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Original Article

Evaluation of Potential Toxicity Associated with Antidiabetic Herbs in Saudi Arabia

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ABSTRACT

Introduction: Diabetes mellitus is a serious, long-lasting disease that is characterized by high blood sugar levels, leading to more severe complications involving other organ systems of the body. Diabetes is becoming more common worldwide. Managing diabetes can be complicated, but many people, especially in Saudi Arabia, often use traditional herbal medicines to treat the condition. Our study concentrates on assessing the safety of commonly used antidiabetic herbs in Saudi Arabia by examining their potential toxicity. **Method:** Using keywords and their variations, we conducted a systematic search of the PubMed and Google Scholar databases to find studies on treatments based on antidiabetic herbs and their toxic effects from 2014 to 2024. **Result:** Our study revealed that the use of medicinal plants for treating and managing diabetes along with its complications is becoming popular around the globe. These medicinal plants are also being used as primary sources of developing modern pharmaceutical antidiabetic drugs. Phytotherapy is safe to treat diabetes as herbal bioactive components act through many biological pathways. They may inhibit α-glucosidase enzyme, enhance GLUT-4 translocation, and also improve lipid profile. **Conclusion:** The use of natural plants having medicinal properties is popular for the treatment of diabetes. Claims of their usefulness by traditional healers are being supported by scientific evidence also. To determine the right dosage of these medicinal herbs, cytotoxicity tests or short-term experiments are done to establish doses of plants used in vitro and in vivo. Toxicity concerns are a primary reason why healthcare professionals hesitate to incorporate herbal products into the healthcare system. That's why it is necessary to screen such plants for their toxicity to differentiate pharmacological efficacy from adverse effects.

Keywords: Herbal medicines, plant extracts, phytotherapy, diabetes, KSA, Saudi Arabia, traditional, Medicinal herbs, antidiabetic, toxicity.

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INTRODUCTION

Diabetes mellitus (DM) is a serious and chronic metabolic condition that arises from various causes and is marked by hyperglycemia along with disruption in the metabolism of carbohydrates, fats, and proteins which leads to damage to multiple organs.[1,2] According to the World Health Organization (WHO) criterion, diabetes is diagnosed when the fasting plasma glucose level is equal to or more than 7.0 mmol/L[3]. There are three types of diabetes, type 1 diabetes (insulin-dependent diabetes mellitus), type 2 diabetes (insulin-independent diabetes mellitus), and gestational diabetes (occurs in the second or third trimester of pregnancy).[1]

The incidence of diabetes is on the rise globally. The International Diabetes Federation (IDF) reported in its Diabetes Atlas that around 463 million adults aged between 20 and 79 years have diabetes. This number is expected to increase to 783 million by 2045.[1,4] In 2012, diabetes was responsible for 1.5 million deaths, and hyperglycemia was linked to an extra 2.2 million deaths because of its association with an increased risk of cardiovascular and other medical issues[5]. Factors like family history, older age, being obese, intake of unhealthy foods, smoking, and lack of physical activity contribute to an increased risk of developing diabetes. The majority of the individuals with diabetes suffer from type 2. The World Health Organization predicts that by 2030, diabetes will become the seventh leading cause of death globally.[6]

In the Kingdom of Saudi Arabia (KSA), there is a common practice among the population to use traditional medicines to treat conditions like hypertension, diabetes mellitus, and infertility. Over 25 different plants are used as medicines in KSA to treat diseases, especially among females. The rate of use of herbal medicines in Saudi is up to 69.9%.[7] The WHO ranks Saudi as the second highest in the Middle East and seventh globally for the fastest-growing rates of diabetes. Within the country, about 7 million people, constituting 20% of the population, suffer from diabetes, and around 3 million others are diagnosed with pre-diabetes.[8] A study conducted in Al Qassim, Saudi Arabia, found that over half of the complementary and alternative medicine (CAM) users (51.06%) were suffering from diabetes compared to other chronic conditions.[4]

