

Product Data Sheet

Product Name: ML241 hydrochloride

Cat. No.: GC13656

Chemical Properties

Cas. No. 2070015-13-1

Chemical Name 2-(2H-benzo[b][1,4]oxazin-4(3H)-yl)-N-benzyl-5,6,7,8-tetrahydroquinazolin-4-amine hydrochlorid

SMILES C1(CNC2=NC(N3CCOC4=CC=CC=C43)=NC5=C2CCCC5)=CC=CC=C1.Cl

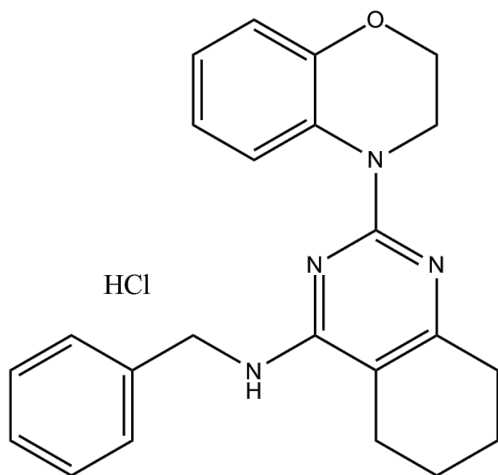
Formula $C_{23}H_{25}ClN_4O$ M.Wt 408.92

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

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

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Cell experiment: HeLa cells stably expressing ODD-luciferase are seeded onto a 96-well white solid bottom plate (5000 cells/well) and cells are grown for 16 h. Cells are treated with DMEM containing MG132 (4 μ M) for 1h and washed with 100 μ L PBS twice. DMEM containing 2.5% FBS, cycloheximide (50 μ g/mL) and ML241 are added into the well. Four 96-well plates are prepared and one of the plates is taken out from incubator at each time point (70, 90, 120, or 150 min). Luciferin (50 μ L of 1 mg/mL in PBS) is added into each well containing 50 μ L of medium and incubated at room temperature with shaking at 500 rpm for 5 min. Luminescence intensity is determined with 0.1 ms integration time on the Synergy HT Microplate Reader[2].

References:

- [1]. Chou TF, et al. Structure-activity relationship study reveals ML240 and ML241 as potent and selective inhibitors of p97 ATPase. ChemMedChem. 2013 Feb;8(2):297-312.
- [2]. Chou TF, et al. Selective, reversible inhibitors of the AAA ATPase p97. Probe Reports from the NIH Molecular Libraries Program. April 14, 2011.

Background

IC50: 100 nM

ML241 is identified as a p97 ATPase inhibitor.

The hexameric p97 protein belongs to the type II AAA (ATPase associated with diverse cellular activities) ATPase protein family and is conserved across all eukaryotes and is essential for life

p97 protein, a member of the type II AAA ATPase protein family, is reported to be conservative for nearly all eukaryotes. p97 is also known as valosin-containing protein and Cdc48p in mammals and yeast, respectively, playing key roles in various cellular processes, such as cell division, homotypic fusion of endoplasmic reticulum and Golgi membranes, as well as autophagosome maturations.

In vitro: Both ML241 and its analog ML240 were found to be able to inhibit the degradation of proteasome substrate in a p97-dependent but not a p97-independent manner. ML241 and ML240

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could also impair the endoplasmic-reticulum (ER) associated degradation pathway. ML240 was able to stimulate accumulation of LC3-II potently, inhibit cancer cell growth, and also mobilize the executioner caspases 3 and 7 rapidly, but ML241 was not able to. Further investigation showed that ML240 had broad antiproliferative activity to the NCI-60 panel of cancer cell lines, but lower activity to normal cells. In addition, ML240 could synergize with proteasome inhibitor to inhibit the growth of various colon cancer cell lines. Moreover, both ML241 and ML240 had low off-target activity toward a panel of protein kinases as well as central nervous system targets [1].

In vivo: Currently, there is no animal in vivo data reported.

Clinical trial: Up to now, ML241 is still in the preclinical development stage.

Reference:

[1] Chou TF, Li K, Frankowski KJ, Schoenen FJ, Deshaies RJ. Structure-activity relationship study reveals ML240 and ML241 as potent and selective inhibitors of p97 ATPase. *ChemMedChem*. 2013 Feb;8(2):297-312.

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