KR-39038

Cat. No.: HY-143248

CAS No.: 2770300-35-9

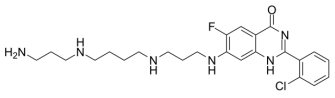
Molecular Formula: $C_{24}H_{32}ClFN_6O$

Molecular Weight: 475

Target: G Protein-coupled Receptor Kinase (GRK); HDAC

Pathway: GPCR/G Protein; Cell Cycle/DNA Damage; Epigenetics

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 115 mg/mL (242.11 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1053 mL	10.5263 mL	21.0526 mL
	5 mM	0.4211 mL	2.1053 mL	4.2105 mL
	10 mM	0.2105 mL	1.0526 mL	2.1053 mL

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

BIOLOGICAL ACTIVITY

Description

KR-39038 is an orally active and potent GRK5 (G protein-coupled receptor kinase 5) inhibitor, with an IC_{50} of 0.02 μM. KR-39038 significantly inhibits angiotensin II-induced cellular hypertrophy through suppression of HDAC5 pathway in neonatal cardiomyocytes. KR-39038 shows profound anti-hypertrophic effects and improved cardiac function. KR-39038 can be used for heart failure research[1].

IC_{50} & Target

HDAC5

In Vitro

KR-39038 (0-1.0 μM, 24 h) significantly inhibits angiotensin II-induced cellular hypertrophy and HDAC5 phosphorylation in neonatal cardiomyocytes[1].

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

Western Blot Analysis[1]

Cell Line:	Primary neonatal cardiomyocytes (isolated from S.D. rats (1-2 days old) using primary myocardial cell isolation kit)
Concentration:	0 μM, 0.03 μM, 0.1 μM, 0.3 μM, 1.0 μM

Incubation Time:	24 h
Result:	Significantly inhibited angiotensin II-induced cellular hypertrophy at a concentration of 0.1 μM and higher concentrations. Decreased angiotensin II-induced HDAC5 phosphorylation at 0.3 μM and higher concentrations.

In Vivo

KR-39038 (0-30 mg/kg, Orally, once daily for 14 days) effectively attenuates both cardiac hypertrophy and dysfunction in experimental heart failure[1].

Pharmacokinetic Parameters of KR-39038 in Sprague-Dawley rats[1].

Parameters	IV (5 mg/kg)	PO (300 mg/kg)
C_{max} (μg/mL)	NA	5.2 ± 2.8
T_{max} (h)	NA	0.7 ± 0.2
$t_{1/2}$ (h)	0.7 ± 0.04	2.3 ± 2.9
$AUC_{0-\infty}$ (μg*h/mL)	3.4 ± 1.0	8.9 ± 5.0
CL (L/h/kg)	1.6 ± 0.5	NA
Vss (L/kg)	1.2 ± 0.2	NA
F (%)		4.3 ± 2.4

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Animal Model:	C57BL/6 mice (male, 20-24 g, transverse aortic constriction)[1]
Dosage:	30 mg/kg
Administration:	Orally, once a day for 2 weeks, starting from 24 h after the operation
Result:	Showed a 43% reduction in the left ventricular weight, and significantly attenuated the development of cardiac hypertrophy.

Animal Model:	Sprague-Dawley (S.D.) rats (male, 380-420 g, coronary artery ligation)[1]
Dosage:	10 mg/kg, 30 mg/kg
Administration:	Orally, once a day for 12 weeks, starting from 24 h after surgery
Result:	Showed significant preservation of cardiac function and attenuation of myocardial remodeling in a rat model of chronic heart failure following coronary artery ligation.

Animal Model:	Sprague-Dawley (S.D.) rats[1]
Dosage:	5 mg/kg (IV), 300 mg/kg (Orally)

Administration:	IV or Orally, single (Pharmacokinetic Analysis)
Result:	The AUC_{∞} values after intravenous injection with 10 mg/kg and oral administration of 300 mg/kg of KR-39038 were 3.4 ± 1.0 and 8.9 ± 5.0 μg·h/mL, respectively, resulting in 4.3% bioavailability.

REFERENCES

[1]. Lee JH, et al. KR-39038, a Novel GRK5 Inhibitor, Attenuates Cardiac Hypertrophy and Improves Cardiac Function in Heart Failure. Biomol Ther (Seoul). 2020 Sep 1;28(5):482-489.

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