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Another 'soberade' on the market: does Outox keep its promise?

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Ein weiterer „Promillekiller" am Markt: Hält Outox, was es verspricht?

Zusammenfassung. *Hintergrund:* Zahlreiche Produkte am Markt werben damit, die Alkoholkonzentration im menschlichen Körper schnell und deutlich zu reduzieren. So soll auch das fructosehältige Getränk Outox die Alkoholeliminationsrate (β60) erheblich steigern. Erklärungen für diesen „Fructose-Effekt" basieren auf der Annahme, dass das Coenzym der Alkoholdehydrogenase, NAD+, in Anwesenheit von Fructose schneller regeneriert wird.

Methoden: In jeweils zwei Trinkversuchen wurde mit 30 Probanden eine randomisierte, doppelblinde, placebokontrollierte Studie im Cross-over Design durchgeführt. Unter strikt identischen Bedingungen wurde jeweils die gleiche Alkoholmenge konsumiert, wobei im Anschluss einmal 250 ml Outox und einmal 250 ml Placebo getrunken wurden. In regelmäßigen Abständen erfolgten Messungen der Alkoholkonzentrationen im Blut (BAK), in der Ausatemluft (AAK) und im Harn (HAK).

Ergebnisse: Die Auswertungen ergaben einen statistisch relevanten Unterschied ($p < 0.0001$) zwischen den gemittelten Alkoholkonzentrationen beider Trinkversuche. Insgesamt betrug die gemittelte BAK-Differenz 0.077 g/l (0.748 g/l ohne vs 0.671 g/l mit Outox), entsprechend 10.3%. Die AAK-Differenz betrug 0.045 mg/l (0.314 mg/l ohne vs 0.269 mg/l mit Outox, 14.3%). Die Unterschiede waren bei den Männern geringfügig größer als bei den Frauen. Bei den jeweiligen Alkoholeliminationsraten (β60) ergab sich kein statistisch signifikanter Unterschied.

Schlussfolgerungen: Unsere Ergebnisse zeigen, dass das fructosehältige Getränk Outox die Alkoholkonzentration um etwa 10% senkt. Die gemessenen Unterschiede der Alkoholkonzentrationen scheinen Folge einer verlangsamten Alkoholresorption im Magen-Darmtrakt zu sein. Eine signifikant gesteigerte Alkoholabbaurate ergab sich nicht. Unsere Studie zeigt, dass die werbewirksamen Versprechungen von Outox, ein „Promillekiller" zu sein, aus wissenschaftlicher Sicht nicht haltbar sind. Es ist sicherlich auch die Aufgabe von Ärzten, potentielle Konsumenten vor übertriebenen Erwartungen, v.a. im Zusammenhang mit dem Straßenverkehr, zu warnen.

Summary. *Objective:* Several products are being widely promoted for reduction of the concentration of alcohol in the human body. One of these preparations, the fructose soft drink Outox, claims to noticeably increase the alcohol elimination rate (β60). Theories to explain this 'fructose effect' are based on the assumption that NAD+, the coenzyme for alcohol dehydrogenase, is regenerated faster in the presence of fructose.

Method: A randomized double-blind, placebo-controlled cross-over study was performed with 30 volunteers in two drinking sessions each. Under strictly identical conditions, the same amount of alcohol was consumed, followed by the consumption of either 250 ml Outox or 250 ml placebo. Periodical measurements of blood (BAC), breath (BrAC) and urine alcohol concentration (UAC) were performed.

Results: Analyses revealed a significant difference ($P < 0.0001$) between the mean alcohol levels of the Outox and the placebo drinking sessions. The overall mean BAC difference was 0.077 g/l (BAC 0.748 g/l without vs 0.671 g/l with Outox), equivalent to 10.3%. The mean BrAC difference was 0.045 mg/l (BrAC 0.314 mg/l without vs 0.269 mg/l with Outox), equivalent to 14.3%. Differences were lower for women than for men. A significant difference between the alcohol elimination rates (β60) was not found.

Conclusions: The results show that the soft drink Outox may decrease the alcohol concentration by about 10%. However, BAC and BrAC differences are rather a consequence of slower gastric absorption of alcohol, because Outox does not increase the alcohol elimination rate. Our study demonstrates that the claim of Outox or other fructose drinks to work as a 'soberade' cannot be proven from a scientific point of view. It should be the task of physicians to warn potential consumers, especially in connection with drinking and driving.

Key words: Ethanol, fructose, blood alcohol concentration BAC, breath alcohol concentration BrAC, Outox.

