Systematic investigation of chelator-radiometals compounds by quantum chemical methods and molecular MD simulations

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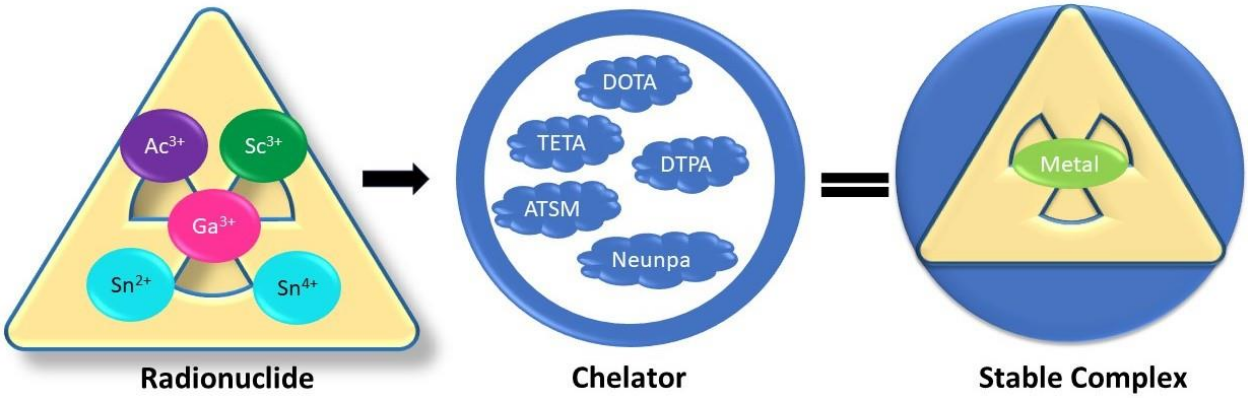
The development of stable radiometal complexes (i.e., a chelator moiety carrying a radionuclide) and the design of chelating systems are crucial aspects in the advancement of radiopharmaceuticals for diagnostic and therapeutic purposes in nuclear medicine (theranostics) [1,4]. Currently, there is no single chelator that is universally effective for all metals or radioconjugates. [2,3,4].



Different radioactive metals may have varying coordination numbers while interacting with the same chelator. The stability of chelators and metal complex structures is affected by the force constant and the coordination numbers [3]. We performed a systematic investigation on different chelator-radiometal compounds taken from the Cambridge Structure Database (CSD). We used quantum mechanics methods at the Density Functional Theory level and generated the General Amber Force Field parameters to perform microsecond-long molecular dynamics simulations in water solution. By considering different chelators (about 30) and radiometals (about 25), we could compare different physical-chemical properties of the chelator radiometal couples, such as selectivity, stability and coordination geometries.

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