There is no precise treatment available for diabetes at present. Several medications have been utilized for managing the disease ever since the blood sugar-lowering effects of sulfonamides were revealed.[9] The management of diabetes is a bit complex because of its severity and effects on multiple systems. It can be controlled through primary preventive measures such as a healthy diet, exercise, oral hypoglycemic agents, and insulin therapy. Multiple types of hypoglycemic drugs are used to manage diabetes. These include sulfonylureas, biguanides,

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α-glucosidase inhibitors, thiazolidinediones, and non-sulfonylurea secretagogues.[6,10] In developing countries, herbal medicines are often used to treat diabetes, especially when the cost of conventional medicines is quite high.[9,11] A wide variety of plants have medicinal properties and can be used to manage diabetes as they have various active ingredients that affect several biological pathways to relieve symptoms of diabetes. They either improve the function of the pancreas to release insulin or decrease the glucose absorption in the intestines. These antidiabetic plants have been used traditionally and are still popular for their effects on lowering blood sugar levels. Bioactive ingredients derived from these medicinal herbs are also an excellent source for the development of new pharmaceutical drugs with reduced toxicity.[6,12] Metformin which is known for its preventive effect on diabetes was derived from Galega officinalis L., the French lilac.[10] The major benefits of medicinal plants are their ease of availability, low cost, and minimal side effects.[11]

Although there are some concerns regarding the safe use of herbal medicines, many studies support the idea of phytotherapy. As herbal medicines contain multiple ingredients that interact with each other and other pharmaceutical drugs that may lead to serious side effects, the proper dosage needs to be determined to lower the risk of potential side effects. The importance of phytotherapy is clear as ingredients obtained from herbs that have low toxicity are significant choices for treating diabetes around the world.[6,9]

AIM

This study aims to assess the safety profile of commonly used antidiabetic herbs in Saudi Arabia by evaluating their potential toxicity.

OBJECTIVE

The objective of this study is to systematically identify and analyze the toxic effects associated with the use of antidiabetic herbs in Saudi Arabia. This will involve the collection of toxicological data, the assessment of interaction between herbs and other drugs, and the documentation of adverse effects.

METHODOLOGY

Search strategy

For our research, we conducted a comprehensive search for articles published between 2014 and 2024 on PubMed and Google Scholar sites. Key terms associated with our study such as "toxicological evaluation" OR "anti-diabetic" OR "phytotherapy" OR "herbal hypoglycemic" OR "Saudi Arabia" and their related variations were used to search and identify relevant articles. We ensured that each selected article had required data like the importance and properties of antidiabetic herbs, as well as evaluation of side effects of their use. We analyzed the titles, abstracts, aims, and objectives with the help of specific keywords to extract relevant data for our study.

Inclusion criteria

- Articles published in the year from 2014 to 2024.
- Those having information about antidiabetic plants along with their significance and toxicity.

Exclusion criteria

- Articles written in languages other than English were not included.
- Studies regarding multi-organ system complications of diabetes were not included.
- All forms of gray literature were also excluded.

Data evaluation

With the help of keywords and their variations, we conducted a systemic search on PubMed and Google Scholar databases for studies with information on the phytotherapy of diabetes and its toxic effects from 2014 to 2024. This strategic search aimed to get relevant studies for our review. Around 18,000 search results were given by Google Scholar and approximately 3500 results were provided by PubMed. 341 records from Google Scholar and 11 records were selected from PubMed. Initially, around 30 articles with suitable titles and abstracts were selected after the process of screening and selection. Then, the inside contents of each article were evaluated to collect data. This included a collection of data by assessing introductions, methodology, results, and discussion parts of the studies to gather information. This final evaluation left us with 6 selected articles in the end. (Figure. 1)

Data collection

The titles and abstracts from relevant journal publications were thoroughly reviewed by the authors. Then, the full texts of the documents that appeared to have the required information were collected. Articles with detailed information such as the traditional use of herbs for the treatment of diabetes, their mechanism of action, how they interfere with bodily functions to treat the disease, their interaction and use with new pharmaceutical drugs, and their possible side effects were considered for our systemic review. (Table 1)

