Published in final edited form as:
Recent Pat Food Nutr Agric. 2012 April 1; 4(1): 50–60.

A Review of the Hypoglycemic Effects of Five Commonly Used Herbal Food Supplements

Ruitang Deng*
Department of Biomedical and Pharmaceutical Sciences, College of Pharmacy, University of Rhode Island, Kingston, Rhode Island

Abstract

Hyperglycemia is a pathological condition associated with prediabetes and diabetes. The incidence of prediabetes and diabetes is increasing and imposes great burden on healthcare worldwide. Patients with prediabetes and diabetes have significantly increased risk for cardiovascular diseases and other complications. Currently, management of hyperglycemia includes pharmacological interventions, physical exercise, and change of life style and diet. Food supplements have increasingly become attractive alternatives to prevent or treat hyperglycemia, especially for subjects with mild hyperglycemia. This review summarized current patents and patent applications with relevant literature on five commonly used food supplements with claims of hypoglycemic effects, including emblica officinalis (gooseberry), fenugreek, green tea, momordica charantia (bitter melon) and cinnamon. The data from human clinical studies did not support a recommendation for all five supplements to manage hyperglycemia. Fenugreek and composite supplements containing emblica officinalis showed the most consistency in lowering fasting blood sugar (FBS) or glycated hemoglobin (HbA1c) levels in diabetic patients. The hypoglycemic effects of cinnamon and momordica charantia were demonstrated in most of the trials with some exceptions. However, green tea exhibited limited benefits in reducing FBS or HbA1c levels and should not be recommended for managing hyperglycemia. Certain limitations are noticed in a considerable number of clinical studies including small sample size, poor experimental design and considerable variations in participant population, preparation format, daily dose, and treatment duration. Future studies with more defined participants, standardized preparation and dose, and improved trial design and size are warranted.

Keywords

Cinnamon; diabetes; emblica officinalis; fenugreek; food supplement; hypoglycemic; green tea; glucose and insulin; momordica charantia

INTRODUCTION

As the most important energy source for human body, glucose plays a vital role in maintaining health [1]. In most cells of human body, glucose molecules are broken down to produce adenosine triphosphate molecules, the fuel that powers numerous cellular processes. Glucose is delivered to cells through blood circulating. To ensure steady supply of glucose

*Address correspondence to this author at the Department of Biomedical and Pharmaceutical Sciences, College of Pharmacy, University of Rhode Island, 41 Lower College Road, Kingston, RI 02881; Tel: 401-874-4950; Fax: 401-874-5787; DengR@mail.uri.edu.

CONFLICT OF INTEREST
The author has no conflict of interest.

as an energy source for cells to function, a relatively constant level of glucose in blood is maintained [1]. Failure to maintain such homeostatic level of glucose in blood results in hypoglycemia or hyperglycemia.

Under the physiological condition, the concentration of blood glucose is tightly regulated by various mechanisms [2, 3]. The major source of glucose comes from the food we eat. After digestion, glucose is released from the food, absorbed by small intestine and finally enters the blood stream. The other source of blood glucose is from the liver in which the storage form of glucose, glycogen, is converted into glucose entering the blood stream. On the other hand, the major pathway that decreases blood glucose levels is the uptake of glucose by the cells for use as a source of energy in most of the tissues or to be stored for future use in the adipose tissue and liver. Therefore, blood glucose concentration reflects the combined effects of food consumption, glucose production, transport into and out of cells and utilization by the body.

Hyperglycemia is a pathological condition characterized by elevated blood glucose levels. It is a manifestation most commonly associated with such disease conditions as pre-diabetes and diabetes mellitus [4–6]. Prediabetes is a condition which does not satisfy the diagnostic criteria for diabetes but the blood glucose levels are elevated. All the diabetes patients go through such non-diabetic hyperglycemia stage before escalating into full-blown diabetes [4, 5]. Studies have shown that both prediabetic and diabetic subjects have significantly increased risk for cardiovascular diseases and other complications [6–9]. The incidence of prediabetes and diabetes is increasing and imposes great burden on healthcare worldwide [10, 11].

Various pharmacological therapies are currently available to control hyperglycemia [12]. However, those pharmacological treatments are associated with various adverse responses such as hypoglycemia and weight gain with sulfonylureas, digestive track problems with most of oral drugs, potential liver toxicity with thiazolidinediones and skin rash with insulin injection [13–17]. In addition, it is not uncommon that the blood glucose levels are not well controlled by pharmacological therapies alone mainly due to poor compliance, inappropriate self-care behavior, and psychological problem with insulin injection [18]. On the other hand, the herbal food supplements reviewed in this article have been used for human consumption for centuries and their safety in human has been well established. With good safety profile and convenience, those food supplements have increasingly become attractive additions to the regular pharmacological therapies in diabetic patients, especially for those whose blood glucose levels are not well controlled by the therapies alone [19–22]. In addition, those food supplements are becoming more and more popular to manage hyperglycemia in prediabetic patients [20, 21], especially for those whose blood glucose levels are on the borderline and pharmacological therapies have not been initiated.

This review summarized current patents and patent applications with relevant literature on five commonly used food supplements with claims of hypoglycemic effects, including emblica officinalis (gooseberry), fenugreek, green tea, momordica charantia (bitter melon) and cinnamon. The focus of this review is on human clinical trials although a large body of evidence is well documented in preclinical studies. The quality of each clinical trial is rated with the Jadad scoring system (Table 1) [23] and the quality of evidence for the hypoglycemic effect of the five food supplements is categorized based on the criteria listed in (Table 2). The results from human clinical studies did not support a recommendation for all five supplements to manage hyperglycemia.

EMBLICA OFFICINALIS

Emblica officinalis, known as India gooseberry or amla, is an edible fruit from the tree of the *phyllanthaceae* family. The fruit is eaten raw, cooked or pickled. In addition to serving as fruit, emblica officinalis has been used to treat a variety of disease conditions including hyperlipidemia and diabetes. In two recent patents, it was claimed that emblica officinalis had hypoglycemic effects and could be used for managing hyperglycemia [24, 25]. Such claims were largely supported by 4 clinical trials with diabetic patients.

The first trial recruited 120 diabetic patients without complication or symptomatically normal [26]. The subjects were randomly assigned into two groups, treatment or control. A composite supplement containing a teaspoon of emblica officinalis juice and other hypoglycemic herbals including 2.5 g of ocimum sanctum leaves powder, aqueous extract of 60 g of syzygium cumini fruit, 10 g seed powder of syzygium cumini, 5 g of momordica charantia juice and 2 g of gymnema sylvestre leaves was given to treatment group daily for 3 months. The control group received normal diet. At the end of the study, fasting blood sugar (FBS) levels were significantly decreased in patients received the composite supplement whereas no changes were detected in control group. Glycated hemoglobin (HbA1c) values were also significantly reduced in experimental group while the values remained unchanged in the control group.

The second trial had 53 participants including 43 patients with type 2 diabetes and 10 healthy volunteers [27]. The diabetic patients were divided into three age groups, age 35–45 (15 patients), 46–55 (13 patients) and over 55 (15 patients). All the diabetic subjects received daily two tablets (500mg/tablet) each containing 25% of emblica officinalis, 25% *curcuma longa L* and 50% *salacia oblonga* wall fort for 3 months. The healthy subjects did not take any tablets serving as normal controls. At the end of the study, a significant reduction in both FBS and HbA1c levels were detected in all the three age groups. When grouping the patients based on initial FBS levels into subjects with FBS levels above or below 145.9 mg/dL, both groups exhibited significant decreases in FBS and HbA1c levels. However, it remained undetermined how much emblica officinalis contributes to the observed hypoglycemic effect.

