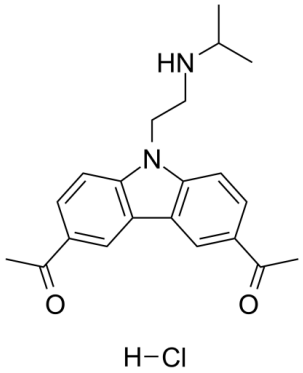
Data Sheet

Product Name:	CBL0137 hydrochloride
Cat. No.:	CS-0033711
CAS No.:	1197397-89-9
Molecular Formula:	C21H25ClN2O2
Molecular Weight:	372.89
Target:	MDM-2/p53; NF-κB
Pathway:	Apoptosis; NF-κB
Solubility:	H2O : 10 mg/mL (26.82 mM; Need ultrasonic); DMSO : 25 mg/mL (67.04 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

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. IC50 & Target: FACT[1]

EC50: 0.37 μM (p53), 0.47 μM (NF-Kb)[2] **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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]. **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]. **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 $L×W^2/2$ 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].

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.

CAIndexNames:

Ethanone, 1,1'-[9-[2-[(1-methylethyl)imino]ethyl]-9H-carbazole-3,6-diyl]bis-, hydrochloride (1:1)

SMILES:

CC(NCCN1C2=C(C3=C1C=CC(C(C)=O)=C3)C=C(C(C)=O)C=C2)C.[H]Cl

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