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Review

Best herbs for managing diabetes: A review of clinical studies

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Diabetes mellitus is a public health problem which leads to serious complications over time. Experimentally, many herbs have been recommended for treating diabetes. In most cases, however, the recommendations are based on animal studies and limited pieces of evidence exist about their clinical usefulness. This review focused on the herbs, the hypoglycemic actions of which have been supported by three or more clinical studies. The search was done in Google Scholar, Medline and Science Direct databases using the key terms *diabetes, plants*, *herbs*, *glucose* and *patients*. According to the clinical studies, *Aegle marmelos*, *Allium cepa, Gymnema sylvestre*, *Momordica charantia*, *Ocimum sanctum*, *Nigella sativa, Ocimum sanctum, Panax quinquefolius, Salacia reticulate, Silybum marianum* and *Trigonella foenum-graecum* have shown hypoglycemic and, in some cases, hypolipidemic activities in diabetic patients. Among them, *Gymnema sylvestre*, *Momordica charantia*, *Silybum marianum* and *Trigonella foenum-graecum* have acquired enough reputation for managing diabetes. Thus, it seems that physicians can rely on these herbs and advise for the patients to improve management of diabetes.

Uniterms: Medicinal plants/diabetes treatment. Diabetes/treatment. Diabetes/clinical trials.

Diabetes mellitus é um problema de saúde pública que leva a complicações graves ao longo do tempo. Experimentalmente, muitas ervas têm sido recomendadas para o tratamento da diabetes. Contudo, na maior parte dos casos as recomendações são baseadas em estudos em animais e existem evidências limitadas sobre a sua utilidade clínica. Esta revisão tem como foco as ervas nas quais as ações hipooglicêmicas são apoiadas por três ou mais estudos clínicos. Realizou-se pesquisa no *Google Scholar, Medline* e *Science Direct* utilizando palavras-chave diabete, plantas, ervas, glicose e pacientes. Segundo os estudos clínicos, *Aegle marmelos*, *Allium cepa*, *Gymnema sylvestre*, *Momordica charantia*, *Ocimum sanctum, Nigella sativa, Ocimum sanctum, Panax quinquefolius*, *Salacia reticulate*, *Silybum marianum* e *Trigonella foenum-graecum* mostraram atividade hipoglicêmica e, em alguns casos, hipolipidêmica em pacientes diabéticos. Entre elas, *Gymnema sylvestre*, *Momordica charantia*, *Silybum marianum* e *Trigonella foenum-graecum* apresentam grande reputação no manejamento da diabetes. Portanto, parece que os médicos podem confiar nessas ervas e aconselhar aos pacientes para que melhorem o tratamento da diabetes.

Unitermos: Planta medicinais/tratamento da diabetes. Diabetes/tratamento. Diabetes/ensaios clínicos.

INTRODUCTION

Diabetes mellitus is a growing public health problem in both developed and developing countries. According to the report of World Health Organization (August, 2011), 346 million people have diabetes worldwide. It is also estimated that 3.4 million patients died from diabetes-related complications in 2004. Without urgent action, this number is likely to double by 2030. Generally, diabetes is classified to two main types: type-1 diabetes (T1D), previously known as insulin-dependent diabetes mellitus, and type-2 diabetes (T2D), formerly called non-insulin-dependent diabetes mellitus. Patients with T1D show a state of insulin deficiency because of severe defect in islet β-cell function while T2D is characterized by a combination of resistance to action of insulin and insufficiency in insulin secretion (Deshpande *et al.*, 2008).

