DNC News

Graham Crackers, Avemar, and Cancer Treatment

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Subject: A product made of fermented wheat germ shows promise in treating cancer

Sylvester Graham (1794-1851)

A forgotten Fanatic:
Sylvester Graham is long forgotten. He was born in 1794 and, as an ordained Presbyterian minister, preached throughout his life on the benefits of vegetarianism, abstinence from alcohol and the value of whole wheat flour. If remembered for anything, he is famous for inventing Graham flour in 1829. He preached that the white bread of the time was unwholesome. Graham made his bread from pure unsifted and unbolted flour. He insisted that bread was dangerous to eat while still fresh. For reasons unclear to me, he argued that dry hard crusty loaves were preferable. He was also down on sex. He made and shipped his hard dry loaves to followers all over the country. Graham crackers are a leftover from his one time fame. His fanatical belief in the danger of white flour also remains in the public domain, even if we are not quite as fanatical as Graham was.

What is Germ?
Everyone knows that whole wheat bread is better for you than white bread. That's a given. Wheat grains are made of three components, the endosperm, the bran and the germ. The endosperm makes up the majority of the grain by weight, about 83%, and contains primarily starch and a little protein. This is the stuff that white flour is made from. It contains calories from the starch and protein but is relatively deficient in vitamins, minerals and other nutrients. The bran comes from the outer protective shell of the wheat kernel and makes up about 14% of the grain by weight. Bran is mostly indigestible fiber, though it does contain more nutrients than the white endosperm. The germ is the most nutritious part of the grain although it makes up only 2-3% of the grains weight. The germ is the actual plant embryo. It is rich in vitamins, minerals and other nutrients. Both bran and germ are removed from wheat during the milling process to make 'white flour.' It is worth remembering these nutrition basics when talking about one of the new entries into the field of nutritional oncology. It is called Avemar

Avemar:
A product called Avemar made from fermented wheat germ extract was invented in the 1990s by a Hungarian scientist named Máté Hidvégi. To make Avemar, wheat germ is fermented with the yeast *Saccharomyces cerevisiae* for about 18 hours and the resultant product dried to a powder. This endproduct is standardized to contain 0.04% of methoxysubstituted benzoquinones which may be one of several active ingredients in Avemar.

Hidvégi isn't the first Hungarian to show interest in these benzoquinones for treating cancer. Albert Szent-Gyorgyi, who received a Nobel Prize for discovering ascorbic acid, was the first to propose their use as anticancer agents.

Safety:
It should come as no surprise to find that this product is safe. After all it's just fermented wheat germ. In animal studies, no adverse effect was seen when giving animal 2 grams per kilogram body weight per day. An equivalent dose for a 150 pound person would be 150 grams or about 5 ounces per day of the powder. Typical doses used in studies have been 9 to 18 grams a day. At these lower doses, human test subjects have reported only mild transient nausea, dizziness, constipation when using Avemar.

Mechanisms:
Quite a bit of work has been published which attempts to explain the mechanisms of action of Avemar. This is a complex substance and probably contains a number of active chemicals. It is assumed that the methoxy-substituted benzoquinones are at least part of the active principles. A number of different mechanisms have been identified by which Avemar acts against cancer. They include apoptosis induction via poly (ADP-ribose) polymerase, the immune system, major histocompatability comples (MHC) class 1, ribonucleotide reductase (RNR), cyclo-oxygenase (cox1 and cox-2) enzyme activity, intracellular adhesion molecule (ICAM) 1, tumor necrosis factor alpha (TNF-a) production, and transketolase (TK). If I write anymore about this, I'm sure to lose readers. [i]

Animal Research:
Numerous animal studies have demonstrated Avemar's benefit in cancer treatment. Scientists measure immune function by timing how long it takes an experimental animal to reject a skin graft from another animal. The faster the rejection, the better the immune system is working. Avemar increases immune function as measured by this skin graft test. [ii] Giving Avemar to test rats prevented them from developing colon cancer when given a cancer causing chemical. In the rats in the control group, 83% developed tumors while only 45% of the rats given Avemar did so. [iii] In a number of animal experiments giving vitamin C at the same time as the Avemar increased the effect at inhibiting metastasis. [iv]

Human Research:
At this point, we are still awaiting a definitive double blinded placebo controlled human trial. There are a number of open human trials and animal trials suggesting benefit.

