

# **Avemar: A Clinically Versatile Functional Food**

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Avemar is a biologically active cultured wheat germ extract developed in Hungary for medical use. It is unique for its unusual potency as an immunomodulator, its well-established safety, and for the body of evidence supporting its efficacy as a therapeutic agent. Animal testing, cell line studies and human clinical studies support the use of Avemar as a medicament in its own right and as an adjuvant to conventional cancer therapy<sup>1-3</sup>.

Avemar has proved to be effective against all cancer cell lines tested and has been shown to have cancer preventive and anti-metastatic properties in animal studies. Avemar has also been shown to have a significantly therapeutic effect in controlled human trials in treatment of primary colorectal cancer, Stage III melanoma and Stages III and IV oral cancer. Avemar consistently enhances quality of life and reduces side effects of chemotherapy, as well as prevents chemotherapy-induced suppression of immune function.

## **Nutritional value**

Avemar is a “functional food,” a food that has proven therapeutic applications based on scientific investigation. The raw material for production of Avemar is wheat germ. The wheat kernel contains 2-4% germ, Wheat germ itself is a food with high nutritional value and is often used in food supplements, breakfast cereals, diet bars and fiber drink mixtures. Some of the chemical characteristics of wheat germ make it unsuitable for the bread baking process, so it is separated out and sold as a source of various nutrients including vitamin E (wheat germ is the richest known source of tocopherols) and B complex. Because Avemar is a “superfood” supplement, it is extremely safe for use with all types of patients. Its toxicological status was first tested in Hungary<sup>4</sup> and it has also been reviewed for safety in the U.S. In the opinion of the independent panel of medical, food safety and toxicology experts that confirmed Avemar’s GRAS status with in accordance with FDA regulations, Avemar has the toxicological profile of bread<sup>5</sup>.

The standardized manufacturing process included the extraction of wheat germ, fermentation of the extract, separation of the fermentation liquid, microencapsulation, drying and granulation. The original composition of wheat germ is substantially modified due to extraction followed by fermentation; therefore, Avemar cannot be replaced by wheat germ, germinated wheat or any extract or derivative of these (quinones liberated by the fermentation process).

The fermentation process increases the nutritional and therapeutic properties of wheat germ. One of the advantages of fermentation of food products is that fermentation “predigests” the raw materials and breaks down chemical constituents to components of a smaller molecular size, which are more bioavailable because they are more absorbable. Another enhancement from the fermentation process is to create new components that did not exist in the base material. In the case of Avemar fermentation produces biologically active quinones, which may be active principles.

### **History**

Avemar was developed in Hungary by a doctor named Máté Hidvégi, assisted by Rita Tömösközi-Farkas who continued the work of the Nobel Laureate Albert Szent-Györgyi in his quest of production of a natural-based quinone-concentrate. From the early 1960s Szent-Györgyi had researched wheat as a potential source of quinones with unique therapeutic properties.

Quinones have been discussed in the popular media in recent years, when researchers speculated that the quinones in red wine were a factor possibly responsible for the “healthy French heart.” The rate of cardiovascular disease has been inexplicably low in France even though there is a similar level of fat consumption in the average French person’s diet. The well-known nutritional supplement coenzyme Q-10 (CoQ-10) is also known as “ubiquinone.” Anthraquinones and naphthoquinones are found to play important roles in a wide range of botanical medicines. Anthraquinones and naphthoquinones have been observed to have anti-tumor and anti-microbial properties.

Quinones are carbonyl group molecules with a wide range of biological activity. One of their properties is to be able to attract and accumulate electrons in the carbon-hydrogen double bond. Benzo- and hydroquinones have anti-microbial activity. Adriamycin, daunorubicin and mitomycin have cytostatic effects. All of these compounds may modulate the immune system. The mechanism they share in common is suggested to be a free radical scavenging capability.