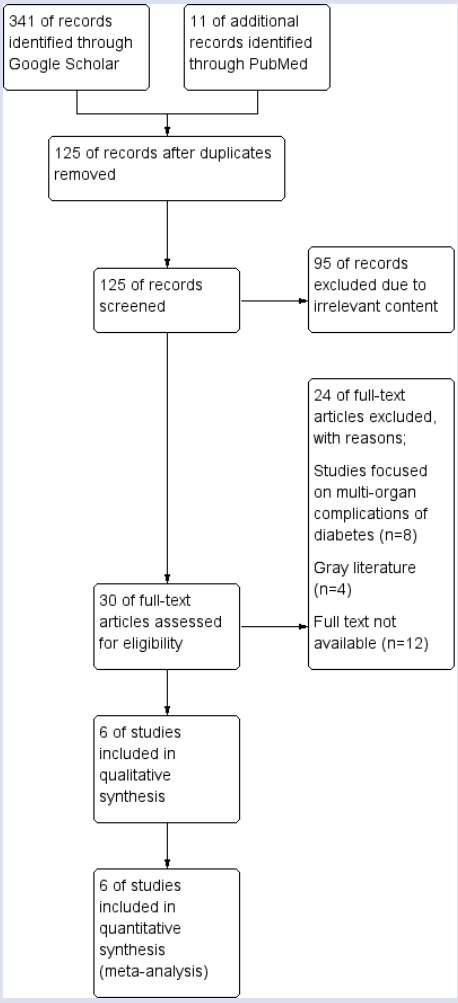

Figure 1: Study selection following PRISMA flow chart.

Table 1: Articles included in this systematic review for data extraction.

Title	Article	Type of study	Country	Herb	Findings
Effect of Fenugreek on Hyperglycemia: A Systematic Review and Meta-Analysis[13]	Shabil M et al., 2023	Systematic Review and Meta-Analysis	India	Fenugreek	Decrease in fasting blood glucose (p value: 0.76), postprandial glucose level (p value: 0.72), and HbA1c levels (p value: 0.00).
In Vitro Anti-Diabetic, Anti-Inflammatory, Antioxidant Activities and Toxicological Study of Optimized *Psychotria malayana* Jack Leaves Extract[14]	Syed Mohamad SNA et al., 2023	Experimental	Malaysia	Psychotria malayana	Toxic effects on zebrafish embryos; highest survival at conc. of 50 µg/mL, highest mortality at conc. 100 µg/mL and higher.
Phytochemical, Antidiabetic, Antioxidant, Antibacterial, Acute and Sub-Chronic Toxicity of Moroccan *Arbutus unedo* Leaves[15]	Doudach L et al., 2023	Experimental	Morocco	Arbutus unedo	Metganolic extracts strongly inhibited glucosidase and amylase. Toxic study on mice and rats showed no significant difference.
Medicinal Plants Used for the Traditional Management of Diabetes in the Eastern Cape, South Africa: Pharmacology and Toxicology[16]	Odeyemi S et al., 2018	Systematic Review	South Africa	Tulbaghia violacea, Catharanthus roseus, Bulbine frutescense, Allium sativum	Decrease in blood glucose levels.
Crocetin: A Systematic Review[17]	Guo ZL et al., 2022	Systematic Review	China	Crocetin	Increased body weight and insulin levels, Improved lipid profile, Decreased blood glucose levels.
Phytotherapy in the Management of Diabetes: A Review[18]	Governa P et al., 2018	Systematic Review	Italy/ Switzerland	Allium cepa L., Azadirachta indica A. Juss., Ocimum tenuiflorum L.	Inhibit α-glucosidase, enhance GLUT-4 translocation Decreased non-enzymatic glycation, inhibit advanced glycation end products, decreased oxidative stress, increased levels of glucose-6-phosphatase Improved fasting glucose levels, glucose tolerance, decreased LDL cholesterol levels.

