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The effect of oral administration of various sugars on blood ethanol concentrations in man

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Urine output and blood ethanol concentrations have been measured in volunteers for 2 h after the administration of a standard oral dose of ethanol (0·798 g kg^{-1}) given 30 min after a large oral dose of one of several sugars in 200 ml water. Both fructose (125 g) and sorbitol (125 g) produced large reductions in urine output and blood-ethanol concentrations for the duration of the experiment when compared with controls. Galactose (125 g) had a similar but transient effect and smaller doses of fructose (62·5 g) were without these actions. It is concluded that the effects observed can be explained in terms of alterations in absorption of ethanol and water from the gastrointestinal tract.

Various reports have appeared in the literature suggesting that fructose has the ability to increase the rate of ethanol metabolism in man and to reduce blood-ethanol concentrations (Merry & Marks, 1967: Pawan, 1968; Patel, Paton & others, 1969; Lowenstein, Simone & others, 1970) although not all workers agree on this point (Camps & Robinson, 1968). The most usual explanation advanced for the observed effect is an enhancement of the action of alcohol dehydrogenase by fructose or its metabolites (Holzer & Schneider, 1955; Lowenstein & others, 1970). A variety of experimental designs have been used in these studies but most frequently fructose has been administered parenterally (4–200 g iv.) or by mouth (30–135 g) at the same time as the ethanol.

METHODS

Experimental design

Student volunteers of either sex took part. They were asked to eat a light meal and to drink one cup of tea or coffee before the experiment. They were then assigned to one of five dose regimens which was not made known to them. The regimens were: I, 125 g fructose; II, 62·5 g fructose; III, 125 g galactose; IV, 125 g sorbitol; or V, control (30 mg sodium saccharin); taken by mouth in 200 ml water.

Approximately 30 min later subjects were asked to drink over a 5 min period 0·798 g kg^{-1} ethanol as 2·53 ml kg^{-1} whisky or gin in an equal volume of water (flavoured with orange if requested). Although this dose may seem excessive, the blood-ethanol concentrations produced were not greatly in excess of the 80 mg ml^{-1} 'driving limit' (Fig 1A) and in 2 of the subjects they were below this limit at all times tested. Subjects were then asked to empty their bladder and at 0·5 h intervals the following were obtained: (*a*) volume of urine produced in the previous 0·5 h; (*b*) ethanol concentration of urine; (*c*) capillary blood ethanol (0·1 ml blood obtained from finger).

In some subjects measurements of blood-ethanol only were made.

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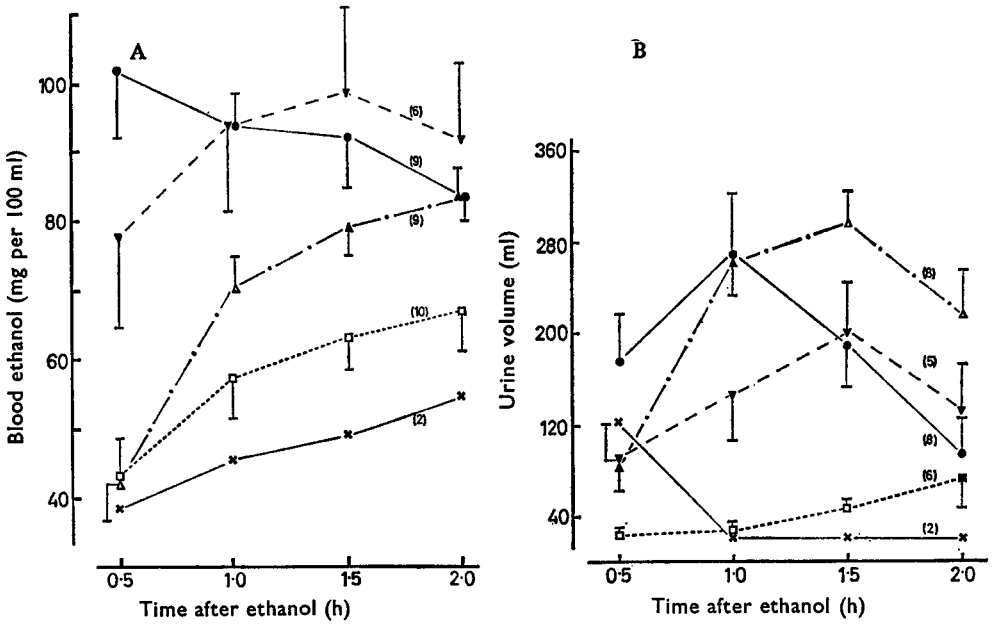

FIG. 1. Showing (A) blood-ethanol concentrations (mean ± s.e.: mg per 100 ml) and (B) urine volumes obtained at various times (h) after administration of a standard dose of ethanol in the following groups of volunteers (number contributing in parentheses): ● —— ● 30 mg sodium saccharin; ▼ — — ▽ and ■ - - - □, 62·5 and 125 g of fructose; ▲ — · — △ 125 g galactose; × —— × 125 g sorbitol. All treatments were given orally in 200 ml water some 30 min before the ethanol (0·798 g kg^{-1}). Open symbols represent statistically significant differences ($P<0·05$) from saccharin controls.

