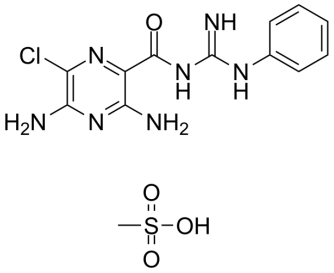
Phenamil methanesulfonate

Cat. No.:	HY-108464A
CAS No.:	1161-94-0
Molecular Formula:	$C_{13}H_{16}ClN_7O_4S$
Molecular Weight:	401.83
Target:	Sodium Channel; TRP Channel
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	-20°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (62.22 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4886 mL	12.4431 mL	24.8861 mL
	5 mM	0.4977 mL	2.4886 mL	4.9772 mL
	10 mM	0.2489 mL	1.2443 mL	2.4886 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 (6.22 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Phenamil methanesulfonate, an analog of Amiloride (HY-B0285), is a more potent and less reversible epithelial sodium channel (ENaC) blocker with an IC_{50} of 400 nM[2]. Phenamil methanesulfonate is also a competive inhibitor of TRPP3 and inhibits TRPP3-mediated Ca^{2+} transport with an IC_{50} of 140 nM in a Ca^{2+} uptake assay[1]. Phenamil methanesulfonate is an intriguing small molecule to promote bone repair by strongly activating BMP signaling pathway[4]. Phenamil methanesulfonate is used for the research of cystic fibrosis lung disease[5].

IC_{50} & Target

TRPC3
140 nM (IC_{50})

In Vitro

TRPP3, a member of the transient receptor potential (TRP) superfamily of cation channels, is a Ca^{2+}-activated channel permeable to Ca^{2+}, Na^+, and K^+. TRPP3 is implicated in regulation of pH-sensitive action potential in spinal cord neurons. Phenamil methanesulfonate (1 μM) decreases $^{45}Ca^{2+}$ uptake in a radiotracer uptake assay. It inhibits TRPP3-mediated Ca^{2+} transport with an IC_{50} value of 0.28 μM in oocytes expressing TRPP3 or H2O-injected oocytes[1].
Phenamil methanesulfonate is a more potent ENaC blocker than Amiloride, it inhibits the epithelial sodium channel (ENaC)

with an IC_{50} of 400 nM (Amiloride=776 nM)[2].
Phenamil methanesulfonate inhibits basal short-circuit currents with IC_{50} values of 75 and 116 nM, respectively in both human and ovine bronchial epithelia cells[3].
Phenamil methanesulfonate (0-20 μM; 14 days) elevates adipogenic gene expression, PPARγ, Fabp4, and lipoprotein lipase expression in a concentration-dependent manner ,and regulates adipogenesis in C3H10T1/2 cells[4].
Phenamil methanesulfonate (0-20 μM; 7 or 14 days) modulates MC3T3-E1 osteoblastic differentiation, it increases Alkaline phosphatase (ALP) activity in MC3T3-E1 cells in a concentration-dependent manner[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

RT-PCR[4]

Cell Line:	C3H10T1/2 cells
Concentration:	0 μM and 20 μM
Incubation Time:	14 days
Result:	Increased PPARγ, Fabp4, and lipoprotein lipase (LPL) mRNA expression.

In Vivo

Phenamil methanesulfonate (subcutaneous injection; 15 or 30 mg/kg; 21 days; infusion rate of 1 ml/h) reduces chronic-hypoxia-induced pulmonary artery hypertension (PAH). Additionally, the mRNA level of SMA, SM22, Id3, and Trb3 from the lung sample are also decreased by Phenamil under hypoxia or normoxia in rats. However, phenamil has little effect on pulmonary vasculature under physiological conditions[5].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Sprague-Dawley rats[5]
Dosage:	15 or 30 mg/kg
Administration:	Subcutaneous injection; 15 or 30 mg/kg; 21 days; infusion rate of 1 ml/h
Result:	Reduced hypoxia-induced pulmonary hypertension and vascular remodeling.

REFERENCES

[1]. Xiao-Qing Dai , et al. Inhibition of TRPP3 channel by amiloride and analogs. Mol Pharmacol. . 2007 Dec;72(6):1576-85.

[2]. Andrew J Hirsh, et al.Design, synthesis, and structure-activity relationships of novel 2-substituted pyrazinoylguanidine epithelial sodium channel blockers: drugs for cystic fibrosis and chronic bronchitis. J Med Chem. 2006 Jul 13;49(14):4098-115.

[3]. Andrew J Hirsh, et al.Evaluation of second generation amiloride analogs as therapy for cystic fibrosis lung disease.J Pharmacol Exp Ther. 2004 Dec;311(3):929-38.

[4]. Mun Chun Chan, et al. The amiloride derivative phenamil attenuates pulmonary vascular remodeling by activating NFAT and the bone morphogenetic protein signaling pathway. Mol Cell Biol

Caution: Product has not been fully validated for medical applications. For research use only.

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