### **Koch and early quinone research**

Carbonyl group molecules play an important role in tissue chemistry. There are innumerable chemical reactions that involve or produce a carbonyl group as an intermediary or as an end product. They are electron donors and therefore hydrogen acceptors and break up congestion from oxidative stress through hydrogen abstraction. They initiate oxidative energy production for normal function and nutrition at the cellular level. Carbonyl group molecules were first researched in the early 20th century by Dr. William F. Koch, the nephew of Robert Koch, the

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famous 19th century microbiologist who discovered the tubercle bacillus, postulated Koch's Law and founded the Koch Institute.

William Koch found that carbonyl group molecules break up deposition and condensation processes, represented by tumors, degeneration, accumulation of all kinds of tissue debris and plaque, and dissolve it because of their extremely powerful properties as electron donors (oxygen) and hydrogen acceptors. They reverse oxidative stress and initiate normal aerobic metabolism by donating negative charge. They also initiate a process of depolymerization that behaves as a type of "chain reaction" such that the therapeutic effects of the administration of a single dose can have far-reaching effects and persist for an extended period of time.

In the 1920's a new approach to cancer treatment pioneered by Dr. Koch, who was a professor of physiology at what is now Wayne State University, took a radically different view of the disease. Koch, like the Nobel Prize winners Otto Warburg<sup>6</sup> and Albert Szent-Györgyi decades after him, believed that cancer was the result of faulty metabolism and that it might be possible to return the malignant cells to a normal state<sup>7</sup>.

Koch's reagents do not destroy cancer cells. They restore the terrain by means of a type of antioxidant chain reaction so that normal cell metabolism can resume. Koch treated hundreds of patients with phenomenal success and with long term stability in cancer patients who were thought to be terminal, as well as patients with a variety of neurological and metabolic disorders<sup>8</sup>.

Quinones similar to the ones developed by Koch are also found pau d'arco, yew trees, in apricot seeds and other natural sources that have been observed to have therapeutic or adjuvant properties in cancer treatment. In 1946 Dr. Willard Dow, President of the Dow Chemical Industries said of Koch: "Koch is so far ahead of the thinking of his profession that he is not understood, and they even ridicule him at times." But Koch suffered legal harassment and persecution in the U.S. and eventually relocated to Brazil where he conducted his research with government sponsorship (see [www.williamfkoch.com](http://www.williamfkoch.com) for detailed history and publications by Koch and his colleagues). Carbonyl group remedies are still used by natural medicine doctors in South America and Europe for chronic viral infections, cancer, asthma, and many types of metabolic disorders

## **Szent-Györgyi's research**

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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 to be 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 help prevent the states of hyper metabolism characteristic of cancer cells. The type of carbonyl group found in Avemar is dimethoxy-benzoquinone. Wheat germ is one of the largest known natural sources of 2-methoxy-p-benzoquinone (2-mbq) and 2,6-dimethoxy-p-benzoquinone (2,6-DMBQ). Early experiments with natural and synthetic forms of DMBQ showed promise and demonstrated the effects that Szent-Györgyi predicted. Several anticancer agents have a quinone structure (eg. adriamycin, daunorubicin, mitomycin C) and quinones are active components of some antibiotics (eg. Tetran-b, Metocylins, Doxycylins). Recent published research shows that benzoquinones inhibit tumor propagation. The benzoquinone derivative 2,6-methoxy-p-benzoquinone (DMBQ), one of two found in Avemar, induced downregulation of MHC Class I proteins in lymphoid tumors cells, although the results were not sustained over an extended time period as with the whole fermented wheat germ extract. Therefore there are probably other components active in the whole compound.

### **Máté Hidvégi's research on wheat germ**

The Hungarian biochemist Dr. Máté Hidvégi resumed Dr. Szent-Györgyi's work, 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”.

### **Animal Studies**

Animal research models were used to study the effects of Avemar for a variety of rationales<sup>11</sup>. Many of the animal studies were undertaken to attempt to understand the mechanism of Avemar's effect on pathophysiology. Research in animal models has shown the cancer-prevention properties of Avemar<sup>12</sup>. Avemar co-administered with vitamin C was shown to have a profound effect of inhibiting the process of metastasis. Another study showed prevention of colon cancer using Avemar. Further studies have also shown that Avemar can inhibit autoimmunity and potentially be effective in some types of arthritis and SLE (systemic lupus erythematosus)<sup>13-16</sup>.

