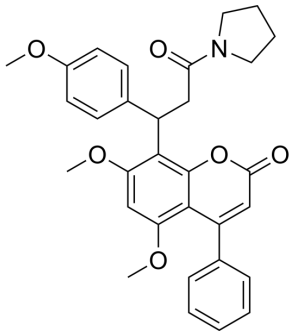
CMLD-2

Cat. No.:	HY-124828
CAS No.:	958843-91-9
Molecular Formula:	$C_{31}H_{31}NO_6$
Molecular Weight:	513.58
Target:	HuR
Pathway:	Epigenetics
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 : 50 mg/mL (97.36 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9471 mL	9.7356 mL	19.4712 mL
5 mM	0.3894 mL	1.9471 mL	3.8942 mL
10 mM	0.1947 mL	0.9736 mL	1.9471 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 (4.87 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.87 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.87 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CMLD-2, an inhibitor of HuR-ARE interaction, competitively binds HuR protein disrupting its interaction with adenine-uridine rich elements (ARE)-containing mRNAs (K_i=350 nM). CMLD-2 induces apoptosis exhibits antitumor activity in different cancer cells as colon, pancreatic, thyroid and lung cancer cell lines. Hu antigen R (HuR) is an RNA binding protein, can regulate target mRNAs stability and translation[1][2].

IC_{50} & Target

HuR[1]

In Vitro

CMLD-2 (1-75 μM; 24-72 h) inhibits thyroid cancer cell viability[2].
?CMLD-2 (20-30 μM; 24-48 h) activates caspases and induces apoptotic cell death in H1299 and A549 cells[3].
?CMLD-2 (30 μM; 24-48 h) induces G1 cell cycle arrest and mitochondrial perturbation in H1299 and A549 cell[3].
?CMLD-2 (30 μM; 24-48 h) reduces expression of HuR and HuR-regulated mRNAs and proteins in H1299 cells[3].
?CMLD-2 (35 μM; 72 h) decreases directional migration capability in SW1736, 8505C, BCPAP and K1 cells. CMLD-2 induces a strong decrease of MAD2 mRNA levels in SW1736, 8505C, BCPAP and K1 cells[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	SW1736, 8505C, BCPAP and K1 cells
Concentration:	1, 5, 10, 25, 35, 50, 75 μM
Incubation Time:	24, 48, 72 hours
Result:	Reduced the viability of all the four cell lines when used at 35, 50 and 75 μM concentration and at different time points.

Apoptosis Analysis[3]

Cell Line:	H1299, A549, H1975, HCC827, MRC-9 and CCD16 cells
Concentration:	20, 30 μM
Incubation Time:	24, 48 hours
Result:	Marked activated the caspase-9 and -3 in lung tumor cells. Induce the cleavage of PARP in lung tumor cells. Significantly increased the annexin-V-positive staining in lung tumor cells.

Cell Cycle Analysis[3]

Cell Line:	H1299, A549, MRC-9 and CCD16 cells
Concentration:	30 μM
Incubation Time:	24, 48 hours
Result:	Induced greater G1 phase cell cycle arrest in H1299 and A549 cells than in MRC-9 and CCD16 cells.

Western Blot Analysis[3]

Cell Line:	H1299, A549, H1975, HCC827, CCD16 and MRC-9 cells
Concentration:	20, 30 μM
Incubation Time:	24, 48 hours
Result:	Diminished protein expression of HuR, Bcl-2, Cyclin E and Bcl-XL and increased expression of p27 and BAX in lung tumor cells.

REFERENCES

[1]. Wu X, et, al. Identification and validation of novel small molecule disruptors of HuR-mRNA interaction. ACS Chem Biol. 2015 Jun 19;10(6):1476-84.

[2]. Allegri , et, al. The HuR CMLD-2 inhibitor exhibits antitumor effects via MAD2 downregulation in thyroid cancer cells. Sci Rep. 2019 May 14;9(1):7374.

[3]. Muralidharan R, et, al. HuR-targeted small molecule inhibitor exhibits cytotoxicity towards human lung cancer cells. Sci Rep. 2017 Aug 30;7(1):9694.

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