Ensifentrine

Cat. No.: HY-119708

CAS No.: 1884461-72-6

Molecular Formula: $C_{26}H_{31}N_5O_4$

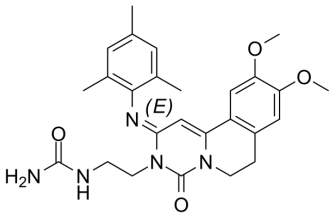
Molecular Weight: 477.56

Target: Phosphodiesterase (PDE)

Pathway: Metabolic Enzyme/Protease

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 : 25 mg/mL (52.35 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0940 mL	10.4699 mL	20.9398 mL
	5 mM	0.4188 mL	2.0940 mL	4.1880 mL
	10 mM	0.2094 mL	1.0470 mL	2.0940 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: ≥ 1.25 mg/mL (2.62 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 1.25 mg/mL (2.62 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Ensifentrine (RPL-554) is an inhaled first-in-class dual inhibitor of phosphodiesterase 3 (PDE3) and PDE4 with IC_{50}s of 0.4 nM and 1479 nM, respectively. Ensifentrine has bronchoprotective and anti-inflammatory activities. Ensifentrine can be used for chronic obstructive pulmonary disease (COPD) research[1][2].

IC_{50} & Target

PDE3	PDE4
0.4 nM (IC_{50})	1479 nM (IC_{50})

In Vitro

Ensifentrine (RPL-554) inhibits, in a concentration-dependent manner, lipopolysaccharide-induced TNF-α release from human monocytes (IC_{50} of 0.52 μM) and proliferation of human mononuclear cells to phytohemagglutinin (IC_{50} of 0.46 μM)[1].

Electrical field stimulation-induced contraction of guinea pig superfused isolated tracheal preparations is significantly inhibited by Ensifentrine (10 μM). Contractile responses are suppressed for up to 12 h after termination of superfusion with RPL-554 demonstrating a long duration of action[1].

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

In Vivo

Ensifentrine (RPL-554; 10 mg/kg; Oral administration; once) significantly inhibits eosinophil recruitment following antigen challenge in ovalbumin-sensitized guinea pigs[1].

The inhalation of dry powder containing Ensifentrine by conscious guinea pigs (25% in micronized lactose) 1.5 h before antigen exposure significantly inhibits the recruitment of eosinophils to the airways[1].

Exposure of conscious guinea pigs to inhalation of dry powder containing Ensifentrine (2.5%) in micronized lactose significantly inhibits histamine-induced plasma protein extravasation in the trachea and histamine-induced bronchoconstriction over a 5.5-h period[1].

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

Animal Model:	Male Dunkin Hartley guinea pigs (200-300 g) injected with ovalbumin[1].
Dosage:	10 mg/kg
Administration:	Oral administration; once
Result:	Significantly inhibits eosinophil recruitment following antigen challenge in ovalbumin-sensitized guinea pigs.

REFERENCES

[1]. Victoria Boswell-Smith, et al. The pharmacology of two novel long-acting phosphodiesterase 3/4 inhibitors, RPL554 [9,10-dimethoxy-2(2,4,6-trimethylphenylimino)-3-(n-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one] and RPL565 [6,7-dihydro-2-(2,6-diisopropylphenoxy)-9,10-dimethoxy-4H-pyrimido[6,1-a]isoquinolin-4-one]. J Pharmacol Exp Ther. 2006 Aug;318(2):840-8.

[2]. Henrik Watz, et al. Symptom Improvement Following Treatment with the Inhaled Dual Phosphodiesterase 3 and 4 Inhibitor Ensifentrine in Patients with Moderate to Severe COPD - A Detailed Analysis. Int J Chron Obstruct Pulmon Dis. 2020 Sep 16;15:2199-2206.

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