Medical Intelligence: A Preliminary Report of Three Cases Influences of AHCC, a Combination Mushroom Extract, on PATIENTS WITH HEPATITIS  Joel S. Edman, D.Sc., and Fred Pescatore, M.D.

Medicinal mushrooms and their extracts have been reported to have a variety of biological effects including immunomodulation, anti-tumor properties, and beneficial influences on blood sugar regulation, serum lipids and blood pressure. Active hexose correlated compound (AHCC), a newly developed extract from a hybridization of several kinds of mushrooms, is one such product whose most active ingredient, among many, is thought to be an oligosaccharide with a molecular weight of approximately 5,000.

AHCC is derived from a process which begins with the culturing of several Basidiomycetes mycelia species, using rice bran as the primary food source. Once the colony reaches maturation, enzymes are added to form more bioavailable oligosaccharides from polysaccharide chains. Final processing includes centrifugation, freeze drying, and then the final product encapsulation consisting of AHCC extract, canola oil and cyclodextrin. Recent clinical and animal research has provided evidence for a variety of beneficial effects from AHCC supplementation.

For example, a retrospective investigation of 126 patients with histologically proven hepatocellular carcinoma, showed that those who took AHCC following hepatectomy had significantly higher overall survival and significantly longer tumor markers one year post-surgery. Animal study data has suggested that AHCC reduces metastasis of rat mammary adenocarcinoma, reduces side effects of anticancer drugs such as anemia, alopecia and liver injury, and is protective of chemically induced liver injury.

The likely influence of AHCC is as a biological response modifier (BRM) which activates or restores host immunity. For example, an investigation of oral AHCC administration to cancer patients produced increased serum levels of tumor necrosis factor (TNF)-a, gamma interferon and interleukin (IL) 12, as well as decreased immunosuppressive acidic protein (IAP) and tumor growth factor (TGF)-b. The previously mentioned study of reduced mammary adenocarcinoma metastasis in rats, suggested increased NK cell activity and increased nitric oxide (NO) production as well as increased cytotoxicity of peritoneal macrophages. This study also reported AHCC's restorative effect on mRNA synthesis for IL-1a and TNF-a which was suppressed by chemotherapy.

With regard to other beneficial mechanisms specific to the liver, there are a few that have been suggested. The study mentioned previously examining protective effects of chemically induced liver injury found that AHCC improved detoxification function by inducing P450 enzymes and by inhibiting the decline of phase II enzyme activity caused by the chemical exposure. In addition, this study found that AHCC reduced free radical activity and associated hepatic injury. This latter finding was supported by an animal study of streptozotocin-induced diabetes in which AHCC was protective and the mechanism was thought to be the reduction of oxidative damage. Whether these mechanisms explain the animal study findings that AHCC appeared to reduce the susceptibility to fatty liver in one investigation and improved serum lipids in another is unknown; however, it is likely that there remain specific influences to be determined.

To illustrate the clinical influence of AHCC therapy in patients with Hepatitis C, we present the following three preliminary case reports of Hepatitis C in which AHCC significantly reduced their viral levels and had other beneficial effects:

CLINICAL CASE REPORTS
Case 1: 64 YO Female with Hepatitis C
M.F. presented 11/98 for treatment of Hepatitis C, irritable bowel syndrome (IBS) and allergies. The hepatitis diagnosis was made 2-3 years earlier when liver enzymes had significantly increased, although there had been some evidence of elevated liver enzymes up to 35 years earlier. At presentation, the liver enzymes Gamma GT and AST were high (100.0 and 67.0 respectively), ALT was normal, and the white blood cell (WBC) count was low (3.4 thous/ml). The Hepatitis C Virus RNA level by the polymerase chain reaction (PCR) method, done 1/99, showed a count of 1,475,000 (n=2000 copies). Nutritional supplementation and IV vitamin therapy did not produce significant results as liver enzymes were still high and the patient was still fatigued, although it was not known what the viral level was at initial presentation compared to its current level. AHCC was begun 3/99, 6 gms in divided doses. Follow-up testing 7/99 showed a Hepatitis C Virus RNA level of 167,000 (a dramatic 89% decrease in 5 months) and testing 10/99 showed a normal level (<2000). The two elevated liver enzyme levels were essentially unchanged, although the patient reported significant improvement in energy and ALT remained normal.

