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The Use of Antidiabetic Herbal Remedies by Jordanian Herbalist: A Comparison of Folkloric Practice vs. Evidence-Based Pharmacology

Reem Issa[1]*, Areen Khattabi[2], Tabarak A.Alkarem[3], Omar Altameemi[3]

[1] Department of pharmaceutical sciences, Faculty of Pharmacy, Yarmouk University, Irbid-Jordan.
[2] Department of pharmaceutics and pharmaceutical sciences, Faculty of Pharmacy, Applied Science Private University, Amman, Jordan.
[3] Undergraduate students, Faculty of Pharmacy, Applied Science Private University, Amman, Jordan.

ABSTRACT

Traditionally used herbal remedies are an essential part of the Jordanian folklore, due to its abundance in vast sources of ethnomedicine.

This study conducted a face to face interview with a random sample of local herbalists, focused on traditionally used antidiabetic herbal remedies. Subsequently, these remedies were validated for evidence-based pharmacological studies, using data in the literature to find out the available information about different clinical, *in vitro* or *in vivo* studies.

Two traditionally used antidiabetic herbal mixtures were found commonly prescribed, composed of twelve different plant species. Nine species proved to be effective in in vitro, in vivo and clinical evaluations for their antidiabetic effect. Only one species was found to be effective on animal models or as enzyme inhibitor, but not in any clinical studies. Another two species were found to be ineffective neither in invitro, invivo nor in clinical evaluations.

This review will help to strengthen the relation between traditional medicine and evidence-based pharmacology. Also, it will shed the light on the ethnomedicine practices in Jordan, revealing some common errors among herbalist's practices and uses of antidiabetic herbal remedies. We recommend for these traditionally used plants, to go for extensive chemical investigations as well as clinical trials, in order to find out potential new antidiabetic agents.

Keywords: Antidiabetic, Ethnomedicine, Evidence-based, Jordan, Pharmacology.

1. INTRODUCTION

Traditional uses of medicinal herbal remedies have been of interest not only in Jordan, but also at the Arab world and at the global level.[1] Historically, a lot of ethnobotanical surveys revealed that medicinal plants are used to treat varied diseases; like the nervous system, cardiovascular systems, respiratory system, digestive and other systems.[2] Because of being natural, there are common believes that they are highly effective and safe.[3] Nevertheless, many previous as well as recent research and reviews revealed that there is a significant gap exists between scientific validation of the traditional uses, and the proved pharmacological activities of herbs used by the public and herbalists. [2,4,5,6]

As the alarming rising trend of diabetes prevalence in the Arab region constitutes a real challenge for heath decision makers,[7] a similar scenario was also shown in Jordan. In a study performed by Al-Nsour and coworkers in 2012 on Jordanian population with chronic diseases, it was estimated that 11% of the study population in 2007 was diagnosed with diabetes by a health professional, and 19% was diagnosed with diabetes according to laboratory testing.[8] In addition; diabetes were also found to cause the proportion of deaths attributable to diabetes in Jordan to increase up to 7% in 2010.[9] Therefore, more research is needed to further discover new potential antidiabetic agents. One of the possible approaches is via searching for remedies that are commonly used among the local herbalists and diabetic patients in the country.[10]

* reem.issa@yu.edu.jo
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The Mediterranean location of Jordan makes it one of the richest countries in the world with a diverse floral source, which can be used in different aspects of medicine.[11] In addition, cultural believes and geographical diversity of the country also encourage the treatment of various diseases with plants in different formulations like crude extracts, whole plants, a paste of plants, infusions, etc.[12,13] In an ethno-pharmacological survey of medicinal herbs in Jordan at the Northern Badia region by Alzweiri *et al.*; rated 10 herbal species that possess anti-diabetic effect as the third among the list of commonly used herbs, after digestive and respiratory problems.[11] Among the previous ethno-pharmacological studies performed in Jordan, 30 different plant species were used as anti-diabetic or hypoglycemic agents in the folk medicine; with only 6 species were not reported in the literature for their claimed uses.[14]

In a cross-sectional study conducted by Otoom *et al.* they interviewed diabetic patients visiting two medical centers at the north of Jordan. In that study they found that 31% of interviewed patients have used herbal products, and that the most commonly used herbs were *Trigonella foenumgraecum* (22.9%).[15] Where in a similar study by Wazaify *et al.*, interviewing diabetes patients in Amman (the capital of Jordan), only 16.6% reported using herbs and the most commonly used was green tea (20.5%).[16]