The third trial was a randomized and controlled study with 49 diabetic patients. The participants were randomly assigned into treatment group (30 patients) and control group (19 patients) [28]. The treatment group took a medium sized fresh amla (~35g) on a daily bases while the control group received no supplementation for 2 months. During the course of study, no modification in the diet or medication was made in both groups. At the end of study, no significant reduction in both FBS and HbA1c levels were detected in the treatment and control group. However, more detailed analysis of the data revealed that a significant reduction in FBS was achieved in subjects with FBS > 150 mg/dl, accompanied by a non significant fall in HbA1c levels. It was thus concluded that consumption of fresh emblica officinalis fruit improved FBS levels in diabetic patients with high FBS levels.

The most recent clinical study recruited 13 uremic diabetic patients and 15 healthy volunteers [29]. The uremic diabetic patients received a daily supplement of 3 tablets each containing 100 mg emblica officinalis extract, 100 mg green tea extract and 50 mg excipient starch for 3 months. The healthy subjects did not receive any supplement serving as controls for normal ranges. Supplementation with a combination of emblica officinalis and green tea extract resulted in a significant reduction in FBS levels compared with the baseline levels prior to treatment. The HbA1c levels were not statistically different before and after treatment. The data thus suggested that a 1:1 combination of emblica officinalis and green tea extract is a safe and effective treatment for uremic patients with diabetes.

In summary, the quality of trials ranges from 0 to 4 of the Jadad scale (Table 3). It is thus concluded that there is strong scientific evidence (Level B1) to support that composite supplements containing emblica officinalis is effective in lowering blood glucose levels in diabetic patients. However, there was not enough evidence to supports the hypoglycemic activity of emblica officinalis alone.

FENUGREEK

Fenugreek, also known as its scientific name of *trigonella foenum-graecum L., leguminosae*, belongs to the plant family *fabaceae* (or *leguminosae*). It grows in most of the countries around world with major production in Asia, Europe and American including United States. The health-promoting property of fenugreek has been long documented when it is taken as vegetables, food supplements or medicinal remedies. Four recent patents or patent applications described usages and applications of fenugreek in managing metabolic diseases including hyperglycemia and diabetes. One patent application described making dietary supplements with fenugreek fibers to control blood glucose [30]. Another patent application claimed making food products with fenugreek seed powder for prevention of obesity and diabetes [31]. The third patent application disclosed an anti-diabetic composition of food supplement with fenugreek seed extract [32]. Clinical studies with human volunteers showed a dosage form of 500 mg given once or twice daily either alone or in combination with standard, synthetic anti-diabetic drugs such as metformin and glipizide provided beneficial effects on controlling plasma glucose levels. One recently issued patent illustrated a composition with fenugreek seeds to lower glucose and cholesterol [33].

Those claims are largely supported by the findings from human clinical trials. Four such trials were conducted with type 1 and 2 diabetic patients before 2000. The first study involved non-insulin dependent diabetic patients [34]. Supplementation of 15 g fenugreek seed soaked in water resulted in a significant reduction in postprandial glucose levels in 21 diabetic patients. The second study was a randomized, controlled crossover trial with 15 diabetic patients [35]. A diet supplemented with 100 g of fenugreek seed powder was given daily for 10 days in treatment group (7 patients) while a regular diet was given to the control group (8 patients). Then the patients were crossed over for additional 10 days. It was found that supplementation with fenugreek seed powder significantly reduced FBS and improved the glucose tolerance test. In the third study, ten non-insulin dependent diabetic patients were enrolled in a randomized, controlled crossover trial [36]. Treatment for 5 subjects included a diet supplemented with 25 g fenugreek daily for 15 days. Without a washout period, the patients were crossed over for additional 15 days. The results showed that fenugreek supplement significantly reduced the area under the plasma glucose curve and improved glucose tolerance. In the fourth trial [37], forty patients with coronary artery disease and non-insulin-dependent diabetes mellitus and 30 healthy volunteers were given a diet containing 5 g of fenugreek for 3 months. At the end of the study, twenty patients with mild hyperglycemia exhibited a significant reduction in FBS and postprandial glucose levels. However, the changes in patients with severe hyperglycemia and healthy subjects were not statistically significant.

Four clinical trials were carried out more recently with diabetic patients. In a small double blind and controlled study [38], twenty five newly diagnosed type 2 diabetic patients were divided into two groups, treatment and control. Twelve patients in the treatment group were supplemented with 1 g hydroalcoholic extract of fenugreek seeds whereas 13 patients in the control group received placebo capsules for daily 2 months. No significant differences in FBS and oral glucose tolerance test were detected between the two groups. However, significant differences in the area under curve of blood glucoses and insulin sensitivity were noticed. Two relatively large clinical trials were carried out in 2005 [39] and 2008 [40]. One

trial involved 60 male subjects with non-insulin dependent diabetes [39]. Thirty patients in one group received a daily dose of 1 g mixed powder containing equal amount of raw fenugreek seed, bitter gourd and jambu seed powder in the form of capsules whereas the other group with 30 patients consumed same dose in the form of salty biscuits for 1.5 months, followed by ingesting an increased daily dose of 2 g mixed powder for another 1.5 months. At the end of the study, a significant reduction in FBS and post-prandial glucose levels was achieved in both groups. The other trial was conducted in 69 type 2 diabetic patients with not well controlled blood glucose levels using oral sulfonylureas [38]. The treatment group with 46 patients received 18 pills of fenugreek daily while the control group with 23 patients took placebo for 12 weeks. All the patients continued their original hypoglycemic drugs during the study. Supplement with fenugreek pills in the treatment group significantly decreased FBS, postprandial blood glucose and HbA1c levels, companied with improved clinical symptoms. It was thus concluded that supplementation of sulfonylureas hypoglycemic drug with fenugreek was an effective therapy to manage diabetic patients with uncontrolled blood glucose with hypoglycemic drug alone. The last trial recruited 18 type 2 diabetic patients [41]. The subjects were divided into two groups. One group with 11 patients received a daily dose of 10 g fenugreek seed powder in hot water whereas the other group with 7 subjects consumed the same amount of fenugreek seeds mixed with yoghurt for 8 weeks. Significant decreases in FBS was detected in group consuming fenugreek in hot water but not in the group given fenugreek mixed with yoghurt. It was concluded that fenugreek seeds was an effective adjuvant in the control of type 2 diabetes in the form of soaked in hot water. Mixing of fenugreek seeds with yoghurt may interfere with the absorption of active ingredients of fenugreek seeds in the gastrointestinal track.

The hypoglycemic activity of fenugreek was also evaluated in three clinical trials with healthy or healthy obese volunteers. The first early trial recruited 20 male healthy subjects [42]. The treatment group received 40mg/kg aqueous extract of fenugreek seeds whereas the control group received placebo. Four hours post-ingestion, blood glucose levels were significantly reduced in the treatment group. The second trial was a single blind, randomized, crossover study and conducted in 18 healthy obese subjects [43]. Two treatment groups received 4g or 8g of isolated fenugreek fiber whereas the control group received a placebo. No significant changes were noticed in postprandial blood glucose levels and insulin sensitivity within 3.5 hours post-ingestion between the three groups. The third trial is a double-blind, randomized, and placebo-controlled study with 38 healthy overweight male volunteers [44]. Treatment group with 18 subjects received 1176mg daily dose of hydroalcohol extract of fenugreek seed for 6 weeks while the control group with 20 subjects received placebo. At the end of the study, no significant differences in FBS and insulin were detected between the control and treatment group.

