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Review

Plants Used in Diabetes Treatment

Pelin Taştan[1,*]

[1] İzmir Katip Çelebi University, Faculty of Pharmacy, Department of Pharmacognosy, Izmir, Türkiye; pelin.tastan@ikcu.edu.tr; https://orcid.org/0000-0003-0913-5369

* Corresponding author: pelin.tastan@ikcu.edu.tr

Abstract: Recently, the interest in herbal products is increasing day by day due to the side effects as well as the medical and economic problems. There are different plants used for different diseases and different extracts prepared from certain parts of these plants. In this study, the plants used in the treatment of diabetes were emphasized; In many different countries, including Türkiye, the plants used for this purpose and their parts are mentioned. For this, articles in many indexes were scanned and scientific studies were compiled following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. In addition, scientific studies on the plants *Panax ginseng* C. A. Meyer, *Trigonella foenum-graecum* L., *Cinnamomum cassia* Blume, *Cinnamomum zeylanicum* Nees. and *Allium sativum* L., which are frequently used in the treatment of diabetes globally, are given in detail. It is also mentioned that these plants are included in pharmacopoeia and monographs. While the place and importance of plants and preparations prepared from plants in medicine and pharmacology is quite large, any work to be done on this subject will shed light on the world of science.

Keywords: Diabetes; *Panax ginseng; Trigonella foenum-graecum; Cinnamomum cassia; Cinnamomum zeylanicum*

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1. Introduction

The developments in chemistry and biochemistry sciences in the 19th-20th centuries gave a great impetus to the pharmaceutical industry. In this way, many drugs that meet the needs of medicine have been developed in laboratories as a result of analytical, toxicological, pharmacological and clinical studies by adopting the principles of effectiveness, harmlessness and quality. 1/4 of the existing drugs are of herbal origin, and in most of them, the active ingredient desired to be obtained from the plant is copied in the laboratory environment (Nathan et al., 1993; Green et al., 1996)

In recent years, many factors such as the medical and economic problems caused by the serious side effects that may occur with synthetic drugs, ecological approaches and movements strengthened by environmental pollution in industrialized countries, the threat of many chronic diseases for which curative treatments are not yet possible, and the thought that naturalness is always effective and free from side effects. As a result, herbal treatment has become popular again. WHO reports that 25% of currently used medicines are prepared from medicinal plants, 30% of medicines sold worldwide contain raw materials of herbal origin, 3-5% of patients receive only herbal treatment as the main treatment, and WHO states that 80% of people, a good indication of this popularity is that (Infrmary, 1995). Today, more than 400 plants and more than 120 products of natural origin, as well as many vitamins and minerals are used by diabetes patients to support treatment. Some herbs can lower blood sugar; however, test results are subject to several factors. First, each herb contains thousands of ingredients, only a few of which can be therapeutically effective. Second, different parts of a plant have different content profiles. Also, different extraction methods may yield different active ingredients. Third, herbal formulas containing more than one herb may have synergistic effects (Marks and Raskin, 2000; Satman et al., 2002).

Diabetes mellitus is a metabolic disease characterized by chronic hyperglycemia, resulting from absolute or relative insufficiency of pancreatic insulin secretion, insulin ineffectiveness or structural defects in the insulin molecule, causing disturbances in carbohydrate, fat and protein metabolism. This disease has heterogeneous features with its etiology, genetic and clinical picture. The effects of diabetes progress with damage, dysfunction and failure in various organs in the long term. This disease may show characteristic symptoms such as thirst, polyuria, loss of vision, and weight loss. Often these symptoms are not severe or not visible. Therefore, before the diagnosis is made, hyperglycemia may cause pathological and functional changes in a long period (Mandrup-Poulsen, 1998). Long-term effects of diabetes include specific complications of retinopathy, nephropathy, and/or neuropathy. In addition, people with diabetes have an increased risk of coronary heart, cerebrovascular and peripheral vascular diseases. In its advanced forms, ketoacidosis and non-ketotic hyperosmolar state may develop. This condition can lead to weakness, coma, and death if left untreated (Başkal, 2005; WHO, 1999a).

Studies on the use of natural resources in the treatment of diabetes and the development of new drug molecules based on these resources began in the first quarter of the 20th century. In the first studies on *Galega officinalis*, it was found that the plant is rich in guanidine derivative compounds with hypoglycemic effect. Due to the toxicities of guanidine derivatives revealed in clinical trials, alkaline diguanidines with lower toxicity were synthesized and Sintalin A and B began

to be used as oral antidiabetic drugs all over Europe in the 1920s. Although the use of diguanidines has decreased with the introduction of insulin into the treatment field, metformin, one of its derivatives, is still used in treatment (Grundy et al.,2002).

Conventional medicines treat diabetes by improving insulin sensitivity, increasing insulin production, and/or reducing the amount of glucose in the blood. Various herbal preparations are used to treat diabetes, but their reported hypoglycemic effects are in some cases complex and even paradoxical.

2. Materials and Methods

This study is a descriptive study on the resolution of diabetes mellitus, which has a high prevalence in the world, using herbal treatments. Diabetes mellitus is one of the most common metabolic diseases seen in all populations and age groups.

This was a screening study, a systematic review of plants used in the treatment of diabetes by epidemiological and geographic characteristics, including their distribution and parts used in Canada, China, Africa, Israel, Jordan, Mexico, Morocco, North America, and Türkiye. In addition, more detailed research was conducted for 5 plants that are often used for this purpose*: Panax ginseng, Trigonella foenum-graecum, Cinnamomum cassia, Cinnamomum zeylanicum* and *Allium sativum*. They were classified according to their inclusion in pharmacopoeias such as the British Pharmacopoeia, the American Pharmacopoeia, the French Pharmacopoeia, and the monographs such as WHO monographs and EMA monographs.