Variations among the previous studies can be explained by the differences in their geographic locations, as in the capital Amman, patients are less familiar with the traditional uses of medicinal herbs. Moreover, the ethno-pharmacological practices by the herbalists allocated in Amman, are not well scientifically validated. Therefore, in the current article, we have surveyed for traditional herbal remedies commonly prescribed by the local herbalists allocated in Amman, for their diabetic customers, with their methods of preparation and use. The aim of this work is to review different clinical, invitro or invivo studies performed on these remedies, which have been published through various reputed scientific journals; in order to validate the reported traditional uses, and hence to assess whether or not these practices are supported by any evidence-based pharmacological studies and/ or medicinal reports.

Methodology

Ethnobotanical survey with the local herbalists

We conducted a random sample of herbalist from local community of Amman areas (n=15), over a period of 2 months in 2017. Interviews were face to face with the herbalists at their shops, without time limit and according to ISE code of ethics (www.ethnobiology.net/ethics.php). Arabic language was the language used. The interviewees were aware of their right to refuse answering any question, to stop the interview at any time, or to simply decline the interview altogether.

In order to determine the traditionally used plant species with antidiabetic effect; data collection regarding the used herbal remedies was comprised of: mixture components, local Arabic common names of the plants, and the method of preparation and use. The identity of each plant species mentioned by herbalists was not able to be checked and confirmed by a botanist; as they were available only as powder materials.

The local Arabic names of the plants were used to search for the botanical names of these species, utilizing previously published studies on the available medicinal plant species in the Jordanian market as reported by the local researchers.[17, 13, 18, 11] These botanical names were then searched in the literature for evidence-based pharmacological studies and medicinal reports supporting their claimed antidiabetic effect.

Literature Review

A literature review was conducted for the plant species that have been used as antidiabetic remedies by the interviewed herbalists. The available information about different invivo, invitro and clinical antidiabetic studies of these species were collected from various electronic

sources like Pubmed, SciFinder, Elsevier, Springer, Scopus, Science Direct, Google Scholar and Web of Science, apart from these locally available books and peer reviewed journal were also used to collect information. The results of this review will be used to evaluate the herbalist's level of knowledge on the herbal remedies that are commonly prescribed by them for their diabetic customers.

Results

Ethnobotanical survey results

As a result of our ethnobotanical survey, two mixture herbal remedies composed of 12 plant species, used for treatment of diabetes were reported. The Arabic common names, botanical names, and methods of preparation for each mixture are shown in Table 1. These species were found to belong to 11 families. Of the reported plant families, Compositae, Brassicaceae, Fabaceae, Asteraceae, Oleaceae and Lamiaceae were previously reported to possess antidiabetic activity.[19] Moreover, only 7 plant species were previously reported as antidiabetic agents by the local researchers namely: *Oleae uropaea* and *Salvia triloba* by Alzweiri *et al.*; [11] *Artemisia vulgaris, Artemisia herba-alba, Rheum ribes, Teucrium polium,* and *Cinnamomum ceylanicum*as by Abu-Irmaileh and Afifi.[13] Up to our knowledge, the other five plant species were not previously reported to be used as antidiabetic agents among the local herbalists in Jordan.

Table (1)
The most commonly used antidiabetic herbal mixtures by the local herbalists

*Plants botanical name	Family name	Local Arabic name
Mixture 1: Take a spoon and then boil and drink, repeated three times a day after each meal		
Artemisia vulgaris L.	Compositae	البعيثران
*Fucusvesicolosus*L.	Fucaceae	الفوقس الحويصلي
Lepidiumsativum L.	Brassicaceae	الرشاد
AstragalusonbrgchisL.	Fabaceae	الكثيراء
Artemisia herba-alba Asso	Asteraceae	الشيح
Oleaeuropaea L.	Oleaceae	ورق الزيتون
Mixture 2: Take a spoon and then boil and drink on empty stomach before bed time		
Artemisia vulgaris L.	Compositae	البعيثران
Artemisia herba-alba Asso	Asteraceae	الشيح
*Rheum ribes*L.	Polygonaceae	الروباص
*Teucriumpolium*L.	Compositae	الجعدة
*Urticapilulifera*L.	Urticaceae	القريص
Salvia triloba L.	Lamiaceae	الميرمية
*Costusigneus*Nak	Costaceae	القسط الهندي
Cinnamomumceylanicum	Lauraceae	القرفة

*Plants botanical name corresponding to the local Arabic name as prescribed by previous researchers. [17, 13, 18, 11]

Literature validation for the featured plant species

Studying and evaluating the local herbalist level of knowledge on using herbal remedies is considered one of the most important issues, since modulating their practices and communicating with target group can be more effective in the treatment process. Therefore, over the past

few decades, a lot of reviews have been done investigating the traditional uses and scientific studies related to the globally or locally antidiabetic herbs used, from which we can validate the efficient use of herbal remedies by the herbalist's for our featured plants species. Those species are discussed below in term of their efficiency in controlling diabetes. Moreover, these plants phyto-constituents and mode of action for their antidiabetic effect were also reviewed.

1. Antidiabetic activity of Artemisia vulgaris

As an antidiabetic herb, *A. vulgaris* has been reported in Jordan to be commonly recommended by the local herbalists for the treatment of diabetes. [20, 13] However, it has been noticed that when mice are treated with a dosage of 5 mg/ 20 g extracts of *A. vulgaris*, there was no significant lowering in their blood glucose levels.[21]

Phytochemical analysis identified 15 out of a total of 22 compounds, all are being classified as phenolic compounds; mainly chlorogenic acid derivatives or flavonoids, with a high radical-scavenging capacity and a strong reducing potential in the methanolic extract.[22]

2. Antidiabetic activity of Fucus vesicolosus

The extracts obtained from *F. vesiculosus* algae have been traditionally used for the treatment of obesity and several gastrointestinal diseases.[23] For instance, in a study performed by Gabbia *et al.*, the ability of the extracts to inhibit the digestive enzymes (like α-amylase and α-glucosidase) and to control the postprandial plasma glucose levels has been evaluated in a mouse model of non-alcoholic steato-hepatitis.[24] The obtained results demonstrated that both the postprandial glycemic peak and the area under curve for the blood glucose were reduced using these algae phytocomplex extracts. This algal extract may also be useful in the control of carbohydrate digestion and absorption, since a delay in carbohydrate digestion resulted from the administrations of the extract in a diet particularly rich in fat, even though a decrease in its assimilation might also occur.

The effect of brown marine algae as hypoglycemic agent was attributed to the presence of fucoidan, a negatively charged water-soluble polysaccharide. Depending on the algal species from which fucoidan was extracted as well as the algae's season of harvest, funcoidan inhibits α-glucosidase differently.[25] Furthermore, Wang *et al.* showed that if fucoidan is orally administered for 13 weeks, a decrease in fasting blood glucose, blood urea nitrogen, serum creatinine, urine protein and collagen levels in non-obese Wistar rat will be observed.[26] These findings suggest that fucoidan has the ability to prevent or impede the development of diabetic nephropathy related to spontaneous diabetes and attenuate hyperglycemia compared with the control Wistar rats.

The effect of *F. vesiculosus* on post challenge plasma glucose and insulin levels in men and women has been investigated by Paradis *et al.* using a randomized crossover placebo-controlled trial. [27] Compared with placebo, administration of 250 mg seaweed capsules resulted in a 12.1% reduction in the insulin incremental area under the curve and a 7.9% increase in the Cederholm index of insulin sensitivity. This, indeed, indicates that insulin homeostasis may be altered by brown seaweed in response to carbohydrate ingestion.