Taken together, the quality of trials with diabetic patients ranges from 0 to 3 in the Jadad scale (Table 4). Therefore, there is good scientific evidence (Level B2) suggesting that fenugreek is effective in reducing blood glucose levels in diabetic patients. The quality of trials with healthy, obese or overweight subjects ranges from 0 to 3 in the Jadad scale with majority of the trials exhibiting no hypoglycemic effect (Table 4). There is thus good scientific evidence (Level B2) to support that fenugreek is not effective in lowering blood glucose in healthy, obese or overweight subjects.

GREEN TEA

Green tea is one of the most consumed beverages in the world, especially in Asian. As a dry product, tea is the processed leaf from the plant *Camellia sinensis*. Health promoting benefits of tea consumption have been indicated in a variety of diseases including metabolic

syndromes and diabetes. Several recent patents and patent applications claimed the hypoglycemic activity of green tea or its main ingredient catechin alone or in combination with other natural products [25, 45–48].

Four clinical trials have been reported to evaluate whether green tea has hypoglycemic effects in patients with type 2 diabetes. The first trial was a randomized and controlled study with 66 diabetic patients [49]. The treatment group took a packet of green tea extract containing 544 mg polyphenols or 456mg catechins daily for 2 months whereas the control group did not take any extract. At the end of the study, the FBS and HbA1c levels were significantly lower than the respective values before treatment. However, when compared with placebo control, there were no significant differences in FBS and HbA1c levels. In conclusion, the daily supplementary intake of green tea did not have significant effects on blood glucose and HbA1c levels.

The second trial was a double-blind, placebo-controlled, randomized multiple-dose study with 49 diabetic patients [50]. The two treatment groups consumed daily 375 mg or 750 mg of green tea for 3 months where the control group received placebo. The results showed that no significant differences in HbA1c were detected among the three groups. Therefore, it was concluded that green tea had no hypogly-cemic effect in patients with type 2 diabetes.

In the third study [51], the effects of continuous ingestion of a catechin-rich beverage in 43 diabetic patients who were not receiving insulin therapy were evaluated with a double-blind controlled study. One group with 23 subjects consumed daily 582.8 mg of catechin-containing green tea whereas the other group with 20 patients ingested 96.3 mg of catechins-containing green tea for 12 weeks. At the end of the study, there were no apparent differences in blood glucose and HbA1c levels between the two groups.

In the most recent study with 80 diabetic patients [52], the effect of a decaffeinated green tea extract on obese individuals with type 2 diabetes was investigated. The study was a randomized, double-blind, placebo-controlled clinical trial. The treatment group received a daily dose of 1500 mg of green tea extract while the control group received placebo for 16 weeks. No statistically significant differences were detected between the treatment and placebo groups in any measured variable including FBS and HbA1c levels.

Four clinical trials were also conducted with healthy or healthy obese volunteers to evaluate the hypoglycemic activity of green tea. The first trial was a crossover study with 60 participants [53]. One group consumed daily a packet of green tea extract containing 544 mg polyphenols (456 mg catechins) for 2 months, followed by 2 month-nonintervention period. Conversely, the other group had a 2 month-nonintervention period, followed by ingesting daily same dose of green tea extract for 2 months. At the end of the study, HbA1c levels were significantly decreased following the intervention. However, no significant changes in FBS levels were detected.

The second trial was to evaluate the effect of acute ingestion of green tea extract on glucose tolerance of healthy volunteers during moderate-intensity exercise [54]. One treatment group with 12 subjects performed a moderate exercise before and after supplementation of green tea extract containing 890 mg polyphenols. The other treatment group with 11 subjects took an oral-glucose-tolerance test before and after supplementation. The results showed that the insulin area under the curve decreased in both treatment groups with a concomitant increase in insulin sensitivity. It was thus concluded that acute green tea extract ingestion improved insulin sensitivity and glucose tolerance in healthy young men. Therefore, it was concluded that a combination of excise and ingestion of green tea may represent a practical approach to prevent prediabetes or diabetes.

The third trial was carried out in 88 overweight or obese male subjects [55]. The participants were randomly assigned into two groups, treatment and control. The treatment group with 46 subjects ingested a daily dose of 800 mg epigallo-catechin-3-gallate (EGCG), the active ingredient of green tea for 8 weeks. The control group with 42 subjects took the placebo lactose. At the end of the study, it was revealed that supplementation with EGCG for 8 weeks had no significant effects on FBS and HbA1c levels, insulin sensitivity, insulin secretion, glucose tolerance.

The most recent trial was a crossover study with 14 healthy volunteers [56]. The subjects were randomized into treatment or control group. The subjects in treatment group took 300ml of green tea with their breakfast whereas control subjects received water. Multiple blood samples were drawn within the 2 hour period after the ingestion. Plasma glucose levels were increased in the treatment group 2 hours after ingestion when compared with the control group. No significant differences were found in serum insulin levels, the area under the curve for glucose or insulin. It was thus concluded that green tea showed no glucose or insulin-lowering effect.

Altogether, the quality of clinical trials ranges from 0 to 4 in the Jadad scale with majority being negative in reducing blood glucose levels (Table 5). There is thus strong scientific evidence (Level B1) indicating that green tea is not effective in controlling hyperglycemia in diabetic patients as well as healthy subjects.

MOMORDICA CHARANTIA (BITTER MELON)

Momordica charantia, known as bitter melon or gourd, is widely consumed as a vegetable and bitter flavoring in cookery, especially in Asian countries such as China and India. Consumption of momordica charantia has been linked to a variety of health-promoting benefits, including lowering blood glucose in hyperglycemic subjects. Five recent patent applications described momordica charantia-containing compositions for managing hyperglycemia [45, 57–60]. A large number of preclinical studies support the claim that momordica charantia is able to lower plasma glucose levels. However, the results from human clinical trials are not conclusive.

The results from three early clinical trials support the hypoglycaemic activity of momordica charantia. The first study recruited 14 diabetic patients and 5 healthy volunteers [61]. Insulin-like substance, called vegetable insulin (v-insulin), was extracted from momordica charantia. Injection of mormordica charantia extract containing 10, 20 or 30 units of v-insulin dependent on the severity of the diabetes in 9 diabetic patients resulted in significant reduction in FBS by 21.5% to 49.2% within the period of 12 hours post-treatment. The control group including 5 diabetic and 5 healthy subjects received a placebo and exhibited a 5% decrease in FBS. The second trial with 9 diabetic patients showed that daily consumption of 230 g fried momordica charantia fruit for 8 to 11 weeks significantly improved glucose tolerance [62]. Drinking of 50 ml of fresh momordica charantia fruit juice also significantly reduced plasma glucose levels and the area under curve within the period of 1.5 hours post-drinking. The third trial is a case study with 100 moderate non-insulin dependent diabetic patients [63]. Drinking of the aqueous homogenized suspension of the vegetable pulp resulted in a significant reduction in FBS and postprandial sugar levels in 86 subjects with a mean reduction of 18%.

However, such claim was challenged by the results from two randomized and placebo-controlled trials. The first trial had 50 type 2 diabetic patients [64]. The participants were randomized into treatment or control group. The 26 subjects in the treatment group took 4 g dry bitter gourd daily for 2 and 4 weeks while the control group with 24 subjects received Riboflavin as placebo. Patients in both group continued with their routine anti-diabetic

treatment including dietary modification and oral hypoglycemic agents such as sulfonylureas and biguanides. At the end of the trial, no significant changes in FBS, postprandial sugar levels and fructosamine were detected in both treatment and control group. The second trial was a randomised, double-blind and placebo-controlled trial with 40 either newly diagnosed or poorly controlled type 2 diabetic patients [65]. The treatment group were given 6 capsules of momordica charantia extract daily for 3 months whereas the control group received a placebo. It was found that supplementation with momordica charantia extract did not significantly reduced FBS and HbA1c levels although the HbA1c levels were decreased in treatment group compared with the control group.

