# ION-EXCHANGE ADSORPTION OF CALCIUM AND STRONTIUM FROM BLOOD AND PLASMA

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Selective adsorption of substances from a medium with many components can be a difficult task which, in most cases, is solved individually, allowing for the particular features of each system. As a result of this, it is essential that the general principles of selective adsorption of substances from such mixtures be determined and utilized. Cases of hypercalcemia occur in burns, circulatory insufficiency in the limbs and rickets. Maintenance of the calcium level within normal limits during hemosorption and hemoperfusion of other substances [3], especially during detoxication of patients from radionuclides, especially $^{89}Sr$ and $^{90}Sr$, also is of great importance.

Cation-exchange adsorption of $Ca^{++}$ and $Sr^{++}$ from blood plasma and from whole blood was investigated. Blood in this case was regarded as a multicomponent physicochemical system of definite composition [8], to which the general principles of adsorption and ion-exchange characteristic of aqueous solutions can be applied. Differences in the properties of blood and aqueous solutions, namely the presence of blood cells, anomalous viscosity, a high protein concentration, were allowed for as a first approximation by the introduction of appropriate corrections.

## EXPERIMENTAL METHOD

The behavior of $Ca^{++}$ and $Sr^{++}$ in plasma and blood was investigated under static and dynamic conditions: The distribution coefficients of these ions in blood plasma and in a mixture of electrolytes stimulating the salt composition of plasma [8] and also the kinetic ion exchange coefficients were determined. The cation-exchange resin KU = 2 × 8, converted beforehand into the equilibrium-salt form for creating selectivity of adsorption of $Ca^{++}$ and $Sr^{++}$ [1, 2].

For $Sr^{++}$ adsorption the KU = 2 × 8 resin ($H^+$-form 0.25-0.5 mm) was washed to pH 7.0 with a solution of the following composition: NaCl 0.11 M, KCl 10 mM, $MgCl_2$ 4 mM, $NH_4Cl$ 0.0001%, $CaCl_2$ 10 mM; in the experiments to study $Ca^{++}$ adsorption, $CaCl_2$ was left out of the washing water.

Experiments were carried out with the radionuclides $^{45}CaCl_2$, $^{89;90}SrCl_2$, and a calcium-selective electrode based on thenoyltrifluoroacetone. In this case the $Ca^{++}$ adsorption curves were recorded by the pH-340 pH-meter and ÉPP-09 automatic writer.

Concentrations of $K^+$, $Na^+$, $Ca^{++}$, proteins, urea, sugars, phosphates, and other components of plasma in experiments on animals were determined with an automatic analyzer.

## EXPERIMENTAL RESULTS

Distribution coefficients of $Ca^{++}$ and $Sr^{++}$ in solutions with successively increasing concentrations of plasma are given in Fig. 1. The character of the change in the distribution coefficients indicates complex formation between ions of the metals and components of plasma. Regarding plasma as a "collective ligand" [2], we calculated the constants of formation ($K_f$) of complexes between $Ca^{++}$ and $Sr^{++}$ and the components of plasma. The electrophoresis results showed that complexes were anionic in nature, thus explaining the absence of their adsorption on the cation-exchange resin. Calculation followed Schubert's method [2, 5], and on the basis of the results a diagram of the states of the $M^{++}$ and $ML^{x-}$ ions was constructed for different

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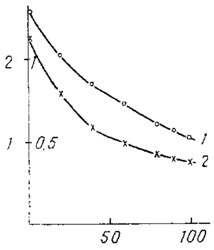

Fig. 1

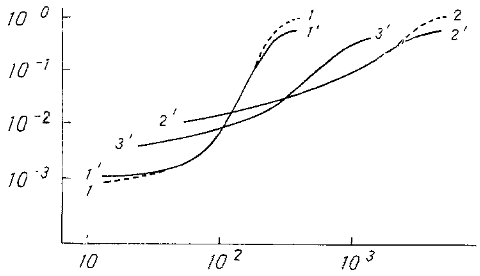

Fig. 2

Fig. 1. Distribution coefficients ($K_d$) of $Ca^{++}$ (1) and $Sr^{++}$ (2) as functions of plasma concentration. Abscissa, concentration of plasma (in %); ordinate: $K_d \times 10^{-2}$ for $Ca^{++}$; $K_d \times 10^{-3}$ for $Sr^{++}$.

