Leptomycin B

Cat. No.: HY-16909

CAS No.: 87081-35-4

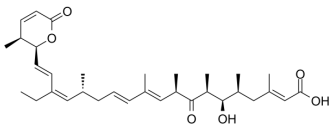
Molecular Formula: $C_{33}H_{48}O_6$

Molecular Weight: 540.73

Target: CRM1; Fungal; Antibiotic

Pathway: Membrane Transporter/Ion Channel; Anti-infection

Storage: -20°C, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (184.94 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8494 mL	9.2468 mL	18.4935 mL
5 mM	0.3699 mL	1.8494 mL	3.6987 mL
10 mM	0.1849 mL	0.9247 mL	1.8494 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 (4.62 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.62 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Leptomycin B (CI 940; LMB) is a potent inhibitor of the nuclear export of proteins. Leptomycin B inactivates CRM1/exportin 1 by covalent modification at a cysteine residue. Leptomycin B is a potent antifungal antibiotic blocking the eukaryotic cell cycle[1].

IC_{50} & Target

CRM1/exportin 1[1]

In Vitro

Leptomycin B (LMB) is very potent in vitro against various cancer cell lines (IC50 values in the 0.1 to 10 nM range). Leptomycin B (LMB) inhibits SiHa, HCT-116, and SKNSH cells with IC_{50}s of 0.4, 0.3 and 0.4 nM for a 72 hour exposure,

respectively[2].
Leptomycin B (LMB) (0.5 nM) displays a synergistic effect on Gefitinib (0–32 μM)-induced cytotoxicity in A549 and H460 cell line. The simultaneous treatments of Gefitinib (0–32 μM) and Leptomycin B (0.5 nM) show synergistic cytotoxic effect on A549 as compared to Gefitinib alone at both 24 and 48 hours[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[3]

Cell Line:	The non-small cell lung cancer (NSCLC) cell lines A549 and H460
Concentration:	0.5 nM
Incubation Time:	24 and 48 hours
Result:	The IC_{50} of Gefitinib at 48 hours was 32.0±2.5 μM while it was significantly reduced to 25.0±2.1 μM with the combination of 0.5 nM Leptomycin B. The significant synergistic cytotoxic effect from co-treatment of 0.5 nM Leptomycin B with Gefitinib was also confirmed in H460 cell line.

Cell Viability Assay[3]

Cell Line:	A549
Concentration:	0.5 nM
Incubation Time:	48 hours
Result:	0.5 nM Leptomycin B plus Gefitinib or Gefitinib alone had a decreased p-EGFR(Tyr1068) expressions compared with controls. p-Akt (Ser473) was inhibited in a dose-response manner by Gefitinib treatments, but it was enhanced by gefitinib+Leptomycin B co-treatments compared with gefitinib alone. A549 treated by Gefitinib+Leptomycin B had a higher expression of p-Erk1/2(Thr202/Tyr204) than A549 treated by Gefitinib alone.

In Vivo

Leptomycin B (LMB) is poorly tolerated in vivo. Maximum tolerated dose (MTD) is 2.5 mg/kg for LMB (single i.v.) in HCT-116 tumor–bearing mice.The limited in vivo efficacy of Leptomycin B is due to off-target effects because our nuclear export inhibitors (NEIs) retain the potent inhibition of CRM1, but are clearly better tolerated in vivo[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Immunol. 2021 May 17;ji2001346.
- Mol Med Rep. 2021 Apr 15.

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REFERENCES

[1]. N Kudo, et al. Leptomycin B inactivates CRM1/exportin 1 by covalent modification at a cysteine residue in the central conserved region. Proc Natl Acad Sci U S A. 1999 Aug 3;96(16):9112-7.

[2]. Sarah C Mutka,et al. Identification of nuclear export inhibitors with potent anticancer activity in vivo. Cancer Res. 2009 Jan 15;69(2):510-7.

[3]. Zhongwei Liu, et al.Leptomycin B reduces primary and acquired resistance of gefitinib in lung cancer cells. Toxicol Appl Pharmacol. 2017 Nov 15;335:16-27.

[4]. Sarah C Mutka, et al. Identification of nuclear export inhibitors with potent anticancer activity in vivo. Cancer Res. 2009 Jan 15;69(2):510-7.

India Contact:
Life Technologies (India) Pvt. Ltd.
306, Aggarwal City Mall, Opposite M2K Pitampura, Delhi – 110034 (INDIA). Ph: +91-11-42208000, 42208111, 42208222, Mobile: +91-9810521400, Fax: +91-11-42208444
Email: customerservice@lifetechindia.com Website: www.lifetechindia.com