Introduction

There is a popular aim to decrease the resulting body ethanol (the term alcohol will be used interchangeably in this paper) concentration after consumption of alcoholic drinks, especially in relation to drinking and driving. Many substances have been attributed as having some effect; for example, coffee beans, vitamin B6, pickled herring or simply water. Evaluation of their potential ability to increase alcohol metabolism has nearly always been without success. However, some investigations have shown a decrease of blood alcohol concentration (BAC) after consumption of sugar solutions [1–3], and fructose (levulose) in particular is widely accepted in this respect. The ability of fructose to decrease ethanol levels was first demonstrated [4] and then confirmed in several studies, e.g. [5–7]. The mechanism of this so called 'fructose effect' was thoroughly investigated but led to partly different conclusions. Elimination of alcohol in the human body is a relatively constant process that mainly uses alcohol dehydrogenase (ADH), although other enzyme systems support this process, especially in chronic alcohol abuse [8]. In rats the alcohol elimination rate increased after fructose was given, but no alteration of hepatic ADH was demonstrated [9]. On the other hand, fructose did not increase ethanol metabolism in ADH-deficient mice, so it was assumed that this enzyme must play a major role [10]. The first step in alcohol metabolism is the oxidation of ethanol by cytosolic ADH in the presence of the coenzyme NAD+, resulting in acetaldehyde, NADH and H^+, provided that acetaldehyde is removed [11]. The (re)oxidation of NADH, respective the dissociation of the ADH-NADH complex, is considered to be the rate limiting step here. Different metabolic pathways have been suggested to explain how fructose is involved. It was proposed that fructose stimulates ethanol oxidation indirectly by increasing the energy consumption of the liver, followed by increased mitochondrial oxidation of NADH [12]. Fructose is metabolized to fructose-1-phosphate and then to D-glyceraldehyde, so it was assumed that in the presence of ethanol further metabolism to glycerol takes place, needing NADH and therefore providing NAD+, instead of the usual metabolism to glycerate [13]. In fact it was shown that in the presence of ethanol the output of glycerate was completely suppressed [6]. However, it was doubted that this mechanism alone is a sufficient explanation, and further metabolism of glycerate to pyruvate and oxaloacetate was proposed, followed by the $NADH_2$-requiring metabolism of oxaloacetate to malate [14].

The fructose effect was repeatedly used for merchandising different products claiming to reduce alcohol levels and prevent hangover. However, none of these kept their promise, and all of them soon vanished from the market, mostly lacking scientific verification [15]. In the forensic community an *in vivo* fructose effect was severely doubted [16, 17], although in these studies the numbers of persons tested were too low to obtain statistically valid results. In other investigations the fructose effect was also judged controversially [18–20], so doubts seem to be justifiable.

In the meantime Outox, a soft drink containing fructose, has been available in several middle European countries. Currently, Outox is being aggressively promoted as a 'soberade' by the merchandiser, promising accelerated alcohol elimination by "production of physiological enzymes and co-enzymes in the body" and therefore diminishing the well known hangover effects. The doubts of physicians and scientists are completely ignored, and reports of enthusiastic consumers are spread on the internet to prove the "amazing" effects of such products. Such information has to be categorized as dangerous, especially in connection with road traffic, unless proper scientific studies were conducted. Statistical data show that up to 24% of the Austrian population can be rated as problem drinkers [21] who can be considered a target group for the soberade market. It is therefore realistic that physicians may be asked by patients if the alcohol concentration really can be decreased by a third with these products, thus impinging on clinical medicine [22]. The present study can help to answer such questions on a scientific basis.

A first study with Outox was conducted in Hungary, testing two blood samples from each of 10 male volunteers after consumption of 400 ml Outox [23], which is higher than a supposed commonly used dose. In order to give a scientific opinion on this topic a new investigation with Outox, including proper statistical analyses, seemed mandatory. In the present study, a total of 60 alcohol profiles of 30 volunteers after consumption of 250 ml Outox and 250 ml placebo were evaluated regarding BAC, breath (BrAC) and urine alcohol concentration (UAC), as well as the alcohol elimination rates in blood and breath.

