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Effect of Beverage Containing Fermented *Akebia quinata* Extracts on Alcoholic Hangover

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ABSTRACT: The present study was conducted to investigate the effects of beverages containing fermented *Akebia quinata* extracts on alcoholic hangover. For this study, 25 healthy young men were recruited. All participants consumed 100 mL of water (placebo), commercial hangover beverage A or B, fermented *A. quinata* leaf (AQL) or fruit (AQF) extract before alcohol consumption. After 1 h, all participants consumed a bottle of Soju, Korean distilled liquor (360 mL), containing 20% alcohol. Blood was collected at 0 h, 1 h, 3 h, and 5 h after alcohol consumption. The plasma alanine transaminase (ALT) activity was highest in the placebo group. Compared with the control group, the AQL and AQF groups showed decreased ALT activity at 5 h after alcohol consumption. Plasma ethanol concentration was increased after alcohol intake and peaked at 3 h after alcohol consumption. Compared with the control group, the A group showed a higher plasma ethanol concentration at 1 h ($P<0.05$). At 3 h after alcohol consumption, the AQF group showed the lowest mean plasma ethanol concentration compared to the other groups; however, there were no statistical differences. After 5 h of alcohol consumption, the AQL and AQF groups showed lower plasma ethanol concentrations compared with the B group. The sensory evaluation score for the fermented *A. quinata* fruit extract was lower than for the commercial hangover beverages. In conclusion, the present intervention study results suggest that fermented *A. quinata* extracts alleviate alcoholic hangover and reduce plasma ethanol concentrations.

Keywords: *Akebia quinata*, hepatoprotection, alcohol, hangover, beverage

INTRODUCTION

Recently, social diversification and economic growth have caused people to drink alcoholic beverages more often than in the past, which may increase the incidence of alcoholism and hangovers (1). Worldwide, people over 15 years of age consumed 6.1 liters of alcohol on average in 2013 (WHO, 2014). Chronic and excessive alcohol consumption can cause many diseases, including diabetes mellitus, neuropsychiatric disorders, cardiovascular disease, cirrhosis of the liver, unintentional injuries, and cancer (2). Acute heavy drinking can cause hangover symptoms due to acetaldehyde, formed by the action of alcohol dehydrogenase, which is further metabolized into acetone by acetaldehyde dehydrogenase (3). Acetaldehyde is known to be a primary metabolite of ethanol and is the main cause of hangovers (4). It has been reported that acetaldehyde causes steatohepatitis, hepatic cirrhosis, and impaired vitamin activity via mitochondrial dysfunction (5).

The increasing rates of alcohol consumption and severe hangover symptoms are sufficient reasons to make a product to relieve hangover symptoms. A few products, such as coffee, tea, fluids, vitamin B6, and painkillers are recommended for relieving hangover symptoms (6). Several plant extracts, like *Hovenia dulcis*, *Radix puerariae*, and ginseng, have undergone scientific evaluation for relieving hangover symptoms (7-10). Moreover, several hangover beverages, like Condition®, which is the best-selling hangover beverage in Korea, are in the market, and the size of the hangover beverage market is 173 million dollars in Korea. However, traditional or natural ingredients have limited effects against hangover symptoms (11,12). Therefore, other alternatives are needed for preventing or treating alcoholic hangover.

Akebia quinata grows naturally in Korea, Japan, and China. In traditional medicine, the dried fruit has been used as an anti-phlogistic, diuretic, and antidote, while the stems reportedly possess diuretic, analgesic, and anti-phlogistic properties (13,14). A number of triterpe-

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noid saponins have been isolated from *A. quinata*, including guaianin N, collinsonidin, kalopanaxsaponin A, hederagenin, and oleanolic acid (15,16). In the previous study, we demonstrated a potential hepatoprotective effect from *A. quinata* extract on acute alcohol-induced hepatotoxicity in mice (17). In addition, oleanolic acid and hederagenin, which are compounds found in *A. quinata* extract, demonstrated hepatoprotective effects and reduced blood ethanol concentration in mice with alcohol induced hepatotoxicity (18). Furthermore, we showed that *A. quinata* extracts relieved oxidative stress by increasing hepatic glutathione levels. However, no human based trials have been conducted to evaluate the effects of *A. quinata* extracts on alcoholic hangovers yet. Therefore, we investigated the effects of extracts from fermented *A quinata*, which is a by-product in the production of the Korean traditional fermented alcoholic beverage, makgeolli, on reducing blood alcohol concentration in healthy men.

MATERIALS AND METHODS

Fermented *A. quinata* extract

Fermented *A. quinata* extracts were provided by Woorisul Co., Ltd. (Gwangju, Korea). In brief, the *A. quinata* leaves and fruits were washed and finely ground. *A. quinata* leaves or fruits were fermented by yeast for 1 month, and alcohol fermentation was performed for 1 week. After the fermentation, alcohol was removed, and fermented extracts were diluted to 30 percent. The detailed method for making fermented *A. quinata* extracts is Woorisul Co., Ltd. property.

Study participants

Inclusion criteria were as follows: generally healthy male, age range from 20 to 30 years old, and body mass index (BMI) range from 10 to 30. For this study, 25 participants were recruited from volunteers who fulfilled the inclusion criteria. The participants were required to be free of alcohol for 3 d and fasted for 1 h before the experiment. All participants provided written informed consent to participate in the study. The Institutional Review Board of Ewha Womans University approved our study protocol (Protocol No. 93-6).

Study design

The participants were randomly assigned to 5 groups based on age and BMI so that the average age and BMI for each group were similar. During testing, the 25 participants were divided into a placebo and 4 test groups. At 0 h, the study participants drank either 100 mL of water (placebo), 100 mL of commercial hangover beverage A (Condition®, CJ, Seoul, Korea) or B (Morningcare, Dong-A Pharm., Seoul, Korea), or fermented *A. quinata* leaf (AQL) or fruit (AQF) extract. After 1 h, all participants consumed a bottle of Soju, Korean distilled liquor (360 mL), containing 20% alcohol (Chamisul classic, Jinro, Seoul, Korea) with 20 pieces of a commercial snack (Saewookkang, Nongshim, Seoul, Korea) within 30 min.

Anthropometric parameters, blood pressure, and blood collection

The body weight and height of the participants were measured before the onset of the study. The BMI was calculated as body weight in kilograms divided by height in square meters (kg/m^2). Body fat percentages were measured with Inbody 520 (InBody Co., Ltd., Seoul, Korea). Venous blood specimens were collected 0, 1, 3, and 5 h after alcohol consumption in ethylenediaminetetraacetic acid-treated Vacutainer tubes, and blood samples were centrifuged at 4°C for 20 min. Separated plasma samples were stored at −80°C until analysis.

Plasma alanine aminotransferase activity and ethanol concentration

Plasma alanine aminotransferase (ALT) activity was measured using a commercial ALT, aspartate aminotransferase assay kit (AM101-K, Asan Pharmaceutical Co., Hwaseong, Korea). Plasma ethanol concentrations were measured with Ethanol assay kits (Sigma-Aldrich Co., St. Louis, MO, USA) using a colorimetric method. Both analyses followed the manufacturer's manual for each product.

Sensory evaluation of characteristics of fermented *A. quinata* extracts

The survey tool consisted of 6 questions about the characteristic traits of fermented *A. quinata* extracts addressing appearance, texture, color, scent, nasty smell, and overall taste. The scores ranged from 0 (negative) to 6 (positive) and the sum of the score for each of the questions was considered to be the preference index. The survey was administered to participants simultaneously with hangover beverage or fermented *A. quinata* extracts consumption.

Statistical analysis

Data are presented as the mean±standard deviation (STD) and standard error (SE). These data were analyzed by one-way analysis of variance (ANOVA) using SAS (ver. 9.3, SAS Institute Inc., Cary, NC, USA). The differences among the treatments were tested with Duncan's new multiple range test.

Table 1. General characteristics of the participants

	Control		A		B		AQL		AQF	
	AVG	STD	AVG	STD	AVG	STD	AVG	STD	AVG	STD
Age	26.0	3.08	26.5	2.89	26.4	3.05	26.0	1.00	27.4	2.70
Height (cm)	176.8	3.96	177.0	5.72	175.4	2.19	178.2	4.76	175.6	5.08
Weight (kg)	71.9	11.13	72.1	9.37	75.0	10.07	74.0	3.76	71.4	7.01
BMI	23.0	3.54	23.0	2.78	24.4	2.98	23.3	1.13	23.1	1.60
Body fat (%)	17.1	4.27	15.4	7.68	18.3	6.56	19.8	7.07	18.1	5.62

A, Condition®; B, Morningcare; AQL, fermented *A. quinata* leaf extract; AQF, fermented *A. quinata* fruit extract.
AVG, average; STD, standard deviation.
Non-significant.

RESULTS AND DISCUSSION

General characteristics of the participants

Table 1 shows the general characteristics of the participants. Age, height, weight, BMI, and body fat percentage for all participants were in the normal range. The average height and weight for 20 to 30 year-old Korean men is 175.8 cm and 75.6 kg (Korean Statistical Information Service, 2014), so the participants were typical young and healthy Korean men. The general characteristics of the participants were not significantly different between the groups.

