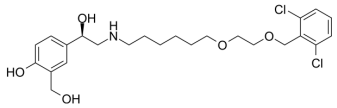
Vilanterol

Cat. No.:	HY-14300
CAS No.:	503068-34-6
Molecular Formula:	$C_{24}H_{33}Cl_2NO_5$
Molecular Weight:	486.43
Target:	Adrenergic Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Pure form -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.14 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.14 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.14 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Vilanterol (GW642444) is a long-acting β_2-adrenoceptor (β_2-AR) agonist with 24 h activity. The pEC_{50}s for β_2-AR,β_1-AR and β_3 -AR is 10.37±0.05, 6.98±0.03 and 7.36±0.03, respectively.

IC_{50} & Target

β adrenergic receptor

In Vitro

The selectivity of Vilanterol 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.

[4]. Calzetta L, et al. Pharmacological characterization of the interaction between umeclidinium and vilanterol in human bronchi. Eur J Pharmacol. 2017 Jul 14. pii: S0014-2999(17)30470-3.

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