3. Antidiabetic activity of Lepidium sativum

The hypoglycemic effect due to *L. sativum* seeds was investigated in normal and streptozotocin induced diabetic rats. A significant decrease in blood glucose levels was produced in diabetic and normal rats after an acute or chronic repeated oral administration of aqueous extract, with no changes in basal plasma insulin concentrations; meaning that this pharmacological activity is based most likely on a mechanism that is independent of insulin secretion.[28] Later, the same research group has performed a similar study and concluded that the aqueous *L. sativum* extract caused a significant inhibition of renal glucose reabsorption, which in turn reduced blood sugar.[29] Moreover, the ethanolic extracts of *L. sativum* showed a high in vitro antioxidant activity, where a higher scavenging activity was exhibited by shoots compared to

the seed. This is most likely due to the higher content of the total polyphenolic compounds in the Leaf extract.[30]

4. Antidiabetic activity of Astragalus onbrgchis

It has been concluded that *A. onbrgchis* total saponins and curcumin, with different distribution ratio, can significantly improve lipid profile and reduce glycosylated serum protein.[31] Moreover, it increases the high density lipoprotein (HDL) content and serum insulin levels; and therefore it can be used for the prevention and treatment of diabetes. Furthermore, Astragalus polysaccharides was used to treat rats with type 2 diabetes mellitus, the results suggested that the expression level of miRNA-203a-3p was up regulated in their liver, indicating insulin resistance attenuation in type 2 diabetes.[32]

In a large meta-analysis study including 1054 participants, a control group was compared with Astragalus aqueous decoction treated group. That study found that Astragalus administration can significantly reduce both fasting and postprandial plasma glucose when compared with control group; thus it may be beneficial as a supplementary therapy in the treatment of type 2 diabetes.[33]

5. Antidiabetic activity of Artemisia herba alba Asso

Artemisia herba alba is one of the most commonly used herbal plants to treat diabetes in Saudi Arabia.[34] In Jordan, as well, this plant has been reported as an antidiabetic herb with both in vitro and in vivo hypoglycemic activity.[35, 20, 36, 13]

When the ethanolic extract of *A. herba alba* aerial part was given orally to both normal and diabetic albino rats, the blood glucose level was significantly reduced in type II diabetic rat.[37] A similar study performed by Boudjelal *et al.* showed that when *A. herba alba* infusion were administered orally to normal and alloxan-induced diabetic rats, a significant reduction in blood glucose content with a much more efficient antidiabetic activity compared to glibenclamide was observed.[38] In addition, a recent study has shown that the aqueous extracts of *A. herba alba* exhibited an α-amylase inhibitory activity.[39] This effect was most likely related to the high phenolic and flavonoidal contents in the extract, which is composed of several polyphenol compounds; with 5-caffeoylquinic (chlorogenic) acid being the main compound.

A considerable lowering of elevated blood sugar was obtained when fifteen patients with diabetes mellitus were treated with *A. herba alba* extract; 14 out of the 15 patients had good remission of diabetic symptoms. More importantly, no side effects were reported either during or after treatment with the extract.[40]

6. Antidiabetic activity of Olea europaea

In Jordan, olives oil and leaves were used traditionally for the treatment of diabetes. [11] Otoom *et al.* stated that 3.1% of diabetic patients in Jordan use this plant to control their diabetes conditions.[15] In addition, Oran and Al-Eisawi and Hudaib *et al.* reported the use of *O. europaea* oil and leaves in Jordan as an antidiabetic herb with both in vitro and in vivo tested hypoglycemic activity.[41, 42]

It has been found that when extracts of *O. europaea* leaves were administrated in low and high doses, an improvement in the physiological, molecular and histopathological alterations on streptozotocin induced diabetic male rats was observed.[43] In addition, a substantial reduction in the digestion and absorption of starch was previously observed in streptozotocin induced diabetic animal models receiving olive leaf extract compared to untreated intestine.[44] These results suggest that the inhibition of disaccharide digestion at the intestinal mucosa might be the reason behind the hypoglycemic mechanism.

The aqueous extract of olive tree leaves was suggested to be potential sources of natural antioxidants and a potent inhibitory of α-amylase activity, due to their high flavonoidal and phenolic contents.[39] Moreover, a study performed by Sato *et al.* showed that mice fed with a high fat diet exhibited lower serum glucose and insulin levels combined with a glucose tolerance enhancement, when exposed to oleanolic acid (triterpene) from *O. europaea*.[45] In addition to this, oleic acid, phenols and squalene, were

all attributed to the use of plant extract in the treatment of diabetes, hypertension and toothache.[46, 36, 47]

Another compound that is also responsible for the biological activities of olive is oleuropeoside, which exhibited an antidiabetic activity in alloxan-induced diabetic animals; with suggested mechanisms for the hypoglycaemic activity involve an increase in peripheral uptake of glucose and also potentiating of glucose-induced insulin release.[48]

In a controlled randomized clinical trial, diabetic patients were treated orally with 500 mg of olive leaf extract tablet once daily.[44] The results showed that HbA1c and fasting plasma insulin levels were significantly lowered after 14 weeks as compared to the control group.

