上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

# 产品名称：N-[4-[(1S)-1-[3-(3,5-二氯苯基)-5-(6-甲氧基-2-萘基)-1H-吡唑-1-基]乙基]苯甲酰]-BETA-丙氨酸
# 产品别名：MK 0893

## 生物活性：

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| **Description** | MK 0893 is a potent, selective glucagon receptor antagonist with $IC_{50}$ of 6.6 nM, and > 200 fold selectivity against GIPR, PAC1, GLP-1R, VPAC1 and VPAC2. |
| **$IC_{50}$ & Target** | IC50: 6.6 nM (glucagon receptor) |
| **In Vitro** | MK 0893 is selective for glucagon receptor relative to other family B GPCRs, showing IC50 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 IC50 of 56 nM in a cAMP assay with CHO cells expressing the rhesus GCGR[1]. |
| **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]. |

**Solvent&Solubility**

***In Vitro:***

**DMSO : ≥ 33.33 mg/mL (56.64 mM)**

**$H_2O$ : < 0.1 mg/mL** (insoluble)

* "≥" means soluble, but saturation unknown.

**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 |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

***In Vivo:***

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (4.25 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.25 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

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| | 2.请依序添加每种溶剂： 10% DMSO →90% corn oil<br>Solubility: ≥ 2.5 mg/mL (4.25 mM); Clear solution<br>此方案可获得 ≥ 2.5 mg/mL (4.25 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **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; |
| **实验参考：** | |
| **Cell Assay** | 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. |
| **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; |