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Oenanthe javanica extract accelerates ethanol metabolism in ethanol-treated animals

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The effect of water dropwort (*Oenanthe javanica* DC) extract in eliminating ethanol was evaluated in New Zealand white rabbit and ICR mice. When a hot-water extract of water dropwort extract and ethanol was injected into New Zealand white rabbit, the plasma ethanol level was rapidly reduced, similar to metadoxine treatment. Specifically, the n-butanol fraction of hot-water extract was the strongest in eliminating plasma alcohol in ICR mice. When ethanol was orally ingested, administration of the hot-water extract eliminated up to 44% of the plasma ethanol in mice while the n-butanol fraction eliminated around 70%. Alcohol removal behaved in a dose-dependent manner in response to 50-200 mg/kg of n-butanol fraction. These data show *O. javanica* extract is effective in overcoming alcohol intoxication by the accelerating ethanol metabolism. [BMB reports 2009; 42(8): 482-485]

INTRODUCTION

Water dropwort (*Oenanthe javanica* DC), cultivated in East Asian countries such as Korea, China and Japan, is consumed as a spicy vegetable especially in early spring because of its distinctive aroma and taste. In traditional Chinese medicine, it has well-known uses in the treatment of jaundice, hypertension and polydipsia. Indeed, Chinese researchers have already shown that *O. javanica* extract has anti-arrhythmic activity (1) and anti-diabetic activity by promoting insulin release from Langerhan's β-cells (2). Recently, the protective effect of *O. javanica* extract against hepatitis induced by hepatitis B virus was also described (3, 4).

As water dropwort soup is often consumed for overcoming alcohol hangovers, its hepatoprotective activity has been extensively studied in Korea. Three major flavonoids including isorhamnetin sulfate, hyperin and persicarin were isolated from the leaves and stems of *O. javanica* (5, 6). Among them persicarin exhibited high hepatoprotective activity against the hepatic lipid peroxidation in bromobenzene or acetaminophen-treated rats (7, 8). Enhanced enzyme activity for alcohol detoxification by persicarin was also recognized in ethanol-treated rats (9).

In general, alcohol hangovers present personal health and socio-economic consequences most often characterized by headache, tremulousness, nausea, diarrhea, and fatigue combined with decreased occupational, cognitive, or visual-spatial skill performance (10). Even though alcohol hangovers are not solely dose-related, acetaldehyde is most likely responsible for hangover symptoms (11). Indeed, the rapid removal of acetaldehyde from the body is necessary for overcoming an alcohol hangover.

Increased understanding of the pathogenesis of alcoholic liver disease and the associated hangover has provided new treatment approaches that alter the liver's glutathione pool in order to counteract oxidative stress generated by cytochrome P450 during ethanol metabolism (12). One such treatment is the molecule metadoxine (pyridoxol and L-2-pyrrolidone-5-carboxylate) which can protect against glutathione depletion by increasing glutathione reductase activity (13).

In this paper ethanol metabolism after administration of *O. javanica* extract was investigated in ethanol-injected rabbits and ethanol-fed mice. Results were compared with metadoxine in order to fully evaluate its mitigating effect on alcohol hangover.

RESULTS AND DISCUSSION

Ethanol elimination in New Zealand white rabbits

The elimination of ethanol was examined in New Zealand white rabbits by monitoring the plasma ethanol concentration following injection of 20% ethanol via the ear vein. Immediately after injection the plasma ethanol concentration increased above 215 mg/dl and then decreased in a first-order pattern dependent upon time (Fig. 1). Three hours after treatment the plasma ethanol concentration of the experimental group fed hot-water extract of water dropwort (*O. javanica* DC) was reduced to 50 ± 2.3 mg/dl, which is nearly identical to the value of the reference group treated with 50 mg/kg of metadoxine. In contrast, the plasma ethanol concentration of

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the control group was 69 ± 3.3 mg/dl, which is 38% higher than values from the experimental group and reference group. Five hours after alcohol injection a plasma ethanol concentration of 33 ± 2.1 mg/dl and 30 ± 2.0 mg/dl was detected in the experimental and references groups, respectively, which is much lower than the plasma ethanol in the control group. observed as 54 ± 2.7 mg/dl.

Ethanol elimination in ICR mice

Hot-water extract of water dropwort was further fractionated using organic solvents in the order of n-hexane, methylene chloride and n-butanol. After each of these fractions was administered orally to ICR mice (200 mg/kg of each fraction; 30% ethanol), the n-butanol fraction was revealed to possess the highest rate of ethanol elimination (Fig. 2). The plasma concentration after treatment with n-butanol fraction was measured to be 22 ± 1.1 mg/dl after 2 h, a value nearly identical to the metadoxine-treated group (21 ± 2.9 mg/dL). When the concentration of n-butanol fraction ranged from 20 mg/kg to 200 mg/kg, plasma ethanol concentration decreased in a dose-dependent manner (Fig. 3). However other fractions did not perform well in removing ethanol from blood, generating similar plasma concentrations as the control group.