7. Antidiabetic activity of Rheum ribes

Rheum ribes is most commonly used in the treatment of diabetes in Jordan.[13] The effect of the water extract was found to exert a dual inhibition of α-amylase and α-glucosidase in a significant dose dependent manner, using an in vitro enzymatic starch digestion bioassay.[49] Also, it was found that the aqueous extract of *R. ribes* to possess glucose homeostasis and diabetic neuropathy protection in alloxan-diabetic mice. Moreover high doses can significantly increase serum catalase and decrease glucose levels.[50] Interestingly, in the same study, the mice were also found to be protected from acquiring diabetes and diabetic neuropathy as they were pretreated with the extract prior to alloxination. Another study performed by Hamzeh and coworkers showed that alloxan-induced diabetic rats exhibited an improvement in their renal dysfunction; due to the effect of hydroalcohlic extract of *R. ribes* root, through controlling blood glucose and renal protective effects.[51]

8. Antidiabetic activity of Teucrium polium

Different studies had confirmed the use of *Teucrium polium* in Jordan as anti-diabetic herb, with both in vitro and in vivo tested hypoglycemic activity. [52, 35, 41, 20, 53, 36, 13, 11]

Recently, Al-Kharabsheh *et al.* demonstrated that the aqueous extract of the Jordanian species of *T. polium* exhibited weak antioxidant and α-amylase inhibitor; due to their relatively low phenolic and flavonoidal contents.[39] These findings are consistent with the previous study by Kasabri *et al.*, who found that the water extract of *T. polium* does not have any in vitro α-amylase inhibitory effect.[54]

On the contrary, in a more detailed study, the ethanol extract of this plant were found to exhibit a tendency to decrease glucose level and increase blood insulin level in streptozotocin diabetic rats.[55] It seems that, as was further confirmed by Stefkov *et al.*, the ethanolic extract has an insulinotropic effect on INS-1E cells and a reduction in blood glucose levels in both normo- and hyperglycemic rats, due to the presence of flavonoids.[56] These findings are in agreement with Mirghazanfari *et al.* and Patel *et al.*, who showed that the crude extract of *T. polium* is able to enhance insulin secretion by the pancreas, due to the presence of apigenin which exists only in methanol fraction but not in aqueous fractions.[57,58] In addition, it seems that this type of extract has an ability to regenerate the islets of Langerhans comparing to the untreated diabetic rats. From these data, we may conclude that the hypoglycemic effect of *T. polium* extract varies as it is largely influenced by the type of the solvent used for extracting the active components.

In a clinical trial, the hypoglycemic effect of this plant was compared with glybenclamide in diabetes mellitus type 2.[59] The results showed that the mean of glycosylated hemoglobin decreased in both treatments; where the mean levels of triglyceride, total cholesterol and body mass index decreased significantly in plant extract treated group, with decreased appetite. On the other hand, HDL-Cholesterol, LDL-Cholesterol and liver function tests showed no change in both groups.

9. Antidiabetic activity of Urtica pilulifera (Urtica dioica)

It was reported that about 8% of diabetic patients in Jordan use *Urtica pilulifera* (Nettle) as antidiabetic herb

with in vitro/in vivo tested hypoglycemic activity and α-amylase/α-glucosidase inhibitory effects.[15] On the contrary, Hamdan and Afifi could not observe any α-glucosidase inhibitory activity for *U. dioica* aqueous extract; [60] while Oenal *et al.* were previously able to demonstrate this inhibitory effect on α-glucosidase for the same plant species.[61]

Similarly, when different extracts of *U. pilulifera* were prepared and tested for their antidiabetic, antioxidant and antiinflammatory effects on type 2 diabetic rat model, big conflicts in their results were observed, which can be explained by the type of the tested plant species that were not clearly distinguished in the literature. The extracts of *U. dioica* showed an ability to enhance insulin secretion by islets of Langerhans and reduce blood sugar levels.[62] On the other hand, no significant decrease in glucose movement in the gastrointestinal tract in an in vitro study was observed.[63] Similarly, not any hypoglycemic effect in alloxan-diabetic rats was observed; however a significant antihyperglycemic effect (lasting for 3 hours) was observed after the oral glucose tolerance test.[64] This indicates that the intestinal glucose absorption was reduced due to aqueous *U. dioica* extract effect.