Additional two clinical trials were carried out to investigate the hypoglycaemic activity of momordica charantia in combination or comparison with oral hypoglycemic drugs. One trial investigated the effect of momordica charantia extract in combination with regular oral hypoglycaemic drugs on type 2 diabetic patients [66]. Fifteen subjects were recruited and randomized into three equal groups. The three groups received oral hypoglycaemic drug metformin, glibenclamide, or combination of metformin and glibenclamide for 7 day, followed by taking half dose of the hypoglycaemic drugs supplemented with a daily dose of 400 mg momordica charantia extracts for 7 additional days. FBS and PPS levels were significantly reduced after oral hypoglycemics for 7 days and a further reduction was achieved at half oral hypoglycemics supplemented with momordica charantia extract. It was thus concluded that momordica charantia extract acted in synergism with oral hypoglycemics and potentiated their hypoglycemic effect in diabetic patients. The second trial was a multicenter, randomized, double-blind, active-control trial [67]. Type 2 diabetic subjects were randomly divided into four groups. Group 1–3 received a daily dose of 500 mg, 1000 mg or 2000 mg of momordica charantia for 4 weeks. Group 4 took a daily dose of 1000 mg metformin for 4 weeks. At the end of the trial, a significant reduction in fructosamine levels was detected in patients receiving 1000 mg metformin or 2,000 mg momordica charantia. No significant changes were noticed in groups consuming 500 mg or 1000 mg momordica charantia. It was thus concluded that momordica charantia had a modest hypoglycemic effect and significantly reduced fructosamine levels at the high dose. However, the hypoglycemic effect of momordica charantia was less than metformin at a dose of 1000 mg/day.

In summary, the quality of trials ranges from 0 to 4 in the Jadad scale with majority being positive in reducing blood glucose levels (Table **6**). Thus there is good scientific evidence (Level B2) to suggest that momordica charantia is effective in reducing blood glucose levels in diabetic patients. However, such hypoglycemic effect was not consistently detected in two clinical trials.

CINNAMON

Cinnamon, obtained from the inner bark of plants *cinnamomum*, has been used as a spice in cookery worldwide and is an important ingredient in the traditional Chinese medicine and Ayurveda for centuries. The dry bark of cinnamon trees is rich in botanical source of polyphenolics and has been used to improve general health and treat a variety of disease conditions including diabetes. Five recent patents and patent applications disclosed compositions with cinnamon for the management of metabolic diseases including diabetes [2, 68–71]. A relatively large number of clinical trials have been conducted to evaluate cinnamon’s hypoglycemic effects in diabetic patients and health volunteers.

The results from four clinical trials with diabetic patients support the claim that cinnamon supplements have hypoglycemic effects. In a study with 60 type 2 diabetic patients [72], the subjects were randomized into 6 groups. Group 1, 2 and 3 ingested 1, 3 or 6 g cinnamon

daily for 40 days. As controls, groups 4, 5 and 6 consumed placebo capsules corresponding to the number of capsules ingested for groups 1, 2 and 3. Patients in all the groups continue their routine sulfonylurea drugs. After 40 days, FBS levels were significantly reduced in groups 1, 2 and 3 by 18–29% while no significant changes were detected in placebo groups.

The second study was a randomized, double-blind and placebo-controlled trial [73]. Seventy nine participants with type 2 diabetes not on insulin therapy but treated with oral antidiabetics or diet were randomly assigned into treatment or control group. The treatment group took aqueous extract of 3 g cinnamon powder daily for 4 months while the control group received placebo capsules. At the end of the study, FBS and postprandial blood glucose levels were significantly reduced in the treatment group compared with placebo group. However, no significant differences in HbA1c levels were detected intra- and inter-group. In addition, it was noted that the decrease in FBS correlated significantly with the baseline concentrations, indicating that subjects with a higher initial plasma glucose level may benefit more from cinnamon intake.

The third trial was also a randomized and controlled clinical study [74]. One hundred nine type 2 diabetic patients were randomized into treatment or control group. In the treatment group, participants were supplemented with 1 g cinnamon capsules daily for 90 days. The control group was not given supplement. Patients in both groups continued with their routine anti-diabetic medications. It was found that supplement with cinnamon significantly lowered HbA1c levels in diabetic patients.

The fourth study was also a randomized and placebo-controlled trial with 58 type 2 diabetic patients [75]. The participants were randomized into treatment or control group. The treatment group received 2 g cinnamon daily for 12 weeks while the control group consumed placebo capsules. At the end of the trial, HbA1c levels were significantly decreased in the cinnamon group compared with placebo group. A significant reduction in FBS levels were also detected compared to the baseline in the cinnamon group. However, the changes were not significant when compared to placebo group.

The hypoglycemic effects of cinnamon supplement were challenged by the results from following three clinical studies. The first study recruited 25 postmenopausal type 2 diabetic patients [76]. The participants received either a supplement of 1.5 g cinnamon or placebo daily for 6 weeks. During the experimental period, all the subjects maintained their normal dietary and physical activity pattern, and continued with their anti-diabetic medications. At the end of the study, no significant changes were detected in FBS, HbA1c and insulin sensitivity after the cinnamon intervention. The second study was a prospective, double-blind and placebo-controlled trial with 72 adolescent type 1 diabetic patients [77]. The subjects were given either a supplement of 1 g cinnamon or an equivalent-appearing placebo daily for 90 days. All patients continued with their daily insulin dose and maintained routine medical care, diet, or exercise. At the end of the trial, there were no significant differences in Hb A1C levels, total daily insulin intake, and the number of hypoglycemic episodes between the cinnamon and placebo arms. The third study was also a randomized, double-blind and placebo-controlled trial with 58 type 2 diabetic patients [78]. The subjects received either a capsule containing 500 mg cinnamon or wheat flour placebo daily for 3 months. Patients in both groups continued with their routine anti-diabetic and lipid-lowering medications. No significant differences between the cinnamon and placebo groups in FBS, HbA1c and insulin levels were detected at the end of the trial. The authors concluded that cinnamon supplement did not have hypoglycemic effects in type 2 diabetic patients and the effects of cinnamon might differ by population.

In addition to the clinical studies with diabetic patients, three small clinical trials were carried out to investigate the hypoglycemic effect of cinnamon in healthy volunteers. The first study recruited 27 healthy subjects to determine whether cinnamon, vinegar or combination of both lowered blood glucose levels [79]. The subjects consumed a normal meal or a normal meal supplemented with either 4 g cinnamon, 28 mM acetic acids or combination of both, followed by multiple detections of blood glucose during the 2 hour period postprandially. A significant reduction in blood glucose level was noted in subjects supplemented with a combination of cinnamon and acetic acids 15 minutes post-ingestion. The second study had 8 male volunteers [80]. The subjects received either 3 g cinnamon or placebo supplement daily for 14 days. Oral glucose tolerance tests were performed multiple time points during the study period. The results showed that cinnamon supplement significantly decreased glucose and insulin response to the glucose tolerance test and improved insulin sensitivity. The third study was a crossover trial with 15 healthy volunteers [81]. The subjects were randomly assigned into three groups. Two treatment groups ate rice pudding with 1 or 3 g cinnamon while the control group ate only rice pudding. Supplement with 1 or 3 g cinnamon had no significant effect on blood glucose level. However, the insulin response at 60 min and the area under the curve at 120 min were significantly decreased after ingestion of rice pudding with 3 g cinnamon.

