Aluminium Biokinetics Studies with ^{26}Al on Rats with Different Iron Status

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In the blood plasma, aluminium is bound to the protein transferrin and to citrate. Two binding places per transferrin molecule are available for iron or for aluminium and other metals. In order to study effects of changes in the aluminium binding to transferrin on the uptake, transport, distribution and excretion of aluminium, a study with three groups of Sprague-Dawley rats with different iron diet was performed. The control group Fe(0) obtained normal diet, a second group Fe(-) obtained iron deficient and a third group Fe(+) iron abundant diet [1]. A single dose of 20 ng ^{26}Al together with 200 μg Al was administered orally to the rats as $AlCl_3$. The rats were sacrificed 24 h after administration. Samples of blood plasma, collected urine, femur, liver and spleen were taken. ^{26}Al was measured in the samples with AMS. The results are shown in fig. 1.

The ratio of ^{26}Al found in the liver to that found in bones is by a factor of 6.1 larger for the Fe(-) group than for the Fe(+) group: N(Fe-, liver)/N(Fe-, bones) $\approx$ 6.1 N(Fe+, liver)/N(Fe+, bones). The uptake R of ^{26}Al for the Fe- group is about 2.3 times larger than for the Fe+ group: R(Fe-) $\approx$ 2.3 (Fe+). These observations can be explained by larger (smaller) compartments for transferrin binding of aluminium for the Fe- (Fe+) group compared to the controls, supply of the liver via transferrin bound aluminium (in the plasma), supply of the bones via citrate bound aluminium (in the interstitial fluid) and uptake of aluminium from the intestinal tract into the plasma half to transferrin and half to citrate binding.

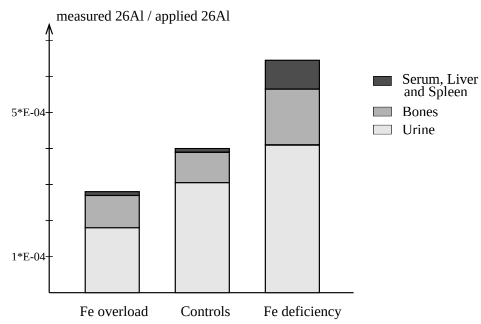

Fig. 1: ^{26}Al contents in urine, in bones and in liver, spleen and serum for the control, iron overload (Fe+) and iron deficiency (Fe-) groups

Simulation calculations of the aluminium biokinetics were performed with compartmental models. For demonstration, a model with two compartments is considered (fig. 2). The sizes of the compartments are N_1^{max} and N_2^{max}, the actual occupation numbers are N_1 and N_2, respectively. The number of particles transported from compartment 1 into compartment 2 is given by N_1 a_{12} $(1-N_2/N_2^{max})$ dt, for the other direction by N_2 a_{21} $(1-N_1/N_1^{max})$ dt. The rate constants a_{12} and a_{21} are inverse time constants T_{12}^{-1} and T_{21}^{-1}. Saturation effects are taken into account by the terms in brackets. In equilibrium, $N_1/N_1^{max} = N_2/N_2^{max}$. From the equilibrium condition it is seen that $a_{12}/a_{21} = N_1^{max}/N_2^{max}$, or a_{12} = a' N_2^{max} and a_{21} = a' N_1^{max}.

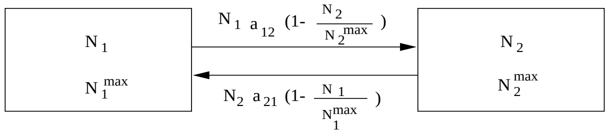

Fig. 2: Compartmental model with two compartments 1 and 2.

This means, the rate constant is proportional to the size of the compartment into which the particles are transported. In the performed experiments, it was found that rate constants for humans and rats were similar. A more universal description is thus obtained if concentrations or normalized sizes are used. Here, we use for normalization the plasma volume V_P. The rate constants are thus expressed by a_{12} = a" N_2^{max}/V_P and by a_{21} = a" N_1^{max}/V_P. The actual compartmental model for aluminium biokinetics is shown in fig. 3.

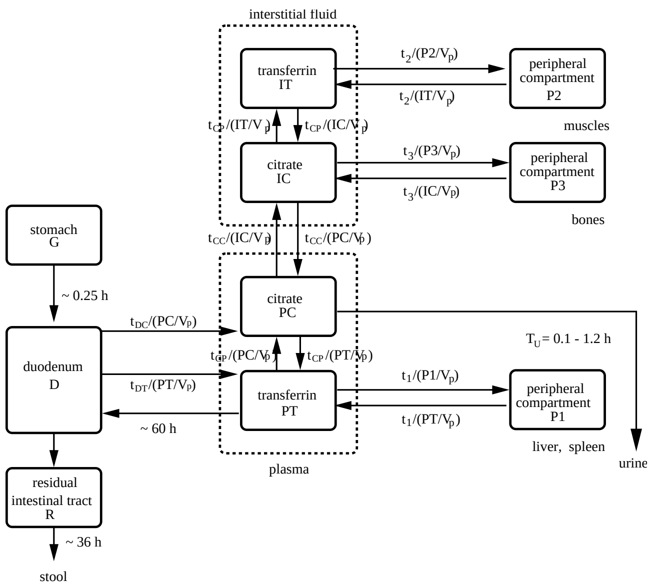

Fig. 3: Compartmental model for aluminium biokinetics used for simulation calculations. PT (PC) transferrin (citrate) bound aluminium in the plasma, IT (PC) transferrin (citrate) bound aluminium in the interstitial fluid, V_P plasma volume.

This model is based on this experiment and on many other experiments with volunteers, patients with renal failure, control rats and nephrectomized rats with p.o. and i.v. administration of ^{26}Al. From these experiments it is seen that the muscles are supplied with aluminium via citrate bound Al (in the interstitial fluid). In the simulation calculations for this study, all parameters were kept constant except for the sizes of the transferrin compartments. The transferrin compartments PT and IT for the Fe- group were taken to be 6.1 times larger than those of the Fe+ group. The simulation calculations reproduce well the measured values.

References

[1] Jahresbericht 1996, p. 72