

# THE TABLET: PALLIATIVE CARE PHARMACY TIPS



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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

## TODAY'S TOPIC: Ginseng for Cancer-Related Fatigue

**Background:**

Ginseng is thought to have unique medicinal properties. Saponin glycosides (ie. ginsenosides or panaxosides) are thought to be responsible for potential biological effects as they are thought to have both stimulatory and inhibitory CNS effects, alter cardiovascular tone, enhance humoral and cellular-dependent immunity, and exert anticancer effects. American Ginseng (AG) is gaining traction for its use in cancer-related fatigue (CRF).

**Importance:**

Fatigue is a common symptom that burdens patients with cancer and adversely affects a person's quality of life. We often utilize medications off-label to help improve fatigue symptoms when other modalities have failed. Palliative care clinicians should be aware of the literature for herbal supplements, like ginseng, that could be used for CRF.

**The Literature:**

[Cancer Nurs. 2022 Feb 21. doi: 10.1097/NCC.000000000001068. Epub ahead of print. PMID: 35184068.](#)

**Effects of Ginseng on Cancer-Related Fatigue: A Systemic Review and Meta-analysis of Randomized Controlled Trials**

**Objective:** Systematically appraise evidence whether ginseng could alleviate CRF and improve QOL

**Methods:**

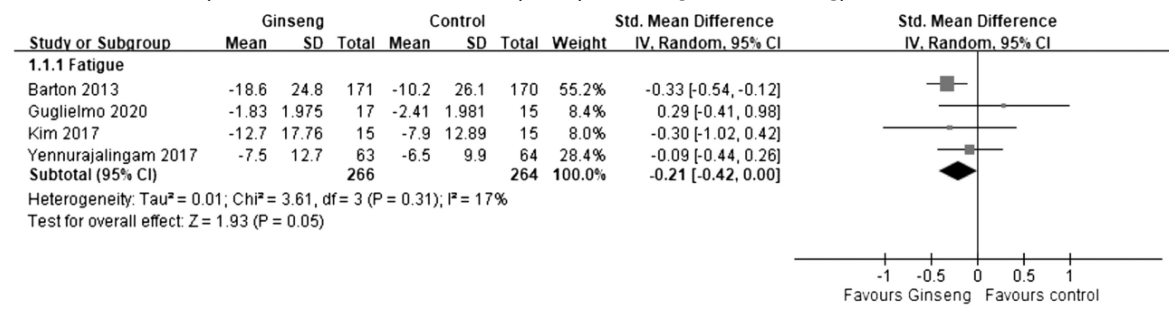
- Literature review through June 2021 based on PRISMA guidelines
- Studies included: RCT design, specific investigation of efficacy of ginseng in CRF, and clear definitions on source and dosage of ginseng and outcomes
- CRF parameters, cancer type and ginseng dose varied across trials
  - o Doses varied between 750-2000mg/day for AG

**Outcomes:**

- Primary: fatigue (variety of outcome measures used between studies)
- Secondary: QOL, anxiety, adverse effects, depression and lab markers

**Results:** N = 7 studies included (all RCTs)

- American ginseng (n = 3), Korean red ginseng (n=2), Chinese ginseng (n=2), four of which had low overall risk of bias
- CRF (n=4 studies)
  - o Reduction in fatigue was greater in the ginseng groups compared to placebo groups (Standard mean difference (SMD) = -0.21 [-0.42 to 0.00])



**Figure 2** ■ Forest plot comparing the effects of ginseng and placebo on cancer-related fatigue.

- Quality of life (n=4 studies)
  - o Ginseng groups exhibited significant improvement in physical well-being (SMD 0.25, [0.09 to 0.41]) and emotional well-being (SMD 0.20, [0.01 to 0.40])
  - o Trends toward significant improvements in vigor (SMD 0.18, [-0.02 to 0.38]) and mitigation of nausea (SMD 0.38, [-0.09 to 0.85]) and dyspnea (SMD 0.27, [-0.04 to 0.59])
  - o No difference in mental well-being, social activity, sleep, or drowsiness
- Anxiety (n=2 studies) and Depression (n=2 studies): no statistical difference
- Adverse effects (n= 5 studies)
  - o N=4 no significant differences in adverse events
  - o N = 1 reported neutropenia more frequently in ginseng group
- Lab values (n=2)
  - o Increases in AST and ALT, lower levels of interleukin 1B in ginseng group
  - o No difference in binucleated cell index and median value of micronuclei yield was lower in ginseng group
- **Of note, 4 studies had multi-time study design**
  - o Effects on fatigue and physical well-being were more significant at week 8 versus week 4
  - o Greater enjoyment of life at week 16 versus week 8
  - o Functional well-being better at week 4 than week 2

**Conclusion:** Weak evidence exists to support efficacy of ginseng in improving CRF and QOL in cancer patients

[Am J Hosp Palliat Care. 2018 Jan;35\(1\):144-150.](#)

**Single institute experience with methylphenidate and American Ginseng in cancer-related fatigue**

**Objective:** Assess clinical safety, feasibility, and potential efficacy of treating CRF with methylphenidate and AG combination therapy

**Methods:** Retrospective chart review between Feb 1, 2015 and Dec 31, 2015

- Adult patients who received a combination of methylphenidate (10-40mg/day) and AG (2000mg/day) undergoing active anti-cancer treatment who scored 4 or higher on NRS for fatigue on ESAS
- NRS prescore from visit date when combination was prescribed and postscore from visit following combination therapy (date interval mean = 30.5 days, SD 7.78)

**Outcomes:**

- Primary: change in numerical rating scale (NRS) score on Edmonton Symptom Assessment Scale (ESAS)

**Results:** n = 15; 53.3% female, average age 52.4 years

- Significant reduction in fatigue score: -2.8, SD 1.61; p <0.0002
- 60% of patients reported subjective reductions in fatigue
- Most commonly prescribed methylphenidate dose was 10mg PO BID (n=12)

**Conclusion:**

- Combination of methylphenidate and AG had not discernible associated toxicities and showed potential clinical benefit in CRF

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## Safety Concerns:

- It is important to note that American ginseng may stimulate the growth of breast cancer cells and should be **utilized with caution in patients with breast cancer**<sup>1</sup>
- **Interaction with warfarin**<sup>2</sup> and may reduce warfarin's efficacy and decrease INR values
- **May induce CYP3A4**, clinical relevance of this interaction has not been established<sup>3,4</sup>

## Bottom Line:

- Given heterogeneity in trials including lack of standardization of quantity, quality, production process, and formulations of ginseng is a limitation, this impacts our ability to compare the findings among RCTs
- Doses of ginseng varied between trials, although might be worth considering doses between 1000mg-2000mg/day
- Given multi-time study design(s), it is worthwhile to consider prognosis and time to benefit of ginseng. It is possible that it may take several weeks to take effect and benefit becomes more significant over time
- American Ginseng may be worth trialing for patients who are struggling with CRF, given lack of adverse effects in the trials
- Keep in mind potential safety concerns listed above, although trials did not support this data
- American Ginseng is available over the counter and should be available at pharmacies (& Amazon!). It comes in many different strengths produced by different manufacturers with unique quantities which impacts cost.
- Cost ranges from ~\$8 per bottle to ~\$30 per bottle depending on strength, manufacturer, and quantity. Generally, would say 30-day supply would be *around* \$20 if recommending doses of 1000mg-2000mg/day

## References:

1. Amato P, Christophe S, Mellon PL. Estrogenic activity of herbs commonly used as remedies for menopausal symptoms. *Menopause* 2002;9:145-150.
2. Yuan CS, et al. Brief Communication: American Ginseng reduces warfarin's effect in healthy patients. *Ann Intern Med* 2004;141:23-27.
3. Hao M, Ba Q, Yin J, et al. Deglycosylated ginsenosides are more potent inducers of CYP1A1, CYP1A2, and CYP3A4 expression in HepG2 cells than glycosylated ginsenosides. *Drug Metab Pharmacokinet.* 2011;26(2)201-205.
4. Hao M, Zhao Y, Chen P, et al. Structure-activity relationship and substrate-dependent phenomena in effects of ginsenosides on activities of drug metabolizing P450 enzymes. *PLoS One.* 2008 Jul 16;3(7):e2697.