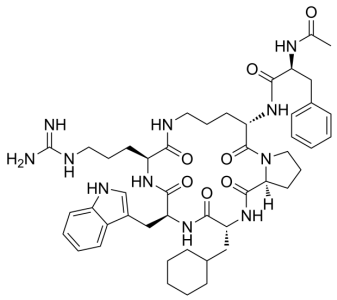
PMX-53

Cat. No.:	HY-106178
CAS No.:	219639-75-5
Molecular Formula:	$C_{47}H_{65}N_{11}O_7$
Molecular Weight:	896.09
Sequence Shortening:	F-{Orn}-P-{d-Cha}-WR (Lactam bridge: Orn2- Arg6)
Target:	Complement System
Pathway:	Immunology/Inflammation
Storage:	Sealed storage, away from moisture and light, under nitrogen Powder -80°C 2 years -20°C 1 year * In solvent : -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture and light, under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (111.60 mM; Need ultrasonic)

H_2O : 2.5 mg/mL (2.79 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.1160 mL	5.5798 mL	11.1596 mL
5 mM	0.2232 mL	1.1160 mL	2.2319 mL
10 mM	0.1116 mL	0.5580 mL	1.1160 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (2.32 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (2.32 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (2.32 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PMX-53 (3D53) is a synthetic peptidic and a potent and orally active complement C5a receptor (CD88) antagonist with an IC_{50} of 20 nM. PMX-53 is also a low-affinity MrgX2 agonist that stimulates MrgX2-mediated mast cell degranulation. PMX-53 specifically binds to C5aR1 and does not bind to the second C5aR (C5L2) and C3aR. PMX-53 has anti-inflammatory, anticancer and antiatherosclerotic effects[1][2][3][4][5][6].

IC_{50} & Target	IC50: 20 nM (Complement C5a receptor)[4] MrgX2[1]
In Vitro	PMX-53 is a potent CD88 antagonist and inhibits C5a-induced neutrophil myeloperoxidase release and chemotaxis with IC_{50} values of 22 nM and 75 nM, respectively[1]. ?PMX-53 (10 nM) inhibits C5a-induced Ca^{2+} mobilization in HMC-1 cells, but at higher concentrations(≥30 nM) it causes degranulation in LAD2 mast cells, $CD34^{+}$ cell-derived mast cells, and RBL-2H3 cells stably expressing MrgX2. Replacement of Trp with Ala and Arg with dArg abolishes the ability of PMX-53 to inhibit C5a-induced Ca^{2+} mobilization in HMC-1 cells and to cause degranulation in RBL-2H3 cells expressing MrgX2[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PMX-53 (0.3-3?mg/kg; subcutaneous injection; once; male Wistar rats) treatment inhibits the hypernociception induced by zymosan-activated serum and C5a but not by the direct-acting hypernociceptive mediators, prostaglandin E2 and dopamine [2]. Local pretreatment of rats with PMX-53 (60-180?μg per paw) inhibits zymosan-, carrageenan-, lipopolysaccharide (LPS)- and antigen-induced hypernociception[2]. Pharmacokinetic analyses have shown that PMX-53 (3D53) appears in the plasma within 5 min of oral administration (3 mg/kg) to rats, with peak blood levels of approximately 0.3 μM being reached within 20 min The plasma elimination half-life was approximately 70 min in this case[3]. The non-acetylated version of PMX-53 (3D53) binds to isolated mouse neutrophils with a K_d value of 30 nM (mouse C5a binds with a K_d value of 0.3 nM) and inhibits mouse C5a-induced chemotaxis with an IC_{50} value of 0.5 nM[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Adult male Wistar rats (weighing 180-200 g) injected with zymosan[2]
Dosage:	0.3 mg/kg, 1 mg/kg or 3 mg/kg
Administration:	Subcutaneous injection; once
Result:	Inhibited the hypernociception induced by zymosan-activated serum and C5a.

CUSTOMER VALIDATION

- Mol Ther. 2023 May 3;S1525-0016(23)00256-3.
- Int Immunopharmacol. 2024 Mar 16:131:111874.
- Research Square Print. November 28th, 2022.

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REFERENCES

[1]. Subramanian H, et al. PMX-53 as a dual CD88 antagonist and an agonist for Mas-related gene 2 (MrgX2) in human mast cells. Mol Pharmacol. 2011 Jun;79(6):1005-13.

[2]. Ting E, et al. Role of complement C5a in mechanical inflammatory hypernociception: potential use of C5a receptor antagonists to control inflammatory pain. Br J Pharmacol. 2008 Mar;153(5):1043-53.

[3]. Holland MC, et al. Synthetic small-molecule complement inhibitors. Curr Opin Investig Drugs. 2004 Nov;5(11):1164-73.

[4]. Finch AM, et al. Low-molecular-weight peptidic and cyclic antagonists of the receptor for the complement factor C5a. J Med Chem. 1999 Jun 3;42(11):1965-74.

[5]. Manthey HD, et al. Complement C5a inhibition reduces atherosclerosis in ApoE-/- mice. FASEB J. 2011 Jul;25(7):2447-55.

[6]. Vadrevu SK, et al. Complement c5a receptor facilitates cancer metastasis by altering T-cell responses in the metastatic niche. Cancer Res. 2014 Jul 1;74(13):3454-65.

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