BPO-27 racemate

Cat. No.: HY-19778A

CAS No.: 1314873-02-3

Molecular Formula: $C_{26}H_{18}BrN_3O_6$

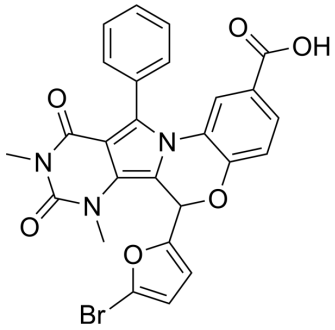
Molecular Weight: 548.34

Target: CFTR; Autophagy

Pathway: Membrane Transporter/Ion Channel; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 16.67 mg/mL (30.40 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8237 mL	9.1184 mL	18.2369 mL
	5 mM	0.3647 mL	1.8237 mL	3.6474 mL
	10 mM	0.1824 mL	0.9118 mL	1.8237 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: 1.67 mg/mL (3.05 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BPO-27 racemate is a potent CFTR inhibitor with an IC_{50} of 8 nM.

IC_{50} & Target

IC50: 8 nM[1]

In Vitro

The benzopyrimido-pyrrolo-oxazinedione BPO-27 is an analogue of PPQ-102, which inhibits CFTR with an IC_{50} of 8 nM. The R enantiomer of BPO-27 inhibits CFTR chloride conductance with an IC_{50} of 4 nM, while S enantiomer is inactive. In vitro metabolic stability in hepatic microsomes shows both enantiomers as stable, with less than 5% metabolism in 4 h[1]. (R)-BPO-27 binds near the canonical ATP binding site. Whole-cell patch-clamp studies shows linear CFTR currents with a voltage-independent (R)-BPO-27 block mechanism. At a concentration of (R)-BPO-27 that inhibits CFTR chloride current by 50%, the EC_{50} for ATP activation of CFTR increases from 0.27 to 1.77 mM[2].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Following bolus interperitoneal administration in mice, serum (R)-1 decays with $t_{1/2} \approx 1.6$ h and gives sustained therapeutic concentrations in kidney[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Whole-cell recordings are done on CFTR-expressing CHO-K1 cells. After establishing the whole-cell configuration, BPO-27 is added for 5 minutes, and then CFTR is activated by the addition of forskolin (10 μM) in the continued presence of BPO-27 (0.5 or 1 μM). Whole-cell currents are elicited by applying hyperpolarizing and depolarizing voltage pulses from a holding potential of 0 mV to potentials between +80 and −80 mV in steps of 20 mV. Recordings are made at room temperature using an Axopatch-200B. Currents are digitized with a Digidata 1440A converter and filtered at 5 kHz[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: (R)-BPO-27 is formulated at 1 mg/mL in 5% DMSO, 2.5% Tween-80 and 2.5% PEG400 in water. Male mice in a CD1 genetic background are administered 300 μL of the (R)-BPO-27 formulation by intraperitoneal injection. At specified times, blood samples are collected by eye bleed. At 4 h, kidneys are removed following renal arterial perfusion with PBS. Kidneys are weighed, mixed with acetic acid and homogenized for analysis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Gastroenterology. 2018 Dec;155(6):1883-1897.e10.

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REFERENCES

[1]. Snyder DS, et al. Absolute Configuration And Biological Properties of Enantiomers of CFTR Inhibitor BPO-27. ACS Med Chem Lett. 2013 May 9;4(5):456-459.

[2]. Kim Y, et al. Benzopyrimido-pyrrolo-oxazine-dione (R)-BPO-27 Inhibits CFTR Chloride Channel Gating by Competition with ATP. Mol Pharmacol. 2015 Oct;88(4):689-96.

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