Sinbaglustat

Cat. No.: HY-129411

CAS No.: 441061-33-2

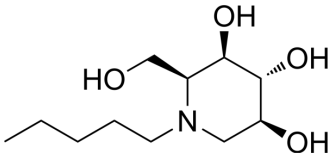
Molecular Formula: $C_{11}H_{23}NO_4$

Molecular Weight: 233.3

Target: Glucosylceramide Synthase (GCS)

Pathway: Neuronal Signaling

Storage: -20°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 : 83.33 mg/mL (357.18 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	4.2863 mL	21.4316 mL	42.8633 mL
	5 mM	0.8573 mL	4.2863 mL	8.5727 mL
	10 mM	0.4286 mL	2.1432 mL	4.2863 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: ≥ 6.25 mg/mL (26.79 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sinbaglustat (OGT2378) is a dual inhibitor of glucosylceramide synthase (GCS) and non-lysosomal glucosyl ceramidase (GBA2). Sinbaglustat is an orally available N-alkyl iminosugar that crosses the blood-brain barrier. Sinbaglustat can be used for the research of central neurodegenerative diseases associated with lysosomal dysfunctions[1][2].

In Vitro

Sinbaglustat (OGT2378; 20 μM) reduces the synthesis of glucosylceramide and ganglioside by 93% and >95% in MEB4 melanoma cells compared with untreated MEB4 cells, respectively, without either cytotoxic or antiproliferative effects[1]. GBA2 is an enzyme involved in the catabolism of glycosphingolipids (GSLs). Sinbaglustat is 50-fold more potent in inhibiting GBA2 than GCS[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Sinbaglustat (OGT2378; administered p.o., in the powdered chow, at a dose of 2500 mg/kg/day, corresponding to 35-40 mg of Sinbaglustat per mouse per day) is highly effective in impeding melanoma tumor growth in vivo. The effectiveness of p.o. Sinbaglustat in this murine model suggests that inhibition of glycosphingolipid synthesis is a promising approach to inhibit

tumor progression[1].

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

Animal Model:	Female syngeneic C57BL/6 mice, 6-8 weeks old bearing MEB4 melanoma tumor[1]
Dosage:	35-40 mg per mouse per day
Administration:	Administered p.o., in the powdered chow, at a dose of 2500 mg/kg/day
Result:	Inhibited MEB4 melanoma tumor growth in a syngeneic, orthotopic murine model.

REFERENCES

[1]. Michael Weiss, et al. Inhibition of melanoma tumor growth by a novel inhibitor of glucosylceramide synthase. Cancer Res. 2003 Jul 1;63(13):3654-8.

[2]. Martine Gehin, et al. Assessment of Target Engagement in a First-in-Human Trial with Sinbaglustat, an Iminosugar to Treat Lysosomal Storage Disorders. Clin Transl Sci. 2021 Mar;14(2):558-567.

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