Over time, both types of diabetes lead to serious complications in the body, which include nephropathy, retinopathy, neuropathy, dyslipidemia and cardiovascular diseases (Deshpande *et al.*, 2008; Ghorbani *et al.*, 2010). Currently, beside insulin, the most widely used medication

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for diabetes are oral hypoglycemic drugs including insulin sensitizers (biguanides, thiazolidinediones), insulin secretagogues (sulfonylureas, meglitinides), α-glucosidase inhibitors, incretin agonists and dipeptidyl peptidase-4 inhibitors (Lorenzati *et al.*, 2010). Although early onset complications of diabetes can be controlled by oral hypoglycemic drugs/insulin treatment, serious late onset complications emerge in many patients (Tzoulaki *et al.*, 2009). Furthermore, clinical uses of the current drugs are accompanied by unpleasant side effects such as severe hypoglycemia, lactic acidosis, peripheral edema and abdominal discomfort (Lorenzati *et al.*, 2010). Therefore, the search for new antidiabetic agents with more effectiveness and less side effects has been continued.

Medicinal plants have always been an important source for finding new remedies for human health problems. Traditionally, numerous herbs have been recommended for treatment of diabetes. Also, antidiabetic effects of so many plants have been reported by many researchers. In most cases, however, these reports are confirmed by animal models and even *in vitro* studies and limited evidence exists about their clinical usefulness. The current review focused on the medicinal plants, the hypoglycemic actions of which have been supported by different clinical studies on diabetic patients.

RESEARCH METHODOLOGY

The search was done in databases of Google Scholar, Medline and Science Direct, using the key terms *diabetes, plants*, *herbs*, *glucose* and *Patients*. Only those medicinal plants with hypoglycemic actions shown by at least three clinical studies were incorporated in the manuscript. Antidiabetic effects of some plants (e.g. *Opuntia streptacantha*, *Ipomoea batatas*, *Urtica dioica*) have been reported by replicated studies of only one group of researchers. Results of these clinical studies have not been included in this paper.

ANTIDIABETIC HERBS

Aegle marmelos

Aegle marmelos, also known as bael, has been reported to have a number of medicinal attributes including antidiabetic effects. In a study by Ismail (2009a), twenty T2D patients with postprandial blood glucose (PPBG) of 201 ± 6 mg/dL were given decoction of 5 g *A. marmelos* leaf powder once a day. After 16 weeks, their PPBG significantly decreased to 159 ± 5 mg/dL. In another study, it was also shown that this decoction (5 g/day for 1 month) potentiated hypoglycemic effect of standard oral drugs in T2D patients (Ismail, 2009b). The same finding was also reported by Sankhla *et al*. (2009). In their double blind placebo trial, T2D patients were given sulfonylurea drug plus *A. marmelos* leaves (2 g/twice a day) or sulfonylurea plus placebo. After 8 weeks, the combined therapy had more effects on the level of fasting blood glucose (FBG), PPBG and urinary glucose (Table I).

Allium cepa

Preliminary, Mathew and Augusti (1975) reported that oral consumption of *Allium cepa* (onion) can improve glycemic control in diabetes. Acute hypoglycemic effect of *A. cepa* was also observed in a self-controlled study on twenty patients with T2D. It was also able to attenuate (37%) rise in plasma glucose 2 h after glucose ingestion (Myint *et al.*, 2009). More recently, it was shown that intake of 100 g *A. cepa* can decrease FBG level and improve glucose tolerance test (GTT) in both T1D and T2D patients (Eldin *et al.*, 2010).

Gymnema sylvestre

Accumulating pieces of evidence demonstrates that leaves of *Gymnema sylvestre* (Gurmar, Meshashringi, Merasingi, Kavali, Dhuleti) can improve glycemic control in diabetes. Shanmugasundaram *et al*. (1990) evaluated effectiveness of *G. sylvestre* leaf extract in controlling hyperglycaemia in 27 T1D patients under insulin therapy. The extract (400 mg/day for 18 months) significantly decreased FBG, HbA1c and serum lipids of the patients when compared with a similar group who received only insulin. Also, administration of this extract (400 mg/day for 18-20 months) as a supplement to conventional oral hypoglycemic drugs reduced FBG and HbA1c of T2D patients and drug dosage could be decreased (Baskaran *et al.*, 1990). In a study by Joffe and Freed (2001), diabetic patients were given a product containing *G. sylvestre* leaf extract (400 mg) twice a day. After 3 months, FBG and PPBG levels decreased by 11 and 13%, respectively. A 0.6-0.8% decrease was also observed in HbA1c. In another trial, treatment of T2D patients with a *G. sylvestre*-based product (1 g/day for 2 months) led to significant decreases in FBG and PPBG levels which were accompanied by increases in circulating insulin and C-peptide. Moreover, it stimulated insulin secretion from isolated human islets of Langerhans (Al-Romaiyan *et al*., 2010). A mild decrease in FBG (1%) and PPBG (1%) levels was also seen in T2D patients (20 cases) treated for 4 weeks with 6 g/day of *G. sylvestre* leaf powder (Paliwal *et al.*, 2009).

