Vilanterol trifenatate

Cat. No.: HY-14300A
CAS No.: 503070-58-4
Molecular Formula: C₄₄H₄₉Cl₂NO₇
Molecular Weight: 774.77
Target: Adrenergic Receptor
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

In Vitro  
DMSO: 100 mg/mL (129.07 mM; Need ultrasonic)  
H₂O: < 0.1 mg/mL (insoluble)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td></td>
<td>1.2907 mL</td>
<td>6.4535 mL</td>
<td>12.9071 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.2581 mL</td>
<td>1.2907 mL</td>
<td>2.5814 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.1291 mL</td>
<td>0.6454 mL</td>
<td>1.2907 mL</td>
<td></td>
</tr>
</tbody>
</table>

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 (3.23 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: 2.5 mg/mL (3.23 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (3.23 mM); Clear solution

BIOLOGICAL ACTIVITY

Description  
Vilanterol trifenatate (GW642444 trifenatate) is a long-acting β₂-adrenoceptor (β₂-AR) agonist with inherent 24-hour activity. The pEC₅₀s for β₂-AR, β₁-AR and β₃-AR are 10.37, 6.98 and 7.36, respectively.

IC₅₀ & Target  
pEC50: 10.37±0.05 (β₂-adrenoceptor), 6.98±0.03 (β₁-adrenoceptor), 7.36±0.03 (β₃-adrenoceptor) [1]
In Vitro

The selectivity of Vilanterol trifenatate for \( \beta_2 \)-AR over the other \( \beta \)-AR receptor subtypes (\( \beta_2 \) and \( \beta_3 \)) is established by testing the ability of Vilanterol to elicit concentration-dependent increases in cAMP in CHO cells expressing human \( \beta_1 \), \( \beta_2 \), and \( \beta_3 \)-AR. Vilanterol is demonstrated to be highly selective for the \( \beta_2 \)-AR with at least a 1000-fold selectivity over both \( \beta_2 \)- and \( \beta_3 \)-AR subtypes. This analysis results in a low-affinity \( pK_D \) for \( [^3H] \)Vilanterol of 9.44±0.07 (n=4) in the presence Gpp(NH)p and a high-affinity \( pK_D \) of 10.82±0.12 (n=4) and a low-affinity \( pK_D \) 9.47±0.17 (n=4) in the absence of Gpp(NH)p. In addition, a low-affinity \( pK_D \) for \( [^3H] \)Vilanterol of 9.52±0.24 (n=4) in the absence of Gpp(NH)p (37°C) is observed[1]. Vilanterol trifenatate is a novel inhaled long-acting \( \beta_2 \)-agonist with inherent 24 h activity in vitro in development as a combination with the inhaled corticosteroid fluticasone furoate for both COPD and asthma[2]. Vilanterol is a novel long-acting \( \beta_2 \)-agonist (LABA) with inherent 24-hour activity for once-daily clinical treatment of chronic obstructive pulmonary disease (COPD) and asthma in combination with the inhaled novel corticosteroid fluticasone furoate, also active for 24 hours[3].

PROTOCOL

Kinase Assay[1]

Saturation, association, and dissociation binding studies are performed for \( [^3H] \)Vilanterol to determine receptor binding kinetics at the \( \beta_2 \)-AR (equilibrium dissociation constant (\( K_D \)), total number of receptors (Bmax), association rate (\( k_{on} \)), and dissociation rate (\( k_{off} \)) are calculated). For saturation binding, membranes (in a volume of 1.4 mL to avoid ligand depletion) are incubated with increasing concentrations of \( [^3H] \)Vilanterol (~0.01-1.3 nM) for 5 h before filtration. For association binding, membranes are incubated with different concentrations of \( [^3H] \)Vilanterol (~0.1-1.9 nM) for varying incubation times up to 1 h before filtration. For dissociation binding, membranes are preincubated for 1 h with a fixed concentration of \( [^3H] \)Vilanterol (~1.1 nM) before dissociation is initiated by a 1:20 dilution in binding buffer (containing 10 µM cold Vilanterol) and then incubated for varying times up to 8 h before filtration. Saturation binding is also completed for \( [^3H] \)CGP12177 (increasing concentrations of ~0.01-2.8 nM) in the same format as described above for \( [^3H] \)Vilanterol. To determine the affinity of \( \beta_2 \)-AR agonists and antagonists, competition binding displacement studies are completed in which membranes are incubated with a fixed concentration of \( [^3H] \)Vilanterol (~0.2 nM) and increasing concentrations of unlabeled agonist/antagonist for 5 h before filtration. All competition binding displacement studies are completed in the presence of 100 µM Gpp(NH)p to ensure that binding curves are monophasic[1].

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

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REFERENCES