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Three tumor models were used to ascertain the metastasis-inhibiting effect of Avemar used along with vitamin C. Vitamin C had a metastasis-inhibiting effect in some models, but not all. When vitamin C was combined with Avemar, however, there was profound inhibition in all of the models. In some models the effect of Avemar was stronger without vitamin C<sup>17</sup>.

Animal models were also used to determine the suitability of co-administration of Avemar with conventional chemotherapy drugs. Experiments using B16 mouse melanoma and c38 mouse colorectal tumor strains were carried out to find out how daily treatment with Avemar would affect the tumor growth and metastasis-inhibiting effect of 5-fluorouracil (5-FU) and dacarbazine (DTIC), which are widely in cancer protocols. The study showed that Avemar synergistically enhanced the the metastasis-inhibitory effect of DTIC. Avemar combined with 5-FU also significantly diminished the number of liver metastases<sup>18</sup>. Despite a substantial therapeutic effect, toxic side effects of cytostatics in both experiments were not observed<sup>19-20</sup>.

### **Cell Line research**

Research on Jurkat T-cell leukemia cells helped to elucidate a previously unknown mechanism of tumor reduction. Jurkat T-cell leukemia cells were treated with Avemar to investigate its effects on various cellular response mechanisms using a C-labeled glucose tracer. Cell cycle modulation, induction of apoptosis, changes in metabolic enzyme activity and substrate flow were examined. Avemar altered the ability of cancer cells to utilize glucose, which triggered their destruction. The greater the metastatic potential of the cancer cell line tested, the higher the glucose utilization rate.

The effect of Avemar was more dramatic in proportion to how high the rate of glucose utilization was. There was no effect on normal cells until the concentration of Avemar was 50 times higher. It was found that Avemar has a strong anti-proliferative effect on Jurkat T-cell leukemia cells. They found multiple mechanisms involved. Avemar targets nucleic acid synthesis enzymes, including G6PDH (involved in direct glucose oxidation), transketolase (non-oxidative glucose utilization toward nucleic acid synthesis), lactate dehydrogenase (glycolysis) and hexokinase (glucose activation). 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)<sup>21</sup>.

Researchers at the National Center for Public Health in Budapest investigated the effect of Avemar in combination with Tamoxifen on MCF-7 breast cancer cells. Tamoxifen is commonly

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used in treatment of estrogen receptor positive breast cancer. The researchers found that estrogen receptor activity was enhanced by the combined treatment of Tamoxifen and Avemar. The data showed that Avemar induces apoptosis, or cell death, in estrogen positive cells and was significantly potentiated by administering Tamoxifen simultaneously. This is an indication that Avemar can be recommended as an adjuvant to cancer therapy with Tamoxifen<sup>22-23</sup>.

The effects of Avemar on glucose oxidation were studied using 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 are hypermetabolic and usually have low oxygen levels. The breakdown of glucose that occurs in the absence of oxygen, called anaerobic glycolysis, results in the conversion of most of the glucose into lactic acid. There is a poor energy yield in anaerobic glycolysis so cancer cells compensate by consuming a large volume of glucose to produce enough ATP to support the survival, and replication of the cells<sup>24-26</sup>.

The anti-tumor activity of Avemar on HT-29 human colon carcinoma cells was researched at the Medical University of Vienna. Both necrosis and apoptosis of the cells were observed, necrosis at lower doses and apoptosis at higher doses. One mechanism previously observed in Jurkat T-cell leukemia cells was the inhibition of glycolysis and pentose cycle enzymes. Another possible mechanism explored was free radical scavenging. Ribonucleotide reductase (RR) converts ribonucleotides to deoxyribonucleoside triphosphates. These are precursors of DNA synthesis. Substances that inhibit RR, an important enzyme of DNA synthesis, can have anti-tumor effects. The researchers were able to confirm that Avemar inhibited RR activity. Cyclogenase (COX) is another enzyme associated with the occurrence of colon tumors. Avemar inhibited both COX-1 and COX-2. COX-2 is associated with inflammation and tumor formation<sup>27</sup>.