Studies in English, Portuguese, and Spanish were retrieved from the Virtual Health Library, MEDLINE/PubMed, and Embase and reported in accordance with PRISMA guidelines as seen in Figure 1.

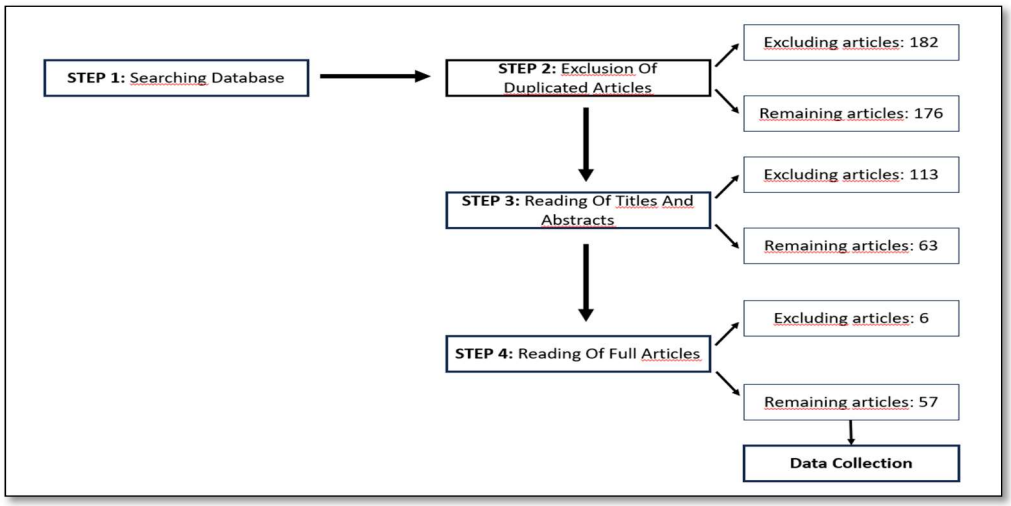

Figure 1. PRISMA flow diagram in the study.

3. Results

The plants that are frequently used in the treatment of diabetes in the countries that actively use phytotherapy in the world are compiled in Table 1 (Jarald et al., 2012; Arıtuluk and Ezer, 2012). Especially in recent years, the number of clinical studies on it has increased and its monographs, including the most recent studies of 5 plants that are widely used in the world and in Turkey, have been prepared.

Table 1. Plants used in the treatment of diabetes in various countries.

Country	**Plants**	**Used Parts**
Africa	*Combretum micranthum*	Folia
	Ficus capensis	Cortex
	Cassia sieberiana	Cortex
	Ocimum sanctum	Bark/twigs
	Anacardium occidentale	Folia
	Jatropha curcas	Cortex
	Allium sativum	Bulbus
	Citrus medica	Folia
	Moringa oleifera	Bark/twigs
	Catharanthus roseus	Cortex
	Tamarindus indica	Pulpa
	Carica papaya	Cortex
	Landolphia dulcis	Bark/twigs
	Mesonerum benthamianum	Folia
	Ocimum viridae	Cortex
	Psidium guajava	Bark/twigs

	Pterocarpus ericens	Bark/twigs
Canada	*Abies balsamea*	Bark/twigs
	Achillea millefolium	Roots
	Acorus calamus	Roots
	Aralia nudicaulis	Roots
	Aralia racemosa	Roots
	Arisaema triphyllum	Roots
	Asarum canadense var. *acuminatum*	Roots
	Celastrus scandens	Roots
	Cornus stolonifera	Bark
	Corylus cornuta	Bark/twigs
	Dirca palustris	Root bark
	Gaultheria procumbens	Leaves
	Heracleum lanatum.	Roots
	Juniperus communis	Bark
	Juniperus virginiana	Leaves/twigs
	Kalmia angustifolia	Leaves/flowers
	Ledum groenlandicum	Leaves
	Nuphar variegatum	Roots
	Picea glauca	Bark/twigs
	Picea mariana	Leaves
	Populus balsamifera	Buds
	Populus tremuloides	Bark
	Prunus serotina	Bark
	Quercus alba	Bark
	Quercus rubra	Bark
	Rhus hirta f. typhina	Fruit
	Sassafras albidum	Bark
	Smilacina racemose	Roots
	Solidago canadensis	Roots
	Sorbus americana	Bark
	Taraxacum officinale	Roots
	Taxus canadensis	Twigs/leaves
	Thuja occidentalis	Leaves
	Tsuga canadensis	Bark
	Verbascum Thapsus	Roots
China	*Astragalus membranaceus*	Roots
	Panax ginseng	Roots
	Polygonatum odoratum	Rhizoma
	Lycium barbarum	Cortex
	Ophiopogon japocicus	Cortex
	Epimedium sagittatum	Bark/twigs
	Lithospermum erythrorhizon	Bark/twigs
	Rheum palmatum	Rhizoma
	Hordeum vulgare	Folia
	Codonopsis pilosula	Cortex
	Momordica charantia	Bark/twigs
	Punica granatum	Cortex
	Dioscorea opposite	Cortex
	Allium cepa	Bulbus
	Trigonella foenum graecum	Semen
	Prunella vulgaris	Folia
	Ephedra sinica	Herba
India	*Asparagus racemosus*	Folia
	Berberis aristate	Cortex
	Catharanthus roseus	Folia
	Costus speciosus	Bark/twigs
	Ficus racemose	Cortex
	Ipomoea batatus	Bark/twigs
	Momordica charantia	Bark/twigs
	Syzygium cuminii	Cortex
	Trigonella foenum graecum	Semen
	Urtica dioica	Folia
	Zingiber officinale	Rhizoma
	Allium cepa	Bulbus
	Allium sativum	Bulbus
	Aloe vera	Folia

