PL-3994

Cat. No.:	HY-P3562
CAS No.:	952295-80-6
Molecular Formula:	$C_{82}H_{127}N_{27}O_{20}S_2$
Molecular Weight:	1875.18
Target:	Others
Pathway:	Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description

PL-3994 is a natriuretic peptide receptor-A (NPR-A) agonist that is resistant to neutral endopeptidase and acts as a bronchodilator. PL-3994 produces concentration-dependent relaxation of pre-contracted guinea-pig trachea with an IC_{50} value of 42.7 nM[1].

In Vitro

PL-3994 has high affinity for recombinant human, dog, or rat NPR-As with K_i values of 1 nM, 41 nM, 10 nM, respectively. And PL-3994 binds to hNPR-C with K_i of 7 nM, while there is no effect on cGMP generation in hNPR-B[1].

PL-3994 induces dose-dependent cGMP generation in human, dog, and rat NPR-As with EC_{50}s of 2 nM, 3 nM, and 14 nM, respectively[1].

PL-3994 (0.1 nM-100 mM; 5-20 min) elicits a potent, concentration-dependent but small relaxation of pre-contracted human precision-cut lung slices (hPCLS)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Intratracheal PL-3994 (1-1000 mg/kg; i.t.; single dose) produces a dose-dependent inhibition of the bronchoconstrictor response evoked by aerosolized methacholine, without significant effect on cardiovascular parameters[1].

PL-3994 is resistant to degradation by human neutral endopeptidase (hNEP) (92% remaining after 2 h), whereas the natural ligands, ANP and CNP, are rapidly metabolized (≤1% remaining after 2 h)[1].

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Animal Model:	Guinea-pig model anaesthetized with urethane (1.75 g/kg, i.p.)[1]
Dosage:	1, 10, 100, 1000 mg/kg
Administration:	Intrathecal; single dose
Result:	Resulted a significant maximum inhibition of 43%, 63% and 70%, respectively, observed after 15-min pretreatment at doses of 10, 100 and 1000 mg/kg.

REFERENCES

[1]. Edelson JD, et al. In vitro and in vivo pharmacological profile of PL-3994, a novel cyclic peptide (Hept-cyclo(Cys-His-Phe-d-Ala-Gly-Arg-d-Nle-Asp-Arg-Ile-Ser-Cys)-Tyr-[Arg mimetic]-NH(2)) natriuretic peptide receptor-A agonist that is resistant to neutral endopeptidase and acts as a bronchodilator. Pulm Pharmacol Ther. 2013 Apr;26(2):229-38.

[2]. Edelson JD, et al. In vitro and in vivo pharmacological profile of PL-3994, a novel cyclic peptide (Hept-cyclo(Cys-His-Phe-d-Ala-Gly-Arg-d-Nle-Asp-Arg-Ile-Ser-Cys)-Tyr-[Arg mimetic]-NH(2)) natriuretic peptide receptor-A agonist that is resistant to neutral endopeptidase and acts as a bronchodilator. Pulm Pharmacol Ther. 2013 Apr;26(2):229-38.

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