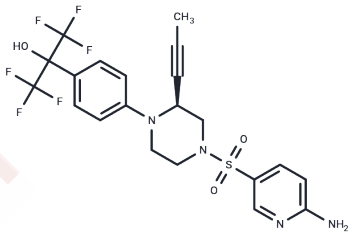
Data Sheet (Cat.No.TQ0055)

TargetMol

AMG-3969

Chemical Properties



CAS No. : 1361224-53-4

Formula: C21H20F6N4O3S

Molecular Weight: 522.46

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	AMG-3969 is an effective glucokinase-glucokinase regulatory protein interaction (GK-GKRP) disruptor (IC50: 4 nM).
Targets(IC50)	Glucokinase
In vitro	AMG-3969 demonstrates significant cellular activity (EC50: 0.202 μM; IC50: 4 nM) [1,2], reversing GKRP's inhibitory effect on GK activity and promoting GK translocation in vitro (isolated hepatocytes) [3].
In vivo	AMG-3969, at a dosage of 100 mg/kg, significantly lowers blood glucose levels, achieving a 56% reduction eight hours post-administration [1]. This compound effectively normalizes blood glucose levels across various rodent diabetes models and exhibits favorable in vivo pharmacokinetic properties in rats (75%). It also progressively reduces blood glucose levels in db/db mice in a dose-responsive manner [2]. Demonstrating efficacy across three diabetes models—diet-induced obese (DIO), ob/ob, and db/db mice, AMG-3969, however, does not impact blood glucose in normoglycemic C57BL/6 (B6) mice. Additionally, it is highly efficient in enhancing carbohydrate metabolism, leading to noticeable prolonged effects on carbohydrate oxidation, evident from the increased respiratory exchange ratio observed up to the following day post a single administration [3].
Animal Research	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 methylcellulose, 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 [1].

Solubility Information

Solubility	DMSO: 100 mg/mL (191.4 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4 mg/mL (7.66 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.914 mL	9.5701 mL	19.1402 mL
5 mM	0.3828 mL	1.914 mL	3.828 mL
10 mM	0.1914 mL	0.957 mL	1.914 mL
50 mM	0.0383 mL	0.1914 mL	0.3828 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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;57(7):3094-116.

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

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.