Intracellular Pu Decorporation in Rat by Different DTPA Formulations

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Cellular internalisation of DTPA appears negligible. Thus, a fast urinary excretion of Pu-DTPA is observed after treatments, but a slow excretion also occurs, explained by Pu-DTPA retention within the interstitium (2.5% of Pu-DTPA, half-life 1 week). One day after 14C-DTPA i.v., 1-2% of the activity was retained in perfused soft tissues, demonstrating its cellular internalisation, whereas blood DTPA was 0.025%. Encapsulation of DTPA has been proposed to improve its cellular internalisation, and a nearly total liver decorporation was obtained using stealth® 100 nm-liposomes. This study estimates intracellular decorporation of Pu by different DTPA formulations. First, a biokinetic study was performed after Pu-DTPA i.v., to help interpretation of decorporation data. About 99% of Pu was excreted via urines for the first 3 days, followed by residual excretion. Similar Pu activities were measured in skeleton, liver, kidneys and urine of day 7 (0.1%). These values, quite different than those measured after Pu-citrate i.v., demonstrated the great stability of Pu-DTPA, in extra and intracellular environments. When DTPA solutions were given i.v., 1 hour after Pu-citrate i.v., both fast and slow excretion (half-life 3-4 days) of Pu-DTPA were observed. The ratio between fast and slow excretions increased with DTPA dosage and, at similar dosage, this ratio was much lower after pulmonary insufflation of dry DTPA powder than after i.v.. Therefore, fast excretion depends on DTPA concentration in blood, whereas slow excretion, associated with intracellular DTPA, depends on total DTPA administered. This was confirmed after specific liver or lung contamination. Then, most of the urinary decorporation involved a slow process observed for 1 month. Moreover, half-life of slow excretion appeared to vary depending on tissues. In a last experiment, a treatment was performed 1 day before Pu-citrate i.v. (30 and 300μmol.kg-1). A decorporation similar to a standard treatment (30μmol.kg-1, i.v. at+1h) was observed for the highest dosage ($\sim$50%), whereas a 25 % decorporation was obtained for the lowest dosage. Altogether, these results underline the importance of intracellular DTPA in the decorporation process which will be discuss in terms of modelling and radioprotection.

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