TABLE I - Best herbs for managing diabetes

Herbs	Cases	Study Design	Effects	References
Aegle marmelos	T2D	Controlled trial	↓PPBG	Ismail, 2009a
	T2D	Controlled trial	↑Oral hypoglycemic drugs actions	Ismail, 2009b
	T2D	RDBP trial	↑Oral hypoglycemic drugs actions	Sankhla *et al*., 2009
Allium cepa	T2D	Pre- & Post-treatment	↓FBG	Mathew *et al*., 1975
	T2D	Pre- & Post-treatment	↓blood glucose 2 h after sugar ingestion	Myint *et al*., 2009
	T1D&T2D	Controlled trial	↓FBG, ↑Glucose tolerance	Eldin, *et al*., 2010
Gymnema sylvestre	T1D	Controlled trial	↑Insulin actions	Shanmugasundaram *et al*., 1990
	T2D	Controlled trial	↑Oral hypoglycemic drugs actions	Baskaran *et al.*, 1990
	T2D	Pre- & Post-treatment	↓FBG, ↓PPBG, ↓HbA1c	Joffe *et al*., 2001
	T2D	Pre- & Post-treatment	↓FBG, ↓PPBG	Al-Romaiyan *et al*., 2010
	T2D	Pre- & Post-treatment	↓FBG, ↓PPBG	Paliwal *et al*., 2009
Momordica charantia	T1D&T2D	Pre- & Post-treatment	↓PPBG	Grover *et al*., 1990
	T2D	Pre- & Post-treatment	↓FBG, ↓PPBG	Ahmad *et al*., 1999
	T2D	Pre- & Post-treatment	↑Glucose tolerance	Welhinda *et al*., 1986
	T2D	Pre- & Post-treatment	↓FBG, ↓HbA1c	Sirvastava *et al*., 1993
	T2D	Pre- & Post-treatment	↓FBG, ↓HbA1c	Leatherdale *et al*., 1981
	T2D	Pre- & Post-treatment	↓FBG	Waheed *et al*., 2008
	T2D	Controlled trial	↓FBG, ↓Lipids, ↓Retinopathy, ↓stroke	Rahman *et al*., 2009
	T2D	Controlled trial	↓Fructosamine	Fuangchan *et al*., 2011
	T1D&T2D	Controlled trial	↓FBG	Baldwa *et al.*, 1977
	T2D	RDBP trial	Without significant effects	Dans *et al.*, 2007
Nigella sativa	MS	Controlled trial	↓FBG, ↓Lipids	Najmi *et al.*, 2008
	T2D	Pre- & Post-treatment	↓FBG, ↑Insulin	Bilal *et al*., 2009
	T2D	Pre- & Post-treatment	↑Oral hypoglycemic drugs actions	Bamosa *et al.*, 2010
	T2D	Controlled trial	↓FBG, ↓Lipids, ↓Blood pressure	Qidwai *et al*., 2009
Ocimum sanctum	T2D	Pre- & Post-treatment	↓Polydypsia, ↓Polyphagia	Kochhar *et al*., 2009
	T2D	Pre- & Post-treatment	↑hypoglycemic drugs actions, ↓Lipids	Rai *et al*., 1997
	T2D	RSBP trial	↓FBG, ↓PPBG, ↓Lipids, ↓Glucosuria	Agrawal *et al*., 1996
Panax quinquefolius	T2D	RSBP trial	↓PPBG	Vuksan *et al*., 2000a
	T2D	RSBP trial	↓Area under curve of BG	Vuksan *et al*., 2000b
	T2D	RDBP trial	↓FBG, ↓HbA1c, ↓Body weight	Sotaniemi *et al*., 1995
Salacia reticulate	T2D	RDBP cross over trial	↓FBG, ↓HbA1c	Kajimoto *et al*., 2000
	T2D	RDBP trial	↓HbA1c	Jayawardena *et al*., 2005
	T2D	Controlled trial	↓FBG, ↓HbA1c, ↓Lipids	Radha *et al*., 2009
Silybum marianum	T2D	RDBP trial	↓FBG,↓HbA1c,↓Lipids,↓Liver enzymes	Fallah Hoseini *et al*., 2006
	T2D	RDBP trial	↓FBG,↓HbA1c,↓Lipids,↓Liver enzymes	Ramezani *et al*., 2008
	T2D	RDBP trial	↑Oral hypoglycemic drugs actions	Hussain, 2007
	CDP	Controlled trial	↓Random BG, ↓Liver enzymes	Jose *et al*., 2011
	CDP	Controlled trial	↓FBG, ↓HbA1c, ↓Glucosuria	Velussi *et al*., 1997
	CDP	Controlled trial	↓hyperinsulinemia, ↓Daily insulin need	Velussi *et al*., 1993
Trigonella foenum	T1D	Cross over trial	↓FBG, ↓Lipids, ↓Glucosuria	Sharma *et al*., 1990b
	T2D	Pre- & Post-treatment	↓FBG, ↓Lipids	Kassaian *et al*., 2009
	T2D	Cross over trial	↓FBG, ↓Lipids, ↑Glucose tolerance	Sharma *et al*., 1990a
	T2D	Pre- & Post-treatment	↓PPBG	Ismail, *et al*., 2009a
	T2D	RDBP trial	↑Oral hypoglycemic drugs actions	Fu-rong *et al*., 2008
	T2D	Controlled trial	↑Glucose tolerance, ↓Lipids, ↓Glucosuria	Sharma, 1986
	T2D	Controlled trial	↓FBG, ↓TG, ↓Lipids	Mitra *et al*., 2006
	T2D	RDBP trial	↓Area under curve of BG, ↓Lipids, No significant effects on FBG or glucose tolerance	Gupta *et al*., 2001