FINDINGS

Fenugreek is a medicinal herb traditionally used in cooking and in medicinal contexts across various cultures. Its seeds are known for lowering blood sugar levels and improve glucose tolerance, benefiting those with diabetes. Trials were conducted by Shabil M. et al. to evaluate changes in fasting blood glucose, postprandial blood glucose, and HbA1c levels among participants and the control group treated with fenugreek. The analysis calculated the mean difference with 95% confidence intervals (CI) from 14 studies including 894 participants. Results indicated a decrease in fasting blood glucose levels (MD: 3.70, 95% CI of −27.02, 19.62; p = 0.76), postprandial blood glucose (MD: −10.61, 95% CI of −68.48, 47.26; p = 0.72), and HbA1c (MD: −0.88, 95% CI −1.49, −0.27; p = 0.00) among those who consumed fenugreek. As fenugreek is both accessible and affordable, it is necessary to conduct thorough double-blinded randomized controlled trials to fully understand its effectiveness as an herbal agent for managing diabetes. Research indicates that fenugreek seeds might reduce insulin and glucose levels after meals. Additionally, some extended studies have observed a decrease in fasting plasma glucose, postprandial glucose, and glycated hemoglobin (HbA1c) levels when using fenugreek, though results have varied across different studies.

Effect of Fenugreek on Fasting Blood Glucose Level

There was a decrease in fasting blood glucose levels in the treatment group as compared to the control group, but the difference was statistically insignificant. The summary effect measure indicated a mean difference of -3.70, with a 95% confidence interval of -27.02 to 19.62 and a p-value of 0.76. Heterogeneity was significant among the studies, with a τ^2 value of 1761.14 and an I^2 value of 99.37%.

Effect of Fenugreek on Postprandial Glucose Level

A decrease in postprandial glucose level was observed in the treatment group when compared to the control group. The summary effect measure indicated a mean difference of -10.61, with a 95% confidence interval of -68.48 to -47.26 and a p-value of 0.72. Heterogeneity among the studies was observed, with a τ^2 value of 5083.61 and an I^2 value of 99.10%.

Effect of Fenugreek on HbA1c

As compared to the control group, the treatment group showed a notable decrease in HbA1c levels. The summary effect measure showed a mean difference of -0.88. The confidence interval was 95% which ranged from -1.49 to -0.27, and the p-value was 0.00, indicating statistical significance. There was also significant heterogeneity among the studies, with a τ^2 value of 0.49, an I^2 value of 74.79%, and a p-value of 0.00.[13]

The therapeutic effectiveness of Psychotria malayana, commonly called Salung, from the Rubiaceae family, was evaluated by Syed Mohamad SNA. et al. by studying its ability to inhibit α-glucosidase activity (AGI). A zebrafish embryo/larvae (Danio rerio) was used for toxicity evaluation. Metabolites in the extracts of P. malayana were analyzed using GC-MS (gas chromatography-mass spectrometry) and LC-MS (liquid chromatography-mass spectrometry). The optimized extract (OE) of P. malayana leaves showed significant α-glucosidase inhibition (AGI) and SLOXI activities, with IC50 values of 2.02 and 4.92µg/mL respectively. It also displayed strong antioxidant properties, with IC50 values of 13.08µg/mL (using the DPPH assay) and 95.44mmol TE/mg DW (using the FRAP assay). Additionally, it showed an LC50 value of 224.29µg/mL, which exceeds its therapeutic index of 111.03. In comparison to the methanol extract, which had a therapeutic index of 13.84, OE showed a higher therapeutic index, indicating lower toxicity and greater safety for use. This finding indicates that OE could be used effectively in treating diabetes with a lower risk of side effects. Liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectrometry (GC-MS) were used to identify different constituents in the extract. Among these, propanoic acid, succinic acid, procyanidin B3, and leucopelargonidin have been found effective for their anti-diabetic activities.

