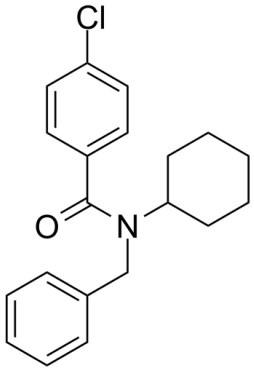
Data Sheet

Product Name:	FPS-ZM1
Cat. No.:	CS-5270
CAS No.:	945714-67-0
Molecular Formula:	C20H22ClNO
Molecular Weight:	327.85
Target:	Amyloid-β
Pathway:	Neuronal Signaling
Solubility:	DMSO : ≥ 100 mg/mL (305.02 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

FPS-ZM1 is a high-affinity **RAGE** specific inhibitor with a K_i of 25 nM. IC50 & 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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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]. **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]. **Animal Administration:** [1][2] Rat: 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].

Mouse: 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].

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.

CAIndexNames:

Benzamide, 4-chloro-N-cyclohexyl-N-(phenylmethyl)-

SMILES:

ClC1=CC=C(C(N(C2CCCCC2)CC3=CC=CC=C3)=O)C=C1

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

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