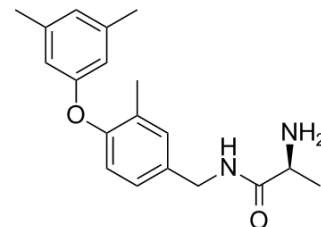


SGC2085

Cat. No.:	HY-100565		
CAS No.:	1821908-48-8		
Molecular Formula:	C ₁₉ H ₂₄ N ₂ O ₂		
Molecular Weight:	312.41		
Target:	Histone Methyltransferase		
Pathway:	Epigenetics		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 32 mg/mL (102.43 mM)
 * "≥" means soluble, but saturation unknown.

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	3.2009 mL	16.0046 mL	32.0092 mL
	5 mM	0.6402 mL	3.2009 mL	6.4018 mL
	10 mM	0.3201 mL	1.6005 mL	3.2009 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (8.00 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
 Solubility: ≥ 2.5 mg/mL (8.00 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (8.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SGC2085 is a potent and selective coactivator associated arginine methyltransferase 1 (CARM1) inhibitor with an IC₅₀ of 50 nM.

IC₅₀ & Target

IC₅₀: 50 nM (CARM1)^[1]

In Vitro

SGC2085 which features a methyl at position R1 and a 3,5-dimethylphenoxy at R2 has an IC₅₀ of 50 nM for CARM1 and is over

100-fold selective for CARM1 over PRMT6. These results indicate that the presence of a substituent at R1 is essential for potent and selective inhibition of CARM1. With the exception of PRMT6 ($IC_{50}=5.2 \mu M$), SGC2085 does not inhibit other PRMTs. Considering its small size ($MW=312.4 Da$), SGC2085 has an excellent selectivity profile, which can probably be further improved by exploiting differences in the binding sites of the two enzymes outside the arginine binding pocket. Compound SGC2085 also shows complete selectivity against a panel of 21 human protein methyltransferases tested at three different concentrations (1, 10, and 50 μM). To characterize the mechanism of action of SGC2085 in solution, IC_{50} values are determined at various concentrations of SAM and peptide substrate. Increasing concentration of substrate peptide or cofactor does not affect IC_{50} values, indicative of a noncompetitive mechanism of inhibition, which has been previously shown for other protein methyltransferase inhibitors binding at the substrate pocket^[1]. No cellular activity is observed for SGC2085 when tested up to 10 μM (48 h exposure in HEK293 cells), while methylation of BAF155 is abrogated by 10 μM of the dual CARM1/PRMT6 inhibitor MS049. We assume that the absence of cellular activity for SGC2085 is due to poor permeability^[1].

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

PROTOCOL

Cell Assay^[1]

SGC2085 is dissolved in DMSO and diluted with appropriate medium before use. HEK293 cells are grown in 12-well plates in DMEM supplemented with 10% FBS, penicillin (100 U/mL), and streptomycin (100 $\mu g/mL$). Thirty percent confluent cells are treated with inhibitors or DMSO. After 48 h, media are removed and cells are lysed in 100 μL of total lysis buffer (20 mM Tris-HCl pH 8.0, 150 mM NaCl, 1 mM EDTA, 10 mM $MgCl_2$, 0.5% Triton X-100, 12.5 U/mL benzonase), complete EDTA-free protease inhibitor cocktail. After 3 min incubation at room temperature, SDS is added to 1% final concentration. Lysates are run on SDS-PAGE, and immunoblotting is done as outlined below to determine the levels of unmethylated and methylated BAF155^[1].

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

REFERENCES

[1]. Ferreira de Freitas R, et al. Discovery of a Potent and Selective Coactivator Associated Arginine Methyltransferase 1 (CARM1) Inhibitor by Virtual Screening. *J Med Chem.* 2016 Jul 28;59(14):6838-47.

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

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