



Active Hexose Correlated Compound:

Immune Booster Extraordinaire

When it comes to our health, few of us get excited about fungus. After all, when we think fungus, we think of candida or tinea's like athletes foot. We rarely consider medicinal mushrooms, but we should, especially when immunity is a concern. For over 7000 years, they have been prized in Oriental medicine. Historically, their use included immune support, the treatment of fatigue, and the promotion of cardiovascular health. Today, an oligosaccharide called active hexose correlated compound (AHCC), extracted from a class of higher fungi grown in rice bran called basidiomycetes, particularly stands out. **AHCC was developed in Japan in 1989 and it has since been used as an immunotherapy by over 100 000 patients. It was shown to be effective in cancer treatment and prevention, for hypertension, to reduce inflammation, to improve the body's response to stress and infection and for diabetics, hepatitis and AIDS patients.**

Feed Your Immunity

AHCC is remarkable because of its function as a Biological Response Modifier (BRM) - immune enhancing agents. Other examples of BRM's include immunotherapy drugs such as Interferon, Interleukin, and Growth Factors. AHCC is also an immunotherapy; it fuels the body's defense system by stimulating the production of certain immune cells. However, AHCC is not a drug, it is a functional food and does not have the side effects that can be associated with pharmaceuticals.

How does AHCC work? **Oral supplementation with AHCC induces interleukin-12 (IL-12) and interferon (IFN)-gamma.**¹ Interleukin and interferon are natural proteins released by immune cells that have been

activated by foreign agents such as bacteria, viruses, parasites or tumor cells. They are part of a larger family called cytokines, the messengers of the immune system. IFN-gamma is released by T cells and it regulates immune function by activating macrophages. It is an important messenger in the control of infections and cancer. Individuals who cannot produce IFN-gamma have a predisposition to microbial infections.² IFN-gamma also promotes host reaction to certain cancers.³ On the other hand, the production of interleukin-12 leads to the proliferation of natural killer (NK) cells and T cells.⁴ It increases the cytotoxicity (the ability to kill other cells such as cancerous or infected cells) of NK-cells, accelerates the differentiation from Th-0 (naïve T cell) to Th-1 (effector T cell) cells, inhibits angiogenesis (the formation of new blood vessels) and suppresses TGF- β (an immunosuppressive cytokine).⁵ IL-12 has suppressed tumor growth in all murine models examined and its antimicrobial activity has been demonstrated in bacterial, yeast, parasitic, and viral models of infection.⁶

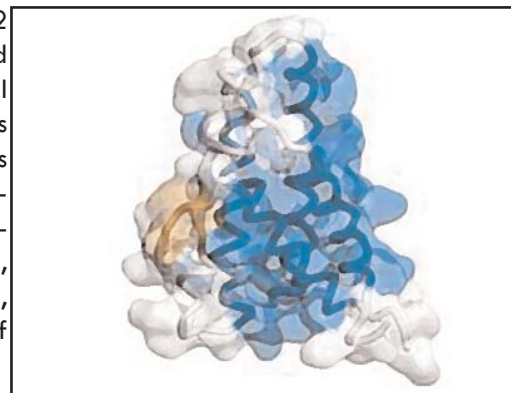


Figure 2: Cytokines, the messengers of the immune system

Sounds complicated? Not really, the function of the immune system is to protect us from potentially pathogenic organisms or substances. In order to accomplish this task, the immune system must recognize the offender - in this case with T cells. Once the threat has been identified, messengers are released -IFN-gamma and IL-12. These messengers are specific and they activate the components of the immune system best suited to eliminate a particular pathogen. Once the appropriate cells are mobilized they attack the foreign substance: If they can eliminate it, health returns; if they cannot, the disease progresses. AHCC feeds your immune reaction, it allows you to produce more of the messengers which up-regulate the production and mobilization of certain key immune cells. It is a valuable ally in several diseases where immunity is lacking.

