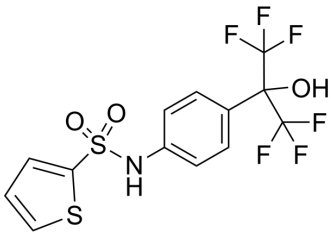
SR3335

Cat. No.:	HY-14413
CAS No.:	293753-05-6
Molecular Formula:	$C_{13}H_9F_6NO_3S_2$
Molecular Weight:	405.34
Target:	ROR
Pathway:	Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor
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 : ≥ 100 mg/mL (246.71 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4671 mL	12.3353 mL	24.6706 mL
5 mM	0.4934 mL	2.4671 mL	4.9341 mL
10 mM	0.2467 mL	1.2335 mL	2.4671 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 (6.17 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.17 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.17 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	SR3335 (ML 176) is a selective RORα inverse agonist that directly binds to RORα with a K_i of 220 nM[1][2].
IC_{50} & Target	Ki: 220 nM (RORα)[1]
In Vitro	SR3335 is a selective RORα partial inverse agonist. In a biochemical radioligand binding assay using [^{3}H]25-hydroxycholesterol as a label it is clear that unlabeled SR3335 dose-dependently competes for binding to the RORα LBD. The

	K_i is calculated as 220 nM using the Cheng-Prusoff equation. In a cell-based chimeric receptor Gal4 DNA-binding domain-NR ligand binding domain cotransfection assay, SR3335 significantly inhibits the constitutive transactivation activity of RORα (IC_{50}=480 nM)(partial inverse agonist activity), but has no effect on the activity of LXRα and RORγ[1]. ?SR3335 suppresses the expression of endogenous RORα target genes in HepG2 cells that are involved in hepatic gluconeogenesis including glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK)[2]. ?SR3335 also blocks IL-25 and IL-33-induced ILC2 proliferation and IL-13 production ex vivo[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SR3335 displays reasonable exposure following an i.p. injection into mice. The ability of SR3335 is assessed to suppress gluconeogenesis using a diet-induced obesity (DIO) mouse model where the mice where treated with 15 mg/kg b.i.d., i.p. for 6-days followed by a pyruvate tolerance test. SR3335 treated mice displays lower plasma glucose levels following the pyruvate challenge consistent with suppression of gluconeogenesis. Importantly, mice treated with SR3335 displayed no difference in body weight or food intake after 7-days of treatment with SR3335[1]. SR3335 (15 mg/kg/day; ip for 7 days) reduces rhinovirus (RV)-induced lung ILC2s in immature mice (RV infection of 6-day-old BALB/c mice)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	HEK293 cells are maintained in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum at 37°C under 5% CO_2. HepG2 cells are maintained and routinely propagated in minimum essential medium supplemented with 10% fetal bovine serum at 37°C under 5% CO_2. 24 h prior to transfection, cells are plated in 96-well plates at a density of 15×10^3 cells/well. Transfections are performed using LipofectamineTM 2000. 16 h post-transfection, the cells are treated with vehicle or SR3335. 24 h post-treatment, the luciferase activity is measured using the Dual-GloTM luciferase assay system. The values indicated represent the means±S.E. from four independently transfected wells. The experiments are repeated at least three times[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] 30 week old Diet induced obese (DIO) C57BL/6 male mice are purchased from Jackson Laboratories that are maintained on a 65% Kcal high-fat diet from weaning. DIO mice are treated twice per day (07:00h and 18:00h) with 15 mg/kg SR3335 or vehicle for 6 days i.p. Pyruvate tolerance test is conducted on day 6 of the treatment. Food is removed from mice in the morning after SR3335 injection, fasted for 6 hours and the pyruvate tolerance test is conducted at 13:00h. Time 0 blood glucose is measured taken from the tail nip and the pyruvate challenge is initiated by injection of 2g/kg of pyruvate i.p. followed by measuring blood glucose at 15, 30 and 60 min following the injection. Blood glucose is measured by one touch ultra glucose-meter. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Pineal Res. 2019 Sep;67(2):e12581.
- Cell Death Dis. 2021 Sep 28;12(10):886.
- NPJ Parkinsons Dis. 2022 Jul 8;8(1):90.
- Antioxidants (Basel). 2022 Apr 8;11(4):748.
- Cell Signal. 2023 Apr 14;107:110678.

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REFERENCES

[1]. Rajput C, et al. RORα-dependent type 2 innate lymphoid cells are required and sufficient for mucous metaplasia in immature mice. Am J Physiol Lung Cell Mol Physiol. 2017;312(6):L983-L993.

[2]. Kumar N, et al. Identification of SR3335 (ML-176): a synthetic RORα selective inverse agonist. ACS Chem Biol. 2011 Mar 18;6(3):218-22.

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