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Are sodium bicarbonate and potassium bicarbonate fully dissociated under physiological conditions?

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In solutions containing 160 mmol/l Na^+ and K^+, respectively, measurements with an ion-selective electrode system (KNA1, Radiometer), showed apparent falls in the respective Na^+ and K^+ concentrations when Cl^- was replaced by HCO_3^-. After correction for the change in liquid junction potential, the fall was 9.2 mmol/l for Na^+ and 7.3 mmol/l for K^+. On the basis of these findings we conclude that sodium bicarbonate and potassium bicarbonate are not fully dissociated in solution, and that $NaHCO_3^0$ and $KHCO_3^0$ do exist as chemical components with association constants of 0.72 and 0.55, respectively. Using these association constants, normal plasma will contain 1.2 mmol/l $NaHCO_3^0$ and 0.03 mmol/l $KHCO_3^0$. Thus $NaHCO_3^0$ accounts for virtually the same amount of CO_2 as the physically dissolved fraction. A review of all the currently known CO_2 species in plasma suggests that there may be a residue of about 2 mmol/l of unknown CO_2 species in normal plasma.

Key words: activity coefficients; ion-pairing; ion-selective electrodes; liquid junction potential

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Measurements with ion-selective electrodes (ISE) show an apparently lower concentration of sodium ion in the presence of bicarbonate ion. This finding has led to a discussion in the literature concerning the interpretation of data from ISE. Some authors [7] have ascribed the changes to liquid junction potential effects alone; some to ion-pair formation [5, 6]; and others to a combination of both effects [1, 8]. The presence of undissociated $NaHCO_3^0$ in plasma is contrary to the classical dissociation theory of Bjerrum [2], which states that both sodium and potassium salts are completely dissociated in solution.

The purpose of this study is to repeat these measurements under controlled conditions and over a wider range of HCO_3^- concentrations, while maintaining pH constant. The results are used to evaluate which of the above explanations is correct in the interpretation of data from ISE.

METHODS

Five solutions were prepared with a total sodium concentration of 160 mmol/l, but with chloride concentrations falling from 160 to 0 mmol/l, chloride being replaced by bicarbonate. Five further solutions were prepared in the same way but with potassium 160 mmol/l instead of sodium. The solutions were equilibrated to varying p_{CO_2} levels ranging from 0 to 35 kPa in order to maintain pH at 7.4 in all solutions. Furthermore, the two solutions of pure $NaHCO_3$ and $KHCO_3$ were measured without CO_2 equilibration (pH 8.4).

The activity of sodium and potassium was measured with ISE (KNA1, Radiometer Copenhagen, Denmark) at 37 °C. The liquid junction is established as an open static junction between the sample and sodium formate 4.6 mol/kg. We have previously investigated this salt bridge solution to eliminate the effect of erythrocytes on the liquid junction potential [15]. The set point of the instrument was calibrated with either pure NaCl or KCl 160 mmol/l. The electrode sensitivities were automatically adjusted with the standard calibration solutions from the manufacturer (ionic strength 0.161 mol/kg), and were found to be 95% of the theoretical for Na^+ and 99% for K^+.

RESULTS

The results are presented in Fig. 1. The measured data were corrected for the different liquid junction potentials for sodium chloride and sodium bicarbonate, calculated from the Henderson equation, using the same limiting ionic equivalent conductances of 66 $S \cdot cm^2 \cdot mol^{-1}$ for both sodium and formate [10]. The apparent fall in sodium ion concentration at pH 7.4 (Fig. 1) was from 160 to 145.7 mmol/l. Even after correction for the change in liquid junction potential, the Na^+ concentration still fell from 160 to 150.8 mmol/l with a slightly larger fall to 149.5 at pH 8.4. However, part of this extra fall (0.3 mmol/l) is due to minor H^+ interference. The corresponding falls in K^+ concentrations were 7.3 mmol/l at pH 7.4 and 8.9 mmol/l at pH 8.4 after correction for the liquid junction potentials (H^+ does not interfere with the K^+ measurements in this pH range).

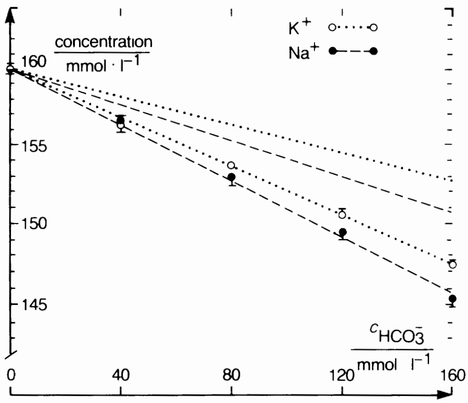

FIG. 1. The apparent fall in Na^+ and K^+ concentrations measured with ISE in 5 solutions containing 160 mmol/l of Na^+ and K^+, respectively, when Cl is replaced by HCO_3^-. pH is maintained at 7.4 by varying p_{CO_2}. Each point is the mean value of 4 determinations, the range also being indicated. The upper lines show the fall after correction for the change in liquid junction potential. In one case ($c_{HCO_3^-}$=80 mmol/l) the values of all c_{K^-} were identical, and hence the range is apparently lacking.

