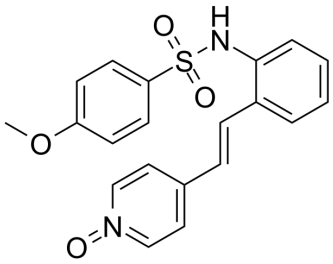
HMN-176

Cat. No.:	HY-13647
CAS No.:	173529-10-7
Molecular Formula:	$C_{20}H_{18}N_2O_4S$
Molecular Weight:	382.43
Target:	Polo-like Kinase (PLK)
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 30 mg/mL (78.45 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6149 mL	13.0743 mL	26.1486 mL
	5 mM	0.5230 mL	2.6149 mL	5.2297 mL
	10 mM	0.2615 mL	1.3074 mL	2.6149 mL

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

BIOLOGICAL ACTIVITY

Description

HMN-176 is a stilbene derivative which inhibits mitosis, interfering with polo-like kinase-1 (plk1), without significant effect on tubulin polymerization.

IC_{50} & Target

PLK1[5]

In Vitro

HMN-176 (2.5 μM) greatly increases the duration of mitosis in hTERT-RPE1 and CFPAC-1 Cell lines. The effect of HMN-176 on spindle morphology does not appear to be related to effects on microtubule polymerization. HMN-176 (2.5, 0.25, and 0.025 μM) inhibits aster formation in a concentration dependent manner[1]. HMN-176 (0.1, 1.0, or 10.0 μg/mL) demonstrates inhibitory effects in multiple tumors, with notable activity seen in breast, nonsmall-cell lung, and ovarian cancer specimens. HMN-176 demonstrates activity towards 63% of the breast (5/8), 67% of the non-small cell lung (4/6), and 57% of the ovarian (4/7) tumor specimens treated with 10.0 μg/mL[2]. HMN-176 shows potent cytotoxicity, with a mean IC_{50} value of 118 nM. HMN-176 displays similar cytotoxicity against tumors with various characteristics from different organs[3]. Treatment with 3 μM HMN-176 suppresses the expression of MDR1 mRNA by 56%. HMN-176 has no significant effect on the residual promoter activity[4].

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

In Vivo	After p.o. of HMN-214 to male rats, the prodrug is not detected in the plasma, while plasma levels of HMN-176 peaks at 2 h and gradually decreases thereafter[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	Cells to be tested are seeded into a 96-well microplate at a density of 3×10^3-1×10^4 cells/well. Drugs are added the next day and the plate is incubated for 72 h at 37 °C in a humidified incubator (5% CO_2, 95% air). The inhibition of growth is measuredby the MTT assay, and the concentration required to produce 50% inhibition of growth (IC_{50}) calculated by the Scansoft 96 software program. The IC_{50} values for HMN-176 andreference agents are presented. Briefly, for each compound the mean IC_{50} value for all cell lines tested is calculated and the difference between the individual IC_{50} values and the mean IC_{50} value (log10) displayed by a bar projecting to the right or left of the mean. The resistance index is calculated as (IC_{50} value for drug-resistant cell line)/(IC_{50} for parent cell line). MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	^{14}C-HMN-214 and ^{14}C-HMN176 are p.o. to male SD rats at doses of 33 (equivalent to 30 mg/kg of HMN-176) and 30 mg/kg, respectively. Blood samples are collected at designated times and plasma levels of radioactivity determined with a liquid-scintillation counter. In addition, unlabeled HMN-214 (33 mg/kg) is administered to male rats and plasma concentrations of HMN-214 and HMN-176 are determined by high performance liquid chromatography. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. DiMaio MA, et al. The small organic compound HMN-176 delays satisfaction of the spindle assembly checkpoint by inhibiting centrosome-dependent microtubule nucleation. Mol Cancer Ther. 2009 Mar;8(3):592-601.

[2]. Medina-Gundrum L, et al. Investigation of HMN-176 anticancer activity in human tumor specimens in vitro and the effects of HMN-176 on differential gene expression. Invest New Drugs. 2005 Jan;23(1):3-9.

[3]. Takagi M, et al. In vivo antitumor activity of a novel sulfonamide, HMN-214, against human tumor xenografts in mice and the spectrum of cytotoxicity of its active metabolite, HMN-176. Invest New Drugs. 2003 Nov;21(4):387-99.

[4]. Tanaka H, et al. HMN-176, an active metabolite of the synthetic antitumor agent HMN-214, restores chemosensitivity to multidrug-resistant cells by targeting the transcription factor NF-Y. Cancer Res. 2003 Oct 15;63(20):6942-7.

[5]. Garland LL, et al. A phase I pharmacokinetic study of HMN-214, a novel oral stilbene derivative with polo-like kinase-1-interacting properties, in patients with advanced solid tumors. Clin Cancer Res. 2006 Sep 1;12(17):5182-9.

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