



## Effect of Nigerian citrus (*Citrus sinensis* Osbeck) honey on ethanol metabolism

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The effect of Nigerian citrus (*Citrus sinensis* Osbeck) honey on ethanol metabolism was tested using 45 consenting individuals in apparent good health and between the ages of 25 and 35 years. The subjects were moderate social drinkers matched in terms of body weight and build. The results obtained showed that on average, honey significantly ( $p < 0.05$ ) increased the blood ethanol clearance rate by 68%

and decreased the intoxication period by 43%, but insignificantly ( $p > 0.05$ ) reduced the degree of intoxication by 9%. Honey could be a promising anti-intoxicating agent, but its long-term biochemical evaluation, possibly as a complement in the management of alcohol intoxication, deserves further study.

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The metabolism of ethanol by alcohol dehydrogenase (ADH, EC. 1.1.1.1.) is coupled to the reduction of oxidised nicotinamide adenine dinucleotide (NAD<sup>+</sup>) to reduced nicotinamide adenine dinucleotide (NADH),<sup>1</sup> thereby increasing the ratio of NADH to NAD<sup>+</sup>. This redox change has been reported to alter liver metabolism leading to hyperlactacidaemia,<sup>2</sup> hyperuricaemia, hypertriglyceridaemia<sup>4</sup> and other serious biochemical consequences.

Fructose, which attenuates the NADH:NAD<sup>+</sup> redox change,<sup>5</sup> has been used to stimulate alcohol clearance from the blood.<sup>6</sup> However, its use as a supportive therapy in the management of alcohol intoxication is not common because the complete mechanisms of fructose absorption in the human intestine and its *in vivo* action in blood containing ethanol are not fully understood. When fructose is given alone in solution, 40 - 80% of subjects experience malabsorption and gastrointestinal symptoms. Flatulence and diarrhoea are common if doses over 50 g are given orally. Fructose infusion can also cause lactic acidosis and severe osmotic diuresis, and this is complicated by its tendency to exacerbate the hyperuricaemic and hypertriglyceridaemic conditions induced by alcohol.<sup>2</sup>

However, if fructose is given in combination with glucose or starch, fructose is completely absorbed, even in subjects who malabsorb fructose alone.<sup>7</sup> On this basis Nigerian citrus (*Citrus sinensis* Osbeck) honey, specifically rich in fructose and glucose, was used to investigate blood alcohol metabolism.

### Materials and methods

#### Honey sample

Freshly harvested *Citrus sinensis* Osbeck honey from the delta region of the River Niger in southern Nigeria was preserved at an

average room temperature of 29°C (range 28 - 30°C) for about 4 months. This storage period is important because evolution of sugars during the first 3 months after harvest has been reported for citrus honey.<sup>8</sup> Thereafter the sugar profile was determined using a previously described method.<sup>8</sup>

#### Subjects

The study involved testing 25 men and 20 women who were moderate social drinkers between the ages of 25 and 35 years. The subjects, enlisted from the Urhobo ethnic group in the Niger-Delta region, southern Nigeria, were screened for drug use, and they were instructed not to drink alcohol or take medication the night before testing. They were asked to eat a light breakfast at about 07h00 and then not to eat, drink or smoke from that time until reporting to the laboratory at 11h00. The 4-hour fast was necessary because food in the stomach often retards the absorption of alcohol. The women were scheduled according to where they were in their menstrual cycle and were tested only during their intermenstrual (ovulation) period. The men were also tested at approximately 1-month intervals to keep the time comparable between testing sessions for women and men.

Upon arriving at the laboratory the participants signed a consent form, and were then weighed and given 0.65 ml 190-proof United States Pharmaceuticals (USP) ethanol per kg body weight. Pure ethanol was used because liquors contain congeners that may compound the effects of alcohol. The ethanol was mixed with orange squash in a ratio of one part ethanol to three parts orange drink. Thus, the same concentration of ethanol (25%) was given to all participants, since concentration has been reported to be related to absorption rate. The time allowed to consume the ethanol mixture was controlled because drinking time has been reported to influence alcohol effects. Therefore, each participant's drinking was paced so that consumption took about 5 minutes.

Blood alcohol level (BAL) was then determined using the method of Busher and Redetzki<sup>9</sup> every 20 minutes for 5 hours,

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with whole blood collected via a cannula placed in a vein of a forearm. This exercise was repeated after about a month. In the third month, the experiment was conducted in a similar manner except that honey was used. On this occasion, 1 ml of the honey sample per kg body weight was administered orally to the men about 40 minutes after and to the women about 30 minutes after ingesting the alcohol dose. This corresponds to about 10 minutes before the attainment of peak BAL. This measure prevents interference with ethanol absorption by the honey. The honey experiment was repeated in the fourth month.

