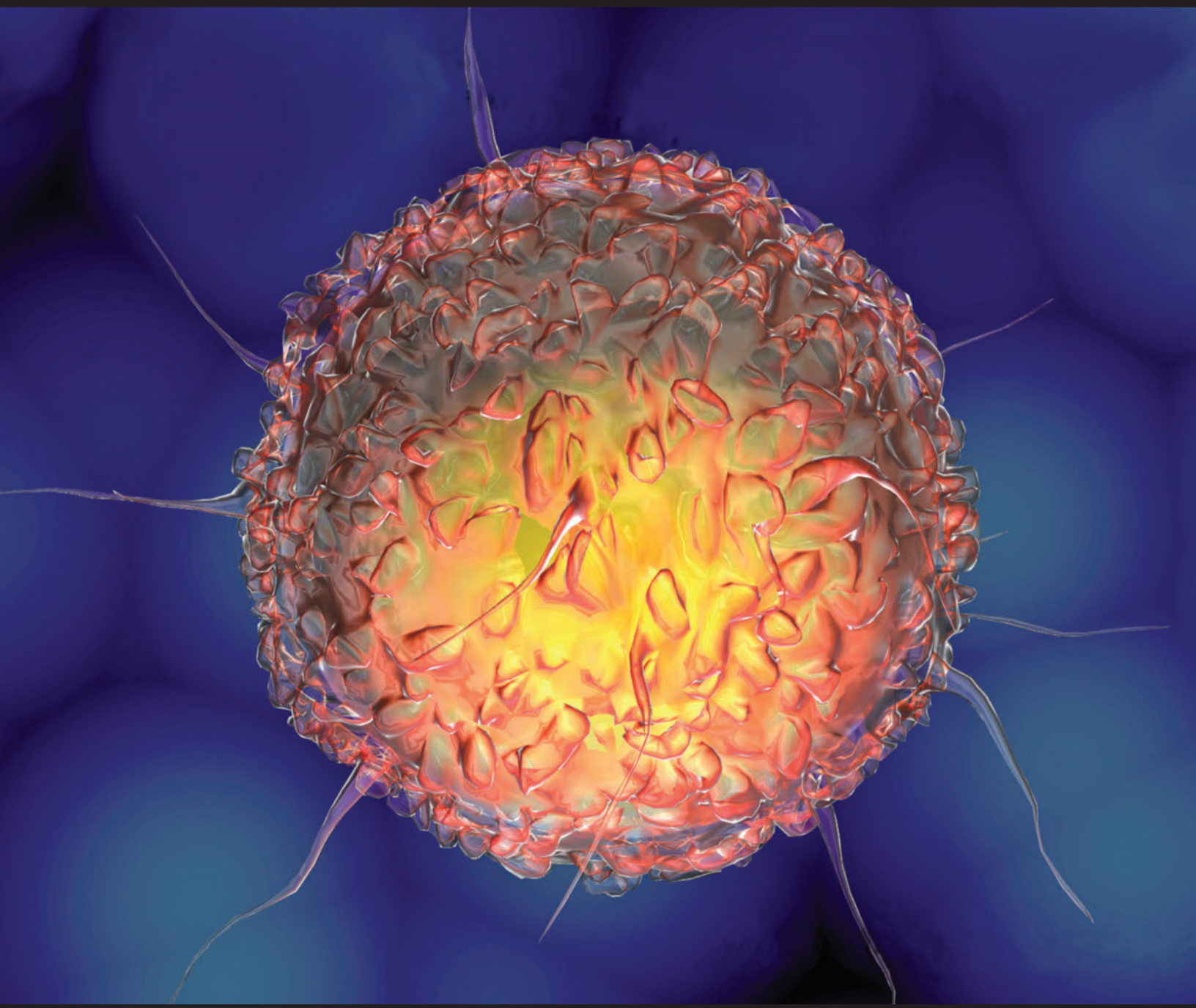
Turbocharging Chemotherapy with Active Hexose Correlated Compound



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A diagnosis of cancer is often terrifying experience. The prospect of having cancer invokes fear of pain, suffering and death. The treatment of cancer is, for many, as terrifying as the disease itself.