In summary, there are four trials scoring 2 or 3 in Jadad scale showing positive in lowering blood glucose in type 2 diabetic patients. Thus there is very strong scientific evidence (Level A) to support that cinnamon is effective in lowering blood glucose levels in type 2 diabetic patients. However, such hypoglycemic effect was not detected in specific subject populations such as type 1 diabetic patients and postmenopausal type 2 diabetic patients.

CURRENT AND FUTURE DEVELOPMENTS

The five herbal food supplements emblica officinalis, fenugreek, green tea, momordica charantia and cinnamon are currently used for controlling hyperglycemia, especially in Asian countries such as India and China and are gaining more and more popularity in western countries including US. However, clinical data did not support a recommendation for all the five supplements to manage hyperglycemia.

For emblica officinalis, there are limited 4 clinical trials reported with only one having high quality [26]. The consistent finding from those clinical studies is the significant reduction in FBS levels after consumption of composite supplements containing emblica officinalis, especially in patients with high initial FBS levels. One limitation associated with the trials is that the composite supplements contain other substances in addition to emblica officinalis, making it impossible to determine how much emblica officinalis contributes to the observed hypoglycemic effects. Additional trials with emblica officinalis as the supplement are required for establishing its possible hypoglycemic activity. In addition, different forms and doses of emblica officinalis were used in the trials, including fresh fruit, juice and extract. It remains to be determined which form and dose provide the most benefits in controlling hyperglycemia.

Despite of the differences in sample size, experimental design, dose and duration among the clinical studies, accumulative results indicate that fenugreek supplement alone or in combination with oral hypoglycemic drugs provide beneficial effects in controlling hyperglycemia in diabetic patients. However, such hypoglycemic effect is not certain or diminished in healthy, obese or overweight subjects. Additional trials with high quality study design and increased sample size are required to substantiate the claim of fenugreek's hypoglycemic effect.

Based on the data from clinical studies, dietary supplement with green tea or its active ingredients has minimal effects on controlling hyperglycemia in diabetic patients. It is thus not recommended to drink green tea to manage high blood glucose levels in diabetic patients. It is still controversial whether consumption of green tea has beneficial benefits in lowering blood glucose levels in healthy or healthy obese subjects. Additional studies with improved experimental design and increased sample size are warranted.

Majority of the clinical studies support the hypoglycemic effects of momordica charantia in diabetic patients. However the effects were not consistently detected in two trials [64, 65]. Differences in methods for making momordica charantia preparations and relative small sizes may explain the discrepancy in the two trials. Overall, the data suggest that combination of momordica charantia with oral anti-diabetic drugs may represent a practical option to better control hyperglycemia in diabetic patients, especially for those whose blood glucose levels are not well controlled by oral hypoglycemic drug alone. Additional clinical studies with improved experimental design, standardized preparation and dose, and increased size are required to firmly establish the hypoglycemic activity of momordica charantia.

Among the five food supplements, cinnamon has been clinically studied the most with relatively good quality trials. There is very strong scientific evidence supporting the hypoglycemic activity of cinnamon in type 2 diabetic patients. However, cinnamon provides limited benefits in lowering blood glucose levels in certain subject populations including type 1 diabetic [77] and postmenopausal type 2 diabetic patients [76]. In addition, the difference in ethnic background may explain the negative result in one trial with type 2 diabetic patients [78]. Therefore, additional clinical studies with more defined subject population are warranted.

Acknowledgments

The author’s research is supported by the National Institutes of Health Grant R01DK087755.

References

1. Osundiji MA, Evans ML. Hypothalamic glucose sensing and glycaemic disease. Curr Diabetes Rev. 2011; 7:84–98. [PubMed: 21329490]
2. Kalsbeek A, Bruinstroop E, Yi CX, Klieverik LP, La Fleur SE, Fliers E. Hypothalamic control of energy metabolism via the autonomic nervous system. Ann N Y Acad Sci. 2010; 1212:114–29. [PubMed: 21070249]
3. Delaere F, Magnan C, Mithieux G. Hypothalamic integration of portal glucose signals and control of food intake and insulin sensitivity. Diabetes Metab. 2010; 36:257–562. [PubMed: 20561808]
4. Rhee SY, Woo JT. The prediabetic period: review of clinical aspects. Diabetes Metab J. 2011; 35:107–16. [PubMed: 21738892]
5. Nyenwe EA, Dagogo-Jack S. Metabolic syndrome, prediabetes and the science of primary prevention. Minerva Endocrinol. 2011; 36:129–45. [PubMed: 21519322]
6. Kolb H, Eizirik DL. Resistance to type 2 diabetes mellitus: a matter of hormesis? Nat Rev Endocrinol. 2011 [Epub ahead of print].
7. Berenson GS, Agirbasli M, Nguyen QM, Chen W, Srinivasan SR. Glycemic status, metabolic syndrome, and cardiovascular risk in children. Med Clin North Am. 2011; 95:409–17. [PubMed: 21281842]
8. Dhingra R, Vasan RS. Diabetes and the risk of heart failure. Heart Fail Clin. 2012; 8:125–33. [PubMed: 22108732]
9. Milman S, Crandall JP. Mechanisms of vascular complications in prediabetes. Med Clin North Am. 2011; 95:309–25. [PubMed: 21281835]

10. Colagiuri S. Epidemiology of prediabetes. Med Clin North Am. 2011; 95:299–307. [PubMed: 21281834]
11. Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus-present and future perspectives. Nat Rev Endocrinol. 2011 [Epub ahead of print].
12. Ho J, Leung AK, Rabi D. Hypoglycemic agents in the management of type 2 diabetes mellitus. Recent Pat Endocr Metab Immune Drug Discov. 2011; 5:66–73. [PubMed: 22074580]
13. Levetan C. Oral antidiabetic agents in type 2 diabetes. Curr Med Res Opin. 2007; 23:945–52. [PubMed: 17407651]
14. Plutzky J. Macrovascular effects and safety issues of therapies for type 2 diabetes. Am J Cardiol. 2011; 108:25B–32B.
15. Madsbad S, Kielgast U, Asmar M, Deacon CF, Torekov SS, Holst JJ. An overview of once-weekly glucagon-like peptide-1 receptor agonists-available efficacy and safety data and perspectives for the future. Diabetes Obes Metab. 2011; 13:394–407. [PubMed: 21208359]
16. Hollander P, Raslova K, Skjøth TV, Råstam J, Liutkus JF. Efficacy and safety of insulin detemir once daily in combination with sita-gliptin and metformin: the TRANSITION randomized controlled trial. Diabetes Obes Metab. 2011; 13:268–75. [PubMed: 21205123]
17. Starner CI, Schafer JA, Heaton AH, Gleason PP. Rosiglitazone and pioglitazone utilization from January 2007 through May 2008 associated with five risk-warning events. J Manag Care Pharm. 2008; 14:523–31. [PubMed: 18693776]
18. Home P. The challenge of poorly controlled diabetes mellitus. Diabetes Metab. 2003; 29:101–9. [PubMed: 12746629]
19. Lee T, Dugoua JJ. Nutritional supplements and their effect on glucose control. Curr Diab Rep. 2011; 11:142–8. [PubMed: 21298562]
20. Davì G, Santilli F, Patrono C. Nutraceuticals in diabetes and metabolic syndrome. Cardiovasc Ther. 2010; 28:216–26. [PubMed: 20633024]
21. Najm W, Lie D. Herbals used for diabetes, obesity, and metabolic syndrome. Prim Care. 2010; 37:237–54. [PubMed: 20493334]
22. Bartlett HE, Eperjesi F. Nutritional supplementation for type 2 diabetes: a systematic review. Ophthalmic Physiol Opt. 2008; 28:503–23. [PubMed: 19076553]
23. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled Clin Trials. 1996; 17:1–12. [PubMed: 8721797]
24. Patell, VM. Screening method (metabolite grid) for therapeutic extracts and molecules for diabetes. US. 20110159118. 2011.
25. Mazed, MA.; Mazed, S. Nutritional supplement for the prevention of cardiovascular disease, alzheimer's disease, diabetes, and regulation and reduction of blood sugar and insulin resistance. US. 8017147. 2011.
26. Mitra A. Effects of a composite of tulsi leaves, amla bitter gourd, gurmur leaves, jamun fruit and seed in type 2 diabetic patients. J Clinical Diagnostic Research. 2007; 6:511–20.
27. Faizal P, Suresh S, Satheesh Kumar R, Augusti KT. A study on the hypoglycemic and hypolipidemic effects of an ayurvedic drug Ra-janyamalakadi in diabetic patients. Indian J Clinical Biochem. 2009; 24:82–7. [PubMed: 23105812]
28. Iyer U, Joshi A, Dhruv S. Impact of Amla (Embilica Officinalis) supplementation on the glycemic and lipidemic status of type 2 diabetic subjects. J Herbal Medicine and Toxicol. 2009; 3:15–21.
29. Chen TS, Liou SY, Wu HC, Tsai FJ, Tsai CH, Huang CY, et al. Efficacy of epigallocatechin-3-gallate and amla (Emblica officinalis) extract for the treatment of diabetic-uremic patients. J Medicinal Food. 2011; 14:718–23.
30. Pilgaonkar, PS.; Rustomjee, MT.; Gandhi, AS.; Suvarnapathaki, RK. Dietary fiber compositions. US. 20110177175. 2011.
31. Losso, JN.; Finley, JW.; Holliday, DL.; Mumphrey, LA. Fenugreek flour for incorporating into food products. US. 20100266665. 2010.
32. Pawan, GK. A novel antidabetic furostanolic saponin rich (FSR) fraction from fenugreek seeds. WO. 2010140165. 2010.