The averages of the two sets of experimental values were used to obtain the individual blood alcohol curves, and from such curves the mean kinetic data for alcohol metabolism were obtained and recorded.

**Statistical analysis**

Two related mean values were compared and the level of statistically significant difference was established at the 5% probability level using the Student's *t*-test.

**Results**

Table I summarises the average sugar profiles and water contents

**Table I. Average water and sugar profiles of *Citrus spp* honeys**

	Nigeria*	Spain (Bonvehi and Coll) <sup>8</sup>	USA (Pancoast and Junk) <sup>10</sup>
Water (%)	16.8	17.2	17.0
Fructose (%)	40.2	36.3	38.0
Glucose (%)	31.4	30.3	31.0
Sucrose (%)	1.3	5.9	1.5
pH	4.0	3.7 <sup>†</sup>	3.9
Appearance	Brownish, sticky and viscous		

\*Data obtained during this study.

†From: Aykroyd.<sup>11</sup>

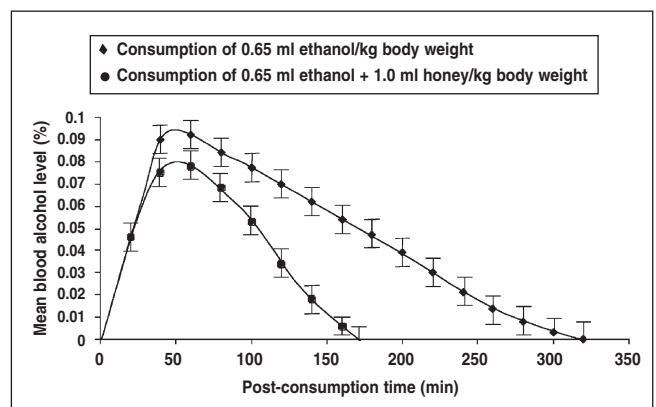
of *Citrus spp.* honeys produced in Nigeria, Spain and the USA.

The data presented (Table I) show that values are similar for comparable variables although the Nigerian honey was richest in fructose and glucose but lowest in sucrose and water content. pH varied minimally, and the Spanish honey was most acidic. The sucrose content of Spanish honey was noticeably the highest. However, these comparisons appear insignificant.

Blood alcohol time curves are given in Figs 1 and 2 and data on the influence of honey on alcohol metabolism are presented in Table II.

The data recorded in Table II show that women had higher peak blood alcohol level (PBAL), faster metabolic and clearance rates, but shorter duration of intoxication, all demonstrated to be statistically insignificant (*p* > 0.05) when compared with the rates of the men.

In the presence of honey, however, PBALs, which represent the extent of intoxication, were reduced by 13.7% and 9.1%, and the time taken to reach such PBALs was shortened by 1.2% and 2.9% in the male and female subjects, respectively. These show that



**Fig. 1. Blood alcohol time curve following the consumption of 0.65 ml ethanol/kg body weight and 0.65 ml ethanol + 1.0 ml honey/kg body weight by the male subjects. (Values are expressed as mean ± SEM of 2N determinations, N = 25).**

**Table II. Citrus honey-induced changes in alcohol metabolic data\***

	Male (N = 25)			Female (N = 20)		
	Control	Test	<i>p</i> -value	Control	Test	<i>p</i> -value
Peak blood alcohol level (PBAL) (%)	0.095 ± 0.003	0.082 ± 0.004	> 0.05	0.099 ± 0.002	0.090 ± 0.002	> 0.05
Time taken to attain PBAL (h)	0.83 ± 0.18	0.84 ± 0.23	> 0.05	0.68 ± 0.16	0.70 ± 0.22	> 0.05
Time taken to attain zero blood alcohol level (h)	5.28 ± 0.43	2.86 ± 0.48	< 0.05	4.72 ± 0.54	2.82 ± 0.33	< 0.05
Blood alcohol metabolic rate (mg/kg/h)	98.6 ± 10.2	189.2 ± 12.3	< 0.05	118.3 ± 9.5	198.3 ± 13.6	< 0.05
Blood alcohol clearance rate (β60) (%/h)	0.019 ± 0.004	0.035 ± 0.003	< 0.05	0.023 ± 0.002	0.041 ± 0.003	< 0.05

\*Values are expressed as mean + SEM of 2N determinations for both control (ethanol alone) and test (ethanol and honey) experiments. N = no. of subjects.



