COMPLEXITIES OF THE INTERACTION OF Ni^{II}, Pd^{II} AND Pt^{II} PYRROLE-IMINE CHELATES WITH HUMAN SERUM ALBUMIN

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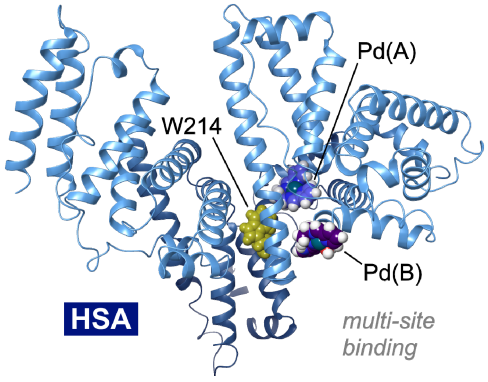
Human serum albumin (HSA) efficiently transports drugs *in vivo*: most are organic. Here, HSA binding affinity and site specificity are shown to depend on the identity of the d^8 metal ion in Ni^{II}, Pd^{II} and Pt^{II} chelates of the bis(pyrrole-imine) ligand H_2PrPyrr [1]. Fluorescence quenching data for native and probe-bound HSA showed sites close to Trp-214 (subdomain IIA) are targeted. The Stern-Volmer constants, K_{SV}, ranged from 10^4 M^{-1} to 10^5 M^{-1} while the affinity constants, K_a, ranged from ~3.5×10^3 M^{-1} to ~1×10^6 M^{-1} at 37 °C, following the order Pd(PrPyrr) > Pt(PrPyrr) > Ni(PrPyrr) > H_2PrPyrr. Ligand uptake is enthalpically driven, hinging mainly on London dispersion forces. Induced CD spectra for the protein-bound ligands could be simulated by hybrid QM:MM TD-DFT methods, proving that the metal chelates neither decompose nor demetallate after uptake by HSA. Transport and delivery of the metal chelates by HSA *in vivo* could therefore be feasible.



[1] Sookai, Sheldon, and Orde Q. Munro. "Complexities of the Interaction of Ni^{II}, Pd^{II} and Pt^{II} Pyrrole-Imine Chelates with Human Serum Albumin." *ChemistryEurope*, June 2023, p. e202300012. *DOI.org (Crossref)*, https://doi.org/10.1002/ceur.202300012.