Product Data Sheet

Product Name: DPDPE
Cat. No.: GC10333

Chemical Properties

Cas. No.	88373-73-3		
Chemical Name	(4S,7R,13R)-13-((R)-2-amino-3-(4-hydroxyphenyl)propanamido)-7-benzyl-3,3,14,14-tetramethyl-6,9,12-trioxo-1,2-dithia-5,8,11-triazacyclotetradecane-4-carboxylic acid		
SMILES	O=C1NCC(N[C@H](CC2=CC=CC=C2)C(N[C@@H](C(O)=O)C(C)(C)SSC(C)(C)[C@@H]1NC([C@@H](CC(C=C3)=CC=C3O)N)=O)=O)=O		
Formula	$C_{30}H_{39}N_5O_7S_2$	M.Wt	645.79
Solubility	10mg/mL in Water	Storage	Desiccate at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	DPDPE		

Protocol

Cell experiment [1]:

Cell lines	CHO cells stably expressing the DOR (CHO/DOR)
Preparation Method	Serum-starved CHO/DOR cells were incubated for 5-30min with 100nM DPDPE. Zero time samples were treated with vehicle. Cell extracts were analyzed for the levels of phosphoGSK-3b (pGSK), total GSK-3b (GSK) and actin.
Reaction Conditions	100nM; 5-30min

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Applications	Treatment of CHO/DOR cells with DPDPE (100nM) caused a rapid increase in phospho-Ser9-GSK-3β levels, which was significant after 5min, peaked at 10min and remained above basal levels up to 30min.

Animal experiment [2]:

Animal models	Sprague Dawley rats
Preparation Method	Rats received intrathecal injections of DPDPE (100nM; 10μL) 10min before hindpaw compression. Rats were anesthetized with sodium pentobarbital, one of the hindpaws was positioned perpendicularly across the jaws of a 6 inch mosquito forceps with nonserrated jaws, and the jaws were closed to the first click of the hemostat ratchet. Compression was applied for 60s. Five minutes after compression, the rats were fixed by aortal perfusion, and the spinal cords were harvested for NK1R immunocytochemistry.
Dosage form	100nM; 10μL; i.t.
Applications	DPDPE treatment significantly inhibited NK1R internalization in the dorsal horn I layer of the spinal cord induced by hind claw compression injury.

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References:
[1] OLIANAS M C, DEDONI S, ONALI P. Signaling pathways mediating phosphorylation and inactivation of glycogen synthase kinase-3β by the recombinant human δ-opioid receptor stably expressed in Chinese hamster ovary cells[J]. Neuropharmacology, 2011, 60(7-8): 1326-1336.
[2] KONDO I, MARVIZON J C G, SONG B, et al. Inhibition by spinal μ- and δ-opioid agonists of afferent-evoked substance P release[J]. Journal of Neuroscience, 2005, 25(14): 3651-3660.

Background

DPDPE is a selective and anticonvulsant δ-opioid receptor (DOR) agonist[1]. DOR is a G protein-coupled receptor (GPCR) primarily distributed in the central nervous system, which mediates various physiological effects such as analgesia and antidepressant actions of both endogenous enkephalins and exogenous ligands[2]. DPDPE is commonly used in studies involving opioid receptor signaling, pain pathways, and addiction mechanisms[3].

In vitro, treatment of HEK293 cells overexpressing or with knocked-down GRK2 with DPDPE (2μM) for 30min showed that GRK2 overexpression enhanced internalization and subsequent recycling of the wild-type receptor, whereas GRK2 knockdown inhibited these processes[4]. Pretreatment of HEK293 cells with DPDPE (1μM) for 60min induced only mild DOR desensitization, which was significantly enhanced in the presence of monensin[5]. Treatment of CHO cells stably expressing human DOR (CHO/DOR) with

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DPDPE (100nM) for 5-30min rapidly and significantly induced phosphorylation of glycogen synthase kinase-3β (GSK-3β) at Ser9, accompanied by a marked inhibition (~35%) of kinase activity[6].

In vivo, subcutaneous injection of DPDPE (0.5, 1, 3, 5mg/kg) in streptozotocin (STZ)-induced diabetic neuropathic mice produced dose-dependent inhibition of mechanical allodynia, thermal hyperalgesia, and thermal allodynia 30min after administration[7]. In Sprague Dawley rats, intrathecal pretreatment with DPDPE (100nM; 10μL) 10min before hindpaw compression significantly inhibited noxious stimulation-induced neurokinin 1 receptor (NK1R) internalization in lamina I of the spinal dorsal horn[8].

References:

[1] TORTELLA F C, ECHEVARRIA E, ROBLES L, et al. Anticonvulsant effects of mu (DAGO) and delta (DPDPE) enkephalins in rats[J]. Peptides, 1988, 9(5): 1177-1181.
[2] NIETO M M, GUEN S L E, KIEFFER B L, et al. Physiological control of emotion-related behaviors by endogenous enkephalins involves essentially the delta opioid receptors[J]. Neuroscience, 2005, 135(2): 305-313.
[3] ABDALLAH K, GENDRON L. The delta opioid receptor in pain control[J]. Delta Opioid Receptor Pharmacology and Therapeutic Applications. 2017: 147-177.
[4] ZHANG X, WANG F, CHEN X, et al. Post-endocytic fates of δ-opioid receptor are regulated by GRK2-mediated receptor phosphorylation and distinct β-arrestin isoforms[J]. Journal of Neurochemistry, 2008, 106(2): 781-792.
[5] AUDET N, CHARFI I, MNIE-FILALI O, et al. Differential association of receptor-Gβγ complexes with β-arrestin2 determines recycling bias and potential for tolerance of delta opioid receptor agonists[J]. Journal of Neuroscience, 2012, 32(14): 4827-4840.
[6] OLIANAS M C, DEDONI S, ONALI P. Signaling pathways mediating phosphorylation and inactivation of glycogen synthase kinase-3β by the recombinant human δ-opioid receptor stably expressed in Chinese hamster ovary cells[J]. Neuropharmacology, 2011, 60(7-8): 1326-1336.
[7] CASTANY S, CARCOLÉ M, LEÁNEZ S, et al. The antinociceptive effects of a δ-opioid receptor agonist in mice with painful diabetic neuropathy: Involvement of heme oxygenase 1[J]. Neuroscience Letters, 2016, 614: 49-54.
[8] KONDO I, MARVIZON J C G, SONG B, et al. Inhibition by spinal μ- and δ-opioid agonists of afferent-evoked substance P release[J]. Journal of Neuroscience, 2005, 25(14): 3651-3660.

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