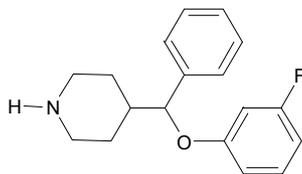


## SYNTHESES AND BINDING STUDIES OF NEW 4-(N-BENZYLAMINO)PIPERIDINE DERIVATIVES AND RELATED COMPOUNDS AS POTENTIAL ANTIDEPRESSANT DRUGS WITH DUAL AFFINITY FOR SEROTONIN AND NOREPINEPHRINE TRANSPORTERS

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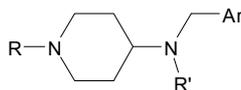
As a result of our research program to obtain new, efficient and fast-acting antidepressant drugs [1], F-98214-TA was found to display a dual binding profile with very high affinity values for serotonin transporter (SERT) and norepinephrine transporter (NET) ( $K_i = 1.9$  nM and  $K_i = 13.5$  nM respectively).



F-98214-TA

We have prepared series of new compounds having a 4-(N-benzylamino)piperidine moiety according to a chemical program based on the previously reported F-98214-TA as lead compound. They have been evaluated for SERT, NET, dopamine transporter (DAT) and  $\alpha_2$ , 5-HT<sub>1A</sub> and 5-HT<sub>2A</sub> receptors.

We have synthesized new arylmethylaminopiperidines which display high affinities for SERT and NET.



A critical, remarkable and common structural feature of these compounds is the necessary requirement of a secondary amine (R=H) for binding to SERT. Whenever the nitrogen atom of the piperidine ring is substituted the compounds lack affinity for this transporter.

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[1] Orjales, A.; Mosquera, R.; Toledo, A.; Pumar, M.C.; García, N.; Cortizo, L.; Labeaga, L.; Inneráritu, A.; Syntheses and Binding Studies of New [(Aryl)(aryloxy)methyl]piperidine Derivatives and Related Compounds as Potential Antidepressant Drugs with High Affinity for Serotonin (5-HT) and Norepinephrine (NE) Transporters. *J. Med. Chem.* **2003**, 46, 5512-5532.