CDP: Cirrhotic diabetic patients; FBG: fasting blood glucose; MS: Metabolic syndrome; PPBG: postprandial blood glucose; RDBP: Randomized double-blind placebo; RSBP: Randomized Single-blind placebo; T1D: type-1 diabetes; T2D: type-2 diabetes; ↓: Decrease; ↑: Increase

Momordica charantia

Momordica charantia (Karela, Ampalaya, bitter melon, bitter gound) has acquired a reputation for management of diabetes. It has passed several animal studies and its clinical trials have been started since many years ago. Administration of *M. charantia* seeds to six T1D and fourteen T2D patients significantly decreased PPBG level in both patient groups (Grover Gupta, 1990). Also, drinking an aqueous suspension of the vegetable pulp resulted in remarkable reduction of FBG and PPBG levels in 86 out of 100 cases with moderate T2D (Ahmad *et al.*, 1999). Similarly, fruit juice of *M. charantia* was found to significantly improve glucose tolerance in 73% of eighteen maturity onset diabetic patients (Welhinda *et al.*, 1986). In a case series study, diabetic patients were given aqueous extract (7 cases) or dried powder (5 cases) of *M. charantia* fruit, as a single dose or thrice a day, respectively. After 3 weeks, the extract and powder caused 54% and 25% reduction in mean blood glucose, respectively (Sirvastava *et al.*, 1993). Also, HbA1c was reduced from 8.37 to 6.1% by the extract. In line with these findings, Leatherdale et al. (1981) found a decreased HbA1c in 9 patients with T2D who consumed fried *M. charantia* fruits (0.23 kg/day for 8-11 weeks) and also an improvement of glucose tolerance in the patients who had taken 50 ml of *M. charantia* juice. Consumption of dried powder of *M. charantia* fruit showed reduction in FBG of 10 T2D patients with no history of previous medication and 10 T2D patients with history of taking oral hypoglycemic agents. The same effect was also obtained with aqueous and alcoholic extracts of *M. charantia* fruit (Waheed *et al*., 2008). Recently, Rahman *et al*. (2009) compared effects of *M. charantia* and rosiglitazone, a thiazolidinedione derivative, between 25 T2D patients treated with *M. charantia* juice (55 mL/day for 5 months). The study showed that *M. charantia* was more effective in the management of diabetes (FBG, total cholesterol and serum sialic acid) and its related complications (retinopathy and myocardial infarction) than rosiglitazone. On the other hand, Fuangchan *et al*. (2011) reported that hypoglycemic effect of *M. charantia* was less than metformin. Besides, in their multicenter randomized double-blind study, fructosamine level significantly decreased in T2D patients who received *M. charantia* for 4 weeks. Unlike the above mentioned studies, Dans *et al*. (2007) reported no significant decrease in FBG and total cholesterol level of T2D patients treated with a *M. charantia* product (2 capsules/three times daily) given for 3 months. They only observed a 0.24% decline in HbA1c following the intervention. In an attempt to test active compound underlying antidiabetic effect of *M. charantia*, a controlled clinical trial was performed on 9 diabetic patients using an insulin-like agent purified from this plant. Subcutaneous injection of the agent led to a remarkable fall in the blood glucose level after 30-60 min (Baldwa *et al*., 1977). Also, a hypoglycemic peptide (polypeptide-p) was isolated from fruits, seeds and tissues of *M. charantia*, which showed hypoglycemic effect when being subcutaneously administered to diabetic patients (Khanna *et al*., 1981).

Nigella sativa

Seeds of *Nigella sativa* (black seed) have been used for centuries as a natural remedy for various ailments. Hypoglycemic, antioxidant, hypotensive, hypolipidemic and antimicrobial effects of *N. sativa* have been experimentally reported (Mehta *et al*., 2012; Shafiee-Nick *et al*., 2012). With clinical studies, its therapeutic effect in metabolic syndrome and diabetes has been shown in recent years. Administration of *N. sativa* oil (2.5 mL twice a day for 6 weeks) to patients with metabolic syndrome has significantly decreased FBG and LDL and increased high density lipoprotein (HDL) levels (Najmi *et al*., 2008). A significant decrease in FBG and increase in insulin and SGOT of 41 T2D patients has been observed after a 40 day treatment with *N. sativa* oil. Levels of blood urea, SGPT, total leukocyte and platelet have remained unchanged after treatment with oil (Bilal *et al*., 2009). In a study, *N. sativa* seeds (1, 2 or 3 g/day) were added to antidiabetic drugs of 94 T2D patients. After three months, a significant reduction occurred in FBG, PPBG and HbA1c levels (Bamosa *et al*., 2010). Favorable impact of *N. sativa* on blood glucose, serum lipids and blood pressure was also reported by Qidwai *et al*. (2009).

Ocimum sanctum

A significant decrease in diabetic symptoms (polydypsia, polyphagia and tiredness) has been seen in 30 T2D patients consuming (2 g/day/for 3 months) leaf powder of *Ocimum sanctum* (Kochhar *et al*., 2009). One month dietary supplement with *O. sanctum* powder has also shown decreased FBG (21%) and glycated protein (11%), total cholesterol (11%), low density lipoprotein (LDL) (14%), very low density lipoprotein (VLDL) (16%) and triglyceride (TG) (16%) in 27 patients with T2D (Rai *et al.*, 1997). Hypoglycemic and hypolipidemic effects were confirmed by Agrawal *et al*. (1996) in a randomized placebo-controlled, single blind trial performed on T2D patients.