Plasma ALT activity

To investigate hepatotoxicity from alcohol consumption, the change in plasma ALT activity at different time points was measured (Fig. 1). Plasma levels of ALT serve as a cytosolic marker reflecting hepatocellular necrosis as the enzymes are released into the blood after cell membrane damage (19). Consequently, ALT is used as a sensitive marker in the diagnosis of hepatic diseases (20). In this study, 1 h after alcohol consumption, ALT activity was decreased in every group but there was no difference among the groups. After 3 h of alcohol consumption, the control, AQL, and AQF groups showed increased ALT activity compared with ALT activity after 1 h. However, the ALT activity in the A and B groups at 3 h was lower than at 1 h. Furthermore, A and B groups showed lower ALT activity than the control and AQF groups ($P<0.05$). ALT activity at 5 h after alcohol consumption was higher in all groups than at 3 h. The ALT activity was highest in the AQL group and lowest in the A group ($P<0.05$). Alcohol induced hepatic damage is mainly assessed by the activity of released cytoplasmic ALT in the circulation (21). In this study, ALT activity in all the groups gradually increased after alcohol consumption. Furthermore, we showed that the increase of ALT activity after alcohol consumption could be ameliorated by pre-administration of fermented *A. quinata* extracts. However, these changes were within a normal range, so it was hard to conclude which group was most effective. However, this result was the same as in our previous study, in which the ALT activity increased with alcohol treatment and *A. quinata* extract reduced the ALT activity in acute alcohol-induced mice (17). To sum these results, *A. quinata* extracts were effective in lowering ALT activity after alcohol consumption.

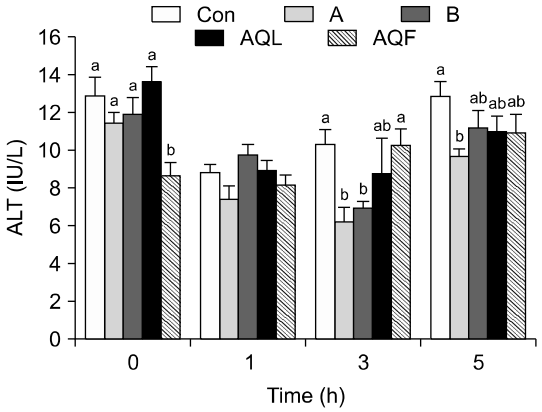

Fig. 1. Serum alanine transaminase (ALT) activity between groups. Con, control; A, Condition®; B, Morningcare; AQL, fermented *A. quinata* leaf extract; AQF, fermented *A. quinata* fruit extract. Means with different letters (a,b) above the bars are significantly different. Each bar represents the mean±SE.

Plasma ethanol concentration

We further measured serum ethanol concentrations before and after alcohol intake by the participants. As shown in Fig. 2, the serum ethanol concentration increased after alcohol intake and peaked at 3 h after alcohol consumption. Compared with the control group, the A group showed higher serum ethanol concentration at 1 h ($P<0.05$). AQL and AQF groups showed no differences compared with the control group at 1 h. At 3 h after alcohol consumption, the AQF group showed the lowest serum ethanol concentration compared to the other groups, however there were no statistical differences. After 5 h of alcohol consumption, the AQL and AQF groups had lower plasma ethanol concentrations compared with the B group.

In this study, we have shown that plasma ethanol concentrations increased in a time-dependent manner for 3 h and decreased at 5 h after alcohol consumption. Fur-

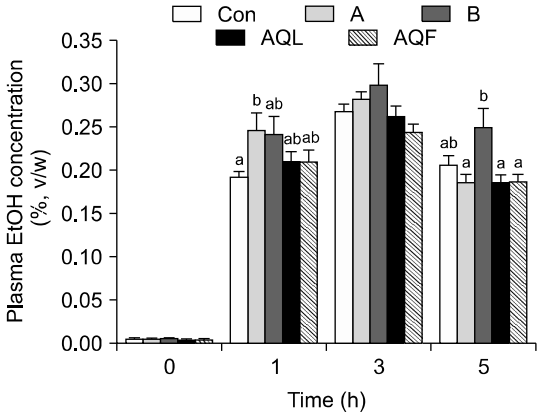

Fig. 2. Serum ethanol concentration before and after alcohol consumption. Con, control; A, Condition®; B, Morningcare; AQL, fermented *A. quinata* leaf extract; AQF, fermented *A. quinata* fruit extract. Means with different letters (a,b) above the bars are significantly different. Each bar represents the mean±SE.

thermore, we confirmed that the administration of fermented *A. quinata* extract before alcohol consumption was effective in reducing plasma ethanol concentrations. The acetaldehyde concentration was not measured in this study because 5 h is not long enough for acetaldehyde conversion from ethanol, and acetaldehyde concentration could be estimated from plasma ethanol concentration.