Chemotherapy, the mainstay of conventional treatment, is perhaps the most feared treatment of all. While singularly effective at destroying cancerous cells, unfortunately chemotherapy causes harm to healthy tissues as well. This harm, in turn, commonly causes nausea, diarrhea and/or constipation, mouth sores, fatigue, and numbness and tingling of the extremities. While the last few decades have witnessed significant advancements in the development of anti-nausea, anti-diarrheal and neuropathy-relieving medications, chemotherapy side-effects still occur. The need for additional therapies that will reduce the toxicity of chemotherapy is great. One such therapy is Active Hexose Correlated Compound, or AHCC. **AHCC is an enzyme-fermented extract of cultured mycelium (vegetative body) of Basidiomycetes mushrooms.** AHCC, through its potent immune enhancing effects, **has the potential to significantly improve tolerance to, and benefit from, chemotherapy.**

What is AHCC?

Mushrooms have been used medicinally in Asia for centuries. Medicinal mushrooms possess strong immune enhancing activity. Unfortunately, the polysaccharide compounds in mushrooms responsible for immune stimulation are bulky, heavy compounds which are poorly absorbed into the blood. AHCC represents an exciting alternative. AHCC was developed in Japan in 1989 by the Amino Up Chemical Company. AHCC is created by reacting several types of mushrooms with enzymes. The resulting product is unique and is not found in mushrooms. The majority of AHCC is made up of streamlined molecules (oligosaccharides, low weight GI-polysaccharides and α- and ß-glucans) that weigh much less than those found in mushrooms. In contrast to medicinal mushrooms, these streamlined molecules are easily absorbed into the bloodstream. In the body, they exert powerful immune enhancing, antioxidant, and anti-cancer actions.

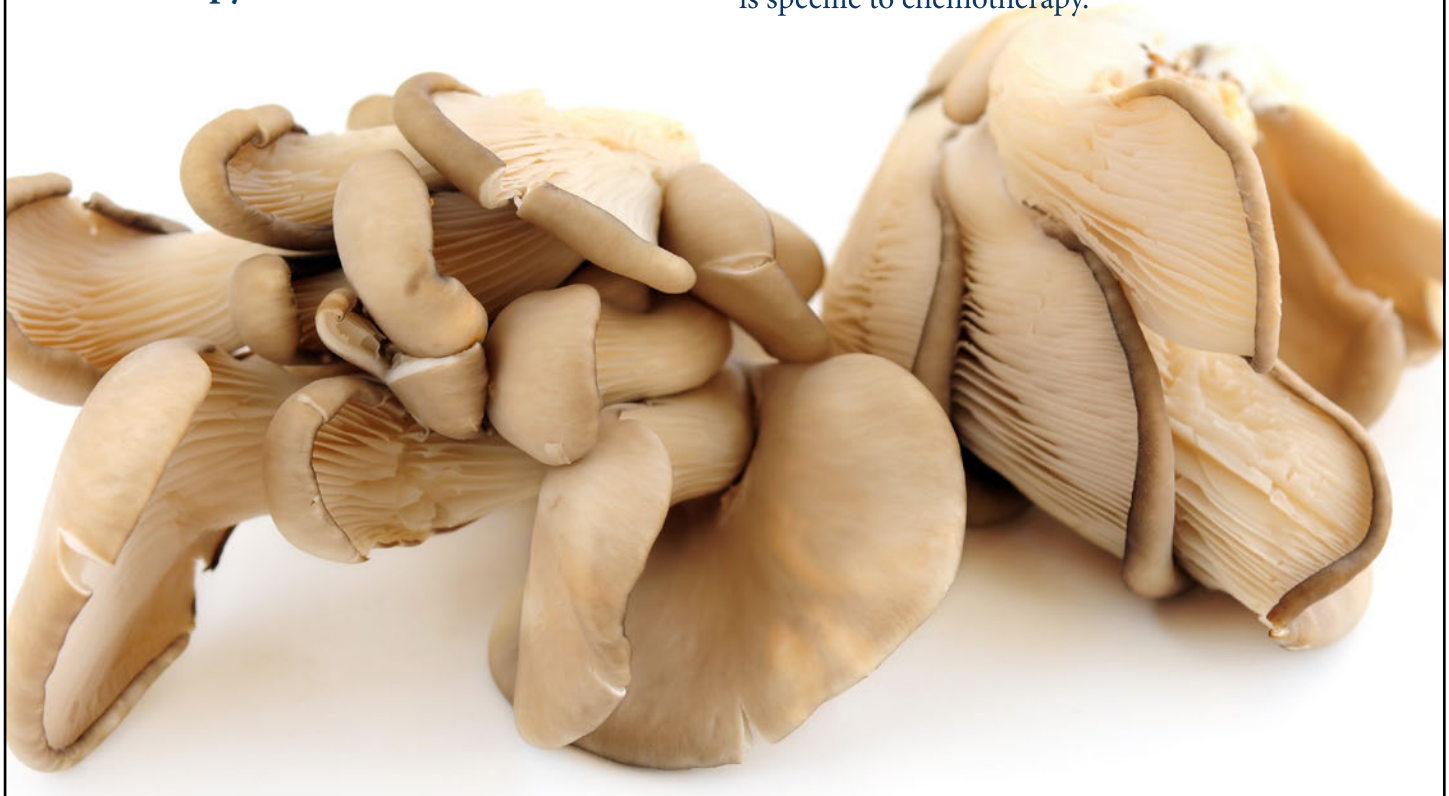
What makes AHCC so exciting in the realm of cancer therapy is its ability to both improve the duration and the quality of life in patients diagnosed with cancer. Two clinical trials of patients diagnosed with highly incurable primary liver cancer, have shown that the individuals who were given AHCC experienced a significant prolongation of life as well as dramatic improvement in their quality of life. Equally as exciting is the benefit of AHCC in patients receiving chemotherapy and radiation. AHCC appears to reduce the negative side effects of chemotherapy and radiation while enhancing the tumor killing effects of chemotherapy and radiation. This translates into higher quality of life and increased survival times for patients with cancer. Before we explore the effects of AHCC on chemotherapy, let's take a peek at its potent immune effects. This is important because AHCC's effects on immune function are the basis of its synergistic actions with chemotherapy. In addition, the majority of people with cancer are already immune suppressed and both chemotherapy and radiation only aggravate this immune deficiency.

