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**FILE: ■ Fermented Wheat Germ Extract
■ Cancer
■ Autoimmune Diseases**

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RE: Treatment of Cancer and Autoimmune Diseases with Wheat Germ Extract

Boros LG, Nichelatti M, Shoenfeld Y. Fermented wheat germ extract (Avemar) in the treatment of cancer and autoimmune diseases. *Ann N Y Acad Sci.* 2005;1051:529–542.

Wheat germ is considered a healthy food; however, it is extracted from flour because it has adverse effects on the functional properties of dough and, thus, on the quality of bread. Wheat germ extracts are often added to "healthy foods" and to vitamin E extracts. A new fermented wheat germ extract for human consumption was invented in Hungary in the 1990s by Professor Máté Hidvégi. This extract, known as Avemar®, is currently manufactured by Biomedicina (Budapest, Hungary) and was approved as a medicinal food by the National Institute of Food Safety and Nutrition of Hungary. Avemar has been shown to inhibit metastatic tumor dissemination and proliferation during and after radiation, surgery, and chemotherapy. The beneficial effects of this extract have been shown in many human cancers, in cultures of cancer cells, in the prevention of chemical carcinogenesis, and in some autoimmune disorders. These benefits as well as the mechanisms of action of Avemar are summarized in this review.

The safety and efficacy of Avemar have been studied in both animal and human studies, none of which have indicated any adverse effects. The long-term administration of Avemar to human cancer patients showed no significant changes in hematologic status after 1, 3, and 5 years of treatment. The no-observable adverse effect level of Avemar was determined to be 3000 mg/kg/day in a subchronic study in mice and rats. In tests of possible drug interactions, it was determined that Avemar can safely be taken concomitantly with cytostatic drugs used for cancer treatment (e.g., cyclophosphamide, doxorubicin, and vinorelbine) and with cytokine preparations. It is recommended that Avemar be taken at least 2 hours before or after the ingestion of vitamin C-containing preparations. In a study in mice, the immunomodulatory effects of mice were demonstrated by a significantly increased degree of blastic transformation of peripheral blood T lymphocytes stimulated by concanavalin A.

Although the specific molecule, or molecules, of Avemar responsible for its beneficial health effects has not been identified, the molecular targets of this medicinal food are known. In human leukemia cells, Avemar has been shown to induce apoptosis (programmed cell death) by activating the capsase-3-catalyzed cleavage of the poly (ADP-ribose) polymerase enzyme and to decrease cell motility, which mitigates metastasis. Avemar has also been shown to decrease the MHC-1 level in human tumor cells, which makes them more susceptible to natural killer cell activity. A common characteristic of metastatic tumor cells is to avoid detection by natural killer cells; therefore, an increase in natural killer cell activity reduces the metastatic potential of tumor cells. Avemar also increases the expression of intercellular adhesion molecule-1 and tumor necrosis factor- α , which have anticancer activities. Cyclooxygenases and ribonucleotide reductase, enzymes that are upregulated in tumor cells, were both shown to be inhibited after treatment with Avemar. The oral intake of Avemar was shown to ameliorate the clinical manifestation of experimental systemic lupus erythematosus in mice, which was the catalyst for a recently initiated study of the efficacy of Avemar in lupus patients.

In clinical cancer trials, Avemar was shown to reduce the progression of disease in patients with head and neck cancers, colorectal cancer, and malignant melanoma of the skin. The quality of life of patients with breast cancer or lung cancer improved significantly ($P < 0.05$) after supportive treatment with Avemar: improvements in the global state of health and fatigue were observed in lung cancer patients, and improvements in physical and emotional function, the global state of health, fatigue, nausea, vomiting, insomnia, and constipation were observed in breast cancer patients. Clinical studies of the efficacy of Avemar in the treatment of other cancers are ongoing. However, observational data indicate that this wheat germ extract has favorable effects on ovarian cancer, gastric cancer, thyroid cancer, non-Hodgkin's lymphoma, and multiple myeloma. "The therapeutic spectrum of Avemar is much wider than it had been thought some years ago."

—*Brenda Milot, ELS*

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