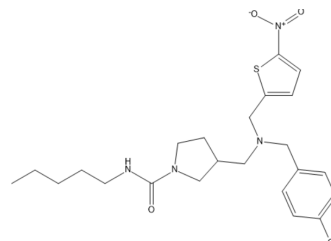


SR9011

Cat. No.:	HY-16988		
CAS No.:	1379686-29-9		
Molecular Formula:	C ₂₃ H ₃₁ ClN ₄ O ₃ S		
Molecular Weight:	479.04		
Target:	REV-ERB		
Pathway:	Metabolic Enzyme/Protease		
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 : ≥ 43 mg/mL (89.76 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.0875 mL	10.4375 mL	20.8751 mL
	5 mM	0.4175 mL	2.0875 mL	4.1750 mL
	10 mM	0.2088 mL	1.0438 mL	2.0875 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 (5.22 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (5.22 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SR9011 is a REV-ERB α / β agonist with IC₅₀s of 790 nM and 560 nM for REV-ERB α and REV-ERB β , respectively.

IC₅₀ & Target

IC₅₀: 790 nM (Rev-ErbB α), 560 nM (Rev-ErbB β)^[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-ERB α IC₅₀=790 nM, REV-ERB β IC₅₀=560 nM). SR9011 potently and efficaciously suppresses transcription in a cotransfection assay using full-length REV-ERB α along with a luciferase reporter driven by the Bmal1 promoter (SR9011 IC₅₀=620 nM). SR9011 suppresses the expression of BMAL1 mRNA in HepG2 cells in a REV-ERB α / 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 G₀/G₁ phase and a decrease of cells in S and G₂/M phase suggesting that activation of REV-ERB may be resulting in decreased transition from G₁ to S phase and/or from S to G₂/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 7 α -hydroxylase (Cyp7a1) and sterol response element binding protein (Srebp1) 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-erba). 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 (ED₅₀=56 mg/kg) is similar to the potency of SR9011-mediated suppression of a REV-ERB responsive gene, Srebf1, in vivo (ED₅₀=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, 3×10³ to 5 × 10³ 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 μ M) 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.
- Br J Pharmacol. 2021 Jan;178(2):328-345.
- Free Radical Bio Med. 2019 Dec;145:312-320.
- Cell Prolif. 2021 Jan 13:e12988.
- Acta Pharmacol Sin. 2019 Jan;40(1):26-34.

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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-ERB α / 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.

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