While the hexan extract of *U. dioica* showed no clear effect, both ethyl acetate and chloroform extracts exhibited a significant antiinflammatory, hypoglycemic and antioxidant effects in diabetic rats.[65] Another recent study evaluated the synergistic effects of hydro-alcoholic extract of *U. dioica* combined with pioglitazoneon on the prevention of diabetic nephropathy in streptozotocin induced-diabetic mice.[66] The results showed that this combination have synergistic protective effects that can be a promising approach for the treatment of diabetic nephropathy.

In a randomized double-blind placebo-controlled clinical trial, a capsule of (500 mg) obtained from Nettle leaf extract and administrated daily to patients with type 2 diabetes, showed that the blood levels of fasting glucose and HbA1c were significantly reduced, without any significant effects on the other parameters compared with placebo.[67]

10. Antidiabetic activity of Salvia triloba (S. fruticosa) (S. officinalis)

In a study by Otoom *et al.* theyreported the use of *S. officinalis* by (3.1%) of diabetic patients in Jordan.[16] Al-Mustafa and Al-Thunibat revealed the use of *S. fruticosa* by 54% of the traditional healers in Jordan for treatment of diabetes and its complications.[68] Moreover, the study showed that the aqueous and the methanol extracts to contain total phenolic compounds of 18.5% and 46.7% respectively, with moderate antioxidant effects. Alzweiri *et al.* reported the use of *S. triloba* in Jordan as antidiabetic herb.[11]

These variations in the type of species used within the same study area were clearly reported by Kasabri *et al.*.[69] Briefly, eleven Jordanian indigenous Salvia spp., were found to modulate gastrointestinal carbohydrate and lipid digestion and absorption, when were screened in vitro for inhibition of pancreatic triacylglycerol lipase, α-amylase and α-glucosidase using the crude aqueous extracts, in dose dependent manner. These data explain the appearance of more than one Salvia species in the literature; that have been traditionally used for treatment of diabetes either by the traditional healers or the citizens in Jordan.

In a study by Perfumi *et al.* investigating the hypoglycemic activity of leaf infusion of *S. fructose* in normo- and alloxan-diabetic rabbits, this infusion was found to cause significant reduction in blood glucose levels in diabetic rabbits without exerting any effect on normal ones.[70] Additionally, the hypoglycemic effect was dependent on the root of administration as changing it from oral to intravenous, rendered the extracts of *S. fructose* ineffective; thus indicating that this plant would reduce the intestinal absorption of glucose leading to hypoglycemic effect.

In a randomized placebo-controlled trial performed on hyperlipidemic type 2 diabetic patients, treated with 500 mg encapsulated hydroalcoholic extract of *S.*

officinalis, a significant reduction in the blood levels of glucose, HbA1c, total cholesterol, triglyceride, and LDL; and an increase of HDL level were reported.[71] Similarly, a randomized placebo-controlled trial performed on type 2 diabetic patients, treated with 150 mg *S. officinalis* extract, a significant reduction of 2 h postprandial glucose and total cholesterol levels were reported but with no observed effects on fasting glucose, HbA1c, triglyceride, LDL and HDL.[72]

11. Antidiabetic activity of Costus igneus (Costus spicatus D. Don)

In in vitro study the ethanolic extract of *C. spicatus* leaf was used to evaluate glucose uptake activity, showed no direct peripheral action comparable with insulin and metformin.[73] A similar previous study investigating insulin tolerance, showed that *C. spicatus* tea consumption did not alter insulin sensitivity in obesity induced hyperglycemic mice, which suggested that *C. spicatus* leaves is not effective in the treatment of obesity-induced hyperglycemia.[74]