### **Clinical trials**

Avemar was shown in a clinical study to significantly reduce the occurrence of febrile neutropenia in pediatric cancer patients. Febrile neutropenia is a serious complication resulting from cytotoxic treatment. Cytotoxic treatment for solid tumors often impairs cellular (Th1) immunity because of the neutropenic, granulocytopenic and myelosuppressive effects of chemotherapeutic agents<sup>28</sup>. The results of a pilot study with 22 patients at the Semmelweis University School of Medicine in Budapest, Hungary were favorable with fewer febrile neutropenic incidences. The two groups of children underwent chemotherapy cycles with no significant differences. The methods used to prevent neutropenic episodes and treatment of them with antibiotics and antipyretics did not differ between the two groups, but there was a significant difference in occurrence of episodes with 30 (24.8%) in the Avemar-treated group

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vs. 46 (43.4%) in the control group. There was also difference in the overall leukocyte and lymphocyte counts (measured daily), with the Avemar-treated group significantly closer to normal<sup>29</sup>.

The immunomodulating and anti-inflammatory effects of Avemar were demonstrated in an unpublished study on rheumatoid arthritis. Fifteen patients studied at the National Institute of Rheumatology and Physiotherapy, Budapest were treated with Avemar over a 12 month period. All patients improved considerably and it was possible to decrease doses of steroids significantly; erythrocyte sedimentation rate decreased significantly and C-reactive protein decreased, but not significantly<sup>30</sup>.

The results of a multi-centered open label clinical trial on 170 subjects with primary colorectal cancer investigating Avemar as an adjuvant to standard treatment compared with standard treatment alone yielded data that were highly favorable to the use of Avemar. The data showed that Avemar, along with surgery and the standard radio/chemotherapy, can significantly inhibit overall tumor progression including the formation of new metastases and can prolong the life of colorectal cancer patients. It is also interesting that Avemar increased the probability of survival by nearly 70% similar to the previously observed 70% in the rat model<sup>31-32</sup>.

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<sup>33</sup>.

In an open label, non-randomized clinical trial on patients with oral cancer (squamous cell carcinomas, stage 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%<sup>34</sup>.

### **Side effects of chemotherapy**

Avemar helps to prevent the chemotherapy-induced suppression of immune function. One

example is the study of the effect of Avemar on pediatric neutropenia mentioned above. Avemar has also been found to reduce side effects associated with chemotherapy and improve quality of life (QOL). A multi-center study of Avemar on QOL during breast cancer treatment has shown significant improvements in physical functions, emotional functions, global state of health, fatigue, nausea, vomiting, insomnia and constipation. Clinical efficacy studies are ongoing. Another 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<sup>35</sup>.

### **Physiological mechanism of Avemar**

There are several mechanisms of the effect of Avemar that have been identified. As mentioned above, the carbonyl group molecules, like DMBQ, are powerful electron donors and work at the cellular level. They clean up deposited metabolic by-products and simultaneously increase the efficiency of metabolic activity. Avemar has been proven to support overall immune strength, coordination and function. There are several mechanisms by which Avemar can favorably influence cancer treatment as well as inflammatory disorders such as rheumatoid arthritis. Listed here are various types of immunological effects, metabolic mechanisms, cytotoxic effects and antitumor effects. Multiple mechanisms in the physiological activity of Avemar open the possibility of a wide spectrum of therapeutic applications.

### **Immunological effects of Avemar**

Avemar can influence the immune system's bias toward humoral (Th2) or cellular (Th1) immunity. In many chronic diseases where antibodies to the pathogen exist, healing does not take place because of a failure of cellular immunity. In a mouse model of SLE Avemar improved clinical manifestations by inhibiting the Th2 response (inhibition of IL-4 and IL-10 production). These results were the motivation for a double-blind clinical study with lupus patients. Avemar also promotes upregulation of one of the primary anticancer cytokines, tumor necrosis factor-alpha (TNF- $\alpha$ ).

