产品名称：氢溴酸替格列汀

产品别名：**Teneligliptin hydrobromide； MP-513 hydrobromide**

生物活性：

Description	Teneligliptin (MP-513) hydrobromide is a potent chemotype prolylthiazolidine-based DPP-4 inhibitor, which competitively inhibits human plasma, rat plasma, and human recombinant DPP-4 in vitro, with IC_{50}s of approximately 1 nM.
IC_{50} & Target	IC50: 1 nM (DPP4)[1]
In Vitro	Teneligliptin (MP-513) inhibits all these DPP-4 enzymes in a concentration-dependent manner. The IC_{50}s of Teneligliptin for rhDPP-4, human plasma, and rat plasma are 0.889, 1.75, and 1.35 nM, respectively. A study of enzyme inhibition kinetics is conducted for Teneligliptin (MP-513) using Gly-Pro-MCA as the substrate and rhDPP-4 as the enzyme source. Plots based on the Michaelis-Menten equation reveals that Teneligliptin (MP-513) inhibits DPP-4 in a substrate-competitivemanner; the residual sum of squares for competitive and non-competitive models is 0.162 and 0.192, respectively. K_i, K_m, and V_{max} values are 0.406 nM, 24 μM, and 6.06 nmol/min, respectively. Teneligliptin (MP-513) inhibits the degradation of GLP-1(7-36)amide with an IC_{50} of 2.92 nM[1].
In Vivo	Oral administration of Teneligliptin (MP-513) in Wistar rats results in the inhibition of plasma DPP-4 with an ED50 of 0.41 mg/kg. Plasma DPP-4 inhibition is sustained even at 24 h after administration of Teneligliptin (MP-513). An oral carbohydrate-loading test in Zucker fatty rats shows that Teneligliptin (MP-513) at ≥0.1 mg/kg increases the maximum increase in plasmaglucagon-like peptide-1 and insulin levels, and reduces glucose excursions. This effect is observed over 12 h after a dose of 1 mg/kg. An oral fat-loading test in Zucker fatty rats also shows that Teneligliptin (MP-513) at 1 mg/kg reduces triglyceride and free fatty acid excursions. In Zucker fatty rats, repeated administration of Teneligliptin (MP-513) for two weeks reduces glucose excursions in the oral carbohydrate-loading test and decreased the plasma levels of triglycerides and free fatty acids under non-fasting conditions. Oral administration of Teneligliptin (MP-513) inhibits plasma DPP-4 in rats in a dose-dependent manner. The ED50 value for Teneligliptin (MP-513) is calculated to be 0.41 mg/kg, while those for Sitagliptin and Vildagliptin, 27.3 and 12.8 mg/kg, respectively[1]. Teneligliptin (MP-513) improves the histopathological appearance of the liver and decreases intrahepatic triglyceride levels in an NAFLD model mouse, which is associated with downregulation of hepatic lipogenesis-related genes due to AMPK activation[2].

In Vitro:

H_2O : ≥ 200 mg/mL (318.04 mM)

DMSO : ≥ 100 mg/mL (159.02 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5902 mL	7.9509 mL	15.9018 mL
5 mM	0.3180 mL	1.5902 mL	3.1804 mL
10 mM	0.1590 mL	0.7951 mL	1.5902 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:

Solvent&Solubility	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 (3.98 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.98 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。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (3.98 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.98 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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (3.98 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.98 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。 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]. Fukuda-Tsuru S, et al. A novel, potent, and long-lasting dipeptidyl peptidase-4 inhibitor, teneligliptin, improves postprandial hyperglycemia and dyslipidemia after single and repeated administrations. Eur J Pharmacol. 2012 Dec 5;696(1-3):194-202. [2]. Ideta T, et al. The Dipeptidyl Peptidase-4 Inhibitor Teneligliptin Attenuates Hepatic Lipogenesis via AMPK Activation in Non-Alcoholic Fatty Liver Disease Model Mice. Int J Mol Sci. 2015 Dec 8;16(12):29207-18.

实验参考：

Animal Administration	Rats[1] Nine-week-old Wistar rats are randomly divided into 13 groups of eight animals each based on body weight (306.2-374.2 g) and plasma DPP-4 activity. Teneligliptin (MP-513) is orally administered to four groups (0.01, 0.1, 1 and 10 mg/2 mL/kg). Sitagliptin and vildagliptin is orally administered to each four groups (0.1, 1, 10 and 100 mg/kg). Vehicle (0.5% hydroxypropyl methylcellulose) is orally administered to one group. Blood samples are collected from the tail vein with heparinized capillary tubes at 0 h (pre dose) and 0.5, 1, 2, 3, 6, 9, 12, and 24 h (post dose) and centrifuged at 1800 g for 15 min at 4°C. Separated plasma is used for the measurement of DPP-4 activity. For dose-response curve using the maximum effect in each dose, the dose of the inhibitors which produce half of the maximum effect; ED_{50} are calculated. Mice[2] Monosodium glutamate (MSG) is administered into the neonatal ICR mice at birth as a single-dose subcutaneous injection (4 mg/g body weight). Among these mice, males are divided into two groups at 4 weeks of age: the MSG/HFD group (n=6, Group 1) and the MSG/HFD/Teneligliptin

	(MP-513)-treated group (n=6, Group 2). The mice in Group 2 are administered Teneligliptin (MP-513) (30 mg/kg per day) in the drinking water from 4 weeks of age. The treatment dose of Teneligliptin (MP-513) is determined according to the data from the animal experiments in the drug development process. Although the dose is relatively higher than that for humans in clinical practice, no notable adverse effect is observed in the treatment with the dose for the experimental animal in the process. Both groups are fed HFD from 4-14 weeks of age. At the termination of the experiment (14 weeks of age), all animals are sacrificed by CO_2 asphyxiation to analyze hepatic histopathology.
References	[1]. Fukuda-Tsuru S, et al. A novel, potent, and long-lasting dipeptidyl peptidase-4 inhibitor, teneligliptin, improves postprandial hyperglycemia and dyslipidemia after single and repeated administrations. Eur J Pharmacol. 2012 Dec 5;696(1-3):194-202. [2]. Ideta T, et al. The Dipeptidyl Peptidase-4 Inhibitor Teneligliptin Attenuates Hepatic Lipogenesis via AMPK Activation in Non-Alcoholic Fatty Liver Disease Model Mice. Int J Mol Sci. 2015 Dec 8;16(12):29207-18.