Phytochemical screening of *C. igneus* and Insulin plant (*C. spictus*) leaves revealed that it is rich in protein, iron, and antioxidant components such as ascorbic acid, α-tocopherol, β-carotene, terpinoids, steroids, and flavonoids, where the methanolic extract varied in its content of phytochemicals including carbohydrates, triterpenoids, proteins, alkaloids, tannins, saponins, and flavonoids.[75] Moreover, the insulin-like protein (ILP) was purified from *C. igneus* grown in Western Ghats of India by affinity chromatography using anti-insulin antibodies. The characterization of ILP showed that it is structurally different from insulin but functionally similar. Interestingly, the purified ILP showed significant hypoglycemic effect; when administered orally in oral glucose tolerance test, compared to insulin in streptozotocin induced diabetic mice.[76]

In a cross- sectional clinical study, patients consuming either one fresh leaf or 1 teaspoon of shade-dried powder/day of *C. igneus* in conjunction with other modalities of treatment had effectively produced glycemic control in diabetics.[77]

12. Antidiabetic activity of Cinnamomum ceylanicum

Abu-Irmaileh and Afifi reported the use of *C. ceylanicum* in Jordan as antidiabetic herb.[13] In vitro incubation of pancreatic islets with cinnamaldehyde isolated from *C. ceylaniucm*, resulted in enhanced insulin release. The insulinotropic effect of cinnamaldehyde was due to increase in the glucose uptake through glucose transporter translocation in peripheral tissues.[78]

A group of type 2 diabetic patients were treated with glibenclamide, and randomly assigned to receive either 1 g of cinnamon or placebo daily for 12 weeks. A highly significant reduction of fasting blood glucose level after 6 and 12 weeks of treatment (10.12% and 17.4%, respectively), was observed. Compared to baseline value and to placebo group at corresponding duration, a similar effect on glycosylated Hb was also found. These findings indicate the beneficial effect of adjuvant cinnamon as antidiabetic agent along with the conventional medications, in order to treat poorly controlled type 2 diabetes mellitus.[79]

Discussion

In the current survey, 9 out of the 12 listed plant species were found clinically studied for their antidiabetic effects. For the rest of the species (*A. vulgaris, L. sativum, R. ribes)* only invitro and invivo studies were available, with not any clinical studies were performed on these species.

Nine species, *F. vesiculosus*, *A. onbrgchis*, *A. herba alba*, *O.europaea*, *T. polium*, *U. Pilulifera*, *S. triloba*, *C. igneus*, and *C. ceylanicum* proved to be effective in invivo, invitro and in clinical studies as hypoglycemic agents, or as adjuvant treatments in order to reduce diabetic complications. Of the other species, *L. sativum* was found effective in invitro/ inviov studies, but not clinically proved for its antidiabetic effectiveness. In spit that the species *R. ribes* and *A. vulgaris*, failed to show any hypoglycemic effects in invitro or in invivo studies; they

showed some evidences to reduce diabetes complications when tested on diabetic animal's models.

The phytoconstituents analysis data of the effective species are in agreement with the previously published data, Mishra *et al.* summarized the most naturally abundant antidiabetic phytoconstituents with their mode of activity as follow: [80] Alkaloids inhibit alpha-glucosidase and decrease glucose transport through the intestinal epithelium. Imidazoline compounds stimulate insulin secretion in a glucose-dependent manner. Polysaccharides increase the levels of serum insulin, reduce the blood glucose levels and improve tolerance of glucose. Flavonoids suppress the glucose level, reduce plasma cholesterol and triglycerides significantly, and increase their hepatic glucokinase activity; probably by enhancing the insulin release from pancreatic islets. Dietary fibers effectively adsorb glucose, retard glucose diffusion, inhibit the activity of alpha-amylase, and may be responsible for decreasing the rate of glucose absorption and concentration of postprandial serum glucose. Saponin stimulates the release of insulin and blocks the formation of glucose in the blood stream. Ferulic acid has stimulatory effects on insulin secretion.

Significant findings

The majority of the experiments confirmed the benefits of the listed plant species; with hypoglycaemic effects, in the management of diabetes mellitus. In addition, numerous mechanisms of actions have also been proposed for these plant species. Therefore, it is assumed that these botanicals have a major role to play in the management of diabetes, but still needs further exploration for development of drugs and nutraceuticals from natural resources.

Many herbal remedies used by the local herbalists, were found to not undergo careful scientific assessment yet. Further scientific validation of several Jordanian plant species is therefore necessarily needed, if the efficacy and safety of the botanicals in reducing diabetes level in the country are required.

