Product Data Sheet

Product Name: Tolcapone
Cat. No.: GC17921

Chemical Properties

Cas. No.	134308-13-7		
Chemical Name	(3,4-dihydroxy-5-nitrophenyl)-(4-methylphenyl)methanone		
SMILES	CC1=CC=C(C=C1)C(=O)C2=CC(=C(C(=C2)O)O)[N+](=O)[O-]		
Formula	$C_{14}H_{11}NO_5$	M.Wt	273.24
Solubility	≥ 12mg/mL in DMSO, ≥ 5.78 mg/mL in EtOH with ultrasonic and warming	Storage	Store at -20°C
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	Tolcapone		

Protocol

Kinase experiment [1]:

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COMT assay	COMT activity was evaluated by the ability of homogenates to methylate adrenaline to metanephrine. Aliquots of 0.5 ml of the homogenate were preincubated for 20 min with 0.5 ml of phosphate buffer (0.5 mM); thereafter, the reaction mixture was incubated for 30 min with increasing concentrations of adrenaline (5 to 500 uM) in the presence of a saturating concentration (100 /M) of the methyl donor (S-adenosyl-L-methionine); the incubation medium contained also pargyline (100 gM), MgCl2 (100 gM) and EGTA (1 mM). The preincubation and incubation were carried out at 37°C, in conditions of light protection, with continuous shaking and without oxygenation. In experiments conducted with the aim of studying the inhibitory effect of tolcapone on COMT activity, tissue homogenates were preincubated for 15 min with increasing concentrations of tolcapone (0.5 to 10,000 nM); the incubation was performed in the presence of a concentration of adrenaline three times the corresponding Km value, as determined in saturation experiments for each age group. At the end of the incubation period the tubes were transferred to ice and the reaction was stopped by the addition of 100 ul of perchloric acid (2 M). The samples were then centrifuged (200 g, 4 min, 4C), and 500 Ml aliquots of the supernatant filtered on Millipore microfilters (MF1) were used for the assay of metanephrine. This procedure allows 99% extraction of catecholamines and their methylated metabolites.

Cell experiment [2]:

Cell lines	SH-SY5Y neuroblastoma cells

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Preparation method	Soluble in DMSO > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 ℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reaction Conditions	6 days
Applications	Tolcapone as an inhibitor of COMT shows a protective effect against HIV associated dendritic and synaptic damage.

Animal experiment [3]:

Animal models	Male albino rats (Fii-albino, 270-300 g)
Dosage form	Orally in a final volume of 2 ml/kg.
Preparation method	Suspended in saline containing 1% Tween 80 using a glass homogenizer.
Applications	Tolcapone is very effective in increasing the striatal extracellular levels of L-DOPA and dopamine in the rat, when given in combination with L-DOPA+benserazide.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

1. Vieira-Coelho MA, Soares-da-Silva P. Ontogenic aspects of liver and kidney catechol-O-methyltransferase sensitivity to tolcapone. Br J Pharmacol. 1996 Feb;117(3):516-520.

2. Lee TT, Chana G, Gorry PR etc. Inhibition of catechol-O-methyl transferase (COMT) by tolcapone restores reductions in microtubule-associated protein 2 (MAP2) and synaptophysin (SYP) following exposure of neuronal cells to neurotropic HIV. J Neurovirol. 2015 Jun 3.

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3. Napolitano A, Zürcher G, Da Prada M. Effects of tolcapone, a novel catechol-O-methyltransferase inhibitor, on striatal metabolism of L-dopa and dopamine in rats. Eur J Pharmacol. 1995 Feb 6;273(3):215-21.

Background

Tolcapone is a novel, reversible and orally-bioavailable small-molecule catechol-O-methyltransferase (COMT) inhibitor used for as an adjunct to levodopa therapy for the treatment of Parkinson’s disease (PD). The chemical structure of tolcapone contains a catechol structure with two electron withdrawing substituents of a tendency to easily deliver a proton resulting in an anion that is highly affinitive for COMT (the value of 50% inhibition concentration IC_{50} of 36 nM in rat liver) and displaces other catechols (such as catecholamines and levodopa) from the COMT catalytic center to prevent methylation. Study results have that the use of tolcapone reduces the dosage but enhances the therapeutic effects of levodopa to control PD symptoms.

Reference

[1].Truong DD. Tolcapone: review of its pharmacology and use as adjunctive therapy in patients with Parkinson's disease. Clin Interv Aging. 2009;4:109-113
[2].Jorga K, Fotteler B, Heizmann P, Gasser R. Metabolism and excretion of tolcapone, a novel inhibitor of catechol-O-methyltransferase. Br J Clin Pharmacol. 1999; 48(4):513-520.

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