THE EFFECT OF AN AMETHYSTIC PRODUCT ON ETHANOL IN HUMANS

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SUMMARY

A putative amethystic product was studied in two cohorts of human subjects. The amethystic product (Sobrietol®) was applied according to the manufacturer's instructions while control subjects received water in place of the Sobrietol® solution. The two cohorts were challenged with 1.2 ml/lb and 1.4 ml/lb of 80 proof liquor, respectively, with subsequent breath alcohol (BrAC) measurement. In cohort 1, Sobrietol® reduced the area under the BrAC curve (AUC) by 15.1% ($p = 0.003$) relative to controls; in cohort 2 the AUC was reduced by 12.5% ($p = 0.011$) relative to controls. It appears that the amethystic product Sobrietol® can eliminate significantly greater ethanol than ethanol eliminated by similar controls.

KEY WORDS

ethanol, pharmacokinetics, amethystic, forensic, alcohol dehydrogenase

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INTRODUCTION

An amethystic agent is any agent that is able to reverse alcohol intoxication or lower blood alcohol. It is so named because historically the gemstone amethyst was believed to reverse alcohol intoxication. More recently agents capable of relieving intoxication without affecting *in vivo* alcohol concentrations as well as agents that reduce alcohol concentrations *in vivo* are both considered amethystic agents.

Numerous products and processes evaluated for amethystic effect were reviewed by Whitmire /1/. Intravenous injection of microbial alcohol oxidase reduced blood alcohol concentration in ethanol challenged rats and rabbits. These injections resulted in a threefold increase in ethanol elimination but numerous experimental animals died shortly after the experiment /2/. Two reports indicate that hemodialysis or peritoneal dialysis was used for emergency ethanol removal resulting in ethanol removal several-fold greater than unaided metabolism, but dialysis is impractical except for emergency use /3,4/. There have been several reports in which fructose variously increased endogenous alcohol elimination; in most of these cases, however, fructose increased alcohol elimination from a prevailing relatively low elimination rate to a more normal alcohol elimination rate /5,6/.

Several experimental drugs have been investigated for reversing or preventing ethanol intoxication. Both DH-524 [2(3,4-dichlorophenoxy)methyl-2-imadazoline)] /7-9/ and ST-587 [2(-chloro-5-trifluoromethyl phenylimino)imidazoline] /10/ reversed intoxication in ethanol challenged rats and prevented intoxication when administered prior to ethanol challenge. The imiadazobenzodiazepine, Ro15-4513 (ethyl-8-azido-5,6-dihydro-5-methyl-6-oxo-4H-imidazo[1,5α][1,4]benzodiazepine-3-carboxylate) was used to stimulate ^{36}Cl uptake at the GABA receptor while blocking the intoxicating effect of ethanol /11/. Importantly, none of these experimental drugs affected blood alcohol concentration.

Drugs such as naltrexone have been described as amethystic /12/ but those drugs are more correctly identified as prophylactics to prevent drinking, somewhat similar in use to cyanamide and disulfiram.

Recently a product named Sobrietol® has been advertised as an amethystic agent /13/. Ingredients of the product include alcohol dehydrogenase (ADH), lactate dehydrogenase (LDH), NADH, calcium pyruvate, methionine, fructose, sodium phosphate dibasic dihydrate,

and glutathione. This product purports to enzymatically oxidize ethanol in the gut by using ADH and LDH to recycle NAD; the LDH substrate calcium pyruvate is used to thermodynamically pump this coupled enzyme reaction /14/. With ethanol thus cleared from the gut, ethanol from the vascular space would diffuse back into the gut and be oxidized in turn. This amethystic principle was demonstrated *in vitro* /14/ and *in vivo* in dogs /1/ but no investigation in humans has been reported. Therefore, the purpose of the present work was to evaluate the amethystic effect of Sobrietol®.

MATERIALS AND METHODS

Human subjects were volunteers from a class training to become Texas highway patrol troopers (Austin, TX). Volunteer subjects currently taking medications prescribed by a physician and subjects with known chronic medical conditions managed by a physician were excluded. Pregnant or nursing female subjects were also excluded. Informed consent was obtained from all remaining volunteers. The volunteers were divided into cohort 1 (19 experimental subjects, six control subjects) and cohort two (23 experimental subjects, five control subjects).