These results were similar to those of our previous study on the effects of *A. quinata* extracts on alcohol induced hepatotoxicity using mice, which confirmed that the hepatoprotective effects of *A. quinata* can be applied to the human system (17). Numerous agents like plant extracts have been proposed for the treatment of alcoholic hangover, and some plant extracts have shown remarkable effects (22-24). In our study results, even though the reduction of plasma ethanol concentration was less than in other studies (9) and there were no significant differences from the control group, the participants had substantially reduced plasma ethanol concentrations, which have not been confirmed in a human-based study. These results indicate that fermented *A. quinata* extracts can be used as a functional food ingredient for attenuating hangover after alcohol consumption.

Sensory evaluation of fermented *A. quinata* extracts

The results of the survey on 6 characteristic traits of fermented *A. quinata* extracts are shown in Table 2. Commercial hangover beverages A and B were more favored in appearance than fermented *A. quinata* extracts. Furthermore, texture, color, scent, and nasty smell were rated more positively by participants for the commercial hangover beverages than for the fermented *A. quinata* extracts. The score for overall taste was lowest in fermented *A. quinata* fruit extract. Fermented *A. quinata* extracts were a pilot product for a hangover beverage, so there are several possible reasons for the low sensory evaluation scores compared to the commercial products. However, these results could be important for the commercialization of *A. quinata* extracts. If more options for tastes are provided and if quality of the taste is improved, fermented *A. quinata* extracts can be used as a competitive hangover beverage with beneficial function on hangover relieve.

Despite our efforts, this study has several limitations. The study included a small sample size and some results are barely significant. In addition, the study included only Korean men and a limited age range. Future larger studies including populations of both genders and a wider age range are therefore warranted to confirm these findings and to determine gender and age differences. Another limitation may be a placebo effect, even though we used an indistinguishable placebo beverage to eliminate the placebo effect. However, this is the first study using *A. quinata* in humans, and we hope it will be useful as an exploratory study to elucidate the effects of *A. quinata* on alcoholic hangover.

In conclusion, the present intervention study results suggest that fermented *A. quinata* extracts alleviate alcoholic hangover and reduce the plasma ethanol concentrations.

Table 2. Sensory evaluation survey of commercial hangover beverages and fermented *A. quinata* extracts

	Control		A		B		AQL		AQF	
	AVG	STD	AVG	STD	AVG	STD	AVG	STD	AVG	STD
Appearance	4.50	2.37	4.38	1.06	4.30	1.34	1.70	1.16	2.90	1.85
Texture	4.00	1.89	5.88	1.46	4.60	1.26	3.20	0.92	2.90	1.79
Color	4.50	2.17	4.75	1.83	4.10	1.37	2.20	1.14	3.20	1.87
Scent	4.00	1.94	5.63	1.51	4.30	1.25	3.10	1.37	2.10	1.66
Nasty smell	3.60	1.96	2.25	1.91	4.50	0.71	4.70	1.95	3.90	1.60
Overall taste	4.00	1.94	6.00	0.53	5.10	1.10	2.70	0.95	2.20	1.48

A, Condition®; B, Morningcare; AQL, fermented *A. quinata* leaf extract; AQF, fermented *A. quinata* fruit extract.
AVG, average; STD, standard deviation.
Non-significant.

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AUTHOR DISCLOSURE STATEMENT

The authors declare no conflict of interest.

