Determination of [K⁺] in Blood Serum with a Valinomycin-Based Silicone Rubber Membrane of Universal Applicability to Body Fluids

To the Editor:

Various ion-selective electrodes based on valinomycin (Table 1) have been widely used for determination of the K⁺ concentration in whole blood, blood plasma, and undiluted and diluted blood serum, as well as in diluted urine (for a review see (1)). Plasticized poly(vinylchloride) membranes (columns 2 and 3 in Table 1) have been of special interest. Although these electrodes, especially the one plasticized with dinonyladiapate (I), exhibit a very high stability of the electromotive force of the cell assembly and lead to reliable determination of [K⁺] in these media, they cannot be used for undiluted urine. This shortcoming is due to anion interference (2), which can be eliminated almost completely (2) by incorporating valinomycin into Silopren (silicone rubber, column 4 in Table 1). Such membranes are now in routine use for the bedside monitoring of undiluted urine (3).

Here we report on the use of these membranes to measure [K⁺] in undiluted blood serum. To test their universal applicability to body fluids, including serum, we prepared silicone rubber membranes and miniaturized electrodes as described earlier (2).

Using the same cell assembly and the same calibration and evaluation procedure as described recently for [Na⁺] determination in serum (4), we correlated measurements made with use of the silicone rubber membrane electrode and a flame photometer (Figure 1). The three solutions for the electrode calibration all contained, per liter, 140 mmol of NaCl, 1.1 mmol of CaCl₂, and 0.6 mmol of MgCl₂. The respective concentrations of KCl were 1.4, and 9 mmol/L.

Results obtained by direct potentiometry agreed well with the indirect measurements made by flame photometry (upper curve in Figure 1). The correlation yields a residual standard deviation of ±0.10 mmol/L and a positive bias of the potentiometrically determined potassium concentrations with a mean of 2.2%. Correcting the values for the protein and lipid volume according to Waugh (4, 5) shifts the bias to −4.3% (lower curve in Figure 1, residual standard deviation: ±0.10 mmol/L).

No bias (6) or only a positive one varying from 0.7% (7) to 4.0% (8) has been found in different potentiometric studies of [K⁺] in serum, if no corrections are made for protein and lipid volume. Correcting the results for typical (6.7%) protein and lipid volumes (4), we obtained negative biases of 7.2%, 6.4%, and 2.9%, respectively. In contrast to corresponding considerations for [Na⁺] determinations (4), the deviations observed for [K⁺] are of minor clinical significance because they are so small as compared with the physiological normal range.

We conclude that the silicone rubber membrane discussed here can be considered as a membrane of universal applicability to body fluids.

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Table 1. Selectivity Factors, Detection Limit, Slope of the Electrode Function and Membrane Resistance of K⁺-selective Solvent Polymeric Membranes

<table>
<thead>
<tr>
<th>Electrode type and membrane composition, in mg/g</th>
<th>Electrode sample</th>
<th>Membrane sample</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>J⁺</strong></td>
<td>Valinomycin 10, II</td>
<td>Valinomycin 13, I</td>
</tr>
<tr>
<td>H⁺</td>
<td>−4.2</td>
<td>−4.1</td>
</tr>
<tr>
<td>Li⁺</td>
<td>−4.3</td>
<td>−4.7</td>
</tr>
<tr>
<td>Na⁺</td>
<td>−4.0</td>
<td>−3.7</td>
</tr>
<tr>
<td>RB⁺</td>
<td>0.0</td>
<td>0.4</td>
</tr>
<tr>
<td>Ca⁺</td>
<td>−0.4</td>
<td>−0.4</td>
</tr>
<tr>
<td>NH₄⁺</td>
<td>−2.0</td>
<td>−1.9</td>
</tr>
<tr>
<td>Mg²⁺</td>
<td>−4.8</td>
<td>−4.8</td>
</tr>
<tr>
<td>Ca²⁺</td>
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<td>−4.8</td>
</tr>
<tr>
<td>Sr²⁺</td>
<td>−4.4</td>
<td>−4.9</td>
</tr>
<tr>
<td>Ba²⁺</td>
<td>−4.5</td>
<td>−5.4</td>
</tr>
</tbody>
</table>

