Product Data Sheet

Product Name: Ro 32-3555
Cat. No.: GC10805

Chemical Properties

Cas. No.	190648-49-8		
Chemical Name	(2R,3R)-3-(cyclopentylmethyl)-N-hydroxy-4-oxo-4-piperidin-1-yl-2-[(3,4,4-trimethyl-2,5-dioxoimidazolidin-1-yl)methyl]butanamide		
SMILES	CC1(C(=O)N(C(=O)N1C)CC(C(CC2CCCC2)C(=O)N3CCCCC3)C(=O)NO)C		
Formula	$C_{22}H_{35}N_4O_5$	M.Wt	436.55
Solubility	Soluble in DMSO	Storage	Store 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	Ro 32-3555		

Protocol

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Animal experiment:

Rats[1]Cipemastat (Ro 32-3555) is formulated in 5% succinylated gelatin and the volume administered to rats is 10 mL/kg, p.o. Female, AHH/R strain rats are used. Rats are anaesthetized in an isoflurane-closed system, and an intra-articular injection of 20 mL of the P. acnes/Freund's incomplete adjuvant emulsion made into the right hind knee. Twenty-eight days later the injection is repeated with the same volume and concentration of antigen to induce the monoarthritis. Animals are orally dosed once daily with either 5% succinylated gelatin as the control vehicle or Cipemastat (50 mg/kg) starting on day 1 after challenge injection. Groups of eight female AHH/R rats are used in these experiments. The animals are dosed twice daily with either 50, 25 or 10 mg/kg Cipemastat, dexamethasone (0.1 mg/kg, s.c. once/day) or vehicle control (10 mL/kg, p.o., b.i.d.). The arthritis is induced by injection into the right hind paws with 0.1 mL of a 5 mg/mL homogenized suspension of Mycobacterium tuberculosis in liquid paraffin. The volume of both the right and left hind paws is measured by water plethysmography by immersing the paw up to the hair line of the ankle. Paw volumes are determined every two or three days[1].

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References:

[1]. E J Lewis, et al. Ro 32-3555, an orally active collagenase inhibitor, prevents cartilage breakdown in vitro and in vivo. Br J Pharmacol. 1997 May; 121(3): 540–546.

Background

Cipemastat is a potent, competitive inhibitor of human collagenases 1, 2 and 3 with Kis of 3.0, 4.4 and 3.4 nM, respectively.

Cipemastat (Ro 32-3555) is a potent, competitive inhibitor of human matrix metalloproteinases. Cipemastat is selective for collagenase 1, 2 and 3 relative to related matrix metalloproteinases. Cipemastat is also a potent inhibitor of rat collagenase (IC50=44.7±3.4 nM (n=4)). In vitro cartilage degradation ± inhibited IL-1a induced cartilage degradation in vitro in a concentration-dependent manner with an IC50=60 nM. The inhibition is not mediated by a cytotoxic action on explant chondrocytes. Cipemastat, at all concentrations tested, fail to modify glucose utilization when compared to explants cultured in the presence of IL-La alone[1].

The amount of hydroxyproline in non-implanted cartilage is 119.3±4.2 nM/mg and this decreases in cartilages implanted in vehicle-dosed animals to 53.6±7.1 nM/mg over a fourteen day period. Animals administered Cipemastat orally at doses of 2.5, 5, 10 and

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25 mg/kg show statistically increased levels of implanted cartilage hydroxypro-line. Fourteen days after the second challenge injection of P. acnes, the area of cartilage most consistently affected by pannus is the lateral femoral condyle, which is the area analysed. In non-arthritic animals the mean cartilage area is 0.17±0.02 mm2 (n=5). In arthritic animals there is a significant decrease to a mean area of 0.086±0.01 mm2 (n=10). The group of animals dosed with Cipemastat (50 mg/kg, p.o.) show a significantly greater area of cartilage with a mean value of 0.126±0.012 mm2 (n=9). The pannus area in vehicle-dosed animals is 0.099±0.017 mm2 and in Cipemastat dosed animals 0.102±0.019 mm2. Adjuvant arthritis injection of adjuvant induced two phases of swelling of the injected paw in vehicle-dosed rats. The primary swelling phase occurred between days 0 to 5 and induced an increase in paw volume of 1.9±0.1 mL; the secondary phase occurrs between day 9 to 14 and there was an increase in paw swelling of 0.98±0.08 mL. The group of animals dosed with dexamethasone (0.1 mg/kg) shows a significant reduction in both primary (0.2±0.03 mL) and secondary inflammation (0.07±0.08 mL) paw swelling as well as total inhibition of the lesion score[1].

Reference:
[1]. E J Lewis, et al. Ro 32-3555, an orally active collagenase inhibitor, prevents cartilage breakdown in vitro and in vivo. Br J Pharmacol. 1997 May; 121(3): 540–546.

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