Late stage organic synthesis radiolabelling with $^{73/75}Se$ by using selenium acceptor chemistry

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Positron emission tomography (PET) is a powerful nuclear medicine imaging technique that enables the visualization of metabolic and physiological processes at a molecular level. Selenium-73 (^{73}Se) is a positron-emitting radionuclide that has significant potential for use in PET imaging methods. Unlike commonly used isotopes such as carbon-11 and fluorine-18, selenium-73 (^{73}Se) has a longer half-life ($\tau_{1/2}$ = 7.1 hours), enabling the visualization of biomolecules with slow pharmacokinetics, such as antibodies and peptides. Its longer half-life also improves the signal-to-background ratio, and its low positron energy ensures high spatial resolution. Furthermore, ^{73}Se forms covalent bonds with carbon, nitrogen and oxygen, eliminating the need for chelating complexes to achieve high in vivo stability of tracers, unlike radiometals. These complexes significantly affect the structure of small biomolecules and are therefore limited in neuroscience applications due to their inability to cross the blood–brain barrier.

Selenium-75 (^{75}Se) is another radioactive isotope with a half-life of 120 days. Although incompatible with tomographic methods, it shares chemical properties with ^{73}Se, is relatively easy to produce, and is ideal for the development and optimization of chemical procedures, as well as for preclinical studies of selenium-based radiotracers.

Despite its numerous advantages, selenium-labelled radiotracers are not yet used in clinical practice due to the inefficient, time-consuming and suboptimal chemical procedures involved, which have hindered the medical application of this isotope.

This study investigates the reaction between radioactive selenium and aromatic ortho-diamines, which leads to the formation of heterocyclic compounds known as selendiazoles. A rapid and efficient procedure for extracting selenium from its matrix was developed based on this reaction. Furthermore, the potential of using aromatic ortho-diamines as selenium acceptor groups was explored. To validate the concept of radiolabelling small molecules and peptides, the direct and indirect radiolabelling pathways of the peptidomimetic compound Glu-C(O)-Lys were studied. This compound targets prostate-specific membrane antigen (PSMA), a prostate cancer biomarker.

The results address key challenges in selenium radiochemistry and pave the way for the development of clinically relevant radiotracers in the near future, thereby expanding the capabilities of positron emission tomography.