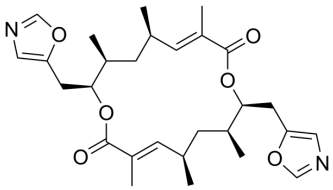
Conglobatin

Cat. No.:	HY-119906
CAS No.:	72263-05-9
Molecular Formula:	$C_{28}H_{38}N_2O_6$
Molecular Weight:	498.61
Target:	HSP; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Conglobatin (FW-04-806), a macrolide dilactone, is isolated from the culture of Streptomyces conglobatus. Conglobatin is an orally active Hsp90 inhibitor. Conglobatin can bind to the N-terminal domain of Hsp90 and disrupt Hsp90-Cdc37 complex formation. Conglobatin induces apoptosis in human breast cancer cells and esophageal squamous cell carcinoma cells, and exhibits antitumor activity in vivo[1][2][3].
IC_{50} & Target	HSP90

In Vitro

Conglobatin (6.25-100 μM; 48 h) markedly inhibits the proliferation of SKBR3 and MCF-7 cells, with IC_{50}s of 12.11 and 39.44 μM, respectively[2].

Conglobatin inhibits cell proliferation in EC109, KYSE70, KYSE450, KYSE150, KYSE180, and KYSE510 cells, with IC_{50}s of 16.43, 15.89, 10.94, 10.50, 10.28, and 9.31 μM, respectively[3].

Conglobatin (10-40 μM; 24 h) displays obvious arrest of SKBR3 and MCF-7 cells in the G2/M phase. Conglobatin induces apoptosis through caspase-dependent pathways in SKBR3 and MCF-7 cells[2].

Conglobatin (10-40 μM; 3-24 h) reduces Hsp90 client protein levels and induces proteasome-dependent degradation[2].

Conglobatin binds to the N-terminal of Hsp90, does not affect ATP-binding capability of Hsp90, but inhibits Hsp90/Cdc37 chaperone/co-chaperone interactions[2].

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

Cell Proliferation Assay[2]

Cell Line:	SKBR3 and MCF-7 cells
Concentration:	6.25, 12.5, 25, 50, 100 μM
Incubation Time:	48 hours
Result:	Inhibited the proliferation of SKBR3 and MCF-7 cells in a dose-dependent manner.

Cell Cycle Analysis[2]

Cell Line:	SKBR3 and MCF-7 cells
Concentration:	10, 20, 40 μM
Incubation Time:	24 hours

Result:	Increased the G2/M cell population and decreased the population in the S and G0/G1 phases.

Western Blot Analysis[2]

Cell Line:	SKBR3 and MCF-7 cells
Concentration:	10, 20, 40 μM
Incubation Time:	3, 6, 12, 24 hours
Result:	Decreased the levels of the client proteins HER2, p-HER2, Raf-1, Akt, and p-Akt in a dose and time-dependent manner in SKBR3 cells. Reduced the the levels of the client proteins Raf-1, Akt, and p-Akt in a dose and time-dependent manner in MCF-7 cells.

In Vivo

Conglobatin (50-200 mg/kg; i.g. q3d for 24 d) inhibits the tumor growth of SKBR3 and MCF-7 human breast cancer xenograft models in a dose-dependent manner[2].
Conglobatin (4-8 mg/kg; i.p. daily for 21 days) inhibits tumor growth in EC109 and KYSE510 tumor xenograft models with low toxicity[3]
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	BALB/c (nu/nu) athymic mice with SKBR3 and MCF-7 tumor xenograft[2]
Dosage:	50, 100, 200 mg/kg
Administration:	Oral gavage every 3 days for 24 days
Result:	Showed inhibition of tumor growth at a rate of 39.1%, 52.7%, and 67.5% in the SKBR3 cell line groups and 27.3%, 39.8%, 54.3% in the MCF-7 cell line groups at the three increasing doses, respectively. Was well tolerated.

REFERENCES

[1]. Westley JW, et, al. Conglobatin, a novel macrolide dilactone from Streptomyces conglobatus ATCC 31005. J Antibiot (Tokyo). 1979 Sep;32(9):874-7.

[2]. Huang W, et, al. FW-04-806 inhibits proliferation and induces apoptosis in human breast cancer cells by binding to N-terminus of Hsp90 and disrupting Hsp90-Cdc37 complex formation. Mol Cancer. 2014 Jun 14;13:150.

[3]. Li LY, et, al. Macrolide analog F806 suppresses esophageal squamous cell carcinoma (ESCC) by blocking β1 integrin activation. Oncotarget. 2015 Jun 30;6(18):15940-52.

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