CBL0137 hydrochloride

Cat. No.: HY-18935A

CAS No.: 1197397-89-9

Molecular Formula: $C_{21}H_{25}ClN_2O_2$

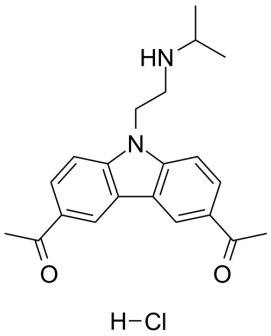
Molecular Weight: 372.89

Target: MDM-2/p53; NF-κB

Pathway: Apoptosis; NF-κB

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 : 33.33 mg/mL (89.38 mM; Need ultrasonic)

H_2O : 10 mg/mL (26.82 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6818 mL	13.4088 mL	26.8176 mL
5 mM	0.5364 mL	2.6818 mL	5.3635 mL
10 mM	0.2682 mL	1.3409 mL	2.6818 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 (6.70 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.70 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CBL0137 hydrochloride is an inhibitor of the histone chaperone, FACT. CBL0137 hydrochloride can also activate p53 and inhibits NF-κB with EC_{50}s of 0.37 and 0.47 μM, respectively.

IC_{50} & Target

p53	NF-κB
0.37 μM (IC_{50})	0.47 μM (IC_{50})

In Vitro

Treatment with CBL0137 hydrochloride leads to complete absence of living cells at concentrations above 2.5 μM. CBL0137 hydrochloride causes a greater reduction in the number of colonies formed of not only MiaPaCa-2 cells when combines with gemcitabine, but also gemcitabine-resistant PANC-1 cells. Treatment of human pancreatic cancer cells with CBL0137

	hydrochloride results in a dose dependent reduction of protein and mRNA levels of RRM1 and RRM2[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The CBL0137 hydrochloride monotherapy group and the CBL0137 hydrochloride-gemcitabine combination group samples show large necrotic fields, numerous apoptotic bodies and loss of tumor cells. Sub-optimal doses of 50 to 60 mg/kg CBL0137 hydrochloride causes similar enhancement of gemcitabine antitumor activity as that produced by the maximum tolerated dose (MTD) of 90 mg/kg as indicated by the lack of statistically significant differences among the combination groups. CBL0137 hydrochloride inhibits FACT function through depletion of the pool of active FACT involved in transcription elongation[1]. CBL0137 hydrochloride, given by oral gavage at a nontoxic dose of 30 mg/kg per day on a 5 days on/2 days off schedule, suppresses tumor growth in xenografts of colon (DLD-1), renal cell carcinoma (Caki-1), and melanoma (Mel-7) tumor cell lines and transplanted surgical samples from patients with pancreatic ductal adenocarcinoma[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	MiaPaca2 and BxPC-3 cells are treated with CBL0137 hydrochloride for 4 or 24 h. Cells are harvested in 1× Cell Culture Lysis Reagent containing protease and phosphatase inhibitors. Lysates 5 to 20 μg are separated on SDS-PAGE gels and transferred to PVDF membranes. Blots are probed with antibodies specific for SSRP1, SPT16, RRM1, and RRM2. GAPDH is used as a loading control. Proteins are visualized using ECL kit[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Cells are resuspended in serum free Dulbecco's Modified Eagle Medium (DMEM) and treated with different concentrations of CBL0137 hydrochloride for 1h. After that 10^5 cells from each treatment condition are plated in 3 wells of 6-well plate in 2 mL of serum-free DMEM/F12 medium supplemented with 0.4% BSA, 0.2×B27, 10 ng/mL recombinant EGF and containing 0.25% agarose. 10^3 cells from each treatment condition are plated in 3 wells of 6-well plate in regular FBS containing medium. Colonies are counted using inverted microscope 7 to 15 days after plating[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	10-week old female athymic nude mice (n=8 per treatment group) are deeply anesthetized with ketamine/xylazine. Using laparotomy, 2×10^6 PANC-1 cells are inoculated into the tail of the pancreas of each mouse. Two weeks following inoculation (tumor presence confirmed by ultrasound), treatment commenced. The following regimens are used: 1) vehicles, 100 mg/kg captisol i.v. and sterile water via gavage, 2) 50 to 90 mg/kg CBL0137 hydrochloride in 100 mg/mL captisol i.v. delivered via tail vein once per week, 3) 10 to 20 mg/kg CBL0137 hydrochloride p.o. via oral gavage, 5 days on/2 days off. Tumor measurement is done with digital calipers. Tumor volume is calculated using the equation $L\times W^2/2$ where L is the longest dimension and W is the dimension perpendicular to W. Mice are followed until at least one tumor per mouse reached 1000 mm^3 or 90 days from start of treatment, whichever comes first[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Res. 2021 Jun 1;81(11):3105-3120.

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REFERENCES

[1]. Burkhart C, et al. Curaxin CBL0137 eradicates drug resistant cancer stem cells and potentiates efficacy of gemcitabine in preclinical models of pancreatic cancer. Oncotarget. 2014 Nov 30;5(22):11038-53.

[2]. Gasparian AV, et al. Curaxins: anticancer compounds that simultaneously suppress NF-κB and activate p53 by targeting FACT. Sci Transl Med. 2011 Aug 10;3(95):95ra74.

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