Summary
Charles University in Prague, Faculty of Pharmacy in Hradec Králové, Department of Pharmacology and Toxicology, Czech Republic
Performed at: University of Bonn, Pharmaceutical Institute, Department of Pharmaceutical Chemistry, Germany
Candidate: Irena Krpelíková
Supervisors: Prof. Dr. Christa Elisabeth Müller
PharmDr. Marie Vopršalová, CSc.

Adenosine, a local modulator, acts in many diverse biological processes. Its effects are mediated through adenosine receptors (ARs). Four types of ARs have been described, A₁, A₂A, A₂B and A₃, which belong to the superfamily of G protein-coupled receptors. AR ligands are being developed as new drugs.
This thesis deals with the study of a novel series of [1,2,4]triazolo[4,3-a]quinoxalines and related compounds as potential adenosine receptor antagonists.
The presented results were obtained using radioligand binding assays.
Series of quinoxalinones and tetrazoloquinoxalines exhibit significant selectivity for human (h) A₃ ARs but their affinity is relatively low for tetrazoloquinoxalines and moderate for quinoxalinones.
Triazoloquinoxalines comprise the largest group of this series. Generally, the R₁ substituent determines the affinity, while the R₄ substituent confers the selectivity. Compounds without any R₄ substituent are not active, conversely compounds with bulky substituents with a lipophilic chain (C₃) are the most potent ones. N-alkyl-(C₂-C₃) substituted pyrrol-2-yl at position 4 dramatically decreases affinity but combination with phenylpropyl at position 1 gives very promising and selective ligands at rat (r) A₁ ARs. These are N4-ethyl-pyrrol-2-yl-1-phenylpropyl[1,2,4]triazolo[4,3-a]quinoxaline (Ki at rA₁ = 4.80 nM) and N4-propyl-pyrrol-2-yl-1-phenylpropyl[1,2,4]triazolo[4,3-a]quinoxaline (Ki at rA₁ = 15.2 nM). Another potent and hA₃ AR selective compound is N4-methyl-pyrrol-3-yl-1-benzyl[1,2,4]triazolo[4,3-a]quinoxaline (Ki at hA₃ = 5.91 nM).
Key words: adenosine receptors, [1,2,4]triazolo[4,3-a]quinoxalines, radioligand binding assays, structure-activity relationships