Toyocamycin

Cat. No.: HY-103248

CAS No.: 606-58-6

Molecular Formula: $C_{12}H_{13}N_5O_4$

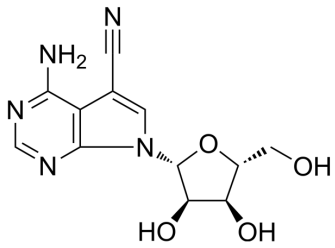
Molecular Weight: 291.26

Target: IRE1; Fungal; Antibiotic; Apoptosis; CDK

Pathway: Cell Cycle/DNA Damage; Anti-infection; Apoptosis

Storage:

Powder	-20°C	3 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (343.34 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.4334 mL	17.1668 mL	34.3336 mL
	5 mM	0.6867 mL	3.4334 mL	6.8667 mL
	10 mM	0.3433 mL	1.7167 mL	3.4334 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (8.58 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.58 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.58 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Toyocamycin (Vengicide) is an adenosine analog produced by Streptomyces diastatochromogenes, acts as an XBP1 inhibitor. Toyocamycin blocks RNA synthesis and ribosome function, and induces apoptosis. Toyocamycin affects IRE1α-XBP1 pathway, and inhibits XBP1 mRNA cleavage with an IC_{50} value of 80 nM with affecting IRE1α auto-phosphorylation. Toyocamycin specifically inhibits CDK9 with an IC_{50} value of 79 nM[1][2][3].

IC_{50} & Target

CDK9/cyclinT1 79 nM (IC_{50})	CDK7/Mat1/cyclinH1 2.8 μM (IC_{50})	CDK2/cyclinA 0.67 μM (IC_{50})	Cdk4/cyclin D3 15 μM (IC_{50})
cdk6/cyclin D3			

	>10 μM (IC_{50})

In Vitro

Toyocamycin (0-0.3 μM; 4 h) inhibits ER stress-induced XBP1 mRNA splicing, and selectively inhibits the ER stress-induced activation of the IRE1α-XBP1 pathway[1].
Toyocamycin (0-0.3 μM; 24 h) inhibits constitutive activation of XBP1 in MM cell lines[1].
Toyocamycin (250 nM; 48 h) inhibits CDK9 enzymatic activity in colon cancer cell lines[2].
Toyocamycin (0.05 nM-50 μM; 48 h and 72 h) doesn't trigger immediate cytotoxicity against YB5 and HCT116 cells with cell viability above 50%, but results eradication of cancer cells 2 weeks later at 10 nM for 24 h treatment[2].
Toyocamycin (0-100 nM; 24 or 48 h) induces apoptosis via mitochondrial pathway in PC-3 cells[3].
Toyocamycin (60 nM; 0-48 h) promotes p38/ERK MAPK activation and regulates ROS-mediated apoptosis by inhibition of p38 on ERK MAPK[3].

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

Western Blot Analysis[1]

Cell Line:	HeLa, HEK293
Concentration:	0, 0.03, 0.1, 0.3 μM
Incubation Time:	4 hours
Result:	Suppressed neither tunicamycin-induced ATF6 nor PERK activation. Inhibited IRE1α-induced XBP1 mRNA cleavage without affecting IRE1α phosphorylation on Ser724.

Western Blot Analysis[3]

Cell Line:	Human prostate cancer PC-3 cells
Concentration:	60 nM
Incubation Time:	12, 24, 36, 48 hours
Result:	Suppressed the phosphorylation level of AKA, while decreasing the phosphorylation level of ERK and p38.

Cell Viability Assay[3]

Cell Line:	PC-3 and RWPE-1 cells
Concentration:	0, 20, 40, 60, 80, 100 nM
Incubation Time:	24 or 48 hours
Result:	Inhibted cell viability and induced cell apoptosis by 62%.

In Vivo

Toyocamycin (0.5 mg/kg, 1.0 mg/kg; i.p.; twice a week; 2 weeks) shows anti-tumor activity in a xenograft model with human multiple myeloma (MM) cells, while the anti-tumor effect enhanced by Bortezomib (HY-10227)[1].

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

Animal Model:	SCID mice injected with human multiple myeloma (MM) cells[1]
Dosage:	0.5 mg/kg, 1.0 mg/kg
Administration:	Intraperitoneal injection; twice a week; 2 weeks
Result:	Reduced the tumor volume significantly.Showed enhancing anti-tumor activity

	represented as smaller tumor volumes when compared with Bortezomib (HY-10227).

CUSTOMER VALIDATION

- Am J Pathol. 2023 Jun 8;S0002-9440(23)00205-5.
- bioRxiv. 2023 Sep 12.

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REFERENCES

[1]. Pandey S, et al. Selective CDK9 Inhibition by Natural Compound Toyocamycin in Cancer Cells. Cancers (Basel). 2022 Jul 8;14(14):3340.

[2]. Park SG, et al. Toyocamycin induces apoptosis via the crosstalk between reactive oxygen species and p38/ERK MAPKs signaling pathway in human prostate cancer PC-3 cells. Pharmacol Rep. 2017 Feb;69(1):90-96.

[3]. Toyocamycin, et al. Identification of Toyocamycin, an agent cytotoxic for multiple myeloma cells, as a potent inhibitor of ER stress-induced XBP1 mRNA splicing. Blood Cancer J. 2012 Jul;2(7):e79.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA