Int J Legal Med (2003) 117 : 276–281
DOI 10.1007/s00414-003-0384-5

ORIGINAL ARTICLE

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Concentration dependency of the BAC/BrAC (blood alcohol concentration/breath alcohol concentration) conversion factor during the linear elimination phase

Received: 19 December 2002 / Accepted: 2 May 2003 / Published online: 5 July 2003

Abstract According to the theoretical pharmacokinetical considerations put forward by Wehner et al. the BAC_{ven}/BrAC conversion factor Q is not a constant value and varies depending on the pharmacokinetic phase deduced from the alcohol concentration curve. Based on these considerations we propose that Q must be inversely proportional to the BrAC during the postabsorptive linear elimination phase, expressed as the hyperbola $Q=1/\kappa+(CT)/BrAC$. The constants κ or $1/\kappa$ and (CT) – where (CT) consists of different parameters which remain constant during the linear elimination phase – can be experimentally determined from the linear relationship $BrAC=\kappa BAC_{ven}-\kappa(CT)$. To test this hypothesis 12 human volunteers received parenteral doses of ethanol. During the elimination phase, BAC and BrAC of each volunteer were measured between 18 and 34 times in a BrAC range between 0.65 mg/l and 0.12 mg/l. The conversion factor Q was either expressed in the form of the hyperbola $Q=1/\kappa+(CT)/BrAC$ or directly calculated from the ratio $BAC_{ven}/BrAC$ and the results obtained using both methods were found to be very similar. The values of $1/\kappa$ of the hyperbolic functions varied between 1.808 and 2.165 and those of (CT) between 0.004 and 0.127. For a BrAC of 0.25 mg/l, an average value of 2.308±0.080 could be calculated for the conversion factor $Q_{0.25}$. On average, the value of $Q_{0.40}$ amounted to 2.207±0.048 and that of $Q_{0.55}$ to 2.160±0.056.

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Key words BAC · BrAC · BAC/BrAC ratio · BAC/BrAC conversion factor · Elimination phase

Introduction

Volatile substances such as ethanol (in this paper referred to by the generic term alcohol) can be detected in blood and exhaled breath. Measurements of the breath-alcohol concentration (BrAC) can be conducted far more easily than the determination of the alcohol concentration in peripheral venous blood (BAC). Therefore, the determination of the BrAC has in most countries superseded the measurement of BAC as forensic proof of alcohol intoxication. However, breath samples cannot always be obtained. For example in cases when the suspect is unconscious, suffers from a lung disease or is uncooperative (e.g. refuses to provide a breath sample). Therefore, both forensic BrAC and forensic BAC determinations are used side-by-side in evidential alcohol testing. The basis for the comparability of BAC and BrAC is the assumption of a conversion factor BAC/BrAC [(g/kg)/(mg/l)] in the following termed Q, which can be used to gain equivalent (venous) BAC values from BrAC values. In most countries conversion factors between 2.0 and 2.3 are used [12].

Numerous investigations have been carried out with regard to the conversion factor Q [1, 2, 3, 4, 7, 9, 10, 11, 12, 15, 16, 20, 21, 24] that reveal a great variability of this value. The most extreme values obtained are 0.74 [24] and 6.00 [15]. This variability of Q can be attributed to the fact that the BAC/BrAC ratio depends on the pharmacokinetic phase of the alcohol metabolism, and Q is remarkably low in the absorption phase [4, 21]. During the elimination phase, however, Q is a nearly constant value [2, 21] and some authors also suggest that even in the definite postabsorptive phase, Q depends on the time that has passed after the end of alcohol consumption [10, 24] or on the alcohol concentration [12].

In a previous publication we presented an attempt to deduce an equation that allows the unambigous calculation of Q at any time during the linear elimination phase [5].

