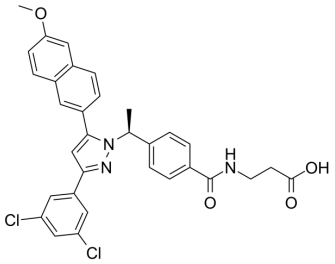
MK 0893

Cat. No.:	HY-50663
CAS No.:	870823-12-4
Molecular Formula:	$C_{32}H_{27}Cl_2N_3O_4$
Molecular Weight:	588.48
Target:	GCGR
Pathway:	GPCR/G Protein
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 : 33.33 mg/mL (56.64 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6993 mL	8.4965 mL	16.9929 mL
	5 mM	0.3399 mL	1.6993 mL	3.3986 mL
	10 mM	0.1699 mL	0.8496 mL	1.6993 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MK 0893 is a potent and selective glucagon receptor antagonist with an IC_{50} of 6.6 nM.

IC_{50} & Target

IC50: 6.6 nM (glucagon receptor)

In Vitro

MK 0893 is selective for glucagon receptor relative to other family B GPCRs, showing IC_{50} values of 1020 nM for GIPR, 9200 nM for PAC1, and >10000 nM for GLP-1R, VPAC1, and VPAC2. MK 0893 is active against the rhesus monkey GCGR, showing an IC_{50} of 56 nM in a cAMP assay with CHO cells expressing the rhesus GCGR[1].

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

In Vivo

MK 0893 blunts glucagon-induced glucose elevation in hGCGR mice and rhesus monkeys. It also lowers ambient glucose levels in both acute and chronic mouse models: in hGCGR ob/ob mice it reduces glucose (AUC 0-6 h) by 32% and 39% at 3 and 10 mpk single doses, respectively. In hGCGR mice on a high fat diet, MK 0893 at 3, and 10 mpk po in feed lowers blood

glucose levels by 89% and 94% at day 10, respectively, relative to the difference between the vehicle control and lean hGCGR mice[1].

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PROTOCOL

Cell Assay [1]

CHO hGCGR cells are grown in Iscove's Modified Dulbecco's Medium (IMDM), 10% FBS, 1 mM l-glutamine, penicillin-streptomycin (100 μ/mL), and 500μg G418/mL for 3-4 days before harvesting using Enzyme-Free Dissociation Media (EFDM). The cells are centrifuged at low speed and resuspended in stimulation buffer. Compounds are diluted from DMSO stocks and added to the assay at a final concentration of 5% DMSO. Cells are preincubated with compound or DMSO controls for 30 min. Glucagon (250 pM) is added, and the samples are incubated at room temperature for an additional 30 min. The assay is terminated with the addition of the FlashPlate kit detection buffer. The assay is then incubated for an additional 3 h at room temperature, and bound radioactivity is measured using a liquid scintillation counter. cAMP levels are determined as per manufacturer's instructions. For Schild Plot analysis, aliquots of cells are preincubated with 56, 100, 178, 300, 560, and 1000 nM 9m for 30 min at room temperature prior to the addition of 0.001-1000 nM glucagon to initiate the assay. Data are analyzed using the linear and nonlinear regression analysis software GraphPad Prism, v4.

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

CUSTOMER VALIDATION

- Nat Metab. 2024 Jan 26.
- Cell Rep. 2018 Oct.
- Endocrinology. 2021 Apr 1;162(4):bqab022.
- J Biol Chem. 2019 Mar 8;294(10):3514-3531.

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REFERENCES

[1]. Xiong Y, et al. Discovery of a novel glucagon receptor antagonist N-[(4-{(1S)-1-[3-(3, 5-dichlorophenyl)-5-(6-methoxynaphthalen-2-yl)-1H-pyrazol-1-yl]ethyl}phenyl)carbonyl]-β-alanine (MK-0893) for the treatment of type II diabetes.J Med Chem. 2012 Jul 12;

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