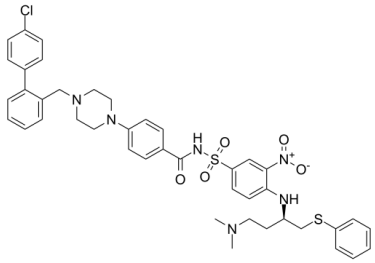
Data Sheet

Product Name:	ABT-737
Cat. No.:	CS-0014
CAS No.:	852808-04-9
Molecular Formula:	C42H45ClN6O5S2
Molecular Weight:	813.43
Target:	Autophagy; Bcl-2 Family; Mitophagy
Pathway:	Apoptosis; Autophagy
Solubility:	DMSO : 50 mg/mL (61.47 mM; Need ultrasonic); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

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. IC50 & Target: EC50: 78.7 nM (Bcl-xL), 30.3 nM (Bcl-2), 197.8 nM (Bcl-w)[3] **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 (Extracted from published papers and Only for reference)

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. **Cell Assay:** ABT-737 is dissolved in DMSO.[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. **Animal Administration:** ABT-737 is dissolved in DMSO, and added to a mixture of 30% propylene glycol, 5% Tween 80, 65% D5W (5% dextrose in water).[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.

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.

CAIndexNames:

Benzamide, 4-[4-[(4'-chloro[1,1'-biphenyl]-2-yl)methyl]-1-piperazinyl]-N-[[4-[[(1R)-3-(dimethylamino)-1-[(phenylthio)methyl]propyl]amino]-3-nitrophenyl]sulfonyl]-

SMILES:

CN(CC[C@@H](NC1=CC=C(C=C1[N+]([O-])=O)S(NC(C2=CC=C(C=C2)N3CCN(CC3)CC4=CC=CC=C4C5=CC=C(C=C5)Cl)=O)(=O)=O)CSC6=CC=CC=C6)C

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