

Product Data Sheet

Product Name: CFTRinh-172

Cat. No.: GC14421

Chemical Properties

Cas. No. 307510-92-5

Chemical Name 4-[(E)-[4-oxo-2-sulfanylidene-3-[3-(trifluoromethyl)phenyl]-1,3-thiazolidin-5-ylidene]methyl]benzoic acid

SMILES C1=CC(=CC(=C1)N2C(=O)C(=CC3=CC=C(C=C3)C(=O)O)SC2=S)C(F)(F)F

Formula $C_{18}H_{10}F_3NO_3S_2$

M.Wt 409.4

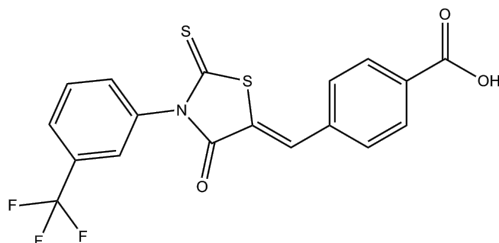
Solubility $\geq 40.9\text{mg/mL}$ in DMSO

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]:

Cell lines T-cell acute lymphoblastic leukemia CCRF-CEM, Jurkat and MOLT-4 cells

Preparation Method T-cell acute lymphoblastic leukemia CCRF-CEM, Jurkat and MOLT-4 cells were incubated in CFTRinh-172 with the concentrations ranged from 5 to $40\mu\text{M}$ for 24h and 48h.

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

Product Data Sheet

Reaction
Conditions 5 to 40µM; 24h and 48h

Applications CFTRinh-172 concentration-dependent inhibited the growth of all three T-ALL cell lines. The IC₅₀ ranged from 7 to 15µM in these cells.

Animal experiment [2]:

Animal models Male Sprague-Dawley rats

Preparation Method The rats were divided into four groups: (1) control group, in which the rats were treated with 0.1% ethanol (vehicle for lipoxin A4) (5mL/kg; iv) 6h after they were treated with 0.9% saline (vehicle for LPS) (4mL/kg; iv); (2) LPS group was identical to the control group except that LPS (20mg/kg; iv) was administered instead of its vehicle; (3) lipoxin A4 treatment group was identical to the LPS group except that lipoxin A4 (2µM/kg; iv) was administered instead of its vehicle; (4) CFTRinh-172 group was identical to the lipoxin A4 treatment group, but 1.5mL of CFTRinh-172 solution (1µM; tracheal instillation) was administered after lipoxin A4.

Dosage form 1.5mL of 1µM; tracheal instillation; administration once

Applications Treatment of rats with lipoxin A4 significantly inhibited IL-6, TNF-α production and increased alveolar fluid clearance with the outcome of decreased pulmonary edema in lung tissue and CFTRinh-172 was able to abolish the beneficial effects of lipoxin A4.

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

Product Data Sheet

References:

- [1]Liu M F, Liao H J, Chen Y, et al. Treatment of human T-cell acute lymphoblastic leukemia cells with CFTR inhibitor CFTRinh-172. Leuk Res. 2019 Nov;86:106225.
- [2]Yang Y, Cheng Y, Lian Q Q, et al. Contribution of CFTR to alveolar fluid clearance by lipoxin A4 via PI3K/Akt pathway in LPS-induced acute lung injury. Mediators Inflamm. 2013;2013:862628.

Background

CFTRinh-172 was identified as a potent and selective blocker of the cystic fibrosis transmembrane conductance regulator (CFTR) Cl^- channel. CFTRinh-172 inhibits Cl^- current in wild-type, G551D, and G1349D CFTR with K_i value of $0.5\mu\text{M}$ ^[1]. 1 and $10\mu\text{M}$ CFTRinh-172 caused 50% and 90% reduction of the original current in chinese hamster ovary (CHO) cells within 1-2s respectively with IC_{50} value of $1.1\mu\text{M}$, and this inhibition is reversible^[2].