Toxicological effect analysis

Zebrafish embryos were treated with OE to access morphological, morbidity, and mortality outcomes. Morphological abnormalities were observed in zebrafish exposed to OE, as well as in the solvent control (1% DMSO in E3 medium), positive control, and E3 medium used as the negative control. No morphological changes were observed in the zebrafish group treated with the extract at a concentration of 50 µg/mL, resembling the negative and solvent controls. However, all morphological defects related to lethality were observed in the remaining zebrafish groups. The highest survival rate was seen in the negative control, solvent control, and zebrafish group treated with OE at a concentration of 50 µg/mL. On the other hand, the highest mortality rates were observed in the positive control and zebrafish groups treated with OE, especially at concentrations of 100 µg/mL and higher.[14]

Arbutus unedo is a perennial medicinal plant from the Ericaceae family, commonly found in North Africa and the Mediterranean region. It is used traditionally as Moroccan medicine to treat various conditions related to the skin, gastrointestinal tract, and urinary tract. Doudach L. et al. assessed the anti-diabetic properties of A. unedo leaves extract to evaluate their ability to inhibit activities of α-glucosidase and α-amylase enzymes.

In vitro Antidiabetic activity

Antidiabetic activity analysis of A. unedo leaves was done in vitro. The methanolic extract showed the strongest inhibition of both glucosidase and amylase, with IC50 values of 0.099 ± 1.21 and 1.350 ± 0.32mg/mL, respectively. The methanolic extract showed stronger inhibition of α-glucosidase than the medication acarbose ($p < 0.05$), with IC50 values of 199.53 ± 1.12 and 396.42 ± 5.16g/mL, respectively. On the other hand, the aqueous extract was less effective than the methanolic extract against both α-glucosidase and α-amylase, with IC50 values of 0.196 ± 4.21 and 1.320 ± 0.26mg/mL, respectively.

Toxicological investigation

Acute toxicity study in mice

Acute oral toxicity of extracts was determined by using Swiss female mice. Throughout the study, all animals were given unrestricted access to tap water and the same type of chow. However, there was a brief period of fasting before the oral administration of the single doses of A. unedo leaf extract. The treatment mice group received oral doses of 2,000mg/kg and 5,000mg/kg, while the untreated control group received distilled water and the vehicle was dosed. The behavior of the mice was continuously observed for the first hour after injection and regularly for the first 24 hours, with specific attention to the initial 4 hours. Also, the mice were observed daily for the subsequent two weeks to observe any change in weight, death, or any other symptomatic disorders during the study duration.

This investigation showed that the A. unedo aqueous leaf extract did not affect the changes in body weight of mice during the observation period compared to the control group.

Sub-chronic toxicity study in rats

Sub-chronic toxicity was evaluated in rats for 90 days. The treatment group was given two dosages (250, 500mg/kg) of aqueous extract daily while the control group received a physiological solution (vehicle). These dosages were given orally to the rats through an esophageal probe. Changes in weight and behavior were calculated and documented weekly. Over time, the results showed that rats gained weight and there was no significant difference in mean weight growth between the treated and control rats.

Arbutus unedo leaves have bioactive properties, which are considered safe for use in pharmaceuticals, chemicals, and the food industry.[15]

Odeyemi S. et al. conducted a majority of laboratory tests at doses ranging from 10 to 50 µg/mL. In the in vivo study of Tulbaghia violacea, the highest dose used was 50µg/mL for INS cells, while it was 10µg/mL for C2C12, Chang liver cells, and 3T3-L1 cells. Catharanthus roseus was studied in Chang liver cells at a maximum concentration of 12.5 µg/mL. Meanwhile, studies indicate that Bulbine frutescent, at a concentration of 50µg/mL, enhances glucose utilization in C1C2 cells more effectively than insulin does, and also stimulates glucose absorption at a concentration of 12.5µg/Ml IN Chang liver cells. Additionally, in vivo studies were conducted using dosage ranges from 300 to 800mg/kg body weight. Human subjects were given Allium sativum (300mg three times per day) and metformin (500mg two times per day), and both showed similar decreases in blood glucose levels.[16]