Sobrietol® (New Paradigm Health Systems, Inc., Seattle, WA) was administered according to instructions on the manufacturer's web site /13/. All subjects were administered 20 mg famotidine p.o. one hour before ethanol challenge. All subjects were fed a sandwich consisting of two slices of bread, a single piece of luncheon meat, and lettuce. Subjects were allowed water or diet soda with the sandwich.

Prior to the first ethanol dose experimental subjects consumed a single packet of Sobrietol® stirred into 4-6 ounces of tap water; control subjects consumed 4-6 ounces of tap water containing no Sobrietol®. Cohorts 1 and 2 were challenged with 1.2 ml/lb body weight and 1.4 ml/lb body weight of 80 proof liquor, respectively, divided into three equal doses. The subjects were allowed to mix the liquor in each dose with 4-6 ounces of water or diet soda. The subjects had a maximum of 15 minutes to consume each of the three ethanol doses. At the end of the third ethanol dose experimental subjects consumed two packets of Sobrietol® stirred into 4-6 ounces of tap water; control subjects consumed 4-6 ounces of tap water containing no Sobrietol®.

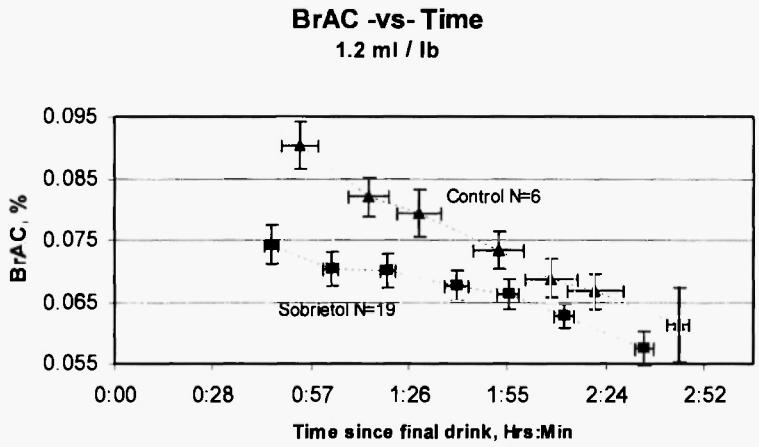

Fig. 1: Mean breath alcohol (BrAC) of volunteers dosed (p.o.) with 1.2 ml of 80 proof liquor per pound of body weight. The abscissa indicates the elapsed time after completion of the final ethanol dose. Triangles indicate control subjects and squares indicate experimental subjects. Error bars indicate standard error of the group mean BrAC at the indicated time. The experimental group AUC was significantly (15.1%) lower than the control group ($p = 0.003$).

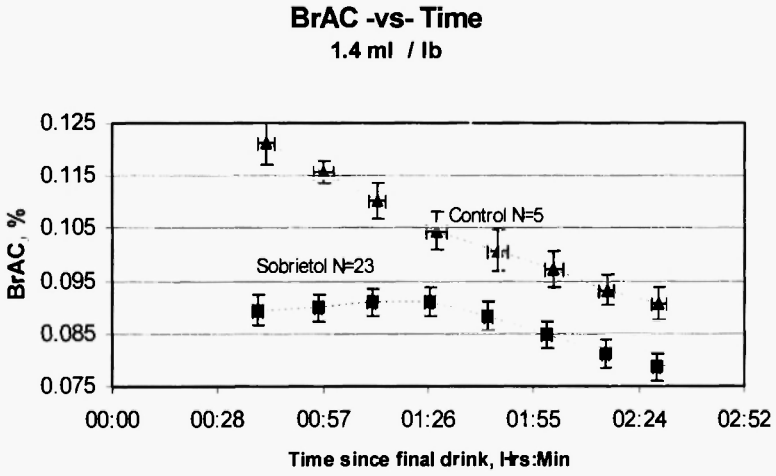

Fig. 2: Mean breath alcohol (BrAC) of volunteers dosed (p.o.) with 1.4 ml of 80 proof liquor per pound of body weight. The abscissa indicates the elapsed time after completion of the final ethanol dose. Triangles indicate control subjects and squares indicate experimental subjects. Error bars indicate standard error of the group mean BrAC at the indicated time. The experimental group AUC was significantly (12.5%) lower than the control group ($p = 0.011$).

All subjects were then evaluated by a sequence of breath alcohol measurements using an Intoxilyzer 5000 (CMI, Inc., Owensboro, KY). Subjects also participated in Standardized Field Sobriety Tests (SFST) /15/ as a training exercise.

