



AHCC and Cancer: A Prospectus

A Different Approach

Is a condition such as acute renal failure specifically a disease of the kidneys? Is pulmonary fibrosis specifically a disease of the lungs? Is cirrhosis specifically a disease of the liver?¹ Perhaps the time is ripe to approach these questions from a broader perspective.

Enter AHCC

AHCC, or Active Hexose Correlated Compound, is a monosaccharide, a simple sugar derived from the mycelium of a member of the basidiomycetes family of mushrooms known as the Shiitake.² The mushroom blend itself, which is in fact a hybrid, is developed in a pre-cultivation tank.³ The basidiomycetes mushroom colonies are then cultured in a main cultivation tank where they undergo a thorough fermentation process that consists of advanced cultivation, enzymatic decomposition, sterilization, concentration and finally freeze-drying.⁴ This is done in tanks as large as 15 tons for as long as 45 days.⁵ This must be done under strict controls.⁶ The fermentation process breaks down nutrients into a form that is most easily assimilated by the body's digestive system.

The tangible end result is a product that has an exceptionally low molecular weight of 5,000 daltons, most

impressive when compared with the molecular weight of most mushroom extracts, which are measured in the hundreds of thousands of daltons.⁷ Arguably the most active nutrient in AHCC is acetylated α -glucan, a component known to enhance the immune system.⁸ However, in addition to merely breaking down nutrients, the cultivation and enzymatic decomposition segments of the fermentation process creates new nutrients.

The beneficial applications of AHCC are centered on its ability to augment the immune system. However, it is also renowned for helping patients with HIV, hypertension, hypoglycemia and endocrine system modulation. It is even known to have cosmetic applications with respect to alopecia (hair loss).⁹ However, it is as a concurrent treatment to chemotherapy that AHCC has carved out the most distinctive role for itself.

There are no fewer than 700 Japanese hospitals dispensing AHCC as part of various protocols.¹⁰ In addition, 15 Japanese medical colleges and universities are conducting research with AHCC, not to mention additional research being undertaken in China, South Korea, Thailand and the United States.¹¹

Enter The Immune System

The immune system is composed mainly of white blood cells, and there are several sub-categories of white blood cells that seem to be exclusively designed by the body to directly resist invasive threats. They are; macrophages, neutrophils, natural killer cells or NK cells, lymphokine activated killer cells (LAK), cytotoxic lymphocytes and T-helper cells.¹² All six of these sub-categories of white blood cells have at least one specific function in common: they serve as the front-line interceptors of the immune system. They circulate throughout the body searching for any abnormal cells as well as foreign substances, often referred to as antigens.¹³ These sub-types of white blood cells, also referred to as leukocytes, destroy the antigens at the point of contact before they have a chance to create any intracellular disturbance. It is the differing specific mechanisms used by these white blood cells to decimate the antigens that distinguish them best from each other.

Macrophages and neutrophils destroy any foreign bacteria through a process called "phagocytosis", which closely matches its literal translation in Greek - cell eating. Macrophages and neutrophils literally engulf and digest any microbes perceived as a threat by the immune system. On the other hand, natural killer cells, lymphokine activated killer cells (LAK), and cytotoxic lymphocytes attach

themselves to the surface of the perceived micro-cellular threat, and like reptilian predators inject their targets with a granule that causes a chemical reaction. That chemical reaction leads to the destruction of the anomaly in question.¹⁴ T-helper cells exert much of their influence by maintaining a favourable balance between two of their manifestations, namely T-helper cell type 1 cells (Th1) and T helper cell type 2 cells (Th2).

It is absolutely critical to stress that the immune response system is inherently dependent on its ability to recognize a foreign protein or bacteria as abnormal before it can direct countermeasures against it. While macrophages and natural killer cells serve as the actual combatants against any cellular abnormality, they require intracellular messengers that would disseminate information between cells in order to initiate and sustain the immune response. These intracellular couriers are a biologically active family of proteins called cytokines.¹⁵ There are numerous types of these intracellular messengers, but the ones most directly pertinent to the immune response are: interferon (specifically gamma interferon); interleukin-2 (IL-2); interleukin-12 (IL-12); and tumor necrosis factor (TNF).¹⁶

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How Does AHCC Work?

AHCC exerts its influence on the immune system in a process that directly involves all of the white blood cells touched upon thus far. This process naturally encompasses biochemical mechanisms that have multiple roles that overlap with one another, but if it were to be described in a step-by-step manner, it would likely resemble the table below:

A great deal of emphasis has been placed on studying AHCC's numerous distinctive benefits, such as its overall enhancement of the immune system, its stimulating effect on the different immune white blood cells such as macrophages, NK cells and CTL cells, its equally stimulating effect on the different cytokines, and finally its improvement of the Th1/Th2 balance.¹⁷

The most common ground that scientists seem to have isolated as the source for all these effects is that AHCC goes to work directly on the macrophage itself. It stimulates both the activity of the macrophages as well as their numbers, perhaps even doubling them.¹⁸ This would of course lead to the increased production of cytokines such as IL-12 and TNF (directly) in turn leading to the increased production of NK, LAK and CTL cells, not to mention more interferon (indirectly).¹⁹

OPTIMAL IMMUNE RESPONSE PROCESS

1. An antigen enters the human bloodstream.
2. Immune cells begin to produce interferon in response.
3. Interferon binds to macrophages and triggers their activation.
4. Macrophages then produce interleukin-12 (IL-12) and tumor necrosis factor (TNF).
5. IL-12 and TNF both simultaneously stimulate the T helper cells to manifest themselves into T helper cell type 1 cells (Th1) and T helper cell type 2 cells (Th2). The IL-12 also directly stimulates the activity and volume of natural killer (NK) cells, while at the same time TNF exerts its inflammatory capabilities to influence the apoptosis of the antigen.
6. It is absolutely critical that the manifested Th1/Th2 balance favours the production of Th1 cells as they produce interleukin-2 and more interferon. In sharp contrast, Th2 cells produce cytokines that suppress the immune response, such as IL-10, IL-6, and TGF- β .
7. The empowered Th1 cells then proceed to increase levels of IL-2 and interferon. The increased IL-2 levels result in the direct stimulation of the activity and volume of cytotoxic lymphocytes (CTL) and lymphokine activated killer cells (LAK). The increased interferon will further enhance the activity of the macrophage, resulting in a "feedback loop" that will perpetually increase the production of IL-12, which in turn will increase the activities of the NK cells.
8. The result of the combined efforts of the LAK, CTL and NK cells will be the apoptosis of the original invading antigen.

This is the optimal method by which the immune system would respond to an antigen. The reality of the matter, of course, is that what is optimal is often very far removed from what is standard. The purpose of AHCC is to make what is standard optimal.

AHCC and the Symptoms of Cancer Treatment

Currently, the standard options for cancer treatment are chemotherapy, radiation, and surgery. Chemotherapy is notoriously aggressive in that it can cause loss of appetite, hair loss, bone marrow suppression and liver damage, severe vomiting, and anemia.²⁰ Many of these symptoms can also be caused by radiation, and both treatments can inflict heavy damage on the patient's immune system. The result for the patient can be a dramatically reduced quality of life, which can easily lead to (or include) depression. Surgery, for all of its power of quick resolution, is infamous for draining its patients' recuperative abilities and very often causes unknown and unexpected complications of its own. This too, can lead to a dramatically reduced quality of life for patients.

A prospective cohort study with AHCC was performed from February 1, 1992 to December 31, 2001. A total of 269 patients with hepatocellular carcinoma (HCC) were studied. 113 of these patients were given AHCC following surgery and the remainder was not, and no placebo was used.²¹ The period of time for which each patient was examined was from immediate post-surgery until either recurrence or death (from any cause). The survival rate of the AHCC group was 79 percent compared to 51 percent for the control group.²² Furthermore, the recurrence rate among the AHCC group was 49 percent compared to 67 percent for the control group.²³ The conclusion of the researchers was that AHCC intake can improve the prognosis of postoperative hepatocellular carcinoma (HCC) patients.

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When the damaging effects of chemotherapy are examined more closely, it becomes increasingly clear how AHCC can play an invaluable role. This is because chemotherapy does not effectively distinguish between healthy cells and tumors. AHCC, on the other hand, stimulates and reinforces the white blood cells and cytokines which attack only the tumors.²⁴

In a large study involving 229 patients suffering from gastrointestinal cancer and undergoing subsequent chemotherapy treatment, the efficacy of AHCC as a chemotherapy support agent was put to the test.²⁵ These patients were being treated with a combination of 5-fluorouracil, CDDP, and other chemotherapy agents. 127 of

these patients were given AHCC while the remaining 102 were not. The results were decisive: 27 months into the study, the survival rate was 66.7% for the AHCC group and 35% for the control group. Among those patients afflicted with colon cancer, the survival rate for the AHCC group was 89.9% after 10.2 months of treatment as opposed to 55.9% for the control group after the same amount of time.²⁶

The chemotherapy drug UFT was also combined with AHCC in a study to determine if the two could produce a synergistic effect. The study determined that AHCC combined with UFT produced results on primary tumor growth and metastasis that UFT alone did not match.²⁷ These results seemed to be mediated by the fact that the AHCC/UFT combination enhanced NK cell activity, whereas UFT alone suppressed it.²⁸ This is most impressive since it implies that AHCC's immune system-enhancing effects more than compensate for UFT's suppressive ones.



