Glenn T. Seaborg Center Seminar

The Quest for Therapeutic Actinide Chelators

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Chelation therapy has been shown to reduce acute radiation damage and chemical toxicity of the actinides and to reduce the severity of late radiation effects by reducing tumor incidence, prolonging tumor latency, and increasing life expectancy. This talk traces the historical time line of the development of actinide chelating agents from its beginnings in the mid 1940s. The subject is brought up-to-date with the inclusion of unpublished data for *in vivo* chelation of Pu(IV), U(VI) and neptunium. Promising highly selective agents have been developed in recent years for *in vivo* chelation of Pu(IV) containing hydroxypyridinoate [1,2-HOPO or Me-3,2-HOPO] metal binding units. Most of these agents also chelate Am(III) and Np(IV). The most efficient and/or facile of the effective ligands appear to be octadentate 3,4,3-(1,2-HOPO) and tetradentate 5-LIO(Me-3,2-HOPO). Low toxicity tetradentate linear ligands with pentylene or diethylether backbone containing catecholoate [CAM(S), CAM(C)], or hydroxypyridinonate [Me-3,2-HOPO] binding groups, have been identified as suitable agents for *in vivo* chelation of U(VI).

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