# CBL0137 hydrochloride

**Cat. No.:** HY-18935A

**CAS No.:** 1197397-89-9

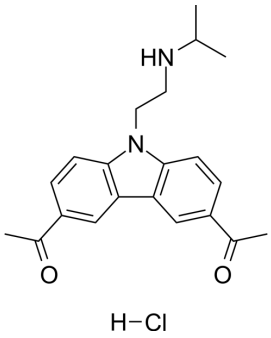
**Molecular Formula:** $C_{21}H_{25}ClN_2O_2$

**Molecular Weight:** 372.89

**Target:** MDM-2/p53; NF-κB

**Pathway:** Apoptosis; NF-κB

**Storage:** 4°C, sealed storage, away from moisture
* In solvent : -80°C, 1 year; -20°C, 6 months (sealed storage, away from moisture)




## 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].<br>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].<br>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].<br>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, $2\times10^6$ 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].<br>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.
- Cell Death Dis. 2020 Dec 2;11(12):1029.
- Oncogene. 2022 Nov 10.

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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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