One reason cancer cells are capable of unrestrained growth because they are able to evade immunological surveillance. Malignant tumor cells are able to protect themselves from immune surveillance by expressing high levels of MHC-I proteins on their surface. These proteins signal the immune system that tumor cells are normal structural cells and this protects them from cytotoxic T-cells such as NK (natural killer) cells. Avemar induced a decrease in MHC (Major Histocompatibility Complex) class I proteins on the surface of tumor cells, making the cancer cells vulnerable to NK cell activity<sup>36</sup>.

Another study in mice showed the benefit of Avemar in protecting the bone marrow from sublethal irradiation and/or cyclophosphamide therapy, as measured by hematopoiesis. Production of platelets began 7 days after irradiation. Erythrocyte and thrombocyte production were both restored by treatment with Avemar following the administration of cyclophosphamide<sup>37</sup>.

### **Metabolic mechanisms**

One mechanism of Avemar is to inhibit glucose metabolism in cancer cells. Hunger for glucose is a well-known characteristic of cancer cells observed by the cancer research pioneer Otto Warburg. Warburg (and Koch) believed that in cancer something blocks the last stages of adenosine triphosphate (ATP) synthesis, perhaps a carcinogen. As explained briefly above, the cell is forced to rely on the breakdown of glucose (glycolysis), an anaerobic reaction, to generate the necessary ATP for energy production. A cell can normally convert glucose to ATP at a ratio of 1 molecule to 35. Because glycolysis is less efficient than aerobic metabolic reactions to produce ATP, the cells' requirement for glucose is dramatically elevated. The first available source of glucose is the glycoproteins in the cell wall structures. Damage to the cell wall also destroys receptor sites that receive and convey information regarding cell functions, such as growth and repair. With the cell wall structures damaged, the cell is unable to repair itself and produce new glycoproteins or to signal the immune system. The degraded cell is thus protected from lysis by the immune system. The cell, because of its voracious need for sugar begins to invade other cells and proliferate until a solid mass of cancer cells forms. By interrupting the supply of glucose carbon atoms available for the production of nucleic acid synthesis, Avemar prevents DNA formation in tumor cells.

The reduced glucose consumption of the tumors that results could explain the effect of Avemar in slowing disease progression and improving 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. This mechanism of shifting tumor metabolism from non-oxidative ribose synthesis to direct glucose oxidation and lipid synthesis is a unique feature described only in connection with Avemar.

### **Antimetastatic action**

Malignant tumors have a decreased expression of ICAM-1 (intercellular adhesion molecule-1) compared to normal endothelial tissue. This protects the tumor from the immune system by preventing infiltration of the tumor with leukocytes.

### **Cytotoxic action**

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Apoptosis of cancer cells is induced by Avemar by several mechanisms. Poly ADP-ribose polymerase enzyme is essential for DNA repair and is extremely active in cancer cells. 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 for DNA synthesis. DNTPs, or deoxyribonucleoside triphosphates, are the monomers that DNA polymerase uses to form DNA. Therefore RR is another target for chemotherapeutic intervention. Avemar significantly inhibits RR activity in a study using HT-29 human colon carcinoma cells, which can further explain its antitumor effect, especially in colorectal cancer.

Avemar has been found to inhibit cyclooxygenase (COX) enzymes. Both COX-1 and COX-2 enzymes were equally affected. COX enzymes are associated with the appearance of colon tumors. Inhibition of cyclooxygenase (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.

### **Signal transduction**

Another reason cancer cells can grow without restraint is because they are able to avoid the normal homeostatic regulatory mechanisms by means of resistance toward apoptotic signals and CD-45 is a regulator of signaling across cell membranes. T-cell receptor calcium signaling can be terminated within seconds of CD-45 phosphatase inactivation.

Antioxidant properties

The powerful electron donor characteristics of the benzoquinones in Avemar have a strong antioxidant effect.