Fig. 2. Elution curves of ion-exchange adsorption of $Ca^{++}$ ($C^\circ = 3 \times 10^{-3}$ M) from salt solution (1), plasma (2), and plasma diluted in the ratio of 1:1 (3). 1, 2 and 1', 2') Theoretical and experimental curves respectively. Here and in Fig. 3, abscissa, time (in sec); ordinate $C/C^\circ$.

TABLE 1. Mass Transfer Coefficients during Ion Exchange of $Ca^{++}$ and $Sr^{++}$

| Ion | Solution | Rate of flow, cm/sec | | | | |
|---|---|---|---|---|---|---|
| | | 0,09 | 0,11 | 0,18 | 0,22 | 0,34 |
| $Ca^{2+}$ | Salt | 0,25 | — | 0,35 | 0 | 0,49 |
| | Plasma | 0,15 | 0,16 | 0,24 | — | 0,37 |
| $Sr^{2+}$ | Salt | 0,22 | 0,23 | — | 0,33 | 0,41 |
| | Plasma | 0,11 | 0,13 | — | 0,24 | 0,35 |

concentrations of plasma. These data agreed closely with results given in the reference literature [4, 7, 8].

The higher values of the distribution coefficients of $Ca^{++}$ and, in particular, of $Sr^{++}$, achieved by special preparation of the resin for selective adsorption, will be noted. This ensured high efficiency of operation of the adsorption column. It was also shown that at $Ca^{++}$ and $Sr^{++}$ concentrations $C^\circ \leq 5 \cdot 10^{-3}$ M the ion-exchange isotherm from aqueous solutions and from plasma was linear.

The type of kinetics of ion exchange and coefficients of mass transfer ($\beta$) for investigation of adsorption of $Ca^{++}$ and $Sr^{++}$ on resin KU = 2 × 8 in equilibrium-salt form from salt solution and from plasma were determined by comparing the experimental elution curves with theoretical curves calculated by computer [6]; the coefficient $\beta$ was determined by the instantaneous overshoot method. Values of the coefficients $\beta$ determined for different flow rates are in good agreement with the $\beta$ vs. $V^{1/2}$ relationship characteristic of external diffusion kinetics (Table 1).

Experimental elution curves for adsorption of $Ca^{++}$ and $Sr^{++}$ from blood plasma coincided with theoretical elution curves with the parameter H = 3.16; this indicates that the external diffusion factor makes the principal contribution to mixed diffusion and, correspondingly, internal diffusion makes only a small contribution. During dilution of plasma with salt solution (for example, with a ratio of plasma to salt solution of 1:1) the experimental elution curve coincided with the theoretical curve characterized by the value H = 1, confirming the tendency for the type of kinetics to approach the external diffusion type during dilution of plasma with salt solution.

Knowing $C^\circ$, $K_d$, and $\beta$ and also the diameter of the column and the flow rate it is possible to calculate any dynamic adsorption curve to an assigned $C/C^\circ$, as is confirmed by the results given in Figs. 2 and 3.

The high efficiency of operation of the column will be noted: 80% of the $Ca^{++}$ was processed by the column in the course of 30 min with a volume of resin $V = \pi \cdot 1.1^2 \cdot 10 = 38\ cm^3$, 0.25-0.5 mm grain size, rate of flow 30-40 ml/min, from a volume of plasma of 600 $cm^3$. The $Ca^{++}$ concentrations before and after adsorption were 5.8 and 1.8 mM, corresponding to absorption of 4.8 mg-eq calcium by the column.

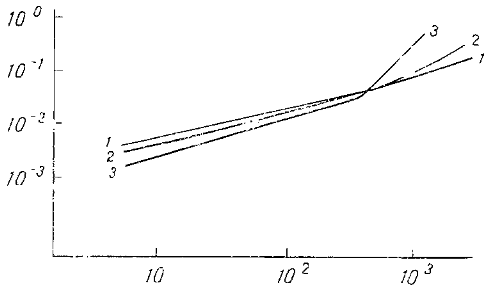

Fig. 3. Elution curves for $^{90}Sr^{++}$ adsorption from blood plasma $C^0$ without carrier (1), $1 \cdot 10^{-4}$ (2) and $1 \cdot 10^{-3}$ M (3).

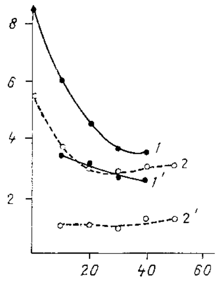

Fig. 4. Time course of $Ca^{++}$ concentration in blood plasma of dogs as a result of adsorption: 1) experiment on February 21, 1975; 2) experiment on February 12, 1976; 1, 2) analysis of $Ca^{++}$ at entrance to column, 1', 2') at exit from column. Abscissa, time (in min); ordinate, $Ca^{++}$ concentration (in mg-eq/liter).

