Manzamine A

Cat. No.: HY-117025

CAS No.: 104196-68-1

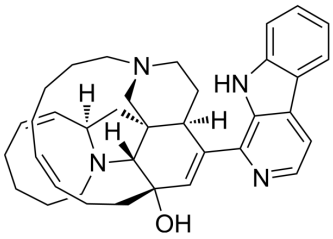
Molecular Formula: $C_{36}H_{44}N_4O$

Molecular Weight: 548.76

Target: GSK-3; CDK; Parasite; Proton Pump; HSV; Autophagy

Pathway: PI3K/Akt/mTOR; Stem Cell/Wnt; Cell Cycle/DNA Damage; Anti-infection; Membrane Transporter/Ion Channel; Autophagy

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 10 mg/mL (18.22 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Concentration \ Mass	1 mg	5 mg	10 mg
	1 mM	1.8223 mL	9.1115 mL	18.2229 mL
	5 mM	0.3645 mL	1.8223 mL	3.6446 mL
	10 mM	0.1822 mL	0.9111 mL	1.8223 mL

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

BIOLOGICAL ACTIVITY

Description

Manzamine A, an orally active beta-carboline alkaloid, inhibits specifically GSK-3β and CDK-5 with IC_{50}s of 10.2 μM and 1.5 μM, respectively. Manzamine A targets vacuolar ATPases and inhibits autophagy in pancreatic cancer cells. Manzamine A has antimalarial and anticancer activities. Manzamine A also shows potent activity against HSV-1[1][2][3][4].

IC_{50} & Target

Plasmodium	GSK-3β 10.2 μM (IC_{50})	CDK5 1.5 μM (IC_{50})	vacuolar ATPases
Malaria	HSV-1		

In Vitro

Manzamine A (5-50 μM, 18 h) decreases tau phosphorylation, measured with ELISA[1].
Manzamine A (10 μM) inhibits yeast S. cerevisiae growth by 30%[2].
Manzamine A displays a few enlarged vacuoles in yeast[2].
Manzamine A (2.5-10 μM, 24 h) increases acidity in pancreatic cancer cells and non-malignant Vero cells[2].
Manzamine A (1 μM, 24 h) inhibits HSV-1 infection in SIRC cells[4].
Manzamine A shows antimalarial activity with an IC_{50} of 8.0 nM (D6 clone) and 11 nM (W2 clone)[5].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[4]

Cell Line:	SIRC cell
Concentration:	0.1, 0.5, 1, 2, 3, 5, and 10 μM
Incubation Time:	72 h
Result:	Inhibited SIRC cell viability with an IC_{50} of 5.6 μM.

In Vivo

Manzamine A (50 and 100 mol/kg, p.o. or i.p.) inhibits the growth of the rodent malaria parasite Plasmodium berghei in infected mice[6].
Manzamine A (8 mg/kg, i.p., daily for 8 consecutive days) prolongs the survival of SW mice to 20 days[7].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Plasmodium berghei in infected mice[6]
Dosage:	50 or 100 mol/kg
Administration:	Intraperitoneal injection (i.p.) or oral administration (p.o.)
Result:	Inhibited the growth of the rodent malaria parasite Plasmodium berghei. Prolonged the survival of highly parasitaemic mice.

REFERENCES

[1]. Hamann M, et al. Glycogen synthase kinase-3 (GSK-3) inhibitory activity and structure-activity relationship (SAR) studies of the manzamine alkaloids. Potential for Alzheimer's disease. J Nat Prod. 2007;70(9):1397-1405.

[2]. Kallifatidis G, et al. The marine natural product manzamine A targets vacuolar ATPases and inhibits autophagy in pancreatic cancer cells [published correction appears in Mar Drugs. 2014;12(4):2305-7]. Mar Drugs. 2013;11(9):3500-3516. Published 2013 Sep 17.

[3]. Winkler JD, et al. Antimalarial activity of a new family of analogues of manzamine A. Org Lett. 2006;8(12):2591-2594.

[4]. Palem JR, et al. Manzamine A as a novel inhibitor of herpes simplex virus type-1 replication in cultured corneal cells. Planta Med. 2011;77(1):46-51.

[5]. Wahba AE, et al. Structure-activity relationship studies of manzamine A: amidation of positions 6 and 8 of the beta-carboline moiety. Bioorg Med Chem. 2009 Nov 15;17(22):7775-82.

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[7]. El Sayed KA, et al. New manzamine alkaloids with potent activity against infectious diseases. J Am Chem Soc. 2001 Mar 7;123(9):1804-8.

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