A Never-Ending War

In 1972, Richard Nixon declared "war on cancer". As a legacy, the US President wanted to eliminate the word cancer from the dictionary. 33 years later, we have made little progress. In Canada, for instance, the incidence of both breast⁷ and prostate⁸ cancers are on the rise. The costs associated with cancer are astonishing. **In 2004, the United States lost \$189.8 billion to cancer⁸ and yet, only \$4.8 billion was spent on research in 2005¹⁰** regardless of the fact that in 2002 it was estimated that 62 % of US

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cancers were preventable.¹¹ Unfortunately, prevention has not been the main focus. For example, since its creation in 1985, the Cancer Research and Prevention Foundation has had a cumulative budget of \$66 million in support of cancer prevention, early detection research and education programs.¹²

Our fight against cancer has been a failure. **According to the World Health Organization, global cancer rates could increase by 50% to reach 15 million cases by 2020.**¹³ We have increased the survival rate for cancer but we have failed to lower the incidence. Cancer will not go away if we cannot prevent it.

So how is cancer prevented? Cancer is a disease of the immune system. **The immune system protects the host against the development of primary cancers but it is also responsible for tumor immunogenicity (eliciting an immune response).**¹⁴ It is up to our immune system to recognize and destroy cancerous cells. Immunosurveillance is the pillar of cancer prevention. Individuals born with immunodeficiencies are 200 times more likely to develop cancer or AIDS and immunosuppressed patients have more malignancies.¹⁵

Hence the great promise of immunotherapies - therapies with the aim of enhancing the immune system instead of trying to kill cancer cells.

A new hope

Stimulating and supporting the immune system's front-line defense has become one of the most promising avenues of cancer treatment and prevention. **Several immune cells**

are involved in the prevention and destruction of cancerous tumors.

If immunity is suppressed, T cells cannot recognize cancer cells and the cancer proliferates.¹⁶ **Natural Killer (NK) cells are some of the most effective cells in the body's fight against cancer.**¹⁷ One month of AHCC supplementation increased NK cells activity for up to 6 months.¹⁸ Therefore, it is not surprising that AHCC is an effective therapy in the prevention and treatment of all cancers, except cancers of the blood.¹⁹ AHCC is a much more humane approach because it is nontoxic. In addition, it alleviates some of the common side effects associated with more conventional cancer therapies. AHCC improved the quality of life (function, performance, psychological state and social interaction) of 28 patients after 2 months of supplementation;²⁰ it also improved the performance status of 38 patients who had used it for 6 months.²¹

The Scent of Wellness

Let's say one of the plants in your garden is dying because it is infested by parasitic insects. Your immediate thought is that you need an insecticide, right? Well, what if the plant, when healthy, naturally produces a scent that attracts beneficial insects that are predators to the harmful insects? Impossible? Not really, as several plants produce scents that attract beneficial insects or repel harmful ones. Wouldn't it make more sense to fertilize your garden then? Well, that is exactly what is happening here. Doesn't it make more sense to feed your body so that it will produce the immune cells that it needs to get rid of the cancer? Impossible?

AHCC was proven effective in several cancer research projects. In a study on 18 cancer patients who had already failed conventional therapy, AHCC and alimentary therapy led to a 22% tumor reduction, and 39% tumor stabilization.²² The combination of AHCC and genistein concentrated polysaccharide (another natural anti-tumor substance derived from soybeans) proved to have synergistic effects and induced apoptosis (the self destruction of unwanted cells).²³ Similarly, supplementation of AHCC with an antioxidant extracted from buckwheat led to the reduction of skin cancer tumors in test rats.²⁴ In another study, 6 months of treatment with AHCC (6g/day) led to a partial response in 49.7% of cancer patients and a complete response in 8.8%.²⁵

