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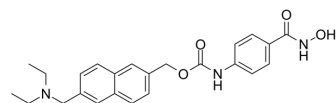
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Givinostat

Cat. No.:	HY-14842
CAS No.:	497833-27-9
Molecular Formula:	C ₂₄ H ₂₇ N ₃ O ₄
Molecular Weight:	421.49
Target:	HDAC
Pathway:	Cell Cycle/DNA Damage; Epigenetics
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (593.13 mM; Need ultrasonic)

	Solvent Concentration	Mass	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		2.3725 mL	11.8627 mL	23.7254 mL
	5 mM		0.4745 mL	2.3725 mL	4.7451 mL
	10 mM		0.2373 mL	1.1863 mL	2.3725 mL

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

BIOLOGICAL ACTIVITY

Description

Givinostat (ITF-2357) is a HDAC inhibitor with an IC₅₀ of 198 and 157 nM for HDAC1 and HDAC3, respectively.

IC₅₀ & Target

hHDAC3 157 nM (IC ₅₀)	HD1-B 7.5 nM (IC ₅₀)	HD1-A 16 nM (IC ₅₀)	HD2 10 nM (IC ₅₀)
hHDAC1 198 nM (IC ₅₀)	hHDAC11 292 nM (IC ₅₀)	hHDAC6 315 nM (IC ₅₀)	hHDAC2 325 nM (IC ₅₀)
hHDAC10 340 nM (IC ₅₀)	hHDAC7 524 nM (IC ₅₀)	hHDAC5 532 nM (IC ₅₀)	hHDAC9 541 nM (IC ₅₀)
hHDAC3 157 nM (IC ₅₀)	hHDAC1 198 nM (IC ₅₀)	hHDAC11 292 nM (IC ₅₀)	hHDAC6 315 nM (IC ₅₀)
hHDAC2 325 nM (IC ₅₀)	hHDAC10 340 nM (IC ₅₀)	hHDAC7 524 nM (IC ₅₀)	hHDAC5 532 nM (IC ₅₀)

	hHDAC9 541 nM (IC ₅₀)	hHDAC8 854 nM (IC ₅₀)	hHDAC4 1059 nM (IC ₅₀)
In Vitro	<p>Givinostat (ITF2357) suppresses total LPS-induced IL-1β production robustly compared with the reduction by ITF3056. At 25, 50, and 100 nM, Givinostat reduced IL-1β secretion more than 70%. Givinostat (ITF-2357) suppresses the production of IL-6 in PBMCs stimulated with TLR agonists as well as the combination of IL-12 plus IL-18. IL-6 secretion decreases to 50% at 50 nM Givinostat, but at 100 and 200 nM, there is no reduction^[1]. As shown by the CCK-8 assay, Givinostat (ITF-2357) inhibits JS-1 cell proliferation in a concentration-dependent manner. Treatment with Givinostat \geq500 nM is associated with significant inhibition of JS-1 cell proliferation (P<0.01). Also, the cell inhibition rate significantly differs between the group cotreated with Givinostat \geq250 nM plus LPS and the group without LPS treatment (same Givinostat concentration) (P<0.05)^[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		
In Vivo	<p>Givinostat (ITF2357) at 10 mg/kg is used as a positive control and, as expected, reduced serum TNFα by 60%. Strikingly, pretreatment of ITF3056 starting at 0.1 mg/kg significantly reduces the circulating TNFα by nearly 90%. To achieve a significant increase in serum IL-1β production, a higher dose of LPS is injected (10 mg/kg), and blood is collected after 4 h. Similarly, when pretreated with lower doses of Givinostat (ITF-2357) (1 or 5 mg/kg), there is a 22% reduction for 1 mg/kg and 40% for 5 mg/kg^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		

PROTOCOL

Cell Assay ^[2]	<p>After the JS-1 cell line is cultured in DMEM with 10% fetal bovine serum for 24 h, 30 wells of JS-1 cells are divided into two groups. In the first group, the culture medium is replaced by complete medium with final Givinostat (ITF-2357) concentrations of 0 nM, 125 nM, 250 nM, 500 nM, and 1000 nM. In the second group, Givinostat of relevant concentrations is added concomitantly with 100 nM of LPS solution. Three replicates are performed for each group. After inoculation at 37°C and 5% CO₂ for 24 h, each well (100 μL) is incubated with 10 μL of CCK-8 solution. The plates are incubated at 37°C for 1 h and the absorbance is measured at 450 nm using a microplate reader^[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Animal Administration ^[1]	<p>Mice^[1] C57BL/6 mice are housed in the animal facility for at least 5 days before use. For the comparison study, Givinostat (ITF2357) at 10 mg/kg is administered orally, and ITF3056 is injected intraperitoneally. One hour after administration of the compounds, the animals are treated intraperitoneally with LPS from Salmonella typhimurium at a dose of 2.5 mg/kg. 90 min after the LPS treatment, mice are sacrificed, and sera are collected and stored at -80°C until further analysis of cytokine productions. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

CUSTOMER VALIDATION

- Cell Death Dis. 2020 Sep 15;11(9):753.
- Cell Prolif. 2021 May 24;e13072.
- Acta Pharmacol Sin. 2021 Apr 13.
- J Orthop Transl. 29 (2021) 106-112.
- Commun Biol. 2021 Oct 29;4(1):1235.

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REFERENCES

- [1]. Li S, et al. Specific inhibition of histone deacetylase 8 reduces gene expression and production of proinflammatory cytokines in vitro and in vivo. J Biol Chem. 2015 Jan 23;290(4):2368-78.
- [2]. Wang YG, et al. Givinostat inhibition of hepatic stellate cell proliferation and protein acetylation. World J Gastroenterol. 2015 Jul 21;21(27):8326-39.
- [3]. Leoni F, et al. The histone deacetylase inhibitor ITF2357 reduces production of pro-inflammatory cytokines in vitro and systemic inflammation in vivo. Mol Med. 2005 Jan-Dec;11(1-12):1-15.
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Caution: Product has not been fully validated for medical applications. For research use only.

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