Zamifenacin fumarate

Cat. No.: HY-107649

CAS No.: 127308-98-9

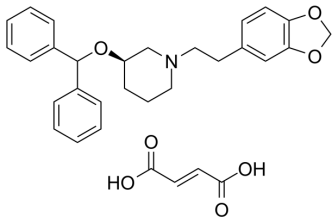
Molecular Formula: $C_{31}H_{33}NO_7$

Molecular Weight: 531.6

Target: mAChR

Pathway: GPCR/G Protein; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (188.11 mM; Need ultrasonic)
H_2O : 1 mg/mL (1.88 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Concentration / Solvent / Mass	1 mg	5 mg	10 mg
1 mM	1.8811 mL	9.4056 mL	18.8111 mL
5 mM	0.3762 mL	1.8811 mL	3.7622 mL
10 mM	0.1881 mL	0.9406 mL	1.8811 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 (3.91 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.91 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zamifenacin fumarate (UK-76654 fumarate) is a potent gut-selective muscarinic M3 receptor antagonist. Zamifenacin significantly reduces colonic motility in irritable bowel syndrome[1].

IC_{50} & Target

Muscarinic M3 receptor[1]

In Vivo

Zamifenacin exhibits moderate oral bioavailability (mouse 26%, rat 64%, dog 100%) and C_{max} (mouse 92, rat 905, dog 416 ng/mL) following oral administration (mouse 13.2, rat 20 and, dog 5 mg/kg)[2].
Zamifenacin exhibits terminal elimination half-lives (mouse 2.1, rat 6.0 and, dog 1.1 h) due to high plasma clearance (68, 35,

and 39 mL/min/kg respectively combined with large volumes of distribution (12.5, 19.0, and 3.5 L/kg respectively) following intravenous administration (mouse 5.3, rat 5.0 and, dog 1.0 mg/kg)[2].

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

Animal Model:	Male CDl mice (mean weight 23 g)[2]
Dosage:	5.3 mg/kg for i.v.; 13.2 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous administration and oral administration
Result:	Oral bioavailability (26%), C_{max} (92 ng/mL), $T_{1/2}$ (1.1 h).

Animal Model:	Male and female CD rats (mean weight 210 g)[2]
Dosage:	5.0 mg/kg for i.v.; 20 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous administration and oral administration
Result:	Oral bioavailability (64%), C_{max} (905 ng/mL), $T_{1/2}$ (6.0 h).

Animal Model:	Male and two female beagle dogs (13-16 kg)[2]
Dosage:	1.0 mg/kg for i.v.; 5 mg/kg for oral (Pharmacokinetic Analysis)
Administration:	Intravenous administration and oral administration
Result:	Oral bioavailability (100%), C_{max} (416 ng/mL), $T_{1/2}$ (1.1 h).

REFERENCES

[1]. Houghton LA, et al. Zamifenacin (UK-76, 654) a potent gut M3 selective muscarinic antagonist, reduces colonic motor activity in patients with irritable bowel syndrome. Aliment Pharmacol Ther. 1997 Jun;11(3):561-8.

[2]. Beaumont KC, et al. Pharmacokinetics and metabolism of Zamifenacin in mouse, rat, dog and man. Xenobiotica. 1996 Apr;26(4):459-71.

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