

Product Data Sheet

Product Name: ML-346
Cat. No.: GC18170

Chemical Properties

Cas. No. 100872-83-1

Chemical Name 5-[3-(4-methoxyphenyl)-2-propen-1-ylidene]-2,4,6(1H,3H,5H)-pyrimidinetrione

SMILES O=C1NC(/C(C(N1)=O)=C/C=C/C2=CC=C(OC)C=C2)=O

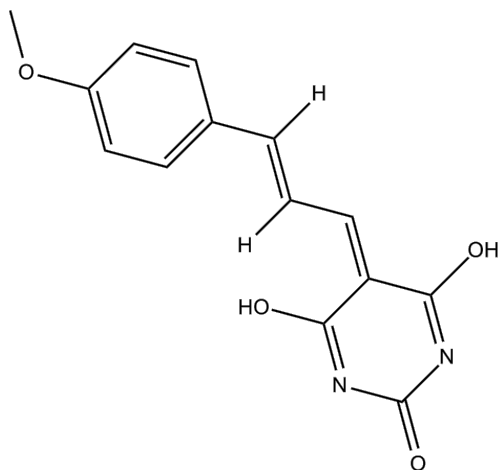
Formula C₁₄H₁₂N₂O₄ M.Wt 272.3

Solubility 0.5mg/mL in ethanol, 30mg/mL in DMSO, or in DMF 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 MDA-MB-435 cells

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

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Preparation Method	MDA-MB-435 cells were cultured in DMEM/F12 medium supplemented with 10% fetal bovine serum, 100U/ml penicillin, and 100µg/ml streptomycin at 37°C with 5% CO ₂ and 95% saturated atmospheric humidity. Cells were seeded into 96-well microplates at a density of 5×10^3 cells/ml for 24h. Various concentrations of ML-346 (0, 2.5, 5, and 10µM) were added to each well. After 24h of incubation, cell viability was analyzed.
Reaction Conditions	0, 2.5, 5, and 10µM; 24h
Applications	ML-346 treatment significantly inhibited the cell viability of MDA-MB-435 cells in a dose-dependent manner.

References:

[1] Chiang S K, Chang W C, Chen S E, et al. CDK7/CDK9 mediates transcriptional activation to prime paraptosis in cancer cells[J]. Cell & Bioscience, 2024, 14(1): 78.

Background

ML-346 is an activator of the heat shock response that induces the expression of the heat shock protein HSP70, with an EC₅₀ value of 4.6µM^[1]. ML-346 molecule covalently modified the cysteine (Cys) at position 208 of the active site of the housekeeping sorting enzyme A (SrtA) of Staphylococcus aureus, significantly reducing the virulence phenotype of Staphylococcus aureus^[2]. ML-346 has been widely used in transplantation tumor models to promote tumor cell apoptosis and reduce tumor growth^[3].

In vitro, ML-346 treatment (10µM) for 24 hours significantly inhibited the viability of MDA-MB-435 cells and reduced the activities of CDK7 and CDK9^[4]. Treatment with 10µM ML-346 for 24 hours significantly inhibited the LC3 I/II conversion in A549 cells, and promoted the accumulation of p62 as well as a significant increase in the phosphorylation level of mTOR at the Ser2448 site^[5]. 15µM of ML-346 pretreatment for 1 hour significantly inhibited the accumulation of sphingomyelin induced by V8 in Jurkat cells and the co-localization with LysoTracker Red^[6]. 10µM of ML-346 pretreatment for 4

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hours alleviated the mitochondrial damage and cell apoptosis induced by the combined action of Fumonisin B1 (FB1) and ochratoxin A (OTA) in pK-15 cells^[7].

References:

- [1] Calamini B, Silva M C, Madoux F, et al. ML346: a novel modulator of proteostasis for protein conformational diseases[M]//Probe Reports from the NIH Molecular Libraries Program [Internet]. National Center for Biotechnology Information (US), 2013.
- [2] Guan X N, Zhang T, Yang T, et al. Covalent sortase A inhibitor ML346 prevents Staphylococcus aureus infection of Galleria mellonella[J]. RSC Medicinal Chemistry, 2022, 13(2): 138-149.
- [3] Chen W, Wang Z, Ji J, et al. The regulatory mechanism of HSP70 in endoplasmic reticulum stress in pepsin-treated laryngeal epithelium cells and laryngeal cancer cells[J]. Aging (Albany NY), 2022, 14(20): 8486.
- [4] Chiang S K, Chang W C, Chen S E, et al. CDK7/CDK9 mediates transcriptional activation to prime paraptosis in cancer cells[J]. Cell & Bioscience, 2024, 14(1): 78.
- [5] Alhasan B, Gladova Y A, Sverchinsky D V, et al. Hsp70 negatively regulates autophagy via governing AMPK activation, and dual Hsp70-autophagy inhibition induces synergetic cell death in NSCLC Cells[J]. International Journal of Molecular Sciences, 2024, 25(16): 9090.
- [6] Qing Y, Guo Y, Zhao Q, et al. Targeting lysosomal HSP70 induces acid sphingomyelinase-mediated disturbance of lipid metabolism and leads to cell death in T cell malignancies[J]. Clinical and translational medicine, 2023, 13(3): e1229.
- [7] Li H, He W, Yue D, et al. Low doses of fumonisin B1 exacerbate ochratoxin A-induced renal injury in mice and the protective roles of heat shock protein 70[J]. Chemico-Biological Interactions, 2023, 369: 110240.

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