33. Murthy, PS.; Moorthy, R.; Prabhu, KM.; Puri, D. Anti-diabetic and cholesterol lowering preparation from fenugreek seeds. US. 7815946. 2010.
34. Madar Z, Abel R, Samish S, Arad J. Glucose-lowering effect of fenugreek in non-insulin dependent diabetics. Eur J Clin Nutr. 1988; 42:51–4. [PubMed: 3286242]
35. Sharma RD, Raghuram TC. Hypoglycaemic effect of fenugreek seeds in non-insulin dependent diabetic subjects. Nutr Res. 1990; 10:731–9.
36. Raghuram TC, Sharma RD, Sivakumar B, Sahay BK. Effect of fenugreek seeds on intravenous glucose disposition in non-insulin dependent diabetic patients. Phytotherapy Research. 1994; 8:83–6.
37. Bordia A, Verma SK, Srivastava KC. Effect of ginger (Zingiber officinale Rosc.) and fenugreek (Trigonella foenumgraecum L) on blood lipids, blood sugar and platelet aggregation in patients with coronary artery disease. Prostaglandins Leukot Essent Fatty Acids. 1997; 56:379–84. [PubMed: 9175175]
38. Gupta A, Gupta R, Lal B. Effect of Trigonella foenum-graecum (fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes mellitus: a double blind placebo controlled study. J Assoc Physicians India. 2001; 49:1057–61. [PubMed: 11868855]
39. Kochhar A, Nagi M. Effect of supplementation of traditional medicinal plants on blood glucose in non-insulin-dependent diabetics: a pilot study. J Med Food. 2005; 8:545–9. [PubMed: 16379570]
40. Lu FR, Shen L, Qin Y, Gao L, Li H, Dai Y. Clinical observation on trigonella foenum-graecum L. total saponins in combination with sulfonylureas in the treatment of type 2 diabetes mellitus. Chin J Integr Med. 2008; 14:56–60. [PubMed: 18219452]
41. Kassaian N, Azadbakht L, Forghani B, Amini M. Effect of fenugreek seeds on blood glucose and lipid profiles in type 2 diabetic patients. Int J Vitam Nutr Res. 2009; 79:34–39. [PubMed: 19839001]
42. Abdel-Barry JA, Abdel-Hassan IA, Jawad AM, Al-Hakiem MH. Hypoglycaemic effect of aqueous extract of the leaves of Trigonella foenum-graecum in healthy volunteers. East Mediterr Health J. 2000; 6:83–8. [PubMed: 11370345]
43. Mathern JR, Raatz SK, Thomas W, Slavin JL. Effect of fenugreek fiber on satiety, blood glucose and insulin response and energy intake in obese subjects. Phytother Res. 2009; 23:1543–8. [PubMed: 19353539]
44. Chevassus H, Gaillard JB, Farret A, Costa F, Gabillaud I, Mas E, et al. A fenugreek seed extract selectively reduces spontaneous fat intake in overweight subjects. Eur J Clin Pharmacol. 2010; 66:449–55. [PubMed: 20020282]
45. Arthur, D. Dietary supplement for promoting control of blood-sugar levels and associated pathology in type 2 diabetics. CA. 2532332. 2005.
46. Yan, L.; Zhang, T.; Cheng, H. A functional food for diabetic. CN. 101156689. 2008.
47. Lelas, A.; Cepanec, I. Formulation based micronized zeolite, green tea extract, and genistein as a therapeutic agent for reduction of body weight and cellulite. WO. 2010097643. 2010.
48. Roozendaal, A. Kit of parts comprising L-glutamine and EGCG. WO. 2010107307. 2010.
49. Fukino Y, Shimbo M, Aoki N, Okubo T, Iso H. Randomized controlled trial for an effect of green tea consumption on insulin resistance and inflammation markers. J Nutr Sci Vitaminol (Tokyo). 2005; 51:335–42. [PubMed: 16392704]
50. Mackenzie T, Leary L, Brooks WB. The effect of an extract of green and black tea on glucose control in adults with type 2 diabetes mellitus: double-blind randomized study. Metabolism. 2007; 56:1340–4. [PubMed: 17884442]
51. Nagao T, Meguro S, Hase T, Otsuka K, Komikado M, Tokimitsu I, et al. A catechin-rich beverage improves obesity and blood glucose control in patients with type 2 diabetes. Obesity (Silver Spring). 2009; 17:310–7. [PubMed: 19008868]
52. Hsu CH, Liao YL, Lin SC, Tsai TH, Huang CJ, Chou P. Does supplementation with green tea extract improve insulin resistance in obese type 2 diabetics? A randomized, double-blind, and placebo-controlled clinical trial. Altern Med Rev. 2011; 16:157–63. [PubMed: 21649457]
53. Fukino Y, Ikeda A, Maruyama K, Aoki N, Okubo T, Iso H. Randomized controlled trial for an effect of green tea-extract powder supplementation on glucose abnormalities. Eur J Clin Nutr. 2008; 62:953–60. [PubMed: 17554248]

