

Product Data Sheet

Product Name: Phenamil

Cat. No.: GC13994

Chemical Properties

Cas. No. 1161-94-0

Chemical Name (E)-3,5-diamino-N-(amino(phenylamino)methylene)-6-chloropyrazine-2-carboxamide methanesulfonate

SMILES C1C(N=C1C(/N=C(N)/NC2=CC=CC=C2)=O)=C(N)N=C1N.OS(=O)(C)=O

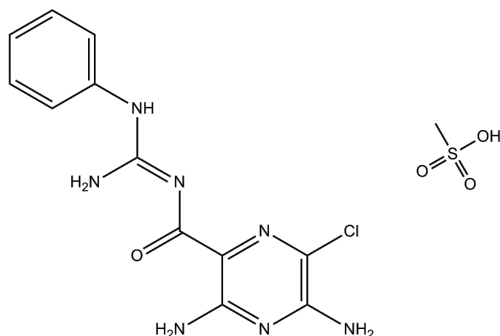
Formula $C_{12}H_{12}ClN_7O \cdot CH_3SO_3H$ M.Wt 401.83

Solubility DMF: 0.1 mg/ml, DMSO: 1 mg/ml, DMSO:PBS (pH 7.2) (1:1): 0.5 mg/ml
Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

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Cell lines	Osteoblast-like MC3T3-E1 cells
Preparation Method	The cells were maintained in regular growth medium, i.e. α -minimal essential medium supplemented with 10% fetal bovine serum (FBS), 100 U/ml penicillin G and 100 mg/ml streptomycin. The culture medium, with or without 10 μ M phenamil, was replaced every 3-4 days.
Reaction Conditions	10 μ M for 14 days
Applications	Phenamil-treated and -untreated control cells showed a statistically significant increase in cell proliferation from day 7 to day 14.
Animal experiment [2]:	
Animal models	Male Sprague-Dawley rats
Preparation Method	Miniature osmotic infusion pumps which deliver saline-DMSO (50% saline-50% DMSO) solution or phenamil in saline-DMSO were implanted subcutaneously in male Sprague-Dawley rats (age, 6 to 7 weeks; weight, 250 to 300 g) between the scapulae and connected via a catheter advanced into the left carotid artery. Four rats were used for each condition. Phenamil (15 or 30 mg/kg of body weight/day) was administered continuously for 21 days at an infusion rate of 1 ml/h. The rats were subjected to hypobaric hypoxia (10.5% oxygen) or normoxia (room air) for 21 days.
Dosage form	15 or 30 mg/kg, Miniature osmotic infusion pump

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Applications Phenamil reduces chronic-hypoxia-induced pulmonary artery hypertension (PAH).

References:

[1] : Lo K W H, Ulery B D, Kan H M, et al. Evaluating the feasibility of utilizing the small molecule phenamil as a novel biofactor for bone regenerative engineering[J]. Journal of tissue engineering and regenerative medicine, 2014, 8(9): 728-736.

[2] :Chan M C, Weisman A S, Kang H, et al. The amiloride derivative phenamil attenuates pulmonary vascular remodeling by activating NFAT and the bone morphogenetic protein signaling pathway[J]. Molecular and cellular biology, 2011, 31(3): 517-530.

Background

Phenamil is a selective inhibitor of transient receptor potentials (TRPs) and acid-sensing ion channels (ASICs) [1]. Phenamil is an amiloride analogs and a more potent and less reversible epithelial sodium channel (ENaC) blocker with an IC₅₀ of 400 nM [2]. Phenamil inhibited TRPP3 - mediated Ca²⁺ transport with an IC₅₀ of 140 nM in a Ca²⁺ uptake assay [3].

Phenamil (10 μM) Treatment of M2-10B4 (M2) mouse (mesenchymal stem cells) MSCs for 6 days with 10 μM phenamil markedly stimulated expression of the genes encoding ALP, Runx2, OCN, and osterix. Phenamil induces osteogenic gene expression and mineralization in both MSC and primary calvariae organ cultures [4]. Phenamil (10 μM) induced the expression of PPARγ within 24 h in 3T3-F442A preadipocyte cell lines. Phenamil act as a new proadipogenic compound [5].

Phenamil (15 or 30 mg/kg; 21 days) reduced chronic-hypoxia-induced pulmonary artery hypertension (PAH). Infusion of phenamil during hypoxia treatment inhibited pulmonary vascular remodeling [6].

References:

[1]. Chan M C, Weisman A S, Kang H, et al. The amiloride derivative phenamil attenuates pulmonary vascular remodeling by activating NFAT and the bone morphogenetic protein signaling pathway[J].

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Molecular and cellular biology, 2011, 31(3): 517-530.

[2]. Hirsh A J, Molino B F, Zhang J, 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]. Journal of medicinal chemistry, 2006, 49(14): 4098-4115.

[3]. Dai X Q, Ramji A, Liu Y, et al. Inhibition of TRPP3 channel by amiloride and analogs[J]. Molecular pharmacology, 2007, 72(6): 1576-1585.

[4]. Park K W, Waki H, Kim W K, et al. The small molecule phenamil induces osteoblast differentiation and mineralization[J]. Molecular and cellular biology, 2009, 29(14): 3905-3914.

[5]. Park K W, Waki H, Choi S P, et al. The small molecule phenamil is a modulator of adipocyte differentiation and PPAR γ expression [S][J]. Journal of lipid research, 2010, 51(9): 2775-2784.

[6]. Chan M C, Weisman A S, Kang H, et al. The amiloride derivative phenamil attenuates pulmonary vascular remodeling by activating NFAT and the bone morphogenetic protein signaling pathway[J]. Molecular and cellular biology, 2011, 31(3): 517-530.

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