A study was done by Elgazar et al. on rats with diabetes induced by alloxan. The results showed that the aqueous extract of saffron increased the body weight and serum insulin levels, improved lipid profile, and decreased the levels of blood glucose. Xi et al. noted that crocetin regulates insulin resistance induced by food rich in fructose and insulin insensitivity caused by free fatty acids. Crocetin replaced the normal levels of adiponectin, leptin, and TNF- α in the experimental group of their study. It was demonstrated by Sheng et al. that crocetin improves insulin sensitivity by increasing the oxidation of non-esterified fatty acids and triglycerides in the liver cells. The therapeutic effects of crocetin on streptozocin (STZ)-induced gestational diabetes mellitus (GDM) in rats were explored by Zheng et al. The findings revealed that crocetin decreased the levels of blood glucose but increased the body weight in the rats.

The safety of crocetin has been thoroughly investigated because of its wide range of medicinal benefits. The effects of crocetin were evaluated by Mori et al. in children with myopia. Soft capsules of crocetin at a dose of 7.5 mg were given one time a day for 24 weeks through oral route to the children. There were no adverse effects related to the use of crocetin.[17]

Allium cepa L., commonly called onion, is a herb from the Amaryllidaceae family. The primary chemical elements are sulfur-containing compounds like I-cysteine sulfoxides, and flavonoids, including quercetin and its glycosides. A. cepa is used in various forms, such as powder, juice, or essential oil, for its antidiabetic effects. An initial investigation done by Governa P. et al., tested the small slices (100g/day) of onions given orally to patients with type 1 and 2 diabetes. The results showed that A. cepa decreased the fasting blood glucose levels to about 89 mg/dL in type 1 diabetes and 40 mg/dL in type 2 diabetes patients. A decrease of 120 mg/dL in type 1 and 159 mg/dL in type 2 diabetes patients with induced hyperglycemia was also observed. Quercetin along with rutin gives A. cepa its antidiabetic properties. They inhibit α-glucosidase and enhance GLUT-4 translocation, improve glucose uptake and the role of insulin.

Governa P. et al., also observed Azadirachta indica A. Juss., most commonly known as neem, is from the family Meliaceae. The dried leaves of this plant are commonly used as herbal remedies. It contains unique compounds called oxidized tetranotriterpenes, specifically azadirachtins. Activities of its chloroform extracts were assessed in vitro and in vivo using rats with streptozocin-induced diabetes at doses from 200 to 300 mg/kg. These extracts reduced non-enzymatic glycation and inhibited the formation of advanced glycation end products (AGEs). They also decreased oxidative stress by increasing the levels of antioxidant enzymes. Also, the extracts increased the levels of glucose-6-phosphatase and hepatic glycogen content, as well as plasma levels of insulin, while decreasing glucokinase activity and lipid peroxidation. The primary mode of action of azadirachtins, such

as azadirachtolide, and azadiradione, is the inhibition of α-glucosidase and α-amylase enzymes.

Tulsi, also known as Ocimum tenuiflorum L., is a shrub in the Lamiaceae family. It is native to India, Taiwan, and some parts of Africa. Its leaves, fresh or dried, are used as herbs because of the presence of tannins and essential oils, primarily eugenol, methyl eugenol, and α- and β-caryophyllene. A randomized, pilot study tested the impact of tulsi extracts on metabolic and biochemical markers in 30 young overweight individuals. O. tenuiflorum capsules of dose 250 mg were given two times daily for 8 weeks. This reduced the plasma insulin levels by 28.49% and insulin resistance by 24.79%. Serum lipid profile became normal and also there was a decrease in body weight and BMI in the treated individuals compared to the control group, which received no intervention. Tulsi, when given orally in the form of aqueous extracts at a dose of 200 mg/kg in animal studies, has been shown to delay the development of insulin resistance. It has been concluded that tulsi significantly improves fasting blood glucose levels and glucose tolerance. It also improves lipid profile by decreasing the LDL cholesterol levels.[18]

