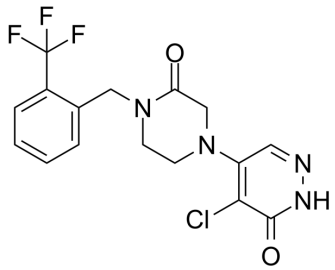
GFB-8438

Cat. No.:	HY-133012
CAS No.:	2304549-73-1
Molecular Formula:	$C_{16}H_{14}ClF_3N_4O_2$
Molecular Weight:	386.76
Target:	TRP Channel
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
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 : 83.33 mg/mL (215.46 mM; Need ultrasonic)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.5856 mL	12.9279 mL	25.8558 mL
5 mM	0.5171 mL	2.5856 mL	5.1712 mL
10 mM	0.2586 mL	1.2928 mL	2.5856 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 (5.38 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.38 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.38 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GFB-8438 is a potent and subtype selective TRPC5 inhibitor, with IC_{50}s of 0.18 and 0.29 μM of hTRPC5 and hTRPC4, respectively. GFB-8438 shows excellent selectivity against TRPC6, other TRP family members, NaV 1.5, as well as limited activity against the hERG channel. GFB-8438 protects mouse podocytes from injury induced by protamine sulfate model[1].

IC_{50} & Target			
	hTRPC5 0.18 μM (IC_{50})	hTRPC4 0.29 μM (IC_{50})	rTRPC5 0.18 μM (IC_{50})

In Vitro

Pretreatment of mouse podocyte with GFB-8438 (1 μM for 30 min), followed by incubation with protamine sulfate, effectively blocked synaptopodin loss and cytoskeletal remodeling[1].

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

In Vivo

GFB-8438 (30 mg/kg; s.c.; daily for 3 weeks) is efficacious in a hypertensive deoxycorticosterone acetate (DOCA)-salt rat model of focal segmental glomerulosclerosis (FSGS), significantly reducing both total protein and albumin concentrations in urine[1].

GFB-8438 (1 mg/kg; i.v.) treatment shows the C_l, V_{SS}, and $t_{1/2}$ were 31 mL/min/kg, 1.17 L/kg, and 0.5 hours, respectively[1].

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

Animal Model:	Sprague Dawley rats (DOCA-salt rat model of FSGS)[1]
Dosage:	30 mg/kg
Administration:	s.c.; daily for 3 weeks
Result:	Significant reduction in urine protein concentrations.

Animal Model:	6-8 weeks old male SD rats[1]
Dosage:	1 mg/kg
Administration:	i.v. (Pharmacokinetic Analysis)
Result:	The C_l, V_{ss}, and $t_{1/2}$ were 31 mL/min/kg, 1.17 L/kg, and 0.5 hours, respectively.

REFERENCES

[1]. Yu M, et al.Discovery of a Potent and Selective TRPC5 Inhibitor, Efficacious in a Focal Segmental Glomerulosclerosis Model.ACS Med Chem Lett. 2019 Oct 22;10(11):1579-1585.

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