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Fractionation of stable chlorine isotopes in the kidneys of mice

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Anion transport across cell membranes is crucial for a variety of physiological functions, including control of electrical excitability of muscles and nerves, salt and water homeostasis, and regulation of cell volume or acidification. Pathogenic mutations in genes encoding chloride ion (Cl^-) transporters lead to a wide range of pathologies including myotonia, cystic fibrosis, renal salt loss in Bartter's, Gitelman's or HELIX syndromes, kidney stones, deafness and osteopetrosis. We are carrying out a pilot study of chloride isotope fractionation ($^{37}Cl/^{35}Cl$) in plasma and urine from mice in order to understand if chloride stable isotopes can be used to better understand their (patho)physiology. Starting from a 200 µl fluid sample, we are able to measure the $d^{37}Cl$ of chloride dissolved in urine or plasma with a sensitivity below 4 µmoles of Cl^- and an accuracy of ± 0.03 ‰ (1sd). Five female and five male mice were fed under standard conditions (food and drink ad libitum). For each of the 10 mice, chloride isotope ratios were measured on 24h-collected urine and on plasma samples at the end of the experiment. We found that urinary chloride is systematically enriched in ^{37}Cl relative to plasma ($d^{37}Cl$ = -0.18 ± 0.05 ‰, sd,n = 10). We take this to indicate that renal reabsorption of chloride favors the light ^{35}Cl isotope. Further, we observed that male mice have plasma chloride ($d^{37}Cl$ = -0.74 ± 0.02 ‰, 1sd, n = 5) systematically more depleted in ^{37}Cl than female mice ($d^{37}Cl$ = -0.62 ± 0.03 ‰, 1 sd, n = 5). Chloride isotope fractionation is thus sex-specific, which may be related to known sex differences in the chloride transport system all along the nephron. This observation paves the way for further investigations in order to identifies chloride transporters that contribute the most to chloride fractionation.