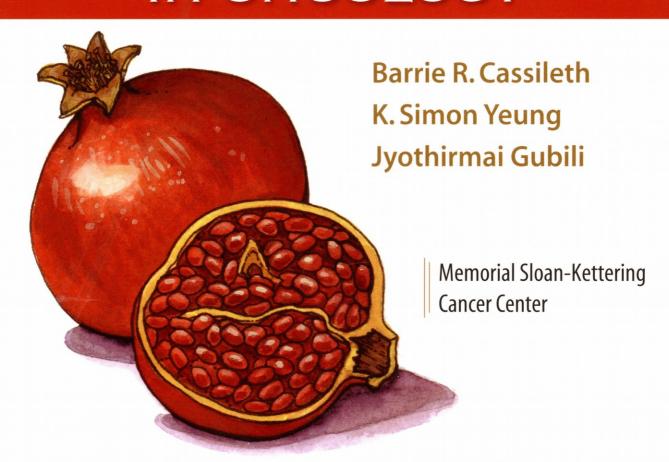
Second Edition



HERB-DRUG INTERACTIONS IN ONCOLOGY



Herb-Drug Interactions in Oncology

Second Edition

Barrie R. Cassileth, PhD

Chief, Integrative Medicine Service Memorial Sloan-Kettering Cancer Center New York, New York

K. Simon Yeung, MBA, PharmD, LAc

Clinical Coordinator and Research Pharmacist Memorial Sloan-Kettering Cancer Center New York, New York

Jyothirmai Gubili, MS

Assistant Editor Memorial Sloan-Kettering Cancer Center New York, New York

Wheat germ extract



Common Names

Fermented wheat germ extract, MSC

Brand Name

Avemar

CLINICAL SUMMARY

Fermented wheat germ extract (WGE) was developed by Mate Hidvegi, a Hungarian chemist, in the 1990s. It should not be confused with wheat germ oil. WGE is used as a dietary supplement by cancer patients in Hungary to improve quality of life. Results from in vitro studies show that WGE has anticancer, antimetastatic, and immunomodulatory effects. It was also shown to increase estrogen receptor (ER) activity in vitro. However, when used along with tamoxifen, an ER antagonist, it enhanced efficacy of tamoxifen in ER positive breast cancer cells. The antitumor effect of WGE is comparable to other endocrine treatments in animal model.² WGE also increased production of tumor necrosis factor and cytokines that are responsible for tumor cell death. Data from pilot studies implicates a beneficial role for WGE in patients with colorectal cancer and in reducing treatment-associated febrile neutropenia in pediatric cancer patients. Another pilot study showed that WGE can prolong survival of patients with melanoma when used with chemotherapy.3 However, these effects must be confirmed by large-scale, well-designed clinical trials. Because it potentiates estrogen receptor activity, patients with hormonesensitive cancers should use WGE with caution. Reported mild side effects include diarrhea, nausea, flatulence, soft stool, constipation, and dizziness. Long-term use of WGE may result in increased body weight.4

PURPORTED USES

Autoimmune diseases Cancer treatment Immunomodulation

CONSTITUENTS

Wheat germ

MECHANISM OF ACTION

Although the exact mechanism of action is not clear, WGE was shown to increase TNF and cytokine production in vitro by activating certain metabolic pathways involved in tumor cell death. WGE also regulates tumor cell proliferation by inhibiting glycolysis and pentose cycle enzymes and induces apoptosis through caspase-3-mediated poly (ADP ribose) polymerase cleavage.

WARNINGS

WGE should be taken under medical supervision only. Diabetics should use this product with caution because of the high carbohydrate content.⁴

CONTRAINDICATIONS

Pregnant and nursing women

Patients with organ or tissue transplants

Patients with bleeding gastric or duodenal ulcers, enteritis/colitis, malabsorption syndrome.

Patients with sensitivity to gluten and those with fructose intolerance.4

ADVERSE REACTIONS

Mild and infrequent side effects may include diarrhea, nausea, flatulence, soft stool, constipation, dizziness. Long term use of WGE may result in increased body weight.³⁻⁴

WGE may have estrogen receptor activity. Patients with hormone-sensitive cancers should consult with a physician before using WGE.

W HERB-DRUG INTERACTIONS

WGE should be taken at least two hours before or after consuming vitamin C.⁴

LITERATURE SUMMARY AND CRITIQUE

Jakab F, et al. A medical nutriment has supportive value in the treatment of colorectal cancer. *Br J Cancer*. 2003;89:465-469.

This study was done to determine if WGE supplementation was beneficial for patients with colorectal cancer. Sixty-six patients were given WGE (9 g once daily) in addition to anticancer treatments, and 104 patients received only anticancer treatments. Data analysis revealed that patients who took WGE had fewer disease progression-related events than the control group. There was also an improvement in overall survival of patients on WGE. More trials are needed with an equal number of patients in the experimental and control groups.

Garami M, et al. Fermented wheat germ extract reduces chemotherapy-induced febrile neutropenia in pediatric cancer patients. *J Pediatr Hematol Oncol.* 2004;26(10): 631-635.

Twenty-two pediatric patients with different malignant tumors participated in this study. Eleven patients were given $12g/m^2/day$ of WGE during cancer treatments, and eleven patients received only cancer treatments. Researchers found that there was no recognizable progression of disease during the follow-up period. But there was a significant difference in the frequency of febrile neutropenic events between the two groups. The overall white blood cell and lymphocyte counts during such events were close to normal values in the WGE group compared to those in the control group. Since this is a pilot study, randomized, controlled trials are warranted with larger sample size to verify these effects.

REFERENCES

- 1. Saiko P, Ozsvar-Kozma M, Madlener S, et al. Avemar, a nontoxic fermented wheat germ extract, induces apoptosis and inhibits ribonucleotide reductase in human HL-60 promyelocytic leukemia cells. *Cancer Lett.* 2007 Jun 8;250(2):323-328.
- Tejeda M, D. Gaál, I. Szûcs, et al. Avemar inhibits the growth of mouse and human xenograft mammary carcinomas comparable to endocrine treatments. ASCO Annual Meeting. 2007. Abstract No: 21132.
- 3. Demidov LV, Manziuk LV, Kharkevitch GY, et al. Adjuvant fermented wheat germ extract (Avemar) nutraceutical improves survival of high-risk skin melanoma patients: a randomized, pilot, phase II clinical study with a 7-year follow-up. *Cancer Biother Radiopharm.* 2008 Aug;23(4): 477-482.
- 4. http://www.avemar.com (Accessed November 26, 2008).