



From isotope geochemistry to isotope biochemistry: A case study on the use of Calcium isotopes in human urine as an indicator of bone demineralization

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Calcium is an essential element for the human body and plays an important role for the skeleton formation, blood coagulation, nerve impulse transmission and muscle contraction. Due to its important role Ca concentrations are kept within small limits in the extracellular space. Ca homeostasis is maintained by three organs, the gastrointestinal tract (input of Ca), the skeleton (store of Ca) and the kidney (output of Ca). Physiological ageing processes and many chronic diseases are associated with disturbances of the calcium homeostasis.

In order to test the use of Ca isotopic composition of urine as an indicator for bone demineralization and generally for a pathological perturbation of the Ca metabolism In a first set of experiments we analyzed $\delta^{44/40}\text{Ca}$ ratios of urine samples from a healthy boy (4 years) and an elderly woman (63 years) burdened with diagnosed osteoporosis. During bone formation Ca isotopes are supposed to become fractionated as the light isotope (^{40}Ca) is preferentially incorporated into the bone. Whereas during bone demineralization the stored isotopically light Ca is released into the blood without any fractionation. Thus any disturbance of the Ca homeostasis should be reflected in by a difference in the $\delta^{44/40}\text{Ca}$. In order to test this hypothesis we collected three urine samples per day (in the morning, at noon and in the evening) over a period of about 5 days from each subject. The $\delta^{44/40}\text{Ca}$ results show huge variations with values ranging from +0.17 permill up to +2.87 permill (relative to SRM915a). As expected we found a clear difference of about 1.12 permill between the mean $\delta^{44/40}\text{Ca}$ values of the healthy boy ($\delta^{44/40}\text{Ca} = +1.46$ permill) and the elderly woman ($\delta^{44/40}\text{Ca} = +0.34$ permill). The measured $\delta^{44/40}\text{Ca}$ values are much higher than expected from the regular diet (~ -1.0 permill). Presumably, the observed fractionation mainly occurs in the

kidney while the formation of urine. This is because during filtration more than 98% of the Ca of the primary urine is reabsorbed (Hoenderop et al. 2005) preferring the light ^{40}Ca whereas the excreted urine is enriched in ^{44}Ca . Alternatively to our hypothesis that disturbances of the Ca balance may account for the observed isotope variations, a higher efficiency of Ca reabsorption in the kidney of the young boy compared to the elderly woman may also account for the observed difference.

References:

Hoenderop J. G. J., Nilius B., and Bindels R. J. M. (2005) *Phys. Rev.* 85, 373–422.