

## The Mushroom *Agaricus blazei* Murill Extract Normalizes Liver Function in Patients with Chronic Hepatitis B

CHUNG-HUA HSU, M.D., Ph.D.,<sup>1,2</sup> KUNG-CHANG HWANG, M.D.,<sup>3</sup> YI-HSIUNG CHIANG, M.D.,<sup>4</sup>  
and PESUS CHOU, Dr.P.H.<sup>2,4</sup>

### ABSTRACT

**Background:** Hepatitis B is a global health problem. Use of complementary and alternative medicine has been popular among patients with hepatitis B. This 1-year open-label pilot study aims to observe whether *Agaricus blazei* Murill extract improves liver function in patients with hepatitis B.

**Methods:** This study involved 12 months of clinical observation. Four (4) patients with hepatitis B who met the criteria (1) aged between 20 and 65 years; (2) being Chinese; (3) having been a hepatic B carrier (HBsAg(+)) for more than 3 years; (4) alanine aminotransferase >100 IU/L; and (5) not taking lamivudine,  $\alpha$ -interferon, or other drugs for hepatitis participated in the study with informed consent. The enrolled patients were given *Agaricus blazei* Murill (ABM) extract of 1500 mg daily for 12 months. The level of alanine aminotransferase was taken as the major outcome measurement.

**Results:** At the end of the study, the mean level of aspartate aminotransferase and alanine aminotransferase decreased from 246.0 ( $\pm$  standard deviation [SD] 138.9) to 61.3 ( $\pm$  SD 32.6) IU/L and 151.0 ( $\pm$  SD 86.9) to 46.1 ( $\pm$  SD 22.5) IU/L, respectively.

**Conclusions:** Our initial observation seems to indicate the potential benefit of ABM extract in normalizing liver function of patients with hepatitis B. Controlled studies with larger samples should be conducted in the future.

### INTRODUCTION

Hepatitis B is a global health problem. Use of complementary and alternative medicine has been popular among patients with viral hepatitis. It is desirable to find a natural product that can help patients with hepatitis B with abnormal liver function.

*Agaricus blazei* Murill (ABM) is a mushroom and natural food, which has been used as a health care product for the prevention of a wide range of illnesses including cancer, diabetes, arteriosclerosis, and chronic hepatitis. It has been reported that ABM has beneficial effects in fighting cancer<sup>1–3</sup> and viruses,<sup>4</sup> improving insulin resistance in type 2 diabetes,<sup>5</sup> as well as enhancing production of antibodies by vaccines.<sup>6,7</sup> Chen et al.<sup>6</sup> have demonstrated that ABM extract might serve as an adjuvant in improving the efficacy

of hepatitis B vaccines *in vivo*. Rich polysaccharides such as  $\beta$ -glucans are found to be the main constituents of ABM.<sup>8,9</sup> In view of the beneficial effects of ABM on patients with hepatitis B observed in our short pilot study, we conducted this 1-year follow-up clinical trial to examine whether ABM extract can improve liver function in patients with chronic hepatitis B.

### METHODS

#### *Study design and population*

This was an open-label pilot study with no placebo given to match. The trial was conducted from August 1, 2004 through July 31, 2006 in Taipei Hospital, Taiwan. Four (4)

<sup>1</sup>Department of Chinese Medicine, Taipei Hospital, Taiwan.

<sup>2</sup>Community Medicine Research Center and Institute of Public Health, National Yang Ming University, Taipei, Taiwan.

<sup>3</sup>Department of Pediatrics, Taipei Hospital, Taiwan.

<sup>4</sup>Department of Internal Medicine, Taipei Hospital, Taiwan.

patients with hepatitis B who met the criteria (1) aged between 20 and 65 years, (2) being Chinese; (3) having been a hepatitis B carrier (HBsAg(+)) for more than 3 years, (4) alanine aminotransferase >100 IU/L; and (5) not taking lamivudine,  $\alpha$ interferon, or other drugs for hepatitis participated in the study. The protocol was approved by the Human Ethics Committee of our hospital. Informed consent was obtained from all 4 enrolled patients. All subjects were free to withdraw at any time during the course of the study.

### Preparation of sample and treatment

ABM is a health care product popularly used in Taiwan. Our ABM extract, obtained from Eng Chiao Bio-Technology Co. Ltd., Taiwan, were extracted from dried fungal bodies of ABM according to the preset standard procedures with certificate of analysis given.<sup>5</sup> The subjects were given one capsule containing 500 mg of ABM extract three times each day for 12 months. This capsule was taken 30 minutes after eating.

### Assessment

The level of alanine aminotransferases was used as the major outcome measurement. Blood samples were taken from the subjects once every 4 months during the study period. The side-effects and complications were also evaluated.

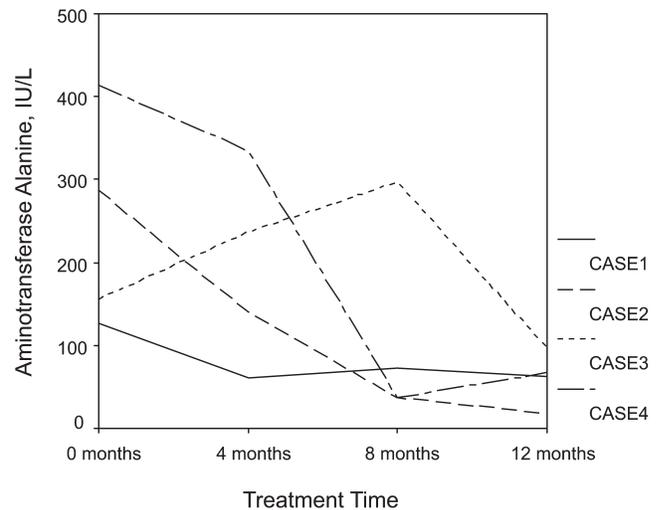
## RESULTS

Figure 1 shows the changes in level of aspartate aminotransferases and alanine aminotransferases during the 12-month follow-up. All of these 4 cases received treatment that involved taking ABM extract.