DISCUSSION

Diabetes is a chronic disease that leads to excessively high blood sugar levels. Recently, the number of people diagnosed with diabetes has risen across almost all parts of the globe, affecting millions. This increase is troubling due to its significant impact on life quality, healthcare demands, and financial burdens. The disease is associated with a series of health issues such as multi-organ complications, and blindness, and may even lead to amputations of lower limbs due to diabetic foot.[19]

For centuries, medicinal plants have been used as the primary source of treatments for many illnesses because of their vast biological and pharmacological effects. There is a common belief that plants are safe to use as medicines without having any adverse effects as they are natural, making them a safer option for treatment as compared to synthetic drugs.[15] Traditionally, plants have always been the main source of medicine for treating various health problems. Nowadays, discovering new compounds that have beneficial effects on the body systems is quite challenging. This can be achieved by identifying phytochemicals from plant extracts. The presence of these phytochemicals and their extracts are the reason why plants are being used as medicines.[16]

It is proven that when herbal medicines are given in combination with antidiabetic drugs, this changes how the drugs affect and are processed in the body. The interactions between herbal and other pharmaceutical drugs are quite complex because the disease involves different biological and medical factors, and herbal medicines are made up of many active components.[2] These herbal ingredients have the ability to inhibit α-glucosidase enzyme which decreases the release of D-glucose from complex sugars like oligosaccharides and disaccharides present in our regular food. This results in slower absorption of glucose, which in turn decreases the blood sugar levels after food intake and prevents the increase of sugar levels in the blood.[14]

In the Kingdom of Saudi Arabia, among all the herbs used for treating diabetes, cinnamon and fenugreek are the most popular herbs. They are also commonly used by individuals in Bahrain, Oman, Iraq, and Jordan due to their ease of availability.[20] Yeung et al. conducted a quantitative review of existing research on antidiabetic herbal products, summarizing the main trends in natural product research for diabetes treatment and management.[19] Many studies show that the presence of these components may have adverse effects on human health as these plants can prove toxic and lead to severe side effects, even death. Although there are concerns regarding the side effects of phytotherapy, the combination of these drugs has generally demonstrated positive outcomes in terms of improved antidiabetic effects.[2] It is necessary to evaluate the safety and toxicity of medicinal herbs as they are easily accessible and affordable, which makes them widely accepted for treatment. That's why it is necessary to screen such plants for their toxicity to differentiate pharmacological efficacy from adverse effects.[16]

CONCLUSION

Diabetes mellitus is widely recognized as a serious health condition that can lead to severe complications. In order to manage these complications, healthcare professionals often combine these herbs with antidiabetic drugs as combination therapies to manage the disease. Our review, supported by numerous studies, indicates that phytotherapy is becoming popular in medicine for treating diabetes. Herbal products are not only being prescribed as medications but also as food additives, antioxidants, and supplements. Ongoing research is developing new drugs by isolating antidiabetic compounds for these herbal drugs. Future studies should also focus on determining the right concentration of herbal drugs that can be given to individuals safely.

