RORγt inverse agonist 29

Cat. No.: HY-143271

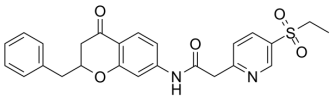
Molecular Formula: $C_{25}H_{24}N_2O_5S$

Molecular Weight: 464.53

Target: ROR

Pathway: Metabolic Enzyme/Protease

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

RORγt inverse agonist 29 is a potent, orally active and selective RORγt inverse agonist (IC_{50}: 21 nM). RORγt inverse agonist 29 can be used in the research of skin inflammation and autoimmune diseases like psoriasis[1].

IC_{50} & Target

RORγt
21 nM (IC_{50})

In Vitro

RORγt inverse agonist 29 (compound b12) demonstrates high RORγt transcriptional inhibitory activity (IC_{50}: 28 nM) in human Jurkat cells[1].
RORγt inverse agonist 29 (10 μM) shows good metabolic stabilities in in vitro human liver microsomes, with comparable half-life ($T_{1/2}$: 4.46 h) and HLM ($CL_{int(liver)}$: 4.8 mL/min/kg)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

RORγt inverse agonist 29 (p.o., 100 mg/kg) reduces the total Psoriasis Area and the development of clinical symptoms in mouse Imiquimod-induced skin inflammation model[1].
RORγt inverse agonist 29 (i.v., p.o., 0.3 or 1 mg/kg) displays an acceptable bioavailability and a half-life in rats[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Mouse Imiquimod-induced skin inflammation model[1]
Dosage:	15 mg/kg, 50 mg/kg, 100 mg/kg
Administration:	Oral administration, twice a day for 13 days.
Result:	Inhibited IL-6 and IL-17A protein in the serum, with inhibition rate of 58.06% (IL-6) and 84.07% (IL-17A) at 100 mg/kg. Reduced the histopathological symptoms on the back skin at dose of 100 mg/kg. Alleviated symptoms including mononuclear and inflammatory cell infiltration, skin layer thickening, and dermal telangiectasia.

Animal Model:	Rats (pharmacokinetic assay)[1]
Dosage:	0.3 mg/kg (i.v.), 1 mg/kg (p.o.)

Administration:	Intravenous injection, oral administration
Result:	Pharmacokinetic profile of RORγt inverse agonist 29 (compound b12).

administration route	$T_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/mL)	AUC_{0-t} (ng•h/mL)	$AUC_{0-\infty}$ (ng•h/mL)	F (%)
i.v. (0.3 mg/kg)	5.8	2.4	88	156	162	
p.o. (1 mg/kg)	6.5	3.1	105	340	352	65

REFERENCES

[1]. Lei Chen, et al. Discovery of N-(2-benzyl-4-oxochroman-7-yl)-2-(5-(ethylsulfonyl) pyridin-2-yl) acetamide (b12) as a potent, selective, and orally available novel retinoic acid receptor-related orphan receptor γt inverse agonist. Bioorg Chem. 2022 Feb;119:105483.

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