EVALUATION OF BLOOD-ETHANOL PROFILES AFTER CONSUMPTION OF ALCOHOL TOGETHER WITH A LARGE MEAL

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ABSTRACT

Sixteen healthy men drank 1.43 g ethanol per kg of body weight as Swedish aquavit, export beer, and cognac during 90 min together with a 3-course meal. Capillary (fingertip) blood was drawn on 8 occasions starting at 0-10 min after the end of drinking and blood alcohol concentration (BAC) was determined by an enzymatic method. The peak BAC ranged from 0.97-1.41 mg/ml (mean 1.20 mg/ml) and this occurred 78 min after the end of drinking (range 0-230 min). The mean rate of disappearance of alcohol from blood (β) was 0.16 mg/ml/h (range 0.13-0.21) and the apparent volume of distribution of ethanol was 0.795 l/kg (range 0.64-0.93). The mean rate of ethanol elimination from the body was 128 mg/kg/h (range 99-160). The BAC increased on the average by 0.17 mg/ml (range 0.0-0.45 mg/ml) before reaching the maximum level. During the absorption phase, the BAC had attained on the average 83%, 91%, 95% and 98% of the final peak BAC within 5 min, 45 min, 109 min and 175 min, respectively, after ingestion. These results suggest that part of the dose of alcohol is rapidly absorbed into the blood despite the presence of undigested food in the stomach. However, the absorption of the remaining dose of alcohol might proceed for several hours.

RÉSUMÉ

Seize hommes en bonne santé ont bu de l'éthanol dans une proportion de 1.43 g pour chaque kg de poids corporel durant une période de 90 minutes tout en consommant un repas à trois services. L'éthanol provenait ou bien d'aquavit suédois, ou de bière importée ou encore du cognac. Une échantillon de sang capillaire (obtenu du bout du doigt) a été prélevé à 8 reprises en commençant 0 à 10 minutes après la fin de la consommation d'alcool. Une méthode enzymatique a été utilisée pour mesurer la concentration sanguine d'alcool. La concentration maximale d'alcool dans le sang variait de 0.97 à 1.41 mg/mL (moyenne de 1.20 mg/mL) et cette concentration a été observée en moyenne 78 min après la fin de la consommation d'alcool (écart de 0 à 230 min). La vitesse moyenne de disparition d'alcool dans le sang (β) était 0.16 mg/mL/h (écart de 0.13 à 0.21) et le volume apparent de distribution de l'éthanol était 0.795 L/kg (écart de 0.64 à 0.93). La vitesse moyenne d'élimination de l'éthanol du corps humain était 128 mg/kg/h (écart de 99 à 160). La concentration sanguine d'alcool a augmenté en moyenne de 0.17 mg/mL (écart de 0.0 à 0.45 mg/mL) avant d'atteindre son maximum. Durant la phase d'absorption, la concentration sanguine d'alcool a atteint en moyenne 83%, 91%, 95% et 98% de la valeur maximale finale et ce dans un délai de 5 min, 45 min, 109 min et 175 min, respectivement, après la fin de la consommation d'alcool. Ces résultats démontrent qu'une partie de la dose d'alcool est rapidement absorbée dans le sang même en présence de nourriture non digérée dans l'estomac. Cependant, l'absorption du restant de la dose d'alcool peut se poursuivre pour plusieurs heures.

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INTRODUCTION

The absorption, distribution and elimination of ethanol[1] depend on a multitude of genetic and environmental factors (1). The magnitude of inter- and intra-individual variations in the pharmacokinetic profile of ethanol is important when the BAC at the time of sampling is used to estimate the BAC at some earlier time, such as, at the time of driving. This procedure, called retrograde extrapolation, is a controversial practice because of the many unknown factors involved (2-4). Although much work has been done to establish the BAC time course in healthy volunteers after ingestion of a bolus dose on an empty stomach (5-10), the pharmacokinetics of ethanol under real-world drinking conditions has not been extensively studied (11-14). It is widely known that ingestion of food together with alcohol delays the emptying time of the stomach and slows the rate of absorption of alcohol into the portal blood (15,16). The resulting BAC profile follows a lower course with a smaller area under the curve, a lower peak BAC (C_{max}) and the time of its occurrence (T_{max}) is also influenced compared with the same dose taken on an empty stomach (17).

