Effects of a Yeast Extract with a High Glutathione Content on Breath Alcohol and Hepatic Function in Human Volunteers

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Key Words: glutathione, GSH, supplementation, yeast extract, human traial

Summary

We obtained the following results in this study conducted to investigate the effectiveness of the oral intake of YH before alcohol consumption, in decreasing breath alcohol concentration and suppressing plasma AST levels after a 2-month long-term intake in human subjects.

1) It was demonstrated that the oral intake of YH immediately before alcohol intake significantly suppressed the breath alcohol compared to that of the placebo group.

2) It was demonstrated that the 2-month oral intake of YH suppressed the plasma AST level.

The results described in 1) and 2) demonstrated the effectiveness of the oral intake of YH on alcohol consumption-related stress, as well as its long-term improvement of hepatic function.

1. Introduction

Glutathione (γ-L-glutamyl-L-cysteine-glycine, GSH) is a tripeptide consisting of glutamic acid, cysteine, and glycine. In Japan, GSH is used medically as an antidote. It plays the role of an antioxidant by protecting cells from active oxygen and oxidants generated in the cells, is known to inhibit melanogenesis [1], and has skin-clearing effects. GSH levels are known to decrease with age and has been reported to decrease owing to alcohol intake [2], medication [3], and stresses such as physical exercise. Alcohol consumption is known to induce hepatic steatosis by promoting hepatic steatogenesis [4] and causes biomembrane disorder [5] because of hepatic lipid peroxidation. Hepatic steatosis may trigger various lifestyle-related diseases as well as hepatic cirrhosis because it decreases hepatic physiological function. Furthermore, it has also been reported that GSH protects the liver against alcohol intoxication [6].

Yeast is rich in GSH, which has been extracted from yeast since ancient times. In Japan, a pioneering study was conducted by Dr. Kuroiwa [7], and we obtained a yeast extract with a high GSH content (YH) after continuous pure cultivation of a developed torula yeast with a high GSH content in a large fermenter. Sugimura *et al*. demonstrated the efficacy of yeast extract with a high GSH content

against hepatic disorders by feeding rats with it; however, the efficacy has not been verified in humans [8].

Therefore, in this study, we focused on real-life stress in humans, especially alcohol consumption, and investigated the effects of YH intake just before drinking on breath alcohol concentration. In addition, we studied changes in the human plasma aspartate aminotransferase (AST) level, an indicator of hepatic function, in patients who had reached the upper limit of the indicator of mild hepatic disorder and had taken YH for a prolonged period. Here, we report the results of these investigations.

2. Methods

2.1 Effects of oral intake of YH on breath alcohol concentration

"HITHION YH-15," which contains reduced GSH 15% (w/w), was the YH used in this study. HITHION YH-15 is a yeast extract manufactured by KOHJIN Life Sciences Co., Ltd. using a fermentative process of torula yeast. The breath alcohol concentration after alcohol consumption was measured in the 20 healthy men and women participants in the study. All the subjects received an explanation of the objectives, methods, and schedule of the study and were informed that they had the option to withdraw from the study at any time. The subjects were adult men and women with drinking experience and no history of drug use and alcoholism. Three study groups were defined, placebo, YH, and curcuma groups, who were treated with the tablets (test meals), consisting of 660 mg lactose; 670 mg YH (equivalent to 100 mg GSH), and curcuma (equivalent to 30 mg curcumin), respectively.

The subjects were requested to abstain from alcohol on the day before the study commenced and consumed rice balls and the test meals approximately 1 hour before drinking alcohol on the day of the study. The whiskey (40 degrees) was double diluted with an amount equal to the subject's weight × 1.25 mL, and the subject was instructed to drink the entire sample within 10 minutes.

The evaluated laboratory parameters were 1) breath alcohol concentration (mg/L) measured using an alcohol checker 20, 60, 120, and 180 minutes after alcohol consumption and 2) subjective feeling questionnaire. Furthermore, the breath alcohol concentration (parameter 1) was measured five times in total before and after drinking alcohol (before and 20, 60, 120, and 180 minutes after drinking alcohol), and parameter 2) consisted of seven items, "sobriety returned," "sleepiness," "headache," "upset stomach," "swelling," "flush," and "light-headedness" in the questionnaire, which were assessed using a five-point scale. Higher points indicated that the symptoms described above such as sleepiness and headache were milder. The study was a crossover comparative study, and each stage was conducted similarly at an interval of 1 week or more.

2.2 Effects of oral YH on human plasma components

12 patients who were confirmed to have reached the upper limit of the indicator of mild hepatic disorder (patients with hepatic steatosis or a tendency to develop hepatic steatosis) participated in the study.

2 study groups, the placebo and YH were defined and administered tablets consisting of dextrin and 333 mg YH (equivalent to 50 mg of GSH), respectively, as the test meals. The subjects took the test meals once daily, and the length of the study was 2 months. After the test substance

administration period, the plasma AST levels were measured.

In the statistical analysis, the mean AST level ± standard deviation (SD) was calculated, and the difference between groups was determined using *t*-test.