Table 1: Mechanisms of action of Avemar

Immunological:

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Th2 response inhibition; MHC downregulation → Increased NK cell activity; TNF-α upregulation → macrophage activation

Metabolic: Pentose cycle + fatty acid synthesis → DNA sugar phosphate chain synthesis

Anti-metastatic: Enhanced ICAM-1 expression → increased cellular activity at tumor site; decreased cell adhesion. Cell adhesion molecules (CAMs) are proteins which anchor cells to each other and to the extracellular matrix (ECM), but whose functions also include signal transduction, differentiation, and apoptosis.

Endothelial cells in the vasculature of human solid tumors have decreased

expression of intercellular adhesion molecule-1 (ICAM-1) compared to normal

endothelial cells. Incubation of tumor-derived endothelial cells with TNF resulted in

expression levels of only 20%, achieved in similarly treated normal tissue-derived en-

dothelial cells because tumor angiogenesis induces anergy in endothelial cells.

This phenomenon may serve as a tumor-protecting mechanism because leukocytes require ICAM-1 to leave the vascular system to infiltrate the tumor tissue. Avemar induced the production of ICAM-1 as well as showing synergy with TNF in this respect.

Signal transduction: Avemar induces apoptosis by tyrosine phosphorylation of intracellular signal proteins resulting in an increased intracellular Ca<sup>++</sup> influx. Apoptosis is triggered in tumor B and T cell lines, but not in healthy peripheral blood mononuclear cells. These events are important components of the cellular response to Avemar treatment. Inhibition of tyrosine

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phosphatase activity causes downregulation of the response of the cell surface MHC class I proteins.

Cytotoxic: Increased apoptosis (PARP); decreased cell proliferation

Antioxidant: Benzoquinone components are powerful antioxidants

### **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<sup>38</sup>. This can be explained by the effect of Avemar on initiating lipid synthesis. Researchers have observed that glucose carbon is redistributed from nonoxidative 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<sup>25</sup>.

Doctors in the U.S. who have used Avemar are reporting favorable results. Michael Broffman, L.Ac. of Pine Street Clinic in San Anselmo, California has been using Avemar for 5 years in a predominately oncological patient population. "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, N.D., founding President of the Oncology Association of Naturopathic Physicians of Scottsdale, Arizona, has been using Avemar during the last year in an integrative setting for people with cancer. "I was pleased to learn that Avemar became available in the

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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. Ave 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.”

Jim LaValle, R.P.H., N.D., C.C.N., 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. “There are multiple layers of value with this product. We have an interdisciplinary and integrative practice that includes detoxification and immune support, but we see cancer patients who have had several courses of chemotherapy and radiation. Not only does Avemar protect immunity, but it also improves the patient’s nutritional status. I have seen consistent good results with reversing cachexia, and even seeing the cachectic condition reappear when the Avemar is discontinued. When Avemar is resumed, the weight increases once again. 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 3 or 4 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. I am encouraged because Avemar acts through several mechanisms to reduce cancer activity at the cellular level. The fermentative pathway downregulation of sugar uptake, the decrease in MHC-1 complexes to unmask the cancer cells, and the triggering of apoptosis make it invaluable as a tool against cancer.

I have also started using Avemar with rheumatoid arthritis and other autoimmune disorders. I think that there is a lot of room for discovery, especially in metabolic syndromes where there is chronic inflammation, problems with lipid metabolism and glucose dysregulation. I think we are likely to see help from Avemar with diabetes and autoimmune disorders that have not yet been formally researched.”

Research into the benefits of Avemar for cancer and other medical problems continues in Europe and North America. Because of its 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 this a valuable new tool for nontoxic and supportive treatment.

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Dear Editor,

The recent article about Avemar, the functional food developed in Hungary, left out a significant part of the history of the therapeutic application of quinones. Quinones have been discussed in the popular media in recent years. Researchers have speculated that the quinones in red wine are a factor possibly partly responsible for the "healthy French heart." The rate of cardiovascular disease has been inexplicably low in France even though there is a similar level of fat consumption in the average French person's diet. The well-known antioxidant coenzyme Q-10 (ubiquinone) is also in the quinone family. Anthraquinones and naphthoquinones are found to play important roles in a wide range of botanical medicines. Anthraquinones and naphthoquinones have been observed to have both anti-tumor and anti-microbial properties.