AHCC in Combination with other Non-Toxic Therapy

AHCC's capabilities as an unparalleled synergist to other treatments is not limited to chemotherapy drugs. In fact, one animal study placed AHCC in combination with Genistein Combined Polysaccharide (GCP).²⁹ GCP is a "functional food" derived from cultivated basidiomycetes and soybean isoflavones, and is reported to have tumor suppressive capabilities.³⁰ Although the tumor growth was slowed in both the AHCC and the GCP groups, the AHCC/GCP combination had a more pronounced effect.³¹

AHCC and Quality of Life

Quality of life (QOL) parameters are a centerpiece of AHCC supplementation. They have been examined heavily in human studies with AHCC primarily because they have

such far-reaching implications. Not only do they improve recovery time and prevent recurrence, but they are also what allow AHCC to be so widely applicable. One indicator of QOL is the patient's ability to perform daily rudimentary tasks, and this was the exclusive indicator in a study used to measure AHCC's effect on QOL among 38 cancer patients who had not undergone surgery, chemotherapy, or radiation.³² It concluded that the QOL parameters were "significantly" improved after 6 months of AHCC therapy.³³ Another study included psychological state and social interaction as indicators of QOL. This particular study examined 28 cancer patients who

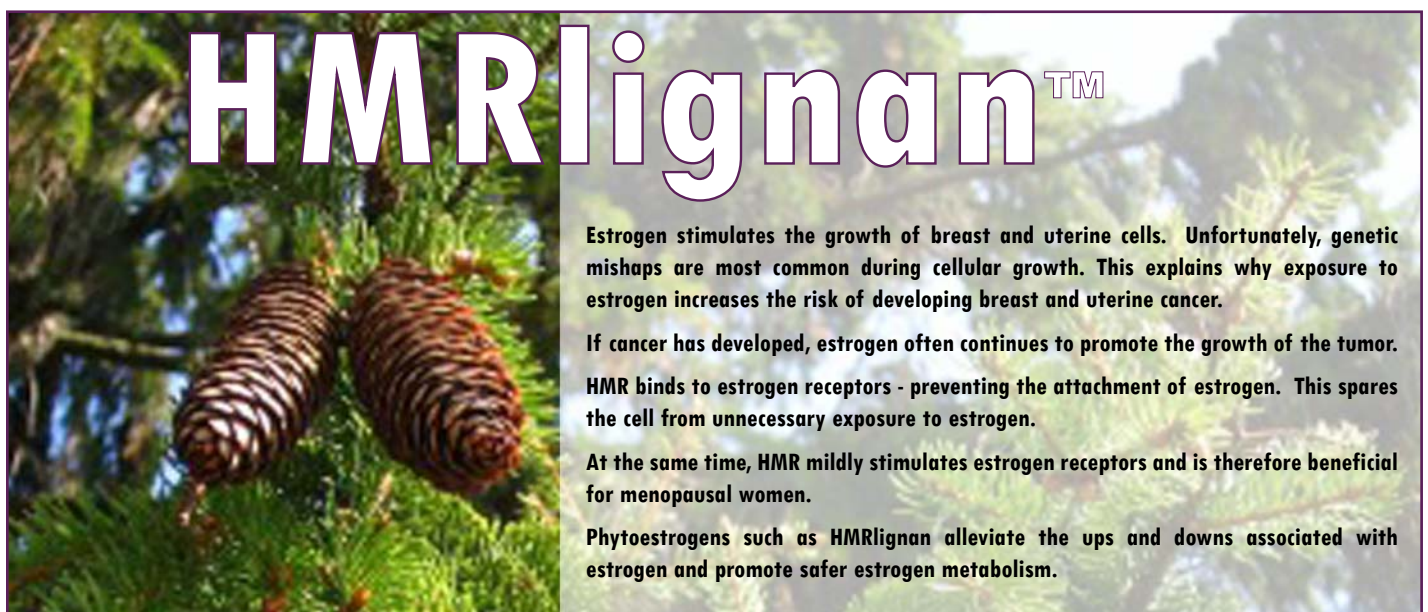
underwent AHCC treatment for 2 months, and it concluded that all parameters of QOL had improved significantly.³⁴

AHCC's effect on QOL makes it a worthwhile treatment for other conditions whose proliferation is dependent on the malfunction of the immune system. This would include autoimmune diseases, inflammation, opportunistic infections and HIV. This is because the improvements in QOL are simply the reflections of AHCC's effect on the immune system, and that effect is so fundamental that the list of afflictions alleviated by its use continues to grow.

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