CALCULATION OF THE ASSOCIATION CONSTANTS

Our results at two different pH values allow the calculation of the thermodynamic association constants from the following equations (exemplified for Na^+):

$$K_{NaCO_3^-} = a_{NaCO_3^-}/(a_{Na^+} \cdot a_{CO_3^{2-}}) = (f_1 - f_2)/(g_2 - g_1)$$

$$K_{NaHCO_3^0} = a_{NaHCO_3^0}/(a_{Na^+} \cdot a_{HCO_3^-}) = (f_1 \cdot g_2 - f_2 \cdot g_1)/(g_2 - g_1)$$

where

$$f = (m_{tNa}/m_{Na^+} - 1) \cdot (m_{Na^+} - m_{Cl^-})^{-1} \cdot (\gamma_{Na^+})^{-1} \cdot [2 \cdot K_2/(a_{H^+} \cdot \gamma_{CO_3^{2-}}) + 1/\gamma_{HCO_3}] \cdot \bar{m}^{\theta}$$

$$g = (m_{tNa} - 2 \cdot m_{Na^+} + m_{Cl^-}) \cdot (m_{Na^+} - m_{Cl^-})^{-1} \cdot K_2/(a_{H^+} \cdot \gamma_{NaCO_3^-})$$

The equations were derived by simple substitution on the basis of the law of conservation of substance and the law of electro-neutrality:

$$m_{tNa} = m_{Na^+} + m_{NaHCO_3^0} + m_{NaCO_3^-}$$
$$m_{Na^+} = m_{HCO_3^-} + 2 \cdot m_{CO_3^{2-}} + m_{NaCO_3^-} + m_{Cl^-}$$

The active molality ($\tilde{m}_B$) is defined as $\tilde{m}_B = m_B \cdot \gamma_B$ and the relative molal activity is $a_B = \tilde{m}_B / \tilde{m}^\theta$, where $\tilde{m}^\theta = 1$ mol·kg^{-1} [14].

Subscript 1 and 2 to *f* and *g* indicate two different solutions, e.g.:

solution 1: $m_{tNa^+} = 160$ mmol·kg^{-1}; $m_{Cl^-} = 0$; $m_{Na^+} = 150{\cdot}8$ mmol·kg^{-1}; $a_{H^+} = 10^{-7{\cdot}4}$

solution 2: $m_{tNa^+} = 160$ mmol·kg^{-1}; $m_{Cl^-} = 0$; $m_{Na^+} = 149{\cdot}8$ mmol·kg^{-1}; $a_{H^+} = 10^{-8{\cdot}4}$.

The activity coefficients are taken to be identical in the two solutions and are estimated by the Debye-Hückel equation:

$$\gamma_{Na^+} = 0.75$$
$$\gamma_{HCO_3^-} = 0.74$$
$$\gamma_{HCO_3^{2-}} = 0.74$$
$$\gamma_{CO_3^{2-}} = 0.30$$
$$K_2 = a_{H^+} . a_{CO_3^{2-}} / a_{HCO_3^-} = 10^{-10\,2} \text{ at } 37\ °\text{C}.$$

We find the following thermodynamic association constants for 37 °C:

$$K_{NaCO_3^-} = 8.3$$
$$K_{KCO_3^-} = 10.6$$
$$K_{NaHCO_3^0} = 0.72$$
$$K_{KHCO_3^0} = 0.55$$

DISCUSSION

Previous studies of the $NaHCO_3^0$ thermodynamic association constant have given quite variable results ranging from 0.56 to 0.78 [3, 4, 11]. Our finding of a lower association for $KHCO_3^0$ than for $NaHCO_3^0$ is to be expected since Na^+ and K^+ belong to a lyotropic series. Thus lithium bicarbonate may be expected to have an even higher K_a and rubidium bicarbonate a lower K_a than sodium or potassium bicarbonate. Our new value of 8.3 for the thermodynamic association constant for Na^+ and CO_3^{2-} is considerably lower than our previous value of 40 [12], which was derived more indirectly from studies of the variation of the carbonic acid p*K* with pH. Garrels *et al.* [11] found a value of 18.6 and Butler & Huston [4] a value of 5.6 at 25 °C. Our finding of a slightly higher value for the association constant for K^+ and CO_3^{2-} than that for Na^+ and CO_3^{2-} (i.e the opposite of what should be expected) indicates that our values for the carbonate association constants are less accurate than those for the bicarbonate associa-

TABLE I. The CO_2 species in normal human plasma at pH 7.4 and p_{CO_2} 5.33 kPa, listed in order of quantitative importance. The values were calculated from the relevant association or dissociation constants. For other relevant data, see footnotes.

