GSK3787

Cat. No.: HY-15577

CAS No.: 188591-46-0

Molecular Formula: $C_{15}H_{12}ClF_3N_2O_3S$

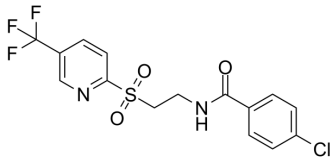
Molecular Weight: 392.78

Target: PPAR

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (127.30 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5460 mL	12.7298 mL	25.4595 mL
5 mM	0.5092 mL	2.5460 mL	5.0919 mL
10 mM	0.2546 mL	1.2730 mL	2.5460 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (6.36 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.36 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK3787 is a selective and irreversible peroxisome proliferator-activated receptor δ (PPARδ) antagonist with pIC_{50} of 6.6.

IC_{50} & Target

PPARδ
6.6 nM (pIC_{50})

In Vitro

GSK3787 is identified as a potent and selective hPPARδ ligand (pIC_{50}=6.6) with no measurable affinity for hPPARα or hPPARγ (pIC_{50} < 5) in our standard in vitro ligand displacement assay. GSK3787 is inactive against hPPARα and hPPARγ in similar functional antagonist assays. GSK3787 fails to activate the receptor in a standard hPPARδ-GAL4 chimera cell-based reporter assay. GSK3787 is a selective PPARδ antagonist with equipotent species activity against the human and mouse receptor[1].

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

In Vivo

GSK3787 has pharmacokinetic properties suitable for use as an in vivo PPARδ antagonist tool compound in mice. GSK3787 is administered intravenously (0.5 mg/kg) and orally (10 mg/kg) to male C57BL/6 mice. Mean clearance (CL) and volume of distribution at steady state (V_{ss}) following iv administration are 39±11 (mL/min)/kg and 1.7±0.4 L/kg, respectively. Following oral administration, good exposure (C_{max}=881±166 ng/mL, AUC_{inf}=3343±332 h•ng/mL), half-life (2.7±1.1 h), and bioavailability (F=77±17%) are observed[1]. Oral administration of GSK3787 (10 mg/kg) leads to a serum C_{max} of 2.2±0.4 μM in C57BL/6 male mice. Oral administration of GW0742 causes an increase in expression of Angptl4 and Adrp mRNA (known PPARβ/δ target genes) in wild-type mouse colon epithelium, and this effect is not found in Pparβ/δ-null mouse colon epithelium. Coadministration of GSK3787 with GW0742 effectively prevents the ligand-induced expression of both Angptl4 and Adrp mRNA in wild-type mouse colon epithelium, and this effect is not found in Pparβ/δ-null mouse colon epithelium. Oral administration of GSK3787 causes a modest increase in promoter occupancy of PPARβ/δ in the PPRE region of both the Angptl4 and Adrp genes, but coadministration of GSK3787 with GW0742 results in markedly less accumulation of PPARβ/δ in the PPRE region of both the Angptl4 and Adrp genes in wild-type mouse colon epithelium[2].

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PROTOCOL

Animal Administration [2]

Mice[2]

For RNA and DNA analysis, male wild-type and ***Ppar***β/δ-null mice are administered vehicle (corn oil), GW0742 (10 mg/kg), GSK3787 (10 mg/kg), or GW0742 and GSK3787 by oral gavage 3 h before euthanasia. After euthanasia, colons are carefully dissected. To isolate colon epithelium, colons are flushed with phosphate-buffered saline, and epithelial cells are scraped from mucosa using a razor blade. The isolated tissues are used for RNA isolation. For glucose-tolerance tests, male wild-type and Pparβ/δ-null mice are administered vehicle (corn oil), GW0742 (10 mg/kg), GSK3787 (10 mg/kg), or Rosiglitazone (20 mg/kg) by oral gavage once a day for 2 weeks.

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CUSTOMER VALIDATION

- Biol Psychiatry. 2021 Mar 15;89(6):615-626.
- Oncol Res. 2019 Aug 8;27(8):923-933.
- iScience. 21 September 2021.
- Front Pharmacol. 2018 Jun 28;9:648.
- Cell Signal. 2020 Aug;72:109628.

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REFERENCES

[1]. Shearer BG, et al. Identification and characterization of 4-chloro-N-(2-{[5-trifluoromethyl)-2-pyridyl]sulfonyl}ethyl)benzamide (GSK3787), a selective and irreversible peroxisome proliferator-activated receptor delta (PPARdelta) antagonist. J Med Chem. 2010 Feb 25;53(4):1857-61.

[2]. Palkar PS, et al. Cellular and pharmacological selectivity of the peroxisome proliferator-activated receptor-beta/delta antagonist GSK3787. Mol Pharmacol. 2010 Sep;78(3):419-30.

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

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