The rate of ethanol elimination following oral administration of extract or fractions was assessed in ICR mice. Two hours after treatment with hot-water extract, the plasma ethanol level was reduced to 42 ± 3.9 mg/dl, which is 44% lower than that of the control group (75 ± 8.2 mg/dl) (Fig. 4A). When n-butanol fraction was administered the plasma ethanol concentration was measured at 22 ± 3.0 mg/dl after 2 h, which is about 70% lower than the control group.

In addition, the plasma acetaldehyde concentration was observed at 0.3-0.4 mg/dl after 2 h when extract or n-butanol fraction was administered to mice. This value is nearly 20-30% lower than the control group and is similar to the acetaldehyde concentration of the metadoxine-treated group (Fig. 4B). This indicated the acetaldehyde produced by ethanol metabolism was nearly all removed from blood by liver detoxification processes. This accelerated removal of plasma acetaldehyde can contribute in preventing alcohol hangover effects after excess alcohol ingestion.

In conclusion, *O. javanica* extract is helpful in preventing the signs and symptoms of alcohol intoxication and overcoming alcohol hangover by inducing rapid ethanol metabolism.

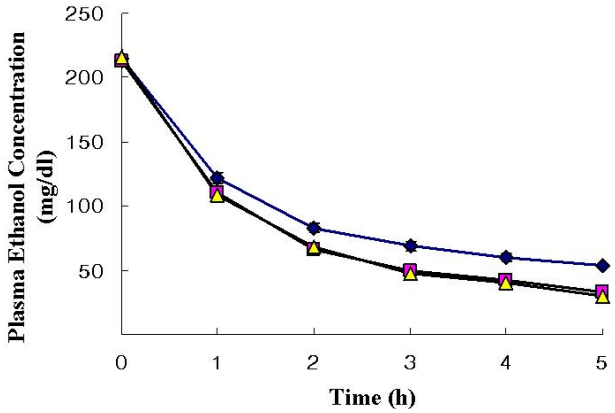

Fig. 1. Time course of plasma ethanol concentration after injecting 20% ethanol via ear vein in New Zealand white rabbits. (◆), simultaneously with 125 mg of hot-water extract (■), or simultaneously with 125 mg of metadoxine (△). Values are mean ± S.D. (n = 9, P < 0.001).

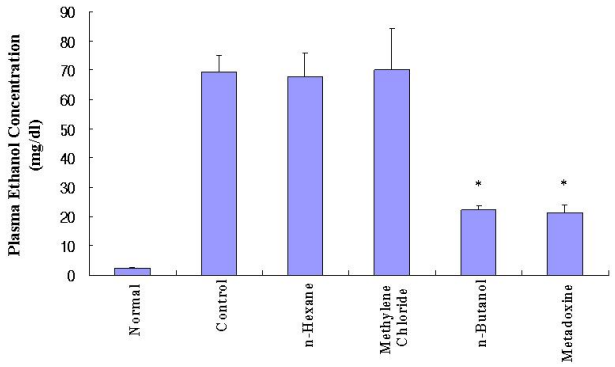

Fig. 2. Plasma ethanol concentration 2 h after administering a mixture of 30% ethanol with 6 mg of various fractions of hot-water extract to ICR mice. Normal systems were fed neither ethanol nor fraction and control systems were provided only ethanol. In the reference system, 1.5 mg of metadoxine was taken simultaneously with ethanol. Values are mean ± S.D. (n = 5, *P < 0.01 vs. control).

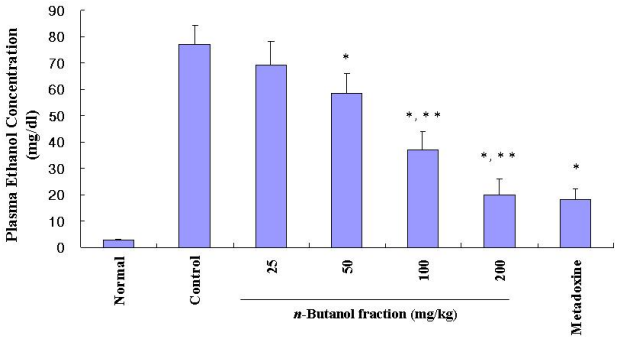

Fig. 3. Comparison of plasma ethanol concentrations 2 h after ingesting 30% ethanol with varying amounts of n-butanol fraction in ICR mice. Normal systems were fed neither ethanol nor fraction and control systems were provided only ethanol. In the reference system, 1.5 mg of metadoxine was taken simultaneously with ethanol. Values are mean ± S.D. (n = 5; *P < 0.01 vs. control; **P < 0.01 vs. 50 or 100 mg/kg of n-butanol fraction).

