose uptake inhibition by *Saccharomyces cerevisiae*, and 71.43±4.92% alpha-amylase inhibition at a concentration of 1 mg mL^{-1}. AgNPs also showed significant anticoagulant activity compared to saline [39].

In vivo anti-diabetic activity

Aniseed is known to have hypoglycemic and hypolipidemic effects in diabetic patients. The antidiabetic potential of *P. anisum* oil was demonstrated by glucose absorption in the rat jejunum, and water absorption from the colon and kidney tubules, according to Kreydiyyeh et al. (2003). The mechanism of hypoglycemic action of aniseed oil was determined by increasing the Na^+-K^+ ATPase activity, which increases the sodium gradient and augments mucosal glucose transport by significantly increasing glucose uptake, even at very low concentration (0.025%) [40].

In a study involving individuals diagnosed with type 2 diabetes, Rajeshwari et al. (2011) conducted a comprehensive examination of the potential therapeutic effects of aniseeds and coriander seeds. Over a course of 60 days, study participants were administered seed powders (5 g/d), which resulted in significant antioxidant, anti-diabetic, and hypolipidemic effects. Notably, significant reductions in FBG levels were observed in patients treated with both *P. anisum* and *Coriandrum sativum*. This intervention also elicited alterations in the lipid profile, LPO, lipoprotein levels, and the high-density lipoprotein (HDL) level. The study further investigated the enzymatic and non-enzymatic antioxidants, highlighting a restoration of balance in these crucial components in treated patients compared to the control group. Among the observed shifts were an elevated catalase (CAT) activity and a mitigation of protein oxidation within erythrocytes. Moreover, the serum levels of essential antioxidants, such as beta carotene, vitamin C, vitamin A, and vitamin E, which are typically decreased in diabetic patients, underwent a reversal due to interventions with both seed samples across the various treated groups. There was also significant improvement in antioxidation of erythrocytes and glutathione-S-transferase (GST). The synergistic actions of the phytocompounds present in the seed samples were responsible for the above-mentioned effects [41].

In another study, *P. anisum* methanol extract was fractionated using solvents of polarity from low-to-high. Then, using column chromatography, the Me extract and ethyl acetate (EA) fraction of the aniseed was sub-fractionated using various eluting systems. Anti-diabetic, antioxidant, and hypolipidemic activities exhibited by sub-fractions (M1, M2, M3, M4, M5), the ethyl acetate fraction, and the Me extract of aniseed was studied using *in vitro* and *in vivo* methods. In addition to antioxidant activity (ABTS and DPPH radical scavenging activities), the aniseed extract fraction decreased the blood glucose level in type 2 DM patients (36%), although not below the normal level (19%), and also decreased the serum cholesterol, triglycerides, and lipoprotein levels (low-density lipoprotein [LDL] and very low-density lipoprotein [VLDL]), and improved the HDL levels. The extract also controlled lipid peroxidation and protein oxidation. These findings indicated that the seeds to be anti-hyperglycemic, hypolipidemic, and antioxidative in nature. The possible mechanism of action for hypoglycemia involved the phytoceuticals in aniseeds decreasing the production of free radicals, which increased the blood glucose levels, i.e., hyperglycemia generates free radicals due to auto-oxidation of glucose and controlling oxidative stress, thereby decreasing diabetic-related complications. Also, α-amylase and α-glucosidase inhibition of the Me extract, ethyl-acetate (Ea) fraction, and the aniseed sub-fractions may be due to the concentration-dependent effect, which may also be the basis for hypoglycemic nature. The highest α-amylase activity was exhibited by the Ea fraction, with values ranging from 43.3%–88.5%, followed by the Me extract (40.6%–62.6%). Sub-fractions of the Me extract (M2 and M3) had poor activity, while other

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sub-fractions (M1, M4, and M5) did not exhibit any inhibitory activity with antioxidants (butylated hydroxytoluene [BHT]) and natural antioxidants (rutin and quercetin) when used as positive controls. A similar response was observed for α-glucosidase inhibition in which the sub-fractions (M1, M4, and M5) did not show any inhibition, while the Ea fraction activity was comparable to natural antioxidants and was better than BHT [42].