AHCC and the Immune System

One of the reasons that cancer cells are so dangerous is that they directly suppress immune function. Specifically, cancer cells suppress macrophages such as dendritic cells. Dendritic cells are like the roving eyes of the immune system. As soon as they 'see' a cancerous cell or an infected cell, they send out chemical signals (namely IL-12) which trigger the rest of the immune system into action. In response to these signals, white blood cells, specifically cell-killing (cytotoxic) T cells and natural killer (NK) cells, either digest the cancerous or infected cell or produce cell killing compounds which are injected into these cells. **This orchestrated sequence of events forms our initial, and most important, defense against cancer.** Unfortunately, in the case of established cancer, this immune reaction comes to a screeching halt. Cancer cells release several kinds of immune suppressive factors which inhibit dendritic cell activity. The suppressed dendritic cells fail to produce IL-12 and thus our normally sophisticated and elegant immune response does not occur. In this way, the immune system is blind to the growing cancerous tumor. **This dangerous situation allows cancerous tumors to grow uncontrollably.**

Immune suppression is of particular concern for those people receiving chemotherapy. **Chemotherapy adds insult to injury in the case of the immune system.** One of the cell populations that is vulnerable to the cell-killing (cytotoxic) effect of chemotherapy are the immune stem cells in the bone marrow. As these cells are destroyed, the body cannot make sufficient white blood cells – the immune cells in our body. Thus, the immunity in people with cancer receiving chemotherapy, is crippled in two ways – there are insufficient white blood cells being produced due to the myelosuppression from chemotherapy and those white blood cells that are available are blinded to the tumor due to the cancer-caused immune suppression. **Thus, reversing and restoring suppressed immune function is a critically important part of treatment for those receiving chemotherapy.**

AHCC is a potent immune enhancing agent. AHCC has been shown in humans to increase both the number of dendritic cells and their ability to stimulate the rest of the immune system. **AHCC increases the production of IL-12 and interferon gamma (IFN-γ).** These are the major signaling molecules secreted by dendritic cells in order to activate cytotoxic, tumor destroying T cells. In addition, AHCC specifically increases the activity of NK cells in cancer patients. The combined effect is to unchain the immune system and to allow it to respond to, and destroy, cancerous cells. These immune-mediated anti-tumor effects have been demonstrated against melanoma and lymphoma cancer cells in tumor bearing rodents. The immune enhancing effect of AHCC is reason enough to consider using it, especially when receiving immune-suppressive chemotherapy treatment. Remarkably, there is additional benefit from AHCC that is specific to chemotherapy.



AHCC and Chemotherapy

AHCC may be a perfect fit for chemotherapy. The effect of AHCC on the actions of cisplatin, one of the most commonly used chemotherapy drugs, illustrates this positive relationship. While cisplatin is effective against the majority of solid tumors, it causes significant toxicities. Nausea, kidney damage, nerve damage, hearing loss, and overall feelings of being unwell (malaise) often accompany its use.