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REFERENCES

1. Tran N, Pham B, Le L. Bioactive Compounds in Anti-Diabetic Plants: From Herbal Medicine to Modern Drug Discovery. Biology (Basel). 2020;9(9).
2. Gupta RC, Chang D, Nammi S, Bensoussan A, Bilinski K, Roufogalis BD. Interactions between antidiabetic drugs and herbs: an overview of mechanisms of action and clinical implications. Diabetol Metab Syndr. 2017;9:59.
3. Chinsembu KC. Diabetes mellitus and nature's pharmacy of putative antidiabetic plants. Journal of Herbal Medicine. 2019;15:100230.
4. Almaqhawi A, Hayim EA, Amer FAA, Almuhanna S, Khteeb NAA, Khwajah SHA. Use of Complementary and Alternative Medicines (CAMs) Among Diabetic Patients in Al Ahsa, Saudi Arabia: A Cross-Sectional Study. Mater Sociomed. 2023;35(4):256-63.
5. El-Tantawy WH, Temraz A. Management of diabetes using herbal extracts: review. Arch Physiol Biochem. 2018;124(5):383-9.
6. Salehi B, Ata A, N VAK, Sharopov F, Ramírez-Alarcón K, Ruiz-Ortega A, et al. Antidiabetic Potential of Medicinal Plants and Their Active Components. Biomolecules. 2019;9(10).
7. Abdelmola AO, Bahri A, Abuallut I, Refaei BA, Hakami WK, Abutaleb AK, et al. Prevalence, knowledge, and perception about the use of herbal medicines jazan - Saudi Arabia. J Family Med Prim Care. 2021;10(6):2386-93.
8. Alzahrani MA, Alsiary KA, Khan MA, Bushnaq A, Alzahrani B, Salama M, et al. Perception of herbs use in treating diabetes among patients attending specialized polyclinics of National Guard Health Affairs, Jeddah. J Family Med Prim Care. 2023;12(2):270-5.
9. Sunmonu TO, Afolayan AJ. Evaluation of Antidiabetic Activity and Associated Toxicity of Artemisia afra Aqueous Extract in Wistar Rats. Evid Based Complement Alternat Med. 2013;2013:929074.
10. El-Abhar HS, Schaalan MF. Phytotherapy in diabetes: Review on potential mechanistic perspectives. World J Diabetes. 2014;5(2):176-97.
11. Arumugam G, Manjula P, Paari N. A review: Anti diabetic medicinal plants used for diabetes mellitus. Journal of Acute Disease. 2013;2(3):196-200.
12. Džamić AM, Matejić JS. Plant Products in the Prevention of Diabetes Mellitus. Mini Rev Med Chem. 2022;22(10):1395-419.
13. Shabil M, Bushi G, Bodige PK, Maradi PS, Patra BP, Padhi BK, et al. Effect of Fenugreek on Hyperglycemia: A Systematic Review and Meta-Analysis. Medicina (Kaunas). 2023;59(2).

14. Syed Mohamad SNA, Khatib A, So'ad SZM, Ahmed QU, Ibrahim Z, Nipun TS, et al. In Vitro Anti-Diabetic, Anti-Inflammatory, Antioxidant Activities and Toxicological Study of Optimized Psychotria malayana Jack Leaves Extract. Pharmaceuticals (Basel). 2023;16(12).

15. Doudach L, Mrabti HN, Al-Mijalli SH, Kachmar MR, Benrahou K, Assaggaf H, et al. Phytochemical, Antidiabetic, Antioxidant, Antibacterial, Acute and Sub-Chronic Toxicity of Moroccan Arbutus unedo Leaves. J Pharmacopuncture. 2023;26(1):27-37.

16. Odeyemi S, Bradley G. Medicinal Plants Used for the Traditional Management of Diabetes in the Eastern Cape, South Africa: Pharmacology and Toxicology. Molecules. 2018;23(11).

17. Guo ZL, Li MX, Li XL, Wang P, Wang WG, Du WZ, et al. Crocetin: A Systematic Review. Front Pharmacol. 2021;12:745683.

18. Governa P, Baini G, Borgonetti V, Cettolin G, Giachetti D, Magnano AR, et al. Phytotherapy in the Management of Diabetes: A Review. Molecules. 2018;23(1).

19. Durazzo A, Lucarini M, Santini A. Plants and Diabetes: Description, Role, Comprehension and Exploitation. Int J Mol Sci. 2021;22(8).

20. Alqathama A, Alluhiabi G, Baghdadi H, Aljahani L, Khan O, Jabal S, et al. Herbal medicine from the perspective of type II diabetic patients and physicians: what is the relationship? BMC Complement Med Ther. 2020;20(1):65.

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