Limitations

The local common names of the plant species are often misleading; as there are not any exclusive authorities in the country, identifying the herbal materials commonly found at the herbalist's shops. Also, many medicinal herbs were cultivated using different breeding procedures, with the aim of increasing the production rate. Presumably, the new cultivated and hybridized crops of the same species may not correspond to the plants described in the literature. In addition, the sources of these plants are not documented to be either imported or locally harvested species, that may bring significant variations in their chemicals composition and therefore might affect their pharmacological activities.

Conclusion

The current data gathered through our literature review and ethnobotanical survey; clearly showed that local herbalists have an important knowledge about the use of medicinal plants in the treatment of diabetes, as been previously proved by evidence-based pharmacological studies including clinical, invivo or invitro evaluations on some of the above mentioned species. These species could be a real natural reservoir of new biomolecule with a potential antidiabetic activity. Therefore, preservation and further investigation of this heritage by documentation and scientific evaluation, are essential requirement and should be considered as a national priority. Such findings support the necessity of proper handling of herbal medicine, which requires proper regulation and licensing as per the WHO regulations.[81, 82, 83]

This review may also help the scientists and researchers working in the field of complementary and alternative medicine, to find out a possible cure for diabetes and explore new agents with hypoglycemic effect. In addition, it may also discover false herbal treatments that have serious harmful and adverse health effects, which are caused by herb-drugs interaction or improper dosage as being described by unqualified healers, without any medical supervisions being followed on these chronically

ill patients.

Conflict of interest statement

The authors declare they have no conflict of interest.

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استخدام العلاجات العشبية المضادة للسكري من قبل العطارين الأردنيين: مقارنة بين الممارسة الشعبية والدراسات الدوائية القائمة على الأدلة

ريم عيسى[1] * ، عرين الخطابي[2]، تبارك عبد الكريم[3] ، عمر التميمي[3]

[١] قسم الكيمياء الصيدلية والعقاقير.

[2] قسم الصيدلة والعلوم الدوائية.

[٣] طلاب جامعيين، كلية الصيدلة.

ملخص

يعدّ التداوي بالأعشاب جزءا أساسيا من الفلكلور الأردني وذلك بسبب كثرة استخدامه في الطب الشعبي. تم إجراء هذه الدراسة بناء على مقابلة (وجها لوجه) مع عينة عشوائية من العطارين حيث تم التركيز على العلاجات العشبية المضادة لمرض السكري. وتم التحقق من صحة هذه العلاجات بالمقارنة مع الدراسات الدوائية القائمة على الأدلة العلمية، وذلك باستخدام البيانات المنشورة لمعرفة المعلومات المتاحة حول الدراسات السريرية المختلفة، والدراسات التي أجريت إما داخل الكائن الحي أو في المختبر.

ووضحت الدراسة الاستقصائية وجود اثنين من الخلطات العشبية المضادة لمرض السكري المستخدمة بشكل واسع التي تتألف من اثني عشر نوعا من النباتات. أثبتت تسعة أنواع من هذه النباتات فعاليتها لعلاج مرض السكري كما تم تقييمها سريريا، ومن خلال التجارب التي أجريت داخل الجسم الحي أو في المختبر. بالمقابل تم العثور على نوع واحد فقط أثبت فعاليته على نماذج حيوانية أو كمثبط للإنزيمات، ولكن ليس في أي من الدراسات السريرية. كما تم رفض نوعين آخرين غير فعالين.

ستساعد هذه الدراسة على تعزيز العلاقة بين الطب الشعبي وعلم الأدوية القائم على الأدلة. أيضا، سوف تلقي الضوء على ممارسات الطب الشعبي في الأردن والكشف عن بعض الأخطاء الشائعة بين العطارين في استخدام الأدوية العشبية المضادة لمرض السكري.

بناء على ذلك فأننا نوصي ونؤكد على أهمية أجراء تجارب كيميائية وسريرية مكثفة لهذه النباتات المستخدمة في الطب الشعبي في الأردن وذلك بهدف استكشاف مركبات دوائية طبيعية لعلاج مرض السكري والتقليل من مضاعفاته.

الكلمات الدالة: مضادات السكري، العلاجات الشعبية، الدراسات الدوائية، الاردن.

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