This paper deals with the absorption, distribution and metabolism of alcohol in healthy men after they ingested a moderate dose together with a large meal lasting for 90 min. Particular attention was given to the rate of increase in BAC after the end of drinking and before the maximum level was reached.

MATERIALS AND METHODS

Subjects and conditions

Sixteen policemen volunteered for this experiment. Their ages ranged from 31 to 54 y (mean 42), their body weights from 73 to 98 kg (mean 84) and their heights from 176 to 198 cm (mean 183). All the subjects were accustomed to moderate drinking and in this study received 1.43 g/kg body weight. Three different alcoholic beverages were available and served in the following order; Swedish aquavit (31.8% w/v ethanol), at a dose of 150 ml/70 kg; export beer containing 4.5% w/v ethanol (450 ml/70 kg) and cognac containing 31.6% w/v ethanol (100 ml/70 kg).

The experiment began at 5.00 p.m. and continued until the following day. The principal aim of the investigation was to record the signs and symptoms of hangover. The results of this study of hangover were reported in detail elsewhere (18). The present article focuses on inter-individual differences in the blood-ethanol profiles obtained. Four subjects took part in each experimental session and alcohol was served together with food. The conditions were made as pleasant as possible in an attempt to reproduce an evening together with friends. The meal consisted of raw herrings, meatballs and potatoes, bread, butter and cheese followed with cold roast beef, potatoes, lettuce and tomatoes and finally ice cream, coffee, cream and sugar. The total caloric value of the meal was about 1900 kcal made up of 120 g carbohydrates, 90 g protein and 120 g fat. Twelve of the subjects smoked several cigarettes during the experiment. After finishing the meal, various tests of performance decrement were conducted or otherwise the subjects relaxed reading magazines. A meal of bread, cheese, cold meat, and coffee was served 5 hours after the experiment started.

Blood sampling and determination of ethanol

Specimens of capillary blood were obtained at approximately 5, 45, 110, 170, 225, 405, 650 and 775 min after the end of drinking. For practical reasons, the times of sampling

1. The words ethanol and alcohol are used interchangeably in this article.

blood were not exactly the same for all subjects. Triplicate samples of capillary (fingertip) blood were taken at each time point and aliquots for determination of ethanol were measured with the aid of 100 μl glass capillaries. The blood was diluted with 900 μl of saponin-fluoride in autoanalyzer cups. The concentration of ethanol was determined by an enzymatic oxidation procedure as described in detail elsewhere (19,20).

Evaluation of blood-ethanol profiles

Blood-ethanol profiles were plotted for each subject. The peak BAC (C_{max}) and the time of its occurrence (T_{max}) were recorded directly from the curves. The pharmacokinetics of ethanol were calculated as described by Widmark (21). In brief, a straight line was fitted to the rectilinear portion of the BAC time profile after the post-absorptive phase was well established. The slope of the disappearance phase corresponds to Widmark's β-slope. The y-intercept of the regression line represents the theoretical BAC obtained if the dose administered was absorbed and distributed in the body immediately at the start of drinking (C_o). The x-intercept of the regression line (h_o) is an estimate of the time needed for complete removal of ethanol from the body neglecting the curvilinear portion of the curve that begins at a BAC below about 0.1 mg/ml. The ratio of dose (g/kg) to C_o is the apparent volume of distribution of ethanol known also as Widmark's r-factor, or the ratio of alcohol in the body to alcohol in the blood at zero time.

