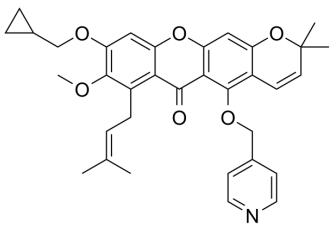
PDE4-IN-12

Cat. No.:	HY-151174
CAS No.:	2901084-32-8
Molecular Formula:	$C_{34}H_{35}NO_6$
Molecular Weight:	553.64
Target:	Phosphodiesterase (PDE)
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PDE4-IN-12 is a potent pan-PDE4 inhibitor, with IC_{50}s of 3.5 and 15 nM for PDE4 and PDE7, respectively (SI=2.71 and 4.27, respectively). PDE4-IN-12 shows well tolerated, can be used in study of inflammatory bowel diseases (IBDs)[1].

IC_{50} & Target

PDE4D2 3.51 nM (IC_{50})	PDE4B2 9.51 nM (IC_{50})	PDE7A 15 nM (IC_{50})	PDE5A1 1.24 μM (IC_{50})
PDE10A 1.02 μM (IC_{50})	PDE8A1 194 nM (IC_{50})		

In Vitro

PDE4-IN-12 (compound 22d) (10, 20 μM; 24 h) reduces the release of NO in LPS induced inflammation cell model (indicates anti-inflammatory effect)[1].

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

Cell Viability Assay[1]

Cell Line:	Raw264.6 cells
Concentration:	10, 20 μM
Incubation Time:	24 h
Result:	Reduced the NO release by dose-dependent manner in the LPS induced inflammatory cell model.

In Vivo

PDE4-IN-12 (5 mg/kg; i.p.; twice daily for 8 days) ameliorates mouse acute colitis induced by DSS (dextran sulfate sodium)[1].

PDE4-IN-12 (10 mg/kg; p.o.; single) shows well tolerated in dogs[1].

PDE4-IN-1 (2.5 mg/kg; i.v.; single) shows great plasma exposure, with $T_{1/2}$ and $AUC_{0\text{-}24\ h}$ values of 4.18 h and 6522 h·ng/mL[1].

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

Animal Model:	Male C57BL/6 mice (5 to 6-week old; 15-17 g; DSS-induced mouse model)[1].
Dosage:	5 mg/kg

Administration:	Intraperitoneal injection; twice daily for 8 days.
Result:	Ameliorated the acute colitis by decreasing disease activity index, increasing the colon length, and also ameliorating the pathological damages.

Animal Model:	Beagle dogs[1].
Dosage:	10 mg/kg (solved in 0.5% CMC-Na solution).
Administration:	Oral administration; single.
Result:	Exhibited good safety, which caused no emesis on beagle dogs at 10 mg/kg.

Animal Model:	Male C57BL/6 mice (5 to 6-week old; 15-17 g)[1].
Dosage:	2.5 mg/kg
Administration:	Intravenous injection; single.
Result:	Pharmacokinetic Parameters of PDE4-IN-12 in Male C57BL/6 mice[1].

	$T_{1/2}$ (h)	$AUC_{0\text{-}24\ h}$ (h·ng/mL)	$MRT_{0\text{-}24\ h}$ (h)	CL (mL/min/kg)	Vss (mL/kg)
IV (2.5 mg/kg)	4.18	6522	1.76	6.40	673

REFERENCES

[1]. Liu H, et al. Discovery of novel PDE4 inhibitors targeting the M-pocket from natural mangostanin with improved safety for the treatment of Inflammatory Bowel Diseases. Eur J Med Chem. 2022 Aug 9;242:114631.

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