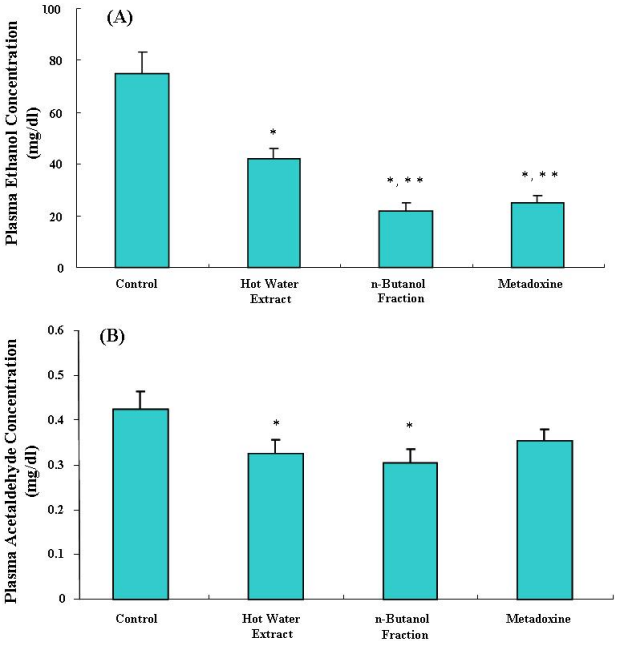

Fig. 4. Plasma level of ethanol (A) and acetaldehyde (B) 2 h after ingesting 30% ethanol with hot-water extract or n-butanol fraction in ICR mice. Control systems were fed only ethanol, and reference systems were provided ethanol with 1.5 mg of metadoxine. Values are mean ± S.D. (n = 5; *P < 0.01 vs. control; **P < 0.01 vs. hot-water extract).

MATERIALS AND METHODS

Materials and chemicals

Water dropwort (*O. javanica* DC) was collected from agricultural farms in Pyongyang-ri, Cheongdo-gun, Gyoungsangbuk-do, Korea. Metadoxine was kindly provided by Ilyang Pharmaceutical Co. Ltd (Yongin, Korea).

Preparation and fractionation of water dropwort extract

The aerial part of water dropwort was washed and dried for 1 wk, and 600 g of dried plant was extracted by reflux with 6 l of boiling water for 3 h. Approximately 165-180 g of residual mass in hot-water extract was obtained. After filtrating insoluble parts, the extract was concentrated to 2 l and re-extracted 3 times with the same volume of n-hexane. The remaining aqueous phase was concentrated into 1.5 l and extracted 3 times with the same volume of methylene chloride. The remaining aqueous phase was then concentrated into 1 l and extracted 3 times with the same volume of n-butanol. Stock solutions of each fraction in ethanol were made to a concentration of 25 mg/ml.

Experimental animals

New Zealand white rabbits around 2.5 kg were supplied from Dept. of Animal Husbandary, Cheonan Yonam College (Cheonan, Korea) and fed with rabbit nutrient pellets of Agribrands Purina Korea (Gimhae, Korea). ICR mice weighing around 30 g were purchased from Daehan BioLink Co., Ltd (Eumsung, Korea), and fed with rat pellets from Superfeed Co. (Wonju, Korea). The animal room was maintained at a temperature of 23 ± 3°C with 50 ± 10% humidity and was illuminated repeatedly at 150-300 lux with 12 h intervals. All animals were adapted for at least 1 week prior to the experiment.

Ethanol metabolism in New Zealand white rabbits

New Zealand white rabbits (n = 9) were injected with 1.25 ml of 20% ethanol with 10% hot-water extract of *O. javanica* through the ear vein. In controls a solution of 20% ethanol in saline was injected, and in the reference group 125 mg of metadoxine was administered instead of hot-water extract. Blood was taken at each time point and the plasma ethanol concentrations were determined by TC ethanol kit (Boeringer Mannheim, Germany).

Ethanol metabolism in ICR mice

Male ICR mice (n = 5) were orally administered 240 µl of 30% ethanol containing either 25 mg/ml of water dropwort extract or fraction. The control set was treated only with 30% ethanol, and the reference set was fed with 30% ethanol containing 6.25 mg/ml of metadoxine. The normal set was fed neither ethanol nor extract. In experiment testing dose-dependency, the extract was diluted in 30% ethanol and the same amount was fed to mice. Two hours after administration blood was withdrawn and the plasma ethanol and acetaldehyde concentrations were determined by TC ethanol kit and TC acetaldehyde kit (Boeringer Mannheim, Germany), respectively. One-way ANOVA was performed for the statistical analysis. When ANOVA showed significant differences, *post hoc* analysis was performed with the Newman-Keuls multiple range test.

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