DESIGN OF THERANOSTIC RADIOPHARMACEUTICALS FOR ENHANCED DRUG DELIVERY

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In the rapidly evolving field of nuclear medicine, the development of targeted radiopharmaceuticals has become a cornerstone strategy for enhancing both diagnostic accuracy and therapeutic efficacy in oncology. Technetium-99m (^{99m}Tc), a versatile gamma-emitting radionuclide, has emerged as a pivotal element in this domain due to its ideal nuclear properties and widespread availability. In the field of nuclear medicine, recent advancements have focused on the development of theranostic radiopharmaceuticals that incorporate both therapeutic and imaging modalities. This innovative approach has garnered substantial interest among researchers and clinicians alike, as it promises to revolutionize both diagnostic and therapeutic applications in nuclear medicine. In the present contribution we utilized advanced computational methodologies to engineer sophisticated protein-based delivery systems for doxorubicin with nuclear imaging capabilities. Specifically, the present study explores the potential of human serum albumin (HSA) as a nanocarrier for doxorubicin (DOX) with radionuclide imaging modalities, focusing on the interaction between HSA and various ^{99m}Tc pharmaceuticals. At the first step of the study we compared the binding affinities of different ^{99m}Tc complexes (TCC) to HSA. Molecular docking studies revealed that most TCCs bind to domain I of HSA, specifically in the region between LEU115 and LYS190. This common binding site suggests a potential competitive binding scenario among these TCCs, which could impact their pharmacokinetics when administered together. Interestingly, TcHYN, which contains a specific peptide sequence, demonstrated the highest affinity for HSA and bound to domain III, partially overlapping with Sudlow site II. This finding highlights the potential of peptide conjugation as a strategy to enhance the albumin-binding properties of radiopharmaceuticals, potentially improving their in vivo stability and target tissue accumulation. Further investigation employed multiple ligand docking to explore ternary HSA-TCC-DOX systems. The results showed that when the binding sites for TCC and DOX do not overlap, DOX binds to a specific region in domain I of HSA (site HSA113-186). However, when TCC and DOX binding sites overlap, DOX binds to an alternative site containing residues from ASP107 to GLN459. The results of the study demonstrate the suitability of albumin as a nanocarrier for DOX with radionuclide imaging capabilities. The findings provide valuable insights into the interactions between HSA, various ^{99m}Tc radiopharmaceuticals, and DOX, which can guide the development of more effective radiopharmaceutical delivery systems. These advancements have the potential to enhance both diagnostic accuracy and therapeutic efficacy in nuclear medicine applications, ultimately improving patient care and treatment outcomes.

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