Solid phase synthesis of arylpiperazine library as potential 5-HT receptors ligands

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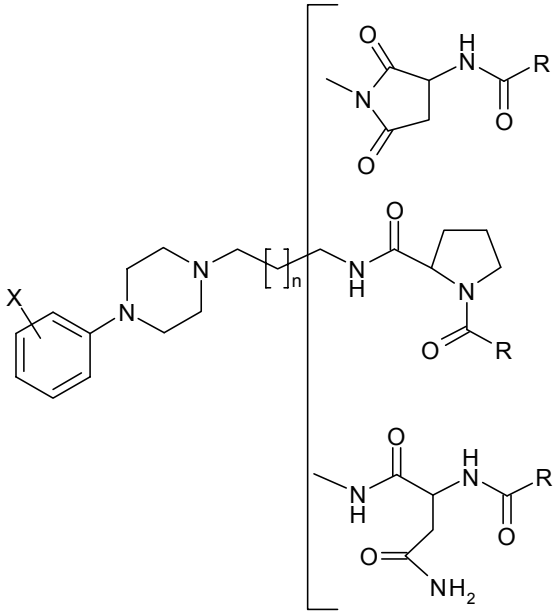
The structure-activity relationship studies in a group of arylpiperazine derivatives showed that the CNS bioactivity, receptor affinity and selectivity depend on the structure of the *N1*-aryl substituents, terminal amide or imide moiety and the length of alkylen spacer (1). We focused our attention on incorporation of the amino acid moieties into the amide pharmacophoric group since its role in the ligand binding mode was still unclear. To get impact of that modification on receptor affinity and selectivity we designed a library of differently substituted arylpiperazine with the amino acids moieties in amide fragment (Figure 1).

Fig. 1



To obtain an easy access to a 100-member focused library we developed and optimized new solid support pathway using BAL linker functionalized Mimotopes Lanterns (2). The sort and combine approach was applied. The analytical data and the results of the primary biological screening of some compounds of the library will be presented.

(1) Lopez-Rodriguez, M.L.; Morcillo, M.J.; Rovat, T.K.; Fernandez, E.; Vicente, B.; Sanaz, A.N.; Hernandez, M.; Orensanz, L. *J. Med. Chem*. **1999**, 42, 36.
(2) Bray, A.M.; Chiefari, D.S.; Valerro, R.M.; Maeji, N.J. *Tetrahedron Lett.* **1995**, 36, 5081.