	Cajanus cajan	Folia
	Gymnema sylvestre	Cortex
	Momordica charantia	Cortex
	Ocimum sanctum	Folia
	Pterocarpus marsupium	Bark
	Tensor cordifolia	Cortex
Israel	*Achillea fragrantissima*	*Folia*
	Allium cepa	*Bark/twigs*
	Coridothymus capitatus	*Cortex*
	Pinus halepensis	*Bark/twigs*
	Silene aspera	*Folia*
	Teucrium polium	*Cortex*
Jordan	*Allium cepa*	Bulbus
	Artemisia vulgaris	Cortex
	Aloe vera	Folia
	Alpinia officinarum	Cortex
	Brassica oleraceae	Bark/twigs
	Cichorium pumilium	Cortex
	Cinnomomum zeylanicum	Cortex
	Hibiscus sabdariffa	Folia
	Juniperus phoenicea	Radix
	Pisum sativum	Bark/twigs
	Quercus coccifera	Cortex
	Rheum ribes	Rhizoma
	Sarcopoterium spinosum	Bark/twigs
	Terminalia chebula	Cortex
	Trigonella foenum graecum	Semen
	Varthemia iphionoides	Bark/twigs
	Zizyphus spina-christi	Cortex
Mexico	*Abutilon trisulcatum*	Bark/twigs
	Agave atrovirens	Folia
	Allium cepa	Bulbus
	Aloe barbadensis	Folia
	Ananas comosus	Cortex
	Argemone mexicanam	Bark/twigs
	Artemisia absinthium	Herba
	Bidens leucantha	Cortex
	Carica papaya	Folia
	Cassia fistula	Radix
	Catharanthus roseus	Radix
	Jatropha elbae	Bark/twigs
	Musa sapientum	Cortex
	Piper hispidum	Cortex
	Plumbago scandes	Bark/twigs
	Quassia amara	Bark/twigs
	Quercus acutifolia	Radix
	Senna multiglandulosa	Folia
	Tamarindus indica	Pulpa
	Trigonella foenum graecum	Semen
	Zizyphus acuminate	Cortex
Morocco	*Ammi visnaga*	Fructus
	Carum carvi	Fructus
	Artemisia absinthium	Herba
	Lactuca sativa	Bark/twigs
	Tetraclinis articulata	Bark/twigs
	Lavandula dentata	Folia
	Trigonella foenum graecum	Semen
	Allium sativum	Bulbus
	Aloe succotrina	Folia
	Linum usitatissimum	Semen
	Eucalyptus globulus	Folia
	Myrtus communis	Fructus, folia
	Sesamum indicum	Semen
	Punica granatum	Cortex
	Nigella sativa	Leaves
	Prunus amygdalus	Cortex
	Citrus bigaradia	Fructıs

	Peganum harmala	Cortex
	Zygophyllum	Cortex
North America	*Abies balsamea*	Bark/twigs
	Aralia nudicaulis	Bark/twigs
	Cornus stolonifera	Cortex
	Juniperus communis	Radix
	Picea mariana	Bark/twigs
	Prunus serotina	Bark/twigs
	Quercus rubra	Radix
	Solidago canadensis	Bark/twigs
	Sorbus americana	Cortex
	Taraxacum officinale	Pulpa
	Verbascum thapsus	Bark/twigs
Turkey	*Cotinus coggyria*	Cortex
	Pistacia terebinthius	Bark/twigs
	Arum conophalloides	Bark/twigs
	Hedera helix	Folia
	Eryngium campestre	Cortex
	Ferula caspica	Radix
	Artemisia absinthium	Herba
	Artemisia vulgaris	Cortex
	Helianthus tuberosus	Bark/twigs
	Helichrysum arenarium	Cortex
	Matricaria chamomilla	Flores
	Onopordum tauricum	Bark/twigs
	Taraxacum macrolepium	Cortex
	Taraxacum officinale	Bark/twigs
	Berberis crataegina	Folia
	Capsella bursa-pastoris	Herba
	Sambucus nigra	Flores
	Juniperus foetidissima	Radix
	Juniperus oxycedrus	Radix
	Trigonella foenum-graecum	Semen
	Quercus coccifera	Cortex
	Hypericum perforatum	Herba
	Melisa officinalis	Folia
	Origanum onites	Bark/twigs
	Origanum vulgare	Cortex

3.1. Panax ginseng C. A. Meyer

While the *Panax ginseng* C. A. Meyer plant, which is in the Araliaceae family, grows naturally in China, Japan and Korea, it does not grow in Turkey. While ginseng varieties get names such as Korean ginseng (*Panax ginseng*), American ginseng (*Panax quinquefolius*) according to the geography where they are grown; They get names such as red ginseng, black ginseng or white ginseng according to the color of the root. Both Korean and American ginseng contain herbal chemicals called ginsenosides. However, the proportional differences between the ginsenosides and the different effects of their contents differentiate the effects of these two ginseng types. Korean ginseng is known as true ginseng; because the substances that make up the ginsenosides in its content have many therapeutic properties. American ginseng is considered a weaker variety (Demirezer, 2011).

The chemical composition of the plant consists of triterpene saponins in the Dammaran structure. Those with oleanolic acid structure are also encountered (ginsenoside Ro). The saponins in Dammaran structure are protopanaxadiol or protopanaxatriol derivatives. Trace amounts of panacene, limonene, terpineol, eucalyptol, α-fellandrene, citral and sesquiterpene alcohols panacinsanol A and B, ginsenol, polyacetylenes, sterols as well as polysaccharides, starch, β-amylase, free sugar, vitamins (B1, B2, B12, pantothenic acid), biotin), choline, oils and minerals (Demirezer, 2011).