TABLE 2. Mass Transfer Coefficients of $Ca^{++}$ (V = 0.212 cm/sec) for Equilibrium Salt Solution and for Solutions of Plasma

| Salt solution | Ratio of solution to plasma | | | | Plasma |
|---|---|---|---|---|---|
| | 1:1 | 2:1 | 3:1 | 5:1 | |
| 0,40 ± 0,03 | 0,24 ± 0,02 | 0,22 ± 0,02 | 0,20 ± 0,03 | 0,18 ± 0.04 | 0,16 ± 0,2 |
| External diffusion kinetics | Mixed diffusion kinetics, H = 1.0 | | | Mixed diffusion kinetics, H = 3.16 | |

Purification of plasma from strontium ($^{90}Sr$) was carried out on a column with volume $V = \pi \times 1.1^2 \times 3 = 11$ cm$^3$. When the radionuclide was used without carrier the state of saturation of the column was not reached during 40 min with a single run through of plasma or during circulation of the solution. The degree of purification from $^{90}Sr$ under these conditions was 85% and calcium was not adsorbed.

The mass transfer coefficients (Table 2) differed for salt solution and plasma by a factor of 2-3, corresponding to the difference between the viscosities of water and blood.

The scheme for correction of plasma with an increase in $Ca^{++}$ concentration, developed under laboratory conditions, was applied in experiments on dogs; altogether eight operations were performed.

TABLE 3. Dynamics of Blood Plasma Parameters during Adsorption of $Ca^{++}$ from Dogs' Blood

| Substances | | Initial data | Sampling time, min | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | 10 | | 20 | | 30 | | 40 | |
| Sodium | mg-eq/liter | 150 | 155 | 133 | 140 | 142 | 140 | 145 | 140 | 145 |
| Potassium | | 2,8 | 2,7 | 2,6 | 2,8 | 2,8 | 3,0 | 3,0 | 3,3 | 3,3 |
| Calcium | | 8,6 | 6,0 | 3,4 | 4,5 | 3,1 | 3,6 | 2,6 | 3,5 | 2,5 |
| Chloride | | 115 | 112 | 110 | 112 | 111 | 111 | 112 | 113 | 112 |
| Protein (total) | % | 5,0 | 4,8 | 4,4 | 5,0 | 5,0 | 4,9 | 4,9 | 4,9 | 4,9 |
| Albumin | | 3,0 | 2,8 | 2,8 | 2,8 | 2,6 | 2,7 | 3,3 | 2,8 | 2,8 |
| Phosphates (inorg) | mg % | 4,7 | 4,9 | 4,5 | 4,7 | 4,7 | 4,8 | 5,0 | 5,0 | 5,3 |
| Cholesterol | | 212 | 210 | 180 | 175 | 195 | 175 | 200 | 180 | 225 |
| Uric acid | | 2,0 | 1,8 | 1,7 | 1,7 | 1,7 | 1,9 | 2,3 | 2,3 | 2,3 |
| Urea nitrogen | | 30 | 30 | 25 | 29 | 29 | 30 | 31 | 31 | 31 |
| Glucose | | 320 | 300 | 250 | 260 | 260 | 275 | 285 | 320 | 320 |
| Hemolysis, % | | — | | 5,3 | | 5,3 | | 7,2 | | 6,5 |

Legend. KU = 2 × 8, 0.25-0.5 mm, equilibrium-salt form, 36-37°C, flow rate 150 ml/min.

As an example the time course of the $Ca^{++}$ concentration during hemosorption for two experiments is illustrated in Fig. 4. It was found that the $Ca^{++}$ values showed little change after 30-40 min of working on the column and the main adsorption process had finished. Meanwhile the concentration of other important biogenic substances in the blood remained virtually at the previous level (Table 3), confirming the scheme of selective hemosorption of $Ca^{++}$.

In the experiments to study adsorption of $Sr^{++}$ from isolated blood plasma, satisfactory agreement also was obtained between the experimental and theoretical values. Incidentally, because the adsorbents were used in the equilibrium-salt form, practically no calcium was adsorbed from the blood plasma, and in that way very high selectivity of adsorption of the radionuclide $^{90}Sr$ was achieved.

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