

Product Data Sheet

Product Name: PMX 53
 Cat. No.: GC50176

Chemical Properties

Cas. No. 219639-75-5

SMILES NC(=NCCCC1NC(=O)C(NC(=O)C(Cc2CCCCC2)NC(=O)C2N(C(=O)C(CCCNC1=O)NC(=O)C(Cc1cccc1)NC(=O)C)CCC2)Cc1c[nH]c2c1cccc2)N

Formula $C_{47}H_{65}N_{11}O_7$ M.Wt 896.1

Solubility DMSO : 100 mg/mL (111.60 mM; Need ultrasonic); H₂O : 2.5 mg/mL (2.79 mM; ultrasonic and warming and heat to 60°C)

Storage Store at -20°C, protect from light, stored under nitrogen

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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 **Ac-Phe-cyclo(Orn-Pro-D-Cha-Trp-Arg)**

Protocol

Cell experiment [1]:

Cell lines Mouse neutrophils

Caution: Product has not been fully validated for medical applications. For research use only.

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Preparation Method Mouse neutrophils were isolated from the bone marrow of tibias and femurs from healthy C57BL/6J mice using the Neutrophil Isolation Kit. Neutrophils (5×10^5) were incubated with PMX 53 (10 μ M) for 1h and then stimulated with recombinant murine C5a (0.1 μ M) for 3h. Quantification of NET formation capacity in vitro shown as the percentage of NET release, which was assessed by immunofluorescence staining. NETosis was measured using a plate reader assay.

Reaction Conditions 10 μ M; 1h

Applications NETosis was observed when C5a was added to neutrophil cultures, and this effect was reversed by PMX 53.

Animal experiment [2]:

Animal models Sprague-Dawley rats

Preparation Method Sprague-Dawley rats received 1mg/kg of PMX 53 via the femoral vein 30min prior to ischemia. Following Basso-Beattie-Bresnahan (BBB) scale assessment, rats were anesthetized and killed. The spinal cord was collected and homogenized, and the expression level of MPO was measured 48h after reperfusion. MPO levels in ischemic spinal cord tissues were measured with a rat MPO ELISA assay kit. MPO activities in spinal cord tissues were calculated by using a standard curve generated with human MPO.

Dosage form 1mg/kg; i.v.

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Applications Pre-treatment with PMX 53 significantly attenuated the increase in MPO activity ($p < 0.05$) and reduced the infiltration of inflammatory cells into the ischemic spinal cord.

References:

- [1] CHEN Y, LI X, LIN X, et al. Complement C5a induces the generation of neutrophil extracellular traps by inhibiting mitochondrial STAT3 to promote the development of arterial thrombosis[J]. Thrombosis journal, 2022, 20(1): 24.
- [2] DONG Q, SUN L, PEN L, et al. PMX53 protects spinal cord from ischemia-reperfusion injury in rats in the short term[J]. Spinal Cord, 2016, 54(4): 254-258.

Background

PMX 53 is a potent, cell-permeable, and orally active C5a receptor (CD88) antagonist with an IC_{50} value of 20nM^[1]. PMX 53 specifically binds to C5aR1, blocking the interaction between complement C5a and its receptor, thereby inhibiting C5a-induced inflammatory responses such as myeloperoxidase (MPO) release and neutrophil chemotaxis. PMX 53 also acts as a low-affinity agonist for MrgX2 and can stimulate MrgX2-mediated mast cell degranulation at higher concentrations^[1, 2]. PMX 53 is commonly used in research on inflammatory mechanisms in autoimmune diseases, sepsis, neurodegenerative diseases, and psoriasis^[3].

In vitro, pre-incubation of C57BL/6J mouse neutrophils with PMX 53 (10 μ M) for 1h, followed by stimulation with recombinant murine C5a (0.1 μ M) for 3h, inhibited C5a-induced NETosis^[4]. The addition of PMX 53 (50, 100, 150nM) to the culture medium of THP-1 and HL-60 cells prior to treatment with LukS-PV (1 μ M) for 24h led to a concentration-dependent suppression of LukS-PV-induced apoptosis^[5].

In vivo, intravenous administration of PMX 53 (1mg/kg) via the femoral vein 30min before ischemia in Sprague-Dawley rats significantly reduced MPO activity in spinal cord tissue 48h after reperfusion^[6]. Oral administration of PMX 53 (10mg/kg/day) to C57BL/6 mice, starting 2 days before intracerebral hemorrhage and continuing for 5 days, significantly decreased mRNA levels of TNF- α , IL-6, and

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iNOS in perihematomal tissues^[7]. Subcutaneous injection of PMX 53 (3mg/kg) 30min before seizure stimulation in fully kindled CD1 mice reduced the proportion of mice experiencing stage 5 seizures by 50%^[8].

References:

- [1] SUBRAMANIAN H, KASHEM S W, COLLINGTON S J, et al. PMX-53 as a dual CD88 antagonist and an agonist for Mas-related gene 2 (MrgX2) in human mast cells[J]. Molecular pharmacology, 2011, 79(6): 1005-1013.
- [2] DICK J, GAN P Y, FORD S L, et al. C5a receptor 1 promotes autoimmunity, neutrophil dysfunction and injury in experimental anti-myeloperoxidase glomerulonephritis[J]. Kidney international, 2018, 93(3): 615-625.
- [3] KÖHL J. Drug evaluation: the C5a receptor antagonist PMX-53[J]. Current opinion in molecular therapeutics, 2006, 8(6): 529-538.
- [4] CHEN Y, LI X, LIN X, et al. Complement C5a induces the generation of neutrophil extracellular traps by inhibiting mitochondrial STAT3 to promote the development of arterial thrombosis[J]. Thrombosis journal, 2022, 20(1): 24.
- [5] ZHANG P, YU W W, PENG J, et al. LukS-PV induces apoptosis in acute myeloid leukemia cells mediated by C5a receptor[J]. Cancer medicine, 2019, 8(5): 2474-2483.
- [6] DONG Q, SUN L, PEN L, et al. PMX53 protects spinal cord from ischemia-reperfusion injury in rats in the short term[J]. Spinal Cord, 2016, 54(4): 254-258.
- [7] LI G, FAN R M, CHEN J L, et al. Neuroprotective effects of argatroban and C5a receptor antagonist (PMX53) following intracerebral haemorrhage[J]. Clinical & Experimental Immunology, 2014, 175(2): 285-295.
- [8] BENSON M J, THOMAS N K, TALWAR S, et al. A novel anticonvulsant mechanism via inhibition of complement receptor C5ar1 in murine epilepsy models[J]. Neurobiology of disease, 2015, 76: 87-97.

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