Product Data Sheet

Product Name: Org 25543 hydrochloride
Cat. No.: GC12436

Chemical Properties

Cas. No.	495076-64-7		
Chemical Name	(Z)-4-(benzyloxy)-N-((1-(dimethylamino)cyclopentyl)methyl)-3,5-dimethoxybenzimidic acid hydrochloride		
SMILES	CN(C1(C/N=C(O)/C2=CC(OC)=C(OCC3=CC=CC=C3)C(OC)=C2)CCCC1)C.Cl		
Formula	$C_{24}H_{32}IN_2O_4$.HCl	M.Wt	448.98
Solubility	<8.98mg/ml in Water; <44.9mg/ml in DMSO	Storage	Desiccate at RT
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Org 25543 hydrochloride		

Background

IC50:16 nM

Org 25543 hydrochloride is a potent and selective glycine transporter type 2 (GlyT2) inhibitor for hGlyT2. Two major subtypes of glycine transporter are type 1 (GlyT-1) and type 2 (GlyT-2) revealed by molecular cloning. The GlyT-2 transporter has a similar distribution to ssGlyR with being confined to the spinal cord and brain stem, whereas the GlyT-1 transporter has a wide distribution throughout the CNS.

In vitro: Org 25543 was identified as the most active compound in the library. Org 25543 has both cyclopentyl and BnO groups. As indicated by its favorable physicochemical parameters, Org 25543 exhibits a well penetration of bloodbrain barrier (logBB 0.6). Since Org 25543 also exhibits good metabolic stability (80% remaining after 30 min) in plasma and mouse hepatic microsomes, the compound should prove to be a valuable agent that might help to establish pharmacology of the GlyT-2 transporter [1].

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In vivo: The administration of the antiallodynia effect of GlyT2 inhibitors ORG25543 and ALX1393 appeared without a time lag. The dose-dependent antiallodynia effect displayed by ORG25543 was effective in a limited-dose range. In glycinergic nerve terminals, dysfunction of GlyT2 function plays a very key role in insufficient transmitter loading of synaptic vesicles. However, no sign of hyperekplexia appeared by the administration of GlyT2 inhibitors. Pharmacological manipulation attenuated Glycine refilling in glycinergic nerve terminals in vivo, when reproduction of the antiallodynia effect by repeated treatment of ORG25543 (i.v.) with similar potency per time. [2].

Clinical trial: So far, no clinical study has been conducted.

References:
[1] Caulfield WL, Collie IT, Dickins RS, Epemolu O, McGuire R, Hill DR, McVey G, Morphy JR, Rankovic Z, Sundaram H. The first potent and selective inhibitors of the glycine transporter type 2. J Med Chem. 2001 Aug 16;44(17):2679-82.
[2] Morita K, Motoyama N, Kitayama T, Morioka N, Kifune K, Dohi T. Spinal antiallodynia action of glycine transporter inhibitors in neuropathic pain models in mice. J Pharmacol Exp Ther. 2008 Aug;326(2):633-45.

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