CBL0137 Hydrochloride

Catalog No.C13442 Batch:C1344203

Product Datasheet

Technical Data

Formula	$C_{21}H_{24}N_2O_2$.HCl					
Molecular Weight	372.89	**CAS No.**	1197397-89-9			
Solubility (25°C)*	In vitro	DMSO	19 mg/mL (50.95 mM)			
		Water	9 mg/mL (24.13 mM)			
		Ethanol	Insoluble			
	In vivo (Add solvents to the product individually and in order)	Oral Administration	Homogeneous suspension	CMC-NA	≥5mg/ml	Taking the 1 mL working solution as an example, add 5 mg of this product to 1 ml of CMC-Na solution, mix evenly to obtain a homogeneous suspension with a final concentration of 5 mg/ml.
		Injection	Clear solution	5%DMSO [1]→ 40%PEG300 [2]→ 5%Tween80 [3]→ 50%ddH2O Validated by Capsid Bio labs. Should you need adjustments to this formulation, contact our sales team for custom testing.	0.750mg/ml (2.01mM)	Taking the 1 mL working solution as an example, add 50 μL of 15 mg/ml clarified DMSO stock solution to 400 μL of PEG300, mix evenly to clarify it; add 50 μL of Tween80 to the above system, mix evenly to clarify; then continue to add 500 μL of ddH2O to adjust the volume to 1 mL. The mixed solution should be used immediately for optimal results.

* <1 mg/ml means slightly soluble or insoluble.
* Please note that Capsid Bio tests the solubility of all compounds in-house, and the actual solubility may differ slightly from published values. This is normal and is due to slight batch-to-batch variations.
* Room temperature shipping (Stability testing shows this product can be shipped at 2-8°C for storage purposes.)

Preparing Stock Solutions

Concentration \ Volume / Mass	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
50 mM	0.0536 mL	0.2682 mL	0.5364 mL

Biological Activity

Description

CBL0137 (CBLC137, Curaxin 137) HCl activates **p53** and inhibits **NF-κB** with EC50s of 0.37 μM and 0.47 μM in the cell-based p53 and NF-kB reporter assays, respectively. It also inhibits histone chaperone **FACT** (facilitates chromatin transcription complex).

Targets

FACT [1]	p53 [1] (Cell-free assay)	NF-κB [1] (Cell-free assay)
	0.37 μM(EC50)	0.47 μM(EC50)

In vitro

CBL0137 is a potent inducer of apoptosis in pancreatic cancer cell lines and is toxic not only for proliferating bulk tumor cells, but also for pancreatic cancer stem cells. CBL0137 and related molecules can simultaneously activate p53 and inhibit cellular stress pathways mediated by NF-κB and HSF-1[2]. CBL0137 binds DNA but does not cause any sort of chemical modifications in DNA and therefore lacks genotoxicity. However, CBL0137 binding to DNA leads to functional inactivation of the Facilitates Chromatin Transcription (FACT) complex, a chromatin remodeling complex involved in transcription, replication, and DNA repair. In CBL0137-treated cells, FACT is lost from the nucleoplasm and trapped in chromatin, resulting in the inhibition of FACT-dependent transcription, including NF-kB-mediated transcription. Additionally, chromatin trapping of FACT leads to casein kinase 2 (CK2)-dependent phosphorylation and activation of p53[3].

In vivo

In mice, CBL0137 is effective against several Pancreatic ductal adenocarcinoma (PDA) models, including patient derived xenografts, in which CBL0137 anti-tumor effect correlated with overexpression of FACT[1]. CBL0137 targets glioblastoma (GBM) according to its proposed mechanism of action, crosses the blood-brain barrier, and is efficacious in both TMZ-responsive and -resistant orthotopic models. The property of crossing the blood-brain barrier, especially when administered i.v, bodes well for the potential of this drug to treat CNS tumors. In orthotopic models, i.v. administration leads to greater tumor tissue accumulation than oral dosing, leading to greater bioavailability. Normal brain tissue accumulation of CBL0137 does not cause observable neurotoxicity[3].

Protocol (from reference)

Cell Assay:[1]

- **Cell lines**
  tumor (HT1080, RCC45, MiaPaca) and normal cells (Wi38, NKE-hTERT)
- **Concentrations**
  2 μM
- **Incubation Time**
  24 h
- **Method**
  Effects of CBLC137 (2 μM for 24 hours) on cell cycle in tumor (HT1080, RCC45, MiaPaca) and normal cells (Wi38, NKE-hTERT) are examined using FACS analysis of propidium iodide-stained cells.

Animal Study:[1]

- **Animal Models**
  xenograft mouse models of cancer (athymic nude mice)
- **Dosages**
  30 mg/kg
- **Administration**
  by oral gavage

References

https://pubmed.ncbi.nlm.nih.gov/21832239/ https://pubmed.ncbi.nlm.nih.gov/25402820/ https://pubmed.ncbi.nlm.nih.gov/27370399/

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