REFERENCES

1. An SW, Kim YG, Kim MH, Lee BI, Lee SH, Kwon HI, Hwang B, Lee HY. 1999. Comparison of hepatic detoxification activity and reducing serum alcohol concentration of *Hovenia dulcis* T_{HUNB} and *Alnus Japonica* Steud. *Korean J Med Crop Sci* 7: 263-268.
2. Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, Patra J. 2009. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. *Lancet* 373: 2223-2233.
3. Swift R, Davidson D. 1998. Alcohol hangover: mechanisms and mediators. *Alcohol Health Res World* 22: 54-60.
4. Kim KW, Yang JS, Lee JS, Cho YS, Kang SK, Chung HK. 1994. Activity of alcohol dehydrogenase and ethanol, acetaldehyde levels in normal adult blood. *Korean Ind Hyg Assoc J* 4: 240-247.
5. Helander A, Tottmar O. 1988. Effect of acute ethanol administration on human blood aldehyde dehydrogenase activity. *Alcohol Clin Exp Res* 12: 643-646.
6. Harvard University Medical School. 2006. How to handle a hangover. Drinking fluids may help with the morning-after misery from getting drunk. *Harv Health Lett* 31: 3.
7. Lee MK, Kim YG, An SW, Kim MH, Lee JH, Lee HY. 1999. Biological activities of *Hovenia dulsis* T_{HUNB}. *Korean J Med Crop Sci* 7: 185-192.
8. Park EM, Ye EJ, Kim SJ, Choi HI, Bae MJ. 2006. Eliminatory effect of health drink containing *Hovenia dulcis* Thunb extract on ethanol-induced hangover in rats. *Korean J Food Culture* 21: 71-75.
9. Kim JS. 2004. Effect of a alcohol detoxification beverage (ADB) contained *Radix puerariae* and *Bambusae caules in Liquamen phyllostachyos* on the alcohol administered mouse. *J Korean Soc Food Sci Nutr* 33: 318-323.
10. Lee MH, Kwak JH, Jeon G, Lee JW, Seo JH, Lee HS, Lee JH. 2014. Red ginseng relieves the effects of alcohol consumption and hangover symptoms in healthy men: a randomized crossover study. *Food Funct* 5: 528-534.
11. Verster JC, Penning R. 2010. Treatment and prevention of alcohol hangover. *Curr Drug Abuse Rev* 3: 103-109.
12. Pittler MH, Verster JC, Ernst E. 2005. Interventions for preventing or treating alcohol hangover: systematic review of randomised controlled trials. *BMJ* 331: 1515-1518.
13. Choi J, Jung HJ, Lee KT, Park HJ. 2005. Antinociceptive and anti-inflammatory effects of the saponin and sapogenins obtained from the stem of *Akebia quinata*. *J Med Food* 8: 78-85.
14. Jung HJ, Lee CO, Lee KT, Choi J, Park HJ. 2004. Structure-activity relationship of oleanane disaccharides isolated from *Akebia quinata* versus cytotoxicity against cancer cells and NO inhibition. *Biol Pharm Bull* 27: 744-747.
15. Higuchi R, Kawasaki T. 1976. Pericarp saponins of *Akebia quinata* D_{ECNE}. I. Glycosides of hederagenin and oleanolic acid. *Chem Pharm Bull* 24: 1021-1032.
16. Ikuta A, Itokawa H. 1988. A triterpene from *Akebia quinata* callus tissue. *Phytochemistry* 27: 3809-3810.
17. Lee SH, Song YS, Lee SY, Kim SY, Ko KS. 2014. Protective effects of *Akebia quinata* fruit extract on acute alcohol-induced hepatotoxicity in mice. *Korean J Food Sci Technol* 46: 622-629.
18. Jung SH, Lee SH, Ko KS. 2016. Effect of oleanolic acid and hederagenin on acute alcohol-induced hepatotoxicity in mice. *Korean J Food Sci Technol* in press.
19. Valentová V, Ulrichová J, Cvak L, Šimánek V. 2007. Cytoprotective effect of a blueberry extract against oxidative damage of rat hepatocytes. *Food Chem* 101: 912-917.
20. Choi JS, Yoon TJ, Kang KR, Lee KH, Kim WH, Suh YH, Song J, Jung MH. 2006. Glycoprotein isolated from *Acanthopanax senticosus* protects against hepatotoxicity induced by acute and chronic alcohol treatment. *Biol Pharm Bull* 29: 306-314.
21. Letteron P, Fromenty B, Terris B, Degott C, Pessayre D. 1996. Acute and chronic hepatic steatosis lead to *in vivo* lipid peroxidation in mice. *J Hepatol* 24: 200-208.
22. Lim AK, Jung MJ, Lee JW, Hong JH, Kim KS, Jung SB, Kim DI. 2011. Effect of alcohol detoxification beverage that contained *Bulnesia sarmienti* on alcohol-metabolizing enzymes and antioxidant enzyme activities. *Korean J Food Preserv* 18: 407-413.
23. Kim JH, Min SS, Kim SH, Hong HD, Kim JS, Kim SU. 1995. Effect of arrowroot flower (*Puerariae flos*) extract on lowering of ethanol concentration in rat blood. *J Korean Soc Agric Chem Biotechnol* 38: 549-553.
24. Lee HS, Isse T, Kawamoto T, Baik HW, Park JY, Yang M. 2013. Effect of Korean pear (*Pyrus pyrifolia* cv. Shingo) juice on hangover severity following alcohol consumption. *Food Chem Toxicol* 58: 101-106.