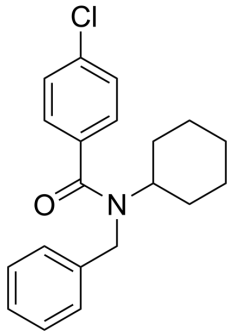
FPS-ZM1

Cat. No.:	HY-19370
CAS No.:	945714-67-0
Molecular Formula:	$C_{20}H_{22}ClNO$
Molecular Weight:	327.85
Target:	Amyloid-β
Pathway:	Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (305.02 mM; Need ultrasonic)

H_2O : 1 mg/mL (3.05 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
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

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.63 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.63 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.63 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.63 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	FPS-ZM1 is a high-affinity RAGE inhibitor with a K_i of 25 nM.
IC_{50} & Target	Ki: 25 nM (RAGE)[1]

In Vitro	FPS-ZM1 inhibits Aβ/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 Aβ40-induced increases inBACE1 mRNA and protein levels and the generation of sAPPβ, an APP cleavage product of BACE1 indicative of BACE1 activity[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	FPS-ZM1 is nontoxic to mice and readily crossed the blood-brain barrier. In aged $APP^{sw/0}$ mice overexpressing human Aβ-precursor protein, a transgenic mouse model of AD with established Aβ pathology, FPS-ZM1 inhibits RAGE-mediated influx of circulating Aβ40 and Aβ42 into the brain. In brain, FPS-ZM1 binds exclusively to RAGE, which inhibits β-secretase activity and Aβ production and suppresses microglia activation and the neuro-inflammatory response[1]. FPS-ZM1 treatment reduces the level of Aβ1-40 and Aβ1-42 in AGEs Rats. It Inhibits AGEs-mediated increase of Aβ-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[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Human sRAGE is immobilized (10 μg/mL) overnight at 4°C in 96-well microtiter plates and blocked with 3% bovine serum albumin. ^{125}I-labeled Aβ40, 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[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	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 μM. The cellular toxicity is determined using the WST-8 Assay Kit[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][2]	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[2]. Mice: FPS2 or FPS-ZM1 are administered i.v. (1 mg/kg) via the femoral vein and arterial blood samples (30 μL) 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[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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 β-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-β 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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