Review Article

Diabetes mellitus and phytotherapy in Turkey

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Abstract

This study reports a literature review aimed to analyse various studies related to the use of phytotherapy in diabetes mellitus in Turkey in order to provide additional information for healthcare professionals. The incidence of Diabetes Mellitus is rising and many of the diabetics frequently use herbal treatments along with modern medical treatment for glycaemic control and/or improve their well-being.

Several electronic databases (such as Medline and Pubmed) were searched for 1990-2010 period (till May, 2010) and 33 related articles were analysed. Many studies - mostly animal trials- have been conducted in this field. Among the herbs most-commonly used along with modern medical therapies and also in folkloric medicine, we searched for bitter melon, cinnamon, fenugreek, olive leaf, black seed and white mulberry. Studies conducted in this field have produced conflicting results and, the necessity to conduct randomized, placebo-controlled clinical human studies to develop new drugs from herbs, as in the case of metformin, still remains important. Besides, further studies are required to address the issues of standardization and quality control of existing preparations. More importantly, healthcare professionals caring for diabetic patients need to be aware of phytotherapy to incorporate phytomedicine into their practices and should undertake more responsibility in relation to these kind of therapies that are commonly-used throughout the world.

Keywords: Phytotherapy, Diabetes Mellitus.

Introduction

Phytotherapy is simply defined as the utilization of plants in prevention or treatment of diseases. Any herbal organ used for treatment purposes, such as leaf, flower, seed, root or bark is called "herbal drug/medicinal herb". The term "phytotherapy" was used first in 1939 by the French Physician, Mr Henri Leclerc (1870-1953) in the journal titled 'La Presse Médical.'[1] Today, this term is used to refer to "herbal treatment" or "treatment with medicinal herbs". The oldest written documents on medicinal herbs are Nineveh Tablets (BC 3000) and Ebers Papyrus (BC 1550).

One third of nearly 11.000 higher plant species found in Turkey is endemic. About 2000-3000 of these species are estimated to have potential for phytotherapeutic use and approximately half of them to be already in use as folk remedies.[2]

There is a growing tendency for using complementary and alternative medicine (CAM) in the whole world as in our country.[3,4] A study conducted on six hundred parents revealed that CAM were used in children, as in adults, at a quite high rate of 49% and that 77% of these treatments were herbal based.[5] In a study performed in Gülhane Military Medical Academy (GATA), Ankara, 41% of the patients with type 2 diabetes mellitus were recorded to have used at least one CAM method.[6] It was also detected that 13.4% of 126 herbal species used in Edirne region as folk remedy was used for diabetes treatment.[7]

A study published in 2009 reported that (by the information collected from their parents) 52% of 100 children living in eastern cities of Turkey and diagnosed with type 1 diabetes for at least six months used at least one CAM method.[8] According to this study, 59.6% of those who applied for CAM methods used herbs or herbal preparations as CAM. Seventy eight percent of them declared that they were satisfied with the results; and 69.2% of them were willing to continue this kind of treatment.

Rate of "applying for CAM" was calculated to be 23% among 194 Canadian children with a chronic disease, 49 of them having diabetes.[9] In the USA, 2-3.6 million people were recorded to be using CAM and this rate was found to be 35-48% in diabetics.[10] In another article on that issue, interviews conducted with 2474 adult diabetics revealed that 48% of them practiced CAM.[11]

It is a known fact that patients tend to seek alternative treatment methods most frequently with chronic diseases and show a greater tendency to "believe without questioning" than other patients. Various reasons can be offered for this tendency:

failure to take the disease seriously due to ignorance, suggestions of close relatives, and friends, effects of advertisements and promotions, effects of cultural or ethnic traditions, aim to improve quality of life, thought that "natural things give no harm," doubts about benefits of present drugs and concerns about their side effects, the expense/cost of present drugs and to support new treatments.