The types of ginsenosides found in Korean ginseng (38 ginsenosides) are greater than those found in American ginseng (19 ginsenosides). In addition, it was determined that Korean ginseng contains more non-saponin main compound, phenol compound, acid polysaccharide and polyethylene compounds than American ginseng (Choi, 2008).

Panax ginseng is mainly used to maintain the homeostasis of the body. Many researchers are trying to verify the effectiveness of *Panax ginseng* based on modern physiological, biochemical and pharmacological knowledge to confirm their experimental observations. In recent years, *Panax ginseng* has become well known in the USA and Europe with frequent studies on it. It is used in modern science to improve brain functions, alleviate pain, antitumor effect, antidiabetic effect, strengthen the immune system, regulate blood pressure, effect against fatigue and stress, increase climacteric disorder and sexual function, have antioxidative and anti-aging effects (Choi, 2008).

Panax ginseng is a species that is used in America as a source of almost all types of medicine. *Panax* species; The Himalayas are spread over a very wide area such as China, Korea, Japan and North America. In Asian countries, it has been used empirically for thousands of years, especially in Korea, Japan, and China. It was also widely used in Russia, the former Soviet Union, and North America. In recent years, the rate of use has increased in European countries, especially in Sweden. It has been reported that at least 5% of the adult population in Sweden uses ginseng. The decoction of the root of *Panax ginseng* is traditionally used among the people for both its tonic feature that helps to increase strength

and power and for the purpose of "a cure-all medicine". The genus name *Panax* also means "healing, panacea". In addition, *Panax ginseng* has been a plant used in preventing the development of cancer. Ginseng tablets have been reported to increase resistance to the adverse effects of antineoplastic drugs. In traditional Chinese medicine, it is used in the treatment of spleen and lung, fluid loss from the body and alleviation of symptoms related to fever (Shin et al., 2000).

Radix Ginseng is given as protective and supportive in increasing mental and physical capacity, in cases such as weakness, exhaustion, fatigue and loss of concentration, and during the healing process (WHO, 1999b). It has been scientifically proven to be effective in improving cerebral functions, improving learning functions and reducing memory loss (Choi, 2008). The Committee on Herbal Medicinal Products (HMPC), based on its long-term use, decided that ginseng root preparations can be used in cases of fatigue and weakness (EMA).

Black ginseng is a new type of processed ginseng with a unique ginsenoside profile. Its pharmacological effects were studied in *in vitro* and *in vivo* models. Although it is argued that the beneficial effect of red ginseng in the prevention of diabetes is mainly due to red ginseng, the relationship of black ginseng with diabetes is not yet known. Therefore, the antidiabetic efficacy of black ginseng extract (BGE) and red ginseng extract (RGE) in streptozotocin-induced diabetic mice was compared. HPLC analyzes showed that BGE had a very different ginsenoside composition compared to RGE. BGE, when given as 200 mg/kg, reduces hyperglycemia, increases the insulin/glucose ratio and improves β-cell function. Inhibition of β-cell apoptosis by BGE was associated with suppression of the cytokine-induced nuclear factor-kB- signaling pathway in the pancreas. In addition, these antidiabetic effects of BGE were stronger than those of RGE. In total, according to the data of this study, BGE protects β-cells from oxidative damage by suppressing cytokine-induced apoptotic signaling and exerts an antidiabetic effect in mice (Wei et al., 2015).

CK is a metabolic product of the protopanaxadiol type ginsenoside. This active ingredient in *Panax ginseng*, which is claimed to inhibit hepatic gluconeogenesis, has been studied *in vivo* and *in vitro* in a study. CK activity was measured *in vivo* in mice with type 2 diabetes by activating adenosine-5'monophosphate kinase (AMPK). 30 mg/kg/day CK was administered orally for 4 weeks, fasting blood glucose and 2 hours OGTT were checked. The results also showed that the effect of CK on inhibiting hepatic gluconeogenesis may be via AMPK activity (Kim et al., 2016).

Another *in vitro* study of CK observed its effect on insulin secretory activity on pancreatic β-cell. The results showed that CK increases insulin secretion and cellular ATP ratio. It has been observed that it has an activity stimulating insulin secretion in MIN6 cells with the glucose transporter isoform-2 (GLUT2) pathway (Gu et al., 2013).

3.2. Trigonella foenum-graecum L.

The plant *Trigonella foenum-graecum* L. in the Fabaceae family is distributed in parts of Central Asia, Europe, North Africa, North America and India and Australia. India ranks first in the world in the production of the plant. The most suitable region for its cultivation is Canada, as the day length is similar (Acharva et al., 2007).

Chemical composition of alkaloids (trimethylamine, neurine, trigonellin, choline, gentian, carpain, betaine), amino acids (isoleucine, 4-hydroxy isoleucine, histidine, leucine, lysine, valine, tryptophan, arginine, tyrosine, cystine, yamogenine, threanin, dioenin smilagenin, sarsasapogenin, tigogenin, neotigogenin, gitogenin), saponins (graecunins, fenugrin B, fenugreekin, trigophoenocytes A-G), steroidal saponins, flavonoids (quercetin, rutin, vetixin, isovetixin), fibers, vitamins, and other components (%) 28 mucilage, 22% protein, fixed fats) (Kirtikar and Basu, 2003; Ram, 1993).

