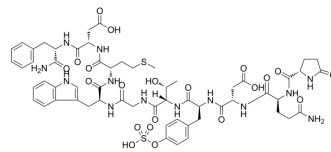


## Ceruletide

**Cat. No.:** HY-A0190  
**CAS No.:** 17650-98-5  
**Molecular Formula:** C<sub>58</sub>H<sub>73</sub>N<sub>13</sub>O<sub>21</sub>S<sub>2</sub>  
**Molecular Weight:** 1352.41  
**Sequence:** {pGlu}-Gln-Asp-Tyr(SO<sub>3</sub>H)-Thr-Gly-Trp-Met-Asp-Phe-NH<sub>2</sub>  
**Sequence Shortening:** {pGlu}-QD-Y(SO<sub>3</sub>H)-TGWMDF-NH<sub>2</sub>  
**Target:** Cholecystokinin Receptor  
**Pathway:** GPCR/G Protein; Neuronal Signaling  
**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 (73.94 mM; Need ultrasonic)  
 DMF : 16.67 mg/mL (12.33 mM; Need ultrasonic)  
 H<sub>2</sub>O : 2.5 mg/mL (1.85 mM; Need ultrasonic)

	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	0.7394 mL	3.6971 mL	7.3942 mL
	5 mM	0.1479 mL	0.7394 mL	1.4788 mL
	10 mM	0.0739 mL	0.3697 mL	0.7394 mL

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

#### In Vivo

- Add each solvent one by one: PBS  
Solubility: 30.3 mg/mL (22.40 mM); Clear solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (1.85 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (1.85 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (1.85 mM); Clear solution
- Add each solvent one by one: Saline  
Solubility: 2 mg/mL (1.48 mM); Clear solution; Need ultrasonic and adjust pH to 12 with 1M NaOH
- Add each solvent one by one: 10% DMF >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 1.67 mg/mL (1.23 mM); Clear solution

7. Add each solvent one by one: 10% DMF >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 1.67 mg/mL (1.23 mM); Clear solution
8. Add each solvent one by one: 10% DMF >> 90% corn oil  
Solubility: 1.67 mg/mL (1.23 mM); Suspended solution; Need ultrasonic

## BIOLOGICAL ACTIVITY

<b>Description</b>	Ceruletide is a decapeptide and a potent cholecystokinin receptor agonist. Ceruletide is a safe and effective cholecystokinetic agent with a direct spasmogenic effect on the gallbladder muscle and bile ducts <sup>[1]</sup> .
<b>IC<sub>50</sub> &amp; Target</b>	Cholecystokinin receptor <sup>[4]</sup>
<b>In Vitro</b>	<p>Ceruletide is similar chemically and biologically to the human gastrointestinal hormones cholecystokinin-pancreozymin (CCK) and gastrin II. Ceruletide stimulates gallbladder contraction, pancreatic exocrine secretion, gastric secretion, and motility in the distal duodenum, jejunum, ileum and colon, while delaying gastric emptying and inhibiting motility in the proximal duodenum<sup>[1]</sup>. Ceruletide in supramaximal but not in physiological doses activates NF-kappaB/Rel in vitro. This activation may induce a self-defending genetic program before the onset of cellular injury, which may prevent higher degrees of damage of pancreatic acinar cells after secretagogue hyperstimulation<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>In Vivo</b>	<p>CeruLetide (0.4-0.5 μg/kg, IV; 3-4 μg/kg, SC) causes vomiting and defecation in conscious intact dogs 15-30 minutes after IV injection and 2-4 hours after full recovery after sc administration . CeruLetide (5-15 ng/kg, iv) exhibits significant spasmogenic effects on the pylorus in rats. CeruLetide also reduces blood pressure in anesthetized dogs <sup>[1]</sup>. CeruLetide serum bile acid (SBA) stimulation circumvents the exogenous and endogenous effects associated with postprandial (PP) SBA stimulation. CeruLetide SBA stimulation may be as effective as PP SBA stimulation in dogs with portosystemic shunts (PSS) and is more sensitive for detecting liver dysfunction in dogs with upper respiratory disease (URD)<sup>[3]</sup>. When S<sup>35</sup>-labeled Ceruletide is injected intramuscularly in rats, rabbits and mice, radioactivity in the blood reached a maximum at 5 and 15 min in rats and rabbits respectively and then decreased rapidly. And the acute toxicity studies in mice show an i.v. LD<sub>50</sub> of 1012 mg/kg<sup>[4]</sup>.</p> <p>Ceruletide-induced pancreatitis is a great characterized animal models of pancreatitis, which is highly reproducible and economical. It has been widely used to generate both acute and chronic pancreatitis in mice and rats<sup>[5]</sup>.</p> <div data-bbox="347 1430 1516 1518" style="border: 1px solid #ccc; padding: 5px; margin: 10px 0;"> <p>1. Induction of Acute Pancreatitis<sup>[6][7][8]</sup></p> </div> <ul style="list-style-type: none"> <li data-bbox="371 1556 526 1583">● Background           <div data-bbox="380 1608 1451 1787" style="border-left: 1px dashed #ccc; border-right: 1px dashed #ccc; padding: 5px; margin-left: 20px;"> <p>Ceruletide acts on CCK receptors, which are often expressed on various species of pancreatic acinar cells. Ceruletide induces dysregulation of the production and secretion of digestive enzymes, leading to cytoplasmic vacuolization and the death of acinar cells, edema formation, and an infiltration of inflammatory cells into the pancreas.</p> </div> </li> <li data-bbox="371 1839 683 1866">● Specific Modeling Methods</li> </ul>