In vitro, CFTR-expressing fischer rat thyroid cells incubated with CFTRinh-172 rapid and dose-dependently inhibited short-circuit current with CFTRinh-172 added to the solution bathing the apical cell surface. The average dose inhibition relationships of CFTRinh-172 is with K_d value of 300nM ^[3]. Human glioblastoma cell line U87 cells pretreated with CFTRinh-172 ($5\mu\text{M}$) for 30min, and then exposed to Forskolin ($50\mu\text{M}$) for additional 48h. CFTRinh-172 significantly increased cell viability and cell density, while partially restored inhibitory effects of Forskolin on U87 cell viability and cell density. CFTRinh-172 pretreatment partially attenuated the effects of Forskolin on Ki67 positive rate and significantly increased cell colony formation number^[4]. CCRF-CEM, Jurkat and MOLT-4 T-ALL cell line were treated with CFTRinh-172 (5 to $40\mu\text{M}$) for 24h or 48h. CFTRinh-172 concentration-dependently inhibited the growth of all three T-ALL cell lines and blocked the cell cycle. CCRF-CEM, JURKAT and MOLT-4 cells treated with $20\mu\text{M}$ CFTRinh-172 for 24h significantly changed the gene expression involved in various signaling pathways, including the Wnt/TGF-beta signaling pathway, the cell cycle, apoptotic process, cell proliferation, programmed cell death, etc^[5].

In vivo, CFTRinh-172 (3mg/kg) was intraperitoneal administrated in *E. coli*-induced acute lung inflammation mouse models. Inhibition of CFTR by CFTRinh-172 deteriorated *E. coli*-induced acute lung inflammation. CFTRinh-172 induced deficiency of CFTR promotes migration of monocytes and neutrophils in *E. coli* pneumonia and peritonitis mouse models^[6]. LPS-Induced Acute Lung Injury rat

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

Product Data Sheet

models were administrated with lipoxin A4 (2 μ M/kg; iv) following CFTRinh-172 treatment. 1.5mL (5mL/kg) of the instillate solution with CFTRinh-172 (1 μ M) was instilled at a rate of 0.08mL/min via tracheal instillation using a syringe pump. Lipoxin A4 significantly improved histology of rat lungs and inhibited IL-6 and TNF- α in LPS-induced lung injury. CFTRinh-172 abolished the effect of lipoxin A4 on alveolar fluid clearance (AFC)[7].

References:

- [1] Taddei A, Folli C, Moran O G, et al. Altered channel gating mechanism for CFTR inhibition by a high-affinity thiazolidinone blocker. FEBS Lett. 2004 Jan 30;558(1-3):52-6.
- [2] Kopeikin Z, Sohma Y, Li M, Hwang T C. On the mechanism of CFTR inhibition by a thiazolidinone derivative. J Gen Physiol. 2010 Dec;136(6):659-71.
- [3] Ma T, Thiagarajah J R, Yang H, et al. Thiazolidinone CFTR inhibitor identified by high-throughput screening blocks cholera toxin-induced intestinal fluid secretion. J Clin Invest. 2002 Dec;110(11):1651-8.
- [4] Zhong X, Chen H Q, Yang X L, et al. CFTR activation suppresses glioblastoma cell proliferation, migration and invasion. Biochem Biophys Res Commun. 2019 Jan 22;508(4):1279-1285
- [5] Liu M F, Liao H J, Chen Y, et al. Treatment of human T-cell acute lymphoblastic leukemia cells with CFTR inhibitor CFTRinh-172. Leuk Res. 2019 Nov;86:106225.
- [6] Gao Z, Su X. CFTR regulates acute inflammatory responses in macrophages. QJM. 2015 Dec;108(12):951-8.
- [7] Yang Y, Cheng Y, Lian Q Q, et al. Contribution of CFTR to alveolar fluid clearance by lipoxin A4 via PI3K/Akt pathway in LPS-induced acute lung injury. Mediators Inflamm. 2013;2013:862628.

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