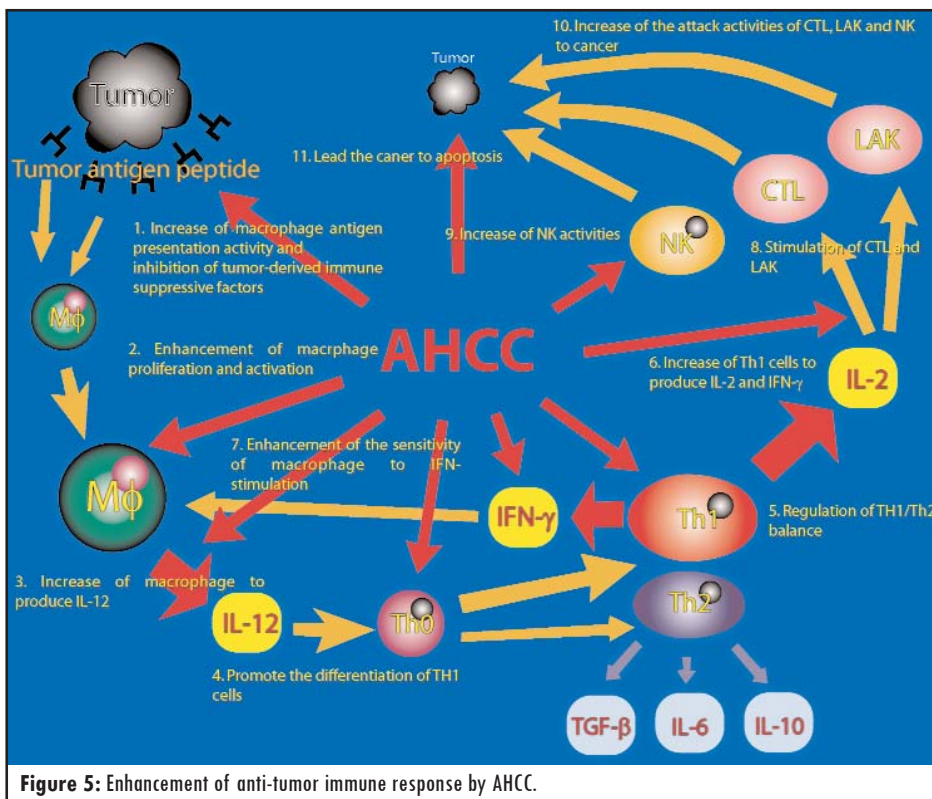


Figure 5: Enhancement of anti-tumor immune response by AHCC.

A More Aggressive Approach

What if you could use the insecticide and fertilize your garden concurrently? Makes sense- you would help your plant to stay healthy while dealing with the infection and the added stress of the toxic insecticide. With cancer, there is always a concern that supplementation with alternative therapies could reduce the efficacy of conventional treatments. **Studies using AHCC in combination with surgery or chemotherapy clearly demonstrated that AHCC safely increases the efficacy of conventional treatments while reducing the frequency of side effects.**²⁶ AHCC and UFT (an oral cytotoxic chemotherapeutic drug) co-administration was more effective at preventing metastases and led to a tumor growth suppression rate of 39.1%,14.4% better than the rate of the patients who were given UFT alone.²⁷ In another study, patients with non-excision pancreatic carcinoma receiving AHCC with chemotherapy and radiation had a better prognosis than the group who only received chemo and radiation. The AHCC-treated group's tumor size shrunk and tumor markers decreased.²⁸ Treatment with AHCC and chemotherapy was more effective than chemotherapy alone in the treatment of incurable or irremovable carcinomatous peritonitis.²⁹