The effect of aqueous aniseed extract on the structure of the pancreas in STZ-induced diabetic rats was investigated in another study. Histologic, immunohistochemical, and biochemical research has been used to better understand the putative underlying mechanisms. Compared to the diabetes control group, anise extract (500 mg/kg orally once daily) had a substantial hypoglycaemic effect. This finding was mostly due to its capacity to stimulate insulin production, as shown by substantial insulin immunoreaction upregulation. The aniseed extract hypoglycaemic impact is attributed to its antioxidant properties, as evidenced by a significant decrease in MDA and an increase in catalase and SOD. The aniseed extract also reduces protein loss caused by hyperglycemia. The structure of the β-cells improves significantly with considerable increases ($p < 0.001$) in insulin immunoreaction and pancreatic acini, as well as a significant decrease in serum amylase levels. Aniseed extract also has a significant impact on the exocrine region of the pancreas, resulting in the preservation of acinar cells. In the pancreas of diabetes-treated rats, considerable decrease downregulation of beclin 1 immunoreaction ($p < 0.001$), an autophagy regulator marker, and caspase 3 immunoreaction ($p < 0.001$), an apoptotic marker, was also shown immunohistochemically compared to diabetic untreated group, confirming the function of autophagy and apoptosis in DM. The antioxidant qualities of beclin 1 and caspase 3 were credited with this effect [43].

Ethnobotanic survey for anti-diabetic use

An ethnobotanic survey was conducted from January 2013 to June 2014 among the Taounate population in northern Morocco to identify plants used in folk medicine. The study surveyed two distinct regions populated by two ethnic groups. Over the past 5 years, 102 medicinal plants were discovered belonging to 48 families. Among 102 plants, 13 were used for DM, which included *P. anisum*. Individuals have reported consuming *P. anisum* raw and in the form of a decoction made from *P. anisum* seeds [44].

An ethnobotanic survey conducted from 1 March to 30 April 2018 among diabetic patients of the SOS Diabetes Center in Rabat, Morocco aimed to inventory and provide ethnobotanic information on medicinal plants used in traditional medicine to treat DM. It was found that 53.6% of diabetic patients use medicinal plants to control DM. The study identified 30 plant species from 18 botanical families, including *P. anisum*. The majority of plants were used for infusions and oral administration. Some plants were used exclusively by type 1 diabetics, while others were used by type 2 diabetics. *P. anisum* was used in type 2 DM only [45].

In a similar study conducted from January 2013 to June 2014, plant species used in diabetes management were inventoried in the Moroccan provinces, Chtouka Ait Baha and Tiznit. The survey involved semi-structured questionnaires and 380 interviews with traditional health practitioners and knowledgeable villagers. It was shown that 48 plant species, with Lamiaceae, Asteraceae, and Apiaceae the most represented families. Based on this data, the oral administration of a decoction made from *P. anisum* has been used for DM treatment [46].

Conclusions

As the diabetic population increases toward unprecedented numbers, this review serves as a guiding beacon for healthcare practitioners, researchers, and those impacted by DM. By offering an encompassing understanding of the disease mechanisms, complications, and available treatment options, the review equips readers with the knowledge needed to make informed decisions. The exploration of plant-based medicines as a potential therapeutic frontier adds an intriguing layer to the discussion, igniting hope for innovative solutions on the horizon. *T. ammi* and *P. anisum*, when administered regularly, can be used to prevent DM and its related complications from worsening. Accumulating evidence underscores the pivotal role of oxidative stress in the onset and progression of DM. This cascade of metabolic events has been hypothesized to originate from heightened oxidative stress due to sustained hyperglycemia, resulting in profound damage to vital macromolecules, including carbohydrates, lipids, proteins, and nucleic acids. This review showed that the hypoglycaemic beneficial effect of *P. anisum* and *T. ammi* are mainly due to the antioxidant properties. The interplay between oxidative stress and DM is profound, triggering an intricate imbalance in cellular antioxidant capacity. As a result, oxidative stress takes root, and this review postulates an intimate interrelationship between autophagy and the generation of ROS as primary pathologic mechanisms driving DM progression. Indeed, the evidence confirms that DM disrupts the cellular antioxidant equilibrium, precipitating oxidative stress, while autophagy and ROS generation remain intrinsically intertwined as central pathogenic components of this metabolic disorder. Hence, the elucidation of the extracts for their antidiabetic nature can also be checked for antioxidant potential because both go hand-in-hand for maintaining the normal glucose levels and also protecting the other organs from damage

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Conflict of interest

None

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