ABT-737

Cat. No.: HY-50907

CAS No.: 852808-04-9

Molecular Formula: $C_{42}H_{45}ClN_6O_5S_2$

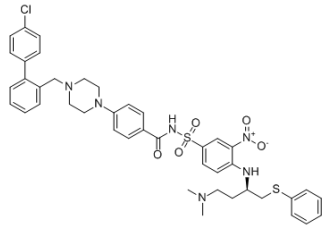
Molecular Weight: 813.43

Target: Bcl-2 Family; Autophagy; Mitophagy

Pathway: Apoptosis; Autophagy

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 (61.47 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2294 mL	6.1468 mL	12.2936 mL
	5 mM	0.2459 mL	1.2294 mL	2.4587 mL
	10 mM	0.1229 mL	0.6147 mL	1.2294 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 (3.07 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: 2.5 mg/mL (3.07 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.5 mg/mL (3.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ABT-737 is a selective and BH3 mimetic **Bcl-2**, **Bcl-xL** and **Bcl-w** inhibitor with **EC_{50}**s of 30.3 nM, 78.7 nM, and 197.8 nM, respectively.

IC_{50} & Target

Bcl-2	Bcl-xL	Bcl-W	Bcl-B
30.3 nM (EC50)	78.7 nM (EC50)	197.8 nM (EC50)	1820 nM (EC50)

	Autophagy	Mitophagy
In Vitro	ABT-737 and ATO inhibits proliferation and induces apoptosis in SGC-7901 and MGC-803 cells in concentration- and time-dependent manner, and shows a synergistic effect. ABT-737 disturbs the binding of B cell lymphoma (Bcl)-2 homologous antagonist killer and Bcl-extra large[1]. ABT-737 induces a BAX/BAK-dependent impairment of maximal O_2 consumption rate in sensitive cells. Stable BCL-2 overexpression in MCF10A cells induces an ABT-737-sensitive primed for death state. ABT-737 induces dose-dependent impairment of maximal O_2 consumption rate in B-cell lymphoma cells[2]. ABT-737 induces apoptosis and synergizes with chemotherapy,and disrups BCL-2/BAX heterodimerization and induces BAX conformational change in AML cells[3].	
In Vivo	ABT-737 (50 mg/kg, i.p.) and ATO significantly suppress SGC-7901 xenograft growth, synergistically inhibit tumour growth and induce apoptosis in vivo[1]. ABT-737 suppresses the leukemia burden by 48% and 53% at the 20 and 30 mg/kg dose levels, respectively[3].	

PROTOCOL

Kinase Assay [3]	To determine the binding affinity of GST-BCL-2 family proteins to the FITC-conjugated BH3 domain of BIM (FITC-Ahx-DMRPEIWIAQELRRIGDEFNAYYAR), FPAs are performed as follows. Briefly, 100 nM of GST-BCL-2 family fusion proteins are incubated with serial dilutions of ABT-737 in PBS for 2 min. Then, 20 nM of FITC-BIM BH3 peptide (FITC-Ahx-DMRPEIWIAQELRRIGDEFNAYYAR) is added. Fluorescence polarization is measured using an Analyst TM AD Assay Detection System after 10 min using the 96-well black plate. IC_{50}s are determined using GraphPad Prism software. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	Cells are treated with ABT-737, ABT-263, or vehicle (DMSO) for 4 h in XF24 assay medium (6×10^4 MCF10A cells, see medium composition below) or RPMI 1640 medium (1×10^6 B-cell lymphoma cells) and apoptosis is analyzed by Annexin-V-binding/PI exclusion or by sub-diploid nuclei determination. FACS analysis is performed on Becton Dickinson FACScan or FACScalibur instruments. Data analysis is performed with CellQuest software. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	For intraperitoneal (i.p.) administration, 1 g/mL stock solution of ABT-737 in DMSO is added to a mixture of 30% propylene glycol, 5% Tween 80, 65% D5W (5% dextrose in water) (pH 4–5; final concentration of DMSO ≤ 1%). Mice injected with FD/ΔRaf-1:ER cells are treated with either ABT-737 (20 and 30 mg/kg/mouse every day i.p. for 21 days starting on day 1 post-cell injection (n=9-10 mice per group) or vehicle or left untreated (control); mice injected with human KG-1 cells are treated with 30 mg/kg ABT-737 starting on day 18 post-cell injection. For noninvasive imaging of FD/ΔRaf-1:ER-luc cells, anesthetized mice are injected with 150 mg/kg of D-luciferin and placed for imaging in the In Vivo Imaging System with total imaging time of 2 min. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **Cancer Lett**. 2019 Jul 15;461:102-111.
- **Haematologica**. 2017 Apr;102(4):755-764.
- **ACS Med Chem Lett**. 2015 Jun 22;6(8):948-52.
- **Eur J Pharm Sci**. 2018 May 31;121:243-250.
- **J Ovarian Res**. 2016 Apr 14;9(1):25.

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REFERENCES

[1]. Sun XP, et al. ABT-737 Induces Apoptosis of Gastric Carcinoma Cells In Vitro and In Vivo.J Int Med Res. 2012;40(4):1251-64.

[2]. Clerc P, et al. Polster BM.Rapid Detection of an ABT-737-Sensitive Primed for Death State in Cells Using Microplate-Based Respirometry.PLoS One. 2012;7(8):e42487. Epub 2012 Aug 3.

[3]. Konopleva M, et al. Mechanisms of apoptosis sensitivity and resistance to the BH3 mimetic ABT-737 in acute myeloid leukemia. Cancer Cell. 2006 Nov;10(5):375-88.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA