

Product Data Sheet

Product Name: [Leu5]-Enkephalin

Cat. No.: GC11236

Chemical Properties

Cas. No. 58822-25-6

Chemical Name (2S,5R,14S)-14-amino-5-benzyl-15-(4-hydroxyphenyl)-2-isobutyl-4,7,10,13-tetraoxo-3,6,9,12-tetraazapentadecan-1-oic acid

SMILES O=C([C@@H](CC1=CC=CC=C1)NC(CNC(CNC([C@H](CC(C=C2)=CC=C2O)N)=O)=O)=O)N[C@H](C(O)=O)CC(C)C

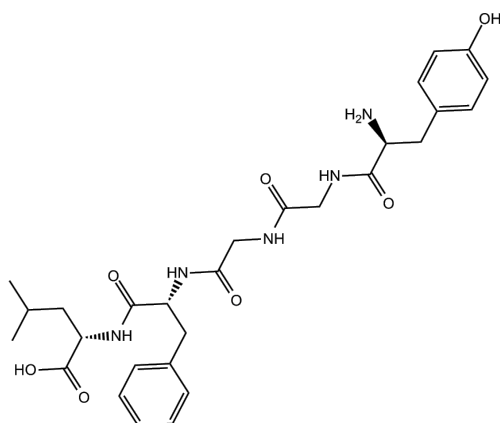
Formula $C_{28}H_{37}N_5O_7$ M.Wt 555.63

Solubility $\geq 55.6\text{mg/mL}$ in DMSO Storage Desiccate at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines HaCaT cells

Caution: Product has not been fully validated for medical applications. For research use only.

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Cells were plated in six-well plates and grown to confluence at 37°C. A scratch wound was created by scraping the cell monolayer with a P100 pipet tip. Cells Preparation Method were washed once and incubated with 2mL of growth media containing [Leu5]-Enkephalin (5-50µM). After 21h, images were acquired immediately using an AxioObserver FL microscope at ×10 magnification.

Reaction Conditions 5, 10, 20, and 50µM; 21h

Applications All the doses tested showed positive wound healing effect with 20µM of [Leu5]-Enkephalin being most remarkable. HaCaT cells migrated steadily across the wound from both sides, moving as an orderly sheet of cells with a smooth leading edge. Cell movement was significantly accelerated by treatment with [Leu5]-Enkephalin in a time dependent manner.

Animal experiment [2]:

Animal models Pathogen-free adult male ddY-strain mice

Preparation Method Intrathecal i.t. injection of [Leu5]-Enkephalin with phosphoramidon (2nM) and bestatin (0.25nM) in mice. The duration of scratching, biting and licking response induced by [Leu5]-Enkephalin (1fM) in combination with phosphoramidon and bestatin was measured every 5min for the 30min period starting immediately after i.t. injection.

Dosage form 1fM; 5µL; i.t.

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Applications The nociceptive responses induced by i.t. combined injection of [Leu5]-Enkephalin with peptidase inhibitors peaked at 10-15min and declined progressively until cessation at 30min post-i.t. injection.

References:

- [1] YANG D J, LEE K S, KO C M, et al. Leucine-enkephalin promotes wound repair through the regulation of hemidesmosome dynamics and matrix metalloprotease[J]. *Peptides*, 2016, 76: 57-64.
- [2] KOMATSU T, KATSUYAMA S, MIZOGUCHI H, et al. Spinal ERK2 activation through δ_2 -opioid receptors contributes to nociceptive behavior induced by intrathecal injection of leucine-enkephalin[J]. *Peptides*, 2014, 54: 131-139.

Background

[Leu5]-Enkephalin is an endogenous δ -opioid receptor agonist that modulates pain perception and emotion by binding to opioid receptors^[1,2]. [Leu5]-Enkephalin is commonly used in the development of novel analgesic drugs and in the treatment and research of neurodegenerative diseases^[3,4].

In vitro, [Leu5]-Enkephalin (5-50 μ M) treatment of human immortalized keratinocyte HaCaT cells for 21h significantly promoted cell migration and scratch wound closure. [Leu5]-Enkephalin (20 μ M) treatment of HaCaT cells for 24h significantly up-regulated the gene expression levels of matrix metalloproteinases MMP-2 and MMP-9^[5]. [Leu5]-Enkephalin (50 μ g/mL) treatment of the scallop *Chlamys farreri* haemolymph for 1h significantly increased catalase (CAT) activity and glutathione (GSH) levels in both haemocyte lysate supernatant (intracellular) and plasma supernatant (extracellular)^[6].

In vivo, [Leu5]-Enkephalin (1mg/kg) administered via subcutaneous injection in a mouse model of colorectal distension-induced visceral pain significantly reduced the visceromotor response elicited by 60mmHg pressure stimulation^[7]. [Leu5]-Enkephalin (1fM; 5 μ L) co-administered intrathecally with the peptidase inhibitors phosphoramidon (2nM) and bestatin (0.25nM) in ddY-strain mice induced characteristic nociceptive behaviors (scratching, biting, licking), which peaked at 10-15min and gradually subsided within 30min^[8].

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References:

- [1] HOHENWARTER L, PUILL E, ROUHOLLAHI E, et al. A Novel Leu-Enkephalin Prodrug Produces Pain-Relieving and Antidepressant Effects[J]. Molecular Pharmaceutics, 2024, 21(2): 688-703.
- [2] CULLEN J M, CASCELLA M. Physiology, enkephalin[J]. 2020.
- [3] MIURA M, YOSHIKAWA M, WATANABE M, et al. Increase in antinociceptive effect of [leu5] enkephalin after intrathecal administration of mixture of three peptidase inhibitors[J]. Tokai Journal of Experimental and Clinical Medicine, 2013, 38(2): 62-70.
- [4] VISWANADHAM K K D R, BÖTTGER R, HOHENWARTER L, et al. An effective and safe enkephalin analog for antinociception[J]. Pharmaceutics, 2021, 13(7): 927.
- [5] YANG D J, LEE K S, KO C M, et al. Leucine-enkephalin promotes wound repair through the regulation of hemidesmosome dynamics and matrix metalloprotease[J]. Peptides, 2016, 76: 57-64.
- [6] LIU D. Effects of Leucine-enkephalin on catalase activity and glutathione level in haemolymph of the scallop Chlamys farreri[J]. International Journal of Peptide Research and Therapeutics, 2008, 14(1): 16-20.
- [7] FABISIAK A, SOBOCIŃSKA M, KAMYSZ E, et al. Antinociceptive potency of enkephalins and enkephalinase inhibitors in the mouse model of colorectal distension—proof-of-concept[J]. Chemical Biology & Drug Design, 2018, 92(1): 1387-1392.
- [8] KOMATSU T, KATSUYAMA S, MIZOGUCHI H, et al. Spinal ERK2 activation through δ_2 -opioid receptors contributes to nociceptive behavior induced by intrathecal injection of leucine-enkephalin[J]. Peptides, 2014, 54: 131-139.

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