WHITE PAPER

Radiochemicals

New Radioligand for Neurochemical Research, [N-Methyl-^{3}H] (S)-(+)-Citalopram

Biochemically derived from tryptophan, serotonin (5-hydroxy-tryptamine) is a major endogenous neurotransmitter in man and implicated in a host of processes including memory, learning as well as the regulation of appetite, mood and sleep. Not surprisingly, defects in the complex serotonin neurobiology can therefore be tied to a host of disease states including depression. The concentration of serotonin in the synaptic cleft is critical and is in part orchestrated by a re-uptake system that transports serotonin into the presynaptic nerve cell. One powerful and successful strategy to beneficially enhance serotonin levels (for instance in the case of depression) is blockade of this re-uptake system with what have been termed "selective serotonin re-uptake inhibitors" (or SSRIs). Among these, the substance citalopram is an especially selective and potent agent.

The structure of citalopram contains a chiral center, giving rise to both an (R)-(-) and (S)-(+) enantiomer. It has been known for over two decades that only the (S)-(+) enantiomer of citalopram results in its clinical efficacy.[1,2] Furthermore, it has been surprisingly discovered that each of the citalopram enantiomers binds to the serotonin transporter in distinctly different conformations[3] and it is suggested that the presence of the citalopram (R)-(-) enantiomer actually inhibits the binding of the (S)-(+) enantiomer at this site.[4,5]

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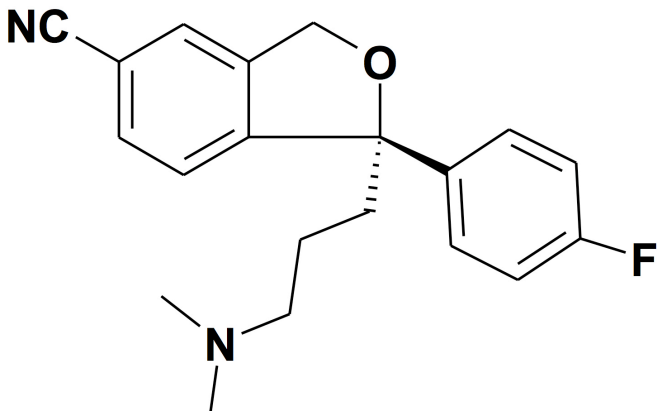
To support this critical neurochemistry research, PerkinElmer has for a number of years made available racemic [N-Methyl-^{3}H] citalopram (NET1039) at high specific activity and radiopurity. In view of the unique efficacy of the (S)-(+) enantiomer of citalopram, we now also offer (S)-(+) [N-Methyl-^{3}H] citalopram (NET1209) at equally high specific activity and chiral purity. Use of these valuable radioligands and especially the new chirally pure version will no doubt advance important research in this area.[6,7,8]

By using radioactive isotopes to directly replace non-radioactive atoms, the biology of the substance you are studying is not altered. The use of radiochemicals is of critical importance in the drug development process for use as radioligands in lead discovery, as metabolic tracers in development, and ADME-Tox studies.

(S)-(+)-Citalopram



References

1. J. Hyttel, K.P. Boegesoe, J. Perregaard, C. Sanchez, *J. Neural Trans: General Section,* **1992,** *88,* 157-160.

2. S.A. Montgomery, H. Loft, C. Sanchez, H. Reines, M. Papp, *Pharmacology & Toxicology,* **2001,** *88,* 282-286.

3. H. Koldso, K. Severinsen, T. Kasper, T. Thuy, L. Celik, H.H. Jensen, O. Wiborg, B. Schiott, S. Sinning, *J. Amer. Chem. Soc.,* **2010,** *132,* 1311-1322.

4. C. Jacquot, D.J. David, A.M. Gardier, C. Sanchez, *Encephale,* **2007,** *33,* 179-187.

5. C. Sanchez, K.P. Bogesoe, B. Ebert, E.H. Reines, C. Braestrup, *Psychopharmacology,* **2004,** *174,* 163-176.

6. H. K. Mueller, G. Wegener, B. Elfving, *Synapse,* **2012,** *66,* 270-272.

7. R.S. Martin, R. A. Henningsen, A, Suen, S. Apparsundaram, B. Leung, Z. Jia, R. K. Kondru, M.E. Milla, *J. Pharmacol. Exp. Ther.,* **2008,** *327,* 991-1000.

8. S. Apparsundaram, D.J. Stockdale, R.A. Henningsen, M. E. Milla, R. S. Martin, *J. Pharmacol. Exp. Ther.,* **2008,** *327,* 982-990.

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