Gefapixant

Cat. No.: HY-101588

CAS No.: 1015787-98-0

Molecular Formula: $C_{14}H_{19}N_5O_4S$

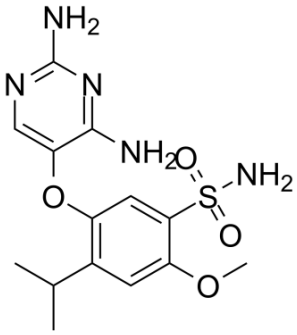
Molecular Weight: 353.4

Target: P2X Receptor

Pathway: Membrane Transporter/Ion Channel

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



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 >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.5 mg/mL (1.41 mM); Clear solution
2. 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
3. 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 (MK-7264) is an orally active P2X3 receptor (P2X3R) antagonist with IC_{50}s of ~30 nM versus recombinant hP2X3 homotrimers and 100-250 nM at hP2X2/3 heterotrimeric receptors[1].

IC_{50} & Target

IC50: ~30 nM (recombinant hP2X3 homotrimers), 100-250 nM (hP2X2/3 heterotrimeric receptors)[1].

In Vitro

The aryloxy-pyrimidinediamine, Gefapixant (AF-219) is an orally active small molecule antagonist at human P2X3-containing receptors. The IC_{50} of Gefapixant has been reported as ~30 nM versus recombinant hP2X3 homotrimers and 100-250 nM at

	hP2X2/3 heterotrimeric receptors, potencies very similar to those reported for recombinant rat receptors, and it 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	In an adjuvant-induced rthritis model in rat (7d following intraplantar administration of complete Freund's adjuvant), AF-353 produces dose-dependent antihyperalgesia in weight-bearing asymmetry and von Frey filament mechanical tests; magnitude of effect is compared with that of the NSAID naproxen. In a rat model of knee osteoarthritis (14d following intra-articular administration of monoiodoacetate), Gefapixant (7d bid, orally; right) attenuates the weight bearing laterality with complete reversal of apparent hyperalgesia at the two higher doses[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]. 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.

[2]. 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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