BIO INDUSTRY

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THE DEVELOPMENT AND APPLICATION OF ACTIVE HEMICELLULOSE COMPOUND (AHCC)

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INTRODUCTION

Recently much interest has been shown involving the research of foods' effectiveness for bodily functions. There has been some progress in food science and medical technology to better understand the relationship between food and health. People in general are worried about cancer and adult diseases. For several years now, at Amino Up Chemical Co., Ltd., we have been researching the components found within foods which have the possibility to control bodily functions. We have researched many kinds of foods, but here let us introduce AHCC.

AHCC, which is a food substance, was first developed in order to decrease the blood pressure and to prevent adult diseases. As our research continued, we found that AHCC contains an immune-active substance. We are continuing basic testing including administering clinical tests at research institutes. These tests are being conducting not only in Japan but also in America, and China. Some of the latest results have come to recognize that AHCC works as both a prevention and a treatment for numerous diseases.

AHCC is a extract of mycelium. We have succeeded to produce AHCC by liquid culture of basidiomycetes in a large quantities, and our own technology of refining and separation as well. We are currently investigating the immune efficacy through clinical testing.

MANUFACTURING PROCESS FOR AHCC

AHCC is extracted of mycelium which is separated and mated in our own way. The manufacturing process is in Figure 1.

In 1989, we have developed the methods of mass production in a large stainless steel tank and now it can be cultured and extracted in a 3,000 L tank.
A long term is needed for the culture to produce AHCC and we must be very cautious about contamination. In our factory, we have succeed to prevent

contamination by our own minute sterilize system.

PROCESSING AHCC

AHCC concentration which is extracted through the manufacturing process (Figure 1) is freeze dried for improvement of preservation quality or quality control. Freeze dried AHCC is easy to dissolve in water, therefore it has much hygroscopicity. The freeze dried AHCC is used for clinical trial or in case of using it in product form, it is used in soft capsules. We also succeeded in processing microcapsules which could control high quality in a powder form as well. We expect to further develop products which have a higher degree of absorption.

PROPERTIES OF AHCC

Nutrition Ingredients (per 100g)

Protein:	8.70g
Lipid:	0.10g
Ash :	5.30g
Iron:	3.70mg
Vitamin B1 :	0.97mg
Vitamin B2 :	0.40mg

Agricultural Chemicals Residue Test

Results of the test are in Table 1.

EFFICACY OF AHCC

Accumulation of Neutrophils

In this study, Stock solution of AHCC was used as specimen. Mice (ddY) were injected in the abdomen with samples. Whereafter abdominal cavity cells were taken and then separated by centrifugation for smear preparation. The

accumulation of neutrophils was indicated by the rate of neutrophils in the total number of abdominal cavity cells. Six hours after the samples were injected, we examined the accumulation of neutrophils. We could see only a few neutrophils from the adminal cavity cells of mice which were injected salin. The amount of neutrophils are less than several percents ordinarily in this study. On the other hand, both of lentinan and picibanil which is kind of BRM and also used as an anticancer drug clinically, made strong humectation blood neutrophil. Each 62.5% and 92.3% of blood neutrophil were recognized in the abdominal cavity. AHCC also indicates the accumulation activity of neutrophils and strong activity (neutrophils 70% - 80%) in the same way as other BRMs. With AHCC, the accumelated neutrophils decreased within a few days, while the macrophage integrated. There is analogy between the accumulation of leukocyte by BRM and AHCC in such progress.

Inhibition Test on Mice with Liver Cancer

AHCC was administered by oral to mice with liver cancer and the level of inhibition was then examined. AHCC (freeze dried powder) was dissolved in water, as the method of taking. The mice began drinking the water treated with AHCC freely from the starting day of the experiment 0 to 20 for 21 days. During the testing period, we stopped the AHCC treatment at interval of 7^{th} day 14^{th} day, and 21^{st} day and we let the mice drink water freely. The result of this experiment showed that tumer was reduced significantly.

TNF Production

We administered AHCC to mice and examined the TNF (Tumor Necrosis Factor) production. The result showed in Table 3. TNF production was recognized by intravenous injection of 5mg AHCC. It can be said there is the possibility that antitumer action is activated by taking AHCC into the blood.

NK Cell Activity

Examination of human lymphocyte

In this study, 7 healthy individuals of both sex (20 - 50 year-old) have taken 3g of AHCC per day for 10 days. 20 cc blood from each individual was drawn

before the start of AHCC treatment, during the treatment (at 3rd day), and after cessation of the treatment (at 1st, 7th, and 30th day).

Effect of AHCC on NK Activity

NK cells activity from control subjects before treatment with AHCC demostrated a moderate level of activity (5 - 20 LU). Treatment with AHCC for 10 days has been done and NK activity has increased significantly on the 3rd day and it maximized at end of treatment course (150 - 500 LU). A high level of NK activity was maintained up to 1 and 2 weeks after cessation of treatment. Although all 7 subjects showed the effect of AHCC on NK cell activity, there was an individual variation towards the immunomodulatory action of AHCC.

Effect of AHCC on Lymphocyte populations

Percentage of lymphocyte subsets (demarcation) was examined by flow cytometry. The result indicated that AHCC did not cause changes in the percentages of T/helper, T/suppressor, total T cells and B cells. On the other hand, there was a remarkable increase in the percentage of NK cell population. This finding was also backed up by morpholog scpy of Giemsa stained anthropo PLB and mice's peritoneal exudate cell.

