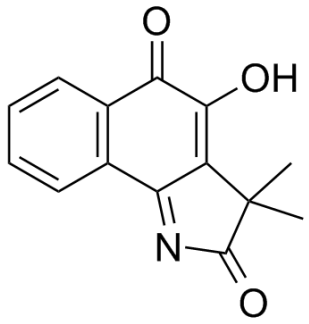
BVT948

Cat. No.:	HY-100625
CAS No.:	39674-97-0
Molecular Formula:	$C_{14}H_{11}NO_3$
Molecular Weight:	241.24
Target:	Phosphatase; Cytochrome P450; Histone Methyltransferase
Pathway:	Metabolic Enzyme/Protease; Epigenetics
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (414.52 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	4.1452 mL	20.7262 mL	41.4525 mL
	5 mM	0.8290 mL	4.1452 mL	8.2905 mL
	10 mM	0.4145 mL	2.0726 mL	4.1452 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 (10.36 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BVT948 is a protein tyrosine phosphatase (PTP) inhibitor which can also inhibit several cytochrome P450 (P450) isoforms and lysine methyltransferase SETD8 (KMT5A).

IC_{50} & Target

PTP[1], P450[1], SETD8[2]

In Vitro

Results show that the effect of BVT948 (BVT.948) is to strengthen the insulin signal and has no effects on the duration of the signal. BVT948 appears to be an effective inhibitor of both protein tyrosine phosphatases (PTP activity and P450 activity)[1]. BVT948 efficiently and selectively suppresses cellular H4 lysine 20 (H4K20me1) at doses lower than 5 μM within 24 h. The cells treated with BVT948 recapitulate cell-cycle-arrest phenotypes similar to what are reported for knocking down SETD8 by RNAi[2]. Treatment of MCF-7 cells with 0.5, 1 or 5 μM of BVT948 for 24 h does not cause any significant changes in cell viability. BVT948 inhibits TPA-induced MMP-9 up-regulation in a dose-dependent manner. Treatment with BVT948 inhibits TPA-stimulated NF-κB binding activity, but not AP-1 binding activity. BVT948 does not affect the MAPK phosphorylation by TPA. Treatment with BVT948 diminishes the TPA-induced cell invasion by 50%[3].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Results show that 3 μmol/kg BVT948 (BVT.948) significantly enhances glucose clearance from the blood stream in response to insulin compare with vehicle-treated controls[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	To determine the reversibility of the inhibition of protein tyrosine phosphatases (PTP) activity by BVT948 (BVT.948), 50 ng of PTP1B is incubated in 100 μL of assay buffer with 20 μM BVT948 for 10 min in a concentration device. The sample is then centrifuged at 14,000 rpm at 4°C for 12 min. The concentrate is subsequently washed three times with 100 μL of assay buffer followed by centrifugation. After washing, 190 μL of assay buffer is added to the sample, increasing the volume to 200 μL. Twenty microliters are used in assays measuring enzyme activity remaining using para-nitrophenyl phosphate (pNPP) as a substrate. Controls includes enzyme, which is treated with inhibitor but not washed, and enzyme, which is not treated with BVT948 but is put through the incubation and washing procedures[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	L6 myocytes are maintained in minimum essential medium-alpha (α-MEM) supplemented with 10% fetal bovine serum and 100 IU/mL penicillin-streptomycin at 37°C in 5% CO_2. Cells are seeded into 24-well plates, and the medium is replaced with α-MEM containing 2% fetal calf serum to induce differentiation into myotubes. The medium is changed every other day, and cytidine (0.24 mg/mL medium) is added to the cultures at days 7 to 9 to suspend cycling cells. The cells are used in experiments after overnight serum starvation at days 11 to 16. They are treated with or without 25 μM BVT948 (BVT.948) for 30 min followed by 5 min of insulin (25 nM) stimulation. After freezing with liquid N_2, the cells are lysed with a Tris-HCl buffer, pH 7.4, containing 1% Nonidet-40, 0.25% sodium deoxycholate, 150 mM NaCl, 1 mM EDTA, 1 mM EGTA, 1 mM sodium orthovanadate, 10 mM β-glycerophosphate, 5 mM sodium pyrophosphate, and complete protease inhibitor cocktail The cell extracts are centrifuged at 14,000 g for 10 min, and the supernatants are used in the Delfia assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Male mice 12 to 14 weeks old are used in this study. They are divided into equal groups (n=9) based on blood glucose levels. At time 0, the mice are injected with vehicle (NaCl with 10% DMSO) or BVT948 (BVT.948) (0.3 and 3 μmol/kg) and 1 U/kg insulin intraperitoneally. Blood glucose is determined from tail vein sampling at 0, 30, 60, and 120 min using a glucometer[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Liljebris C, et al. Oxidation of protein tyrosine phosphatases as a pharmaceutical mechanism of action: a study using 4-hydroxy-3,3-dimethyl-2H-benzo[g]indole-2,5(3H)-dione. J Pharmacol Exp Ther. 2004 May;309(2):711-9.

[2]. Blum G, et al. Small-molecule inhibitors of SETD8 with cellular activity. ACS Chem Biol. 2014 Nov 21;9(11):2471-8.

[3]. Hwang BM, et al. Protein tyrosine phosphatase controls breast cancer invasion through the expression of matrix metalloproteinase-9. BMB Rep. 2013 Nov;46(11):533-8.

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