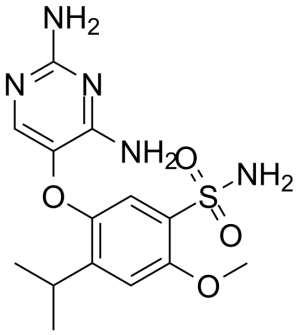
Gefapixant

Cat. No.:	HY-101588
CAS No.:	1015787-98-0
Molecular Formula:	$C_{14}H_{19}N_5O_4S$
Molecular Weight:	353.4
Target:	P2X Receptor
Pathway:	Membrane Transporter/Ion Channel
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 : 5 mg/mL (14.15 mM; ultrasonic and adjust pH to 5-6 with HCl)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8297 mL	14.1483 mL	28.2965 mL
	5 mM	0.5659 mL	2.8297 mL	5.6593 mL
	10 mM	0.2830 mL	1.4148 mL	2.8297 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% PBS
   Solubility: ≥ 2.5 mg/mL (7.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.5 mg/mL (1.41 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.5 mg/mL (1.41 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.5 mg/mL (1.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Gefapixant is an orally active and potent purinergic P2X3 receptor (P2X3R) antagonist, with IC_{50} values of ~30 nM versus recombinant hP2X3 homotrimers and 100-250 nM at hP2X2/3 heterotrimeric receptors. Gefapixant can be used for the research of chronic cough and knee osteoarthritis[1][2][3].

IC_{50} & Target

P2X3 Receptor

In Vitro	Gefapixant displays no inhibitory impact on any non-P2X3 subunit containing receptors (IC_{50} values >10,000 nM at recombinant homotrimeric hP2X1, hP2X2, hP2X4, rP2X5 and hP2X7 channels)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Gefapixant (7d bid, orally) attenuates the weight bearing laterality with complete reversal of apparent hyperalgesia at the two higher doses in a rat model of knee osteoarthritis (14d following intra-articular administration of monoiodoacetate)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Rats[2] A rodent model often employs for assessing potential for drug effect in osteoarthritis (OA) pain is based on intraarticular injection of monoiodoacetate (mIOA) into one knee joint of the rat. Progressive loss of chondrocytes leads to histological changes of the articular cartilage over subsequent weeks that resemble the changes which occur in human OA, leading to joint discomfort exemplified by a shift in the weight distribution (asymmetry) to favor the unaffected limb. To measure the effect of Gefapixant on the weight bearing laterality and apparent hyperalgesia, Gefapixant is given by intraplantar or oral administration to the rats, with different concentrations (6, 20, and 60 mg/kg) two times a day and continues up to a week[2] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Martin Nguyen A, et al. Validation of a visual analog scale for assessing cough severity in patients with chronic cough. Ther Adv Respir Dis. 2021 Jan-Dec;15:17534666211049743.

[2]. Anthony P. Ford, et al. The therapeutic promise of ATP antagonism at P2X3 receptors in respiratory and urological disorders. Front Cell Neurosci. 2013; 7: 267.

[3]. Ford AP, In pursuit of P2X3 antagonists: novel therapeutics for chronic pain and afferent sensitization. Purinergic Signal. 2012 Feb;8(Suppl 1):3-26.

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