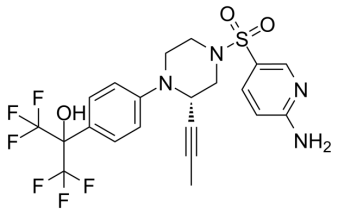
AMG-3969

Cat. No.:	HY-12411
CAS No.:	1361224-53-4
Molecular Formula:	$C_{21}H_{20}F_6N_4O_3S$
Molecular Weight:	522.46
Target:	Glucokinase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (191.40 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9140 mL	9.5701 mL	19.1402 mL
5 mM	0.3828 mL	1.9140 mL	3.8280 mL
10 mM	0.1914 mL	0.9570 mL	1.9140 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 (4.79 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.79 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.79 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	AMG-3969 is a potent glucokinase-glucokinase regulatory protein interaction (GK-GKRP) disruptor with an IC_{50} of 4 nM.
IC_{50} & Target	IC50: 4 nM (GK-GKRP)[1]
In Vitro	AMG-3969 exhibits potent cellular activity with an EC_{50} of 0.202 μM and IC_{50} of 4 nM[1], [2]. It potently reverses the inhibitory effect of GKRP on GK activity and promotes GK translocation in vitro (isolated hepatocytes)[3].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AMG-3969 has good in vivo pharmacokinetic (PK) properties in rats (75%) and significantly lowers blood glucose levels in a dose-dependent manner db/db mice[1]. AMG-3969 (100 mg/kg) demonstrates significant reductions in blood glucose with robust efficacy (56% reduction) observed at the 8 h time point[2]. AMG-3969 demonstrates dose-dependent efficacy in three models of diabetes: diet induced obese (DIO), ob/ob and db/db mice; however,AMG-3969 is ineffective in lowering blood glucose in normoglycaemic C57BL/6 (B6) mice. AMG-3969 is highly effective in promoting carbohydrate substrate. AMG-3969 exhibits extended changes to carbohydrate oxidation as observed by increased respiratory exchange ratio into the next night and day after a single dose[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice: Diabetic db/db mice are used in the study. At 8:00 AM, mice are bled via retro-orbital sinus puncture and blood glucose values are determined and used to randomize the animals in which their averages are similar, and only mice with blood glucose ranges between 300 and 500 mg/dL are included. Vehicle (2% hydroxypropyl methycellulose, 1% Tween 80, pH 2.2 adjusted with MSA) or AMG-3969 (10, 30, 100 mg/kg) are gavaged at 9:00 AM. Blood glucose is measured at 4, 6, or 8 h posttreatment. At each time point, a 15 µL sample of whole blood is analyzed for drug exposure[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2021 Nov 10;12(1):6486.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Lloyd DJ, et al. Antidiabetic effects of glucokinase regulatory protein small-molecule disruptors. Nature. 2013 Dec 19;504(7480):437-40.

[2]. Nishimura N, et al. Small molecule disruptors of the glucokinase-glucokinase regulatory protein interaction: 3. Structure-activity relationships within the aryl carbinol region of the N-arylsulfonamido-N'-arylpiperazine series. J Med Chem. 2014 Apr 10;5

[3]. St Jean DJ Jr, et al. Small molecule disruptors of the glucokinase-glucokinase regulatory protein interaction: 2. Leveraging structure-based drug design to identify analogues with improved pharmacokinetic profiles. J Med Chem. 2014 Jan 23;57(2):325-38.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA