

Abstract

Charles University

Faculty of Pharmacy in Hradec Králové

Department of pharmacology and toxicology

Student: Daulet Balmagambetov

Supervisors: Prof. Dr. Christa Elisabeth Müller

Dr. Aliaa Abdelrahman

Mgr. Lucie Hyršová

Title of diploma thesis: Pharmacological characterization of novel P2X3 receptor's ligands.

The P2X3 receptor takes a part in transferring painful signals through neuronal and non – neuronal cells. The agonist of the receptor, ATP, is released from afferent neurons or from damaged cells or from non–neuronal peripheral tissue by stimuli through various mechanisms including active transport. Before ATP is being degraded, it may activate P2X3 receptors at nociceptive cells endings and stimulate pain pathway. SP2X3 receptor antagonists may therefore be useful for the treatment of severe pain, e.g. in cancer or in chronic pain disorders. Therefore, completely new allosteric antagonists based on a screening hit were synthesized and tested in vitro at the slowly desensitizing P2X3-S15V receptor mutant expressed in human astrocytoma 1321N1 cells. Some of the new compounds have shown promising activity.