Dihexa

Cat. No.: HY-16969

CAS No.: 1401708-83-5

Molecular Formula: $C_{27}H_{44}N_4O_5$

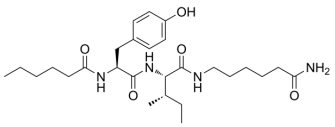
Molecular Weight: 504.66

Target: c-Met/HGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



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

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.95 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.95 mM); Clear solution

BIOLOGICAL ACTIVITY

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

PROTOCOL

Animal Administration [2]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Chemosphere. 2023 Jan:310:136924.
- Sci Total Environ. 2020 Jul 10;725:138433.
- Stem Cell Res Ther. 2020 Sep 11;11(1):393.
- Brain Sci. 2021 Nov 11;11(11):1487.
- Methods Mol Biol. 2022;2429:127-142.

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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.

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