A Stake For Your Plant

Just like a fertilizer, AHCC nourishes the body that has been depleted by cancer and conventional treatments. Comparable to a stake for the plant in your garden, it supports your body and more specifically your immune system. **A weakened immune system is one of the most serious side effects of chemotherapy.**³⁰ At a time when a viable immune response is crucial to prevent the spread and growth of cancer, the body is weakened by a toxic chemo-therapeutic agent used to kill the tumor cells. AHCC helps to preserve immunity even when anti-cancer drugs are administered. For example, AHCC restored the NK cell activity in rats given UFT.³¹ It also increased macrophage activity, IL-12 levels³² and inhibited the immuno suppressive cytokine TGF- β .³³ **AHCC's benefits are not limited to improved immune function; it also reduces the toxicity and side effects associated with chemotherapy.** One of the most distressing side effects of chemotherapy is alopecia (hair loss).³⁴⁴ Researchers showed that AHCC-treated rats were protected from chemotherapy-induced alopecia. Myelosuppression (the suppression of the bone marrow's production of blood cells and platelets) is another common and serious consequence of chemotherapy. Chemotherapy regularly leads to a 50% decrease in red and white blood cells.³⁵ Myelosuppression

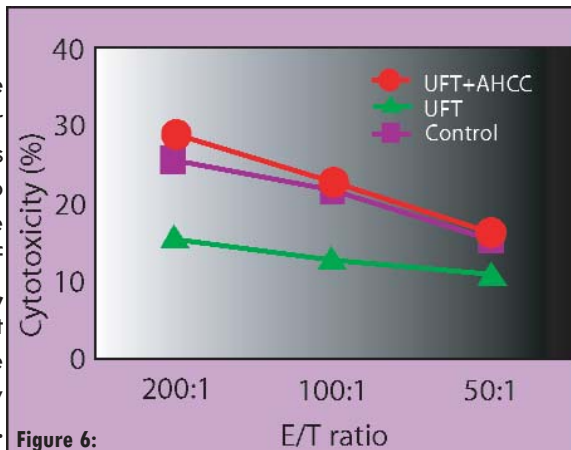


Figure 6: NK cell activity of spleen cells in ST-2 bearing rats administered AHCC.

leaves the patient susceptible to infections. In rats given fluorouracil and cyclophosphamide monohydrate - two chemotherapeutic drugs, AHCC co-administration normalized the red blood cell count.³⁶ Chemotherapeutic agents tend to be toxic for the liver. However, in a group of mice treated with 6-mercaptopurine and methotrexate concurrently with AHCC, liver enzymes remained normal - indicating that **AHCC is effective at preventing liver damage induced by chemotherapy.**³⁷ Patients taking

AHCC also reported less nausea and vomiting,³⁸ and AHCC is currently being used to increase patient's bodyweight and appetite.

Strength From Within

Now that the harmful insects are gone, how do you keep them away? The best way to keep them at bay would be to keep your plants and your garden healthy so that any further infestations could be avoided. Unfortunately, at present, there are very few proven strategies to reduce the risk of recurrence of tumors or cancer among survivors.³⁹ NK cells have been shown to be important in cancer incidence.⁴⁰ Chemotherapy and other conventional cancer therapies weaken the immune system and reduce the efficiency of NK cells,⁴¹ leaving the host more susceptible to recurrences. As we have seen, AHCC helps maintain the NK cell's competence. Therefore, it's no surprise that AHCC and chemotherapy completely inhibited lymph node metastases in rats.⁴² **AHCC also increased the survival rate and the recurrence free period in postoperative hepatocellular carcinoma patients,** a cancer where the recurrence rate is high. Only 34.5% of patients treated with AHCC had recurrences while 66.1% of the patients in the control group regressed. Similarly, 79.6% of the AHCC patients survived whereas 46.8% of the control patients died by the end of the follow-up period.⁴³

A Lesson In Immunity

There is a serious immunological disorder that we have all heard of, acquired immune deficiency syndrome (AIDS). The infection caused by the HIV retrovirus leads to a deficient cell-mediated immune response that is manifested by increased susceptibility to opportunistic infections and to certain rare cancers, especially Kaposi's sarcoma. The virus is transmitted primarily by exposure to contaminated body fluids, especially blood and semen. There are currently approximately 39 million HIV positive people worldwide.