The rise in BAC after taking the first sample of blood (0-10 min post-drinking) until reaching the peak BAC was noted for each subject. The BAC at various times during the absorption phase (C_t) was expressed as a percentage of the observed peak BAC (C_{max}) for each of the subjects. Note that those subjects that had already reached their peak BAC were not included when average values of (C_t/C_{max}) were computed at later time points. The quantity of alcohol (g) absorbed and distributed in the body at the time the first sample of blood was taken between 0 and 10 min after the meal, was calculated as follows:

$$\text{Alcohol (g)} = [(\text{BAC}/0.84) \times \text{TBW}] + [(\text{dose}/h_o) \times t]$$

In the above equation, BAC (mg/ml) is the concentration of alcohol in capillary blood at the time of interest (t) measured from the start of drinking, 0.84 is the fraction of water in whole blood in mass/volume units (22), TBW is the volume of total body water (liters) for each individual subject. The dose of alcohol administered is given by (1.43 $\times$ body weight) and h_o is the estimated time to zero BAC. Note that the ratio dose/h_o is the rate of ethanol metabolism from the whole body. TBW was derived from a multiple regression equation with age (y), body weight (kg) and height (cm) of each subject as the independent variables (23):

$$\text{TBW (l)} = 2.447 - 0.09516\ \text{Age} + 0.1074\ \text{height} + 0.3362\ \text{weight}$$

RESULTS

Figs 1 and 2 show the concentration-time profiles of ethanol for each of the 16 subjects. The absorption/distribution phases differ widely despite the standardized drinking conditions and similar intake of food. Subjects 6 and 16 had already reached their peak BAC by the time the first sample of blood was taken between 0-10 min after drinking. By contrast, subject 15 did not reach a peak BAC until 230 min after the end of drinking. Subjects 1, 3 and 5 showed an alcohol concentration plateau and the BAC remained more or less unchanged for 2-3 hours. Subject 12 vomited 150 min after the start of drinking or 60 min after end of drinking.

