Vilanterol trifenatate

Cat. No.: HY-14300A

CAS No.: 503070-58-4

Molecular Formula: $C_{44}H_{49}Cl_2NO_7$

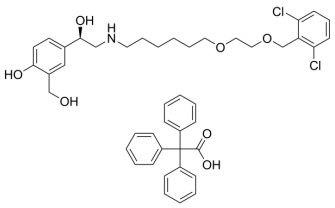
Molecular Weight: 774.77

Target: Adrenergic Receptor

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 : 50 mg/mL (64.54 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2907 mL	6.4535 mL	12.9071 mL
	5 mM	0.2581 mL	1.2907 mL	2.5814 mL
	10 mM	0.1291 mL	0.6454 mL	1.2907 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 mg/mL (2.58 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2 mg/mL (2.58 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2 mg/mL (2.58 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Vilanterol trifenatate (GW642444 trifenatate) is a long-acting β_2-adrenoceptor (β_2-AR) agonist with inherent 24-hour activity. The pEC_{50}s for β_2-AR, β_1-AR and β_3-AR are 10.37, 6.98 and 7.36, respectively.

IC_{50} & Target

β adrenergic receptor

In Vitro

The selectivity of Vilanterol trifenatate for β_2-AR over the other β-AR receptor subtypes (β_2 and β_3) is established by testing the ability of Vilanterol to elicit concentration-dependent increases in cAMP in CHO cells expressing human β_1-, β_2-, and β_3-AR. Vilanterol is demonstrated to be highly selective for the β_2-AR with at least a 1000-fold selectivity over both β_2- and β_3-AR subtypes. This analysis results in a low-affinity pK_D for [^{3}H]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 [^{3}H]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 β_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 β_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].

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

PROTOCOL

Kinase Assay [1]

Saturation, association, and dissociation binding studies are performed for [^{3}H]Vilanterol to determine receptor binding kinetics at the β_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 [^{3}H]Vilanterol (~0.01-1.3 nM) for 5 h before filtration. For association binding, membranes are incubated with different concentrations of [^{3}H]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 [^{3}H]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 [^{3}H]CGP12177 (increasing concentrations of ~0.01-2.8 nM) in the same format as described above for [^{3}H]Vilanterol. To determine the affinity of β_2-AR agonists and antagonists, competition binding displacement studies are completed in which membranes are incubated with a fixed concentration of [^{3}H]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.

CUSTOMER VALIDATION

- Eur J Pharmacol. 2017 Oct 5;812:147-154.
- J Pharmaceut Biomed. 2020, 113870.
- J Neuroimmunol. 2019 Jul 15;332:37-48.
- Mental Health and Neuroscience Institute. University of Alberta. 2016 Sep.
- Centre for Neuroscience. University of Alberta. 2016.

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REFERENCES

[1]. Slack RJ, et al. In vitro pharmacological characterization of vilanterol, a novel long-acting β2-adrenoceptor agonist with 24-hour duration of action. J Pharmacol Exp Ther. 2013 Jan;344(1):218-30

[2]. Kempsford R, et al. Vilanterol trifenatate, a novel inhaled long-acting beta2 adrenoceptor agonist, is well tolerated in healthy subjects and demonstrates prolonged bronchodilation in subjects with asthma and COPD. Pulm Pharmacol Ther. 2013 Apr;26(2):256-

[3]. Harrell AW, et al. Metabolism and disposition of Vilanterol, a long-acting β(2)-adrenoceptor agonist for inhalation use in humans. Drug Metab Dispos. 2013 Jan;41(1):89-100.

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

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