In an article published in August 2003 in the British Journal of Cancer, Jakab Shoenfeld and his colleagues reported on an open trial of 66 patients with colorectal cancer. They received standard therapy plus 9 grams of Avemar a day. These patients were compared to 104 patients who received only standard treatment but no Avemar. The primary endpoint of the study was progression-free survival. Tumor progression was defined as an increase in size of tumor of at least 25% or the appearance of new lesions. Progression related events, including recurrent disease, metastasis, or death were more common in the control group than in those taking Avemar. In all, 42.3% of the control group had progression events while only 16.7% of the Avemar group did. This was an open trial, patients decided if they wanted to take this 'experimental product.' They were not randomized. It seems that the sicker someone was at the start of the experiment, the more inspired they were to try something unusual. At the start of the trial 27% of the Avemar patients had stage IV disease while the control group only 4% were this advanced. [v]

Event	Control	Avemar	p value
New Reccurences	17.3%	3.0%	<0.01
New Metastases	23.1%	7.6%	<0.01
Deaths	31.7%	12.1%	<0.01
Progression related events	42.3%	16.7%	<0.001

[vi]

Another study from 2004, this one published in the Journal of Pediatric Hematological Oncology looking at the incidence of febrile neutropenia in children undergoing immunosuppressive chemotherapy. [vii] Avemar was given at the same time as chemotherapy in an open label matched-pair pilot trial. Control patients did not receive Avemar. Tumor staging was the same at the start of the study. The number and frequency of febrile illnesses was monitored and differed significantly between the two groups of patients. The Avemar patients had 30 febrile episodes in total in contrast to the control patients who had 46 episodes.

In another open-label, pilot trial but this one randomized clinical trial, Avemar was given along with chemotherapy to patients with stage III melanoma. Twenty-two patients were given Avemar in addition to the chemotherapy drugs DTIC. They were compared against twenty-four patients who only received the drugs. Again there was a significant difference in favor of the patients consuming Avemar in terms of progression-free survival. [viii]
Dosing: Avemar comes as powder in single serving packages that are stirred into water. The powder is flavored and sweetened. Human trials have used 9 grams of powder once or twice a day.

The question: Before any of you write to ask, I will confess that I do not know if you can make this at home. Since Avemar is made by fermenting wheat germ with yeast, someone is bound to write me and ask, "Could I bake bread at home using loads of wheat germ and produce the same chemicals as in Avemar?" I don't know but it is an intriguing thought.

Further Information:

A nice review article on Avemar from the Annals of the New York Academy of Science is posted at:

http://www.avemar.hu/docs/43_Boros_et_al-NY.pdf

Links to full text of the human clinical trials can be found at:

http://www.avemarresearch.com/TOC.html

Research summary on Sloan-Kettering's website:

http://www.mskcc.org/mskcc/html/69418.cfm

References:

[i] Integrative Medicine vol 6 no 2 April/May 2007

[ii] Immunopharmacology 1999 Apr;41(3):183-186
Hidvegi M, Raso E, Tomoskozi Farkas R, Lapis K, Szende B.
Birochem, Budapest , Hungary .
Effect of MSC on the immune response of mice
The supposed immunostimulatory actions of MSC, a new fermented wheat germ extract standardized to its benzoquinone composition (trade name: AVEMAR) were studied examining blastic transformation of peripheral blood lymphocytes of mice treated with MSC. It was found that MSC significantly increased the degree of blastic transformation caused by Concanavalin A. Using the B10LP to C57Bl skin graft system, MSC (0.03 and 3.0 g kg(-1) applied orally) acted in favour of restoring the immune function. On the other hand, 2,6-dimethoxy-p-benzoquinone (DMBQ), applied in equivalent doses (0.012 and 1.2 mg kg(-1)), did not shorten the rejection time of skin grafts. The immune restoring effect, as well as the blastic transformation enhancing potential of MSC may be exploited in various cases of decreased immune response.

[iii] Carcinogenesis. 2001 Oct;22(10):1649-52.