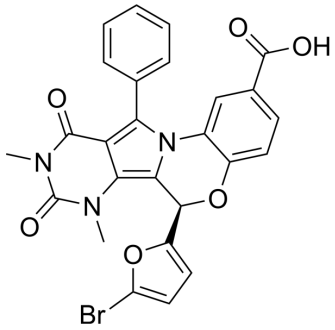
(R)-BPO-27

Cat. No.:	HY-19778
CAS No.:	1415390-47-4
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 : ≥ 14.28 mg/mL (26.04 mM)

* "≥" means soluble, but saturation unknown.

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.

BIOLOGICAL ACTIVITY

Description

(R)-BPO-27, the R enantiomer of BPO-27, is a potent, orally active and ATP-competitive CFTR inhibitor with an IC_{50} of 4 nM.

IC_{50} & Target

IC50: 4 nM[1]

In Vitro

(R)-BPO-27 exhibits a dose-response inhibition and inhibits the CFTR current by 50% at 0.53 nM in HEK-293T cells. (R)-BPO-27 acts from the cytoplasmic side and has low membrane permeability[1].

(R)-BPO-27 reduces the channel open probability (NPo) from 0.29 to 0.08, modestly reduces in mean channel open time, and strongly increases mean channel closed time in HEK-293T cells expressing human wild-type CFT in a single-channel patch-clamp experiment. Meanwhile, (S)-BPO-27 does not affect any of these parameters[1].

(R)-BPO-27 is applied directly to the cytoplasmic membrane surface and stabilizes the CFTR channel closed state with an IC_{50} of 600 pM in Single-channel electrophysiology assay[2].

(R)-BPO-27 (10 μM, 10 min pretreatment) inhibits Cl^- current with apparent IC_{50} values of 5 and 10 nM for CPT-cAMP and 8-Br-cGMP, respectively, in CFTR-expressing FRT cells after CFTR stimulation by cAMP agonist. the IC_{50} of 4 nM for inhibition of forskolin-stimulated CFTR Cl^- current in FRT cells[3].

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

In Vivo

(R)-BPO-27 (interperitoneal administration; 10 mg/kg) decays with $t_{1/2}$≈1.6 h and gives sustained therapeutic concentrations in kidney in a PK study[1].

(R)-BPO-27 (intraperitoneal injection; 5 mg/kg; 30 min before abdominal surgery) prevents fluid accumulation in closed midjejunal loops produced by cholera toxin, giving an intestinal loop weight/length ratio similar to that in PBS-injected loops. This effect is dose-dependently and the IC_{50} value is 0.1 mg/kg[3].

(R)-BPO-27 (intraperitoneal injection or oral administration; 5 mg/kg) shows a slow (R)-BPO-27 metabolism and produces sustained serum (R)-BPO-27 levels for at least 4 h. The AUC analysis gave an oral bioavailability of -94% for (R)-BPO-27 in mouse pharmacokinetics and toxicity study[3].

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

Animal Model:	Female CD1 mice (age 8–10 wk)[3]
Dosage:	0.05, 0.15, 0.5, 1.5, and 5 mg/kg
Administration:	Intraperitoneal injection; 5 mg/kg; 30 min before abdominal surgery
Result:	Exhibited apparent efficacy in mice models of cholera and traveler's diarrhea.

CUSTOMER VALIDATION

- Gut Microbes. 2023 Jan-Dec;15(1):2225841.

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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.

[3]. Onur Cil, et al.Benzopyrimido-pyrrolo-oxazine-dione CFTR inhibitor (R)-BPO-27 for antisecretory therapy of diarrheas caused by bacterial enterotoxins. FASEB J. 2017 Feb;31(2):751-760.

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