BRD9876

Cat. No.: HY-110208

CAS No.: 32703-82-5

Molecular Formula: $C_{16}H_{14}N_2$

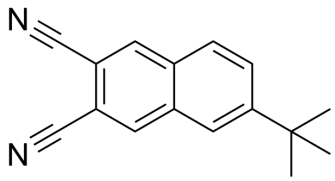
Molecular Weight: 234

Target: Kinesin; Microtubule/Tubulin

Pathway: Cell Cycle/DNA Damage; Cytoskeleton

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (213.68 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.2735 mL	21.3675 mL	42.7350 mL
	5 mM	0.8547 mL	4.2735 mL	8.5470 mL
	10 mM	0.4274 mL	2.1368 mL	4.2735 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (10.68 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BRD9876 is the “rigor” inhibitor that locks kinesin-5 (Eg5) in a state with enhanced microtubules (MTs) binding, leading to bundling and stabilization of MTs. BRD9876 interacts with the tyrosine 104 residue that is part of the α4-α6 allosteric binding pocket. BRD9876 specifically targets microtubule-bound Eg5 and selectively inhibits myeloma over CD34 cells. BRD9876 has the potential for multiple myeloma (MM) research[1][2][3][4].

In Vitro

BRD9876 (10 μM; 24 hours) reveals rapid arrest of cells at the G2/M phase starting as early as 2h of treatment in MM1S cells [1].

BRD9876 exhibits approximately 3-fold selectivity for MM1S myeloma cells (IC_{50}=3.1 μM) over CD34+ derived hematopoietic cells (IC_{50}=9.1 μM)[1].

BRD9876 (0.1, 1, 10, 100 uM) is able to overcome, in MM1S cells, stromal resistance of bone marrow stromal cells (BMSCs) from MM bone marrow aspirates but only minimal effects are observed with BRD9876 against primary MM cells[1].

BRD9876 is completely ineffective at inhibiting the basal ATPase activity of Eg5, in contrast to loop L5-binding monastrol or α4/α6-binding BI8 which shows greater activity against basal Eg5 ATPase activity[1].

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

Cell Cycle Analysis[1]

Cell Line:	MM1S cells and CD34 hematopoietic cells
Concentration:	10 μM
Incubation Time:	24 hours
Result:	Revealed rapid arrest of cells at the G2/M phase starting as early as 2h of treatment in MM1S cells. Showed markedly less G2/M arrest in CD34 hematopoietic cells.

REFERENCES

[1]. Shrikanta Chattopadhyay, et al. Niche-Based Screening in Multiple Myeloma Identifies a Kinesin-5 Inhibitor with Improved Selectivity over Hematopoietic Progenitors. Cell Rep. 2015 Feb 10;10(5):755-770.

[2]. Geng-Yuan Chen, et al. Eg5 Inhibitors Have Contrasting Effects on Microtubule Stability and Metaphase Spindle Integrity. ACS Chem Biol. 2017 Apr 21;12(4):1038-1046.

[3]. Chieh-Ting Fang, et al. HSP70 regulates Eg5 distribution within the mitotic spindle and modulates the cytotoxicity of Eg5 inhibitors. Cell Death Dis. 2020 Sep 1;11(8):715.

[4]. Anke Maes, et al. The therapeutic potential of cell cycle targeting in multiple myeloma. Oncotarget. 2017 Jun 28;8(52):90501-90520.

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