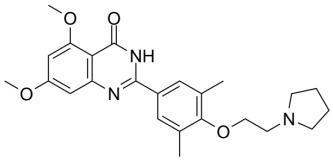
RVX-297

Cat. No.:	HY-114504
CAS No.:	1044871-04-6
Molecular Formula:	$C_{24}H_{29}N_3O_4$
Molecular Weight:	423.5
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
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 : 50 mg/mL (118.06 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3613 mL	11.8064 mL	23.6128 mL
	5 mM	0.4723 mL	2.3613 mL	4.7225 mL
	10 mM	0.2361 mL	1.1806 mL	2.3613 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: ≥ 2.08 mg/mL (4.91 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.91 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RVX-297 is a potent, orally active BET bromodomain inhibitor with selectivity for BD2. RVX-297 shows IC_{50}s of 0.08, 0.05, and 0.02 μM for BRD2(BD2), BRD3(BD2), and BRD4(BD2), respectively. RVX-297 suppresses inflammatory gene expression in multiple immune cell types. RVX-297 is effective in acute inflammation and autoimmunity models[1][2].

IC_{50} & Target

BRD2 (BD1) 3.76 μM (IC_{50})	BRD2 (BD2) 0.08 μM (IC_{50})	BRD3 (BD1) 2.34 μM (IC_{50})	BRD3 (BD2) 0.05 μM (IC_{50})
BRD4 (BD1)	BRD4 (BD2)	BRDT (BD1)	

	1.16 μM (IC_{50})	0.02 μM (IC_{50})	2.69 μM (IC_{50})

In Vitro

RVX-297 (1-30 μM; 24 hours) decreases proinflammatory gene expression in synovial fibroblasts[1].
RVX-297 displaces BET proteins from the promoters of sensitive genes and disrupted recruitment of active RNA polymerase II, a property shared with pan-BET inhibitors that nonselectively bind BET BDs[1].
RVX-297 reduces gene expression of inflammatory mediators in vitro. RVX-297 suppresses IL-6 gene induction in human U937 macrophages, mouse primary B cells isolated from the spleen, mouse BMDMs, and THP-1 monocytes in a dose-dependent manner. RVX-297 represses IL-1β expression in LPS-stimulated mouse BMDMs, with an IC_{50} of 0.4-3 μM. RVX-297 inhibits MCP-1 expression in unstimulated human PBMCs with an IC_{50} of 0.4 μM. RVX-297 inhibits antigen stimulation of T cells and the induction of IL-17 expression[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

RT-PCR[1]

Cell Line:	Synovial fibroblasts
Concentration:	1-30 μM
Incubation Time:	24 hours
Result:	Downregulated IL-6 and VCAM-1 gene expression in synovial fibroblasts.

In Vivo

RVX-297 (25-75 mg/kg; p.o.; per day for 6 day) inhibits progression of pathology in the rat collagen-induced arthritis model[1].
RVX-297 (75-150 mg/kg) inhibits progression of pathology in the mouse collagen-induced arthritis model[1].
RVX-297 suppresses cytokine production in LPS-treated mice[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female Lewis rats are 6-8 weeks old, approximately 150 g (rat collagen-induced arthritis) [1]
Dosage:	25, 50, and 75 mg/kg
Administration:	P.o.; per day for 6 days
Result:	Prevented swelling and inflammation of the ankle and knee joints.

REFERENCES

[1]. Jahagirdar R, et al. RVX-297, a BET Bromodomain Inhibitor, Has Therapeutic Effects in Preclinical Models of Acute Inflammation and Autoimmune Disease. Mol Pharmacol. 2017;92(6):694-706.

[2]. Kharenko OA, et al. RVX-297- a novel BD2 selective inhibitor of BET bromodomains. Biochem Biophys Res Commun. 2016;477(1):62-67.

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