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Influence of the substituent(s) at aromatic ring of arylidene hydantoin and of the length of carbon chain on affinity for $5HT_6$ serotonin receptor in the group of 3,4-dichlorophenylpiperazine derivatives

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Recently serotonin receptors have been the subject of intense research because of their potential role in many neurological disorders. They are family of G-coupled (excluded $5HT_3$ type), seven transmembrane receptors which have many subtypes.

One of them are $5HT_6$ receptors which play role in functions like cognitive impairment, emotionality. Modulation of this type of receptor could be also useful for dementia patients and in AD disease [1, 2]

Studies of these type of receptors have shown that the numerous compounds with affinity to serotonin receptors contain arylpiperazine moiety.

In our recent studies 3,4-dichlorophenylpiperazine derivatives of arylidene hydantoins were obtained. Chemical modifications were focused on introduction of one or two- methoxy substituents at arylidene ring of the lead and different carbon chain (from 3 to 8 atoms of carbons, excluded 4 and 7- carbon chain) between hydantoin and phenylpiperazine.

The new compounds were obtained within four-step synthesis [3]: (1) Knoevenagel condensation, (2) Mitsunobu reaction, (3) N-alkylation under microwave irradiation and (4) conversion of the obtained basic derivatives into the corresponding hydrochloric form.

The new hydantoin derivatives were evaluated on their affinity for $5HT_6$ radioligand binding assay. Ki values in the group of investigated compounds were in the very wide range: 37- 1693nM.

SAR-studies indicated a profitable influence of only one methoxy substituent at arylidene ring. We also noticed that the compounds with longer carbon chain have shown better affinity for $5HT_6$ serotonin receptors.

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