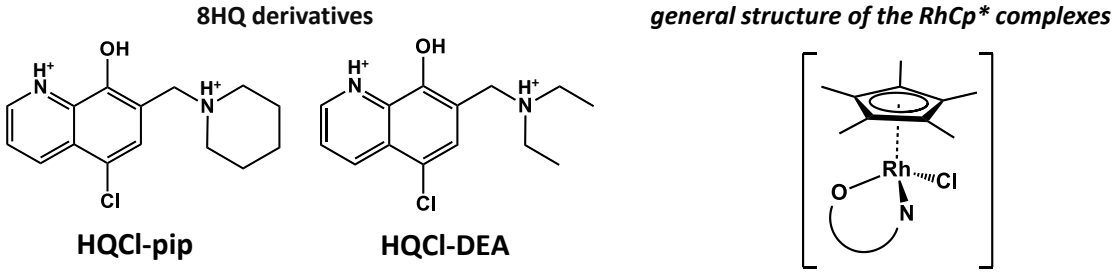
A MULTIDRUG RESISTANCE SELECTIVE ANTICANCER 8-HYDROXYQUINOLINE DERIVATIVE AND ITS RhCp* COMPLEX

Laura C. Erdei, Éva A. Enyedy, Orsolya Dömötör

Department of Molecular and Analytical Chemistry, University of Szeged, H-6720 Szeged, Dóm tér 7, Hungary
e-mail: erdeilaura21@gmail.com

In the field of developing more effective chemotherapeutic drugs with fewer severe side effects, 8-hydroxyquinoline (8HQ) derivatives are promising compounds. A group of these molecules was found to be selective against multidrug resistant (MDR) cancer cells, which occurs frequently when treating cancer [1]. Furthermore, several studies showed that these molecules form complexes with essential metal ions which is associated with the therapeutic effect [2]. In our research group several 8HQ Mannich base compounds have been developed and tested against MDR cancer cells, including HQCl-pip. Its complexation with half-sandwich Rh(III)(η^5-petamethylcyclopentadienyl)$(H_2O)_3]^{2+}$ (RhCp*) cation (see figure), has actually enhanced, rather than diminished the toxicity on MDR cells; moreover, the complex has better aqueous solubility in comparison to HQCl-pip alone [3].



HQCl-DEA is a close derivative of the former compound showing selective toxicity on MDR cancer cells. Therefore, we found it worth to investigate its behaviour in aqueous solution, complex formation with RhCp* cation and their interaction with human serum albumin. Proton dissociation processes and stability of HQCl-DEA and its RhCp* complex was followed by UV-Vis spectrophotometry and ^{1}H NMR spectroscopy. The same techniques were applied to determine the Cl^-/H_2O exchange constant of the complex. Lipophilicity was determined by *n*-octanol/water partitioning experiments at various pH values and chloride ion concentrations. Albumin binding was investigated by equilibrium dialysis, ultrafiltration, UV-Vis and fluorescence spectroscopies. Based on our results, the complex shows promise as an anticancer agent against MDR.

Acknowledgements
This work was supported by the National Research, Development and Innovation Fund through projects ANN 149481 and TKP2021-EGA-32. We thank Prof. István Szatmári and Dr. Szilárd Tóth for their help in ligand synthesis and cytotoxicity assays, respectively.

References

[1] G. Szakács et al., Nat. Rev. Drug Discovery 5 (2006) 219.
[2] V. F. S. Pape et al., Dalton Trans. 47 (2018) 17032.
[3] T. Pivarcsik et al., Inorg. Chem. 63 (2024) 23983.