# GSK2945 hydrochloride

**Cat. No.:** HY-117147A

**Molecular Formula:** $C_{20}H_{19}Cl_3N_2O_2S$

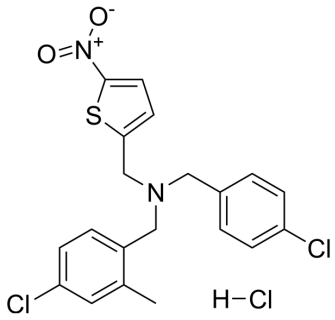
**Molecular Weight:** 457.8

**Target:** Cytochrome P450

**Pathway:** Metabolic Enzyme/Protease

**Storage:** 4°C, stored under nitrogen

* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 20.83 mg/mL (45.50 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.1844 mL | 10.9218 mL | 21.8436 mL |
| | 5 mM | 0.4369 mL | 2.1844 mL | 4.3687 mL |
| | 10 mM | 0.2184 mL | 1.0922 mL | 2.1844 mL |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.54 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.54 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

GSK2945 hydrochloride is a class of tertiary amine, and is a highly specific Rev-erbα/REV-ERBα (mouse/human reverse erythroblastosis virus α) antagonist with $EC_{50}$s of 21.5 μM and 20.8 μM, respectively. GSK2945 hydrochloride enhances cholesterol 7α-hydroxylase (CYP7A1) level and cholesterol metabolism[1].

**In Vitro**

GSK2945 dose-dependently enhances the transcriptional activity of Rev-erbα and a Bmal1 (a target gene of REV-ERBs) luciferase reporter ($EC_{50}$ of 2.05 μM)[1].

?GSK2945 (20 μM; 12 hours and 24 hours; mouse and human primary hepatocytes) treatment increases levels of Cyp7a1/CYP7A1 in mouse and human primary hepatocytes. GSK2945 (20 μM) treatment also increases Lrh-1/LRH-1 (a known hepatic activator of Cyp7a1/CYP7A1) mRNA and protein[1].

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

RT-PCR[1]

| | |
|---|---|
| Cell Line: | Mouse (male, CD1) and human (male, Caucasian) primary hepatocytes |
| Concentration: | 20 μM |
| Incubation Time: | 12 hours and 24 hours |
| Result: | Led to significant increases in mRNA and protein (at 24-h) expression of Cyp7a1. mRNA and protein (at 24-h) levels of CYP7A1 were increased in human primary hepatocyte. Lrh-1/LRH-1 was upregulated. |

**In Vivo**

GSK2945 (0-10 mg/kg; intraperitoneal injection; twice every day; for 7 days; male C57BL/6 mice) treatment increases hepatic mouse cholesterol 7α-hydroxylase (Cyp7a1) level and lowers plasma cholesterol in wild-type mice[1].

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

| | |
|---|---|
| Animal Model: | Male C57BL/6 mice (8-10 weeks of age)[1] |
| Dosage: | 0 mg/kg or 10 mg/kg |
| Administration: | Intraperitoneal injection; twice every day; for 7 days |
| Result: | Increased hepatic mouse cholesterol 7α-hydroxylase (Cyp7a1) level and lowered plasma cholesterol in wild-type mice. |

## REFERENCES

[1]. Zhang T, et al. REV-ERBα Regulates CYP7A1 Through Repression of Liver Receptor Homolog-1. Drug Metab Dispos. 2018 Mar;46(3):248-258.



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