产品名称：Givinostat (ITF2357)
产品别名：ITF-2357 hydrochloride monohydrate；Givinostat hydrochloride monohydrate

生物活性：

Description	Givinostat (ITF-2357) is a HDAC inhibitor with an IC_{50} of 198 and 157 nM for HDAC1 and HDAC3, respectively.

IC_{50} & Target

hHDAC3	hHDAC1	hHDAC11	hHDAC6	hHDAC2
157 nM (IC_{50})	198 nM (IC_{50})	292 nM (IC_{50})	315 nM (IC_{50})	325 nM (IC_{50})
hHDAC10	hHDAC7	hHDAC5	hHDAC9	hHDAC8
340 nM (IC_{50})	524 nM (IC_{50})	532 nM (IC_{50})	541 nM (IC_{50})	854 nM (IC_{50})
hHDAC4	HD1-B	HD1-A	HD2	
1059 nM (IC_{50})	7.5 nM (IC_{50})	16 nM (IC_{50})	10 nM (IC_{50})	

In Vitro

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 (ITF2357) 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 (ITF2357), but at 100 and 200 nM, there is no reduction[1]. As shown by the CCK-8 assay, Givinostat (ITF2357) inhibits JS-1 cell proliferation in a concentration-dependent manner. Treatment with Givinostat (ITF2357) ⩾500 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 ⩾250 nM plus LPS and the group without LPS treatment (same Givinostat concentration) ($P<0.05$)[2].

In Vivo

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 (ITF2357) (1 or 5 mg/kg), there is a 22% reduction for 1 mg/kg and 40% for 5 mg/kg[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (210.10 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1010 mL	10.5049 mL	21.0097 mL
5 mM	0.4202 mL	2.1010 mL	4.2019 mL
10 mM	0.2101 mL	1.0505 mL	2.1010 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

	——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.17 mg/mL (4.56 mM); Clear solution 此方案可获得 ≥ 2.17 mg/mL (4.56 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 21.7 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.17 mg/mL (4.56 mM); Clear solution 此方案可获得 ≥ 2.17 mg/mL (4.56 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 21.7 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.17 mg/mL (4.56 mM); Clear solution 此方案可获得 ≥ 2.17 mg/mL (4.56 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 21.7 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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 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% CO_2 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].
Animal Administration	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 Givinostat (ITF2357) 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.
	[1]. Li S, et al. Specific inhibition of histone deacetylase 8 reduces gene expression and production

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