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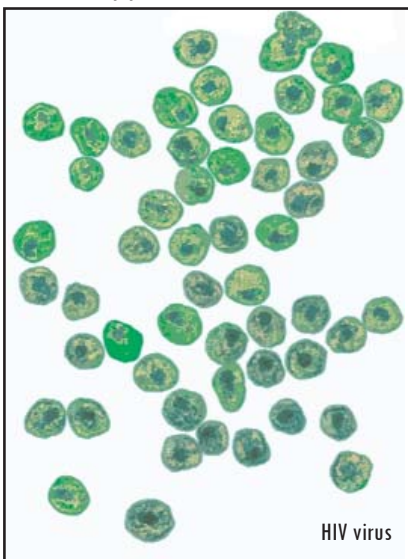
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Newer drugs have been successful in the treatment of HIV infection. For instance, highly active antiretroviral therapy (HAART) can slow the rate of progression from HIV to AIDS by 86% when compared with patients receiving no treatment.⁴⁴ Unfortunately, U.K. health experts found that after two years on HAART, 10% of the patients had become resistant to some of the drugs, 20% had developed resistance after four years and 30% had become resistant after six years.⁴⁵ Once the virus becomes drug resistant, outcome worsens.

Cast For The Same Mould

In cancer, the cancerous cells escape the wrath of the immune system by avoiding recognition. In HIV infection, the process is slightly different. The viral infection eventually leads to the destruction of the immune system and the patient becomes immunodeficient. **HIV attacks activated T helper cells, the very cells that should coordinate the body's antiviral defenses.** The virus is then left unchecked and ravages the host. Conventional approaches have focused on the suppression of the HIV virus. **In HIV, as with cancer, the immune system has been incapacitated.** Couldn't immune enhancement also prove to be beneficial in HIV infection? Perhaps there is a way for the immune system to keep the HIV virus in check. After all, other viruses such as chicken pox or mono remain in the body even after recovery.



A team of researchers at the Massachusetts General Hospital showed that HIV levels can remain suppressed without drugs if the immune system is functioning adequately.⁴⁶ This suggests that immunotherapies may be useful in HIV infection. In one study, AHCC was used in the treatment of 20 HIV positive men. NK cell cytotoxicity was increased by 220% after one month and by 440% after 3 months. Blood analysis also showed that CD4+ T cell (Helper T cells) counts increased in 14 patients by 120% and CD8+ T cell (cells that can remove HIV infected cells) counts increased in 12 patients by 137%.⁴⁷

Caught Off Guard

An infection, whether it is bacterial, viral, fungal or parasitic is caused by the invasion and the multiplication of pathogenic microorganisms. Infections can cause tissue injury and progress to disease through cellular or toxic mechanisms. Approximately one hundred thousand billion bacteria, most of which are beneficial, inhabit our body.

Consequently, we hold ten times as many bacterial cells as human cells. It is estimated that we carry 500 to 1000 different species of bacteria. Many of the microorganisms normally found in humans are opportunistic pathogens. Adequate immunity is therefore crucial in preventing infections.

Conventional treatment of infection relies on antibacterial drugs, antifungal drugs, antiviral drugs, antiprotozoal drugs and antihelminthics. Unfortunately, the resistance to drugs such as antibiotics is increasing at an alarming rate.⁴⁸ For instance, about three per cent of all newly diagnosed tuberculosis patients have multidrug-resistant tuberculosis.⁴⁹ Once again, immunotherapies hold a promising role as new modalities of treatment will need to be developed. **Several experiments confirmed AHCC's competence in the control of infections.** Immuno-suppressed rats were administered AHCC for 4 days before *Candida Albicans* (a fungus) and *Pseudomonas aeruginosa* (a bacterium) were introduced intravenously. AHCC supplementation continued for 2-4 weeks after inoculation. When compared to the control group, the group fed AHCC had a longer survival period.⁵⁰ AHCC was also shown effective for patients with chronic viral hepatitis, destroying the hepatitis type B virus through enhanced immune activity. Supplementation increased antibody levels.⁵¹ Once again, protecting the immune system's resources proves to be an effective strategy in disease treatment and prevention.

