Product Data Sheet

Product Name: CGH 2466 dihydrochloride
Cat. No.: GC14674

Chemical Properties

Cas. No.	1177618-54-0		
Chemical Name	4-(3,4-dichlorophenyl)-5-(pyridin-4-yl)thiazol-2(3H)-imine dihydrochloride		
SMILES	ClC1=C(Cl)C=C(C(NC2=N)=C(S2)C3=CC=NC=C3)C=C1		
Formula	$C_{14}H_9N_3SCl_2.2HCl$	M.Wt	395.13
Solubility	<3.95mg/ml in DMSO; <1.98mg/ml in ethanol	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	CGH 2466 dihydrochloride		

Background

CGH 2466 dihydrochloride is a combined adenosine receptor antagonist. It is an inhibitor of phosphodiesterase type 4 and p38 mitogen-activated protein kinase. It inhibited the phosphodiesterase 4D (PDE4D) isoenzyme with an IC50 value of 22±5 nM. It inhibited the p38 mitogen-activated protein (MAP) kinases α and β with IC50 values of 187±18, 400±38 nM, respectively [1].

There are four adenosine receptor subtypes of the G protein-coupled receptor family, designated as A1, A2A, A2B and A3 [2]. Adenosine plays a role in the control of inflammation [3]. Phosphodiesterases can inactivate cAMP. In inflammatory cells, phosphodiesterase-4 (PDE4) is the predominant isoenzyme [4]. In mammalian cells, the p38 MAPK was thought to be important for regulating cellular responses during infection via its effects on the expression of proinflammatory molecules [5].

CGS15943 is a broad spectrum adenosine antagonist, SB203580 is a prototypical inhibitor of the p38 MAP kinase, and cilomilast is a standard inhibitor of PDE4. Data

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showed that CGH2466 was similar to SB203580 in potency as a p38 MAP kinase inhibitor, and was similar to cilomilast in activity to inhibit PDE4D. Compared to CGS15943, CGH 2466 showed similar potency to inhibit A1, A2B and A3 adenosine receptors. In contrast to CGS15943, CGH2466 was not active at the A2A receptor. Compared with other above compounds, CGH2466 was an inhibitor of the highest potency to inhibit selected enzymes or receptors in leucocyte-based assays [1].

48 h after the allergen challenge, bronchoalveolar lavage recovered eosinophil numbers. In sensitized mice, aerosol challenge of ovalbumin was able to increase these eosinophil numbers. In this animal model of asthmatic inflammation, 15 min before and 24 h after the challenge, the intranasal administration of CGH2466, dose-dependently inhibited the airway eosinophilia induced by ovalbumin, reaching significant levels at doses of 3 and 10 mg.kg-1 [1].

References:
[1]. Trifilieff A, Keller TH, Press NJ, et al. CGH2466, a combined adenosine receptor antagonist, p38 mitogen-activated protein kinase and phosphodiesterase type 4 inhibitor with potent in vitro and in vivo anti-inflammatory activities. British journal of pharmacology, 2005, 144(7): 1002-1010.
[2]. Klotz KN, Hessling J, Hegler J, et al. Comparative pharmacology of human adenosine receptor subtypes-characterization of stably transfected receptors in CHO cells. Naunyn-Schmiedeberg's archives of pharmacology, 1997, 357(1): 1-9.
[3]. Yang D, Zhang Y, Nguyen HG, et al. The A2B adenosine receptor protects against inflammation and excessive vascular adhesion. The Journal of clinical investigation, 2006, 116(7): 1913-1923.
[4]. Gamble E, Grootendorst DC, Brightling CE, et al. Antiinflammatory effects of the phosphodiesterase-4 inhibitor cilomilast (Ariflo) in chronic obstructive pulmonary disease. American journal of respiratory and critical care medicine, 2003, 168(8): 976-982.
[5]. Han J, Jiang Y, Li Z, et al. Activation of the transcription factor MEF2C by the MAP kinase p38 in inflammation. 1997, 386(6622):296-299.