Quinones are carbonyl group molecules with a wide range of biological activity. One of their properties is to be able to attract and accumulate electrons in the carbon-hydrogen double bond. Benzo- and hydroquinones have anti-microbial activity. Adriamycin, daunorubicin and mitomycin have cytostatic effects and all of these compounds may modulate the immune system. The mechanism they share in common is suggested to be a free radical scavenging capability.

Carbonyl group molecules play an important role in tissue chemistry. There are innumerable chemical reactions that involve or produce a carbonyl group as an intermediary or as an end product. They are electron donors and therefore hydrogen acceptors and break up congestion from oxidative stress through hydrogen abstraction. They initiate oxidative energy production for normal function and nutrition at the cellular level. Carbonyl group molecules were first researched in the early 20th century by Dr. William F. Koch, the nephew of Robert Koch, the famous 19th century microbiologist who discovered the tubercle bacillus, postulated Koch's

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Law and founded the Koch Institute.

William Koch found that carbonyl group molecules break up deposition and condensation processes, represented by tumors, degeneration, accumulation of all kinds of tissue debris and plaque, and dissolve it because of their extremely powerful properties as electron donors (oxygen) and hydrogen acceptors. They reverse oxidative stress and initiate normal aerobic metabolism by donating negative charge. They also initiate a process of depolymerization that behaves as a type of "chain reaction" such that the therapeutic effects of the administration of a single dose can have far-reaching effects and persist for an extended period of time.

In the 1920's a new approach to cancer treatment pioneered by Dr. Koch, who was a professor of physiology at what is now Wayne State University, took a radically different view of the disease. Koch, like the Nobel Prize winners Otto Warburg<sup>6</sup> and Albert Szent-Györgyi decades after him, believed that cancer was the result of faulty metabolism and that it might be possible to return the malignant cells to a normal state<sup>7</sup>.

Koch's reagents do not claim to destroy cancer cells. They restore the terrain by means of a type of antioxidant chain reaction so that normal cell metabolism can resume. Koch treated hundreds of patients with phenomenal success and with long term stability in cancer patients who were thought to be terminal, as well as patients with a variety of neurological and metabolic disorders<sup>8</sup>.

Quinones similar to the ones developed by Koch are also found pau d'arco, yew trees, in apricot seeds and other natural sources that have been observed to have therapeutic or adjuvant properties in cancer treatment. In 1946 Dr. Willard Dow, President of the Dow Chemical Industries said of Koch: "Koch is so far ahead of the thinking of his profession that he is not understood, and they even ridicule him at times." But Koch suffered legal harassment and persecution in the U.S. and eventually relocated to Brazil where he conducted his research with government sponsorship (see [www.williamfkoch.com](http://www.williamfkoch.com) for detailed history and publications by Koch and his colleagues). Carbonyl group remedies are still used by natural medicine doctors in South America and Europe for chronic viral infections, cancer, asthma, and many types of metabolic disorders

The most recent chapter of the Koch carbonyl group story takes us to India where researchers have been working for over ten years using a methylglyoxal-based formulation on advanced stage cancer patients that has had "a dramatic positive effect on the patients."

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According to Manju Ray, a biochemist at the Indian Association of the Cultivation of Science (IACS), where the drug was developed under a project funded by the Department of Science and Technology and the Council of Scientific and Industrial Research, "We have what we think is a magic bullet against cancer." The scientists have observed that methylglyoxal was successful against different types of cancer including acute myeloid leukemia, colon cancer, non-Hodgkin's lymphoma, and cancers of ovary, breast, liver, lung, bone, gall bladder, pancreas and oral cavity. Administered orally, no toxic reactions were observed. Perhaps these powerful antioxidants, which have such enormous potential for malignancy and chronic viral infections, will finally become available.