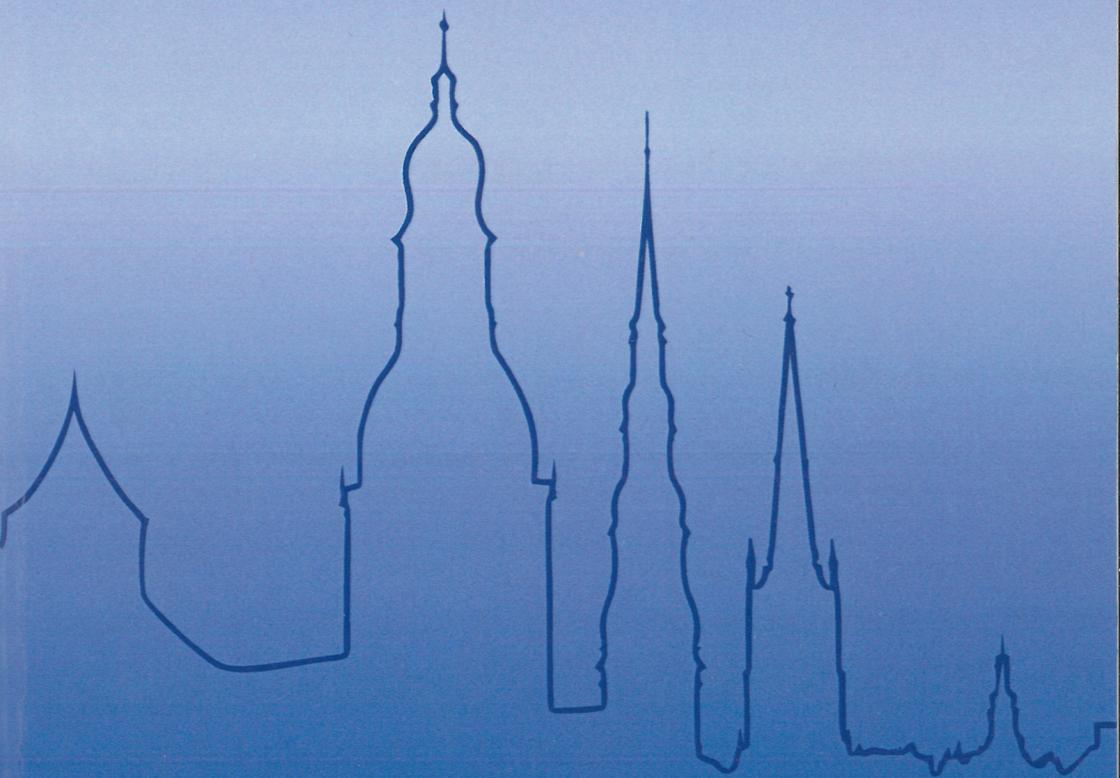




Drug Discovery Conference

August 27-29, 2015, Riga, Latvia



OP13. INHIBITORS OF CARBONIC ANHYDRASES – CHALLENGES OF DESIGN AND SYNTHESIS

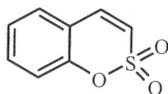
Raivis Žalubovskis,¹ Aiga Grandāne,¹ Jekaterīna Ivanova,¹ Ilona Domračeva,¹
Kaspars Tārs,² Claudiu T. Supuran³

¹ Latvian Institute of Organic Synthesis, Aizkraukles 21, Rīga LV-1006, Latvia; e-mail: raivis@osi.lv; phone: +371 67014826

² Biomedical Research and Study Center, Ratsupites 1, Rīga LV-1067, Latvia

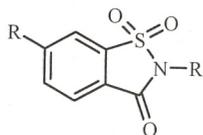
³ NEUROFARBA Department, Section of Pharmacology and Toxicology, Università degli Studi di Firenze, Viale Pieraccini 6, 50139 Florence, Italy

Carbonic anhydrases (CA) are zinc containing enzymes which catalyze reversible hydration and transport of carbon dioxide and, along with other functions, provide pH regulation in cells. Among 15 isoforms of human CA special attention is dedicated to inhibition of tumor associated CA IX and CA XII,¹ where good inhibitory activities and selectivities for series of sulfocoumarin have been recently demonstrated.² We have found interesting design of saccharin derivatives which was driven by protein-inhibitor crystallization experiment.³



Sulfocoumarin

(1,2-Benzoxathiine 2,2-dioxide)



Saccharin

Design and synthesis of derivatives of sulfocoumarin and saccharin will be discussed. Overview of their inhibition of CA and cytotoxicity on tumor cell lines will be presented.

Acknowledgements:



References:

1. Alterio, V.; Di Fiore, A.; D'Ambrosio, K.; Supuran, C. T.; De Simone, G. *Chem. Rev.* 2012, 112, 4421-4468.
2. Tars, K.; Vullo, D.; Kazaks, A.; Leitans, J.; Lends, A.; Grandane, A.; Zalubovskis, R.; Scozzafava, A.; Supuran C.T. *J. Med. Chem.* 2013, 56, 293-300; Grandane, A.; Tanc, M.; Zalubovskis, R.; Supuran, C.T. *Bioorg. Med. Chem.* 2014, 22, 1522-1528; Grandane, A.; Tanc, M.; Zalubovskis, R.; Supuran, C.T. *Bioorg. Med. Chem. Lett.* 2014, 24, 1256-1260.
3. Ivanova, J.; Leitans, J.; Tanc, M.; Kazaks, A.; Zalubovskis, R.; Supuran, C.T.; Tars, K. *Chem. Commun.* 2015, 51, 7108-7111.