Materials and methods

Study participants and conditions:

The study was evaluated by the ethical committee of Innsbruck Medical University. Experiments were performed at our Institute between December 2004 and February 2005. Thirty healthy volunteers, 14 women and 16 men, gave their written informed consent for participating in two drinking sessions. Data are given as mean ± standard deviation, if not indicated otherwise. The 30 volunteers ranged in age from 20 to 40 years (29 ± 5.1 years), body weight varied between 45 kg and 100 kg (67.9 ± 13 kg), body length between 157 cm and 200 cm (175.7 ± 9.9 cm) and calculated body mass indices between 17.6 and 28.7 (21.8 ± 2.6). Identical physical activity, food and beverage intake and possible medication on the testing day and on the day before were documented and proved by questionnaires for both experiments. None of the volunteers was taking any medication that might influence gastric emptying, e.g. ranitidine. Soberness of each individual was proved by a BrAC measurement at the beginning of the experiments and confirmed by BAC analysis of a simultaneously drawn blood sample. In the first drinking session the participants were allowed to drink beer, wine and vodka in amounts of their own choosing during a two-hour period; juices containing fructose were not allowed. The average amount of alcohol consumed by the participants was 1.06 ± 0.24 g per kg body weight. Deprivation of food was for at least four hours. The second drinking session was performed under strictly identical conditions with the same volunteers, i.e. the time of day of the experiment, possible medication, physical activity, time and kind of food intake (each of these topics checked on the testing day and the day before). The type and amount of the alcoholic beverages and the dura-

tion of the alcohol intake during the second experiment were also exactly the same. In both experiments either 250 ml of Outox (Outox experiment) or 250 ml of a placebo drink (placebo experiment) was consumed within 15 min of completing the alcohol intake. Starting 30 min after the end of alcohol consumption, BrAC was measured and a blood sample drawn every 30 min. In addition, a urine sample was collected every 60 min. Comparison of the sample times did not reveal any statistically significant differences between the two experiments, therefore the measurement values at each time point were directly comparable. Blood samples were taken from an indwelling catheter in the cubital vein using a blood collection system without preservatives (Monovette, Sarstedt, Wiener Neudorf). Measurements were made up to five hours after the end of drinking or until a BrAC $\leq$ 0.1 mg/l was reached.

OUTOX and placebo drink

According to the product specification of the manufacturer, the composition of Outox is based on carbonated water (6 g/l CO_2), fructose, citric acid, malic acid, ascorbic acid, 'tutti frutti' flavor and carminic acid (E120). Density is indicated as 1.083 ± 0.005, pH as 3.0 ± 0.3 and acidity as 4.0 ± 0.5. Outox contains 20.3 g carbohydrates, 3.0 mg sodium and no fat or protein; the energy value is stated as 81.2 kcal (345.1 kJ) per 100 ml. The drink is subjected to Belgian legislation for soft drinks (Health Certificate 2003, Ministerie van Sociale Zaken, Volksgezondheit en Leetmilieu), which means that Outox complies with European legislation and European hygiene guidelines. The Outox drinks used in this study were obtained from the distributor for Austria, Germany and Switzerland (Brunner Getränkevertriebs GmbH, Bayreuth, Germany).

Placebo drinks were prepared on the basis of a sugar-free carbonated soft drink, adding food flavoring and liquid artificial sweetener (containing cyclamate and saccharin) until a sufficient similarity in color and flavor was obtained. The placebo therefore did not contain any relevant energy value. Both drinks were served in dark-colored, non-transparent cups.

Determination of blood and urine alcohol concentrations

Blood and urine samples were stored at 4°C. All samples were analyzed within two days after the drinking experiments. BAC was measured according to Austrian forensic standards [24]. Sample preparation involved pipetting a mixture of 100 µl sample and 600 µl of t-butanol as internal standard into a headspace vial. The headspace injection volume was split into two different columns, PE-BAC1 (30 m x 0.32 mm x 1.8 µm) and PE-BAC2 (30 m x 0.32 mm x 1.2 µm) (Perkin Elmer, Vienna), each connected with a flame ionization detector. Headspace conditions were: thermostatting 20 min at 60 °C, needle and transfer temperature 90 °C, pressurization time: 1 min, injection temperature 100 °C. GC conditions were: 3 min at 35 °C, FID:

Table 1. Mean, minimal and maximal blood (BAC) and breath alcohol concentration (BrAC) measured in samples drawn at different time points, and the resulting mean differences between the two drinking experiments

BAC (n = 30)[a]	Placebo			Outox			Diff (%)
	Mean (SD)	Min	Max	Mean (SD)	Min	Max	
1.	1.010 (0.287)	0.486	1.675	0.976 (0.286)	0.579	1.543	–0.034 (–3.5)
2.	0.997 (0.286)	0.478	1.642	0.934 (0.288)	0.521	1.482	–0.063 (–6.8)
3.	0.931 (0.279)	0.435	1.540	0.859 (0.294)	0.413	1.397	–0.072 (–8.4)
4.	0.844 (0.267)	0.347	1.417	0.770 (0.302)	0.262	1.251	–0.074 (–9.6)
5.	0.754 (0.263)	0.236	1.240	0.663 (0.299)	0.129	1.190	–0.091 (–13.7)
6.	0.658 (0.258)	0.147	1.117	0.579 (0.283)	0.053	1.098	–0.079 (–13.6)
7.	0.593 (0.239)	0.133	1.013	0.547 (0.267)	0.105	1.019	–0.046 (–8.4)
8.	0.555 (0.201)	0.140	0.918	0.487 (0.257)	0.056	0.943	–0.068 (–13.9)
9.	0.505 (0.179)	0.211	0.818	0.463 (0.215)	0.113	0.891	–0.042 (–9.1)
10.	0.465 (0.168)	0.259	0.732	0.470 (0.217)	0.231	0.842	0.005 (1.1)
BrAC (n = 30)[a]	Placebo			Outox			Diff (%)
	Mean (SD)	Min	Max	Mean (SD)	Min	Max	
1.	0.470 (0.118)	0.245	0.730	0.441 (0.121)	0.255	0.670	–0.029 (–6.6)
2.	0.430 (0.121)	0.220	0.700	0.401 (0.128)	0.210	0.655	–0.030 (–7.4)
3.	0.392 (0.123)	0.200	0.680	0.362 (0.130)	0.150	0.585	–0.029 (–8.1)
4.	0.351 (0.117)	0.150	0.575	0.315 (0.134)	0.090	0.545	–0.036 (–11.4)
5.	0.307 (0.119)	0.095	0.545	0.261 (0.129)	0.030	0.490	–0.046 (–17.6)
6.	0.260 (0.118)	0.045	0.480	0.222 (0.127)	0.000	0.470	–0.038 (–17.0)
7.	0.230 (0.108)	0.000	0.420	0.207 (0.121)	0.000	0.440	–0.023 (–11.3)
8.	0.213 (0.094)	0.000	0.380	0.177 (0.112)	0.000	0.385	–0.036 (–20.1)
9.	0.191 (0.079)	0.060	0.335	0.168 (0.102)	0.000	0.370	–0.024 (–14.2)
10.	0.171 (0.070)	0.090	0.295	0.174 (0.099)	0.060	0.340	0.004 (2.1)

[a] Sample number per time point: the number decreases with ongoing measurements because the number of volunteers reaching zero increases; *Mean* mean value; *BAC* blood alcohol concentration [g/l]; *BrAC* breath alcohol concentration [mg/l]; *SD* standard deviation; *Min* minimal value; Max maximal value; *Diff* absolute difference; (in %): relative difference in percent.

240 °C. Each sample was pipetted twice, giving four independent results. Results never varied more than 5% and the average value was calculated.

Determination of breath alcohol concentration

BrAC was measured using a calibrated Alcotest 7110 MK III A (Dräger Austria, Vienna), which is also used by the police in Austria for evidential BrAC measurement in road traffic. Two independent breath samples are necessary for a valid result. An infrared optical measurement system and an electrochemical system are used, whereby the electrochemical system is needed to control the environmental air and for an internal comparison of the two measurements. The displayed measurement results are both obtained from the infrared optical system that is known to be the more reliable and more accurate measurement system. According to Austrian law, the lower of the two measured values is taken as valid result. The device is warmed to prevent water condensation. BrAC values are given as milligrams of alcohol per liter of exhaled air (mg/l).

Statistical analyses

The study was a randomized, placebo-controlled, double-blind study in cross-over design with Outox versus placebo as evaluated substances. The primary aim of the study was evaluation of the BAC elimination rate (β60) and the difference of BAC at each time point. The secondary aim was the evaluation of BrAC. The main hypothesis concerns the mean reduction of the alcohol concentration during a period of five hours; this was evaluated for the study collective as a whole and for men and women separately using mixed-effects models. The mixed model analysis was used to adjust for additional factors that may influence the alcohol concentration, especially measurement time, sex and body weight. In addition, the alcohol elimination rates were modeled in linear regression analysis using a paired t-test. The significance level was set at 0.05 for the comparison of the full study group and at 0.025 for the sex-specific calculations (Bonferroni correction). The sample size of the study was prespecified at 24 individuals in order to detect a BAC difference of 0.05 g/l as significantly different with a statistical power of 90%. To compensate for possible drop-outs among the volunteers, 30 persons were enroled. Randomization, meaning whether placebo or Outox was consumed in the first or the second experiment, was achieved according to a scheme based on random numbers. All statistical analyses were calculated using MS Excel 2002 or SPSS 11.0 for Windows.

