Improving the Decorporation Efficacy of DTPA and HOPO Using Nanoparticles

PROJECT TEAM:

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OBJECTIVE

Improve decorporation efficacy of sequestering agents currently employed to remove accidentally inhaled spent nuclear reactor fuel.

- Significant health effects to humans when they ingest/inhale radioactive materials becomes lodged in the lungs or other organs and continues to irradiate the body until the material is excreted or decays.
- Decorporating/chelating agents accelerate the removal of these particles from the body to significantly reduce the radiation dose experienced by the organs.
- Chelating agents bind and sequester radioactive materials that get into the body. Once bound to a radioactive material, the chelating agent is then excreted from the body in the urine. These drugs have great potential to be used to remove inhaled insoluble materials from the lungs.
- The aim of this project is to mitigate toxic effects of human contamination with radioactive heavy metals (i.e., Pu, U) using biomimetic synthetic chelators having extremely high affinity and specificity for targeted radionuclides.
- Diethylene triaminepentaacetate (DTPA-Zn or DTP-Ca) has been used to decorporate internal radionuclide contaminations (Pu, Am etc.) in nuclear industry, however, frequent (daily) dosage is required as a result of its short retention time in the body.
- In addition, a new “drug”, 3,4,3-LI(1,2-HOPO), has been developed by the University of Berkeley (in partnership with partnered with Bayer Pharmaceuticals) and is under FDA pre-clinical review.
- In this project, new formulations of HOPO and DTPA will be encapsulated with polymeric particles and tested for potentially enhanced efficacy for decorporation of internal alpha contamination using an animal model (rat)

Experimental design

Test Groups: 1) DTPA 2) Chitosan-DTPA nanoparticles 3) 3,4,3-LI (1,2 HOPO) 4) Chitosan-HOPO nanoparticles

- Prepare drug formulations for testing.
- Perform pilot studies to examine the toxicological effects of the novel drug formulation with repeat dosing by intra-nasal dosing over a week long period.
- Contaminate animals (study groups and the control groups) with the fuel particle samples via intra-tracheal instillation.

- Examine clearance of fuel particles from the lungs by collecting daily urine samples from the animals and lung tissue samples at conclusion of the experiments in the study groups and control groups and measuring target radionuclides in the urine and lung samples
- Compare daily excreted radionuclides from the rats and evaluating the decorporation efficiency.

Expected outcomes

Development of novel agents to improve the decorporation efficiency of treatments for internalized radionuclides /actinide s following internal exposures

Progress/results

1. Chitosan (nanoparticle) and DTPA and HOPO formulations prepared: (Health Canada and Carleton University)
2. Completed pilot studies to examine the toxicological effects of the novel drug formulations
    - Drug formulations were given per day for 5 days (intranasal delivery). Tc-99m was mixed with the drugs on day of euthanasia.
    - Lung pathology results showed presence of only slight to moderate irritation for all drug formulations;
    - Delivery efficiency of drug formulations found to be adequate: 20 to 30 %, depending on drug tested.
3. Collection, isotopic characterization and size fractionation of irradiated UO2 fuel particles

Future work fy 2019/20

Perform main animal decorporation study; documentation of results in scientific manuscript