Abstract

This diploma thesis deals with preparation of modified ligands of mu, delta and kappa opioid receptors, following up on the author’s bachelor’s thesis. The main goal of the submitted thesis is ligand tethering at an appropriate position using oligoethylene glycol linkers, to enable their use in the innovative iBodies concept.

Ligands chosen for modifications were: naltrexone (μ-opioid receptor), naltrindole (δ-opioid receptor) and nalfurafine (κ-opioid receptor). Naltrexone was modified, according to the bachelor’s thesis results, at the C-6 position with linker attachment via ether and amide. At the same time, the influence of the configuration at the newly formed C-6 stereogenic center on biological activity was studied. In case of naltrindole, access through indole nitrogen was chosen based on the information in literature. Nalfurafine was modified on the furane fragment.

Series of fluorescently labeled ligands were prepared. Attachment of the fluorescent tag allowed us to study the affinity and selectivity of these modified ligands. Based on the results, ligands for development of DIANA method and for preparation of synthetic iBodies were synthesised.

Key words: naltrexone, receptor, conjugate, opioid receptor

1 M. Hadzima. Fluorescenčně značené ligandy μ-opioidních receptorů, 2016.