

Product Data Sheet

Product Name: SR 8278

Cat. No.: GC15275

Chemical Properties

Cas. No. 1254944-66-5

Chemical Name (S)-ethyl 2-(5-(methylthio)thiophene-2-carbonyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate

SMILES O=C([C@H]1N(C(C2=CC=C(SC)S2)=O)CC3=CC=CC=C3C1)OCC

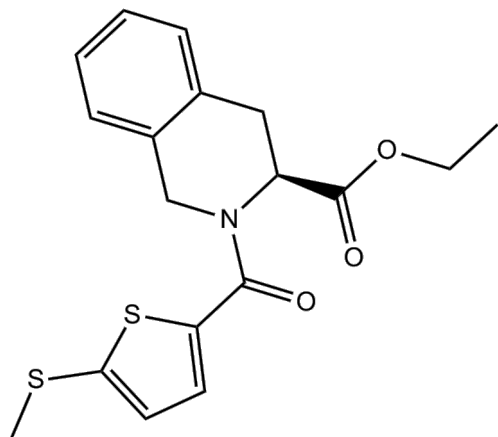
Formula $C_{18}H_{19}NO_3S_2$ M.Wt 361.48

Solubility $\leq 15\text{mg/ml}$ in ethanol; $\leq 10\text{mg/ml}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



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

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Protocol

Cell experiment [1]:

Cell lines HaCaT keratinocytes

Preparation Method HaCaT cells were pre-treated with DMSO vehicle, SR 8278 (50 μ M), KS15 (50 μ M), or both KS15 and SR 8278 (KS+SR) for 24h before exposure to the indicated fluences of UVB radiation. MTT assays were performed 3 days later to determine relative viability.

Reaction
Conditions 50 μ M; 24h

Applications The REV-ERB inhibitor SR 8278 protects keratinocytes against UVB radiation.

Animal experiment [2]:

Animal models Sprague-Dawley rats

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The present study employed a randomized experimental design in which rats were assigned to one of eight groups. These included a control group that received DMSO, a drug control group that received 50mg/kg of SR9009 (i.p.), a group subjected to lung IR, and three groups that received different doses of SR9009 (12.5mg, 25mg, or 50mg/kg) along with lung IR, IR+SR8278 (5mg/kg), or IR+SR 8278 (5mg/kg)+SR9009 (50mg/kg) group. To facilitate intraperitoneal

Preparation Method injection, SR9009 was dissolved in 0.5% DMSO and administered 60 min before inducing lung IR. In the IR + SR 8278 + SR9009 group, rats were pretreated with SR 8278 for 30min prior to SR9009 injection. Lung IR was induced by stopping ventilation and perfusion, leading to ischemia, and then maintaining the lungs in a deflated state for 40min, followed by 60min of ventilation and perfusion. In contrast, the control group received perfusate alone for 100min.

Dosage form 5mg/kg; i.p.

Applications SR 8278 abolished the protective effects of SR9009 in IR-ALI. In this model, SR9009 had previously demonstrated a dose-dependent reduction in lung edema, along with significant inhibition of TNF- α , IL-6, and CINC-1 production in BALF. Additionally, SR9009 restored suppressed I κ B- α levels and reduced nuclear NF- κ B p65 accumulation in lung tissues. It also mitigated IR-induced apoptosis and suppressed MAPK activation in injured lung tissue. However, SR 8278 treatment completely reversed these protective mechanisms.

References:

- [1] Cvammen W, Kemp M G. The REV[?]ERB antagonist SR8278 modulates keratinocyte viability in response to UVA and UVB radiation[J]. Photochemistry and Photobiology, 2024, 100(6): 1864-1873.
[2] Chu S J, Liao W I, Pao H P, et al. Targeting Rev-Erb α to protect against ischemia-reperfusion-induced acute lung injury in rats[J]. Respiratory Research, 2023, 24(1): 247.

Background

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SR 8278 is an antagonist of the nuclear receptor REV-ERB α that can inhibit the transcription of REV-ERB α with an EC₅₀ value of 0.47 μ M^[1]. SR 8278 can be used to regulate metabolism in vivo, study biological rhythms, and treat mood disorders caused by Parkinson's disease^[2, 3]. SR 8278 can effectively enhance the tear secretion function of jet-lagged mice by targeting NR1D1 inhibition^[4].

In vitro, SR 8278 (50 μ M) pretreatment of HaCaT keratinocytes for 24h can protect keratinocytes from UVB radiation damage, but can make keratinocytes sensitive to UVA radiation and produce reactive oxygen species^[5].

In vivo, SR 8278 (20 μ g/mouse) was slowly injected into the ventral tegmental area (VTA) of the midbrain to treat Parkinson's disease mice, which restored the emotion-related behavioral defects exhibited by the mice and restored the binding activity of REV-ERB α and NURR1^[3]. SR 8278 (5mg/kg) was intraperitoneally injected into rats with acute lung injury (ALI) induced by ischemia-reperfusion (IR). It completely abolished the protective effect of SR9009 in IR-ALI and reversed the protective mechanisms of SR9009, including reducing pulmonary edema, inhibiting the production of inflammatory factors in bronchoalveolar lavage fluid (BALF), and reducing the accumulation of nuclear NF- κ B p65 in lung tissue^[6].

References:

- [1] Kojetin D, Wang Y, Kamenecka T M, et al. Identification of SR8278, a synthetic antagonist of the nuclear heme receptor REV-ERB[J]. ACS chemical biology, 2011, 6(2): 131-134.
- [2] Dong D, Sun H, Wu Z, et al. A validated ultra-performance liquid chromatography-tandem mass spectrometry method to identify the pharmacokinetics of SR8278 in normal and streptozotocin-induced diabetic rats[J]. Journal of Chromatography B, 2016, 1020: 142-147.
- [3] Kim J, Park I, Jang S, et al. Pharmacological rescue with SR8278, a circadian nuclear receptor REV-ERB α antagonist as a therapy for mood disorders in Parkinson's disease[J]. Neurotherapeutics, 2022, 19(2): 592-607.
- [4] Huang S, QI D, Pei X, et al. Transcriptomic analysis of SR8278 improving lacrimal gland dysfunction in-duced by jet lag in mice[J]. Recent Advances in Ophthalmology, 2024: 264-269.
- [5] Cvammen W, Kemp M G. The REV-ERB antagonist SR8278 modulates keratinocyte viability in response to UVA and UVB radiation[J]. Photochemistry and Photobiology, 2024, 100(6): 1864-1873.
- [6] Chu S J, Liao W I, Pao H P, et al. Targeting Rev-Erb α to protect against ischemia-reperfusion-

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