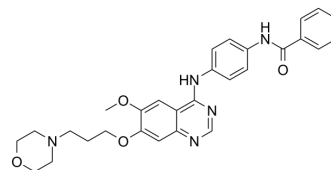


ZM-447439

Cat. No.:	HY-10128		
CAS No.:	331771-20-1		
Molecular Formula:	C ₂₉ H ₃₁ N ₅ O ₄		
Molecular Weight:	513.59		
Target:	Aurora Kinase; Apoptosis		
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Apoptosis		
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 : ≥ 100 mg/mL (194.71 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent	1 mg	5 mg	10 mg
	Concentration			
	1 mM	1.9471 mL	9.7354 mL	19.4708 mL
	5 mM	0.3894 mL	1.9471 mL	3.8942 mL
	10 mM	0.1947 mL	0.9735 mL	1.9471 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (4.87 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (4.87 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ZM-447439 is an aurora kinase inhibitor with IC₅₀s of 110 and 130 nM for aurora A and B, respectively.

IC₅₀ & Target

Aurora A	Aurora B
110 nM (IC ₅₀)	130 nM (IC ₅₀)

In Vitro

Cells treated with ZM-447439 progress through interphase, enter mitosis normally, and assemble bipolar spindles. However, chromosome alignment, segregation, and cytokinesis all fail. ZM-447439 inhibits cell division and inhibit mitotic phosphorylation of histone H3. ZM-447439 prevents chromosome alignment and segregation. ZM-447439 compromises spindle checkpoint function. ZM-447439 inhibits kinetochore localization of BubR1, Mad2, and Cenp-E^[1]. Inhibition of

Aurora kinase by ZM-447439 reduces histone H3 phosphorylation at Ser10 in Hep2 carcinoma cells. Multipolar spindles are induced in these ZM-treated G2/M-arrested cells with accumulation of 4N/8N DNA, similar to cells with genetically suppressed Aurora-B. ZM-447439 treatment induces cell apoptosis. ZM-447439 inhibition of Aurora kinase is potently in association with decrease of Akt phosphorylation at Ser473 and its substrates GSK3 α/β phosphorylation at Ser21 and Ser9^[2]

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

PROTOCOL

Kinase Assay ^[1]

1 ng purified recombinant enzyme is added to a reaction cocktail containing buffer, 10 μ M peptide substrate, 10 μ M for Aurora A or 5 μ M ATP for Aurora B, and 0.2 μ Ci γ [³³P]ATP, and is then incubated at room temperature for 60 min. Reactions are stopped by addition of 20% phosphoric acid, and the products are captured on P30 nitrocellulose filters and assayed for incorporation of ³³P with a Betaplate counter. No enzyme and no compound control values are used to determine the concentration of ZM-447439, which gave 50% inhibition of enzyme activity^[1].

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

Cell Assay ^[1]

To determine cloning efficiency, MCF7 cells are plated in phenol red free DME plus 5% stripped serum, and are then treated with or without the anti-estrogen ICI 182780 at 1 μ M for 48 h. ZM-447439 is then added at the indicated concentrations for 72 h. The cells are harvested, washed, and ~400 cells plated in each well of a 6-well plate in complete media without ZM-447439. After 10 d, the colonies are fixed, stained with crystal violet, and counted. The cloning efficiency represents the number of colonies on ZM-447439-treated plates compared with DMSO-treated controls^[1].

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

CUSTOMER VALIDATION

- Elife. 2020 Dec 7;9:e61405.
- EBioMedicine. 2021 Aug 5;70:103510.
- bioRxiv. 2021 Feb 5.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Ditchfield C, et al. Aurora B couples chromosome alignment with anaphase by targeting BubR1, Mad2, and Cenp-E to kinetochores. *J Cell Biol.* 2003 Apr 28;161(2):267-80.

[2]. Long ZJ, et al. ZM 447439 inhibition of aurora kinase induces Hep2 cancer cell apoptosis in three-dimensional culture. *Cell Cycle.* 2008 May 15;7(10):1473-9.

Caution: Product has not been fully validated for medical applications. For research use only.

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