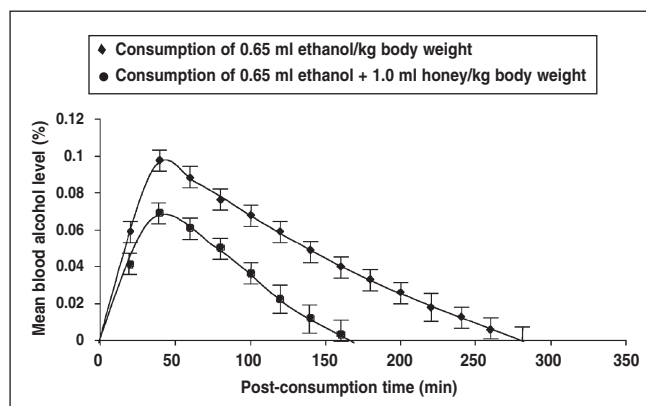


Fig. 2. Blood alcohol time curve following the consumption of 0.65 ml ethanol/kg body weight and 0.65 ml ethanol + 1.0 ml honey/kg body weight by the female subjects. (Values are expressed as mean  $\pm$  SEM of 2N determinations, N = 20).

honey did not significantly ( $p > 0.05$ ) affect the alcohol absorption rate. The total intoxication time, i.e. the time taken to record zero BAL, was reduced by 45.8% in the men and by 40.3% in the women. Blood ethanol clearance ( $\beta_{60}$ ) and metabolic rates in men versus women, respectively, increased by 58.0% v. 78.3% and 92.0% v. 67.6%. The reduction in total intoxication time and the increase in clearance and metabolic rates were demonstrated to be statistically significant at the 5% probability level in both genders. Note that, biochemically, the degree of intoxication has been directly related to PBAL in previous studies.<sup>12</sup> Conventionally, it follows that the higher the PBAL, the more intoxicated the individual, although this has been observed to bear no relationship to behavioural and/or speech disorders.

## Discussion

The gender differences in alcohol time curves (Figs 1 and 2) show that the females were more intoxicated, although for a shorter period, i.e. the women had a higher rate of alcohol clearance from the blood, and this possibly suggests that the rate of initial descent obeys first order kinetics, that is, the higher the PBAL, the higher the rate of the initial descent, and hence the faster the clearance of alcohol from blood. The difference in PBAL is probably related to body water content. The total body weight of men is composed of 55 - 65% water, while that of women is 45 - 55% water,<sup>13</sup> and since alcohol distribution throughout the body is proportional to water content of the body tissues, alcohol tends to be more diluted in the body of males than females.

Honey, a sweet, sticky substance made from flower nectar by certain bees, primarily the honey bee (*Apis mellifera*), is produced in almost every country of the world.<sup>15</sup> The composition of a particular honey sample will depend greatly on the composition of the nectar(s) from which it originates.

The Nigerian citrus honey sample used in this study contains about 40% fructose and 31% glucose. These figures compare well with those for honey produced in Spain and the USA (Table I). The honey sample promoted the clearance of alcohol from the blood in both genders, although faster in women. This stimulatory response in blood alcohol metabolism may be due to the fructose present in the honey sample, since fructose has been reported to increase blood alcohol oxidation by about 80%.<sup>16</sup>

The mechanism by which fructose promotes alcohol metabolism is uncertain, but fascinating hypotheses have been proposed. The most famous seems to be that since the rate of alcohol oxidation by hepatic ADH is 30% dependent upon the rate of re-oxidation of NADH, the metabolism of fructose to sorbitol or glycerol in the presence of alcohol<sup>6</sup> utilises NADH, and so offers the means of re-oxidising NADH to NAD<sup>+</sup> which facilitates further alcohol metabolism.

As previously reported,<sup>17</sup> honey appears to possess an improved anti-intoxicating property when compared with fructose, and this suggests that fructose may be well absorbed and utilised in the presence of other constituents (especially glucose) present in citrus honey. Citrus honey seems to be a promising adjunct in the management of alcohol intoxication because of its sugar (fructose and glucose) content, but because fructose use has been reported to further increase the hyperuricaemic and hypertriglyceridaemic conditions induced by alcohol,<sup>2</sup> the long-term effects of honey on blood urate and lipids deserve further investigation before the potential benefit(s) is declared for possible clinical application.

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