Water In Your Wine

There are several ways to injure our liver. Heavy alcohol consumption, certain drugs, viral hepatitis and poor nutrition are common causes of liver pathology. The liver is the largest organ in our body and it is responsible for over 500 vital functions. One of the functions of the liver is to breakdown harmful substances and to excrete them in the blood or bile. An excess of toxins can damage the liver. Injury leads to the lysis of liver cells and, as a result, liver enzymes increase in the blood circulation. Liver function and disease are usually monitored through those enzymes. **Trials have demonstrated that AHCC protects the liver and improves hepatic function.** Three of ten mice given galactosamine to induce acute liver injury died within 24 hours, whereas the mice given AHCC and galactosamine all survived. The AHCC-fed group also had much lower ALT and AST (liver enzymes).⁵² The protective effect of AHCC on the liver was demonstrated in another study on mice receiving 1g/kg/day of AHCC for 3 days followed by 0.4ml CCL4 (a liver poisoning substance used to induce experimental liver injury) administered by peritoneal injection for 4 days.

Treatment with AHCC prevented the decrease of cytochrome P-450 (a family of the body's more powerful detoxification enzymes) and prevented the increase in ALT from 365.9 IU versus 164.7 IU in the AHCC group. AHCC

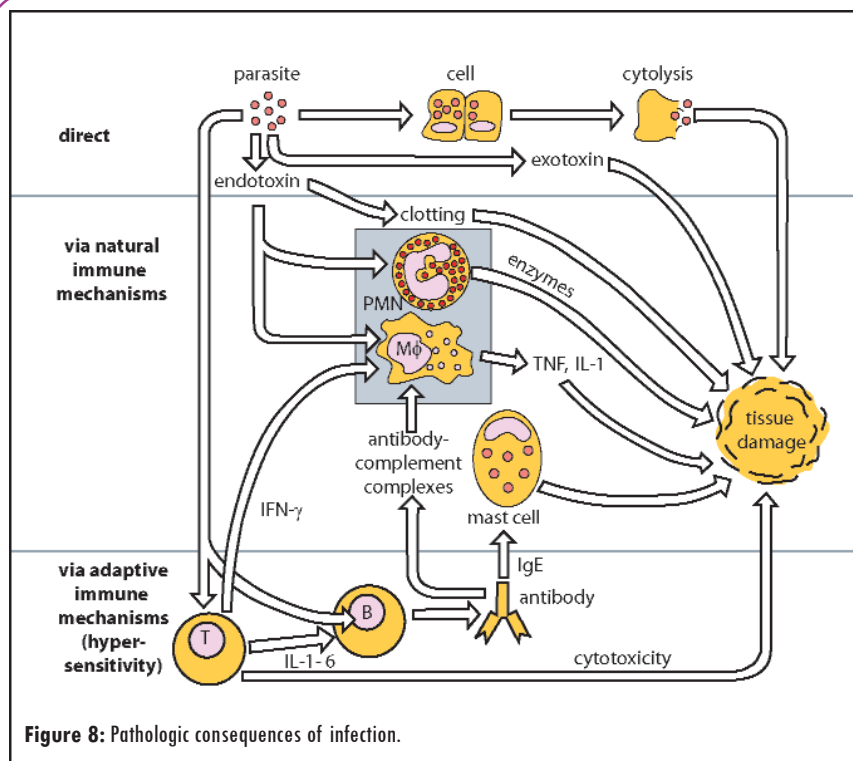


Figure 8: Pathologic consequences of infection.

cytokine), levels were lower in the AHCC treated group.⁵⁷ AHCC also inhibited cell death induced by calprotectin (a marker of inflammation).⁵⁸ It was also reported that patients taking AHCC to prevent the recurrence of cancer had significant improvements in rheumatoid arthritis.⁵⁹ **It is thought that AHCC reduces inflammation by modulating the immune system and by improving fat metabolism through the hormone leptin.**