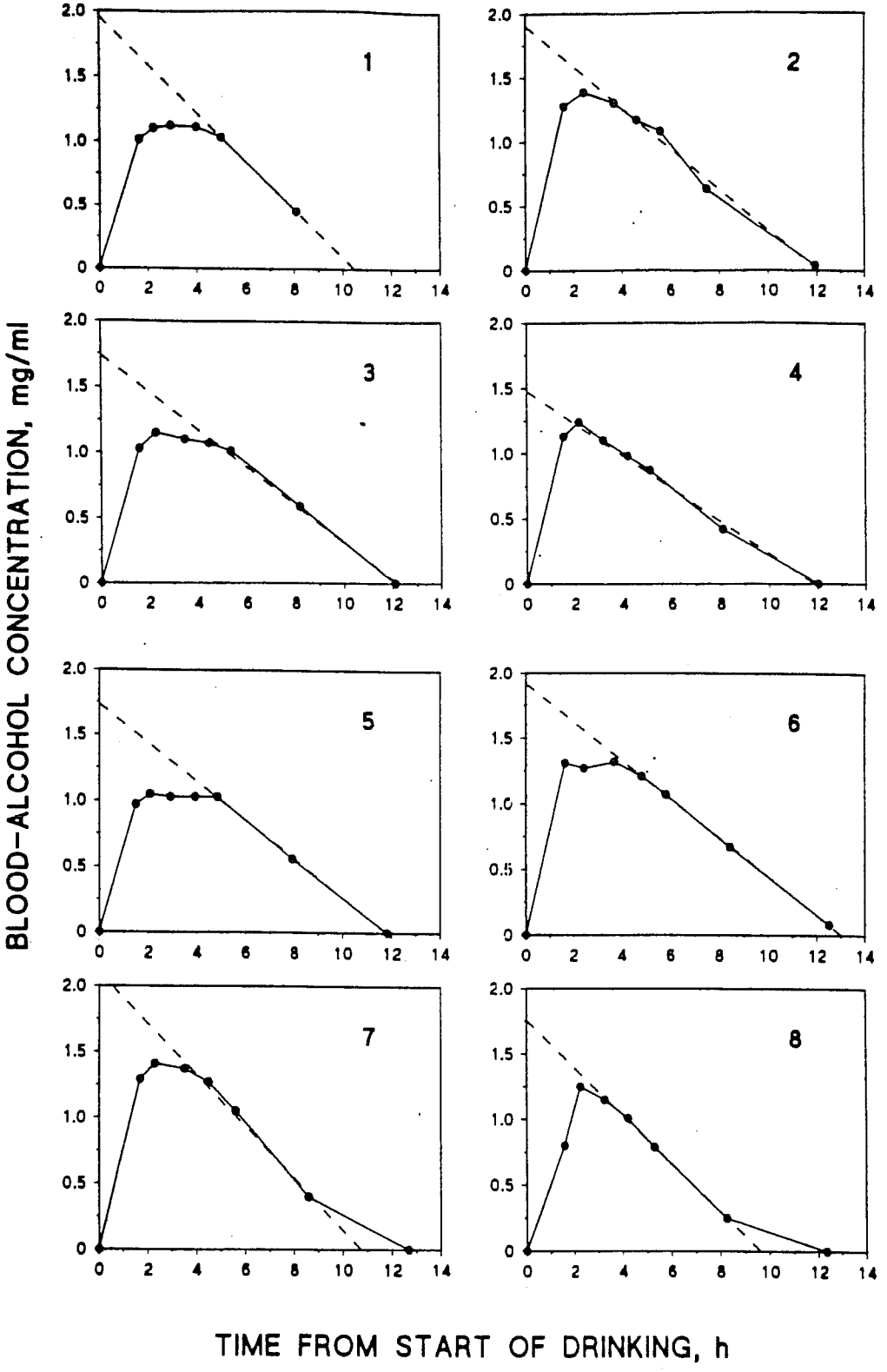

Figure 1. Concentration-time profiles of ethanol in capillary blood of healthy men (1-8) after they consumed 1.43 g/kg ethanol as mixed drinks together with a meal lasting 90 min.

