SR9011 hydrochloride

Cat. No.: HY-16988A

CAS No.: 2070014-94-5

Molecular Formula: $C_{23}H_{32}Cl_2N_4O_3S$

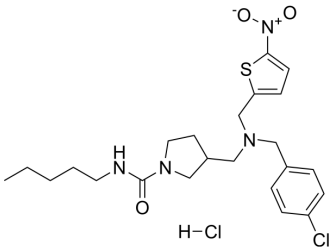
Molecular Weight: 515.5

Target: REV-ERB

Pathway: Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor

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

DMSO : ≥ 32 mg/mL (62.08 mM)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.9399 mL	9.6993 mL	19.3986 mL
5 mM	0.3880 mL	1.9399 mL	3.8797 mL
10 mM	0.1940 mL	0.9699 mL	1.9399 mL

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

BIOLOGICAL ACTIVITY

Description

SR9011 hydrochloride is a REV-ERBα/β agonist with IC_{50}s of 790 nM and 560 nM for REV-ERBα and REV-ERBβ, respectively.

IC_{50} & Target

IC50: 790 nM (Rev-ErbBα), 560 nM (Rev-ErbBβ)[1]

In Vitro

SR9011 dose-dependently increases the REV-ERB-dependent repressor activity assessed in HEK293 cells expressing a chimeric Gal4 DNA Binding Domain (DBD) - REV-ERB ligand binding domain (LBD) α or β and a Gal4-responsive luciferase reporter (REV-ERBα IC_{50}=790 nM, REV-ERBβ IC_{50}=560 nM). SR9011 potently and efficaciously suppresses transcription in a cotransfection assay using full-length REV-ERBα along with a luciferase reporter driven by the Bmal1 promoter (SR9011 IC_{50} =620 nM). SR9011 suppresses the expression ofBMAL1 mRNA in HepG2 cells in a REV-ERBα/β-dependent manner[1] SR9011 suppresses proliferation of the breast cancer cell lines regardless of their ER or HER2 status. SR9011 appears to pause the cell cycle of the breast cancer cells prior to M phase. Cyclin A (CCNA2) is identified as a direct target gene of REV-ERB suggesting that suppression of expression of this cyclin by SR9011 may mediate the cell cycle arrest. Treatment with SR9011 results in an increase in cells in the G_0/G_1 phase and a decrease of cells in S and G_2/M phase suggesting that activation of REV-ERB may be resulting in decreased transition from G_1 to S phase and/or from S to G_2/M phase[2].

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

In Vivo	SR9011 displays reasonable plasma exposure, thus, the expression of REV-ERB responsive genes is examined in the liver of mice treated with various doses of SR9011 for 6-days. The plasminogen activator inhibitor type 1 gene (Serpine1) is a REV-ERB target gene and displays dose-dependent suppression of expression in response to SR9011. The cholesterol 7α-hydroxylase (Cyp7a1) and sterol response element binding protein (Srepf1) genes have also been shown to be responsive to REV-ERB and are dose-dependently suppressed with increasing amounts of SR9011. After 12 days in D:D conditions mice are injected with a single dose of SR9011 or vehicle at CT6 (peak expression of Rev-erbα). Vehicle injection causes no disruption in circadian locomotor activity. However, administration of a single dose of SR9011 results in loss of locomotor activity during the subject dark phase. Normal activity returns the next circadian cycle, consistent with clearance of the drugs in less than 24h. The SR9011-dependent decrease in wheel running behavior in the mice under constant darkness conditions is dose-dependent and that the potency (ED_{50}=56 mg/kg) is similar to the potency of SR9011-mediated suppression of a REV-ERB responsive gene, Srebf1 , in vivo (ED_{50}=67mg/kg)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	MCF10A, MDA-MB-231, MCF-7, MDA-MB-361, SKBR3, BT474 cells are plated in 6-well plates one day before treatment. The MTT cell proliferation assays are performed. Briefly, 3×10^3 to 5×10^3 cells per well are plated in 96-well plates. Twenty-four hours later, cells are treated with SR9011 (0, 2, 4, 6, 8 and 10 μM) or DMSO. Seventy-two hours after treatment, the cells are labeled with 1.2 mM MTT and incubated for 4 hours. DMSO is then added and readings are taken on a plate reader at 540 nm [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] For circadian gene expression experiments male C57BL6 mice (8-10 weeks of age) are either maintained on a L:D (12h:12h) cycle or on constant darkness. At circadian time (CT) 0 animals are administered a single dose of 100 mg/kg SR9011 (i.p.) and groups of animals (n=6) are sacrificed at CT0, CT6, CT12 and CT18. Gene expression is determined by real time QPCR. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Res. 2022 Apr 15;82(8):1503-1517.
- Cell Prolif. 2021 Jan 13;e12988.
- Acta Pharmacol Sin. 2019 Jan;40(1):26-34.
- Free Radical Bio Med. 2019 Dec;145:312-320.
- Br J Pharmacol. 2021 Jan;178(2):328-345.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Solt LA, et al. Regulation of circadian behaviour and metabolism by synthetic REV-ERB agonists. Nature. 2012 Mar 29;485(7396):62-8.

[2]. Wang Y, et al. Anti-proliferative actions of a synthetic REV-ERBα/β agonist in breast cancer cells. Biochem Pharmacol. 2015 Aug 15;96(4):315-22.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA