Avemar – A Functional Food with Proven Anti-Cancer Effects

by Dan Kenner, PhD, LAc

Avemar is concentrated and extracted from fermented wheat germ via a patented process and has been shown in cell, animal, and human clinical studies to have potent anti-cancer and immune system-modulating effects. Extensive published research supports the use of Avemar both as a medicament in its own right and as an adjuvant to conventional cancer therapy.[1-3] Avemar has proven effective against all cancer cell lines tested, including breast, prostate, lung, pancreatic, lymphoma, and leukemia. It has been shown to have both cancer-preventive and anti-metastatic properties in animal studies and has demonstrated highly significant therapeutic effects in controlled human trials against primary colorectal cancer, Stage III melanoma, and Stages III and IV oral cancer.

Avemar also has been shown to reduce side effects of conventional cytotoxic cancer therapy, such as suppression of immune function, and to improve quality of life in cancer patients. Developed in Hungary and widely used throughout Europe and parts of the Middle East and Asia, Avemar is newly available in the United States and now rapidly gaining wider use following its recent GRAS (Generally Recognized As Safe) designation.

History: Nobel Beginnings

The development of Avemar can be traced back to the work of the Nobel Laureate Dr. Albert Szent-Györgyi, who was awarded the Nobel Prize in Physiology or Medicine in 1937 for his discovery of the physiological role of vitamin C. In his later life, Szent-Györgyi studied various extracts of the wheat plant extensively for their immune enhancing effects. According to his theory, the two quinones 2-methoxy benzoquinone and 2,6-dimethoxy benzoquinone, present in wheat germ as glucosides and liberated by yeast glucosidase, are likely responsible for the biological properties of fermented wheat germ. He theorized that quinones, 2,6-DMBQ, and related compounds called methoxy-substituted benzoquinones, when provided in supplemental quantities, would help to chaperone the cellular metabolism and prevent the states of hypermetabolism characteristic of cancer cells. Early experiments with DMBQ showed promise and demonstrated the effects that Szent-Györgyi predicted. Recent published research shows that benzoquinones inhibit tumor propagation.[4]

Máté Hidvégi Continues the Work

The Hungarian biochemist Dr. Máté Hidvégi resumed Dr. Szent-Györgyi's work, developing and patenting a technique of fermenting wheat germ with baker's yeast to produce a laboratory-standardized compound for research and later

commercialization. Research was promising, but limited by financial constraints, and it seemed that fermented wheat germ might again fade into obscurity. Dr. Hidvégi, being a devout Catholic, prayed to Mary, Mother of God, for guidance – and an investor: "Avé Maria, if it is your will, that this research should be continued, please send an investor." The next day, an entrepreneur whom Dr. Hidvégi had never met offered him the necessary funding. In thanks, he named his new product "Avemar." Several years of intense research followed, and as cell and animal studies confirmed that the promise that Szent-Györgyi, Hidvégi and others had suspected was indeed real, Dr. Hidvégi moved to make the compound more widely available to researchers and then to patients and physicians.

Many Years of Research

As with most proven therapies, Avemar's research began with the most basic laboratory experiment, progressing to the most advanced controlled human clinical trials.

Cell Studies

Treatment of Jurkat T-cell leukemia cells with Avemar lessened their ability to utilize glucose, triggering their destruction. The greater the metastatic potential of the cancer cell line tested, the higher the glucose utilization rate and the more pronounced the effect of Avemar. Normal cells were unaffected below 50 times the therapeutic dose.[5] In a study of estrogen receptor positive MCF-7 breast cancer cells, Avemar potentiated the apoptosis-inducing effects of Tamoxifen, indicating that Avemar can be recommended as an adjuvant to cancer therapy with Tamoxifen.[6-7] In MIA pancreatic adenocarcinoma cells, Avemar regulated tumor-cell proliferation by redistributing glucose carbon from non-oxidative nucleic acid ribose synthesis to direct glucose oxidation and lipid synthesis, which is a unique anti-proliferative mechanism. Cancer cells utilize a large volume of glucose to produce enough ATP to support the survival and promote replication of the cells.[8-9] In HT-29 human colon carcinoma cells, Avemar promoted tumor cell necrosis at lower doses and apoptosis at higher doses, inhibiting glycolysis and pentose cycle enzymes and free radical scavenging. Substances that inhibit ribonucleiotide reductase (RR), an important enzyme for DNA synthesis, can have anti-tumor effects; Avemar was shown to inhibit RR activity.[10] Cyclooxygenase (COX) is an enzyme associated with the occurrence of colon tumors. Avemar inhibited COX-2, associated with inflammation and tumor formation.[11]

