SAG dihydrochloride

Cat. No.: HY-12848C

CAS No.: 2702366-44-5

Molecular Formula: $C_{28}H_{30}Cl_3N_3OS$

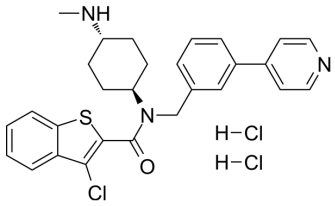
Molecular Weight: 562.98

Target: Smo

Pathway: Stem Cell/Wnt

Storage: 4°C, sealed storage, away from moisture

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



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (177.63 mM; Need ultrasonic)

DMSO : 33.33 mg/mL (59.20 mM; Need ultrasonic)

Preparing Stock Solutions

Concentration / Solvent / Mass	1 mg	5 mg	10 mg
1 mM	1.7763 mL	8.8813 mL	17.7626 mL
5 mM	0.3553 mL	1.7763 mL	3.5525 mL
10 mM	0.1776 mL	0.8881 mL	1.7763 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 50 mg/mL (88.81 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.44 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.44 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.44 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SAG dihydrochloride is a potent Smoothened (Smo) receptor agonist (EC_{50}=3 nM; K_d=59 nM). SAG dihydrochloride activates the Hedgehog signaling pathway and counteracts Cyclopamine (HY-17024) inhibition of Smo[1][2][3].

IC_{50} & Target

EC50: 3 nM (Smo)[1]

In Vitro

SAG (0.1 nM-100 μM; 30 h) induces firefly luciferase expression in Shh-LIGHT2 cells with an EC_{50} of 3 nM and then inhibits

expression at higher concentrations[1].
SAG (1-1000 nM; 1 h) competes for the binding of BODIPY-cyclopamine to Smo-expressing Cos-1 cells, yielding an apparent dissociation constant (K_d) of 59 nM for the SAG/Smo complex[1].
SAG (100 nM) inhibits the inhibitory effect of ShhN-induced pathway activation by Robotnikinin[2].
SAG (250 nM; 48 h) significantly increases SMO mRNA and protein expression in MDAMB231 cells[3].
SAG (250 nM; 24 and 48 h) increases CAXII mRNA expression in MDAMB231 cells at 24h in normoxic and hypoxic conditions in MDAMB231 cells[3].
SAG (250 nM; 24 h) increases MDAMB231 cells migration[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

SAG (1.0 mM) induces more osteogenesis mainly at the defect borders and a significant increase in BV/TV at the eight week timepoint in CD-1 mice[4].
SAG (15-20 mg/kg; i.p.) induces pre-axial polydactyly prevalently in a dose-dependent manner in mice[5].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Pregnant C57BL/6J mice[5]
Dosage:	15, 17, 20 mg/kg
Administration:	A single i.p.
Result:	Effective in ca. 80% of the embryos and increased Gli1 and Gli2 mRNA expression in the limb bud, with Gli1 mRNA being the most upregulated at the dose of 20 mg/kg.

CUSTOMER VALIDATION

- Cell Res. 2022 Mar;32(3):288-301.
- Sci Adv. 2023 Jun 16;9(24):eadf6927.
- Cell Rep. 2020 Apr.
- Glia. 2021 Mar 11.
- iScience. 2022 Dec 26;26(1):105898.

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REFERENCES

[1]. Guerrini G, et, al. Inhibition of smoothened in breast cancer cells reduces CAXII expression and cell migration. J Cell Physiol. 2018 Dec; 233(12): 9799-9811.

[2]. Chen JK, et al. Small molecule modulation of Smoothened activity. Proc Natl Acad Sci U S A. 2002 Oct 29;99(22):14071-6.

[3]. Stanton BZ, et al. A small molecule that binds Hedgehog and blocks its signaling in human cells. Nat Chem Biol. 2009 Mar;5(3):154-6.

[4]. Lee S, et al. Combining Smoothened Agonist (SAG) and NEL-like protein-1 (NELL-1) Enhances Bone Healing. Plast Reconstr Surg. 2017 Feb 13.

[5]. Fish EW, et al. Preaxial polydactyly following early gestational exposure to the smoothened agonist, SAG, in C57BL/6J mice. Birth Defects Res A Clin Mol Teratol. 2016 Nov 1.

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

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