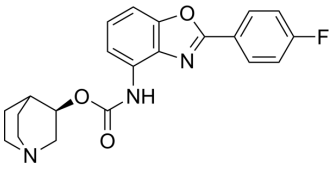
Glucosylceramide synthase-IN-3

Cat. No.:	HY-144270
Molecular Formula:	$C_{21}H_{20}FN_3O_3$
Molecular Weight:	381.4
Target:	Glucosylceramide Synthase (GCS)
Pathway:	Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Glucosylceramide synthase-IN-3 (compound BZ1) is a potent, brain-penetrant and orally active glucosylceramide synthase (GCS) inhibitor with IC_{50}s of 16 nM for human GCS.Glucosylceramide synthase-IN-3 can be used for Gaucher's disease research[1][2].
In Vitro	Glucosylceramide synthase-IN-2 (compound BZ1) causes measuring the reduction of glucosylceramide and the cellular IC50 was determined to be 94 nM in human and 160 nM in mouse with cellular activity was confirmed using a fibroblast assay[1]. Glucosylceramide synthase-IN-2 has the IC50 of 20 nM in primary neurons[1]. Glucosylceramide synthase-IN-2 (10, 30, 100, 300 nM) produces a dose-dependent reduction in glycosphingolipids in WT and D409V mouse cortical neurons. Glucosylceramide synthase-IN-2 decreases the amount of detergent-insoluble pS129 α-syn[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Eight hours after a single dose of Glucosylceramide synthase-IN-2 (compound BZ1; 6, 20 or 100 mg/kg; oral gavage; formulated in 30% captisol), plasma GlcCer C:16:0 is reduced in a dose-dependent fashion up to ~75% of concentration in vehicle treated animals. Brain GlcCer is also significantly reduced to concentrations of ~48% of vehicle treated controls in C57BL6 mice (8 weeks of age, male)[1]. Glucosylceramide synthase-IN-2 (6, 20 or 100 mg/kg/day for 4 days; oral gavage) causes larger reductions in GlcCer[1]. Glucosylceramide synthase-IN-2 has good pharmaceutical properties with high permeability (pApp=26.54) and is not a substrate of P-gp[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Mali Cosden, et al. A novel glucosylceramide synthase inhibitor attenuates alpha synuclein pathology and lysosomal dysfunction in preclinical models of synucleinopathy. Neurobiol Dis. 2021 Nov;159:105507.

[2]. Yuta Tanaka, et al. Discovery of Brain-Penetrant Glucosylceramide Synthase Inhibitors with a Novel Pharmacophore. J Med Chem. 2022 Mar 10;65(5):4270-4290

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

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