1. Mice: C57Bl/6n mice • 8-12 week-old

Administration: Ceruletide 50 µg/kg • i.p. • 8 hourly, total 8 times;

2. Mice: C57BL6/J mice • male • 6-8 week-old

Administration: Ceruletide 100 µg/kg plus LPS (5 mg/kg, i.p. immediately after the last injection of Ceruletide) • i.p. • 10 hourly, total 10 times;

or Ceruletide (50 µg/kg, 7 hourly, total 7 times) plus LPS (10 mg/kg, once) • i.p.

#### Note

(1) Cerulein induces rapid pancreatitis and rapid spontaneous recovery within one week in mammals.

Therefore, mice are usually euthanized within 24h after the first Ceruletide injection.

- Modeling Indicators

Molecular changes: Increased serum amylase, serum lipase, TNF- $\alpha$ , and IL-1 $\beta$  level.

Histology analysis: Pancreatic edema, inflammatory infiltration, and acinar cell necrosis (H&E staining).

- Correlated Product(s): Lipopolysaccharides(HY-D1056)

- Opposite Product(s):

## 2. Induction of Chronic Pancreatitis<sup>[9]</sup>

- Background

Chronic pancreatitis (CP) model can be established by repeated injection of mice with Ceruletide. Histologic characteristics of chronic pancreatitis include inflammatory infiltrates, fibrosis, acinar cell atrophy, duct distortion, and squamous metaplasia of the duct epithelium.

- Specific Modeling Methods

Mice: C57BL/6 • female • 6 week-old

Administration: Ceruletide 50 µg/kg • i.p. • 3 days per week, for a total of 4 weeks.

#### Note

Mice were sacrificed 3 days after the last injection.

- Modeling Indicators

Histology analysis: Glandular atrophy, infiltration of immune cells and distorted and/or blocked ducts.

- Correlated Product(s): Pevonedistat (HY-70062)
- Opposite Product(s):

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

## PROTOCOL

### Animal Administration <sup>[3]</sup>

Dogs<sup>[3]</sup>

All dogs undergo serum bile acid (SBA) stimulation with food (<5 kg/body weight [BW] 2 teaspoons, >5 kg BW 2 tablespoons) or 0.3 µg/kg BW Ceruletide IM, respectively, on consecutive days. A diet of moderate protein content and with an increased concentration of fiber is chosen to minimize metabolic complications such as hepatic encephalopathy. Before each test, the dogs are fasted for 12 hours. Blood samples are drawn at baseline, 60 and 120 minutes after feeding, and 20, 30, and 40 minutes postinjection, respectively. The blood samples are collected in plain tubes and left to clot; they are then centrifuged at 6,500 ×g for 1 minute, and the serum is used to measure SBA by a colorimetric test with endpoint determination<sup>[3]</sup>.

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

## CUSTOMER VALIDATION

- Cell Discov. 2023 Jan 3;9(1):1.
- Gut. 2024 Mar 29;gutjnl-2023-330788.
- Chem Eng J. 15 October 2022, 136792.
- Sci Adv. 2020 Aug 5;6(32):eaba8415.
- J Exp Clin Cancer Res. 2021 Jan 9;40(1):25.

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- [1]. Ke-You Zhang, et al. Chemically Induced Models of Pancreatitis. 2022. Pancreapedia: Exocrine Pancreas Knowledge Base, DOI: 10.3998/panc.2022.01
- [2]. Wu Z, et al. Dopamine D2 Receptor Signaling Attenuates Acinar Cell Necroptosis in Acute Pancreatitis through the Cathepsin B/TFAM/ROS Pathway. Oxid Med Cell Longev. 2022 Jul 26;2022:4499219.
- [3]. Kong L, et al. Sitagliptin activates the p62-Keap1-Nrf2 signalling pathway to alleviate oxidative stress and excessive autophagy in severe acute pancreatitis-related acute lung injury. Cell Death Dis. 2021 Oct 11;12(10):928.
- [4]. Malla SR, et al. Early trypsin activation develops independently of autophagy in caerulein-induced pancreatitis in mice. Cell Mol Life Sci. 2020 May;77(9):1811-1825.
- [5]. Lin Y, et al. Neddylation pathway alleviates chronic pancreatitis by reducing HIF1α-CCL5-dependent macrophage infiltration. Cell Death Dis. 2021 Mar 15;12(3):273.
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- [7]. Steinle AU, et al. NF-kappaB/Rel activation in cerulein pancreatitis. Gastroenterology. 1999 Feb;116(2):420-30.

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[8]. Bridger N, et al. Comparison of postprandial and ceruletide serum bile acid stimulation in dogs. J Vet Intern Med. 2008 Jul-Aug;22(4):873-8.

[9]. Zarrindast MR, et al. Effects of cholecystokinin receptor agonist and antagonists on morphin dependence in mice. Pharmacol Toxicol. 1995 Dec;77(6):360-4.

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

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