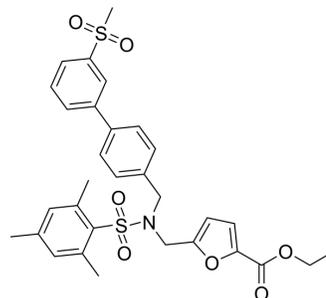


## SR9238

<b>Cat. No.:</b>	HY-101442		
<b>CAS No.:</b>	1416153-62-2		
<b>Molecular Formula:</b>	C <sub>31</sub> H <sub>33</sub> NO <sub>7</sub> S <sub>2</sub>		
<b>Molecular Weight:</b>	595.73		
<b>Target:</b>	LXR		
<b>Pathway:</b>	Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : 50 mg/mL (83.93 mM; Need ultrasonic)					
		Solvent Concentration	Mass	1 mg	5 mg	10 mg
	<b>Preparing Stock Solutions</b>	1 mM		1.6786 mL	8.3931 mL	16.7861 mL
		5 mM		0.3357 mL	1.6786 mL	3.3572 mL
10 mM			0.1679 mL	0.8393 mL	1.6786 mL	
Please refer to the solubility information to select the appropriate solvent.						
<b>In Vivo</b>	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: 2.5 mg/mL (4.20 mM); Suspended solution; Need ultrasonic  2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (4.20 mM); Clear solution					

### BIOLOGICAL ACTIVITY

<b>Description</b>	SR9238 is a synthetic liver X receptor (LXR) inverse agonist with IC <sub>50</sub> s of 214 nM and 43 nM for LXR $\alpha$ and LXR $\beta$ , respectively.
<b>IC<sub>50</sub> &amp; Target</b>	IC <sub>50</sub> : 43 nM (LXR $\beta$ ), 214 nM (LXR $\alpha$ ) <sup>[1]</sup>
<b>In Vitro</b>	Results from the cell-based cotransfection assays demonstrate that SR9238 is a synthetic LXR inverse agonist with IC <sub>50</sub> s of 214 nM and 43 nM for LXR $\alpha$ and LXR $\beta$ , respectively. SR9238 also effectively suppresses transcription from a fatty acid synthase (Fasn) promoter driven luciferase reporter. It is found that SR9238 induces increased interaction of CoNR box peptides derived from NCoR (NCoR ID1 and NCoR ID2) with both LXR $\alpha$ and LXR $\beta$ , while causing decreased interaction with a coactivator NR box peptide derived from TRAP220. SR9238-induced recruitment of CoNR box peptides is dose-dependent for both LXR $\alpha$ and LXR $\beta$ . HepG2 cells treated with SR9238 result in a significant decrease in Fasn and Srebp1c mRNA

expression<sup>[1]</sup>.

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

#### In Vivo

Approximately 6  $\mu$ M SR9238 is detected in the liver 2h after the injection of SR9238, but no compound is detected in the plasma. SR9238 is also detected in the intestine with either ip or oral administration. SR9238-treated mice display greatly reduced lipid content in the liver. Results demonstrate that both Tnfa and Il1b expression are substantially reduced (~80% and >95%, respectively) in the SR9238-treated mice when compare to the vehicle-treated mice. SR9238-treated DIO mice display considerably lower intensity of F4/80 staining versus vehicle-treated DIO mice consistent with a beneficial effect of SR9238 on non-alcoholic steatohepatitis (NASH). SR9238 treatment does not alter body weight or percent body fat composition relative to vehicle treated animals during the experiment. Treatment with SR9238 suppresses diet-induced hepatosteatosis, hepatic inflammation, and hepatocellular injury<sup>[1]</sup>.

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## PROTOCOL

#### Cell Assay <sup>[1]</sup>

HepG2 cells are seeded at  $5 \times 10^5$  cells/mL in a 4-chamber culture slide. The following day the media is removed and replaced with antibiotic-free media containing 10  $\mu$ M of DMSO or SR9238 and cells are allowed to grow for 48 h. Cells are washed in TBS, fixed and fluorescently stained for SREBP2 according to the assay protocol<sup>[1]</sup>.

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#### Animal Administration <sup>[1]</sup>

Twenty-one-week-old male C57BL6 DIO mice are used. Animals are individually housed and fed a high fat diet (60% kcal/fat diet, 20% carbohydrate) for the duration of the experiment that includes SR9238 administration for 30 days (30 mg/kg, qd, ip). Prior to initiation of the experiment, animals are provided the high fat diet for 10-weeks. Animals are acclimated to the environment for one week and sham dosed with vehicle for 3 days prior to SR9238 administration. Body weight and food intake are monitored daily. Pre- and post-experiment body composition analysis is performed on all the mice. Blood is collected by cardiac puncture and used for plasma cholesterol and triglyceride measurements. Livers are weighed and immediately flash-frozen in liquid nitrogen for gene expression analysis or put in formalin on ice for histology<sup>[1]</sup>.

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

## REFERENCES

[1]. Griffett K, et al. A liver-selective LXR inverse agonist that suppresses hepatic steatosis. ACS Chem Biol. 2013 Mar 15;8(3):559-67.

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

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