18th International Conference on
PHARMACEUTICS & NOVEL DRUG DELIVERY SYSTEMS
May 27-28, 2019 Istanbul, Turkey

Development of novel therapeutic molecules for targeting multiple G protein coupled receptors (GPCRs) as anti-Parkinson's agents

Essam Hamied Ahmed Hanashalshahaby, Ozge Sensoy and Mustafa Guzel
Medipol Remer Regenerative And Restorative Medicine Research Center, Turkey

Background & Aim: Parkinsons Disease (PD) is a long-term degenerative disorder of the central nervous system that mainly affects the motor system. It is caused by the destruction of dopamine cells in the striatum region of the brain. The main approach in treatment of the disease is to increase the dopaminergic effect. However, it has been shown that simultaneous binding of Adenosine 2A receptor (A2AR) agonist and antagonist to the tetramer, which is the dominant oligomer formed by A2AR and D2R in the striatum, can increase D2R signalling more than that exerted by antagonist alone. These findings suggest that heterobivalent ligands might be used for this purpose. They can provide opportunity of using lower dose of L-dopa than being currently used for the therapy of the disease. Therefore, the risk of onset of motor complications such as motor fluctuations and dyskinesia might be alleviated1. This study has been aimed to synthesize novel heterobivalent ligands consisting of the A2AR antagonist/ A2AR agonist that are targeting the heterotetramer (A2AR - A2AR homodimer) structure as shown in Figure1. Synthesized therapeutic molecules are expected to reduce the side effects expected by administration of L-dopa alone via preventing antagonistic effect of A2AR on D2R, thus treating Parkinson's disease.

Method and Results: The pharmacophore groups of the heterobivalent ligands have been developed by combining certain parts of A2AR antagonist (istradefylline) and A2AR agonist (CGS-21680). The synthesis strategy of one of the developed heterobivalent ligands has been investigated as shown in Scheme1. A2AR antagonist (istradefylline) and A2AR agonist (CGS-21680) were synthesized according to the literature reports2,3 with some modification. We will investigate in vitro studies as well as blood brain barrier cell penetration studies of these novel heterobivalent laigands.

Biography

Essam Hamied Ahmed Hanashalshahaby is a Member in the Staff at Chemistry Department, Faculty of Education, Sana'a University. He has completed his PhD in the field of Synthetic Organic Chemistry (Synthesis of Biologically Active Heterocyclic Compounds Using Ketonic Mannich Bases) at Faculty of Science, Hacettepe University. He has worked as a postdoctoral researcher (Bioactive Secondary Metabolites from Marine-Derived Fungi) at Pharmacognosy Department, Faculty of Pharmacy, Ankara University. He is curretly working as a Postdoctoral Researcher in the field of Drug synthesis at Molecular Discovery and Development of Biologically Active Compounds Laboratory, Regenerative and Restorative Medicine Research Center (REMER), Istanbul Medipol University.