Revefenacin

Cat. No.: HY-15851
CAS No.: 864750-70-9
Molecular Formula: C₃₅H₄₃N₅O₄
Molecular Weight: 597.75
Target: mAChR
Pathway: GPCR/G Protein; Neuronal Signaling
Storage: Powder
-20°C 3 years
4°C 2 years
In solvent
-80°C 6 months
-20°C 1 month

**SOLVENT & SOLUBILITY**

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass (1 mg)</th>
<th>Mass (5 mg)</th>
<th>Mass (10 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO</td>
<td>1.6729 mL</td>
<td>8.3647 mL</td>
<td>16.7294 mL</td>
</tr>
<tr>
<td>DMSO</td>
<td>0.3346 mL</td>
<td>1.6729 mL</td>
<td>3.3459 mL</td>
</tr>
<tr>
<td>DMSO</td>
<td>0.1673 mL</td>
<td>0.8365 mL</td>
<td>1.6729 mL</td>
</tr>
</tbody>
</table>

DMSO: ≥ 125 mg/mL (209.12 mM)

*“≥” means soluble, but saturation unknown.

**BIOLOGICAL ACTIVITY**

Description
Revefenacin (TD-4208; GSK1160724) is a potent mAChR antagonist; has a high affinity on M3 receptor with a \( K_i \) of 0.18 nM.

IC₅₀ & Target
Kᵢ: 0.42 nM (M1), 0.32 nM (M2), 0.18 nM (M3), 0.56 nM (M4), 6.7 nM (M5)[¹]

In Vitro
The \( Kᵢ \)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 \( Kᵢ \)’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 \( Kᵢ \).[¹]

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\textsuperscript{[2]}.

## PROTOCOL

**Animal Administration** \textsuperscript{[2]}

Rats: To determine the bronchoprotective and antisialagogue potency after a single dose, rats are exposed by inhalation to a nebulized solution of revafenacin (3–300 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\textsuperscript{[2]}. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## REFERENCES


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

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