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产品名称：SR1078
产品别名：SR1078

生物活性：

Description	SR1078 is an agonist of retinoic acid receptor-related orphan receptor α/γ (RORα/RORγ).
IC_{50} & Target	RORα/γ[1]
In Vitro	SR1078 is a synthetic RORα/RORγ ligand. SR1078 modulates the conformation of RORγ in a biochemical assay and activates RORα and RORγ driven transcription. Furthermore, SR1078 stimulates expression of endogenous ROR target genes in HepG2 cells that express both RORα and RORγ. In a cell-based chimeric receptor Gal4 DNA-binding domain-NR ligand binding domain cotransfection assay, SR1078 significantly inhibits the constitutive transactivation activity of RORα and RORγ, but has no effect on the activity of FXR, LXRα and LXRβ. In a RORα cotransfection assay, treatment of cells with SR1078 (10 μM) results in a significant increase in transcription. Similarly, in the RORγ cotransfection assay, SR1078 treatment results in a stimulation of RORγ-dependent transcription activity[1].
In Vivo	The pharmacokinetic properties of SR1078 are examined in mice and noted significant exposure. Plasma concentrations reach 3.6 μM 1h after a 10 mg/kg i.p. injection of SR1078 and sustained levels of above 800 nM even 8h after the single injection. These levels are sufficient to perform a proof-of-principle experiment to determine if SR1078 treatment would stimulate ROR target gene expression in an animal model. Mice are treated with SR1078 (10 mg/kg i.p.) and 2h after the injection the livers are harvested and mRNA purified for assessment of G6Pase and FGF21 gene expression.T he expression of both FGF21 and G6Pase is significantly stimulated by SR1078 treatment vs. vehicle control[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 33.33 mg/mL (77.29 mM;** Need ultrasonic)

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.3188 mL	11.5942 mL	23.1884 mL
	5 mM	0.4638 mL	2.3188 mL	4.6377 mL
	10 mM	0.2319 mL	1.1594 mL	2.3188 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: 2.5 mg/mL (5.80 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.80 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

	以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.80 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.80 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.80 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.80 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Wang Y, et al. Identification of SR1078, a synthetic agonist for the orphan nuclear receptors RORα and RORγ. ACS Chem Biol. 2010 Nov 19;5(11):1029-34.

实验参考：

Cell Assay	HEK293 cells are maintained in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% (v/v) fetal bovine serum at 37°C under 5% CO_2. HepG2 cells are maintained and routinely propagated in minimum essential medium supplemented with 10% (v/v) fetal bovine serum at 37°C under 5% CO_2. In experiments where lipids and sterols are depleted, cells are maintained on charcoal treated serum (10% (v/v) fetal bovine serum) and treated with 7.5 μM lovastatin and 100 μM mevalonic acid. 24 h prior to transfection, HepG2 or HEK293 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 SR1078. 24 h post-treatment, the luciferase activity is measured using the Dual-GloTM luciferase assay system. The experiments are repeated at least three times[1].
Animal Administration	Mice[1] Plasma levels of SR1078 are evaluated in C57BL6 mice (n=3 per time point) administered by i.p. injection. After 1, 2, 4, and 8h blood is taken. In the 2h time point liver is taken for target gene analysis. Plasma is generated using standard centrifugation techniques, and the plasma and tissues are frozen at −80°C. Plasma and tissues are mixed with acetonitrile (1:5 (v/v) or 1:5 (w/v), respectively), sonicated with a probe tip sonicator, and analyzed for drug levels by liquid chromatography/tandem mass spectrometry.
Kinase Assay	The ALPHA screen assays are performed. Assays are performed in triplicate in white opaque 384-well plates under green light conditions (<100 lux) at room temperature. The final assay volume is 20 μL. All dilutions are made in assay buffer (100 mM NaCl, 25 mM Hepes, 0.1% (w/v) BSA, pH 7.4). The final DMSO concentration is 0.25% (v/v). A mix of 12 μL of GST-RORγ-LBD (10 nM), beads (12.5 μg/mL of each donor and acceptor), and 4 μL of increasing concentrations (210 nM-50 μM) of compound SR1078 are added to the wells, the plates are sealed and incubated for 1h. After

	this preincubation step, 4 μL of Biotin-TRAP220-2 peptide (50 nM) is added, the plates are sealed and further incubated for 2h. The plates are read on PerkinElmer Envision 2104 and data analyzed using GraphPad Prism software[1].
References	[1]. Wang Y, et al. Identification of SR1078, a synthetic agonist for the orphan nuclear receptors RORα and RORγ. ACS Chem Biol. 2010 Nov 19;5(11):1029-34.