Our hypothesis is based on the fundamentals of alcohol pharmacokinetics in venous and arterial blood and in alveolar breath air [18, 22, 23], i.e. arterial blood alcohol concentration (BAC_{art}) and alveolar breath air alcohol concentration (BrAC) are proportional according to the equation

$$BrAC = \kappa BAC_{art} \quad (1)$$

According to Wehner et al. [22], the relationship between venous blood alcohol concentration, BAC_{ven}, and arterial blood alcohol concentration, BAC_{art}, is expressed as:

$$BAC_{ven} = BAC_{art} + \Phi_G/(\eta^m V_G)\,[(\eta^s \Delta BAC_{art}/\Delta t) - (\Delta BAC_{ven}/\Delta t)] \quad (2)$$

or

$$BAC_{art} = BAC_{ven} - \Phi_G/(\eta^m V_G)\,[(\eta^s \Delta BAC_{art}/\Delta t) - (\Delta BAC_{ven}/\Delta t)] \quad (3)$$

where Φ_G expresses the flow rate of arterial blood, V_G represents the distribution volume for alcohol, η^m or η^s the mixed or shunt stream portion in or around the distribution space V_G, $(\Delta BAC_{art}/\Delta t)$ and $(\Delta BAC_{ven}/\Delta t)$ the concentration changes of arterial and venous blood per unit time.

The term

$$\Phi_G/(\eta^m V_G)\,[(\eta^s \Delta BAC_{art}/\Delta t) - (\Delta BAC_{ven}/\Delta t)]$$

in Eq. 2 and 3 is referred to as correction term by Wehner et al. [22] and will be abreviated as (CT) subsequently. In this correction factor (CT), Φ_G, V_G as well as η^m and η^s are nearly constant, whereas $(\Delta BAC_{art}/\Delta t)$ and $(\Delta BAC_{ven}/\Delta t)$ depend on absorption and elimination. In the definite postabsorptive linear elimination phase $(\Delta BAC_{art}/\Delta t)$ and $(\Delta BAC_{ven}/\Delta t)$ are also to a large degree constant, so that the entire correction factor (CT) can be considered as a constant value.

BrAC can be related to BAC_{ven} when BAC_{art} of Eq. 3 is inserted into Eq. 1:

$$BrAC = \kappa[BAC_{ven} - (CT)] \quad (4)$$

or

$$BrAC = \kappa BAC_{ven} - \kappa(CT) \quad (5)$$

When the correction term (CT) is constant, there is a linear relationship between BrAC and BAC_{ven}.

Equations 4 and 5 can then be converted into

$$BAC_{ven}/BrAC = 1/\kappa + (CT)/BrAC \quad (6)$$

or, because $BAC_{ven}/BrAC$ corresponds to the conversion factor Q, into

$$Q = 1/\kappa + (CT)/BrAC \quad (7)$$

The conversion factor Q takes the shape of a hyperbola and thus depends on the concentration of breath-alcohol. This means that Q is inversely proportional to the BrAC as a result of being affected by $1/\kappa$.

Material and methods

The experiments were approved by the Ethics Commission of the Medical Faculty of the University of Heidelberg and conducted on 12 volunteers, 3 women and 9 men between 19 and 47 years old. The alcohol was administered parenterally by way of a 7% ethanol/5% glucose solution through an indwelling cannula. Thus, possible sources of inaccuracy of the measurements in the first phase after the application of alcohol are eliminated. Had the alcohol been administered orally, a waiting period of at least 2 h would have been necessary to ensure that absorption was complete. However, the postabsorptive elimination phase, i.e. the actual period of measurement, is not affected by the way alcohol is administered. The flow speed of the infusion solution was controlled via an infusion pump and retained at 0.40 g alcohol/kg body weight h^{-1} in males and 0.33 g alcohol/kg body weight h^{-1} in females. The final concentration of approximately 0.65 mg/l was reached after 2.5–3 h. Alcohol administration was reduced and kept at a dose that was specifically calculated for each volunteer to retain the final concentration for 30 min (0.105 g alcohol/kg body weight h^{-1} in males; 0.090 g alcohol/kg body weight h^{-1} in females). The measurements were started 20 min after the infusion was stopped in order to rule out potential disturbances brought about by unterminated diffusion. Figure 1 shows an example of the experimental set-up.

The measurement of breath alcohol was carried out with a calibrated Dräger Alcotest 7110 Evidential MK III, a device that is used to measure the alcohol concentration of two breath samples, which are taken at time intervals of 2 and 5 min. The alcohol concentration in the first breath sample is determined electrochemically, that in the second sample optically using infrared light. The temperature of breath air is measured and the results corrected to a