54. Venables MC, Hulston CJ, Cox HR, Jeukendrup AE. Green tea extract ingestion, fat oxidation, and glucose tolerance in healthy humans. Am J Clin Nutr. 2008; 87:778–84. [PubMed: 18326618]
55. Brown AL, Lane J, Coverly J, Stocks J, Jackson S, Stephen A, et al. Effects of dietary supplementation with the green tea polyphenol epigallocatechin-3-gallate on insulin resistance and associated metabolic risk factors: randomized controlled trial. Br J Nutr. 2009; 101:886–94. [PubMed: 18710606]
56. Josic J, Olsson AT, Wickeberg J, Lindstedt S, Hlebowicz J. Does green tea affect postprandial glucose, insulin and satiety in healthy subjects: a randomized controlled trial. Nutr J. 2010; 9:63. [PubMed: 21118565]
57. Ye, Y.; James, DE.; Tan, M.; Cooney, GJ.; Ke, C.; Kraegen, EW.; Chen, T.; Ye, J.; Li, X. Use of compounds extracted from momordica Charantia L. in the manufacture of medicaments for prevention and treatment of diabetes and obesity. US. 20110152208. 2011.
58. Dixit, A.; Vashishta, A.; Sahu, T.; Choudhary, SK.; Murugesan, A. Antidiabetic protein. US. 20110046054. 2011.
59. Ye, Y.; James, DE.; Tan, M.; Cooney, GJ.; Ke, C.; Kraegen, EW.; Chen, T.; Ye, J.; LI, X. Use of compounds extracted from momordica charantia L. in the manufacture of medicamedicaments for prevention and treatment of diabetes and obesity. EP. 2255816. 2010.
60. Lee, SY. Composition comprising an extract of herbal combination thereof for preventing and treating diabetes mellitus. US. 20110027305. 2011.
61. Baldwa VS, Bhandari CM, Pangaria A, Goyal RK. Clinical trials in patients with diabetes mellitus of an insulin-like compound obtained from plant source. Ups J Med Sci. 1977; 82:39–41. [PubMed: 20078273]
62. Leatherdale BA, Panesar RK, Singh G, Atkins TW, Bailey CJ, Bignell AH. Improvement in glucose tolerance due to Momordica charantia (karela). Br Med J (Clin Res Ed). 1981; 282:1823–4.
63. Ahmad N, Hassan MR, Halder H, Bennoor KS. Effect of Momordica charantia (Karolla) extracts on fasting and postprandial serum glucose levels in NIDDM patients. Bangladesh Med Res Counc Bull. 1999; 25:11–3. [PubMed: 10758656]
64. John AJ, Cherian R, Subhash HS, Cherian AM. Evaluation of the efficacy of bitter gourd (momordica charantia) as an oral hypoglycemic agent--a randomized controlled clinical trial. Indian J Physiol Pharmacol. 2003; 47:363–5. [PubMed: 14723327]
65. Dans AM, Villarruz MV, Jimeno CA, Javelosa MA, Chua J, Bautista R, et al. The effect of Momordica charantia capsule preparation on glycemic control in type 2 diabetes mellitus needs further studies. J Clin Epidemiol. 2007; 60:554–9. [PubMed: 17493509]
66. Tongia A, Tongia SK, Dave M. Phytochemical determination and extraction of *Momordica charantia* fruit and its hypoglycemic potentiation of oral hypoglycemic drugs in diabetes mellitus (NIDDM). Indian J Physiol Pharmacol. 2004; 48:241–4. [PubMed: 15521566]
67. Fuangchan A, Sonthisombat P, Seubnukarn T, Chanouan R, Chotchaisuwat P, Sirigulsatien V, et al. Hypoglycemic effect of bitter melon compared with metformin in newly diagnosed type 2 diabetes patients. J Ethnopharmacol. 2011; 134:422–8. [PubMed: 21211558]
68. Hayes, KC.; Greenberg, NA.; Troup, JP.; Falk, AL.; Biolo, G. Method and composition for nutritionally improving glucose control and insulin action. US. 20110305791. 2011.
69. Romero, T.; Miller, P. Methods and materials for reducing or eliminating risk factors associated with syndrome x. US. 20110052736. 2011.
70. Tjandrawinata, RR.; Sinambela, JM.; Mayasari, O.; Deasy Diah Dwi, RW.; Puspasari, M. Herbal extract as sensitivity enhancer toward insulin and antidiabetes. US. 20110177177. 2011.
71. Patell, VM.; Henjarappa, JB.; Siddaiah, CB.; Ullant, R. Synergistic herbal composition and process of preparation thereof. US. 20110064833. 2011.
72. Khan A, Khattak KN, Safdar M, Anderson RA, Ali Khan MM. Cinnamon improves glucose and lipids of people with type 2 diabetes. Diabetes Care. 2003; 26:3215–8. [PubMed: 14633804]
73. Mang B, Wolters M, Schmitt B, Kelb K, Lichtinghagen R, Stichtenoth DO, et al. Effects of a cinnamon extract on plasma glucose, HbA1c, and serum lipids in diabetes mellitus type 2. Eur J Clin Invest. 2006; 36:340–4. [PubMed: 16634838]

74. Crawford P. Effectiveness of cinnamon for lowering hemoglobin A1C in patients with type 2 diabetes: a randomized, controlled trial. J Am Board Fam Med. 2009; 22:507–12. [PubMed: 19734396]

75. Akilen R, Tsiami A, Devendra D, Robinson N. Glycated haemoglobin and blood pressure-lowering effect of cinnamon in multi-ethnic Type 2 diabetic patients in the UK: a randomized, placebo-controlled, double-blind clinical trial. Diabet Med. 2010; 27:1159–67. [PubMed: 20854384]

76. Vanschoonbeek K, Thomassen BL, Senden JM, Wodzig WK, van Loon LJ. Cinnamon supplementation does not improve glycemic control in postmenopausal type 2 diabetes patients. J Nutr. 2006; 136:977–80. [PubMed: 16549460]

77. Altschuler JA, Casella SJ, MacKenzie TA, Curtis KM. The effect of cinnamon on A1C among adolescents with type 1 diabetes. Diabetes Care. 2007; 30:813–6. [PubMed: 17392542]

78. Blevins SM, Leyva MJ, Brown J, Wright J, Scofield RH, Aston CE. Effect of cinnamon on glucose and lipid levels in non insulin-dependent type 2 diabetes. Diabetes Care. 2007; 30:2236–7. [PubMed: 17563345]

79. Mettler S, Schwarz I, Colombani PC. Additive postprandial blood glucose-attenuating and satiety-enhancing effect of cinnamon and acetic acid. Nutr Res. 2009; 29:723–7. [PubMed: 19917452]

80. Solomon TP, Blannin AK. Changes in glucose tolerance and insulin sensitivity following 2 weeks of daily cinnamon ingestion in healthy humans. Eur J Appl Physiol. 2009; 105:969–76. [PubMed: 19159947]

81. Hlebowicz J, Hlebowicz A, Lindstedt S, Björgell O, Höglund P, Holst JJ, et al. Effects of 1 and 3 g cinnamon on gastric emptying, satiety, and postprandial blood glucose, insulin, glucose-dependent insulinotropic polypeptide, glucagon-like peptide 1, and ghrelin concentrations in healthy subjects. Am J Clin Nutr. 2009; 89:815–21. [PubMed: 19158209]

Table 1

The Jadad Scoring System

	Trial Profile	Scoring
1	The trial was a randomized study (this includes words such as randomly, random, and randomization)	+1
2	The method used to generate the sequence of randomization was described and appropriate (table of random numbers, computer-generated, etc)	+1
3	The trial was described as double blind	+1
4	The method of double blinding was described and appropriate (identical placebo, active placebo, dummy, etc)	+1
5	There was a description of withdrawals and dropouts	+1
6	If the method used to generate the sequence of randomization was described and it was inappropriate (patients were allocated alternately, or according to date of birth, hospital number, etc)	−1
7	If the study was described as double blind but the method of blinding was inappropriate (e.g., comparison of tablet vs. injection with no double dummy).	−1

