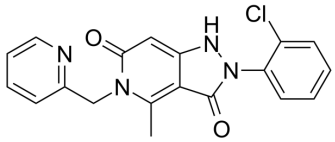
GKT136901

Cat. No.:	HY-101499
CAS No.:	955272-06-7
Molecular Formula:	$C_{19}H_{15}ClN_4O_2$
Molecular Weight:	366.8
Target:	NADPH Oxidase
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 : 33.33 mg/mL (90.87 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7263 mL	13.6314 mL	27.2628 mL
5 mM	0.5453 mL	2.7263 mL	5.4526 mL
10 mM	0.2726 mL	1.3631 mL	2.7263 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 (6.82 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GKT136901 is a potent, selective and orally active inhibitor of NADPH oxidase (NOX1/4), with K_is of 160 and 165 nM, respectively. GKT136901 is also a selective and direct scavenger of peroxynitrite. GKT136901 can be used for the research of diabetic nephropathy, stroke, and neurodegeneration. GKT136901 also has anti-inflammatory activity[1][2][3].

IC_{50} & Target

Ki: 160 (NOX1), 165 (NOX4)[1]

In Vitro

GKT136901 (10 μM; 30 min) significantly attenuates high-D-glucose-induced increase in $O_2^{\bullet-}$ production and in H_2O_2 generation in MPT cells[4].

GKT136901 (10 μM; 30 min) abolishes the effect of high D-glucose on p38MAP kinase activation in MPT cells[4].

GKT136901 (10 μM; 2 h) attenuates methamphetamine (METH)-induced oxidative stress in HBMECs[5].

GKT136901 (10 μM; 2 h) protects HBMECs against METH-induced blood-brain barrier (BBB) dysfunction[5].

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

In Vivo

GKT136901 (30-90 mg/kg; daily p.o. for 16 weeks) has renoprotective effects in a mouse model of Type 2 diabetes[6].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male db/db and db/m mice (8 weeks)[6]
Dosage:	30, 90 mg/kg
Administration:	Daily p.o. for 16 weeks
Result:	Reduced albuminuria, thiobarbituric acid-reacting substances (TBARS) and renal ERK1/2 phosphorylation and preserved renal structure in diabetic mice. Had no effect on plasma glucose, BP (blood pressure), and body weight.

CUSTOMER VALIDATION

- Int J Mol Sci. 2023 Nov 13;24(22):16260.

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REFERENCES

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[2]. Teixeira G, et, al. Therapeutic potential of NADPH oxidase 1/4 inhibitors. Br J Pharmacol. 2017 Jun;174(12):1647-1669.

[3]. Schildknecht S, et, al. The NOX1/4 inhibitor GKT136901 as selective and direct scavenger of peroxynitrite. Curr Med Chem. 2014;21(3):365-76.

[4]. Sedeek M, et, al. Critical role of Nox4-based NADPH oxidase in glucose-induced oxidative stress in the kidney: implications in type 2 diabetic nephropathy. Am J Physiol Renal Physiol. 2010 Dec;299(6):F1348-58.

[5]. Hwang JS, et, al. GKT136901 protects primary human brain microvascular endothelial cells against methamphetamine-induced blood-brain barrier dysfunction. Life Sci. 2020 Sep 1;256:117917.

[6]. Sedeek M, et, al. Renoprotective effects of a novel Nox1/4 inhibitor in a mouse model of Type 2 diabetes. Clin Sci (Lond). 2013 Feb;124(3):191-202.

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