AUC values indicate the amount of initial ethanol dose not metabolized over a specified period of time and available for measurement as BrAC. Therefore, the amethystic effect was determined by comparing the area under the BrAC curve for control and experimental subjects. AUC values were computed using the trapezoid rule.

Another measure of amethysis is the fraction of initial ethanol dose that does not appear in the vascular space and thus is not measurable as BrAC. Therefore, the fraction of the initial ethanol dose eliminated in both control and experimental subjects was also compared. The volume of the total body water (TBW) compartment for each subject was estimated using the height and weight for each subject with the anthropometric correlations of Hume and Weyers /16/.

RESULTS

Cohort 1 contained 19 experimental subjects (two females) and six control subjects (one female). Cohort 2 contained 23 experimental subjects (four females) and five control subjects (one female). Mean BrAC values for control and experimental subjects in both cohorts are shown in Figures 1 and 2, respectively. Time = 0 indicates the endpoint in time of the last of the three ethanol doses. Error bars indicate the standard error of mean BrAC values.

Cohort 1 (Fig. 1) AUC (mean ± SD) values were 6.67 ± 1.0 %-minute and 5.66 ± 0.88 %-minute for control and experimental groups, respectively; the difference in AUC values was significant ($p = 0.003$). In cohort 1 the experimental group mean AUC was 15.1% lower than the control group mean AUC. Also in cohort 1, 18 of 19 (95%) experimental subjects had AUC values lower than the control group mean AUC.

Cohort 2 (Fig. 2) AUC values were 7.67 ± 0.64 %-minute and 6.71 ± 0.79 %-minute for control and experimental groups, respectively; the difference in AUC values was significant ($p = 0.011$). In cohort 2 the experimental group mean AUC was 12.5% lower than the control group mean AUC. Also in cohort 2, 19 of 23 (83%) experimental subjects had AUC values lower than the control group mean AUC.

The mean estimated TBW for females of both cohorts was 34.75 ± 2.98 l. The mean estimated TBW for males of both cohorts was 45.31 ± 4.19 l.

The estimated AUC based on the initial dose for cohort 1 was 16.68 ± 1.77 %-minute. The fraction of the initial dose eliminated by the control group was 0.593 ± 0.045 while the fraction eliminated by the experimental group was 0.660 ± 0.051; the difference of the mean fraction of the initial dose eliminated between control and experimental groups was significant ($p = 0.003$).

The estimated AUC based on the initial dose for cohort 2 was 17.87 ± 1.22 %-minute. The fraction of the initial dose eliminated by the control group was 0.576 ± 0.019 while the fraction eliminated by the experimental group was 0.623 ± 0.047; the difference in the mean fraction of the initial dose eliminated between control and experimental groups was significant ($p = 0.001$).

DISCUSSION

In both cohorts the mean BrAC values of the experimental subjects were lower than the mean BrAC values for the control subjects.

Cohort 1 was investigated the day before cohort 2. Cohort 1 received an ethanol dose of 1.2 ml/lb, a dose that traditionally produced sufficient intoxication to successfully demonstrate the SFST. However, in cohort 1 the mean BrAC for the experimental group did not reach 0.08% while the mean BrAC for the control group exceeded 0.08% for approximately 30 minutes. Several complaints originated from the cohort 1 SFST training that there were insufficient numbers of acceptably intoxicated subjects. As a result, the ethanol dosing was increased to 1.4 ml/lb for cohort 2. The increased dosing yielded numerous subjects with BrAC values greater than 0.08% for as long as 2 hours; no complaints of insufficient intoxication originated from SFST training with cohort 2.

By every measure applied here, it appears that the amethystic product Sobrietol® eliminated up to 15% on average more ethanol than did unaided metabolism in control subjects.

It should be noted that since the ethanol dose was computed based only on body weight the experimental group in cohort 1 was slightly overdosed relative to the control group. Based on the ethanol dose and the TBW, the estimated initial BAC for the experimental group was

0.195% compared with the control group value of 0.185% ($p = 0.001$). There was no significant difference between groups in the initial dose in cohort 2 ($p = 0.21$). This discrepancy in initial ethanol dosing is likely due to the slight under-representation of females in the cohort 1 experimental group. Thus the amethystic effect observed in cohort 1 could possibly be less than the maximum possible if there were no discrepancy in initial ethanol dosing between control and experimental groups.

CONCLUSION

Based on the work presented here, it appears that the amethystic product Sobrietol® when used as described can eliminate significantly greater ethanol than ethanol eliminated by similar controls.

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