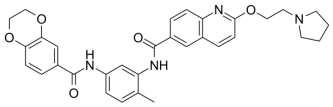
CCT251236

Cat. No.:	HY-101026
CAS No.:	1693731-40-6
Molecular Formula:	$C_{32}H_{32}N_4O_5$
Molecular Weight:	552.62
Target:	HSP
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 150 mg/mL (271.43 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Mass / Solvent / Concentration	1 mg	5 mg	10 mg
1 mM	1.8096 mL	9.0478 mL	18.0956 mL
5 mM	0.3619 mL	1.8096 mL	3.6191 mL
10 mM	0.1810 mL	0.9048 mL	1.8096 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 (4.52 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CCT251236 is an orally available pirin ligand from a heat shock transcription factor 1 (hsf1) phenotypic screen with an IC_{50} of 19 nM for inhibition of HSF1-mediated HSP72 induction.

IC_{50} & Target

HSP72

19 nM (IC_{50}, SK-OV-3 cells)

In Vitro

CCT251236 (0-100 nM; 24hours) displays a desired balance of in vitro properties, while maintaining excellent cellular activity with a pIC50=7.73 ± 0.07 (IC_{50}=19 nM) for inhibition of HSF1-mediated HSP72 induction. The free GI_{50} is 1.1 nM in SK-OV-3 cells that calculated from the free fraction in the cell assay[1].

CCT251236 (0-100 nM; 24 hours) blocks 17-AAG induced he HSF1-mediated heat-shock proteins, HSP72 and HSP27 expression as a concentration manner in SK-OV-3 cells[1].

CCT251236 (0-100 nM; 24 hours), pre-treated with 250 nM 17-AAG for 6h, blocks the induction of HSPA1A mRNA by 17-AAG in a dosedependent manner[1].

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

Western Blot Analysis[1]

Cell Line:	SK-OV-3 cells
Concentration:	0 nM; 10 nM; 100 nM
Incubation Time:	24 hours
Result:	Inhibited HSP72 and HSP27 expression at the dose of 10 nM.

RT-PCR[1]

Cell Line:	SK-OV-3 cells
Concentration:	0 nM; 10 nM; 100 nM and 1000 nM
Incubation Time:	24 hours
Result:	Decreased HSPA1A mRNA level.

In Vivo

CCT251236 (oral adminstation; 5 or 20 mg/kg) in nontumor bearing immunocompetent BALB/c mice exhibits free $C_{av}^{0\text{-}24h}$ value of 2.0 nM and 1.2 nM, respectively[2].

CCT251236 (oral adminstation; 20 mg/kg; 33 days) has a clear therapeutic efficacy in mice with a tumor growth inhibition (%TGI) of 70% based on final tumor volumes. After 33 days, the mean tumor weights decreases 64% when compares to control group. In addition, the compound's basicity and high volume of distribution shows in tumor withtumor concentrations of CCT251236 as high as 940 nM[2].

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

Animal Model:	Athymic mice with SK-OV-3 cells[2]
Dosage:	20 mg/kg; 33 days
Administration:	Oral adminstation
Result:	Was efficacious in SK-OV-3 cell induced-tumor mice model.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2021 Feb 16;118(7):e2014457118.
- Mol Oncol. 2019 Feb;13(2):322-337.
- Mol Med. 2021 May 30;27(1):53.

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REFERENCES

[1]. Cheeseman MD, et al. Discovery of a Chemical Probe Bisamide (CCT251236): An OrallyBioavailable Efficacious Pirin Ligand from a Heat ShockTranscription Factor 1 (HSF1) Phenotypic Screen. J Med Chem. 2017 Jan 12;60(1):180-201.

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

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