Case 1, a 38-year-old male patient, had hepatitis B for 22 years. His initial levels of aspartate aminotransferases and alanine aminotransferases were 72 and 127 IU/L, respectively, which dropped to 43 and 63 IU/L, respectively, after 12 months. Case 2, a 22-year-old male patient, had hepatitis B for 4 years. His initial levels of aspartate aminotransferase and alanine aminotransferase were 125 and 227 IU/L, respectively, and decreased to 17 and 18 IU/L, respectively, at the end of the study period.

Case 3, a 65-year-old male patient, had been suffering from hepatitis B for 30 years with abnormal liver function. Both his aspartate aminotransferases and alanine aminotransferase levels exceeded 100 IU/L throughout these 30 years. Before the ABM treatment, his initial levels were 132 and 156 IU/L, respectively. No improvement was observed during the first 9 months of treatment, but aspartate aminotransferases and alanine aminotransferase levels eventually decreased to 69 and 97 IU/L, respectively, 1 year later.

Case 4 was a 54-year-old woman who had been a hepatitis B carrier for 25 years. General malaise, poor appetite, and abdominal fullness had been noted for 1 month. Her serum levels of aspartate aminotransferases and alanine



**FIG. 1.** Changes in levels of aspartate aminotransferase and alanine aminotransferases among four cases during 12-month follow-up.

aminotransferase were high at 275 and 414 IU/L, respectively, before taking the ABM extract. Soon after the treatment, she began to feel better with symptoms relieved, and the levels of aspartate aminotransferases and alanine aminotransferase became 58 and 67 IU/L, respectively, at the end of the study.

### Adverse effects

No major or minor adverse effects were noted during the 12 months of ABM treatment. The renal function was also evaluated and was within normal limits.

## DISCUSSION

This 1-year clinical observation shows the potential benefits of ABM extract as a supplement for normalizing liver function in subjects with chronic hepatitis B.

Chronic hepatitis B is an escalating health problem. The recommended treatment regimen incurs considerable expenses, not to mention the side-effects and reduced efficacy in some patients. The serum level of liver enzymes is an important marker for evaluating the severity of the disease. Normalization of liver enzymes in patients with hepatitis B would imply a better prognosis and reduced chance of developing other liver diseases.

This study observed a significant reduction in the levels of liver enzymes, which were close to being normalized, among the 4 patients with chronic hepatitis B abnormal liver function after receiving ABM extract for 12 months. For cases 1, 2, and 4, the levels of aspartate aminotransferase and alanine aminotransferase were found to decrease with time. For case 3, who suffers from chronic hepatitis B and C, the levels of aspartate aminotransferase and alanine

aminotransferase decreased after 9 months of ABM treatment. This can be attributed to his liver disease being more serious and complicated. Symptoms of malaise, poor appetite, and abdominal fullness in case 4 improved soon after the patient took the extract of ABM. Since there were no adverse side-effects or discomfort reported during the study period, we can consider the ABM extract safe for taking as a supplement.

Our previous study has demonstrated the benefits of ABM extract as a supplement for reducing the homeostasis model assessment for insulin resistance in subjects with type 2 diabetes treated with gliclazide and metformin.<sup>5</sup> Rich polysaccharides such as  $\beta$ -glucans are found to be the main compounds of ABM.<sup>8,10</sup>  $\beta$ -Glucans from ABM have demonstrated antidiabetic activity.<sup>10</sup> Thiazolidinediones have been found to improve peripheral insulin resistance and have been employed for treating type 2 diabetes.<sup>11,12</sup> However, some adverse side-effects on liver function have also been reported.<sup>12</sup> Hence, ABM can be a possible supplement for type 2 diabetes with hepatitis B and abnormal liver function.

Use of complementary medicine has been common among patients with hepatitis B. There is a tradition in Chinese medicine of using the fungus ABM as a medicine.<sup>13</sup> The ABM extract was obtained from dried fungal bodies of ABM, which has been widely taken as a health care product in Taiwan and Japan for years.<sup>5,13</sup> ABM is rich in polysaccharide, which vitalizes production of interferon and interleukin that prevent viruses from entering the tissue.<sup>7</sup> The benefit of ABM on hepatitis B has been demonstrated in an *in vivo* study.<sup>6</sup> The potential beneficial effects of ABM for patients with chronic hepatitis B are worth further exploration in detailed clinical studies.

Despite the encouraging results, our work still had limitations, such as the absence of controls and a small study sample. In fact, this is only an initial clinical observation. Future research should be performed with well-designed protocols.

In conclusion, our initial observation seems to indicate the potential benefits of ABM extract in normalizing liver function of patients with chronic hepatitis B. Controlled studies with large samples should be conducted in the future.

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Address reprint requests to:  
 Chung-Hua Hsu, M.D., Ph.D.  
 Department of Chinese Medicine  
 Department of Health  
 Taipei Hospital  
 127 Su-Yuan Road  
 Hsin Chuang City, Taipei County 242  
 Taiwan

E-mail: owlherbs@yahoo.com.tw

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