Panax quinquefolius

The most commonly used ginsengs are *Panax ginseng* (Korean or Chinese ginseng), *Panax quinquefolius* (American ginseng) and *Panax japonicus* (Japanese ginseng). American ginseng has been reported to attenuate PPBG level in 9 T2D patients. The area under curve of blood glucose is reduced by about 20% in patients receiving 3 g of ginseng (Vuksan *et al*., 2000a; Vuksan *et al*., 2000b). In a double blind placebo-controlled study, administration of ginseng (unknown species, 100 or 200 mg/day for 8 weeks) to 36 T2D patients significantly decreased FBG, HbA1c and body weight (Sotaniemi *et al*., 1995). In contrast with *P. quinquefolius*, more recently, Reeds *et al*. (2011) showed that *P. ginseng* can not improve glucose tolerance in newly diagnosed T2D patients.

Salacia reticulate

It has been shown that a diet containing aqueous extract from the stem of *Salacia reticulate* (240 mg/day for 6 weeks) can decrease FBG and HbA1c levels in T2D patients (Kajimoto *et al*., 2000). Also, a significant reduction in HbA1c has been reported in the patients receiving a preparation of *S. reticulate* tea for 3 months (Jayawardena *et al*., 2005). Clinical usefulness of *S. reticulate* consumption (2 g/day for 3 months) in the management of diabetes has been also observed in 30 patients (Radha, Amrithaveni, 2009).

Silybum marianum

The fame of *Silybum marianum* (milk thistle) seed in herbal medicine is owing to its therapeutic effects for liver-related disorders. However, beneficial effects of *S. marianum* and its flavonolignans (silymarin) on reducing glucose and lipids have been also shown in diabetic patients (Dixit *et al*., 2007). In a 2-month randomized double blind clinical study, silymarin (200 mg thrice a day) could decrease FBG, HbA1c, total cholesterol, LDL, TG, serum glutamic oxalacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) in T2D patients (30 cases) receiving conventional therapy (Fallah Hoseini *et al*., 2006). Reduction in glucose, lipids and hepatic enzymes is consistent with the results of another trial on 25 T2D patients receiving the same dose of silymarin for 4 months (Ramezani *et al*., 2008). Beneficial effects of silymarin (200 mg/day) on FBG, HbA1c and PPBG have been also seen in T2D patients maintained on glibenclamide (Hussain, 2007). It has been also reported that silymarin administration to diabetic patients with liver disease could reduce insulin resistance, endogenous insulin production and need for exogenous insulin administration (Jose *et al*., 2011; Velussi *et al*., 1993; Velussi *et al*., 1997). Oral consumption of silymarin (600 mg/day for 4 months) significantly decreased FBG, HbA1c and glucosuria in insulin-treated diabetics with alcoholic cirrhosis (Velussi *et al*., 1997). Also, in another study, percentage reduction in FBG, SGOT and SGPT was about 8, 29 and 35%, respectively, after a 5 month treatment of the patients with silymarin (Jose *et al*., 2011).