3. Results

3.1 Effects of oral intake of YH on breath alcohol concentration

The results of this study, which investigated the effects of the intake of YH on the breath alcohol concentration after alcohol consumption in 12 healthy subjects, are shown in **Figure 1**. The breath alcohol concentration of the YH group significantly decreased 20, 60, 120, and 180 minutes after alcohol consumption compared to that of the placebo and curcuma groups. Therefore, the results suggest that YH intake possibly decreased the breath alcohol concentration.

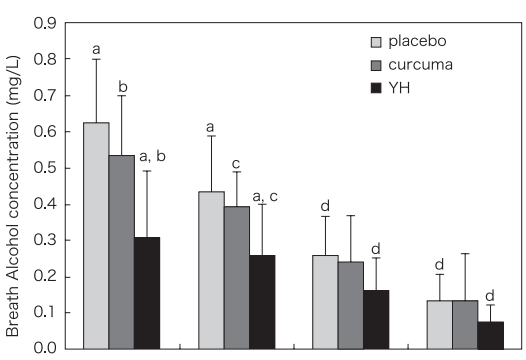

Figure 1 Effects of Oral Intake of Yeast Extract (YH) with a High Glutathione Content on Breath Alcohol Concentration

The results of the analysis of the subjective feeling questionnaire also demonstrated higher points in the YH and curcuma groups than in placebo group. Furthermore, the YH group was confirmed to have scored higher points in the "sleepiness," "headache," and "upset stomach"

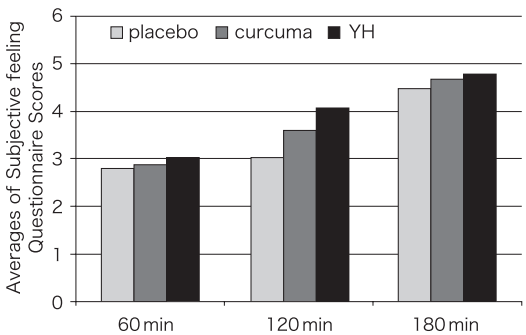

Figure 2 Effects of Oral Intake of Yeast Extract (YH) with a High Glutathione Content on Subjective Feeling Questionnaire Scores

items than the curcuma group did (**Figure 2**).

3.2 Effects of oral intake of YH on human plasma AST

The rate of change in the plasma AST levels of the subjects after 2 month, which is shown in **Figure 3**, reveals that the rate of the YH group was significantly lower than that of the placebo group. Therefore, the AST levels showed a tendency to decrease significantly after YH intake.

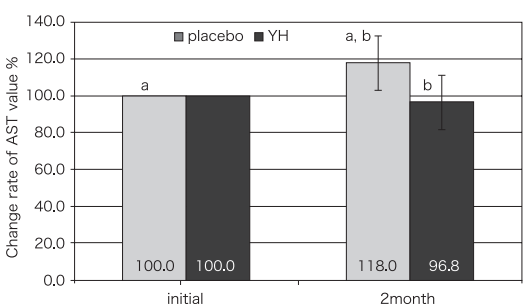

Figure 3 Changes in Human Plasma Aspartate Aminotransferase (AST) Concentration after Intake of Yeast Extract (YH) with a High Glutathione Content for 2 Months

4. Discussion

Following its absorption in the stomach and small intestine and circulation into the blood, alcohol is broken down into acetaldehyde by oxidation by hepatic enzymes. Acetaldehyde is the causative

substance responsible for the symptoms of alcohol intoxication such as headache and nausea. The results of this study showed a significant decrease in the breath alcohol concentration following the intake of the GSH-containing yeast extract 1 hour before alcohol consumption. Park *et al*. reported that the oral intake of GSH increased the plasma GSH levels after 60 to 120 minutes [9]. As shown in our study, the increase was probably due to the ingested GSH, which circulated to the liver via the plasma 1 or 2 hours after the intake and subsequently converted the alcohol to acetaldehyde.

Considering that the subjects in the YH group showed a lower tendency to experience headache or nausea as a subjective feeling than those in the placebo group did, GSH, which is a principal component of YH-15, appeared to metabolize the acetaldehyde promptly. In addition, the changes in plasma AST after the 2-month intake of YH suggest that YH had a long-term effect on improving hepatic function, in addition to its immediate effects after alcohol consumption.

The production of active oxygen is considered to be involved in the progression of the alcoholic hepatic disorder. GSH acts as antioxidant to protect cell from reactive oxygen or peroxide compounds inside cells [10, 11]. GSH appears to delay this progression by removing active oxygen. Also GSH is reported to enhance the lipid metabolism by activating PGC-1α which upregulates the mitochondrial biogenesis.[12] This fact might suggest that GSH intake prevented the progress of the hepatic disorder by enhancing the hepatic lipid metabolism, which eventually suppressed AST level. Another possibility is that YH contains a small percentage of the amino acids, arginine and gamma-aminobutyric acid (GABA), as well as GSH. Some reports have indicated that the amino acids not only promote alcohol metabolism but they also effectively improve hepatic function[13, 14]. Therefore, the amino acids in the yeast extract used in our study might also have worked synergistically, to the delays observed in this study. Further investigation should be needed.

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