Abstract

My PhD research plan concerns the exploration of the structural requirements determining TRPM8 modulation. We prepared a series of N-substituted tryptamines and identified two compounds acting, respectively, as an activator (21) or an inhibitor (12) of calcium influx in HEK293 cells. To develop more potent and selective derivatives we designed and synthetized new series of potential tetrahydroisoquinoline- and tetrahydro-β-carboline-based TRPM8 modulators. The synthetic approach used for the preparation of these compounds led to indole-fused aminoacetal derivatives. Optimization of reaction conditions allow us to obtain ring-fused aminals, which could be useful for preparing analogues of biologically active natural and synthetic products.

At the same time I worked on the synthesis of potential varicella zoster virus replication inhibitors: tryptamine derivative 17a was found to have a selective activity against this herpesvirus family member. A second part of my PhD was dedicated to the identification of small heterocyclic compounds as GRK2 inhibitors.

Lastly, I spent an abroad semester in the University of Graz, where I collaborated to the development of a continuous flow difluoromethylation protocol employing fluoroform as reagent. The protocol is applicable for the direct Cα-difluoromethylation of protected α-amino acids, and enables a highly atom efficient synthesis of the active pharmaceutical ingredient eflornithine.