Diabetes and Pyhtotherapy

Due to its micro and macrovascular complications, diabetes ranks 6th in the list of mortality reasons in the USA.[12] Parallel to the increase in the number of diabetics, related costs on health economy will increase as well. For this reason, there is urgent need for higher number of more economical and effective alternatives for treatment. In addition, treatment of diabetes is still a challenging issue for the medical community. Diabetes is a chronic disease which requires "lifestyle modification" such as exercise, balanced nutrition and weight control as well as regular drug use; in turn, it requires discipline and regular monitoring and follow-up. It has been observed that the percentage of diabetic patients who achieve treatment targets in the world (including Turkey) is unfortunately about 43%.[13] Some of the results behind this low rate can be listed as problems related to healthcare professionals and health system, insufficiency of present therapies and patients' poor compliance with the recommended treatments. In addition, as the case in many other chronic diseases, diabetes has a degenerative and progressive character, which may raise feelings of despair, helplessness and even tiredness in patients.

Particularly in the treatment of type 2 Diabetes Mellitus, medicinal herbs have been used since ancient times. Diabetes was described in historical documents 2000 years ago and was referred to in Egyptian Papyruses, in the works of Hippocrates and Chinese medicine and Ayurveda texts. These resources also mentioned about herbal antidiabetic treatment. However, there is only one antidiabetic drug generated from a plant: "metformin" which originates from French Lilac (Galega officinalis L.). Having gained gradual importance in recent years, metformin has been successfully used in diabetes treatment for the last five decades.

Medicinal Herbs Used in Diabetes Therapy

Bitter Melon (Momordica charantia L.) (Cucurbitaceae):

Herb known as "bitter melon" or "karela" is a member of the Cucurbitaceae family and commonly grows in India, China, Africa and some regions of the USA. Its fruits include triterpen glycosides, protein and lectin. It has been used in Turkey and in the world for many years, particularly in ulcer and diabetes treatment.

In 4 small-scale non-randomized clinical trials, bitter melon was shown to have moderate hypoglycaemic effects.[14]

In another study published in 2009, M. charantia was recorded to have in vitro effects on human PPAR β/δ (Peroxisome proliferator-activated receptor) gene.[15] This gene is thought to be effective on HDL cholesterol and glycaemic control. A mini-review analyzing 5 clinical trials published in 2009 underlined that these five trials produced insufficient and conflicting results in terms of statistics and design.[16]

A review of 3 clinical trials was published in 2010.[17] In the first two trials analyzed in this review, preparations obtained from different parts of this herb were compared to placebo in terms of glycaemic control and no statistically significant difference was found. But in the third trial, preparations obtained from leaves of M. charantia were reported to have antiglycaemic effects comparable to those of glibenclamide and not to have serious side effects.

These evaluations showed that there is no sufficient evidence to recommend regular use of bitter melon in type 2 diabetic patients. However, it can be suggested to be highly reliable as a food supplement due to its long use as a folk remedy. It was reported that children drinking bitter melon tea may develop hypoglycaemic coma and that its seeds may lead to favism in those with G6PD (Glucose 6 phosphate dehydrogenase) enzyme deficiency. Since it has been recorded to produce teratogenic effects in animal trials, bitter melon is not recommended for pregnant women.

Preclinically detected antidiabetic effects of bitter melon have to be analyzed in the scope of well-designed human studies. Full comprehension of activation and isolation of insulin-potentializing capacity of bitter melon will be quite beneficial for standardization and reproducible efficiency of this herb. The main components of bitter melon, Charantia, viscin and polypeptide B are thought to be responsible for its hypoglycaemic and insulin-like effects. Therefore, when administered together, bitter melon has the capacity to increase the effects of oral antidiabetics.

Cinnamon (Cinnamomum zeylanicum L, Cinnamomum cassia L) (Lauraceae):

Cinnamon, used to flavour deserts and cookies, was recorded to be used as a kind of spice in the Chinese documents dating back to 4000 years ago. Cinnamaldehyde is the key flavour compound of both types of cinnamon in their essential oil. However, Chinese cinnamon has been subject to diabetes treatment due to its higher cinnamaldehyde content (85%).

Mechanism of activation of cinnamon on glycaemic control has not been duly understood as yet; however, it has been reported to have insulin-like effects and improve insulin sensitivity by its active compound, classified as Methyl Hydroxy Chalcone Polymer (MHCP).[18,19]

A meta-analysis published in 2008 suggested that cinnamon is not found to be effective in diabetes therapy.[20] In clinical trials analyzed in the scope of this meta-analysis, a total of 282 diabetic patients were administered C. cassia (40 days and 4 months, 1-6 g/day dosage). One of these trials was

nonrandomized, another one was conducted on type 1 DM patients. However, since cinnamon is suggested to improve insulin effects and sensitivity, it should not be expected to possess beneficial effects on type 1 DM. In another study in this meta-analysis, cinnamon amount used was quite low (1.5 g). On the contrary, in a randomized and placebo-controlled study, 1 g/day of cinnamon capsules were added to the current treatment of 109 type 2 DM patients with HbA1c levels above 7% for 90 days.[21] At the end of the treatment, HbA1c levels of cinnamon-administered group (case group) decreased by 0.83% while this decrease was recorded to be only 0.37% in the cinnamon-free (control) group.

No significant adverse effect has been recorded on any of these studies on cinnamon. The only adverse effect reported is contact dermatitis, mainly resulting from essential oil of cinnamon. Cinnamon has not yet been tested for any adverse effects in pregnant women.

In conclusion, there is mid-level evidence for cinnamon's beneficial effects on blood glucose levels; however, its effects on HbA1c are conflicting. For this reason, before it is recommended in clinical routine, cinnamon should be subjected to well-designed and large-scaled clinical trials.

Fenugreek (Trigonella foenum-graecum L.) (Fabaceae):

Native to eastern Mediterranean countries, fenugreek has spread over a vast geographical area from Morocco to China and lately to America. It has been cultivated and used for medical purposes since 2500 BC. It grows in Thrace, Marmara, Central-Southern and Southeastern Anatolia regions of Turkey as well.

Seeds and leaves of fenugreek are reported to possess mucilage (25-40%), oil acids (7-8%) and flavonoids. It includes proteins and amino acids (20-30%) and alkaloids (0.5%). 4-hydroxyisoleucine, the most-frequently studied active substance of fenugreek, has been suggested to stimulate insulin secretion from pancreas in a glucose-dependent manner.[22]

In the experimental studies on the effects of fenugreek seed on diabetic animals, the seeds were reported to reduce blood glucose and cholesterol levels. Mechanism of activation of fenugreek seed has been emphasized to function by delaying gastric emptying, slowing carbohydrate absorption in the intestine and ensuring glycaemic control by increasing insulin sensitivity of tissues.[23]

Studies on patients with type 2 DM point out the efficiency of 12.5-100 g fenugreek powder/day.[24] Its effects can be observed as improvement of fasting blood glucose level, lipid levels, HbA1c level, 24-hour urine glucose excretion and oral glucose tolerance test.[25] Particularly with more than 50% fiber content of fenugreek seed may improve possible benefits in diabetes treatment.[26]

No significant adverse effect of fenugreek has been recorded and it has been tolerated well in the studies performed to date; however, it is noted that special attention should be paid to the use of fenugreek in pregnant women along with other oral antidiabetics. Although there are small-scale studies conducted at National Institute of Health (NIH) on investigation of blood glucose-lowering effects of fenugreek seed in diabetics, however, it is stated that no scientific data are sufficient enough to recommend fenugreek seed.