Species	Concentration (mmol·l^{-1})	Relevant constants		
HCO_3^-	20.41	$a_{H^+} \cdot a_{HCO_3^-} / (a_{CO_2} \cdot a_{H_2O})$	$= 10^{-6.32}$	[13]
CO_2	1.23	$c_{CO_2} / p_{CO_2} = \alpha$	$= 0.23$ mmol·l^{-1}·kPa^{-1}	[13]
$NaHCO_3^0$	1.22	$a_{NaHCO_3^0} / (a_{Na^+} \cdot a_{HCO_3^-})$	$= 0.72$	(Present study)
$CaHCO_3^+$	0.19	$a_{CaHCO_3^+} / (a_{Ca^{2+}} \cdot a_{HCO_3^-})$	$= 24.5$	[9]
$PrNHCOO^-$	0.16			(Ref. 13, p. 20)
CO_3^{2-}	0.08	$a_{H^+} \cdot a_{CO_3^{2-}} / a_{HCO_3^-}$	$= 10^{-10.2}$	[13]
$MgHCO_3^+$	0.05	$a_{MgHCO_3^+} / (a_{Mg^{2+}} \cdot a_{HCO_3^-})$	$= 14.5$	[11]
$NaCO_3^-$	0.03	$a_{NaCO_3^-} / (a_{Na^+} \cdot a_{CO_3^{2-}})$	$= 8.3$	(Present study)
$KHCO_3^0$	0.03	$a_{KHCO_3^0} / (a_{K^+} \cdot a_{HCO_3^-})$	$= 0.55$	(Present study)
$CaCO_3^0$	0.01	$a_{CaCO_3^0} / (a_{Ca^{2+}} \cdot a_{CO_3^{2-}})$	$= 1585$	[11]
$MgCO_3^0$	0.01	$a_{MgCO_3^0} / (a_{Mg^{2+}} \cdot a_{CO_3^{2-}})$	$= 2512$	[11]
	23.42			
Total CO_2	25.69	$10^{-pH} \cdot (c_{tCO_2} - \alpha \cdot p_{CO_2}) / \alpha \cdot p_{CO_2}$	$= 10^{-6.10}$	[13]

1. $pa_{H^+} = 7.412$ after correction for liquid junction potential difference ($\triangle E_j = +0.7$ mV).
2. $a_{H_2O} = 0.9947$, $a_{CO_2} = 0.247 \cdot 10^{-3} \cdot p_{CO_2} \cdot$kPa^{-1}.
3. The activity coefficients (γ) are taken to be 0.75 for sodium and 0.74 for the other monovalent ions, and 0.30 for divalent ions. The water concentration is taken to be 0.933 kg·l^{-1}.
4. The molalities for Na^+, K^+, Ca^{2+} and Mg^{2+} are taken to be 150, 5.0, 1.25 and 0.6 mmol·kg^{-1}, respectively.

tion constants. More accurate measurements of the former should be made with carbonate solutions instead of bicarbonate solutions.

For many years a discrepancy has been known to exist between the concentration of HCO_3^- calculated from the thermodynamic equilibrium constant, pH and p_{CO_2} and that calculated by subtracting the physically dissolved CO_2 from total CO_2. Our data suggest that undissociated $NaHCO_3^0$ and $KHCO_3^0$ do exist as chemical components in solution. Using the calculated association constants in this study of 0.72 for $NaHCO_3^0$ and 0.55 for $KHCO_3^0$, a plasma molality for Na^+ of 0.150 mol/kg, a molal activity coefficient for Na^+ of 0.75, and a relative molal activity for HCO_3^- of 0.0162, normal plasma will contain 1.22 mmol/l $NaHCO_3^0$ and 0.03 mmol/l $KHCO_3^0$. It is interesting to note (Table I) that the ion-pair $NaHCO_3^0$ appears to be quantitatively equal to the physically dissolved CO_2 and that $CaHCO_3^+$ is the fourth most important CO_2 species in plasma. Generally these species are not mentioned in current textbooks of acid-base physiology. However, even allowing for all the known CO_2 species listed in Table I, there is still a residue of about 2 mmol/l of CO_2 which cannot be accounted for in normal plasma. The explanation for this discrepancy may be the presence of other species, e.g. protein-bound compounds, or due to inaccuracy of some of the equilibrium constants, especially the thermodynamic dissociation constant for carbonic acid ($10^{-6.32}$), or because of a higher residual liquid junction potential for the pH measurement than we have taken into account (0.7 mV).

The presence of $NaHCO_3^0$ could be important in facilitating sodium transport through the cell membrane, as has been suggested for $NaCO_3^-$, which, however, exists in much lower concentrations [16].

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