Trigonella foenum-graecum

Hypoglycemic effect of *Trigonella foenum-graecum* (fenugreek) seeds has been demonstrated in cell culture, animal models and human with more than 30 studies (Ghorbani, Rakhshandeh, 2012). In human studies, usefulness of fenugreek seeds has been reported in management of both T1D and T2D. Sharma *et al*. (1990b) showed that defatted *T. foenum-graecum* seeds (100 g/day for 10 days) significantly reduced FBG, TG, total cholesterol, LDL, VLDL and glucoseuria in patients with T1D. In another study, patients with T2D were placed on 10 g/day *T. foenum-graecum* seeds soaked in hot water (11 subjects) or mixed with yoghurt (7 subjects). After 8 weeks, FBG, TG and VLDL significantly decreased in cases which received the seeds in soaked form (Kassaian *et al*., 2009). Similarly, addition of *T. foenum-graecum* seeds (100 g) to diets of patients with T2D for 10 (15 subjects) or 20 (15 subjects) days improved GTT and led to significant decrease in FBG, TG and LVDL levels (Sharma, Raghuran, 1990a). Ismail (2009a) extended period of study to 16 weeks, administrated 20 g/day of *T. foenum-graecum* seeds to 20 non-insulin dependent diabetic patients and reported a significant decrease in PPBG level. In a double blind placebo trial, T2D patients (46 cases) were given sulfonylureas drug plus *T. foenum-graecum* seeds (in the form of pill; 6 pills/3 times per day) or sulfonylureas drug plus placebo (23 cases). After 12 weeks, the combined therapy had more effect on level of FBG, HbA1c and PPBG (Fu-rong *et al*., 2008). With a similar trial design, Gupta *et al*. (2001) administrated 1 g/day hydroalcoholic extract of the seeds to 12 newly diagnosed patients with T2D for two months and found that the extract failed to change FBG and GTT; but, it could decrease serum TG and the area under curve of blood glucose. Also, an increase in HDL level and percent of insulin sensitivity (according to homeostatic model assessment) was observed in the treated subjects. According to the study of 5 non-insulin dependent diabetic patients by Sharma (1986),

administration of defatted *T. foenum-graecum* seeds (25 g) for 3 weeks produced a significant improvement in GTT and insulin response and a significant decrease in serum cholesterol and 24 h urinary glucose output. In this study, a single dose of whole seeds, defatted seeds, gum isolate and cooked seeds (but not degummed seeds) of *T. foenum-graecum* was also able to prevent the rise of plasma glucose after meal or glucose ingestion in non-diabetic subjects. Unlike the seeds, effect of *T. foenum-graecum* leaves on reducing blood glucose level was not consistent. While Sharma (1986) observed negative results with cooked leaves, Abdel-Barry *et al*. (2000) reported that 40 mg/kg of aqueous extract of *T. foenum-graecum* leaves can diminish blood glucose level of healthy subjects 4 h after ingestion, which may be due to methodological issues such as difference in methods of extract preparation.

CONCLUSION

Plants have always been an important source for finding new remedies for human diseases. Among hundreds of plants that have been studied for diabetes, only a small fraction has been tested in animal studies and is under clinical trials. The plants described in this paper, particularly *Gymnema sylvestre*, *Momordica charantia* and *Trigonella foenum-graecum*, had some clinical evidence for their antidiabetic effects. Therefore, it seems that physicians can rely on these herbs, at least as complementary therapeutics, along with current hypoglycemic drugs to improve management of diabetic patients.

Although a list of other plants could be also included in this paper, it is better to wait until more clinical pieces of evidence are available to support their hypoglycemic effect. For example, *Allium sativum, Aloe vera, Azadirachta indica, Citrullus colocynthis*, *Eugenia jambolana,* green tea, *Morus indica*, *Pterocarpus marsupium*, *Phyllanthus amarus* and *Salacia oblonga*, each of which has two supporting studies, could be on the list. On the other hand, regarding some herbs (e.g. *Cinnamomum cassia*), although a significant hypoglycemic effect has been found in some studies (Crawford, 2009; Khan *et al*., 2010; Mang *et al*., 2006), other reports have disapproved the findings (Blevins *et al*., 2007; Suppapitiporn, Kanpaksi, 2006). Furthermore, in a number of studies, there are still some methodological flaws (e.g. small sample size, short duration of trial and lack of control or placebo groups). Therefore, based on the currently available evidence, it is too early for making conclusions on benefits of such plants in diabetes.

Taken together, it seems that *Gymnema sylvestre*, *Momordica charantia*, *Silybum marianum* and *Trigonella foenum-graecum* have acquired enough reputation for their hypoglycemic action and physicians can advise them for patients to improve management of diabetes.

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