Ginseng for cognitive function in Alzheimer's disease: a systematic review

Lee MS, Yang EJ, Kim JI, Ernst E

CRD summary
The authors concluded that there was insufficient evidence that ginseng (*Panax ginseng* herb) was an effective treatment for Alzheimer's disease, and that further research is needed. Given the small number and low quality of available trials, the authors' cautious conclusions appear to be reliable.

Authors' objectives
To assess the effectiveness of ginseng (*Panax ginseng* herb) on the cognitive function of patients with Alzheimer's disease.

Searching
The following databases were searched, up to January 2009, for articles in any language: MEDLINE, EMBASE, AMED, CINAHL, PsycINFO, the Cochrane Library, six Korean Medical databases, four Chinese Medical databases, and Japan Science and Technology Information Aggregator. Search terms were reported. Two relevant journals and department files were also searched. Bibliographies of retrieved articles were handsearched. Dissertations and abstracts were included in the search.

Study selection
Randomised controlled trials (RCTs) of *Panax ginseng* as sole or adjunct treatment in patients with Alzheimer's disease were eligible for inclusion. Trials of Siberian ginseng, or those comparing different types of ginseng, were excluded. Trials were excluded if there were insufficient clinical data for comparison.

Included trials were of red ginseng (4.5g daily or 9.0g daily) or white ginseng (4.5g daily) administered for 12 weeks as an adjunct to conventional drug therapy compared with conventional drug therapy alone. Where reported, conventional therapy was donepezil (5 to 10mg daily), galantamine (16 to 24mg daily), memantine (20mg daily) or rivastigmine (6 to 12mg daily). Patients included in the trials were diagnosed with Alzheimer's disease using National Institute for Neurological and Communicative Disorders and Stroke-Alzheimer's disease and Related disorder Association criteria. Outcome measures were Mini-Mental State Examination (MMSE), the Alzheimer's Disease Assessment Scale (ADAS), and the Clinical Dementia Rating (CDR).

Two reviewers independently selected the studies for review. Discrepancies were resolved by discussion and in consultation with a third reviewer if necessary.

Assessment of study quality
The methodological quality of the included trials was assessed using Jadad scoring (a three-item checklist) assessing randomisation, blinding, and withdrawals/drop-outs; the maximum score was 5 points. Allocation concealment was also assessed using the Cochrane classification.

Two reviewers independently assessed the methodological quality of the included studies. Discrepancies were resolved by discussion and in consultation with a third reviewer if necessary.

Data extraction
The mean change in cognitive function (using MMSE and ADAS measures) was extracted for intervention and control groups. This was used to calculate the mean difference between groups.

Two reviewers independently extracted the data for review. Discrepancies were resolved by discussion and in consultation with a third reviewer if necessary.
**Methods of synthesis**

The studies were combined in meta-analyses using a random-effects model. Weighted mean differences (WMD) with 95% confidence intervals (CIs) were calculated. Statistical heterogeneity was assessed using the $\chi^2$, $I^2$ and $T^2$ tests. Subgroup analyses were carried out to investigate the effectiveness of ginseng at doses of 4.5g daily.

**Results of the review**

Two RCTs were included for review (n=158 patients). Both trials scored 1 point on the Jadad scale; neither reported sufficient detail on randomisation, blinding, allocation concealment or withdrawals.

Ginseng combined with conventional therapy significantly improved cognitive function compared to conventional therapy alone, as assessed using the Mini-Mental State Examination (MMSE, WMD 1.85, 95% CI 0.88 to 2.82; n=158 patients) and the Alzheimer's Disease Assessment Scale (ADAS) cognitive subscale (WMD 3.09, 95% CI 1.08 to 5.09; n=158 patients). Addition of ginseng to conventional therapy did not significantly improve non-cognitive function as assessed using the ADAS. There was no evidence of statistical heterogeneity for any of these outcomes ($I^2 = 0\%$).

Subgroup analyses revealed that ginseng continued to significantly improve cognitive function at doses of 4.5g daily as measured using the MMSE (WMD 1.80, 95% CI 0.71 to 2.90; n=128 patients) and the ADAS (WMD 3.03, 95% CI 0.93 to 5.14; n=128 patients).

Adverse events reported in the included studies were fever, nausea, diarrhoea, headache, dizziness, sensitivity to heat and anorexia.

**Authors’ conclusions**

There was insufficient evidence that ginseng was an effective treatment for Alzheimer's disease. Further research is needed.

**CRD commentary**

The review addressed a clear question with well-defined inclusion criteria for intervention, study design and participants. Inclusion criteria for outcomes were implicit in the review question. Several relevant databases were searched for articles in any language, minimising the risk of language bias. Unpublished data were eligible for inclusion, but an extensive search was not carried out for unpublished data, so there was a possibility of publication bias. Appropriate steps were taken in the review process to minimise the risk of reviewer error and bias.

The methodological quality of the included trials was assessed using an appropriate scale. The quality of the included trials was low. Suitable methods were used to combine the trials. Statistical heterogeneity was assessed and ruled out.

Given the small number and low quality of available trials, the authors' cautious conclusions appear to be reliable.

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

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further research is needed comparing ginseng to an indistinguishable placebo and investigating the optimal dose. Long-term studies should be carried out to investigate the incidence of adverse events of ginseng compared to conventional drug therapy.

**Funding**

Korea Institute of Oriental Medicine

**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.