Olive Leaf (Olea europea L.) (Oleaceae):

Leaves of olive tree yield two potent antioxidants namely oleuropein and hydroxytyrosol which may also act as antidiabetics. Alcohol-extract of olive leaves has been reported to increase insulin secretion in diabetic rats- but not in healthy rats- and the antiglycaemic effects were higher when compared to glibenclamide.[27]

Olive leaf, which includes poliphenols such as oleuropein and hydroxytyrosol, was observed to improve cardiac, hepatic and metabolic parameters by decreasing inflammation and oxidative stress in high fat fed rats.[28] Examination of the biological effects of olive leaf extract on type 1 diabetic rats has shown that it suppresses the production of proinflammatory and cytotoxic mediators. For this reason, olive leaf is suggested to be useful in the prophylaxis in autoimmune diabetes.[29] A study on olive leaf found a statistically significant decrease in serum glucose and cholesterol levels of diabetic rats and proved that extract had an antioxidant effect after use of olive leaf extract for 4 weeks.[30]

Black Seed (Nigella sativa L) (Ranunculaceae):

N. sativa seed creates insulin-like effects that increase glucose uptake in skeletal muscles and adipose tissue due to its thymoquinone content. Its seed, extract and oil can be used.

In a prospective clinical trial, 60 patients were divided into two groups; 1st group was administered 10 mg atorvastatin, 2x500 mg metformin, 50 mg atenolol and 5 mg amlodipin while 2nd group was administered 2.5 ml Nigella sativa oil twice a day in addition to the above-listed drugs.[31] Six-weeks follow-up revealed improvement in terms of fasting blood glucose and lipid profile.

N. sativa was suggested to be effective in reducing diabetic complications due to its antioxidant effects in rats.[32] In another study, it was suggested to be used against obesity and metabolic syndrome due to its PPAR- stimulating effects as well as its effects on adiposities.[33] In the light of all the data above, N. sativa seed extract and oil can be considered quite promising as a supportive care in diabetics; however, these

data have to be supported via randomized and placebo-controlled studies.

White Mulberry (Morus alba L.) (Moraceae):

White Mulberry leaf extract is used as a folkloric remedy for treatment of diabetes.

In vivo examination of the antidiabetic effects of extract and powder of Morus alba leaves on animals pointed out its antioxidant capacity and the fact that it decreased postprandial blood glucose probably by preventing glucose absorption in intestine via inhibition of alpha glycosidase enzyme.[34] In 2 studies by Naowaboot et al. on diabetic rats, Morus alba leaf extract was found to lower vascular reaction due to its long-lasting antioxidant effect and was recorded to have antihyperglycaemic effect.[35]

In conclusion, taking into consideration the high number of adverse effects due to conventional oral antidiabetic drugs, Morus alba leaves seem to possess potential complementary effect on glycaemic control in diabetes.

Discussion

The importance of phytotherapy in treatment of type 2 Diabetes Mellitus seems to gradually increase in coming years. Phytotherapy can be effective in prevention of diabetes and its complications as well as optimization of the treatment and life standards. As in case of many chronic metabolic diseases, the mechanism is closely related, particularly in diabetes, to oxidative stress and inflammation in the body. Therefore, due to the antioxidant properties herbs should be considered for both prevention and treatment of diabetes.

It is a well known fact that herbs constitute a part of culture in the whole world for quite a long time and that nutrients have beneficial effects on health. It is quite important to utilize and use the richness of the nature in the most efficient way. Special attention should be paid to these treatments, which are traditionally used by people for hundreds of years and use of which is gradually on the increase. Making of more scientific studies on these treatments will open new horizons in diabetes treatment. At the moment, scientific evidence and findings to support the efficiency of herbal remedies routinely in clinical practice remain insufficient. On the other hand, adverse effects and/or drug interactions in these widely used therapies should be definitely taken into consideration by the healthcare professionals.

Moreover, it should be kept in mind that phytotherapy is not an alternative but a complementary and supportive treatment to the conventional diabetes therapy and should be accompanied by diet and exercise treatment. The most important support and information source for reliability, efficiency and/or side effects of herbs and herbal preparations should be health professionals who can undertake leadership role effectively by improving and updating themselves in this field, as has to be in all other fields.

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