Phthalazinone pyrazole

Cat. No.: HY-12564

CAS No.: 880487-62-7

Molecular Formula: $C_{18}H_{15}N_5O$

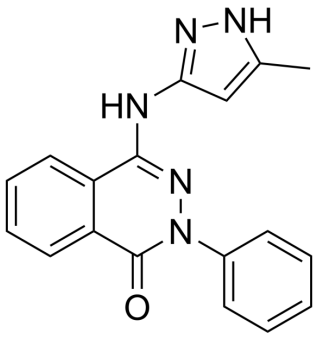
Molecular Weight: 317.34

Target: Aurora Kinase; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 11.11 mg/mL (35.01 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	3.1512 mL	15.7560 mL	31.5119 mL
5 mM	0.6302 mL	3.1512 mL	6.3024 mL
10 mM	0.3151 mL	1.5756 mL	3.1512 mL

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

BIOLOGICAL ACTIVITY

Description

Phthalazinone pyrazole is a potent, selective, and orally active inhibitor of Aurora-A kinase with an IC_{50} of 0.031 μM. Phthalazinone pyrazole can arrests mitosis and subsequently inhibit tumor growth via apoptosis of proliferating cells. Phthalazinone pyrazole suppresses the epithelial-mesenchymal transition (EMT) during the differentiation of hepatocyte-like cells (HLCs) from human embryonic stem cells[1][2].

IC_{50} & Target

Aurora-A

0.031 μM (IC_{50})

In Vitro

Phthalazinone pyrazole (1 and 10 μM; 30 hours) enhances the proliferative capacity of HLCs[2].

Phthalazinone pyrazole (1, 10, and 100 μM; 5 days) enhances hepatic morphological changes in differentiated HLCs without cytotoxicity[2].

Phthalazinone pyrazole (1 and 10 μM; 5 and 17 days) suppresses the EMT and induced maturation of HLCs through the inhibition of the AKT signaling pathway by the off target effect with concomitant upregulation of HNF4α rather than direct inhibition of Aurora-A. The result is confirmed by western blot and qPCR[2].

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

Cell Proliferation Assay[2]

Cell Line:	Hepatocyte-like cells (HLCs)
Concentration:	1 and 10 μM
Incubation Time:	30 hours
Result:	Enhanced the proliferative capacity of HLCs.

Cell Cytotoxicity Assay[2]

Cell Line:	ES-HLCs, iPS-HLCs, Huh7 cells
Concentration:	1, 10, and 100 μM
Incubation Time:	5 days
Result:	Showed no cytotoxic effects on HLCs.

Western Blot Analysis[2]

Cell Line:	HLCs
Concentration:	1 and 10 μM
Incubation Time:	5 and 17 days
Result:	Markedly inhibited the phosphorylation of AKT and activated GSK-3β, which in turn inhibited Snail expression and increased HNF4α. Phthalazinone pyrazole didn't significantly reduce the phosphorylation of Aurora-A.

RT-PCR[2]

Cell Line:	HLCs
Concentration:	1 and 10 μM
Incubation Time:	5 and 17 days
Result:	Markedly inhibited the phosphorylation of AKT mRNA and activated GSK-3β mRNA, which in turn inhibited Snail mRNA expression and increased HNF4α mRNA. Phthalazinone pyrazole didn't significantly reduce the phosphorylation of Aurora-A mRNA.

REFERENCES

[1]. Prime ME, et al. Phthalazinone pyrazoles as potent, selective, and orally bioavailable inhibitors of Aurora-A kinase. J Med Chem. 2011;54(1):312-319.

[2]. Choi YJ, et al. Phthalazinone Pyrazole Enhances the Hepatic Functions of Human Embryonic Stem Cell-Derived Hepatocyte-Like Cells via Suppression of the Epithelial-Mesenchymal Transition. Stem Cell Rev Rep. 2018;14(3):438-450.

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