Among the active ingredients in its content, especially quercetin, galactomannan, diosgenin, 4-hydroxy isoleucine and trigonellin show antidiabetic effects. Strong antioxidant compounds such as quercetin show antioxidant, anti-inflammatory, antitumor, immunomodulatory, antiulcer, anticancer, antidiabetic activities, and are effective in improving mental and physical performance (Phani et al., 2010). Recently, it has been reported that quercetin has antidiabetic effects *in vivo* and *in vitro* (Abdelmoaty et al., 2010). Quercetin mechanism; reducing intestinal glucose absorption, increasing insulin secretion from the pancreas, increasing glucokinase activity, preventing degeneration of β cells, increasing glycosidase inhibition, reducing insulin resistance and increasing adiponectin activity (Aguirre et al., 2011).

Semen foenu-graecum is known for its characteristic odor and the presence of Indian curry in it. It is traditionally used to increase breast milk, treat diabetes, and treat cough and bloating. It also has anti-inflammatory and aphrodisiac effects. Its use is limited, as it contains an unpleasant odor and taste; Mint leaves are frequently used to facilitate consumption. Its antidiabetic properties are mainly due to galactomannan, 4-Hydroxysoleucin, diosgenin and trigonelline. In clinical studies, these substances increase insulin secretion, reduce insulin resistance and provide regeneration of β cells. In addition to these main effects, it also has neuroprotective (trigonelline) and antioxidant (diosgenin, trigonellin) properties to regulate the blood lipid profile. The antidiabetic effect of trigonellin is comparable to glibenclamide therapy, but more effective than sitagliptin therapy. Compared to standard pharmacotherapy, fenugreek has good potential to be a new source of antidiabetic drugs (Koupy et al., 2015).

In an *in vivo* study, the effect of diosgenin, a saponin derived from Trigonella foenum-graecum, on lipid profile in plasma, liver, heart and brain was investigated in high-fat diet and STZ-induced diabetic rats. Diosgenin was administered to diabetic rats for 30 days at a dose of 60 mg/kg. After all; administration of diosgenin was observed to cause a significant decrease in body weight, blood glucose, insulin and insulin resistance in diabetic mice. It also modulated the lipid profile in plasma and tissues. At the end of this study, the effect of fenugreek and its components on both lipid profile and hyperglycemia was observed and it was concluded that it is a potential antidiabetic (Naidu et al., 2015).

In another *in vitro* study, 4-HIL, a compound obtained from Trigonella seeds traditionally used for the treatment of diabetes, reduced glucose level, hepatic glucose production, glucose/insulin ratio, liver damage markers, triglyceride and total cholesterol levels; It has been reported to increase glucose utilization and HDL-cholesterol. It was concluded that further clinical studies are needed to conclude that 4-HIL is more effective and safe than current drugs used in the treatment of type 2 diabetes (Zafar and Gao, 2016).

According to a review published in 2015; It has been reported that diosgenin, 4-hydroxyisoleucine and fiber compounds, which are the active substances in *Trigonella foenum-graecum*, have healthy physiological effects in terms of glucose tolerance, inflammation, insulin activity, liver function, blood lipids and cardiovascular function. Although there are some opinions about the underlying mechanism, there is still no definitive research proving it as a therapeutic agent in metabolic diseases. Therefore, it was concluded that further clinical studies are needed (Fuller and Stephens, 2015).

3.3. Cinnamomum cassia Blume

The countries where the *Cinnamomum cassia* Blume plant in the Lauraceae family is widely cultivated are India, China, Uganda, Vietnam, Bangladesh and Pakistan (Jain et al., 2011). The bark parts of the plant, known as Chinese cassia or Chinese cinnamon, are used as a drug.

The major active chemical components of *Cinnamomum cassia* are cinnamaldehyde (75-90%), coumarin (7%), and essential oils (4%). It also contains low amounts of eugenol, benzoic acid, cinnamic acid, salicylic acid, cinnamyl alcohol and related esters and aldehydes. The daily dosage of cinnamaldehyde has been determined by the FDA (US Food and Drug Administration) and WHO. It has been reported that the active chemical compounds in Cinnamomum cassia have anti-inflammatory, antioxidant, anticancer, antifungal, antipyretic, antimicrobial, antiangiogenic and larvicidal activities (Lean and Shu-Jing, 2011). Antihepatoma activities have also been reported, and the proposed mechanism may involve induction of signaling factors in hepatic cells (Lee et al., 2007). Studies are also examining whether *Cinnamomum cassia* has a positive effect on markers such as glycemic index, insulin resistance and glucose tolerance in diabetic individuals. Some studies support its antidiabetic effect by suggesting various molecular mechanisms; however, there are only a few studies supporting the antidiabetic effect of *Cinnamomum cassia* with clinical trials (Markey et al., 2011; Rafehi et al., 2012). Various studies conducted in recent years have reported the medicinal use of the plant in peptic ulcer and various cancers (Jain et al., 2011).

Cinnamomum cassia is currently marketed as a supplement for obesity, glucose intolerance, diabetes and dyslipidemia. Integrative medicine is a new concept that combines evidence-based complementary therapies with traditional therapies. *Cinnamomum cassia* has the potential to be useful in the management of type 2 diabetes. Currently, the evidence is insufficient and long-term studies are needed for efficacy and safety. However, the high coumarin content in *Cinnamomum cassia* raises concerns, while *Cinnamomum zeylanicum* is a safer alternative with its low coumarin content (Medagama, 2015).

In the *in vivo* study, STZ-induced diabetic mice received the herbal solution orally once daily for 4 weeks. At the end of the experiment, plasma glucose, malondialdehyde (MDA), superoxide dismutase activity (SOD) and serum aldose reductase (AR) were investigated, the effect of traditional drugs on α-glucosidase and angiotensin-converting enzyme was also investigated *in vitro.* Thirteen of 34 plant species significantly lowered plasma glucose. In this study, *Cinnamomum cassia* showed an antidiabetic effect by both preventing the decrease in SOD activity and suppressing the increase in MDA (He et al., 2011).

