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# Systematic Review of Randomized Controlled Trials on Herbs for Glycemic Control in Diabetes Mellitus

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## Introduction

Diabetes Mellitus (DM) is a chronic metabolic disorder indicated by abnormal metabolism of carbohydrate, protein and lipid causing blood glucose increment.[1] According to World Health Organization, 346 million people globally are having diabetes and this number may increase every year.[4] It is reported by International Diabetes Federation (IDF) that currently around 415 million people are living with diabetes, however this number is likely to increase to nearly 642 million people with diabetes in 2040 worldwide. Although, most of the commercially available anti-hyperglycemic medications are efficient in controlling the blood glucose levels among patients who do not meet target glycemic goals; most of these drugs have certain adverse effects. Adverse effects may range from heart failure, edema, weight gain, increased risk of cardiovascular events, abdominal distension, fractures, gastrointestinal disturbance, nausea, and diarrhea.[1,16,17] These adverse effects are commonly associated with non-compliance as well as use of herbal remedies to treat these ADRs. Currently, diabetes mellitus is one of the disease which is most broadly treated with herbal remedies.[12] Herbals are preferable as it is less harmful, assumed to be therapeutically effective, better compatibility with physiological flora, and affordable cost.[14,15] Many herbs possess anti-hyperglcemic properties but not many have been tested in randomized controlled trials. Thus, it could be of value to identify safe herbs with anti-hyperglycemic effects which can be used to compliment conventional treatment. Thus, this study aims to conduct a systematic review of randomized controlled trials on herbs for glycemic control in diabetes mellitus. The richness of knowledge on medicinal herbs will lead to a better opportunity for research and the discovery of new medicines to prevent or treat diseases such as diabetes mellitus.

## Methods

### *Data source and research strategy*

The databases used for this review were Medline, Science Direct and PubMed. The search strategy was developed using combination of the following Medical Subject Headings (MeSH) terms such as diabetes mellitus, diabetes, diabetic, glucose, plants, herbs, herbal, phytomedicine, phytotherapy, medicinal remedies, herbal remedies, herbal medicine, anti-hyperglycemic medication, anti-diabetic, alternative therapies and traditional medicines. Initially the retrieved papers were glanced through by title and abstract to select related journals. Additional relevant studies were manually searched by screening the listing references of identified Randomized controlled trials (RCTs) and review articles.

***Study selection criteria***

This paper restricts the findings focused on herbs for glycemic control; journals that are published in English language and RCTs. We excluded trials of herbal remedies for diabetes mellitus complications for example nephropathy, retinopathy and neuropathy as well as herbs to treat the symptoms of hyperglycemia. Minerals, vitamins and also supplements were also excluded. The journals selected were published from 1996 to 2016.

***Data extraction and quality assessment***

Two researchers performed the search. Additional relevant studies were manually searched by screening the reference lists of the journals. Titles and abstracts were reviewed o to select studies that met the inclusion criteria. Full text articles of relevant abstracts were screened. . PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and JADAD scale were used as tools for quality assessment. Total number of full text articles retrieved were 27.

## Results

**Table 1:** RCT studies of herbs for glycemic control.

| Herbs | Reference | Country | Outcomes | Side Effects |
|---|---|---|---|---|
| *Aloe vera* | Fallah et al 2011 | Iran | Decrease FBG, HbA1c, TC, LDL [5] | No reported ADR |
| *Capparis spinosa L. (Caper)* | Fallah et al 2013 | Iran | Decrease FBG, TG [6] | No ADR |
| *Cinnamon* | Mang et al., 2006 | Germany | Decrease FBG<br>No change HbA1c, lipid profiles [11] | No ADR |
| | Lu et al., 2012 | China | Decrease HbA1c, FBG, TG.<br>No change TC, HDL, LDL [10] | No adverse effect on liver function |
| *Coccinia indica*<br>*(Ivy gourd)* | R.Kuriyan et al., 2008 | India | Decrease FBG, PPG, HbA1c [9] | Abdominal distention, flatulence, constipation & gastritis. |
| *Curcuminoids (Turmeric)* | Na et al., 2012 | China | Decrease FBG, HbA1c, insulin resistance, TG.<br>Increase LPL[13] | Not stated |
| *Momordica charantia*<br>*(Bitter melon)* | Miguel et al., 2007 | Philippines | No change FBG, TC[7] | Diarrhea, epigastric pain |
| | Fuangchan et al., 2011 | Thailand | Decrease fructosamine (bitter melon 2000 mg/day, group)<br>No decrease fructosamine (500 and 1000 mg/day )[3] | Headache<br>& dizziness |
| *Salvia officinalis L. (Sage)* | Kianbakht et al., 2013 | Iran | Decrease FBG, TC ,TG HbA1c, LDL-C<br>Increase HDL-C[8] | No reported ADR |
| *Silybum marianum*<br>*(Silymarin)* | Huseini et al., 2006 | Iran | Decrease Hba1c, FBG, TC, LDL, TG[7] | No ADR |

FBG: Fasting blood glucose; HbA1c: haemoglobin A1c; TC: Total cholesterol; LDL: Low density lipoprotein; TG: Total glycerides; HDL: High density lipoprotein; PPG: Postprandial Glucose; LPL: Lipoprotein lipase;

Herbs that have Jadad score less than 5:

- Allium sativum (Garlic),
- Citrullus colocynthis (Colocynth),
- Ginseng Red ginseng (Panax ginseng),
- Korean Red Ginseng (KRG, Panax ginseng),
- American ginseng (AG, Panax quinquefolius L.),
- Matricaria chamomilla L. (Chamomile),
- Portulaca oleracea (Purslane),
- Trigonella foenum-graecum
- Vaccinium arctostaphylos (Caucasian whortleberry),
- Zingiber officinale (Ginger)

## Discussion

A total of 27 randomized control trials examining 18 herbs for glycemic control were acquired. Most conducted trials tested herbs as an adjunct to conventional treatment with diet and/or medication. The RCTs were conducted specifically in individuals with diabetes mellitus. Most trials examined herbs or herbal preparations as an adjunct to conventional treatment with diet and/or medication. The most common outcome measures encountered in these studies were fasting and postprandial blood glucose and HbA1c. In addition, there were generally few trials per herbs, making it difficult to draw definitive conclusions regarding efficacy. Nevertheless, no major safety concerns were reported in these trials. Few mild adverse effects, mainly gastrointestinal irritation, were reported for garlic, ivy ground, ginseng and bitter melon (Table 1). Less than half of the RCTs (11 of 27, 41%) scored 5 on the Jadad scale. However, certain studies had 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, few herbs have promising antidiabetic effects which warrant larger studies.

## Conclusion

A total of 18 herbs were identified to be effective in reducing hyperglycemia to some extent, thus can be used as a complementary treatment. However, future studies should consider larger trials with clear documentation of intervention and outcomes reporting both safety and effectiveness of the herbs.

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