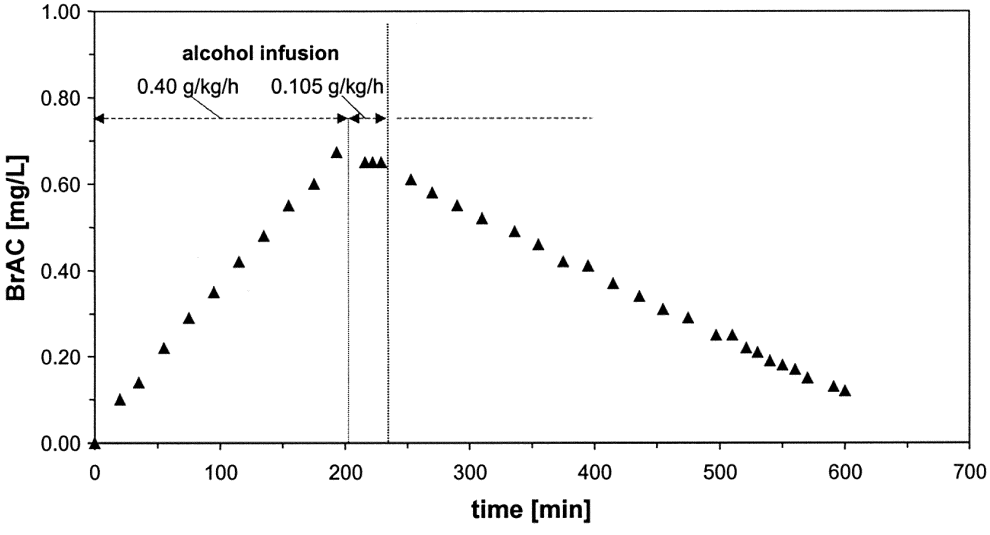

Fig. 1 Example of the experimental set-up

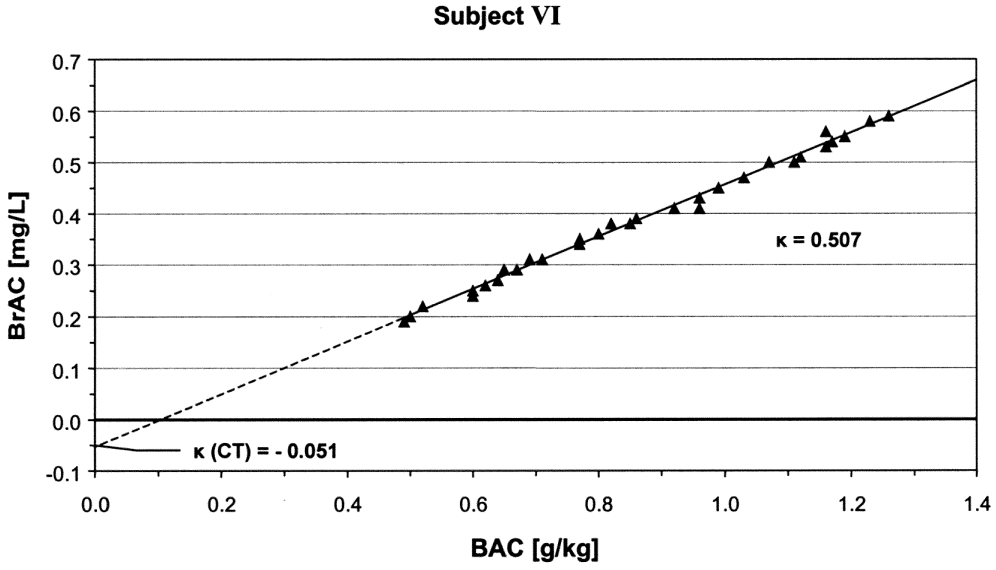

Fig. 2 Breath-alcohol concentrations dependent on the simultaneously measured blood-alcohol concentrations; proband VI

Table 1 Results obtained for the 12 subjects using BrAC as a linear function of BAC