Results

Mean BAC levels of all the volunteers were calculated for each measurement and showed that the highest mean concentration was at the first time point, i.e. on average 36 min after drinking ended. Mean BAC was 1.010 ± 0.286 g/l (range 0.486–1.675 g/l) in the placebo experiment and 0.976 ± 0.286 g/l (0.579–1.543 g/l) in the Outox experiment. The mean, minimal and maximal alcohol concentrations of all blood and breath samples at each time point are listed in Table 1. In addition, the absolute and relative difference of the alcohol concentrations between the two experiments was calculated. The number of measured values decreased with ongoing sample collection because the experiment was individually stopped when a sufficiently low BrAC value was reached.

Peak BAC levels were not reached at the first time point in all the volunteers, indicating that alcohol absorption had not finished at that point. The individual peaks for BAC and BrAC values are listed in Table 2. These values were proved to be significantly different in the two experiments, using a double-sided paired t-test ($P<0.05$ for BAC and $P<0.02$ for BrAC).

The mixed model analysis revealed a significant difference between the BAC values of the Outox and the placebo experiments ($P<0.0001$, $F = 14.2$). Similarly, evaluation of the BrAC values showed a significant difference in the two experiments ($P<0.0001$, $F = 24.5$).

Average differences of the overall measurements of BAC and BrAC that were adjusted for age, body-weight and measurement time were calculated for the total study group as well as separately for males and females. Detailed results are listed in Table 3.

UAC values of both drinking experiments were evaluated in the same way using the mixed model analysis (Table 3). Urine samples were collected every 60 min,

Table 2. Peak blood and breath alcohol levels of each volunteer in the two experiments

Volunteer	Peak BAC		Peak BrAC	
	Outox	Placebo	Outox	Placebo
1 (m)	1.140	1.188	0.465	0.510
2 (f)	0.755	1.036	0.335	0.475
3 (f)	0.751	0.639	0.345	0.325
4 (m)	0.927	0.976	0.420	0.450
5 (f)	0.580	0.805	0.255	0.360
6 (m)	1.374	1.363	0.645	0.635
7 (m)	1.385	1.292	0.620	0.585
8 (f)	1.205	1.330	0.545	0.620
9 (f)	0.652	0.709	0.310	0.355
10 (f)	0.653	0.748	0.295	0.320
11 (m)	1.131	1.068	0.475	0.445
12 (m)	0.877	0.911	0.375	0.395
13 (f)	0.612	0.486	0.265	0.245
14 (m)	1.242	1.414	0.545	0.625
15 (f)	0.703	0.840	0.350	0.395
16 (m)	0.706	0.699	0.325	0.365
17 (m)	1.030	1.018	0.440	0.470
18 (f)	1.543	1.531	0.670	0.665
19 (m)	0.710	0.951	0.320	0.430
20 (f)	1.343	1.356	0.550	0.605
21 (m)	1.261	1.308	0.545	0.490
22 (f)	1.511	1.675	0.655	0.730
23 (m)	1.157	1.262	0.535	0.575
24 (f)	0.830	0.735	0.405	0.350
25 (m)	0.759	0.931	0.320	0.450
26 (f)	0.978	0.906	0.480	0.465
27 (m)	0.972	1.066	0.440	0.515
28 (f)	0.819	0.703	0.420	0.355
29 (m)	0.801	0.893	0.435	0.425
30 (m)	1.254	1.156	0.520	0.490
Mean	0.989	1.033	0.444	0.471
SD	0.287	0.291	0.120	0.118

BAC blood alcohol concentration [g/l]; *BrAC* breath alcohol concentration [mg/l]; *m* male, *f* female; *Mean* overall mean value; *SD* standard deviation.

Table 3. Mean alcohol concentrations and differences between the placebo and Outox drinking experiments

		BAC (95% CI)	BrAC (95% CI)	UAC (95% CI)
Total[a]	Placebo	0.748 (0.719–0.776)	0.314 (0.301–0.327)	1.010 (0.979–1.041)
	Outox	0.671 (0.642–0.700)	0.269 (0.256–0.282)	0.901 (0.844–0.958)
	Diff [%]	10.3	14.3	10.8
Male[b]	Placebo	0.814 (0.789–0.839)	0.332 (0.322–0.342)	
	Outox	0.716 (0.692–0.741)	0.284 (0.273–0.295)	
	Diff [%]	12.0	14.5	
Female[c]	Placebo	0.706 (0.672–0.740)	0.300 (0.282–0.319)	
	Outox	0.656 (0.653–0.660)	0.270 (0.262–0.279)	
	Diff [%]	7.1	10.0	