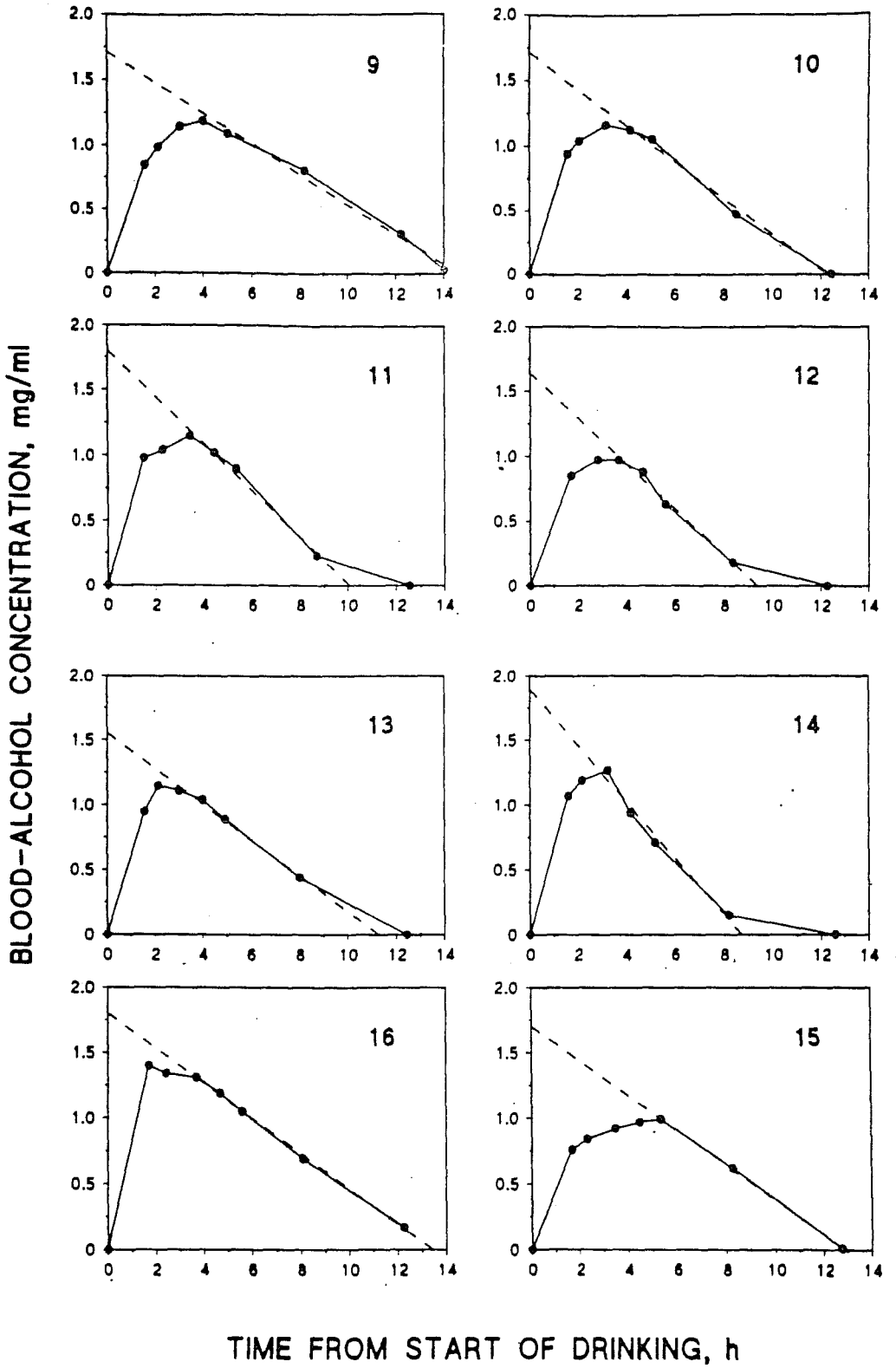

Figure 2. Concentration-time profiles of ethanol in capillary blood of healthy men (9-16) after they consumed 1.43 g/kg ethanol as mixed drinks together with a meal lasting 90 min.

TABLE 1

AMOUNT OF ALCOHOL ABSORBED AND DISTRIBUTED INTO THE BODY AT THE TIME THE FIRST SAMPLE OF BLOOD WAS TAKEN AT 0-10 MIN POST-DRINKING. HEALTHY MEN DRANK 1.43 G/KG ETHANOL TOGETHER WITH A SUBSTANTIAL MEAL LASTING FOR 90 MIN.

PARAMETER	MEAN	SD	CV %	RANGE
Alcohol ingested (g)	118	14.4	12.2	104 - 151
TBW (liters)*	46.2	3.46	7.4	42 - 54
Ethanol turnover (g/h)	10.6	1.77	16.6	8.4 - 14.6
BAC (mg/ml)#	1.03	0.19	18.4	0.76 - 1.41
Alcohol absorbed (g)	73.4	11.4	15.5	51 - 96
Per cent absorbed	61.6	8.7	14.1	48 - 74

* Total body water was derived from a nomogram based on age, weight and height. # Blood-alcohol concentration 0-10 min post-drinking.

