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Datasheet (Version 1.0)

Product Name	:	N-Desmethylclozapine
Synonyms	:	Desmethylclozapine | Normethylclozapine | Norclozapine
Cat No.	:	M19964
CAS Number	:	6104-71-8
Molecular Formula	:	C17H17ClN4
Formula Weight	:	312.8
Chemical Name	:	8-Chloro-11-(1-piperazinyl)-5H-dibenzo(be)(14)diazepine
Description	:	N-Desmethylclozapine is an antagonist of serotonin (5-HT) receptor subtype 5-HT2C (IC50: 7.1 nM). It also is an antagonist at dopamine D4 receptors an agonist at δ-opioid receptors.(In Vitro):The brain penetrant metabolite N-desmethylclozapine preferentially bound to M1 muscarinic receptors with an IC50 of 55 nM and was a more potent partial agonist (EC50, 115 nM and 50% of acetylcholine response) at this receptor than clozapine.N-desmethylclozapine exhibits slight agonistic effects on the M1 mAChR, and agonistic properties at the 5-HT1A receptor in the cerebral cortex and hippocampus. This compound also behaves as an agonist at the δ-opioid receptor in the cerebral cortex and striatum.N-desmethylclozapine (3 μM) greatly decreases the outward current in excitatory neurons, but not in inhibitory neurons. In excitatory neurons, N-desmethylclozapine alone is more effective than either clozapine alone or the combination of clozapine and N-desmethylclozapine. The effect of N-desmethylclozapine in excitatory neurons is significantly suppressed by 0.1 μM pirenzepine and 1 μM atropine. N-desmethylclozapine, but not clozapine, suppressed K+ channels via M1 receptors in excitatory cells.N-desmethylclozapine leads to a decrease in TxB2 levels under unstimulated conditions as well as under TSST-1 stimulation. Clozapine, N-desmethylclozapine and CPZ possibly act on neurotransmitter systems via modulation of TxA2 or TxB2 production.The IC50s of N-desmethylclozapine, fluoxetine hydrochloride, and salmeterol xinafoate in Huh-7 cells infected with DENV-2 are 1 μM, 0.38 μM, and 0.67 μM, respectively. The levels of NS3 are reduced in cells treated with all three inhibitors compared to DMSO treatment, suggesting that the inhibitors act at a stage prior to viral protein translation. N-Desmethylclozapine-treated cells show a >75% reduction in negative-strand RNA levels.(In Vivo):N-desmethylclozapine in rat and human at M2 and M4 mAChRs underlying presynaptic modulation of GABA and glutamate release, respectively. In particular, N-desmethylclozapine maybe a M2 mAChR antagonist in the rat but has no activity at this receptor in human neocortex. However, N-desmethylclozapine has an agonistic effect at M4 mAChR in the human but no such effect in the rat neocortex.
Pathway	:	Endocrinology/Hormones
Target	:	5-HT Receptor
Receptor	:	5-HT2C| D4| δ-opioid receptor
Solubility	:	DMSO: 30 mg/mL; Ethanol: 30 mg/mL
SMILES	:	Clc1ccc2Nc3ccccc3C(=Nc2c1)N1CCNCC1
Storage	:	(-20℃)
Stability	:	≥ 2 years
Reference	:	

1.Kuoppam?ki M et al. Clozapine and N-desmethylclozapine are potent 5-HT1C receptor antagonists. Eur J Pharmacol. 1993 Apr 15;245(2):179-82.