Increase of hito NK Cell in vivo by AHCC

10 healthy individuals and 2 cancer patients were given 3g of AHCC respectively per day. PBL- NK activity was measured by Cr-release method. K562 Cell and resistant Raji Cell were used as a mark. 14LU NK activity became over 100 LU after administration of AHCC. For 1 week its high level was maintained and it descends after 2 weeks. Taking 6g of AHCC per day could destroy even Raji Cell. The amount of Granule which controls anti cancer reaction of NK Cell increases 2 to 3 times bigger compared to before given. And also PBL increases 20% to 30%.

AHCC treatment for cancer patients

3g or 6g of AHCC per day were administered by oral to 3 cancer patients respectively (rhabdomyoblastoma, multiple myeloma, and brest carcinoma) for 2 weeks. NK activity was examined by Cr-release method and the numbers of NK Cell

are measured by flow cytometry. In every case, activity and the numbers of NK Cell has increased.

APPLICATION OF AHCC

AHCC enhances the control of bodily functions, accumulation of neutrophils, and TNF production as indicated in the above research data. There is close resemblance in the function between AHCC and BRM (Biological Response Modifiers) which is the general term for the function of medicine.

There are many kinds of BRMs. Some such as BCG and MER originate from the bacillus. Other BRMs such ass pyrancopolymer and bestatin are syntheses compounds. Lentinan too, is a BRM. AHCC is different from BRMs in that AHCC is a food substance and not a medicine. AHCC is also effective through oral absorption.

Diseases have been attracted nowadays such as Cancer, AIDS, and MRSA are related to immune reactions of the body's defense system. The function of Immune-reinforcement by AHCC effectively works both for prevention and as a treatment.

From this point of view, positive research work and trials have been done so far in Japan, America, and in China. And the significant progress of AHCC is inspiring us to continue and to further our efforts. It is not only efficacy that enhances immune system. AHCC is also rich in polysaccharide and dietary fiber, and it may be valid food ingredient in modern society. It is our hope that AHCC will help many people who suffer from diseases. We will continue to further develop our research.

*The general term "AHCC" has been revised in 1995. The abbreviation "AHCC" remains unchanged. The general term stands for **Active Hexose - correlated Compound**. Through our recent research it has been found that "Active Hemicellulose Compound" does not appropriately represent its active component, therefore, the above mentioned term is now applied, conveying a better description.*

Figure 1 AHCC Manufacturing Process

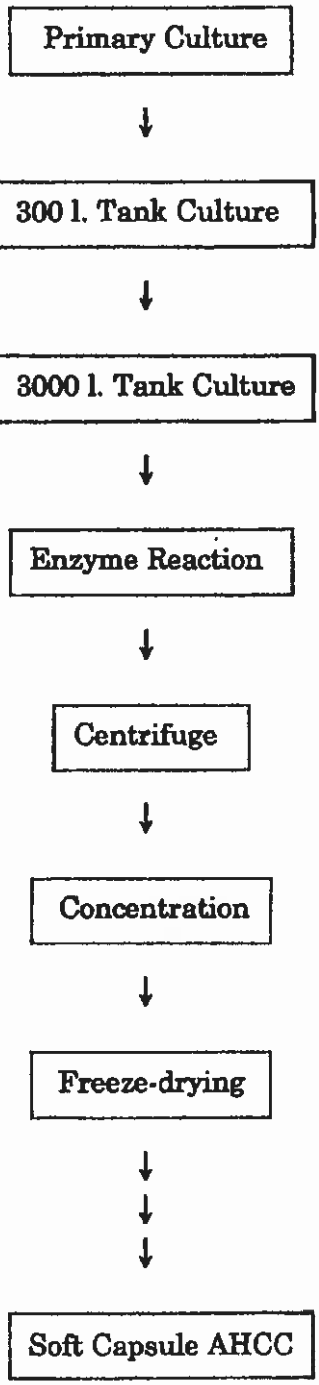

Table 1 Agricultural Chemicals Residue Test

DRIN	BHC	DDT
ALDRIN :Nil DILDRIN :Nil ENDRIN : Nil	α - BHC : Nil β - BHC : Nil γ - BHC : Nil δ -BHC : Nil	PP - DDE : Nil OP - DDY : Nil PP - DDD : Nil PP - DDT : Nil

Table 2 Effect of orally administrated FD on MH 134 hepatoma

Group	Tumor (g)	Inhibition (%)	Body weight (g)
H2O	2.70 ± 0.03	-	27.1 ± 1.4
FD 2mg/ml	2.68 ± 0.45	0.8	27.1 ± 1.8
FD 10mg/ml	2.82 ± 0.66	-4.4	27.1 ± 2.4
FD 50mg/ml	1.74 ± 0.28	35.9	22.9 ± 1.2

Table 3 Effect of FD - priming on TNF production

Dose	Tumor (g)	TNF (U/ml)	
5mg/ mouse	i.v. x 1 p.o. x1 p.o. x 1 p.o. x 1	72.1±14.1 9.3±6.5 8.5±2.6 14.8±6.5	p<0.01