COMPARISON OF E099-25011 AND ITS RIGID OR STERICLY CROWDED ANALOGUES STRUCTURES IN VIEW OF THEIR PHARMACOLOGICAL ACTIVITY

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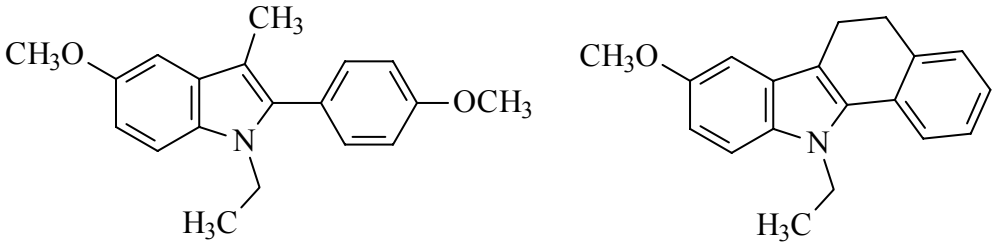
Glutamate is one of the most important excitatory neurotransmitters in the central nervous systems and plays a significant role in the pathophysiology of different neurological and psychiatric diseases [1,2]. This presentation deals with the structural studies (X-ray analysis and theoretical calculation) of the non-competitive GluR5/GluR6 antagonist E099-25011 [1-ethyl-2-(methoxyphenyl)-3-methyl-5-methoxy-indole] found in a HTS and its analogues having rigidly bonded or stericly hindered C-2 pharmacophoric aromatic substituent.



E099-25011

Basic structural and conformational information obtained from X-ray investigations were used to explain the dramatic changes in the glutamate receptor GluR5/6 affinity with the changes of the spatial location of the C-2 substituent. The molecular modeling studies using molecular mechanic method and MNDO-AM1 approximation were undertaken to investigate the conformational preferences of searched derivatives.

[1] S. Bleich, K. Romer, J. Wiltfang, J. Kornhuber, *International Journal of Geriatric Psychiatry*, **2003**, 18 (Suppl. 1), 33.
[2] M. Nedergaard, T. Takano, A. J. Hansen, *Nature Reviews Neuroscience*, **2002**, 9, 748.