[a]Mean age: 29.2 years; mean weight: 68.9 kg; [b]Mean age: 30.3 years; mean weight: 76.4 kg; [c]Mean age: 27.7 years; mean weight: 58.4 kg; mean time point after end of alcohol drinking: 166.5 min; *BAC* blood alcohol concentration [g/l]; *BrAC* breath alcohol concentration [mg/l]; *UAC* urine alcohol concentration [g/l]; *CI*: confidence interval; *Diff [%]* relative difference in percent.

giving too few results to permit statistical analysis for males and females separately, but for the group as a whole the differences of the urine alcohol concentrations were statistically significant ($P<0.001$, F = 11.7).

The mean values of BAC and BrAC at any time point showed a nearly linear alcohol elimination rate (Fig. 1 a,b). Evaluation of the interaction of time, i.e. minutes after beginning drinking, within the Outox and the placebo drinking experiments did not reveal any significant effect on the alcohol concentrations ($P>0.05$ for both BAC and BrAC). In addition, the alcohol elimination rates in the sure linear elimination phase were calculated for each volunteer, i.e. beginning two hours after the end of drinking and ending when a BAC of 0.15 g/l was reached. For BrAC, the concomitant measurement values were taken. The resulting individual blood alcohol elimination rates per hour (β60) are listed in Table 4. Linear regression analysis modeled separately for each person using a paired t-test revealed no statistical difference ($P = 0.6$ for BAC, $P = 0.3$ for BrAC). Furthermore, it can be seen that with Outox, 15 volunteers (7 women, 8 men) showed a higher β60, but in the other 15 volunteers the elimination rate

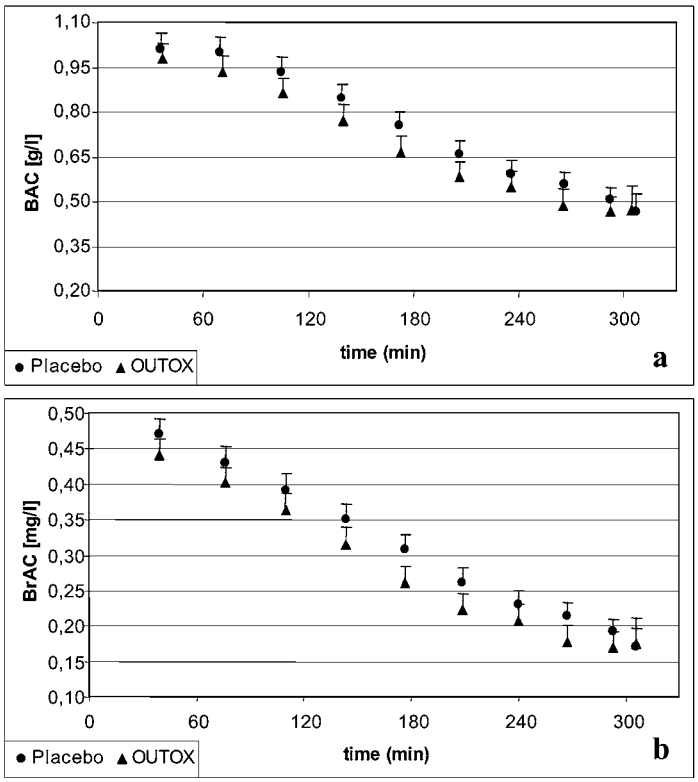

Fig. 1. The calculated mean values of blood alcohol concentration BAC (**a**) and breath alcohol concentration BrAC (**b**), including standard errors for each time point are shown. A linear elimination rate can be seen. There is no statistical difference between the regression rates of the placebo and the Outox drinking experiments

Table 4. The individual blood alcohol elimination rates per hour (β60) of each individual, calculated from the elimination phase