Follow the light

AHCC has shown promise in the treatment of a variety of other conditions. Diabetic patients have been shown to respond to AHCC.⁶⁰ In rats given Streptozotocin to induce diabetes,⁶¹ AHCC treatment prevented the onset of diabetes. In patients given 3g per day of AHCC for 6 months, both blood glucose levels and glycated hemoglobin levels decreased.⁶² AHCC also appears to be an adaptogen - capable of producing changes in the body to combat stress. In AHCC pre-treated rats

subjected to immobilization stress, norepinephrine, epinephrine, dopamine and glucose plasma levels did not increase.⁶³ AHCC could also be effective in the treatment of stress-induced hypertension.⁶⁴

AHCC is very safe even at extremely high doses. The research has shown that dosages of 3g per day and 6g per day both increase NK cell activity. In active cancer, the recommendation is 3g per day for at least 2 weeks followed by a maintenance dose of 1g per day. Dosages of 6g per day have been used in hepatitis and for support in patients undergoing chemotherapy.⁶⁵

Everyday we rely on our immune system to remain healthy. We are exposed to a variety of bacteria, viruses and other potential pathological organisms on a daily basis. Why is it that when we get sick we direct the treatment on those pathogens and not on our innate and acquired aptitude to fight and prevent disease? The great promise of immunotherapies lies in their ability to stimulate our defense

also averted necrosis of liver cells.⁵³ In postoperative hepatocellular carcinoma patients, AHCC supplementation led to a significant improvement in AST, GGT and cholinesterase (liver markers).⁵⁴ The exact mechanism through which AHCC exerts its protective effect on the liver is unknown, but in clinical studies AHCC proved to be effective at preventing hepatic injury.

Better Than Your Ice Pack

In 2003, non-steroidal anti-inflammatory drugs (NSAID's) ranked at number 4 in global pharmaceutical sales. The treatment of inflammation is a huge market, and in 2001, \$265 million was spent on promoting Vioxx® and Celebrex® to consumers, more than for any other drug.⁵⁵

Inflammatory conditions are becoming more and more problematic. **An estimated 40 million people in the United States have arthritis and by the year 2020, 59 million Americans are expected to suffer from the disease.** Furthermore, arthritis is the leading cause of disability among adults aged 65 and older.⁵⁶ Side effects are common with the long-term use of NSAID's. Heartburn, nausea, indigestion and constipation are some of the most frequent side effects. More serious consequences include gastrointestinal bleeding and cardiovascular problems. AHCC has been evaluated for its capacity at reducing inflammation. AHCC was effective at diminishing inflammation in a group of mice injected with dead enterococcus faecalis (a bacterium) to induce inflammation. Tumor necrosis factor (TNF- a proinflammatory

Rank	Audited World Therapy Class	2003 Sales (\$bn)	% Global sales (\$)	% Growth (constant \$)
1	Cholest. & Triglyceride Reducers	26.1	6%	+14%
2	Anti-ulcerants	24.3	5	9
3	Antidepressants	19.5	4	10
4	Antirheumatic Non-Steroidals	12.4	3	6
5	Antipsychotics	12.2	3	20
6	Calcium Antagonists, Plain	10.8	2	2
7	Erythropoietins	10.1	2	16
8	Anti-Epileptics	9.4	2	22
9	Oral Antidiabetics	9.0	2	10
10	Cephalosporins & Combinations	8.3	2	3
	Total Leading 10 ATCs at Level 3	\$142.0bn	30%	+11%

Table 1: Leading therapy classes in 2003 global pharmaceutical sales

system. AHCC's ability to improve immunity has been demonstrated. It is supported by research as an effective treatment for cancer, AIDS and infections; it also has the ability to protect us from toxic substances such as chemotherapeutics. It is a much more humane treatment with far fewer side effects. After all, it addresses our health, not the disease.

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