Procyanidin oligomers are thought to be responsible for the antidiabetic activity of *Cinnamomum cassia*. To investigate the hypoglycemic effect of different procyanidin oligomer species, two different extracts rich in procyanidin oligomer were prepared from two different *Cinnamomum* species. Type B and A procyanidin oligomers were obtained from *Cinnamomum cassia* extract and *Cinnamomum tamala* extract, respectively, using high performance liquid chromatography. Both were administered to mice at 200 mg/kg for 4 weeks. Both extracts showed antidiabetic effect; however, according to histopathological studies, *Cinnamomum cassia* extract contributed more to lipid accumulation in liver and adipose tissue, while *Cinnamomum tamala* extract improved insulin concentration in blood and pancreas (Chen et al., 2012).

In a study conducted to compare the effect of *Cinnamomum cassia* and *Cinnamomum zeylanicum, Cinnamomum cassia* was found to be significantly more effective than *Cinnamomum zeylanicum* in lowering blood glucose level and increasing plasma insulin secretion (Verspohl et al., 2005).

In an *in vitro* study on the use of several plant species used in South Africa in the treatment and management of type 2 diabetes; α-amylase and α-glucosidase activity, as well as Langerhans release activity were measured to evaluate the antidiabetic activity. *Sena alexandrina* Mill. (Fabaceae), *Cymbopogon citrates* Stapf. (Poaceae), *Cucurbita pepo* L. (Cucuribitaceae), *Nuxia floribunda* Benth (Stilbaceae), *Hypoxis hemerocallidea* Fisch and Mey (Hypoxidaceae) and *Cinnamomum cassia* Blume (Lauraceae). When all plants were evaluated, only *H. hemerocallidea* Fisch increased insulin secretion. Therefore, according to this study, it cannot be said with certainty that other herbs have a significant role in postprandial hyperglycemia (Boaduo et al., 2014).

According to these results, it is not possible to draw a definite conclusion that *Cinnamomum cassia* can be an antidiabetic treatment method. It has also been observed that it does not have the necessary potential to reduce postprandial hyperglycemia. More research is needed to elucidate the relationship between fasting blood glucose and blood glucose reduction and to quantify the potential for the use of *Cinnamomum cassia* supplement to prevent pathogenic complications of diabetes (Kirkham et al., 2009).

3.4. Cinnamomum zeylanicum Nees.

Dried stem and branch bark and leaf essential oils of *Cinnamomum zeylanicum* Nees. plant, which is also in the Lauraceae family, are used as drugs. The plants synonym names are *Cinnamomum verum* J.S. Presl, *Laurus cinnamomum* L. Although it is cultivated in Africa, Indonesia, India, Seychelles, South America and the West Indies, it mainly originates from Sri Lanka in the southeast of India (WHO, 1999b; Leela et al., 2008).

Three of the main components of essential oils obtained from the bark of *Cinnamomum verum* are trans-cinnamaldehyde, eugenol and linalool, representing 82.5% of the total composition (Chericoni et al., 2005).Trans-cinnamaldehyde accounts for approximately 49.9-62.8% of the total amount of bark essential oil (Simic et al., 2004; Singh et al., 2007). Cinnamaldehyde and eugenol are also major components of *Cinnamomum verum* extracts (Usta et al., 2003). One of the most important differences between *Cinnamomum verum* and *Cinnamomum cassia* is the coumarin (1,2-benzopyrone) content. The coumarin levels in *Cinnamomum cassia* are observed to be very high and pose health risks when taken regularly in high doses (Archer, 1988).

Cinnamomum verum is an herb that has been used by different cultures around the world for several centuries. Besides its culinary use, it is considered in Ayurvedic medicine as an aid to the treatment of respiratory, digestive, and gynecological ailments. Almost every part of the plant, such as bark, leaves, flowers, fruits and roots, has medicinal or culinary uses. Essential oils obtained from the bark, leaf and root parts are quite diverse in terms of chemical composition; therefore, it causes a variety of pharmacological effects (Shen et al., 2002).

One of the most important differences between *Cinnamomum verum* and *Cinnamomum cassia* is the coumarin (1,2-benzopyrone) content. The coumarin levels in *Cinnamomum cassia* are observed to be very high and pose health

risks when taken regularly in high doses. According to the German Federal Institute for Risk Assessment (BfR), 1 kg of *Cinnamomum cassia* powder contains approximately 2.1-4.4 g of coumarin, suggesting that 1 teaspoon of *Cinnamomum cassia* powder contains 5.8-12.1 mg of coumarin. This dose is above the tolerable daily intake for 0.1 mg/kg coumarin recommended by the European Food Safety Authority (EFSA) (Abraham et al., 2010).

Cinnamomum zeylanicum is a phytotherapeutic that has been used in many complaints among the people for centuries. There are *in vivo* and *in vitro* studies on spasmolytic, antiviral, antifungal, antidiabetic, antibacterial, antiparasitic, insecticide, antioxidant, anti-inflammatory, spermicidal effects, cytotoxic, hypoglycemic, hypolipidemic, wound healing effects. A study was conducted to evaluate the curative role of cinnamon oil on early stage diabetic nephropathy due to its antioxidant and antidiabetic effect. Cinnamon oil was extracted by aqueous distillation of the dried inner bark of *Cinnamomum zeylanicum*. IR, (1) 1 H-NMR, and (13) C-NMR techniques were used to further characterize the extracted oil. Early stage diabetic nephropathy was induced by alloxan (150 mg/kg). Cinnamon oil was applied at various doses (5, 10, 20 mg/kg), during which fasting blood glucose, total cholesterol, HDL-cholesterol, urea, thiobarbituric acid reagents, reduced glutathione and catalase levels were investigated. These parameters were compared in the cinnamon oil-treated groups and those receiving standard treatment (glipizide; 10mg/kg). Thus, it was investigated whether cinnamon oil has a significant protective effect for diabetic nephropathy. Studies in kidney tissues have proven that cinnamon oil has a protective effect on the kidneys by reducing glomerular enlargement, eliminating hyaline attacks and reducing tubular dilatation. The results show that cinnamon essential oil contains more than 98% cinnamaldehyde. This confers a dose-dependent significant protective effect against alloxan-induced renal injury. The maximum reduction in fasting blood glucose was achieved at a dose of 20 mg/kg (Mishra et al., 2010).