Proband	$BrAC=\kappa BAC_{ven}-\kappa(CT)$	κ (±95% CI)	κ (CT) (±95% CI)	(CT) (calculated)
I	BrAC=0.504 BAC–0.044	0.504 (±0.014)	0.044 (±0.018)	0.088
II	BrAC=0.487 BAC–0.034	0.487 (±0.015)	0.034 (±0.015)	0.070
III	BrAC=0.531 BAC–0.062	0.531 (±0.032)	0.062 (±0.026)	0.116
IV	BrAC=0.553 BAC–0.070	0.553 (±0.017)	0.070 (±0.014)	0.127
V	BrAC=0.511 BAC–0.061	0.511 (±0.018)	0.061 (±0.017)	0.119
VI	BrAC=0.507 BAC–0.051	0.507 (±0.015)	0.051 (±0.013)	0.101
VII	BrAC=0.464 BAC–0.010	0.464 (±0.012)	0.010 (±0.009)	0.022
VIII	BrAC=0.478 BAC–0.009	0.478 (±0.008)	0.009 (±0.005)	0.019
IX	BrAC=0.462 BAC–0.002	0.462 (±0.015)	0.002 (±0.012)	0.004
X	BrAC=0.473 BAC–0.019	0.473 (±0.020)	0.019 (±0.016)	0.040
XI	BrAC=0.475 BAC–0.030	0.475 (±0.015)	0.030 (±0.011)	0.063
XII	BrAC=0.464 BAC–0.019	0.464 (±0.010)	0.019 (±0.008)	0.041

reference temperature of 34°C. The final output is the mean value of the two individual measurements [17]. The precision of the device is relatively high with a coefficient of variation of less than 3% [8]. Measurements were taken from a maximum of 0.60 mg/l down to about 0.15 mg/l.

Blood samples were collected at the same time as the alcohol concentration in breath air was measured. They were withdrawn from a second indwelling cannula, which was inserted in the contralateral arm of alcohol administration. Blood samples were centrifuged, stored at 4°C and subsequently examined twice using gas chromatography. The serum values were converted into blood alcohol values using a factor of 1.2, as is required for the forensic determination of blood alcohol levels in Germany. The final concentration was determined as the mean value of the two individual measurements.

Measurement was terminated when the BrAC values dropped to approximately 0.15 mg/l. Thus, sufficient time been allowed to reach the exponential final phase of the elimination of BAC in which it is no longer possible to regard (CT) as constant. The lowest concentration obtained for breath alcohol that was included in the analysis was 0.12 mg/l. The corresponding value for blood alcohol was 0.29 g/kg.

Results

For each volunteer 18–34 BrAC and BAC measurements were obtained and plotted on the same graph as shown in Fig. 2. The data for volunteer VI was used as an example as in this case, the parameters κ und (CT) were closest to the mean value of the volunteer group. Linear regression lines were calculated that in all cases had a negative y-intercept. The values κ and (CT) were calculated according to Eq. 5 (Table 1) and inserted into Eq. 7.The hyperbolas were determined and illustrate the relationship between Q and BrAC (Table 2). As an example, Fig. 3 depicts the hy-

Table 2 Results obtained for the 12 subjects with the BAC/BrAC conversion factor Q as a hyperbolic function of BrAC

Proband	Q=1/κ+(CT)/BrAC
I	Q=1.985+0.088/BrAC
II	Q=2.053+0.070/BrAC
III	Q=1.882+0.116/BrAC
IV	Q=1.808+0.127/BrAC
V	Q=1.957+0.119/BrAC
VI	Q=1.972+0.101/BrAC
VII	Q=2.155+0.022/BrAC
VIII	Q=2.092+0.019/BrAC
IX	Q=2.165+0.004/BrAC
X	Q=2.105+0.040/BrAC
XI	Q=2.128+0.063/BrAC
XII	Q=2.155+0.041/BrAC

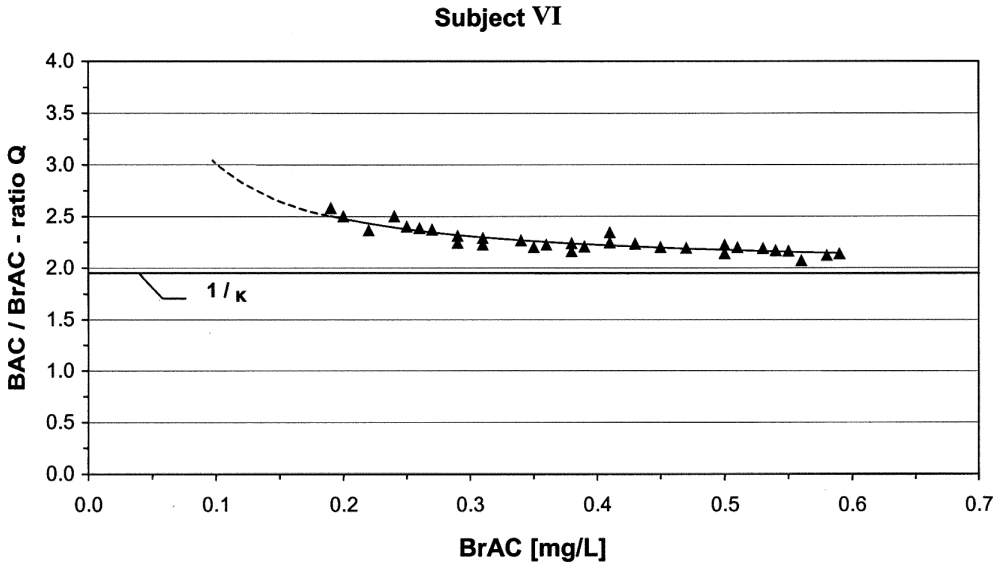

Fig. 3 BAC/BrAC-ratio Q dependent on the value of breath-alcohol concentration; proband VI: Q=1.972+0.101/BrAC

Table 3 BAC/BrAC conversion factors $Q_{0.25}$ for a BrAC of 0.25 mg/l, $Q_{0.40}$ for a BrAC of 0.40 mg/l and $Q_{0.55}$ for a BrAC of 0.55 mg/l

Proband	Conversion factors		
	$Q_{0.25}$	$Q_{0.40}$	$Q_{0.55}$
I	2.337	2.205	2.145
II	2.333	2.228	2.180
III	2.346	2.172	2.093
IV	2.316	2.125	2.039
V	2.433	2.254	2.173
VI	2.376	2.224	2.156
VII	2.243	2.210	2.195
VIII	2.168	2.139	2.126
IX	2.181	2.175	2.172
X	2.265	2.205	2.177
XI	2.380	2.285	2.242
XII	2.319	2.257	2.229
Mean and standard deviation	2.308±0.080	2.207±0.048	2.160±0.056

perbola obtained for volunteer VI. For comparison, this figure also includes the Q values which were calculated as a BAC/BrAC ratio for each individual measurement point and excellent agreement was observed. Table 3 depicts the conversion factors $Q_{0.25}$ for a BrAC of 0.25 mg/l, $Q_{0.40}$ for a BrAC of 0.40 mg/l and $Q_{0.55}$ for a BrAC of 0.55 mg/l.

It was not possible to extend the concentration range in which the measurements were carried out to much lower values because these would no longer be in the linear elimination range. Thus, the measurement values were mainly in the scale in which the curve of the hyperbola is not very prominent. According to purely optical criteria it would be possible to express the measured values also as a linear function, although it is not possible to provide a pharmacokinetic justification for doing so. Therefore, we compared the adjustment of the measured values to a hyperbola with that to a linear function (comparison of the standard deviations $s_{y.x}$). The results of nine volunteers showed a better adaptation to a hyperbola; in one case no difference could be observed, in 2 cases the adaptation to a linear function was better (p=0.05; sign test). The Wilcoxon matched pairs signed rank test showed a significant difference in the case of unilateral testing (p=0.046), in the case of bilateral tests it showed at least a certain tendency (p=0.092). However, after adjustment to a hyperbola and to a straight line, one of the differences of the standard deviations ranged outside of the 4×sigma range of the remaining differences and could thus be eliminated. For the remaining 11 cases, the Wilcoxon matched pairs signed rank test provided a significantly better adjustment to a hyperbola (p=0.022), even in bilateral tests.

Discussion

As early as 1978 Jones [10] suggested that the BAC/BrAC conversion factor Q in the postabsorptive elimination phase depends on the alcohol concentration. This was at least partially confirmed with regard to the dependency of the BAC/BrAC ratio from the time interval after the end of drinking [22, 24]. If this is taken for granted, it is impossible to depict the relation between BAC values and simultaneously measured BrAC values as a straight line that crosses the origin of the coordinate system (i.e. x=0 and y=0), which has been the case up to now. Straight lines always express direct proportionality, which under these circumstances is certainly not the case.

First, it had to be shown that the relationship between BrAC and BAC in the form of the function BrAC=f(BAC) cannot be represented by a straight line that crosses the origin of the axes. This could be confirmed by the experimental findings gained in our investigations. As has been theoretically predetermined, the linear functions revealed negative y-intercepts in all 12 cases. This could thus not be taken as an accidental deviation from the origin and results obtained by other authors also suggest similar curves.

