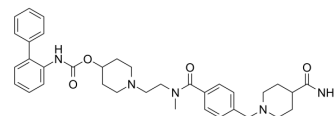


## Revefenacin

<b>Cat. No.:</b>	HY-15851		
<b>CAS No.:</b>	864750-70-9		
<b>Molecular Formula:</b>	C <sub>35</sub> H <sub>43</sub> N <sub>5</sub> O <sub>4</sub>		
<b>Molecular Weight:</b>	597.75		
<b>Target:</b>	mAChR		
<b>Pathway:</b>	GPCR/G Protein; Neuronal Signaling		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 100 mg/mL (167.29 mM; Need ultrasonic)

Concentration	Mass		
	1 mg	5 mg	10 mg
1 mM	1.6729 mL	8.3647 mL	16.7294 mL
5 mM	0.3346 mL	1.6729 mL	3.3459 mL
10 mM	0.1673 mL	0.8365 mL	1.6729 mL

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

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (4.18 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (4.18 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (4.18 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Revefenacin (TD-4208; GSK1160724) is a potent mAChR antagonist; has a high affinity on M3 receptor with a K<sub>i</sub> of 0.18 nM.

#### IC<sub>50</sub> & Target

K<sub>i</sub>: 0.42 nM (M1), 0.32 nM (M2), 0.18 nM (M3), 0.56 nM (M4), 6.7 nM (M5)<sup>[1]</sup>

#### In Vitro

The K<sub>i</sub>s of revefenacin are 0.42, 0.32, 0.18, 0.56, and 6.7 nM at human M1, M2, M3, M4 and M5 receptors, respectively. In a functional assay, revefenacin is shown to be a functional antagonist with inhibition constants similar to binding K<sub>i</sub>'s. Revefenacin also inhibits agonist-induced contraction of guinea pig isolated tracheal ring preparation with an affinity of 0.1

nM, similar to the measured M3 binding  $K_i$ <sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

In anesthetized dogs, revefenacin, along with tiotropium and glycopyrronium, produce sustained inhibition of acetylcholine-induced bronchoconstriction for up to 24 hours. In anesthetized rats, inhaled revefenacin exhibits dose-dependent 24-hour bronchoprotection against methacholine-induced bronchoconstriction. The estimated 24-hour potency is 45.0 µg/mL and the bronchoprotective potencies are maintained after 7 days of once-daily dosing<sup>[2]</sup>.

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## PROTOCOL

#### Animal Administration <sup>[2]</sup>

Rats: To determine the bronchoprotective and antisialagogue potency after a single dose, rats are exposed by inhalation to a nebulized solution of revefenacin (3–3000 µg/mL), tiotropium (0.3–300 µg/mL), glycopyrronium (1–1000 µg/mL), or vehicle (sterile water). Bronchoprotective activity is assessed 24 hours postdose. For the antisialagogue effect, inhibition of Pilo is assessed 1, 6, or 12 hours after inhalation of an efficacious dose of test compound to determine the time point at which peak effect occurred. All subsequent doses are measured at this time point<sup>[2]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## REFERENCES

[1]. Steinfeld T, et al. In vitro characterization of TD-4208, a lung-selective and long-acting muscarinic antagonist bronchodilator (Abstract). Am J Respir Crit Care Med 179:A4553.

[2]. Pulido-Rios MT, et al. In vivo pharmacological characterization of TD-4208, a novel lung-selective inhaled muscarinic antagonist with sustained bronchoprotective effect in experimental animal models. J Pharmacol Exp Ther. 2013 Aug;346(2):241-50.

**Caution: Product has not been fully validated for medical applications. For research use only.**

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA