Interaction study of sugammadex with phytotoxins – new indications for an old antidote?

Eszter KALYDI [1], Fanni SEBÁK [2], Béla FISER [3], Babak MINOFAR [4], Andrea BODOR [2], Milo MALANGA [5], Konstantina YANNAKOPOULOU [6], Szabolcs BÉNI [1]

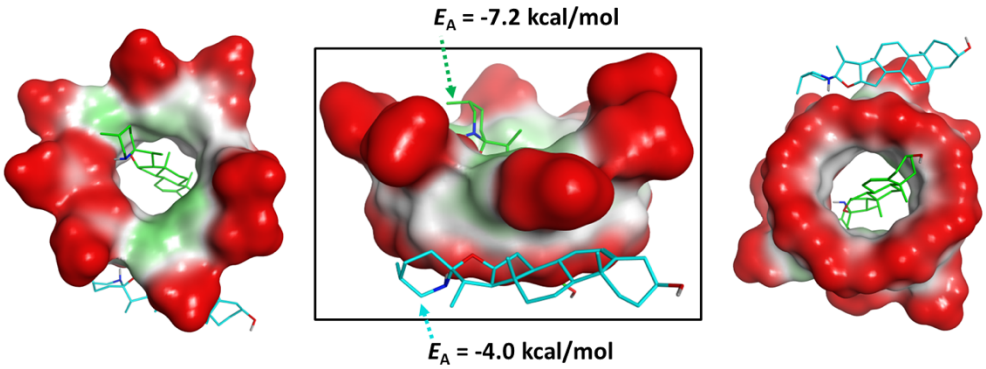
[1] Department of Pharmacognosy, Semmelweis University, Budapest, HUNGARY; [2] Eötvös Loránd University, HUNGARY, [3] University of Miskolc, HUNGARY [4] University of South Bohemia, CZECH REPUBLIC, [5] CarboHyde Zrt., HUNGARY, [6] Institute of Nanoscience and Nanotechnology National Center for Scientific Research, GREECE

kalydi.eszter@phd.semmelweis.hu

Sugammadex (SGM), - an octacarboxylic acid derivative of the native gamma-cyclodextrin - is used in the clinical practice to reverse the neuromuscular blockade of aminosteroid anesthetics. The selective binding is enabled by the formation of a particularly strong host-guest complex, driven by the ionic interactions with the cyclodextrin side chains and the tight fit of the steroid backbone into the cyclodextrin cavity [1].

Toxic glycoalkaloids with similar aminosteroid structures are abundant in nature. Various species of the *Solanaceae* family accumulate toxic glycoalkaloids during ripening. Consumption of part of these species (e.g., immature or sprouted potatoes, berries of *Solanum nigrum*) leads to poisoning, manifesting in gastrointestinal and nervous system symptoms, in extreme cases with fatal outcome. To date, the intoxication is only treated by supportive therapy as there is no known antidote available for these phytotoxins.

Considering the structural similarities between the anesthetics and the toxins of the *Solanaceae* family, we investigated the interactions of SGM with two phytotoxin aglycons, solasodine and solanidine, aiming to find a potentially applicable antidote. Using NMR spectroscopy, particularly stable host-guest complexes were identified between both solasodine and solanidine and SGM. A slow-exchange system in the NMR timescale was recognized, indicating particularly stable supramolecular binding. Through-space magnetic dipole correlation methods were used to identify the structure of the complexes and computational methods were also performed to support the identified structure.



Bibliographic references:

[1] A. Bom, M. Bradley, K. Cameron, J.K. Clark, J. van Egmond, H. Feilden, E.J. MacLean, A.W. Muir, R. Palin, D.C. Rees, M.-Q. Zhang (2002), Angew. Chemie Int. Ed. 41 265-270.