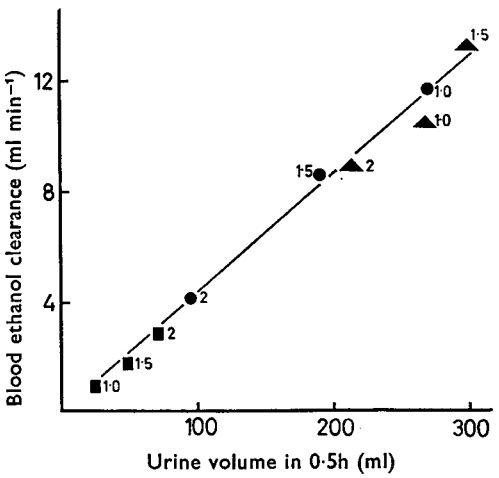

FIG. 2. Showing mean ethanol clearance values (ml min^{-1}) plotted against urine volume (ml) (at appropriate times after ethanol administration as indicated by figures in parentheses) for groups of volunteers treated with 125 g fructose (■), 125 g galactose (▲) or 30 mg sodium saccharin (●) each contained in 200 ml of water and administered 30 min before 0·798 g kg^{-1} ethanol.

Measurements of ethanol concentration

Ethanol concentrations were measured using a modification of the method of Curry, Walker & Simpson (1966). The sample (0·1 ml) was diluted with 0·9 ml of 6·0 mg per 100 ml n-propanol in water containing approximately 200 mg per 100 ml sodium citrate and 1–2 μl of this mixture was then injected into a Pye Gas Chromatograph (Series 104) fitted with a flame ionization detector and connected to a Kent Chromalog 2 integrator. The single column (1·5 m × 4 mm: 10% Carbowax on 100–110 mesh Anakrom U) was maintained at 85° and the retention times for ethanol and n-propanol were 76 and 126 s respectively. The amount of ethanol in the sample was computed from a linear calibration curve relating the ratio of the areas under the ethanol and n-propanol peaks to the ethanol concentration (mg per 100 ml) in known samples. Duplicate determinations were within ±1·5% for known samples.

General

Results are quoted as means (plus or minus standard errors where appropriate) and tests for significance were performed by Student's *t*-test.

RESULTS

Four of the subjects vomited at some stage of the trial and results from them have been excluded. No other unexpected adverse reactions were noted except with sorbitol which at the dose used exerted a gentle but compulsive cathartic action and after results had been obtained from two subjects this regimen was discontinued.

Following the control treatment a blood-ethanol concentration of 101·9 ± 10·2 mg 100 ml^{-1} was attained 0·5 h after the dose and thereafter declined by about 12 mg 100 ml^{-1} h^{-1} (Fig. 1A). A diuresis was also observed which reached a peak about 1 h after the ethanol (Fig. 1B). The ethanol concentrations in the urine samples at the various times and the total amount of urine produced in the 2 h period are shown in Table 1.

After the 125 g doses of both fructose and sorbitol the blood-ethanol concentrations attained 0·5 h after ingestion of the ethanol were very low (42·3 ± 5·9 and

Table 1. *Showing the mean (± s.e.) urine-ethanol level at 0·5, 1, 1·5 and 2 h after administration of ethanol, the total volume of urine produced (mean ± s.e.) and the total amount of ethanol eliminated in the urine for three groups of subjects who had previously taken either fructose (125 g), galactose (125 g) or sodium saccharin (30 mg) (each contained in 200 ml water) 30 min before 0·798 g kg^{-1} ethanol.*

Treatment	Number of subjects	Total urine produced in 2 h (ml)	Total ethanol in urine (mg in 2 h)	Urine-ethanol concentration (mg 100 ml^{-1}) at 0·5 h	1 h	1·5 h	2 h
Fructose (125 g)	7	170·7 ± 27·1	102	17·0 ±4·3	48·1 ±7·0	67·7 ±7·9	74·4 ±8·9
Galactose	8	854·1 ± 55·7	690	22·1 ±3·2	63·8 ±4·8	98·5 ±7·2	100·4 ±6·4
Control	8	723·0 ± 92·3	756	79·1 ±9·9	110·5 ±8·5	119·3 ±6·4	105·2 ±5·2

38·5 mg 100 ml^{-1} respectively) when compared with the concentrations attained after the control treatment. The levels then rose slowly but not to control values (Fig. 1A). Urine output was reduced throughout most of the experiment but with the fructose 125 g treatment, it rose after 1·5–2 h (Fig. 1B, Table 1).

