

Peer Review

Review of: "Chelation Therapy for Rare Earth Element Toxicity: Current Evidence, Challenges, and Future Directions"

Martin Hruby¹¹. Institute of Macromolecular Chemistry, Prague, Czech Republic

The review is very nicely written on a very actual topic and is very interesting to read. I recommend the review to be published after the following points are addressed:

1. The highly society-relevant discussion concerning chelator-assisted detoxication of rare earth element radionuclides (REE) from nuclear fission fallout (especially relevant for ¹⁴¹-Ce, ¹⁴⁴-Ce/¹⁴⁴-Pr, and ¹⁴⁷-Pm, being most prominent in the „late“ fallout radiotoxicity several years after the nuclear fission bomb detonation/reactor failure event after short-lived radionuclides such as ¹³¹-I have decayed) should be included. In fact, one of the major fission products, ⁹⁰-Sr, also decays via its radiotoxic ⁹⁰-Y radionuclide daughter.
2. Anticoagulant activity of lanthanides, given by the antagonistic effect of lanthanides on calcium-dependent steps in the blood clotting cascade, is known for decades and is very typical for these elements; please add more discussion concerning this.
3. Table 2: Please add tetrathiomolybdate as another chelating agent used for the treatment of metal overload; it is used for the therapy of Wilson's disease (i.e., copper overload).
4. The inability of free DTPA to penetrate into the cells is correctly discussed. However, there exists a strategy widely used in cell biology to overcome the poor permeability of cell membranes to hydrophilic chelators: the administration of suitable esters that freely penetrate the cell membranes, and inside cells, cell esterases hydrolyze these esters, releasing the free metal chelator in active form. E.g., for calcium, BAPTA-AM (1,2-bis(2-aminophenoxy)ethane-N,N',N'-tetraacetic acid

tetrakis(acetoxymethyl ester)) and Calcein-AM (Calcein O,O'-diacetate tetrakis(acetoxymethyl ester) are such examples.

Declarations

Potential competing interests: No potential competing interests to declare.