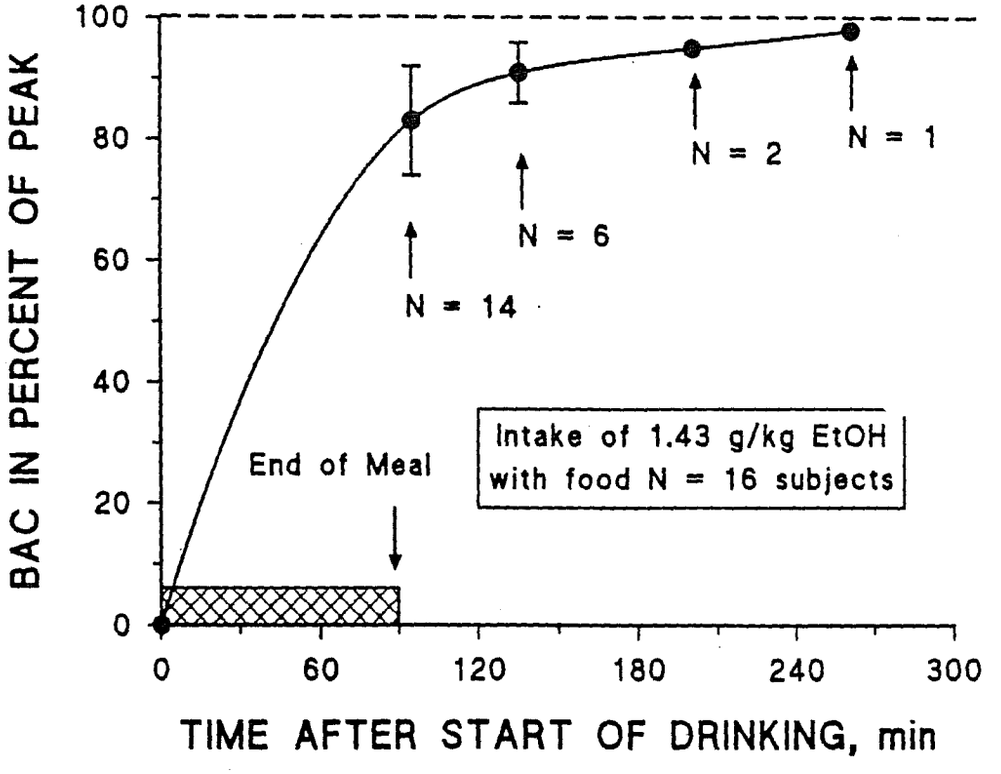

Figure 3. Percent of peak BAC reached at various time points during the absorption phase. N = 16 subjects drank 1.43 g/kg ethanol together with food. N = the number of subjects included in calculating mean values. At various times during absorption, 2, 10, 14 and 15 subjects respectively had already reached their peak BAC.

Despite the presence of food in the stomach, an initial rapid absorption of alcohol occurred in all subjects. The mean BAC was 1.03 mg/ml (range 0.76-1.41) when the first blood sample was drawn 0-10 min post-drinking. Table 1 shows that on the average 61.6% (range 48-74) of the dose of alcohol consumed has already become absorbed and distributed in the blood within 0-10 min of finishing the meal. The remaining part of the alcohol consumed is then absorbed much more slowly and without necessarily increasing the BAC. Figure 3 shows the

TABLE 2

OD-ALCOHOL PARAMETERS DERIVED FROM THE BAC PROFILES SHOWN IN FIGS. 1 AND 2. SD = STANDARD DEVIATION, CV = COEFFICIENT OF VARIATION, N = 16 SUBJECTS

ARAMETER	MEAN	SD	CV	RANGE
Peak BAC (mg/ml)	1.20	0.136	11.3	0.97 - 1.41
Time to peak#	78	*	*	0 - 230
BAC rise (mg/ml)†	0.17	*	*	0 - 0.45
C_0 (mg/ml)	1.80	0.160	8.9	1.54 - 2.22
Widmark's β-slope (mg/ml/h)	0.16	0.025	15.4	0.13 - 0.21
Distribution volume (l/kg)	0.795	0.069	8.7	0.64 - 0.93
Time to reach zero BAC (h)	11.38	1.56	13.6	8.9 - 14.4
Rate of alcohol turnover (mg/kg/h)	128	17.3	13.5	99 - 160

Time (min) to peak is not normally distributed and can take only fixed values. † Measured from the time of obtaining the first blood sample.

rate of rise in BAC in relation to the observed peak BAC at various times after the end of drinking. Evidently, about 80% of the final peak BAC was reached between 0-10 min after the end of drinking. The blood-alcohol parameters when alcohol was taken together with food are shown in Table 2. These values were derived from linear regression analysis of the concentration-time profiles in Figs. 1 and 2. The broken diagonal lines were used in this analysis and the correlation coefficients were greater than 0.99.

DISCUSSION

The blood-alcohol concentration at the time of offence cannot be reported with certainty unless a specimen of blood is available for quantitative determination of ethanol. Nevertheless, based on information about the drinking scenario, such as the duration of intake, the quantity and kind of alcoholic beverages consumed, whether the individual ate any food during the drinking, and the time of last drink in relation to the time of driving, scientists can assist the court in reaching a decision about whether or not the BAC was above or below the legal limit at the time of offence.

