

CHS-828

Chemical Properties

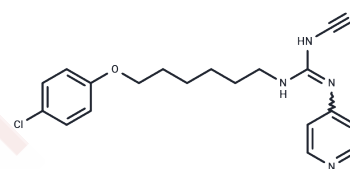
CAS No. : 200484-11-3

Formula: C₁₉H₂₂ClN₅O

Molecular Weight: 371.86

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Actual storage temperature shall be subject to the COA.



Biological Description

Description	CHS-828 (GMX1778), a pyridyl cyanoguanidine, is an effective inhibitor of NAD ⁺ biosynthesis enzyme NAMPT (IC ₅₀ <25 nM).
Targets(IC ₅₀)	Apoptosis, NAMPT
In vitro	GMX1778 induces NAD ⁺ depletion through inhibition of NAD ⁺ biosynthesis, followed by ATP depletion and ultimately resulted in cell death. [1] GMX1778 induces programmed cell death with apoptotic features. [2] GMX1778 suppresses nuclear factor-kappa B activity in cancer cells through downregulation of IKK activity (IC ₅₀ =8 nM). [3]
In vivo	GMX1778 (250 mg/kg, p.o.) shows marked antitumoural activity against three different human neuroendocrine tumours, midgut carcinoid (GOT1), pancreatic carcinoid (BON), and medullary thyroid carcinoma (GOT2), transplanted in nude mice. [4]
Kinase Assay	In vitro coupled-enzyme NAMPT assay: Recombinant NAMPT activity is assessed using a coupled-enzyme assay based on the quantitation of NAD ⁺ . Reactions are performed at room temperature for 180 min using mixtures consisting of 50 mM HEPES (pH 7.4), 50 mM KCl, 5 mM MgCl ₂ , 0.5 mM β-mercaptoethanol, 0.005% bovine serum albumin, 1% DMSO, 2.0 U/ml lactate dehydrogenase, 4 mM sodium L-lactate, 0.4 U/ml diaphorase, 6 μM resazurin sodium salt, 0.4 mM PRPP, 3.0 nM NMNAT1, 125 μM ATP, 50 μM NM, and 2 to 5 μM recombinant NAMPT. Fluorescence is measured with a Tecan Safire plate reader (excitation wavelength, 560 nm; emission wavelength, 590 nm). Ki values are calculated using Graphpad Prism 4.0 software and the Cheng-Prusoff equation.
Cell Research	Serial dilutions of GMX1778 in DMSO are performed to achieve a final concentration of 0.2% DMSO. Relative ATP levels after 72 h are determined using a ViaLight HS high-sensitivity cytotoxicity and cell proliferation BioAssay kit per the manufacturer's instructions. For GMX1778 cytotoxicity rescue experiments, cells are treated with NA (10 μM) or NMN (100 μM) simultaneously with GMX1778. Sigmoidal dose-response curves are generated by nonlinear regression analysis of variable slope using GraphPad Prism version 4.00 (GraphPad Software) to calculate 50% inhibitory (IC ₅₀) values. (Only for Reference)

Solubility Information

A DRUG SCREENING EXPERT

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 69 mg/mL (185.55 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Corn Oil: 2.5 mg/mL (6.72 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.6892 mL	13.4459 mL	26.8918 mL
5 mM	0.5378 mL	2.6892 mL	5.3784 mL
10 mM	0.2689 mL	1.3446 mL	2.6892 mL
50 mM	0.0538 mL	0.2689 mL	0.5378 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

- Watson M, et al. Mol Cell Biol. 2009, 29(21), 5872-5888.
Hansen CM, et al. Anticancer Res. 2000, 20(6B), 4211-4220.
Olsen LS, et al. Int J Cancer. 2004, 111(2), 198-205.
Johanson V, et al. Neuroendocrinology. 2005, 82(3-4), 171-176.

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