Volunteer	BAC elimination rate β60		
	Outox	Placebo	Diff [%]
13 (f)	0.264	0.168	36.4
27 (m)	0.240	0.193	19.5
5 (f)	0.147	0.113	22.8
14 (m)	0.196	0.167	14.7
4 (m)	0.197	0.176	10.8
15 (f)	0.164	0.144	11.8
1 (m)	0.159	0.144	9.1
23 (m)	0.223	0.210	5.8
26 (f)	0.133	0.121	9.3
8 (f)	0.226	0.215	5.2
12 (m)	0.150	0.144	3.9
11 (m)	0.133	0.128	4.3
25 (m)	0.175	0.169	3.1
28 (f)	0.199	0.194	2.4
3 (f)	0.169	0.165	2.4
22 (f)	0.238	0.240	–0.7
7 (m)	0.185	0.188	–2.0
24 (f)	0.189	0.193	–2.4
10 (f)	0.142	0.147	–4.0
30 (m)	0.138	0.145	–4.8
2 (f)	0.205	0.213	–4.0
9 (f)	0.163	0.175	–7.1
17 (m)	0.140	0.156	–11.2
19 (m)	0.136	0.152	–11.8
6 (m)	0.146	0.165	–13.1
29 (m)	0.164	0.185	–12.5
21 (m)	0.156	0.179	–14.4
16 (m)	0.153	0.176	–14.8
20 (f)	0.190	0.227	–19.8
18 (f)	0.182	0.236	–29.5
Mean	0.177	0.174	
SD	0.035	0.033	

BAC blood alcohol concentration, β60 [g/l per hour]; *Diff [%]* relative difference in percent; *m* male; *f* female; *Mean* overall mean value; *SD* standard deviation.

was actually lower. In addition, no differences between men and women were obvious. These results show that Outox did not increase the elimination rate of alcohol.

Figure 2 shows typical examples of elimination curves of two of the volunteers, one showing lower (a) and one showing higher (b) alcohol levels with Outox.

Discussion

Alcohol consumption, especially chronic alcohol abuse, not only causes severe physical damage directly and indirectly [25, 26] but can also cause secondary injuries, especially in connection with road traffic. Consequently, many products are currently offered as soberades, such as 'Bangout' in Hungary, 'Break-Down' in the USA and 'alcokill' in Austria and Germany, all containing fructose as the main ingredient. There have already been warnings about uncritically believing the merchandising promises of these manufacturers, that fructose is able to remarkably decrease alcohol concentrations, especially when there may be legal consequences of believing these claims, e.g. in connection with drinking and driving [15–17]. However, both *in vitro* and animal studies have partly proved a fructose effect, therefore this topic is of ongoing interest. Nevertheless, it has not yet been satisfactorily established whether fructose shows a measurable impact on alcohol elimination in humans. The present study evaluated whether the newly introduced fructose-containing drink Outox that is extensively merchandised in several European countries is really able to increase the alcohol elimination rate and thus influence body alcohol concentrations. The experiments were performed under practical conditions: Outox was evaluated as if consumed during usual leisure activities, which is usually shortly after drinking alcohol or between alcoholic beverages. As each of the 30 volunteers served as his/her own control, the results are based on calculations of a total of 60 alcohol concentration profiles.

The overall reduction of BAC was proved to be 10.3% in the present study, being somewhat lower than the reductions of 20% [27], 25% [28] or 43% [29] reported from other investigations. This may be partly due to different experiment settings but also to the smaller, but therefore realistic, fructose dose given in our study (50 g in total) compared with, if stated, 1 g/kg body weight [28], 75 g [29] or even 200 g fructose in total [5]. In a Hungarian study 400 ml Outox (81 g fructose) was consumed [23], which may explain the greater reduction of BAC (up to 28.1% reduction 4 hours after beginning drinking) compared with our results. Since common side effects of fructose consumption are nausea, abdominal cramps and diarrhea, as was reported for all participants in the Hungarian study, we opted for 250 ml Outox. At the moment, Outox is sold in 200 ml bottles, but according to the distributor the introduction of 250 ml cans is planned. Under these conditions, six of the 30 volunteers (20%) complained about nausea for 15–30 min after consumption. An appropriate warning declaration on the bottles would be desirable, as is generally done e.g. for certain artificial sweeteners.

The reduction of breath alcohol levels, in total 14.3%, was a little greater than reduction of the blood alcohol levels. It is known that at the beginning of alcohol absorption relatively too high BrAC values are obtained in comparison with a corresponding BAC [30], but the slightly greater impact of fructose on BrAC did not occur only in the absorption phase (Fig. 1b). Bilzer et al have observed the relatively too high BrAC values in the absorption phase also in the presence of fructose, therefore concluding that this phenomenon was independent from absorption [31]. Altogether, the small differences observed in our study were probably less than the intra-individual variations of the alcohol concentrations in the two drinking experiments. Further research on BrAC may be interesting.

Two independent statistical calculations did not prove a significant increase of the blood alcohol elimination rate (β60) in our study. The mixed-effects model analysis for the overall calculations and the statistical comparison of individual regression parameters and β60 values did not reveal significant differences between the two drinking experiments. Also the slope of the BrAC curve did not

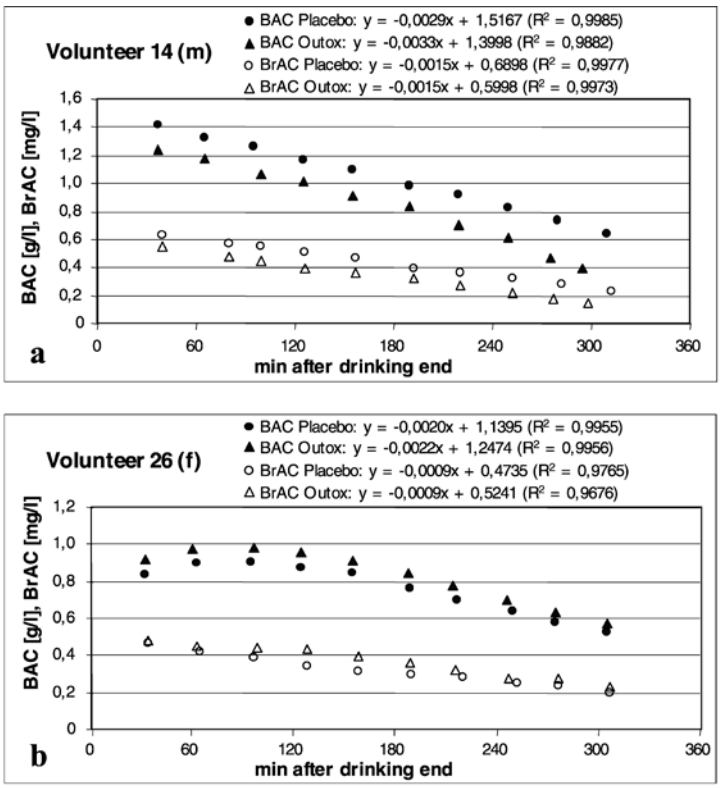

Fig. 2. Two examples of typical alcohol elimination curves are depicted. Examples were chosen in order to demonstrate that the alcohol levels were not necessarily lower in all volunteers in Outox experiments (**b**). Alcohol absorption time and the elimination characteristics were not changed by Outox, as can be also seen by the nearly parallel curves

show a statistically relevant difference between Outox and placebo. This is consistent with results of single experiments that found lowering of the peak alcohol concentrations without a change of β60 [3, 27, 20]. However, a significant increase of the *in vivo* BAC elimination rate was reported after intravenous infusion of 200 g fructose [5], maybe on account of the excessive and unrealistic amount of the sugar given. The placebo drink used in our study was prepared without a sugar to avoid possible interference with alcohol metabolism, as was indicated previously [1–3], so it is possible that the slight lowering of the alcohol concentrations may be due to slower gastric absorption or emptying.

Our results indicate that the alcohol-lowering effect was less among the women volunteers, although the fructose amount in relation to body weight was higher than for the men. The alcohol concentrations in men and women did not differ much, so it is not likely that the observed difference is a consequence of diverse alcohol concentrations in the body. It could be argued that possible sex differences in ethanol elimination may be the cause. If β60 of BAC in both drinking experiments is compared, the mean value for the women lies above the value for the men (0.179 ± 0.036 *versus* 0.161 ± 0.027 g/l*h^{-1}), which is statistically significant ($P < 0.04$). Perhaps the basic enzyme activity in women is higher than in men, as already reported in literature [32, 33], so that in comparison the lowering of alcohol concentrations due to Outox plays a minor role in women.

The relative difference in BAC values of the Outox and placebo experiments was on average 10.3%, for BrAC values 14.3%. Outox therefore has a statistically significant effect on alcohol concentrations if consumed in close connection with alcoholic beverages. However, the difference is much lower than the third as is promised by the manufacturers. Moreover, an increase of the alcohol elimination rates and therefore a 'fructose effect' could not be proven. It is likely that 50 g of any other caloric drink or food would have had the same effect. Furthermore, the mean absolute decrease of 0.77 g/l for BAC and 0.045 mg/l for BrAC is much too low to significantly reduce alcohol-induced impairment, especially in relation to road traffic. It also seems that the 'fructose effect' may be self-limiting in humans because of the unpleasant side effects on the gastrointestinal tract that may occur if greater amounts of fructose are consumed; hardly a positive finding for the sale of Outox. In addition, significant variances in the decrease of the alcohol concentrations were observed among the volunteers, therefore individuals cannot be sure if and to what extent Outox can possibly diminish their personal alcohol concentration. Consequently the claim of Outox being a 'soberade' cannot be proven from a scientific point of view.

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