In the present work, the concentration-time profiles of ethanol showed appreciable inter-subject variation. The peak BAC ranged from 0.97-1.41 mg/ml and the time of its occurrence ranged from 0-230 min after the end of the meal. The faster the absorption, as reflected in an early occurring peak, the higher the concentration of alcohol in the blood. The average rate of disappearance of alcohol from blood was 0.16 mg/ml/h (range 0.13-0.21) and this agrees well with the values normally cited in forensic case work of 0.15 mg/ml/h (range 0.10-0.20) (24). However, if the β-slope is computed using the concentration-time data immediately after reaching C_{max}, abnormally low results are obtained. This underscores the need to construct the complete BAC time-profile in order to make a reliable pharmacokinetic analysis. Calculation of β-slopes without knowledge about the shape of the entire BAC time-profile can lead to erroneous results. This might explain, at least in part, the wide range of β values reported in the literature (25,26). The broken diagonal lines in Figs. 1 and 2 show the segments of the post-peak phase used in the calculation of β-values.

The present work suggests that when ethanol is ingested together with food the absorption occurs in two phases. This supports the conclusions of Schultz et al (27) who advanced a two-pool hypothesis based on extensive experiments with fed and fasted rats. One part of the dose of alcohol becomes trapped by food particles and is not immediately available for absorption through the stomach wall. Another part of the dose, corresponding to the

"unbound pool", is rapidly absorbed just as if the stomach was empty. This explains the initial rapid rise in BAC reaching about 80% of the final peak concentration within 0-10 min after the end of eating and drinking. However, the bound-pool of alcohol is absorbed slowly and the BAC either increases gradually over the next few hours, remains unchanged, or even decreases slowly. Direct support for this hypothesis was obtained by monitoring the rate of absorption of alcohol from the stomach and the duodenum at fixed intervals after ingestion of an experimental test meal of alcohol (0.8 g/kg) and nutrients (28).

Note that a decreasing BAC does not necessarily signify the existence of the post-absorptive state. Instead this indicates that the rate of absorption of alcohol into the systemic circulation is equal to or less than the rate of distribution and elimination of alcohol from the circulating blood. The wide inter-individual differences in the rate of absorption of alcohol might depend on differences in the size and shape of the stomach or the physiology of gastric emptying (1). Uptake of alcohol into the portal blood occurs at a much faster rate if the pylorus valve opens to release stomach contents into the large surface area of the duodenum. Food in the stomach delays gastric emptying and will accordingly retard the rate of absorption of alcohol into the portal blood (29). The C_{max} and T_{max} parameters might also depend to some extent on the composition of the food in the stomach (fat, protein, carbohydrate) and even the particular alcohol formulation, such as, intake of beer, wines, spirits, or cocktails (30-33). Although subject 12 vomited 60 min post-drinking this event had no appreciable effect on the BAC time profile compared with the other subjects. This might suggest that most of the alcohol had already been absorbed from the gut at the time of vomiting. Smoking seems to delay gastric emptying and this might have contributed to the prolonged absorption phase for some subjects in this study (34).

The results presented in this paper emphasise the need for caution when engaging in retrograde extrapolation of BAC for legal purposes. In some individuals, the absorption of alcohol might proceed for several hours after the end of drinking. However, despite this prolonged absorption phase, about 80% of the final peak BAC seems to be reached within 0-10 minutes after the end of eating and drinking. This is an important observation. The problems and uncertainties associated with back estimation of BAC could be avoided if drinking and driving statutes were defined as the BAC existing at the time of sampling as the relevant figure for prosecution. Until the necessary legislation is formulated, forensic scientists are obliged to provide the court with expert opinions on the BAC at the time of offence. The problems and pitfalls associated with retrograde extrapolation are not new. More experiments are needed to establish the concentration-time profiles of ethanol under real-world drinking.

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