In contrast to our observations gained from individual volunteers, these authors analysed the relation of BrAC and BAC on large proband collectives. Thus they could calculate a mean graph which can be expected to have a large variation due to the larger interindividual differences, but should in principle be similar to the graphs which we obtained using single individuals [9, 11, 13, 14, 15, 19]. The majority of authors [10, 11, 13, 14, 15] also provided the mathematical equation of the calculated regression line, which in all cases gave a y-intercept. These y-intercepts were, however so small that they can be regarded as being within the range of statistical error. By comparing the results of the individual research groups, it is noteworthy that the y-intercept is always unidirectional. When the regression line is provided as the function BrAC=f(BAC) it is negative, when provided as the inverse function BAC=f(BrAC) it is positive. The results obtained by Köhler et al. [15] are of particular interest. In addition to providing a regression line with a positive y-intercept, the authors also present the BAC/BrAC quotient in relation to BAC as a cloud of points forming a hyperbola.

The depiction of the relationship between BrAC and BAC as a straight line is based on the idea that BrAC and BAC must reach the origin simultaneously. This is necessary for physiological reasons. Negative y-intercepts in the function BrAC=f(BAC) seem to contradict this as the concentration of breath alcohol reaches the origin while that of blood alcohol still ranges between 0.05 and 0.15 g/kg. In this section, the functions presented here are, however only of theoretical importance. They describe, as detailed above, the relationship during the linear elimination phase and cannot be extended to the exponential end section of the elimination curve. Here the concentration changes ($\Delta BAC_{art}/\Delta t$) and ($\Delta BAC_{ven}/\Delta t$) are no longer constant, therefore, the entire correction term (CT) can no longer be regarded as a constant. The point of axis intersection is therefore only an extrapolation of the function for the linear section of the BAC curve, and may not hold true for values smaller than 0.15 g/kg [25].

On the basis of the relationship BrAC=f(BAC) the conversion factor Q can easily be calculated by dividing the formula by BrAC. This leads to a hyperbolic function, which describes the dependency of the BAC/BrAC conversion factor Q from BrAC. Q is inversely proportional to the BrAC, as a result of being affected by $1/\kappa$. The greater BrAC becomes, the closer Q comes asymptotically to the value of $1/\kappa$. With decreasing BrAC, the slope of the curve however increases continuously. This is of particular importance with regard to forensic aspects, because lower concentration ranges are most important in evidential breath tests.

If the dependency of the BAC/BrAC conversion factor Q from the BrAC is taken into consideration, it is not particularly meaningful to combine Q values which have been obtained from different concentrations or without mentioning the concentration of reference. The presentation of the results in the form of a hyperbolic formula seems most meaningful and can be used for scientific comparisons without restriction, because hyperbolas allow the calculation of Q from any given BrAC. If only selected measurements are used, Q_{BrAC} must be detailed as $Q_{0.25}$, $Q_{0.40}$ oder $Q_{0.55}$ for alcohol concentrations of 0.25 mg/l, 0.40 mg/l or 0.55 mg/l, respectively (Table 3).

Until recently the dependency of the conversion factor Q from the concentration has not been investigated thoroughly. Greater interest in this field was to be expected following the introduction of BrAC legal limits so far as they can be derived from pre-existing BAC limits and/or so far as they can be applied in parallel to the BAC limits. The different values of the conversion factor do not only have an influence on the different concentration levels, the range of variation is equally important. If the depency of the factor Q from the concentration is taken into account, significantly lower standard deviations will be obtained. This does not only have a major influence on the statistical calculation of the probability of an advantage or disadvantage through the determination of breath alcohol determination in contrast to the determination of blood alcohol concentrations [6, 20]. There is another practical aspect with regard to the elimination kinetic of the concentration of breath alcohol. On the one hand, the rate of BrAC elimination and its range of variation cannot simply be derived or converted from the elimination curve of BAC. The form of the BrAC elimination curve is much flatter because of the conversion factors which decrease with increasing concentration. On the other hand, the nearly linear form of the BrAC elimination curve can only be assumed for as long as the value of the conversion factor changes continuously. On the basis of the presented hyperbolic function, this can be assumed for higher concentrations whereas this is not the case with lower concentrations. The elimination curve of BrAC must therefore deviate from its linear course much earlier as is the case for the BAC curve which relies on the Michaelis-Menton kinetics. Such considerations are most important if the BrAC is taken to calculate the degree of alcoholisation retrospectively.

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