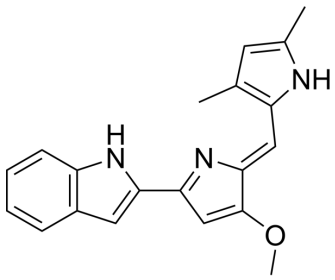
Obatoclax

Cat. No.:	HY-10969A
CAS No.:	803712-67-6
Molecular Formula:	$C_{20}H_{19}N_3O$
Molecular Weight:	317.38
Target:	Bcl-2 Family; Autophagy; Parasite
Pathway:	Apoptosis; Autophagy; Anti-infection
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



BIOLOGICAL ACTIVITY

Description

Obatoclax (GX15-070), a BH3 mimetic, is a pan-BCL-2 family proteins inhibitor with a K_i of 220 nM for BCL-2[1][2]. Obatoclax induces autophagy-dependent cell death and targets cyclin D1 for proteasomal degradation. Obatoclax has anti-cancer and broad-spectrum antiparasitic activity[3][4].

IC_{50} & Target

BCL2	Mcl-1	Bcl-xL	Bcl-W
200 nM (Ki)	1-7 μM (Ki)	1-7 μM (Ki)	1-7 μM (Ki)

Bcl-B
1-7 μM (Ki)

In Vitro

Obatoclax (GX15-070) inhibits BCL-2, BCL-XL, MCL-1, BCL-w, A1, and BCL-b with Ki values≈1-7 μM[2].

Obatoclax (50-200 nM; 24-72 hours) induces a dose- and time-dependent reduction of cell numbers in all human colorectal cancer cell lines. In particular, the IC_{50} of cell proliferation at 72 h are 25.85, 40.69, and 40.01 nM for HCT116, HT-29, and LoVo cells, respectively[1].

Obatoclax (400 nM; for 24 hours) induces autophagy in OSCC cells[3].

Obatoclax (50-200 nM; for 24 hours) provokes a dose-dependent increase in the G1-phase cell populations[1].

Obatoclax (25-200 nM; for 24 hours) indicates a marked drop in cyclin D1 levels as low as 50 nM[1].

Obatoclax induces T286 phosphorylation-dependent or -independent cyclin D1 degradation.in HCT116 and LoVo cells, the steady-state levels of p-Cyclin D (T286) began to decline once exposed to obatoclax (200 nM; 1, 3, 6, 12, 24 hours). Obatoclax inhibits GSK3β but activates p38 MAPK, while barely affecting ERK1/2 activity in HT-29 cells[1].

Obatoclax (50, 100, 150, 200, 250, 300, 350, 400, 450 nM) potently inhibits the clonogenic potential of oral cancer cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	human colorectal cancer HCT116, HT-29 and LoVo cells
Concentration:	50, 100, 200 nM
Incubation Time:	24, 48, and 72 hours
Result:	Induced a dose- and time-dependent reduction of cell numbers.

Cell Autophagy Assay[3]

Cell Line:	AW8507 and SCC029B cells
Concentration:	400 nM
Incubation Time:	24 hours
Result:	Induced autophagy in OSCC cells.

Cell Cycle Analysis[1]

Cell Line:	HCT116 and HT-29 cells
Concentration:	50, 100, 200 nM
Incubation Time:	24 hours
Result:	Provoked a dose-dependent increase in the G1-phase cell populations.

Western Blot Analysis[1]

Cell Line:	HCT116, HT-29 and LoVo cells
Concentration:	50, 100, 200 nM
Incubation Time:	24 hours
Result:	Indicated a marked drop in cyclin D1 levels as low as 50 nM.

In Vivo

Obatoclax (GX15-070; 1.15-5 mg/kg; intravenously injected; five consecutive days) exhibits potent antitumor activity in xenograft mouse models in a dose-dependent manner[4].

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

Animal Model:	6-8 weeks old female BALB/C nude mice bearing subcutaneous tumors[4]
Dosage:	1.15, 2.5, 5 mg/kg
Administration:	Intravenously injected (through lateral tail vein); five consecutive days (i.e. 5 injections)
Result:	Exhibited potent antitumor activity in xenograft mouse models in a dose-dependent manner.

CUSTOMER VALIDATION

- Cancer Lett. 2022 Nov 30;216028.
- Acta Pharmacol Sin. 2021 Aug;42(8):1298-1310.
- Biomed Pharmacother. 2020 Sep;129:110371.
- iScience. 13 August 2022, 104925.
- Am J Cancer Res. 2019 Mar 1;9(3):546-561.

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REFERENCES

[1]. Or CR, et al. Obatoclax, a Pan-BCL-2 Inhibitor, Targets Cyclin D1 for Degradation to Induce Antiproliferation in Human Colorectal Carcinoma Cells. Int J Mol Sci. 2016 Dec 27;18(1).

[2]. Sulkshane P, et al. BH3 mimetic Obatoclax (GX15-070) mediates mitochondrial stress predominantly via MCL-1 inhibition and induces autophagy-dependent necroptosis in human oral cancer cells. Oncotarget. 2016 Aug 5;8(36):60060-60079.

[3]. Ehrenkaufer G, et al. Identification of anisomycin, prodigiosin and obatoclax as compounds with broad-spectrum anti-parasitic activity. PLoS Negl Trop Dis. 2020 Mar 20;14(3):e0008150.

[4]. Nguyen M, et al. Small molecule obatoclax (GX15-070) antagonizes MCL-1 and overcomes MCL-1-mediated resistance to apoptosis. Proc Natl Acad Sci U S A. 2007 Dec 4;104(49):19512-7. Epub 2007 Nov 26.

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