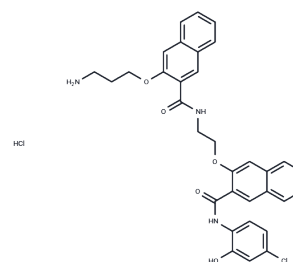


666-15

Chemical Properties

CAS No. : 1433286-70-4
Formula: C33H31Cl2N3O5
Molecular Weight: 620.52
Appearance: no data available
Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year



Biological Description

Description	666-15 (CREB inhibitor) is a potent and selective CREB inhibitor (IC ₅₀ : 81 nM).
Targets(IC ₅₀)	Epigenetic Reader Domain
In vitro	666-15 is a potent and selective inhibitor of CREB-mediated gene transcription (IC ₅₀ = 0.081 ± 0.04 μM). 666-15 also potently inhibited cancer cell growth without harming normal cells [1]. Isoproterenol (ISO) induced cardiac hypertrophy. The rate of ROS production, CREB phosphorylation, and miR-132 expression increased after the addition of ISO. Upregulation of miR-132 was blocked by the specific inhibitor of CREB transcription, 666-15 [2].
In vivo	In an in vivo MDA-MB-468 xenograft model, 666-15 completely suppressed the tumor growth without overt toxicity [1]. 666-15 was found to be readily bioavailable to achieve pharmacologically relevant concentrations for CREB inhibition. The mice treated with 666-15 showed no evidence of changes in body weight, complete blood count, blood chemistry profile, cardiac contractility and tissue histologies from liver, kidney, and heart [3].
Cell Research	HEK 293T cells in a 10 cm plate were transfected with pCRE-RLuc (6 μg) with Lipofectamine2000 following the manufacturer's instructions. Three hours after transfection, the cells were collected and replated into 96-well plates at ~ 10 ⁴ cells/well. The cells were allowed to attach to the bottom of the plates overnight. The cells were then treated with different concentrations of different compounds for 30 min when forskolin (10 μM) was added to each well. The cells were incubated for further 5 h before cell lysis using 1× 30 μL Renilla luciferase lysis buffer. An amount of 5 μL of the lysate was combined with 30 μL of benzyl-coelenterazine solution in PBS (pH 7.4, 10 μg/mL). The protein concentration in each well was determined. The Renilla luciferase activity was normalized to protein content in each well and expressed as relative luciferase unit/μg protein (RLU/μg protein). The IC ₅₀ was derived from nonlinear regression analysis of the RLU/μg protein-concentration curve [1].
Animal Research	Each 6- to 8-week old BALB/c nude mouse was inoculated subcutaneously at the right flank with MDA-MB-468 cells (5 × 10 ⁶) in 0.1 mL of HBSS with Matrigel (1:1) for tumor development. When the tumor volume reached approximately 100 mm ³ , the mice were randomized to be treated with either vehicle or 666-15 at 10 mg/kg. 3i was dissolved in 1% N-methylpyrrolidone (NMP), 5% Tween-80 in H ₂ O. The dosing solution was prepared

weekly. The mice were treated once a day for 5 consecutive days a week, and the treatment lasted for 5 weeks. During the treatment, the tumor size and body weight were measured 2-3 times a week. The tumors were measured in two dimensions using a digital caliper, and the volume was expressed in mm³ using the formula $V = 0.5ab^2$, where a and b represent the long and short diameters of the tumor, respectively. The tumor volume was normalized to the initial tumor volume at the time of the first treatment [1].

Solubility Information

Solubility	DMSO: 60 mg/mL (96.7 mM), (< 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.6116 mL	8.0578 mL	16.1155 mL
5 mM	0.3223 mL	1.6116 mL	3.2231 mL
10 mM	0.1612 mL	0.8058 mL	1.6116 mL
50 mM	0.0322 mL	0.1612 mL	0.3223 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.

Reference

Xie F, et al. Identification of a Potent Inhibitor of CREB-Mediated Gene Transcription with Efficacious in Vivo Anticancer Activity. J Med Chem. 2015 Jun 25;58(12):5075-87.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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