# Aluminium Biokinetics and Speciation

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The multicompartmental model for aluminium biokinetics in humans and rats was refined. The refined model is shown in Fig. 1. In the central compartment, it is now distinguished between blood plasma and interstitial fluid and between transferrin bound and citrate bound aluminium. Transferrin is a protein molecule with 71000 D. Its concentration in human blood plasma is typically 3 g/l (42 $\mu$mol/l). One transferrin molecule can bind two iron or two aluminium ions. One third of transferrin is used for iron binding, 2/3 are available for aluminium binding. 45 % of the total transferrin in the body are found in the blood plasma. The remaining 55 % are given into the interstitial fluid. The interstitial fluid has about four times the volume of the blood plasma.

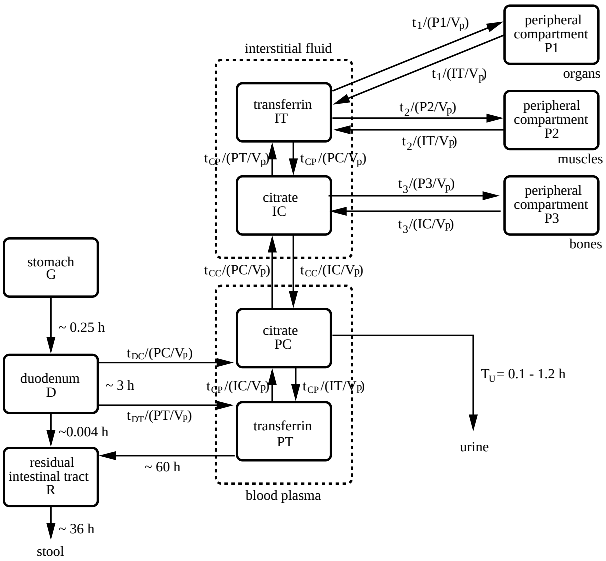


Fig. 1: Compartimental model for the aluminium biokinetics with the central compartment consisting of transferrin and citrate bound Al in blood plasma and interstitial fluid (PT, PC, IT and IC), of three peripheral compartments for organs (P1), muscles (P2) and bones (P3), and of the gastro-intestinal tract with stomach (G), duodenum (D) and residual intestinal tract (R). The time constants which describe the transport are also given.

In order to determine the aluminium distribution in the plasma, a speciaton measurement with $^{26}$Al was performed. $^{26}AlCl_3$ was given i. v. to a human volunteer. At time intervals of 5, 20 and 60 min after administration, blood samples were taken. With ultracentrifugation, the ultrafiltrable percentage of $^{26}$Al in the plasma was determined as function of time. This preliminary measurement of a series of speciation experiments showed that 5.6 % of the aluminium in the plasma are bound to the ultrafiltrable citrate. The time constant for the transition from chloride bound aluminium to transferrin bound aluminium was found to be in the range of 4 min. The result of our speciation measurement of 5.6 % has to be compared with values of about 4 % obtained with $^{26}$Al [1], of 12 ($\pm$5) % [2] and 20 % [3] obtained with stable Al and HPLC, of 15 ($\pm$7) % proposed in a speciation equilibrium model [4] and of 11 ($\pm$5) % deduced with the help of chemical equilibrium constants [5].

With 5.6 % of citrate bound aluminium in the plasma, the maximum compartmental aluminium sizes with respect to the plasma volume are: plasma transferrin PT 56 $\mu$mol/l, plasma citrate PC 3.3 $\mu$mol/l, interstitial fluid citrate IC 13 $\mu$mol/l and interstitial fluid transferrin IT 68 $\mu$mol/l.

The studies with rats have shown that three peripheral compartments P1, P2 and P3 are needed for organs, muscles and bones, respectively. These studies have also shown that organs (P1) and muscles (P2) are supplied with aluminium from the transferrin bound part of the interstitial fluid IT and bones (P3) from the citrate bound part of the interstitial fluid IC.

The aluminium absorption from the gastro-intestinal tract takes place in the duodenum. Two absorption channels can be used, one into the transferrin bound part and the other into the citrate bound part of the blood plasma. For rats under normal conditions, half of the aluminium is taken up via the citrate channel and the other half via the transferrin channel. For humans older than 50 years, the simulation calculations show better agreement with experimental $^{26}$Al concentrations in the blood plasma for a dominant uptake via the citrate channel. The last finding is not significant.

In box models, the transport between compartments is described by rate constants (inverse time constants). From equilibrium conditions, it is seen that the ratio of the rate constant for forward and backward directions is given by the ratio of the sizes (maximum numbers of available Al places) of the two involved boxes. This means that the rate constant can be written as product of a rate parameter and the size of the final compartment. Since humans and rats are described by similar time constants, the sizes which enter the rate constants have been normalized to the plasma volume $V_P$.

The main excretion of aluminium takes place from the ultrafiltrable part PT of the citrate bound aluminium of the blood plasma via the kidneys into the urine. A minor excretion channel exists from transferrin bound Al of the plasma (PT) via the liver into the intestinal tract. Renal Al clearances $C_R$(Al) are determined by the urine excretion time $T_U$ and the ultrafiltrable part PC/(PT+PC) of Al in the plasma, $C_R(\mathrm{Al}) = V_P/[T_U(\mathrm{PT+PC})/\mathrm{PC}]$.

## References

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