Case 2: 35 YO Female with Hepatitis C
A.G. presented 8/93 for treatment of Hepatitis C. She was diagnosed 7/92 with elevated liver enzymes and positive Hepatitis C antibodies, and had a history of IV drug abuse. She was prescribed a dietary and nutritional supplement regimen as well as intravenous (IV) vitamin treatments, all of which were focused on immune support and anti-viral effect. Blood work was largely normal for five years except for slight, fluctuating elevations in the liver enzymes ALT (GPT), AST (GOT) and GGT. She also reported occasional pain and tingling in the area of the liver.
Blood work 11/98 showed a Hepatitis C Virus RNA level of 2,160,900 by PCR testing. AHCC was added within a week after this test - 6 gms in divided doses and no other adjustments to the patient's treatment protocol were made. Follow-up testing 3/99 showed a decrease in Hepatitis C Virus RNA to 1,573,400 (a 27.2% decrease in 4 months).

**Case 3: 47 YO Male with Hepatitis C and Prostate Cancer**

D.F. presented 1/98 with Hepatitis C and prostate cancer (PSA 14.2, Gleason 6). He was diagnosed with moderately differentiated adenocarcinoma with high heterogeneity, when he experienced painless hematuria 11/97. Hepatitis C was first treated in 1974 with acupUNCTure and homoeopathy with resolution of increased liver enzymes.

The patient was treated with total androgen blockage (TAb) starting in 5/98 to stabilize the prostate cancer - his PSA decreased to 4.9. The last Lupron was administered 1/99 and the last Casodex was taken 2/99. Measurement 12/98 of Hepatitis C Virus RNA by PCR testing was 2,498,200. D.F. began AHCC 1/99. 2/99 AHCC was increased to 6 gms per day in divided doses. Follow-up testing done 7/99 showed a significant decrease in the level of Hepatitis C Virus RNA to 499,600 (an 80% reduction in 6 months).

These cases illustrate the significant influence that AHCC can have on Hepatitis C viral loads. More controlled studies are required, however, to evaluate the benefits of AHCC, to establish the success rate in larger numbers of Hepatitis C patients and to compare its effectiveness with other available treatments. In addition, it is difficult to completely separate out the effect of AHCC and that of other nutritional approaches used in these cases.

Interferon alpha is considered the "treatment of choice" for Hepatitis C even though its long-term effectiveness is estimated at 10-20%. While this success rate appears poor, it is important to understand that the accepted research criteria for evaluating effectiveness includes: (a) 6 month duration of treatment with resulting eradication of viremia and normalization of serum alanine aminotransferase (ALT); and (b) maintenance of remission for 6 months following the end of treatment. Due to the small sample size and lack of control, the effects of AHCC cannot be evaluated. However, it did appear at least capable of approaching a comparable degree of effectiveness.

The consequences of untreated or ineffective treatment of Hepatitis C is the development of cirrhosis and hepatocellular carcinoma. Natural and immunostimulatory therapies can be effective and should be investigated. At the same time, these approaches are likely to have less side-effects and be less costly than other approaches, and these criteria are important in evaluating appropriate and effective therapies. One recent study of combined therapy with alpha interferon and riboviron produced influenza-like symptoms in >60% of subjects and anemia in >80% of subjects. AHCC appeared to have no negative side effects in our three subjects.

AHCC has been used in Japan for over 10 years and in many hospitals without evidence of toxicity. Research is necessary, however, to comprehensively evaluate AHCC's immunomodulatory effects as well as to determine the specific mechanisms by which it may be helpful in Hepatitis C patients. As described previously, other specific influences of AHCC on liver function such as detoxification and reducing oxidative damage should be examined as well. Until these studies can be done, however, our preliminary clinical experience suggests that AHCC has significant potential benefit in Hepatitis C treatment worthy of further study and clinical consideration.

**References**