Systematic review of herbs and dietary supplements for glycemic control in diabetes

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CRD summary
The review assessed the efficacy and safety of herbal therapies and vitamin and mineral supplements for glucose control in patients with diabetes. The authors concluded that there is insufficient evidence to draw definitive conclusions about the efficacy of individual herbs and supplements. The authors’ tentative conclusions are in line with the limitations of the current trials.

Authors’ objectives
To assess the efficacy and safety of herbal therapies and vitamin and mineral supplements for glucose control in patients with diabetes.

Searching
MEDLINE, HealthSTAR and the Cochrane Library were searched from 1960 to March 2002; the search terms were reported. References of key articles were handsearched and experts in the field were contacted for additional studies. Only English language publications were eligible for inclusion.

Study selection
Study designs of evaluations included in the review
The authors did not state any inclusion criteria relating to study design prior to conducting their search for literature. However, their review focused on controlled clinical trials. The other studies identified were not included in the tables of included studies or in the synthesis of studies, therefore, they are not summarised in this abstract. The included studies were randomised controlled trials (RCTs) and non-randomised controlled trials.

Specific interventions included in the review
Studies of herbs and supplements for glycaemic control and symptoms of hyperglycaemia were eligible for inclusion in the review. Studies of supplements made from animal components and soluble fibre supplements were not eligible for inclusion. The interventions were classified as single herbs, combination herbs, and vitamin and mineral supplements.

The single herbs were Allium sativum (garlic), Aloe vera, Artocarpus heterophyllus, Astera canthus longifolia, Bauhinia forficata, Coccinia indica, Ficus carica (fig leaf), ginseng, American ginseng, Gymnema sylvestre, Momordica charantia, Myrcia uniflora, Ocimum sanctum (holy basil), Opuntia streptacantha (nopal), Silymarin (milk thistle) and Trigonella foenum (fenugreek). The combination herbs were three traditional Chinese medicine (TCM) herb combinations (including Xiaoke and SPDPA), a Native American herb combination and a Tibetan medicine herb combination. The vitamin and mineral supplements were alpha-lipoic acid, a branched chain AA, carnitine, chromium, chromium with zinc, magnesium, magnesium with vitamin C, vanadium, and vitamin E. Details of the dosages and duration of treatment were provided. Groups consisted of placebo, distilled water, no treatment, an oral hypoglycaemic agent, a bitter commercial tea blend, fresh spinach leaf powder, broiled zucchini squash, ordinary tea, saline infusion, and Torula yeast capsule.

Participants included in the review
Studies of patients with impaired glucose tolerance, or those at risk for diabetes, were eligible for inclusion. The authors also stated that they examined studies of healthy volunteers, as supporting evidence; however, these studies were not included in the tables of included studies or the synthesis of studies, therefore, they are not summarised in this abstract. The vast majority of studies included patients with type 2 diabetes.

Outcomes assessed in the review
Studies that reported glycaemic control and symptoms of hyperglycaemia were eligible for inclusion. Studies that primarily examined diabetic complications were not eligible for inclusion. The outcomes reported by the included
studies included parameters of glycaemic control: fasting and postprandial plasma glucose; response to glucose tolerance tests; insulin and C-peptide levels; protein glycosylation; and clinical insulin requirements. Other outcomes reported were insulin sensitivity, hepatic glucose production, glucose oxidation and glucose uptake.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors used the validated Jadad scale for assessing the quality of RCTs. This scale assesses the following criteria: appropriateness of randomisation, blinding, and description of study withdrawals or drop-outs. The authors did not state how non-randomised controlled trials were evaluated for quality. Two independent investigators assessed the methodological quality of the RCTs.

Data extraction
The authors stated that the data were extracted in a standardised manner, but did not state how many reviewers performed the data extraction. Data were extracted on the study design, Jadad score, number and type of participants, supplement name and regimen, control, outcomes, direction of evidence and reported adverse events.

Methods of synthesis
How were the studies combined?
A narrative synthesis of the studies was undertaken.

How were differences between studies investigated?
The studies were grouped by the type of intervention: single herbs, combination herbs, and vitamin and mineral supplements, and the results presented separately for each group.

Results of the review
From a total of 108 clinical studies identified by the search strategy, 58 were included in the review: 42 RCTs (1,846 participants) and 16 non-randomised controlled trials (593 participants).

Many trials were of a poor quality: 24 of the 42 RCTs scored 2 or less on the quality scale, out of a maximum possible 5 points. There were few trials per supplement.

Statistically significant positive effects were reported in 23 of the 26 studies examining single herbs, 3 of the 5 studies examining combination herbs, and 18 of the 27 studies examining vitamin and mineral supplements. No major safety concerns were reported.

Single herbs or plant derivatives for glycaemic control.

The following herbs were found to significantly positively change at least one outcome measure: Aloe vera, Artocarpus heterophyllus, Asteracanthus longifolia, Ficus carica (fig leaf), ginseng (unspecified), ginseng (American), Momordica charantia and Trigonella foenum (fenugreek). The following herbs were found to significantly positively change more than 50% of the outcomes measured: Coccinia indica, ginseng (American), Gymnema sylvestre, Ocimum sanctum (holy basil), Opuntia streptacantha (nopal), Silymarin (milk thistle) and Trigonella foenum (fenugreek).

Adverse effects with Aloe vera (1 patient had ketosis) and ginseng (1 patient had mild insomnia) were reported.

Combination herbs for glycaemic control.

The TCM herb combination and SPDPA (TCM) formula were found to significantly positively change at least one outcome measure. The Tibetan medicine herb combination was found to significantly positively change more than 50% of the outcomes measured.
Adverse effects with a TCM herb combination (1 patient had diarrhoea, 1 patient had dry mouth) and a Native American herb combination (1 patient had minor gastrointestinal discomfort) were reported.

Vitamin and mineral supplements for glycaemic control.

Alpha-lipoic acid, chromium, magnesium and vitamin E supplements were found to significantly positively change at least one outcome measure. Carnitine, chromium, magnesium, vanadium and vitamin E supplements were found to significantly positively change more than 50% of the outcomes measured.

Adverse effects with magnesium supplements (1 patient had exanthema and 1 patient had gastrointestinal pain) and vanadium supplements (5 of 6 patients had transient gastrointestinal discomfort in one study; all 7 patients in another study had transient gastrointestinal discomfort) were reported.

**Authors' conclusions**

There is insufficient evidence to draw definitive conclusions about the efficacy of individual herbs and supplements for diabetes. However, most of the herbs and supplements reviewed appeared to be generally safe. The best evidence for efficacy from adequately designed RCTs is available for Coccinia indica and American ginseng. Other supplements with positive preliminary results include Gymnema sylvestre, Aloe vera, vanadium, Momordica charantia and Opuntia streptacantha (nopal). Further evaluation of several herbs, vitamins and mineral supplements for glucose control in diabetes is warranted.

**CRD commentary**

The review question was clear in terms of the participants, interventions and outcomes of interest. However, the authors did not state which study designs were eligible for inclusion prior to conducting their search for literature. Their review focused on the controlled clinical trials that their search identified. Three relevant electronic databases were searched and the search terms and dates were reported. This search was supplemented by handsearching references and contacting experts in the field in an attempt to identify additional studies. However, no additional searches for unpublished literature were undertaken and only English language publications were eligible for inclusion. The possibility of publication bias and language bias cannot, therefore, be excluded. Two reviewers applied a validated scale for assessing the quality of RCTs; the authors did not state how non-randomised controlled trials were evaluated for quality. The methods used to select the studies for the review and to extract the data from the primary studies were not described; hence, the possibility of reviewer bias and error cannot be assessed.

Adequate details of the individual studies were tabulated and discussed further in the text. The narrative synthesis was appropriate given the heterogeneity between the trials and the small number of studies evaluating each supplement. The authors' tentative conclusions are supported by the results of their review.

**Implications of the review for practice and research**

Practice: The authors stated that there is insufficient evidence to actively recommend or discourage the use of any particular supplement for glucose control in diabetes, although most of the supplements reviewed appeared to be generally safe. Clinicians should keep an open mind when advising patients on the use of these supplements; they should be guided by the patients' preferences, needs and values, in addition to their own clinical judgement.

Research: The authors stated that further evaluation of herbs, vitamins and mineral supplements for glucose control in diabetes is required. Future research should benefit from defining populations more precisely with regard to disease classification and severity, optimal adjunctive interventions and nutrient deficiencies. Mechanisms of action need elucidation so that the applicability to type 1 or type 2 diabetes can be clarified.

**Bibliographic details**

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.