Table 2

Categories of the Quality of Evidence for Health Benefits

Levels	Evidence
A	Very strong scientific evidence from systematic review or meta-analysis
B1	Strong scientific evidence from one or more randomized controlled trials
B2	Good scientific evidence from one or more randomized controlled trials of limited size or methodology
C	Fair scientific evidence from one or more cohort studies or outcome studies or case control studies
D	Weak scientific evidence from case series
E	Indirect evidence from case reports or expert opinion or laboratory studies
F	Historical or traditional evidence

Table 3

Clinical Trials Evaluating the Hypoglycemic Effect of Emblica Officinalis

Clinical Trials	Subjects	Treatments	Size	Hypoglycemic Effect	Jadad Score	Reference
Mitra A	Type 2 diabetic patients	A composite supplement daily for 3 months	120	Yes	4	[26]
Faizal P *et al.*	Type 2 diabetic patients	A composite supplement daily for 3 months	43	Yes	0	[27]
Iyer U *et al.*	Type 2 diabetic patients	35g fresh Alam fruit daily for 2 months	49	No	1	[28]
Chen TS *et al.*	Diabetic-uremic patients	A composite extract daily for 3 months	13	Yes	0	[29]

Table 4

Clinical Trials Evaluating the Hypoglycemic Effect of Fenugreek

Clinical Trials	Subjects	Treatments	Size	Hypoglycemic Effect	Jadad Score	Reference
Madar Z *et al.*	Type 2 diabetic patients	Fenugreek seeds, 15g	21	Yes	0	[34]
Sharma RD *et al.*	Type 2 diabetic patients	Fenugreek seeds, 100g/daily for 10 days	15	Yes	1	[35]
Raghuram TC *et al.*	Type 2 diabetic patients	Fenugreek seeds, 25g daily for 15 days	10	Yes	1	[36]
Bordia A *et al.*	Type 2 diabetic patients	Fenugreek seeds, 5g daily for 3 months	40	Yes/No[a]	0	[37]
Gupta A *et al.*	Type 2 diabetic patients	Fenugreek seed extract, 1g daily for 2 months	25	Yes/No[a]	2	[38]
Kochhar A *et al.*	Type 2 diabetic patients	A composite supplement daily for 3 months	60	Yes	1	[39]
Lu FR *et al.*	Type 2 diabetic patients	Fenugreek extract, 18 pills daily for 12 weeks	69	Yes	3	[40]
Kassaian N *et al.*	Type 2 diabetic patients	Fenugreek seeds, 10g daily in water for 8 weeks	11	Yes	0	[41]
Kassaian N *et al.*	Type 2 diabetic patients	Fenugreek seed, 10g daily in yoghurt for 8 weeks	7	No	0	[41]
Abdel-Barry JA *et al.*	Healthy volunteers	40 mg/kg aqueous extract powder of Fenugreek seeds	20	Yes	1	[42]
Mathern JR *et al.*	Healthy obese volunteers	4 or 8g of isolated fenugreek fiber	18	No	2	[43]
Bordia A *et al.*	Healthy volunteers	Fenugreek seeds, 5g daily for 3 months	30	No	0	[37]
Chevassus H *et al.*	Healthy overweight volunteers	1176mg fenugreek seed extract daily for 6 weeks	38	No	3	[44]

[a]One of the following four measurements was significantly different between the treatment and control group: FBS, HbA1c, postprandial glucose levels and area under curve of blood glucose.

Table 5

Clinical Trials Evaluating the Hypoglycemic Effect of Green Tea

Clinical Trials	Subjects	Treatments	Size	Hypoglycemic effect	Jadad Score	Reference
Fukino Y *et al.*	Type 2 diabetic patients	Green tea extract containing 544mg polyphenols daily for 2 months	66	No	1	[49]
Mackenzie T *et al.*	Type 2 diabetic patients	375 or 750mg green tea daily for 3 months	49	No	2	[50]
Nagao T *et al.*	Type 2 diabetic patients	582.8 or 96.3mg catechin-containing green tea daily for 12 weeks	43	No	0	[51]
Hsu CH *et al.*	Type 2 diabetic patients	a daily dose of 1500 mg of green tea for 16 weeks	80	No	3	[52]
Fukino Y *et al.*	Healthy obese volunteers	A pack of green tea powder and extract containing 545mg catechins daily for 2 months	60	Yes/No[a]	2	[53]
Venables MC *et al.*	Healthy volunteers	Green tea extract containing 890 mg polyphenols with moderate exercise	23	Yes	0	[54]
Brown AL *et al.*	Overweight/obese volunteers	800 mg EGCG daily for 8 weeks	88	No	4	[55]
Josic J *et al.*	Healthy volunteers	300ml of green tea	14	No	1	[56]

[a]One of the following four measurements was significantly different between the treatment and control group: FBS, HbA1c, postprandial glucose levels and area under curve of blood glucose.

Table 6

Clinical Trials Evaluating the Hypoglycemic effect of Momordica Charantia

Clinical Trials	Subjects	Treatments	Size	Hypoglycemic effect	Jadad Score	Reference
Baldwa VS *et al.*	Type 2 diabetic patients	10, 20 or 30 units of v-insulin	14	Yes	0	[61]
Leatherdale BA *et al.*	Type 2 diabetic patients	230g fried omordica charantia fruit for 8 to 11 weeks	9	Yes	0	[62]
Ahmad N *et al.*	Type 2 diabetic patients	Aqueous homogenate of the vegetable pulp	100	Yes	0	[63]
John AJ *et al.*	Type 2 diabetic patients	4g dry bitter gourd daily for 2 and 4 weeks	50	No	1	[64]
Dans AM *et al.*	Type 2 diabetic patients	6 capsules of momordica charantia extract daily for 3 months	40	No	2	[65]
Tongia A *et al.*	Type 2 diabetic patients	400mg momordica charantia extracts daily for 7 days	15	Yes	0	[66]
Fuangchan A *et al.*	Type 2 diabetic patients	2000mg momordica charantia daily for 4 weeks	143	Yes	4	[67]

Table 7

Clinical Trials Evaluating the Hypoglycemic effect of Cinnamon

Clinical Trials	Subject	Treatment	Size	Hypoglycemic effect	Jadad Score	Reference
Khan A *et al.*	Type 2 diabetic patients	1, 3 or 6g cinnamon daily for 40 days	60	Yes	2	[72]
Mang B *et al.*	Type 2 diabetic patients	3g aqueous extract cinnamon powder daily for 4 months	79	Yes	3	[73]
Crawford P *et al.*	Type 2 diabetic patients	1g cinnamon daily for 90 days	109	Yes	2	[74]
Akilen R *et al.*	Type 2 diabetic patients	2g cinnamon daily for 12 weeks	58	Yes	3	[75]
Vanschoonbeek K *et al.*	Postmenopausal type 2 diabetic patients	1.5g cinnamon daily for 6 weeks	25	No	1	[76]
Altschuler JA *et al.*	Type 1 diabetic patients	1g cinnamon daily for 90 days	72	No	2	[77]
Blevins SM *et al.*	Type 2 diabetic patients	500mg cinnamon daily for 3 months	58	No	3	[78]
Mettler S *et al.*	Healthy volunteers	4g cinnamon and 1.68g acetic acids	27	Yes	1	[79]
Solomon TP *et al.*	Healthy volunteers	3g cinnamon daily for 14 days	8	Yes	1	[80]
Hlebowicz J *et al.*	Healthy volunteers	3g cinnamon	15	Yes/No[a]	2	[81]

[a]One of the following four measurements was significantly different between the treatment and control group: FBS, HbA1c, postprandial glucose levels and area under curve of blood glucose.

Recent Pat Food Nutr Agric. Author manuscript; available in PMC 2013 April 15.