Slope, mV⁻¹: 59.8 ± 0.1; 59.2 ± 0.1; 59.5 ± 0.2
Detection limit (log a₀): 5.3; 5.3; 4.8
Specific membrane resistance Ω · cm²: 9.8 · 10⁷; 3.2 · 10⁸; 2.1 · 10⁹

**References**

Serum 5'-Nucleotidase and γ-Glutamyltransferase Compared in Alcoholic Patients after Detoxification

To the Editor:

Ethanol intake induces liver γ-glutamyltransferase (EC 2.3.2.2), so this can be used as an indicator of chronic alcohol intake or abstinence (1, 2).

5'-Nucleotidase (EC 3.1.3.5) activity in serum correlates closely with γ-glutamyltransferase in various forms of liver disease, and it is specific for hepatobiliary disorders (3). Thus it was desirable to study changes in the nucleotidase activity before and after ethanol intake.

Blood was sampled from each of 28 fasting patients, 18 men and 10 women, at the time they were admitted to a local alcoholism clinic and on followup 90 days after professed abstinence from ethanol. During detoxification the treatment consisted of emetine and pilocarpine-induced regurgitation of ethanol and the parenteral administration of multi-vitamins.

Activities of the two enzymes in serum and their respective reference intervals were determined as described elsewhere (4, 5). To establish the reference intervals, we chose about 40 serum samples from an equal number of men and women who were free of apparent liver disease or ethanol intake.

We found a sex-related difference for γ-glutamyltransferase but not for 5'-nucleotidase.

Table 1 summarizes the data collected before and after ethanol abstinence. Of 28 patients, 17 had an increased value for γ-glutamyltransferase on admission, and for 15 it reverted to normal in 90 days. At admission 20 of the subjects showed above-normal 5'-nucleotidase activity; in only five did it later revert to normal. Twenty-three patients had above-normal values for either one or the other enzyme at admission; only 14 had increased values for both. We used sex-related reference intervals for γ-glutamyltransferase in evaluating these results.

As can be seen from Figure 1, there is a reasonable degree of correlation (r = .77) between the two enzymes. γ-Glutamyltransferase is the more sensitive. All data for γ-glutamyltransferase shown in Figure 1 are based on normal reference intervals for men.

Because γ-glutamyltransferase and 5'-nucleotidase have been localized to the lipoprotein fraction of plasma membranes lining the bile canaliculi (6, 7), it might be expected that these enzymes will be increased in serum in various phases of cholestasis: obstruction, regeneration, and fibrosis (8). In this study, however, the data for patients having increased activities for these two enzymes only partly overlap.

Of significance was a persistent small increase in 5'-nucleotidase in serum of patients whose γ-glutamyltransferase values had returned to normal. In chronic alcoholic hepatitis or progressive cirrhosis, or both, activity of the latter enzyme remains increased. Thus another mechanism is needed to explain the observations.

It is postulated that 5'-nucleotidase is induced in human alcoholism. Induction of 5'-nucleotidase has been previously reported in a patient receiving glutethimide (9). The enzyme had returned to normal by about 120 days, and the γ-glutamyltransferase by about 80 days, after discontinuance of the drug. Nishimura and Teschke (10) report an increase of plasma 5'-nucleotidase and γ-glutamyltransferase and hepatic-membrane γ-glutamyltransferase, but a suppression of membrane 5'-nucleotidase in rats fed alcohol. They suggest that the enzymes may be released from the liver in different ways. These observations may relate to the frequently prolonged increase in human serum 5'-nucleotidase after ethanol intake has been discontinued, the clinical significance of which is yet to be elucidated.

References