Glucosylceramide synthase-IN-2

Cat. No.: HY-144267

CAS No.: 2597958-02-4

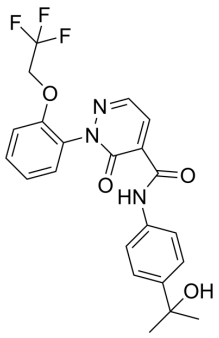
Molecular Formula: $C_{22}H_{20}F_3N_3O_4$

Molecular Weight: 447.41

Target: Glucosylceramide Synthase (GCS)

Pathway: Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (223.51 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2351 mL	11.1754 mL	22.3509 mL
	5 mM	0.4470 mL	2.2351 mL	4.4702 mL
	10 mM	0.2235 mL	1.1175 mL	2.2351 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 (5.59 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.59 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Glucosylceramide synthase-IN-2 (compound T-690) is a potent, brain-penetrant and orally active glucosylceramide synthase (GCS) inhibitor with IC_{50}s of 15 nM and 190 nM for human GCS and mouse GCS, respectively.Glucosylceramide synthase-IN-2 exhibits noncompetitive type inhibition with C8-ceramide and UDP-glucose.Glucosylceramide synthase-IN-2 can be used for Gaucher's disease research[1].

In Vitro

Glucosylceramide synthase-IN-2 (compound T-690) has no SERT inhibitory activity (IC_{50}>10 μM). Glucosylceramide synthase-IN-2 does not affect GCase activity (EC_{50}>300 μM)[1].
Glucosylceramide synthase-IN-2 (30 μM) does not potently inhibit hERG, $Ca_V1.2$, and $Na_V1.5$ channels[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Glucosylceramide synthase-IN-2 (compound T-690; po; 30, 100, 300 mg/kg) reduces GlcCer concentrations in the plasma and

cerebral cortex in a dose-dependent manner in C57BL/6J mice[1].

Glucosylceramide synthase-IN-2 (po; 5 mg/kg) has a C_{max} of 416 ng/mL. Glucosylceramide synthase-IN-2 shows good oral exposure (BA = 31%)[1].

Glucosylceramide synthase-IN-2 reveals good brain exposure (Cu,brain = 0.21 μM at 30 mg/kg dosing, 1 h)[1].

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

REFERENCES

[1]. 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

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