PZ-128

Cat. No.: HY-107146

CAS No.: 371131-16-7

Molecular Formula: $C_{55}H_{99}N_{13}O_9$

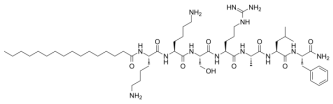
Molecular Weight: 1086.46

Sequence Shortening: {Palmitate}-KKSRALF-NH2

Target: Protease Activated Receptor (PAR)

Pathway: GPCR/G Protein

Storage: Sealed storage, away from moisture
Powder -80°C 2 years
-20°C 1 year
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (92.04 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	0.9204 mL	4.6021 mL	9.2042 mL
	5 mM	0.1841 mL	0.9204 mL	1.8408 mL
	10 mM	0.0920 mL	0.4602 mL	0.9204 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: ≥ 2.5 mg/mL (2.30 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (2.30 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (2.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PZ-128 (P1pal-7), a cell-penetrating lipopeptide pepducin, is a first-in-class, specific and reversible protease-activated receptor-1 (PAR1) antagonist. PZ-128 targets the cytoplasmic surface of PAR1 and interrupts signaling to internally-located G (PAR1-G) proteins. PZ-128 has antiplatelet, anti-metastatic, anti-angiogenic and anticancer effects[1][2][3][4].

IC_{50} & Target

PAR1

In Vitro	PZ-128 (P1pal-7; 3 μM) blocks 90-94% of OVCAR-4 migration toward human ovarian ascites and fibroblast conditioned media. The OVCAR4-treated peritoneal fibroblast conditioned media elicits a 2.2-fold increase in endothelial barrier permeability which could be nearly completely inhibited by PZ-128[1]. PZ-128 is a lipidated 'pepducin' which targets the cytoplasmic surface of PAR1 and interrupts signaling to internally-located G proteins. The structure of PZ-128 is found to mimic the off-state of the corresponding intracellular region of PAR1 which is critical for coupling to G proteins[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PZ-128 (P1pal-7; 10 mg/kg; intraperitoneal injection; every other day; for 6 weeks) treatment significantly reduces mean ascites fluid volume by 60%. PZ-128 treatment also causes a highly significant 84-96% reduction in blood vessel density in both the center and edge of the OVCAR-4 tumors[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female NCR Nu/Nu mice (5-7 weeks) injected with OVCAR-4 or SKOV-3 cells[1]
Dosage:	10 mg/kg
Administration:	Intraperitoneal injection; every other day; for 6 weeks
Result:	Significantly reduced mean ascites fluid volume by 60%.

REFERENCES

[1]. Anika Agarwal, et al. Targeting a metalloprotease-PAR1 signaling system with cell-penetrating pepducins inhibits angiogenesis, ascites, and progression of ovarian cancer. Mol Cancer Ther. 2008 Sep;7(9):2746-57.

[2]. Lidija Covic, et al. Protease-Activated Receptor 1 as Therapeutic Target in Breast, Lung, and Ovarian Cancer: Pepducin Approach. Int J Mol Sci. 2018 Jul 31;19(8):2237.

[3]. Paul A Gurbel, et al. Cell-Penetrating Pepducin Therapy Targeting PAR1 in Subjects With Coronary Artery Disease. Arterioscler Thromb Vasc Biol. 2016 Jan;36(1):189-97.

[4]. Ping Zhang, et al. Suppression of arterial thrombosis without affecting hemostatic parameters with a cell-penetrating PAR1 pepducin. Circulation. 2012 Jul 3;126(1):83-91.

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