Animal Studies

Animal research models were used to study the effects of Avemar for a variety of rationales.[12] Research in animal models has shown the cancer-prevention properties of Avemar.[13] Avemar co-administered with vitamin C was shown to have a profound effect of inhibiting metastasis. In a study of Vitamin C alone or with Avemar in three colon cancer tumor models, vitamin C alone had a metastasis-inhibiting effect in some models, but not all. Vitamin C combined with Avemar produced considerable inhibition of metastasis in all the models. In some models, the effect of Avemar was stronger without vitamin C.[14]

In experiments using B16 mouse melanoma and C38 mouse colorectal tumor models, Avemar synergistically enhanced the metastasis-inhibitory effect of the chemotherapy drug dacabazine (DTIC). Avemar combined with 5-FU also significantly diminished the number of liver metastases.[15] Despite a substantial therapeutic effect, toxic side effects of cytostatics in both experiments were not observed.[16-17]

Clinical Trials

In a multi-centered, open-label clinical trial involving 170 subjects with primary colorectal cancer, Avemar, along with surgery and standard radio/chemotherapy, significantly inhibited overall tumor progression, including the formation of new metastases, and prolonged the life of colorectal cancer patients, compared to standard radio/chemotherapy alone. Avemar increased the probability of survival by nearly 70%, similar to a previously observed 70% improvement in the rat model.[18-19]

Risk analysis revealed that the 12 months of Avemar treatment significantly reduced the overall progression (death, new loco-regional recurrences, new distant metastases) by 85%.[21]

A randomized study of 46 Stage III melanoma patients also showed significant benefits of using Avemar along with standard of care treatment. At end-point analysis, there were significantly more control patients with progressive disease (Avemar: 36% vs. control: 75%), and there were also generally fewer toxic side effects in patients receiving the combined treatment.[20]

In an open-label, non-randomized clinical trial involving patients with oral cancer (squamous cell carcinomas, stages III and IV), the end-point was disease progression. Incidences of local recurrences and disease progression differed significantly between the control group and the group treated with Avemar. Risk analysis revealed that the 12 months of Avemar treatment significantly reduced the overall progression (death, new loco-regional recurrences, new distant metastases) by 85%.[21]

Side Effects of Chemotherapy

Febrile neutropenia – abnormally low white blood cell counts accompanied by high fever – is a serious complication that can result from cytotoxic treatment. In a pilot study with 22 pediatric patients, two groups of children underwent cytotoxic chemotherapy cycles with no significant regimen differences and no difference in preventive measures for febrile neutropenia or treatment of its symptoms with antibiotics and antipyretics. Febrile neutropenia occurred 30 times during or following chemotherapy in the Avemar-treated group (24.8%) vs. 46 times (43.4%) in the control group. Overall leukocyte and lymphocyte counts (measured daily), in the Avemar-treated group were significantly closer to normal.[22]

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A multi-center study of Avemar on quality of life (QOL) during breast cancer treatment showed significant improvements in physical functions, emotional functions, global state of health, fatigue, nausea, vomiting, insomnia, and constipation.

A study on lung cancer patients showed significant improvements in global state of health and fatigue and modest improvements in pain relief, loss of appetite, and mood parameters. An unpublished study on quality of life in 17 lung cancer patients using a questionnaire concluded that there were substantial benefits of using Avemar concurrently with other therapies.[23]

Mechanisms of Action

There are several mechanisms of action identified through which Avemar produces the anti-cancer effects shown in cell, animal, and human studies.

Immunological Effects of Avemar

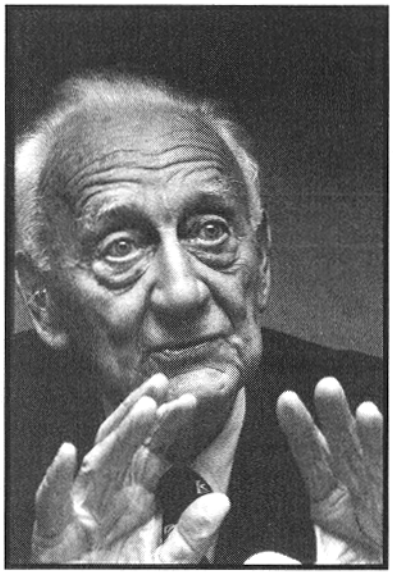
Malignant tumor cells are protected from immune surveillance because they express high levels of MHC-I (Major Histocompatibility Complex-Class I) proteins on the cell membrane, a signal to the immune system that the tumor cells originate within the body, a status that protects them from cytotoxic T-cells such as NK (natural killer) cells. Avemar has been shown to induce a decrease in MHC-I proteins on the surface of tumor cells, making the cancer cells vulnerable to NK cell activity.[24]

