

Interactions of Organometallic Galectin Ligands with Serum Albumin Using Electrochemical Approaches

Marek Zelinka^{1,†}, Lucie Žaloudková¹, Peter Šebest¹, Hana Černocká¹, Vojtěch Hamala², Jindřich Karban², Veronika Ostatná¹

¹Institute of Biophysics of the CAS, v. v. i., Královopolská 135, 612 00 Brno, Czech Republic

²Institute of Chemical Process Fundamentals of the CAS, v. v. i., Rozvojová 1/135, 165 00 Praha, Czech Republic

† corresponding author's email: zelinka@ibp.cz

Galectin protein interactions play a crucial role in numerous biological processes, such as cell adhesion, immunosuppression, cell signaling, and, notably, tumor metastasis. Studying these interactions with natural or synthetic ligands is essential for understanding their nature and for the development of potential therapeutics [1].

Electrochemical properties of ferrocene ligands containing one or two ferrocene moieties attached to mono- or disaccharide scaffolds were studied using cyclic voltammetry (CV), AC voltammetry (ACV), and chronopotentiometric stripping analysis (CPS) at hanging mercury drop electrode (HMDE), as well as fluorescence spectroscopy. Their interactions with the electrode surface and bovine serum albumin (BSA) were also investigated. Due to the hydrophobic nature of the ligands, an organic cosolvent was required for effective dissolution. Dimethyl sulfoxide (DMSO) was chosen for this purpose. DMSO can also influence ligand affinity to surfaces and proteins, and this effect was examined in the study.

Monoferrocene ligands, being more hydrophilic, exhibited diffusion-controlled electrode processes, while bisferrocene analogs showed better adsorption onto the surface due to their more hydrophobic character. Dissociation constants for interactions with BSA were determined using fluorescence of tryptophan and tyrosine residues, with the highest affinity observed for the bisferrocene disaccharide (thiodigalactoside). These interactions were also studied using CPS. The influence of DMSO on ligand interactions with the surface and BSA was analyzed using ACV and CPS. Around a potential of -0.5 V, strong adsorption onto the mercury drop was observed, which was more pronounced for biferrrocene ligands and inhibited by increasing concentrations of DMSO. Low DMSO concentrations (up to 1 %) enhanced ligand binding to BSA, while higher concentrations (up to 5 %) significantly reduced this binding.

This work provides insight into the interactions of ferrocene ligands with the mercury drop surface and serum albumin, and demonstrates the influence of an organic cosolvent on interaction affinity. The presented electrochemical methods can serve as simple, fast, and cost-effective techniques for studying these interactions.

Acknowledgments

This work was funded by Czech Science Foundation (GAČR, project no. 23-06115S).

References

- [1] V. Hamala, M. Kurfírt, L. Červenková Šťastná, H. Hujerová, J. Bernášková, K. Parkan, J. Kaminský, N. Habanová, J. Kozák, A. Magdolenová, M. Zavřel, T. Staroňová, V. Ostatná, L. Žaloudková, A. Daňhel, J. Holčáková, P. Voňka, R. Hrstka, J. Karban, Ferrocene- and ruthenium arene-containing glycomimetics as selective inhibitors of human galectin-1 and -3, *Inorg. Chem. Front.* 11 (2024) 7588–7609. <https://doi.org/10.1039/D4QI01555J>.