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Highly purified chitosan reduce blood alcohol concentration, aspartate aminotransferase, and alanine aminotransferase levels in human

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SUMMARY

The purpose of this study was to examine the effect of supplementary highly purified chitosan (HPC) on blood alcohol concentration in healthy human. The human study was performed with two sections. Each section of the study was conducted by two-phase cross-over design with a week wash-out period. All volunteers took HPC in one phase, and took a placebo in the next phase. Blood alcohol concentrations were different between in those taking HPC and in those taking the placebo in the human. And the concentration of serum aspartate aminotransferase (AST, GOT) and alanine aminotransferase (ALT, GPT), the indicator of liver cell damage, was lowered in those taking HPC, compared to those taking the placebo. In conclusion, taking HPC prior to drinking alcohol can somewhat reduce alcohol concentration in human blood and liver cell damage.

Key Words: Highly purified chitosan; Alcohol; Aspartate aminotransferase; Alanine aminotransferase

INTRODUCTION

Alcoholic beverages have been used since the dawn of history, and a great amount of alcohol is still consumed by adults and youths all over the world. According to death rate statistics, alcohol-related morbidity and mortality is a serious problem both in Korea and the United States (Jeon and Lim, 1998). Excessive alcohol consumption can cause widespread damage to all tissues and organs of the body, although moderated drinking might have a beneficial cardioprotective effect (Boffetta and Garfinkel, 1990).

Most of all, alcoholic liver disease is one of the critical medical problems of chronic alcoholic use, because the liver is the primary site of alcohol metabolism, generating a number of potentially dangerous by-products (Kurose *et al.*, 1996). Alcohol is absorbed in the stomach and intestines into the blood, and most of the alcohol consumed is metabolized in the liver, which retains many properties for detoxification through oxidative and/or reductive process (Wallgren, 1970). In the liver, alcohol is converted to acetaldehyde by alcohol dehydrogenase (ADH) or cytochrome P450IIE1, and then acetaldehyde is rapidly oxidated to acetate by aldehyde dehydrogenase (ALDH), which is followed by conversion to carbon dioxide and water (Lieber, 1994).

Highly purified chitosan (HPC), having a molecular weight of 150,000-200,000 Da, can be produced through ultrasonic waves system. In the present study, it is shown that the HPC reduced blood alcohol concentration, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels.

MATERIAL AND METHODS

Clinical study

This study was conducted in accordance with Good Clinical Practice. A single center, single blind (blinded to the volunteers), 2-phase crossover design with a week wash-out period was chosen. Twenty healthy, male and female volunteers aged 23 to 38

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years were recruited from among the staffs or students of Wonkwang University. None used any drugs regularly. All subjects were given a standard breakfast either with empty capsule (placebo) or HPC (capsule of Thank you™, Chong Kun Dang Pharm) obtained from Chito153 Co., Ltd. (Seoul, South Korea). They drank 25% alcohol 300 ml after 30 min within 1 h. Blood sample for blood alcohol determinations were obtained from a forearm vein into heparinized tubes at 0, 2 and 3 h after alcohol administration. Blood samples were centrifuged and plasma sample were kept at 4°C until analysis.

Determination of blood alcohol concentration

For the analysis of blood alcohol level, blood was centrifuged for 15 min at 3000 rpm. Reaction buffer, 20 mM glycine buffer (pH 9.2) containing 72 mM semicarbazide was mixed 0.5 mM NAD^+ and 36 unit/ml yeast alcohol dehydrogenase, and added 10 ml plasma. Absorbance was determined at 340 nm after standing for 10 min at room temperature.

Liver function tests

Plasma AST and ALT activities were assessed to evaluate hepatic dysfunction. Enzyme activities were measured by means of standard spectrophotometric methods. The results were expressed in international units per liter.

RESULTS

Effect of HPC on blood alcohol concentration

Two and three h after the ingestion of an acute dose of alcohol the blood alcohol level of the control group (receiving 500 mg of placebo capsule with alcohol) was 0.104% and 0.090%, respectively. While that of the test group (receiving 500 mg of HPC with alcohol) was 0.094% and 0.084%, showing a blood alcohol level of 11% and 9% lower than the control value, respectively (Table 1).

Table 1. Effect of HPC on blood alcohol concentration

Drinking time (h)	Blood Alcohol Concentration (%)	
	Placebo	HPC
0	0.0023±0.0010	0.0038±0.0015
2	0.1036±0.0098	0.0941±0.0079
3	0.0895±0.0101	0.0838±0.0079

All subjects were given a standard breakfast either with empty tablet (placebo) or tablet of HPC, 500 mg. Healthy volunteers consumed 25% ethanol 300 ml. Blood samples were obtained from a forearm vein at 0, 2 and 3 h after alcohol administration. Data are presented as the mean±SE of twenty volunteers.

Table 2. Effect of HPC on AST level according to drinking time

Drinking time (h)	AST (IU/L)	
	Placebo	HPC
0	19.291.79	19.672.13
2	24.002.48	21.202.47
3	26.112.35	24.262.73

All subjects were given a standard breakfast either with empty tablet (placebo) or tablet of HPC, 500 mg. Healthy volunteers consumed 25% ethanol 300 ml. Blood samples were obtained from a forearm vein at 0, 2 and 3 h after alcohol administration. Data are presented as the mean±SE of twenty volunteers.

Table 3. Effect of HPC on ALT level according to drinking time

Drinking time (h)	ALT (IU/L)	
	Placebo	HPC
0	20.612.25	18.611.90
2	22.062.29	19.721.93
3	22.892.47	20.722.10

All subjects were given a standard breakfast either with empty tablet (placebo) or tablet of HPC, 500 mg. Healthy volunteers consumed 25% ethanol 300 ml. Blood samples were obtained from a forearm vein at 0, 2 and 3 h after alcohol administration. Data are presented as the mean±SE of twenty volunteers.

Effect of HPC on ALT and AST levels

Blood was extracted on 0, 2 and 3 h after administration of 25% alcohol 300 ml. ALT and AST in the test groups were lower than that in the control group (Table 2 and Table 3).

DISCUSSION

These results demonstrate that HPC enhances blood alcohol clearance and reduces ALT and AST increment in human, although variations exist in its effected on each subject.

Chitosan carries a positive charge on the acetyl remnants and, when solubilised in an acid environment, the chitosan polymers bind to

negatively charged molecules such as fats and lipids. (Sugano *et al.*, 1980; Ebihara and Schneeman, 1989). Although the precise mechanism by which HPC decreases blood alcohol concentration, AST and ALT level remains to be elucidated, it is reasonable to postulate that alcohol clearance by HPC could be attribute to the disturbance alcohol absorption similar to chitosan polymers bind to negatively charged molecules such as fats and lipids.

The major pathway for alcohol metabolism involves the ADH (Ehrig *et al.*, 1990). This enzyme converts alcohol to acetaldehyde through a chemical process called oxidation. Through oxidation, alcohol is detoxified and removed from the blood, preventing the alcohol from accumulating and destroying cells organs. In this respect, it is possible that HPC could be attributed to the elevation of alcohol ADH and ALDH activity.

The present findings that the ingestion of HPC along with alcohol accelerates blood alcohol clearance and lowers ALT and AST in human may render clinical applications in the treatment of alcoholic patients and help alleviate many detrimental effects caused by acute ethanol intoxication.

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