A study in mice demonstrated Avemar protected bone marrow function from sub-lethal irradiation and/or cyclophosphamide therapy, as measured by hematopoiesis. Platelet production began seven days after irradiation. Erythrocyte and thrombocyte production were restored by Avemar following the administration of cyclophosphamide.[25]

Metabolic Mechanisms

Greatly increased use of glucose is a well-known characteristic of cancer cells, as observed by the cancer research pioneer Otto Warburg (the Warburg effect). Much of the glucose is used to help synthesize ribose at rates fast enough to support cell proliferation. By inhibiting transketolase (an enzyme necessary to facilitate the non-oxidative pathway of ribose synthesis supportive of proliferation), Avemar restricts the flow of glucose carbon atoms to tumor cell nucleic acid synthesis, preventing rapid cell proliferation. The reduced glucose consumption of the tumor cells both slows disease progression and improves the nutrition of patients, promoting weight gain in even advanced cases of cachexia. The improved nutritional status improves the patient's general resistance to the rigors of surgery, radiation, or further chemotherapy.Avemar also targets other nucleic acid synthesis enzymes, including G6PDH (involved in direct glucose oxidation), lactate dehydrogenase (glycolysis), and hexokinase (glucose activation).

Forcing a shift of tumor cell metabolism from non-oxidative ribose synthesis to direct glucose oxidation and lipid synthesis is a feature unique to Avemar. These effects are not seen with either conventional cytotoxic chemotherapy, radiotherapy, or other cancer treatments, yet this phenomenon augments conventional treatment, without diminishing any of the beneficial effects of those other treatments.



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Albert Szent-Györgyi, MD, PhD
Speaking at Cancer Dialogue '80
Grand Hyatt Hotel, New York, NY
October, 1980

Apoptosis-Promoting Mechanisms

Avemar also induces cell cycle arrest and apoptosis through a caspase-based mechanism. Caspases have been found to induce apoptosis by means of cleaving a DNA repair enzyme (PARP, or Poly ADP-Ribose Polymerase).[26]

Antimetastatic Action

Malignant tumors have a decreased expression of a cytokine called intercellular adhesion molecule-1 (ICAM-1), compared to normal endothelial tissue. This protects the tumor from the immune system by preventing infiltration of the tumor with leukocytes. Avemar enhances production of ICAM, improving the ability of T-cells and macrophages to travel through blood vessel walls and invade and attack tumors.[27]

Cytotoxic Action

Apoptosis of cancer cells is induced by Avemar by several mechanisms. The Poly ADP-ribose polymerase (PARP) enzyme is essential for DNA repair and is extremely active in cancer cells. Avemar promotes cleavage of PARP by caspase-3.[28] Cleavage of PARP by caspase enzymes causes fragmentation of DNA and leads to apoptosis of tumor cells.

Another enzyme important to the survival of cancer cells is ribonucleotide reductase (RR). RR is upregulated in tumor cells to meet the increased need for dNTPs (deoxyribonucleoside triphosphates) for DNA synthesis. DNTPs are the monomers that DNA polymerase use to form DNA. Avemar has been shown to significantly inhibit RR activity,[29] which can further explain its anti-tumor effects, particularly in colorectal cancer.

Inhibition of Inflammatory Enzymes

Avemar has been found to inhibit cyclooxygenase (COX) enzymes. Both COX-1 and COX-2 enzymes are equally affected. COX enzymes are associated with the appearance of colon tumors. Inhibition of COX enzymes also has therapeutic and preventive effects in colon cancer, and this can explain the effect of Avemar as a cancer preventive in animals.

Avemar Boosts Immune System Response by Increasing TNF Levels

Avemar has also been shown to enhance the production of an immune compound called Tumor Necrosis Factor alpha (TNF-α) by white blood cells called macrophages, which directly attack cancer cells.[30]

Avemar Stimulates Immune System Response by Increasing Interleukin Production

The hormone-like proteins called cytokines are especially important in coordinating immune system attacks on abnormal organisms in the body, including cancer cells. Avemar has been shown to increase activity of genes that express the cytokines interleukin-1-alpha, interleukin-1-beta, interleukin-5, and interleukin-6, helping increase the numbers, growth, and mobility of immune system cells.[31]

Antioxidant Properties

The powerful electron donor characteristics of the benzoquinones in Avemar have a strong antioxidant effect. Antioxidants help reduce cancer risk by protecting DNA from gene damage that can lead to cancer.