These side effects make treatment with cisplatin quite distressing for the patient and, if severe enough, can limit the dose and duration of therapy, thereby decreasing its **potential to destroy the cancer.** This is where AHCC comes in. In an animal study, co-administration of AHCC with cisplatin increased tumor destruction while simultaneously decreasing toxicities associated with cisplatin.

Specifically, kidney toxicity, bone marrow suppression and weight loss were all improved when AHCC was given along with cisplatin. Another rodent study showed that AHCC worked synergistically with chemotherapeutic agents tegafur and uracil (UFT). Rats who received the AHCC in addition to the UFT experienced greater reduction in their mammary tumors (rodent model of breast cancer) and decreased metastasis (spread). In the AHCC-fed rodents, macrophage and NK cell activity was significantly increased, suggesting that the immune enhancing effect of AHCC was responsible for this synergistic effect with UFT chemotherapy.

Researchers in Japan have reported some preliminary findings that further support the syngergistic role of AHCC and many other chemotherapy agents. The side-effects of 5-FU, paclitaxel (Taxol), cyclophosphamide (cytoxan), 6-mercaptopurine (Purinethol), methotrexate, and cytosine arabinoside (Ara-C) were all significantly decreased in mice that were fed AHCC along while receiving the chemotherapy. The AHCC-fed mice experienced less kidney damage, less bone marrow suppression and therefore increased white blood cell, and decreased liver toxicity. **Reiki Ishizuka of the Tajima Clinic in Sapporo Japan has reported on increased survival and improved quality of life in patients with lung, breast and colon cancers who were taking AHCC along with their conventional chemotherapy treatments.** All patients taking AHCC had improved immune function, indicating that the immune enhancing actions of AHCC are how AHCC improves the benefits of chemotherapy. Although these findings are preliminary, there is a growing body of evidence to support the use of AHCC along with chemotherapy – to improve its benefits and to reduce its side effects.

Safety of AHCC

AHCC appears to be a very safe compound. Animal toxicology studies have failed to show toxicity at extremely high doses. AHCC has also been shown to be safe in humans. In a phase I clinical trial, AHCC given in doses of 9g a day failed to cause any abnormalities in blood values. This high dose was also well-tolerated by the majority of the subjects. Mild and transient nausea, diarrhea, bloating, headache and fatigue occurred in 15% of the subjects taking 9g daily – a dose much higher than typical doses used clinically.

Whenever using a natural substance alongside conventional chemotherapy, it is important that the natural agent does not interfere with the intended action of the chemotherapy agent. When a natural substance interferes with chemotherapy, it typically does so by interfering with the metabolism of the chemotherapy drug. This interference occurs in one of two ways. The natural substance may decrease the activity of the enzyme that normally breaks down the chemotherapy agent. **When this occurs, the drug is not broken down efficiently so it remains in the bloodstream longer.** This allows more time for side effects to occur. The other way that a natural substance can interfere with a chemotherapy agent is by increasing the activity of the enzyme that breaks down chemotherapy agent. When this occurs, the chemotherapy drug is metabolized too quickly, jeopardizing the effectiveness of the chemotherapy.

These interactions affect the cytochrome P450 enzyme family. This family of enzymes are located primarily in the liver, but also throughout the body. These are the major enzymes responsible for both breaking down and for activating toxins, drugs, and hormones in our body. Many substances affect the activity of these enzymes and concurrent consumption of certain of these substances creates the potential for changing the metabolism of drug(s). Fortunately, AHCC does not inhibit any of the major drug metabolizing cytochrome P-450 enzymes (2C8/C9, 3A4) thus interference with chemotherapy drugs is highly unlikely. AHCC was shown to increase the CYP450 2D6 enzyme pathway in a cell study with hepatocytes. Tamoxifen, a commonly prescribed anti-estrogen hormonal therapy for women with breast cancer, requires CYP450 2D6 to be activated. Thus, there is a possibility that concurrent use of tamoxifen and AHCC may increase the activity and toxicity of tamoxifen. Although there are some case studies on breast cancer patients showing efficacy of AHCC with Tamoxifen, it is not known how significant this interaction is, and until more is known about the significance of these interactions, concurrent use of AHCC with tamoxifen should be approached with caution. At this point, caution is limited to tamoxifen as the metabolism of all other chemotherapy agents studied thus far appears to be unaffected by AHCC.