KPT-185

Cat. No.: HY-15611

CAS No.: 1333151-73-7

Molecular Formula: $C_{16}H_{16}F_3N_3O_3$

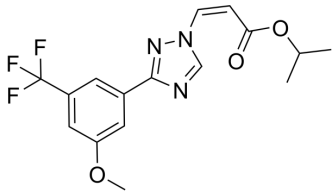
Molecular Weight: 355.31

Target: CRM1

Pathway: Membrane Transporter/Ion Channel

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (140.72 mM; Need ultrasonic)
Ethanol : 50 mg/mL (140.72 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8144 mL	14.0722 mL	28.1444 mL
5 mM	0.5629 mL	2.8144 mL	5.6289 mL
10 mM	0.2814 mL	1.4072 mL	2.8144 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (7.04 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.04 mM); Clear solution
3. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.04 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KPT-185 is an orally bioavailable and selective inhibitor of CRM1 and displays potent antiproliferative properties at submicromolar concentrations (IC_{50}=100-500 nM), induces apoptosis, cell-cycle arrest, and myeloid differentiation in AML cell lines and patient blasts[1].

IC_{50} & Target

CRM1[1]

In Vitro

KPT-185 results in a significant decrease in the level of CRM1 protein and a significant accumulation of p53 in the nucleus of MV4-11 and OCI-AML3 cells[1].

KPT-185 (1-1000 nM; 72 hours) dramatically reduces HPB-ALL, Jurkat, CCRF-CEM, MOLT-4, KOPTK1, LOUCY cells growth with IC_{50}s of 16-395 nM[4].

KPT-185 leads to cell cycle arrest in G1 phase in the MOLT-4 cell line[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[4]

Cell Line:	HPB-ALL, Jurkat, CCRF-CEM, MOLT-4, KOPTK1, LOUCY cells
Concentration:	1, 10, 100, 1000 nM
Incubation Time:	72 hours
Result:	The growth of those lines was dramatically reduced with IC_{50}s of 16–395 nM after 72 h of exposure.

REFERENCES

[1]. Ranganathan P, et al. Preclinical activity of a novel CRM1 inhibitor in acute myeloid leukemia. Blood. 2012 Aug 30;120(9):1765-73.

[2]. Zhang K, et al. Novel selective inhibitors of nuclear export CRM1 antagonists for therapy in mantle cell lymphoma. Exp Hematol. 2013 Jan;41(1):67-78.e4.

[3]. Salas Fragomeni RA, et al. CRM1 and BRAF inhibition synergize and induce tumor regression in BRAF-mutant melanoma. Mol Cancer Ther. 2013 Jul;12(7):1171-9.

[4]. Etchin J, et al. KPT-330 inhibitor of CRM1 (XPO1)-mediated nuclear export has selective anti-leukaemic activityin preclinical models of T-cell acute lymphoblastic leukaemia and acute myeloid leukaemia. Br J Haematol. 2013 Apr;161(1):117-27.

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