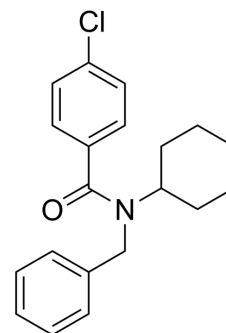


## FPS-ZM1

Cat. No.:	HY-19370
CAS No.:	945714-67-0
Molecular Formula:	C <sub>20</sub> H <sub>22</sub> ClNO
Molecular Weight:	327.85
Target:	Amyloid- $\beta$
Pathway:	Neuronal Signaling
Storage:	<div> <div>Powder</div> <div>-20°C</div> <div>3 years</div> </div> <div> <div></div> <div>4°C</div> <div>2 years</div> </div> <div> <div>In solvent</div> <div>-80°C</div> <div>2 years</div> </div> <div> <div></div> <div>-20°C</div> <div>1 year</div> </div>



## SOLVENT & SOLUBILITY

### In Vitro

DMSO : 100 mg/mL (305.02 mM; Need ultrasonic)  
H<sub>2</sub>O : 1 mg/mL (3.05 mM; ultrasonic and warming and heat to 60°C)

	Solvent Concentration	Mass	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		3.0502 mL	15.2509 mL	30.5018 mL
	5 mM		0.6100 mL	3.0502 mL	6.1004 mL
	10 mM		0.3050 mL	1.5251 mL	3.0502 mL

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

### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility:  $\geq$  2.5 mg/mL (7.63 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE- $\beta$ -CD in saline)  
Solubility:  $\geq$  2.5 mg/mL (7.63 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility:  $\geq$  2.5 mg/mL (7.63 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE- $\beta$ -CD in saline)  
Solubility:  $\geq$  2.5 mg/mL (7.63 mM); Clear solution

## BIOLOGICAL ACTIVITY

### Description

FPS-ZM1 is a high-affinity RAGE inhibitor with a K<sub>i</sub> of 25 nM.

### IC<sub>50</sub> & Target

K<sub>i</sub>: 25 nM (RAGE)<sup>[1]</sup>

<b>In Vitro</b>	<p>FPS-ZM1 inhibits A<math>\beta</math>/RAGE binding in CHO cells with approximately 2-fold greater affinity than its parent molecule, FPS2. FPS-ZM1 inhibits binding of other known RAGE ligands to sRAGE, including S100 calcium-binding protein B and amphoterin. FPS-ZM1 is more effective than FPS2 in reducing A<math>\beta</math>40-induced increases in BACE1 mRNA and protein levels and the generation of sAPP<math>\beta</math>, an APP cleavage product of BACE1 indicative of BACE1 activity<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>In Vivo</b>	<p>FPS-ZM1 is nontoxic to mice and readily crossed the blood-brain barrier. In aged APP<sup>sw/0</sup> mice overexpressing human A<math>\beta</math>-precursor protein, a transgenic mouse model of AD with established A<math>\beta</math> pathology, FPS-ZM1 inhibits RAGE-mediated influx of circulating A<math>\beta</math>40 and A<math>\beta</math>42 into the brain. In brain, FPS-ZM1 binds exclusively to RAGE, which inhibits <math>\beta</math>-secretase activity and A<math>\beta</math> production and suppresses microglia activation and the neuro-inflammatory response<sup>[1]</sup>. FPS-ZM1 treatment reduces the level of A<math>\beta</math>1-40 and A<math>\beta</math>1-42 in AGEs Rats. It Inhibits AGEs-mediated increase of A<math>\beta</math>-metabolism-related proteins and downregulates AGEs-mediated increase of pro-inflammatory cytokines in the hippocampus. FPS-ZM1 up-Regulates anti-oxidant defense system and attenuated AGEs induced memory impairment in AGEs rats<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## PROTOCOL

<b>Kinase Assay</b> <sup>[1]</sup>	<p>Human sRAGE is immobilized (10 <math>\mu</math>g/mL) overnight at 4°C in 96-well microtiter plates and blocked with 3% bovine serum albumin. <sup>125</sup>I-labeled A<math>\beta</math>40, HMGB1, or S100B at 5 nM in the absence and presence of various concentrations of FPS2 or FPS-ZM1 (10 to 1,000 nM) is added to the wells containing immobilized sRAGE and incubated for 1 hour at room temperature in PBS. Wells are washed with cold PBS to remove unbound radiolabeled ligands, and the radioactivity is analyzed<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>Cell Assay</b> <sup>[1]</sup>	<p>To determine whether FPS2 and FPS-ZM1 are toxic to CHO cells, the cells are treated for 72 hours with different concentrations of inhibitors ranging from 10 nM to 10 <math>\mu</math>M. The cellular toxicity is determined using the WST-8 Assay Kit<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>Animal Administration</b> <sup>[1][2]</sup>	<p>Rats: Starting from 1 week before intrahippocampal injection, FZM1 and AGEs+FZM1 rats are intraperitoneally injected with FPS-ZM1 (1 mg/kg/d at a volume of 2 mL) for 4 weeks; rats in the AGEs and the control groups are intraperitoneally injected with normal saline with the same volume for 4 weeks. Three weeks after AGEs intrahippocampal injection, the escape latency time of rats is assayed with Morris water maze test, and then all rats are sacrificed<sup>[2]</sup>.</p> <p>Mice: FPS2 or FPS-ZM1 are administered i.v. (1 mg/kg) via the femoral vein and arterial blood samples (30 <math>\mu</math>L) collected at 1, 5, 10, 15, and 20 minutes via the cannulated femoral artery. Plasma is separated by centrifugation at 4°C and immediately stored at -80°C until analysis<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## CUSTOMER VALIDATION

- Brain Behav Immun. 2017 Jan;59:322-332.
- Theranostics. 2020 Apr 27;10(13):5687-5703
- Nano Res. 04 March 2022.
- J Neuroinflammation. 2020 Oct 9;17(1):295.
- Int J Biol Sci. 2024 Jan 1;20(2):784-800.

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## REFERENCES

- [1]. Deane R, et al. A multimodal RAGE-specific inhibitor reduces amyloid  $\beta$ -mediated brain disorder in a mouse model of Alzheimer disease. J Clin Invest. 2012 Apr;122(4):1377-92.
- [2]. Hong Y, et al. Effects of RAGE-Specific Inhibitor FPS-ZM1 on Amyloid- $\beta$  Metabolism and AGEs-Induced Inflammation and Oxidative Stress in Rat Hippocampus. Neurochem Res. 2016 May;41(5):1192-9.
- [3]. Lian YJ, et al. Ds-HMGB1 and fr-HMGB induce depressive behavior through neuroinflammation in contrast to nonoxid-HMGB1. Brain Behav Immun. 2017 Jan;59:322-332.
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**Caution: Product has not been fully validated for medical applications. For research use only.**

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: [tech@MedChemExpress.com](mailto:tech@MedChemExpress.com)

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA