

Product Data Sheet

Product Name: ML-SI1
Cat. No.: GC19764

Chemical Properties

Cas. No.

SMILES O=C(N1C2=CC=C(C=C2C(C1C)CCN3CCOCC3)OC)C4=C(Cl)C(Cl)=CC=C4. [Mixture of diastereomers]

Formula $C_{23}H_{26}Cl_2N_2O_3$ M.Wt 449.37

Solubility DMSO : 100 mg/mL (222.53 mM) 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.

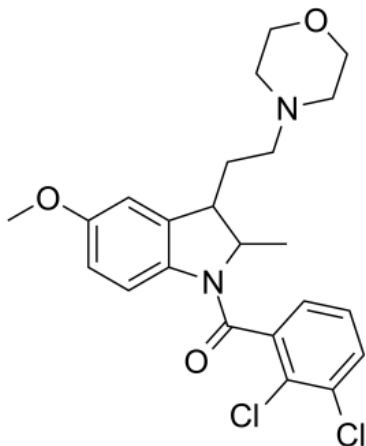
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Mixture of diastereomers

Protocol

Cell experiment [1]:

Cell lines PANC1 cells

Preparation Method Cells were treated with ML-SI1 for 48h, and then incubated with 2mg/mL MTT solution at 37°C in the dark for 3h. After incubation, DMSO was added to dissolve the formazan crystals produced by the living cells. Absorbance was then measured at 540nm using a microplate reader.

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Reaction
Conditions 0-100µM; 48h

Applications Pharmacological inhibition of TRPML1 using ML-SI1 significantly decreased PANC1 cell viability.

References:

[1] Kim B, Jung J. Metabolomic approach to identify potential biomarkers in KRAS-Mutant pancreatic cancer cells[J]. Biomedicines, 2024, 12(4): 865.

Background

ML-SI1 is a racemic mixture and an inhibitor of transient receptor potential cation channel (TRPML), with an IC₅₀ value of 15µM for TRPML1 [1, 2]. TRPML1 is a lysosomal cation channel involved in lysosomal biogenesis, endolysosomal trafficking (including trafficking in neuronal dendrites), and autophagy[3]. ML-SI1 and ML-SI3 are currently the only two published TRPML inhibitors [4].

In vitro, treatment of PANC1 cells with ML-SI1 (0-100µM) for 48h significantly reduced cell viability and induced significant changes in the metabolic profile[5]. Treatment of hippocampal neurons with ML-SI1 (20µM) for 2h blocked the lysosomal localization changes induced by LAMTOR1 knockdown[6]. Treatment of IPEC-J2 cells with ML-SI1 (1.25µM) for 24h significantly reduced ROS and Ca²⁺ levels induced by AFB1, and significantly decreased cell apoptosis and autophagy [7].

References:

[1] Reeks J, Mahajan P, Clark M, et al. High throughput cryo-EM provides structural understanding for modulators of the lysosomal ion channel TRPML1[J]. Structure, 2025.

[2] Leser C, Keller M, Gerndt S, et al. Chemical and pharmacological characterization of the TRPML calcium channel blockers ML-SI1 and ML-SI3[J]. European journal of medicinal chemistry, 2021, 210: 112966.

[3] Wang W, Zhang X, Gao Q, et al. TRPML1: an ion channel in the lysosome[J]. Mammalian Transient Receptor Potential (TRP) Cation Channels: Volume I, 2014: 631-645.

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- [4] Kriegler K, Leser C, Mayer P, et al. Effective chiral pool synthesis of both enantiomers of the TRPML inhibitor trans-ML-SI3[J]. Archiv der Pharmazie, 2022, 355(2): 2100362.
- [5] Kim B, Jung J. Metabolomic approach to identify potential biomarkers in KRAS-Mutant pancreatic cancer cells[J]. Biomedicines, 2024, 12(4): 865.
- [6] Sun J, Lin W, Hao X, et al. LAMTOR1 regulates dendritic lysosomal positioning in hippocampal neurons through TRPML1 inhibition[J]. Frontiers in Cellular Neuroscience, 2024, 18: 1495546.
- [7] Cheng X, Liang J, Wu D, et al. Blunting ROS/TRPML1 pathway protects AFB1-induced porcine intestinal epithelial cells apoptosis by restoring impaired autophagic flux[J]. Ecotoxicology and Environmental Safety, 2023, 257: 114942.

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