The 62·5 g dose of fructose was less effective in reducing blood-ethanol than the 125 g dose. Thus although ethanol levels at 0·5 h were relatively low (77·7 $\pm$ 13·1 mg 100 ml^{-1}), they quickly rose to equal those attained after the control treatment (Fig. 1A). Urine output was initially reduced but this effect was not as marked or as prolonged as that seen after the 125 g dose of fructose (Fig. 1B).

Galactose treatment depressed the 0·5 h blood-ethanol concentrations to a similar degree to that seen after the 125 g dose of fructose but control values were reached by 2 h (Fig. 1A). Urine output was also depressed initially but thereafter rose quickly (Fig. 1B) and the total amount eliminated in the 2 h period was greater than that eliminated after the control treatment (Table 1).

To test the possibility that the sugars might alter the renal handling of ethanol, ethanol clearance values were calculated 1, 1·5 and 2 h after its ingestion for fructose, galactose and control pretreatments and plotted against the volume of urine produced (Fig. 2). In addition, the total amount of ethanol cleared from the body in the 2 h of the experiment has been calculated (Table 1). Although there are large differences in the relative amounts eliminated by this route after the different treatments it must be remembered that since the total dose of ethanol was about 55 g, total urinary clearance represents only 0·2, 1·2 and 1·3% of the total dose for the three treatments respectively.

DISCUSSION

The results show that large (125 g) doses of fructose, galactose and sorbitol administered orally in 200 ml of water 0·5 h before a standard dose of ethanol reduced the blood-ethanol concentrations attained when compared with those after 200 ml of water plus 30 mg sodium saccharin. The magnitude of the reduction was large amounting to about 60% at the 0·5 h period. Smaller doses of fructose (62·5 g) were relatively ineffective.

The explanation for this effect probably does not lie in an alteration in the renal handling of ethanol since there is a linear relation of common slope between the average minute ethanol clearance and the volume of urine produced for all three pretreatments tested as would be expected for a substance handled passively and capable of reabsorption. In addition, although there were differences in the amounts of ethanol eliminated from the body in the urine after the different pretreatments, this never amounted to more than 1·3% of the total dose during the 2 h period. Any variation in this small amount eliminated cannot account for the gross differences in blood-ethanol concentrations observed.

It seems more likely that the reduced blood-ethanol concentrations are due to an effect of the large doses of the sugars on the absorption of ethanol from the gastrointestinal tract. Since equi-osmolar doses of fructose, galactose and sorbitol produced different blood-ethanol concentrations, differences in the intestinal absorption of these substances should perhaps be sought. Sorbitol pretreatment produced a pronounced cathartic effect probably because this material is poorly absorbed and therefore holds, iso-osmotically, a volume of water and ethanol in the gastrointestinal tract. At the doses used (125 g; 694 mmol) sorbitol would require dilution with

approximately 2·5 litre of water to give a solution isotonic with plasma and the fluid intake during the experiment (about 600 ml) is far short of this value. This proposal is supported by the fact that sorbitol produced a gross fall in urine output for the whole of the experimental period. Fructose treatment (125 g) produced no cathartic action but did produce a large fall in urine output for most of the experiment. Both of these sugars may, therefore, hold iso-osmotically appreciable quantities of water and ethanol in the gastrointestinal tract for a considerable time and so alter the absorption of ethanol. Galactose also reduced urine output initially and this coincided with a reduced blood-ethanol concentration. However, within 1 h both urine output and blood-ethanol concentrations rose sharply suggesting that galactose was appreciably absorbed by this time along with a quantity of water and ethanol.

In this context it is interesting to note that Groen (1937) has shown that following the administration of hypertonic sugar solutions, water moves into the gastrointestinal tract to produce an isotonic solution within 0·5 h. After this time galactose is absorbed approximately twice as fast as fructose. In addition, Holdsworth & Dawson (1964) have indicated that the absorption of 1 g of galactose from an isotonic solution is accompanied by absorption of approximately 10 ml of water while absorption of a similar quantity of fructose involves little water transfer.

It is suggested, therefore, that the marked reductions in blood-ethanol concentrations seen *in this trial* after treatment with fructose, galactose and sorbitol can be mainly explained in terms of alterations in ethanol absorption from the gastrointestinal tract after oral administration of these sugars. It seems unlikely however, that this factor could explain the results of other workers where fructose has been shown to increase ethanol metabolism.

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