Safety

Avemar is extremely safe for use with all types of patients. Its toxicological status was first tested in Hungary, and it has also been reviewed for safety in the US. In the opinion of the independent panel of medical, food safety, and toxicology experts that confirmed Avemar's GRAS (Generally Regarded as Safe) status in accordance with FDA regulations, Avemar has the toxicological profile of bread.[32]

The patented fermentation and extraction processes involved in Avemar production increase the nutritional and therapeutic properties of the wheat germ and create new components – biologically active quinones – that did not exist prior to the fermentation and may be the most important active constituents. Hence, Avemar cannot be replaced by wheat germ, germinated wheat, or any extract or derivative of these.

Clinicians Using Avemar

Clinicians in Hungary were the first to report that Avemar appeared to improve the nutritional status of cancer patients with cachexia. Doctors conducting a trial on the use of Avemar with colorectal cancer patients noticed weight gain as well as slowed disease progression in the patient group treated with Avemar.[33] This can be explained by the effect of Avemar on initiating lipid synthesis. Researchers have observed that glucose carbon is redistributed from non-oxidative nucleic acid ribose synthesis to direct glucose oxidation and lipid synthesis. This improvement in the nutrition of cancer patients is a distinctive feature of Avemar and a strong justification for using it even in patients with advanced cases.[34]

Doctors in the US who have used Avemar are reporting favorable results. Michael Broffman, LAc, of Pine Street Clinic in San Anselmo, California has been using Avemar for five years in a predominately cancer patient population. Dr Broffman reports:

> I have used Avemar mostly in the types of cases supported by the literature, especially gastrointestinal cancers and melanoma. We have also used it for Tamoxifen enhancement, and we have a number of patients who were able to cut the dose of Tamoxifen in half and still respond well to the treatment with stable results after five years. We have had over 150 patients who have used Avemar regularly over an extended time period, and I feel that it is effective. More isn't always better, but I believe that we might see even better results in some cases by increasing the dosage. That's something we would like to research.

Daniel Rubin, ND, of Scottsdale, Arizona, founding President of the Oncology Association of Naturopathic Physicians, has been using Avemar during the last year in an integrative setting for people with cancer:

> I was pleased when Avemar became available in the United States. The supportive background science affords a feeling of safety regarding its use in the clinic; I appreciate responsible data collection in the nutraceutical industry, especially in this era of molecular oncology. Avemar is generally well tolerated, and I am becoming more familiar with its clinical effects. I employ it as part of comprehensive protocols and at times alongside conventional treatments for its various well-described effects. I also use it in post-conventional treatment phases to aid in maintenance of remission.

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Jim LaValle, RPH, ND, CCN, co-founder of the Living Longer Institute in Cincinnati, Ohio, has witnessed firsthand the clinical use of Avemar in Hungary. He has been using it clinically for over a year and a half. He notes:

> There are multiple layers of value with this product. We have a holistic practice that includes detoxification and immune support, but we see cancer patients who have had several courses of chemotherapy and radiation as well. Not only does Avemar protect immunity, but it also improves the patient's nutritional status. I've seen consistent good results with reversing cachexia, and I've even seen the cachectic condition reappear when the Avemar is discontinued and the patient's weight increase again when Avemar is resumed. I use it to help prevent metastasis and when there is low NK-cell activity. This product really seems to do what it is supposed to do according to the scientific literature. The progression of cancer slows down significantly and there are fewer negative side effects of conventional cancer therapy, even in patients who have had three or four rounds. I feel very confident that it can be useful to almost any cancer patient, even in advanced stages, and that it will protect immunity and improve nutritional status.

Research into the benefits of Avemar for cancer and other medical problems continues in Europe and North America. Because of Avemar's multiple mechanisms of action, it is likely that the range of disorders that Avemar can benefit will increase. Its record of safety and support from the scientific research literature make Avemar a valuable new tool for nontoxic and supportive treatment.

"The progression of cancer slows down significantly and there are fewer negative side effects of conventional cancer therapy, even in patients who have had three or four rounds."

– Jim LaValle, RPH, ND, CCN, co-founder of the Living Longer Institute in Cincinnati, Ohio

Notes

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