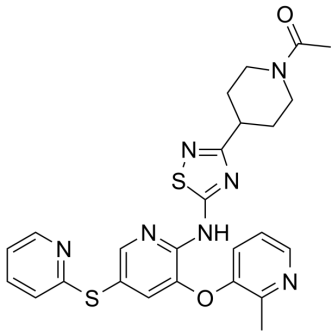
AR453588

Cat. No.:	HY-133127
CAS No.:	1065609-00-8
Molecular Formula:	$C_{25}H_{25}N_7O_2S_2$
Molecular Weight:	519.64
Target:	Glucokinase
Pathway:	Metabolic Enzyme/Protease
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 : 100 mg/mL (192.44 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9244 mL	9.6220 mL	19.2441 mL
	5 mM	0.3849 mL	1.9244 mL	3.8488 mL
	10 mM	0.1924 mL	0.9622 mL	1.9244 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: ≥ 2.5 mg/mL (4.81 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.81 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.81 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AR453588 is a potent and orally bioavailable anti-diabetic glucokinase activator, with an EC_{50} of 42 nM. AR453588 shows anti-hyperglycemic activity[1].

In Vivo

AR453588 (3-30 mg/kg; p.o) lowers post-prandial glucose in normal C57BL/6J mice[1].

AR453588 (3-30 mg/kg; p.o.; once-daily for 14 days) shows anti-hyperglycemic activity in a dose-ranging 14 day ob/ob mouse [1].

AR453588 (10 mg/kg; p.o.) treatment shows that the T_{max}, AUC_{inf}, Vss, C_{max} and F are 1.0 mL/min/kg, 4.65 h μg /mL, 1.67 μg

/mL and 60.3%, respectively[1].

AR453588 (1 mg/kg; i.v.) treatment shows that the CL, AUC_{inf}, Vss, and $t_{1/2}$ are 21.6 mL/min/kg, 0.77 h μg /mL, 0.746 L/kg and 1.28 hours, respectively[1].

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

Animal Model:	Male diabetic ob/ob mice[1]
Dosage:	3, 10, 30 mg/kg
Administration:	Orally once-daily for 14 days
Result:	Lowered the fasted blood glucose from the control animals on day 14 as well as the AUC of the OGTT (oral glucose tolerance tests).

Animal Model:	Male CD-1 mice[1]
Dosage:	10 mg/kg
Administration:	p.o. (Pharmacokinetic Analysis)
Result:	The T_{max}, AUC_{inf}, Vss, C_{max} and F were 1.0 mL/min/kg, 4.65 h μg /mL, 1.67 μg /mL and 60.3%, respectively.

REFERENCES

[1]. Hinklin RJ, et al. Discovery and preclinical development of AR453588 as an anti-diabetic glucokinase activator. Bioorg Med Chem. 2020 Jan 1;28(1):115232.

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