

Treatment of PuO₂ lung contamination using a dry powder formulation of DTPA

**O. Grémy¹, N. Tsapis², Q. Chau¹, F. Tourdes¹,
D. Renault¹, J.-L. Poncy¹, A. Van der Meeren¹**

¹CEA/DSV/IRCM/, Laboratory of Radiotoxicology, Bruyères le Chatel, 91297 Arpajon cedex-France

²Univ. Paris-Sud, CNRS UMR 8612, Physico-chimie-Pharmacotechnie-Biopharmacie, F-92296,
Châtenay-Malabry, France

e-mail: anne.vandermeeren@cea.fr

Lung contamination can result from accidental release of transuranic actinides such as Pu and Am. The therapeutic approach to reduce the effective radiation dose is to remove the α -emitting radionuclides from the body by promoting their decorporation. Diethylene triamine pentaacetic acid (DTPA) is the most commonly used treatment of internal contamination by plutonium, and represents the only available ligand for *in vivo* chelation of this actinide. The present work investigates the decorporation efficacy of a dry powder formulation of CaNa₃-DTPA on a pulmonary contamination with the insoluble physicochemical form of Pu, PuO₂. Adult male Sprague-Dawley rats were exposed to PuO₂ aerosols generated from an industrial powder (47.3% ²⁴¹Am of α activity equivalent to 3.3% of mass). Two hours after contamination, rats received an intratracheal insufflation of CaNa₃-DTPA (18.2 \pm 1.4 μ mol DTPA/kg) formulated into porous particles of a dry powder. Urines were collected daily for 7 days. Initial lung deposit (ILD) was determined by x-ray spectrometry counting 7 days post-inhalation. Fourteen days post-inhalation, rats were euthanized, liver, femurs and lungs were collected and broncho alveolar lavages (BAL) were carried out. The total α activity of samples was measured by liquid scintillation counting, in BAL, BAL cells and BAL fluids, isolated from alveolar immune cells by centrifugation.

The ILDs of contaminated untreated rats and contaminated DTPA-treated rats were respectively 15.6 \pm 2.3 kBq and 13.6 \pm 2.3 kBq. The cumulative activity urinary excretion over 7 days was 7-fold higher after DTPA administration as compared to untreated rats, and represented approximately 7% of the ILD for DTPA-treated animals. In the main retention tissues, liver and skeleton, the deposit of activity in DTPA-treated rats was less than 5% of the one of untreated animals (1.13% of ILD in liver of untreated rats vs 0.05% in DTPA-treated rats; 2.75% in skeleton vs 0.1%).

Distribution of α activity within lungs of treated or untreated rats was determined. Alpha activity recovered in the BAL fluids from DTPA-treated rats was 7.3-times lower than in BAL fluids from non-treated animals. However, although the activity associated with BAL cells (mainly alveolar macrophages) tended to decrease, the difference between treated and non-treated animals remained non significant, suggesting that pulmonary surfactant and/or serum-derived proteins represented the major accessible lung compartment for DTPA decorporation. However, no significant decrease in whole lung activity was obtained.

Our study shows the efficacy of a dry DTPA powder administered directly to the lungs on Pu decorporation. By inhibiting actinide deposit in skeleton and liver, a limitation of the dose delivered to these tissues is expected, thus limiting the risks for radiation-induced diseases. In addition, DTPA treatment modified distribution of activity within lungs. It is generally admitted that soluble compounds leading to more homogeneous irradiation of the lungs cause higher lung damage than insoluble forms, trapped in macrophages. The decorporation of the most soluble fraction of radionuclide present in the acellular fraction of BAL, could thus also limit lung damage. Finally, direct pulmonary administration of DTPA offers the potential for needle-free treatment, which would be convenient in case of several contaminated people at the same time as a first pass emergency treatment.