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：Dihexa
产品别名：PNB-0408; N-hexanoic-Try-Ile-(6)-amino hexanoic amide; Hexanoyl-Tyr-Ile-Ahx-NH2

生物活性：

Description	Dihexa, an oligopeptide drug, is an orally active and blood-brain barrier-permeable angiotensin IV analog. Dihexa binds to hepatocyte growth factor (HGF) with high affinity (K_d=65 pM) and potentiates its activity at its receptor, c-Met. Dihexa exhibits excellent antidementia activity and improves cognitive function in animal models. Dihexa may have therapeutic potential as a treatment Alzheimer's disease[1][2].
IC_{50} & Target	Kd: 65 pM (HGF)[1]
In Vitro	Dihexa binds with high affinity to HGF and both dihexa and its parent compound Norleucine 1-AngIV induce c-Met phosphorylation in the presence of subthreshold concentrations of HGF and augment HGF-dependent cell scattering. Further, dihexa and Nle1-AngIV induce hippocampal spinogenesis and synaptogenesis similar to HGF itself. Dihexa effectively inhibits HGF dimerization at 1 μM. While dihexa at 1 nM and 10 pM alone does not activate c-Met, it markedly augments the capacity of HGF at 1.25 and 2.5 ng/mL to activate c-Met[1].
In Vivo	Dihexa has a long circulating half-life. Dihexa exhibits procognitive activity. Dihexa reverses scopolamine-dependent spatial learning deficits. It improves spatial learning in aged rats. Dihexa induces spinogenesis in cultured hippocampal neurons[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 100 mg/mL** (**198.15 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9815 mL	9.9077 mL	19.8153 mL
	5 mM	0.3963 mL	1.9815 mL	3.9631 mL
	10 mM	0.1982 mL	0.9908 mL	1.9815 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 (4.95 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.95 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% corn oil Solubility: ≥ 2.5 mg/mL (4.95 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.95 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]. Benoist CC, et al. The procognitive and synaptogenic effects of angiotensin IV-derived peptides are dependent on activation of the hepatocyte growth factor/c-met system. J Pharmacol Exp Ther. 2014 Nov;351(2):390-402. [2]. McCoy AT, et al. Evaluation of metabolically stabilized angiotensin IV analogs as procognitive/antidementia agents. J Pharmacol Exp Ther. 2013 Jan;344(1):141-54.

实验参考：

Animal Administration	Rats: Serial dilutions of dihexa in 50% DMSO or water (for dilutions of 50 μg/mL or less) are prepared from the stock used to dose the animals to be used for preparation of a standard curve. 10 μL of each serial dilution is then added to 90 μL of blank plasma for final concentrations of 0.01, 0.02, 0.05, 0.1, 0.2, 1, 10, 20, 50, and 100 μg/mL. 80 μL of each plasma sample is transferred to previously prepared tubes containing 240 μL of ice-cold acetonitrile and vortexed vigorously. 10 μL of isotonic saline containing 100 μg/mL Nle-YI-(6) aminohexanoic amide as an internal standard is added to each sample on ice. The standard-curve plasma samples are then stored at −20°C and further processed alongside the pharmacokinetic study samples[2].
References	[1]. Benoist CC, et al. The procognitive and synaptogenic effects of angiotensin IV-derived peptides are dependent on activation of the hepatocyte growth factor/c-met system. J Pharmacol Exp Ther. 2014 Nov;351(2):390-402. [2]. McCoy AT, et al. Evaluation of metabolically stabilized angiotensin IV analogs as procognitive/antidementia agents. J Pharmacol Exp Ther. 2013 Jan;344(1):141-54.