[MS25-P22] The Crystal Structure of Arylsulphonamide Derivatives - Novel Dopamine D2 Receptor Antagonists

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The dopamine system in organism plays an important role in the regulation of many vital functions controlled by the Central Nervous System (CNS), including: locomotion, cognition, attention, emotion and reward system [1]. Dysfunctions of this system are related to several neurological and psychiatric disorders. Among them most known are: Parkinson's disease, schizophrenia, depression, Tourette's syndrome, ADHD, bipolar disorder and Huntington's disease [2].

Dopamine D2 receptors are biological targets in the treatment of different types of psychosis. The blocking effect of D2 receptor is required for the antipsychotic action, therefore antagonists such as: amisulpride, clozapine or fluphenazine, are currently in a clinical use in treatment of schizophrenia and acute manic phases of bipolar disorder [3].

We are focused on the search of the structure-activity relationship of the new putative drugs based on the single-crystal X-ray analysis. Presented compounds were designed as multireceptor antagonists, acting in CNS [4]. They belong to the chemical group of arylsulphonamides with benzoxazole moiety attached to the piperidine ring. The latter chemical groups are well known fragments of several neuroleptics [5].

Crystal structures of two different arylsulphonamide derivatives in hydrochloride form have been determined. The intermolecular interactions and molecular conformation in chemical environment of the crystal were examined. The receptor affinity assay performed for both compounds shows that one of them (**1**) binds five times more effectively to the D2 receptor comparing to other investigated derivative (**2**). Single molecule of presented structures forms two hydrogen bonds N-H...Cl-, from which one is a charge-assisted hydrogen bond with positive charge localised on protonated piperidine heteroatom. Mentioned interactions create different motives in the crystal. In case of (**1**) centrosymmetric dimers are observed, whereas for (**2**) the zig-zag motive was found along [010] axis. Additionally, several weaker hydrogen bonds with C-H donors and sulphonyl group as an acceptor are recognised, what makes the last mentioned moiety an interesting pharmacophore fragment from the viewpoint of structural analysis.

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