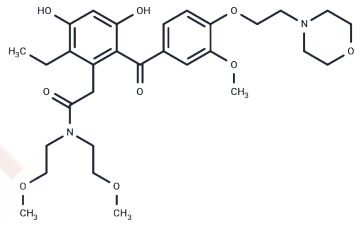
Data Sheet (Cat.No.T6558)

TargetMol

KW-2478

Chemical Properties



CAS No. : 819812-04-9

Formula: C30H42N2O9

Molecular Weight: 574.66

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	KW-2478 is a non-ansamycin HSP90 inhibitor with IC50 of 3.8 nM.
Targets(IC50)	HSP
In vitro	KW-2478 inhibits the binding of bRD to Hsp90α with IC50 of 3.8 nM. KW-2478 degradates the Hsp90 client proteins, including FGFR3 and IGF-1Rβand c-Raf-1. KW-2478 reduces the level of phosphorylated Erk1/2. KW-2478 induces apoptosis by cleavage of PARP, a substrate of caspase-3 In U266 cells,. KW-2478 has Time dependency of antiproliferative activity, consecutive drug exposure for at least 12 hours is necessary to to exert potent antitumor activity. KW-2478 downregulates the translocation products of IgH locus. KW-2478 inhibits the transcription of c-Maf and cyclin D1 genes by mainly suppressing the function of Cdk9. [1] KW-2478 has potent and broad growth inhibitory activities against various cell lines, KW-2478 inhibites cancer cell growth in all cell lines, with EC50 of 101-252 nM, 81.4-91.4 nM and 120-622 nM for B-cell lymphoma, mantle cell lymphoma and multiple myeloma, respectively. KW-2478 also shows potent growth inhibitory activity in primary CLL and NHL cells with EC50 of 40-170 nM and 200-400 nM, respectively. [2].
In vivo	KW-2478 suppresses tumor growth and induces the degradation of client proteins in tumors in NCI-H929 s.c. inoculated model at doses of 100 mg/kg or more. KW-2478 reduces both serum M protein and MM tumor burden in the bone marrow in OPM-2/GFP i.v. inoculated mouse model at doses of 100 mg/kg. [1]
Kinase Assay	Hsp90 Binding Assay: Human Hsp90α solution (0.5 μg/mL) is fixed on 96-well plates, followed by blocking with TBS containing 1% bovine serum albumin. KW-2478 solutions is added to the wells, and bRD is added to a concentration of 0.1 μmol/L. After removal of solution, poly-HRP streptavidin solution dilutes with poly-HRP dilution buffer is added to the wells. After removal of solution, equal volumes of TMB peroxidase substrate and peroxidase solution B are added to the wells. To stop the HRP reaction, 2 mol/L H2SO4 are added, followed by measurement of absorbance at 450 nm using a microplate spectrophotometer.
Cell Research	To measure the IC50, OPM-2/green fluorescent protein (GFP) cells, KMS-11 cells, OPM-2/GFP and other cells are plated into 96-well plates and treat with KW-2478. After 72 hours of cultivation, cell viability is determined using Cell Proliferation Reagent WST-1. WST reagent is added to the wells, followed by incubation for 4 hours at 37 °C. After that, the absorbance at 450 nm with reference at 650 nm is measured with a microplate

	spectrophotometer. To examine time dependency of antiproliferative activity of KW-2478, the cells are plated into 96-well V-bottomed plates and treated with KW-2478. After 0 hour and at intervals from 3 to 72 hours at 37 °C, the supernatant is aspirated. After drug-free medium is added to the wells, the supernatant is aspirated again. Finally, drug-free medium is added to the wells, and the plates are further incubated for the remainder of the 72-hour period, followed by measurement of cell viabil(Only for Reference)

Solubility Information

Solubility	DMSO: 106 mg/mL (184.46 mM),Sonication is recommended. Ethanol: 3 mg/mL (5.22 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.7402 mL	8.7008 mL	17.4016 mL
5 mM	0.348 mL	1.7402 mL	3.4803 mL
10 mM	0.174 mL	0.8701 mL	1.7402 mL
50 mM	0.0348 mL	0.174 mL	0.348 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Takayuki Nakashima, et al. Clin Cancer Res, 2010, 16(10), 2792-2802.
Zeng D, Gao M, Zheng R, et al. The HSP90 inhibitor KW-2478 depletes the malignancy of BCR/ABL and overcomes the imatinib-resistance caused by BCR/ABL amplification. Experimental Hematology & Oncology. 2022, 11(1): 1-14
Zeng D, Gao M, Zheng R, et al. The HSP90 inhibitor KW-2478 depletes the malignancy of BCR/ABL and overcomes the imatinib-resistance caused by BCR/ABL amplifcation. Experimental Hematology & Oncology. 2022, 11(1): 1-14
Juliger S, et al. ASH Annual Meeting and Exposition, 2008.
Li H J, Wang Q S, Han W, et al. Anti-NSCLC activity in vitro of Hsp90N inhibitor KW-2478 and complex crystal structure determination of Hsp90N-KW-2478. Journal of Structural Biology. 2021, 213(2): 107710.
Ishii T, et al. Blood Cancer J, 2012, 2(4), e68.

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