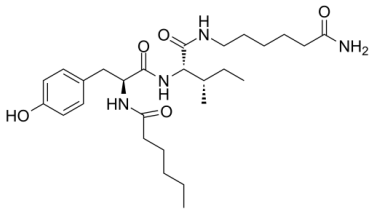
Data Sheet

Product Name:	Dihexa
Cat. No.:	CS-6864
CAS No.:	1401708-83-5
Molecular Formula:	C27H44N4O5
Molecular Weight:	504.66
Target:	c-Met/HGFR
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 100 mg/mL (198.15 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

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]. IC50 & 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].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: Dihexa is dissolved in 75% DMSO.[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].

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.

CAIndexNames:

L-Isoleucinamide, N-(1-oxohexyl)-L-tyrosyl-N-(6-amino-6-oxohexyl)-

SMILES:

OC1=CC=C(C[C@H](NC(CCCCC)=O)C(N[C@H](C(NCCCCCC(N)=O)=O)[C@@H](C)CC)=O)C=C1

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA