Tarafenacin D-tartrate

Cat. No.: HY-14825A

CAS No.: 1159101-48-0

Molecular Formula: $C_{25}H_{26}F_4N_2O_8$

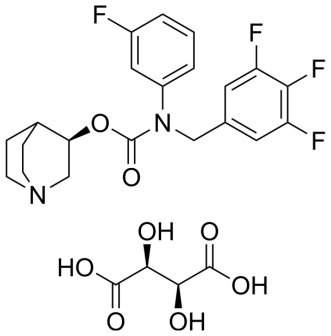
Molecular Weight: 558.48

Target: mAChR

Pathway: GPCR/G Protein; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (179.06 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7906 mL	8.9529 mL	17.9057 mL
5 mM	0.3581 mL	1.7906 mL	3.5811 mL
10 mM	0.1791 mL	0.8953 mL	1.7906 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.48 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.48 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.48 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tarafenacin D-tartrate (SVT-40776 D-tartrate) is a highly selective M3 muscarinic receptor antagonist (Ki= 0.19 nM), ~200 fold selectivity over M2 receptor.IC50 value: 0.19 nM (Ki) [1]Target: M3 muscarinic receptorin vitro: SVT-40776 is highly selective for M(3) over M(2) receptors (Ki = 0.19 nmol.L(-1) for M(3) receptor affinity). SVT-40776 was the most potent in inhibiting carbachol-induced bladder contractions of the anti-cholinergic agents tested, without affecting atrial contractions over the same range of concentrations. SVT-40776 exhibited the highest urinary versus cardiac selectivity (199-fold) [1]. SVT-40776 has a much higher binding affinity (K(d) = 0.4 nM) to M5 mAChR than that of solifenacin (K(d) = 31 nM) with the same reeptor. The calculated binding free energy change (-2.3 ± 0.3 kcal/mol) from solifenacin to SVT-40776 is in good agreement with the experimentally derived binding free energy change (-2.58 kcal/mol), suggesting that our modeled M5 mAChR structure and

	its complexes with the antagonists are reliable [2].in vivo: In the guinea pig in vivo model, SVT-40776 inhibited 25% of spontaneous bladder contractions at a very low dose (6.97 microg.kg(-1) i.v), without affecting arterial blood pressure [1].
IC_{50} & Target	mAChR3

REFERENCES

[1]. Salcedo C, et al. In vivo and in vitro pharmacological characterization of SVT-40776, a novel M3 muscarinic receptor antagonist, for the treatment of overactive bladder. Br J Pharmacol. 2009 Mar;156(5):807-17.

[2]. Huang X, et al. Microscopic binding of M5 muscarinic acetylcholine receptor with antagonists by homology modeling, molecular docking, and molecular dynamics simulation. J Phys Chem B. 2012 Jan 12;116(1):532-41.

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