Product Data Sheet

Product Name: Phosphoramidon Disodium Salt
Cat. No.: GC16768

Chemical Properties

Cas. No.	164204-38-0		
Chemical Name	sodium (S)-3-(1H-indol-3-yl)-2-((S)-4-methyl-2-((oxido(((2S,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)phosphoryl)amino)pentanamido)propanoate		
SMILES	O=C([O-])[C@@H](NC([C@@H](NP(O[C@@H]1O[C@@H](C)[C@H](O)[C@@H](O)[C@H]1O)([O-])=O)CC(C)C)=O)CC2=CNC3=C2C=CC=C3.[Na+].[Na+]		
Formula	$C_{23}H_{34}N_3O_{10}P \cdot 2Na$	M.Wt	589.5
Solubility	14mg/mL in DMSO; 10 mg/ml in DMF; PBS (pH 7.2): 10 mg/ml	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			

Protocol

Cell experiment [1]:

Cell lines	ECs isolated from fresh porcine thoracic aortas

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Preparation method	The solubility of this compound in DMSO is >10mM. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting condition	10- 7-10-4 M
Applications	In ECs, phosphoramidon (10- 7-10-4 M) suppressed dose-dependently the apparent converting activity of the membrane fraction and suppressed the membrane fraction induced apparent conversion of big ET-l to ET-l (Endothelin-1). ET-l is a 21 amino acid peptide isolated from the culture medium of vascular endothelial cells (ECs), the secretion of ET-l from cultured ECs was abolished by the addition of phosphoramidon.

Animal experiment [2]:

Animal models	Wild-type mice, NEP/NEP2-deficient mice
Dosage form	24 μl (30 mM) once per day for 5 days.

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Application	Intranasal administration of phosphoramidon produced significantly elevated cerebral Aβ (Beta-amyloid peptide) levels in wild-type mice. In NEP/NEP2-deficient mice, Aβ levels were significantly elevated by phosphoramidon, in the absence of NEP (Aβ degrading enzymes) and NEP2, phosphoramidon clearly elevates Aβ1–40 levels relative to Aβ1–42 levels. NEP and NEP2 may be the major “NEP-like” Aβ1–42-degrading (phosphoramidon-sensitive) enzymes in the rodent brain.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1]. Matsumura Y, Ikegawa R, Hisaki K., et al. Conversion of big endothelin-1 to endothelin-1 by phosphoramidon-sensitive metalloproteinase derived from aortic endothelial cells. J Cardiovasc Pharmacol, 1991, 17 Suppl 7: S65-7.

[2] . Hanson LR., et al. Intranasal phosphoramidon increases beta-amyloid levels in wild-type and NEP/NEP2-deficient mice.J MolNeurosci. 2011 Mar;43(3):424-7.

Background

Phosphoramidon Disodium Salt is a potent inhibitor of metalloproteinase [1].

Metalloproteinase is an enzyme whose catalytic mechanism involves a metal. Most metalloproteases require zinc and some require cobalt.

Phosphoramidon Disodium Salt is a potent metalloproteinase inhibitor. In porcine aortic endothelial cells, phosphoramidon (10-4 M) inhibited immunoreactive-endothelin (IR-ET) release by 10-20% and increased IR-CTF levels. These results suggested that phosphoramidon reduced the IR-ET release through affecting the conversion of big ET-1 to ET-l [1]. In cultured endothelial cells, phosphoramidon inhibited the increase of ET-1 and C-terminal fragment (CTF) of big ET-1. However, phosphoramidon increased big ET-1 secretion [2].

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In anesthetized rats, phosphoramidon inhibited the hypertensive effect of big ET-1 [2]. In mice, phosphoramidon inhibited big ET-1 induced lethality and increased plasma IR-ET-1 through inhibition of the enzyme that converted big ET-1 to ET-1 [3].

References:

[1]. Ikegawa R, Matsumura Y, Tsukahara Y, et al. Phosphoramidon, a metalloproteinase inhibitor, suppresses the secretion of endothelin-1 from cultured endothelial cells by inhibiting a big endothelin-1 converting enzyme. Biochem Biophys Res Commun, 1990, 171(2): 669-675.
[2]. Matsumura Y, Ikegawa R, Hisaki K, et al. Conversion of big endothelin-1 to endothelin-1 by phosphoramidon-sensitive metalloproteinase derived from aortic endothelial cells. J Cardiovasc Pharmacol, 1991, 17 Suppl 7: S65-7.
[3]. Matsuura A, Okumura H, Ashizawa N, et al. Big endothelin-1-induced sudden death is inhibited by phosphoramidon in mice. Life Sci, 1992, 50(21): 1631-1638.

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