In a study that provided *in vitro* and *in vivo* conditions to evaluate the therapeutic potential of the medicinal use of cinnamon in type 2 diabetes, a functional food was formed with water-soluble polyphenols by placing *Cinnamomum zeylanicum* aqueous extract (CE) on a protein-rich matrix developed. Extracted soybean meal (CDSF) enriched with CE and cinnamon polyphenols was effective in lowering fasting blood glucose in the acute phase of rats in a diet-induced hyperglycemia picture at doses of 300 and 600 mg/kg body weight, respectively. To determine their mechanism of action, rat hepatoma cells were exposed to CE and CDSF washes in the range of 1-25 µg/ml. CE and CDSF washing liquid significantly inhibited hepatic glucose production in a dose-dependent manner at 25 µg/ml. In addition, CE reduced the gene expression of two major regulators of hepatic gluconeogenesis, phosphoenolpyrivate carboxykinase and glucose-6-phosphatase enzymes. It was concluded that the hypoglycemic and insulin-like effects of CE and CDSF may be helpful in the management of type 2 diabetes (Cheng et al., 2012).

Beneficial effects of *Cinnamomum zeylanicum* on animals; diabetes-related weight loss, decrease in fasting blood glucose, decrease in LDL-cholesterol and HbA1c, increase in HDL-cholesterol and insulin levels. In addition, *Cinnamomum* zeylanicum is effective in improving metabolic disorders associated with insulin resistance. It also has beneficial effects against diabetic neuropathy and nephropathy. No toxic effects on the liver and kidneys have been reported and it has a significantly high therapeutic effect. According to this meta-analysis, *Cinnamomum zeylanicum* is a potential therapeutic agent for type 2 diabetes in both *in vitro* and *in vivo* studies. However, more randomized clinical trials are needed to determine its therapeutic safety and efficacy (Ranasinghe et al., 2012).

3.5. Allium sativum L.

Synonym of the *Allium sativum* L. plant in the Asphodelaceae (Liliaceae) family is *Portivum sativum* Rehb, and the onion part is generally used as a drug. The most important chemical component of bulbus allii sativi is sulfur compounds (Roberts, 2011).

The most important chemical component of bulbus allii sativi is sulfur compounds. Organosulfur compounds (allin, methylin, isoallylin, cycloallyin), other sulfur compounds (allyl sulfites, allyl cysteine sulfoxide, methyl allyl thiosulfinate and related compounds), 0.1-0.2% sulfur essential oil (alicin, diallyl disulfide, diallyl trisulfide, ajoene), enzymes (alliinase, myrosinase, peroxidase), trace elements (selenium), carbohydrates (fructans, sucrose, glucose), vitamins (A, B, C), free amino acids (arginine), minerals (K, P, Mg, Na, Ca , Fe), lipids, phytoestrogens (genistein, daidzein), lignans, phytic acid, saponins, steroids (β-sitosterol), adenosine, fibers (1.5%) and water (up to 65% in spring onions, up to 7% in onions)) is found (Demirezer, 2011).

Organosulfur compounds (allin, methylin, isoallylin, cycloallyin), other sulfur compounds (allyl sulfites, allyl cysteine sulfoxide, methyl allyl thiosulfinate and related compounds), 0.1-0.2% sulfur essential oil (alicin, diallyl disulfide, diallyl trisulfide, ajoene), enzymes (alliinase, myrosinase, peroxidase), trace elements (selenium), carbohydrates (fructans, sucrose, glucose), vitamins (A, B, C), free amino acids (arginine), minerals (K, P, Mg, Na, Ca , Fe), lipids, phytoestrogens (genistein, daidzein), lignans, phytic acid, saponins, steroids (β-sitosterol), adenosine, fibers (1.5%) and water (up to 65% in spring onions, up to 7% in onions)) is found (Demirezer, 2011).

It is used for many purposes, both orally and topically. It is most commonly used to prevent and treat infections and maintain general health. It is mainly used in modern phytotherapy for the prevention of hypercholesterolemia and atherosclerosis. Recent studies on *Allium sativum* have focused on its dermatological effects, anticancer, antidiabetic, antithrombotic, antiplatelet, antihypertensive, neuroprotective, antioxidant effects in dementia and heart diseases. It has antidiabetic, antibacterial, antiviral, antifungal, antihypertensive, antihyperglycemic, antithrombotic, antimutagenic, antiplatelet pharmacological effects. These activities are associated with sulfur compounds (alliin, allicin, diallyl sulfide, ajoene, etc.) responsible for the pungent odor of the plant (Borrelli et al., 2007). Allicin is a sulfur-containing component responsible for the pungent odor of the plant and has a significant hypoglycemic effect (Sheela and Augusti, 1992). It is thought that this effect is achieved by increasing hepatic metabolism, increasing insulin secretion from pancreatic β cells, and/or insulin-sparing effect (Bever and Zahnd, 1979). S-allyl cysteine sulfoxide, another amino acid containing sulfur compound, controls lipid peroxidation better than glibenclamide and insulin, and improves diabetes complications (Augusti and Shella, 1996).

An *in vivo* study from 2010 examined the possible protective effects of S-allylcysteine (SAC) in STZ-induced diabetic mice. Blood glucose in plasma and pancreas was determined in the experimental group and the control group. To evaluate the changes in the cellular antioxidant defense system, reduced glutathione level, superoxide dismutase and catalase activities in plasma and pancreas were tested in pancreatic tissue homogenate. Glucose and enzymatic antioxidant levels

were altered in diabetic mice. These changes returned to the control level after SAC treatment. The antidiabetic and antioxidant effect of SAC was compared with gliclazide, a well-known hypoglycemic drug; This suggests that SAC therapy has therapeutic and protective properties in diabetes through the reduction of oxidative stress (Saravanan and Ponmurugan, 2010).

The classification of the pharmacopoeia and monographs that include the 5 plants mentioned above in detail is given in Table 2.

Table 2. Presence of some plants in pharmacopoeias and monographs.

Plants	***Panax ginseng***	***Trigonella foenum***	***Cinnamomum cassia***	***Cinnamomum zeylanicum***	***Allium sativum***
Pharmacopeia and monographs	American Pharmacopoeia	WHO Monographs	European Pharmacopoeia	European Pharmacopoeia	American Pharmacopoeia
	German Pharmacopoeia	Commission E Monographs	French Pharmacopoeia	Austrian Pharmacopoeia	African Pharmacopoeia
	European Pharmacopoeia	European Pharmacopoeia	WHO Monographs	Brazilian Pharmacopoeia	European Pharmacopoeia
	Austrian Pharmacopoeia	African Pharmacopoeia	British Pharmacopoeia	French Pharmacopoeia	Ganha Plant Pharmacopoeia
	Czech Pharmacopoeia	British Pharmacopoeia	African Pharmacopoeia	Dutch Pharmacopoeia	British Plant Pharmacopoeia
	Chinese Pharmacopoeia	Indian Pharmacopoeia	German Pharmacopoeia	British Plant Pharmacopoeia	ESCOP Monographs
	French Pharmacopoeia	Chinese Pharmacopoeia	Chinese Pharmacopoeia	British Pharmacopoeia	Commission E Monographs
	British Plant Pharmacopoeia		Commission E Monographs	Swiss Pharmacopoeia	WHO Monographs
	Swiss Pharmacopoeia		Japanese Pharmacopoeia	Mexican Pharmacopoeia	
	Japanese Pharmacopoeia			Egyptian Pharmacopoeia	
	Russian Pharmacopoeia			Portuguese Pharmacopoeia	
	ESCOP Monographs			Romanian Pharmacopoeia	
	Commission E Monographs			Greek Pharmacopoeia	
	PDR Plant Monographs			Martindale	
	WHO Monographs			ESCOP Monographs	
				Commission E Monographs	
				PDR Plant Monographs	
				WHO Monographs	

4. Discussion and Conclusions

The use of plants and preparations prepared from plants in many diseases has an increasing interest day by day. When the plants used for the treatment of diabetes are examined, it is seen that they are widely used in many countries. Figure 2 shows the distribution of plants used in the treatment of diabetes by country.

It can be clearly seen from here that plants are frequently used in the treatment of diabetes in Turkey. The use of plants in the treatment of diseases is frequently seen in ethnobotanical studies, including their use among the public. Not only in our country, but also in many countries around the world, plants have a great place in the treatment and prevention of diseases. For this reason, the importance of the values that every possible study in the field will add to the scientific world is obvious.

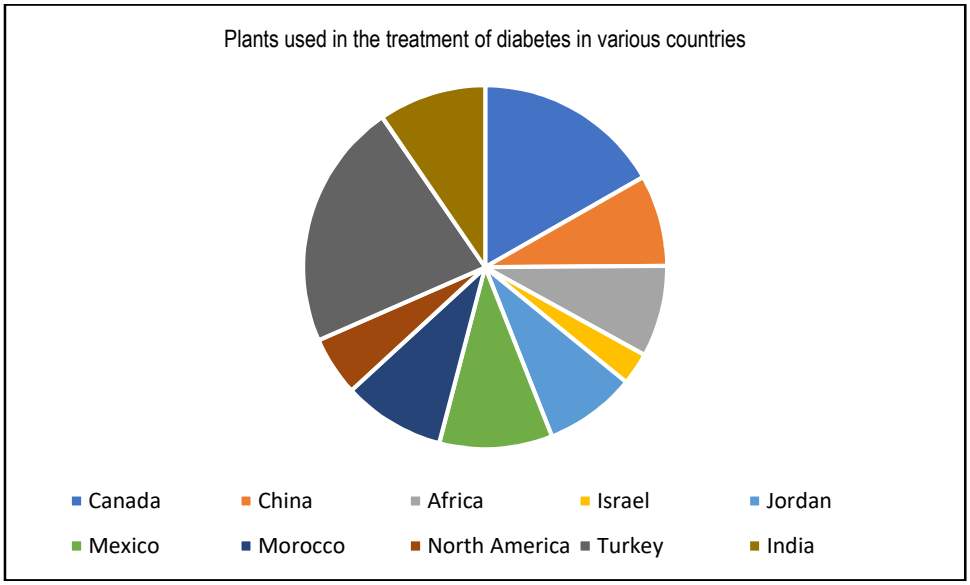

Figure 2. Distribution rates of plants used in the treatment of diabetes by country.

Conflict of Interest

The author have no conflict of interest to declare.

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Authors' Contributions

This study's experimentation, analysis and writing, etc. all steps were made by the author.

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