

Product Data Sheet

Product Name: Cilomilast

Cat. No.: GC17598

Chemical Properties

Cas. No. 153259-65-5

Chemical Name 4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)cyclohexane-1-carboxylic acid

SMILES COC1=C(C=C(C=C1)C2(CCC(CC2)C(=O)O)C#N)OC3CCCC3

Formula $C_{20}H_{25}NO_4$ M.Wt 343.42

Solubility ≥ 12.95 mg/mL in DMSO, ≥ 49.9 mg/mL in EtOH with ultrasonic and warming
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.

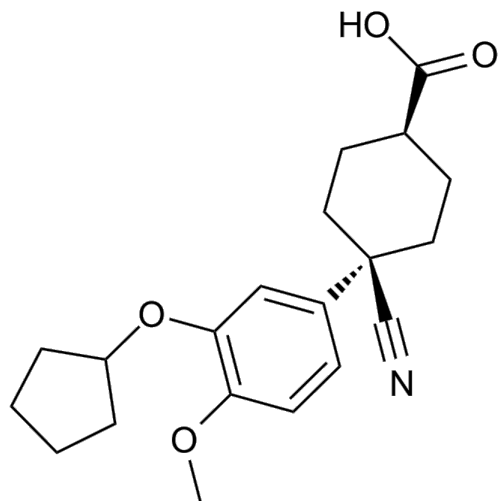
Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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Structure



Protocol

Cell experiment [1]:

Cell lines MCS cell lines

Preparation method The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reaction Conditions 11 d; 40 µM

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Applications

The results demonstrate that inhibition of PDE (Cilomilast) enhances ALP expression in MSCs via the cAMP pathway. The increase in the level of ALP activity is dependent on the dose of cilomilast. To study the effect of the inducers on MSC differentiation at similar proliferation rates, we treated MCSs, except those cultured in osteogenic medium, with 1% DMSO. We compared MSCs cultured for 11 days in the presence of different inducers with MSCs cultured in osteogenic medium in order to quantify the osteogenetic effects of the inducers. We found that the ALP activity levels of MCSs treated with a combination of PDE4 inhibitor (40 μ M) and BMP-2 (300 ng/mL) were almost double the ALP activity level of MSCs treated with osteogenic medium, suggesting that the mineralisation process is more rapid.

Animal experiment [2]:

Animal models

Female C57BL/6 mice

Dosage form

Cilomilast 0.05%; ocular surface instillation three times per day over a period of 7 days.

Applications

Real-time PCR was used to quantify the expression of transcripts encoding IL-1 α , IL-1 β , and TNF- α in the corneas and conjunctivae of DED-induced mice. Treatment with topical cilomilast significantly decreased the corneal expression of TNF- α as compared with the vehicle-treated group. Compared with the DED-untreated corneas, treatment with cilomilast significantly reduced IL-1 α and TNF- α expression.

Other notes

Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

- [1] Munisso M C, Kang J H, Tsurufuji M, et al. Cilomilast enhances osteoblast differentiation of mesenchymal stem cells and bone formation induced by bone morphogenetic protein 2[J]. Biochimie, 2012, 94(11): 2360-2365.
- [2] Sadrai Z, Stevenson W, Okanobo A, et al. PDE4 inhibition suppresses IL-17-associated immunity in dry eye disease[J]. Investigative ophthalmology & visual science, 2012, 53(7): 3584-3591.

Background

Cilomilast, also known as SB-207499 or Ariflo, is a potent second generation inhibitor of type 4 phosphodiesterase (PDE4), an enzyme metabolizing cellular cyclic adenosine monophosphate (cAMP) which acts as a second messenger to disrupt the function of inflammatory cell and induce airway smooth muscle relaxation. Cilomilast is currently used for the treatment of chronic obstructive pulmonary disease (COPD) due to its strong anti-inflammatory activity as well as inhibitory effects against the release of neutrophil chemoattractants (such as tumor necrosis factor TNF- α , interleukin IL-8 and granulocyte-macrophage colony stimulating factor GM-CSF) and suppression of the recruitment of neutrophils into tissues and the LTB4 production.

Reference

- [1].M Profita, G Chiappara, F Mirabella, RCDi Giorgi, L Chimenti, G Costanzo, L Riccobono, V Bellia, J Bousquet, and A M Vignola. Effect of cilomilast (Ariflo) on TNF- α , IL-8, and GM-CSF release by airway cells of patients with COPD. Thorax 2003; 58: 573-579
- [2].Barry D. Zussman, Lisa J. Benincosa, Dawn M Webber, David j. Clark, Hugh Cowley, John Kelly, Robert D. Murdoch, James Upward, Peter Wyld, Andreas Port and Hermann Fuder. An overview of the pharmacokinetics of cilomilast (Ariflo), a new, orally active phosphodiesterase 4 inhibitor, in healthy young and elderly volunteers. J Clin Pharmacol 2001; 41: 950-958

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