Product Data Sheet

Product Name: UK 370106
Cat. No.: GC16579

Chemical Properties

Cas. No.	230961-21-4		
Chemical Name	(3R)-3-[[(2S)-1-[[(1S)-2-methoxy-1-phenylethyl]amino]-3,3-dimethyl-1-oxobutan-2-yl]carbamoyl]-6-(3-methyl-4-phenylphenyl)hexanoic acid		
SMILES	CC1=C(C=CC(=C1)CCCC(CC(=O)O)C(=O)NC(C(=O)NC(COC)C2=CC=CC=C2)C(C)(C)C)C3=CC=CC=C3		
Formula	$C_{35}H_{44}N_2O_5$	M.Wt	572.73
Solubility	<57.27mg/ml in DMSO; <14.32mg/ml in ethanol	Storage	Store at 4°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	UK 370106		

Background

IC50: 23 nm (MMP-3)

Stromelysin-1 also known as matrix metalloproteinase-3 (MMP-3) is an enzyme that in humans is encoded by the MMP3 gene. Proteins of the matrix metalloproteinase (MMP) family are involved in the breakdown of extracellular matrix and during tissue remodeling in normal physiological processes, such as embryonic development and reproduction, as well as in disease processes, such as arthritis, and tumour metastasis (http://en.wikipedia.org/wiki/MMP-3).

In vitro: UK-370106, a potent inhibitor of MMP-3 (IC50) 23 nM) with >1200-fold weaker potency vs MMP-1, -2, -9, and -14. MMP-13, may contribute to the pathology of chronic wounds. UK-370106 potently inhibited cleavage of [3H]-fibronectin by MMP-3 (IC50) 320 nM) but not cleavage of [3H]-gelatin by either MMP-2 or -9 (up to 100 íM). UK-370106 had little effect, at MMP-3 selective concentrations, on keratinocyte migration over a collagen matrix in vitro, which is a model of the re-epithelialization process [1].

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In vivo: Following iv (rat) or topical administration to dermal wounds (rabbit), UK-370106 was cleared rapidly (t1/2=23 min) from plasma, but slowly (t1/2 ~ 3 days) from dermal tissue. In a model of chronic dermal ulcers, topical administration of UK-370106 for 6 days substantially inhibited MMP-3 ex vivo. These data suggest UK-370106 is sufficiently potent to inhibit MMP-3-mediated matrix degradation while leaving unaffected cellular migration mediated by MMPs 1, 2, and 9. These properties make UK-370106 a suitable candidate for progression to clinical trials in human chronic dermal wounds, such as venous ulcers [1].

Clinical trial: Pfizer described the discovery of UK-370106, a highly selective peptidicMMP-3 inhibitor, which was identified as a clinical candidate for the topical treatment of chronic dermal ulcers [2], however, it is now still in the preclinical stage and no clinical trial is ongoing.

References:
[1] Fray MJ, Dickinson RP, Huggins JP, Occleston NL. A potent, selective inhibitor of matrix metalloproteinase-3 for the topical treatment of chronic dermal ulcers. J Med Chem. 2003;46(16):3514-25.
[2] Whitlock GA, Dack KN, Dickinson RP, Lewis ML. A novel series of highly selective inhibitors of MMP-3. Bioorg Med Chem Lett. 2007;17(24):6750-3.

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