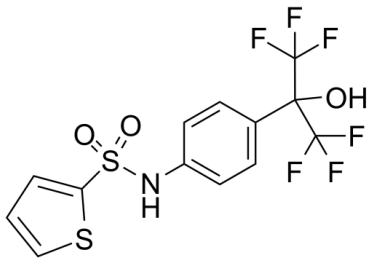
Data Sheet

Product Name:	SR3335
Cat. No.:	CS-1044
CAS No.:	293753-05-6
Molecular Formula:	C13H9F6NO3S2
Molecular Weight:	405.34
Target:	ROR
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 100 mg/mL (246.71 mM)



BIOLOGICAL ACTIVITY:

SR3335 is a selective **RORα** inverse agonist that directly binds to RORα with a K_i of 220 nM. IC50 & 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]. **In Vivo:** Pharmacokinetic studies indicate that 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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: SR3335 is prepared in DMSO and stored, and then diluted with appropriate medium before use[1].[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]. **Animal Administration:** SR3335 is prepared in DMSO and diluted with saline or PBS (Mice)[1].[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.

References:

[1]. 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.

CAIndexNames:

2-Thiophenesulfonamide, N-[4-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-

SMILES:

O=S(C1=CC=CS1)(NC2=CC=C(C(C(F)(F)F)(C(F)(F)F)O)C=C2)=O

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