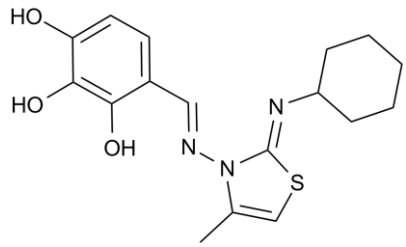
Product Name: MIM1

Revision Date: 6/30/2016

Product Data Sheet

Chemical Properties



Product Name:	MIM1
Cas No.:	
M.Wt:	347.43
Formula:	C17H21N3O3S
Chemical Name:	4-((E)-(((Z)-2-(cyclohexylimino)-4-methylthiazol-3(2H)-yl)imino)methyl)benzene-1,2,3-triol
Canonical SMILES:	OC1=CC=C(/C=N/N2C(C)=CS/C2=N\C3CCCCC3)C(O)=C1O
Solubility:	>12.15mg/mL in DMSO
Storage:	Store at 4°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.
Shopping Condition:	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request

Biological Activity

Targets :	Apoptosis
Pathways:	Bcl-2 Family

Description:

MIM1 effectively competed with FITC-MCL-1 SAHBA and FITC-BID BH3 for MCL-1ΔNΔC binding with IC50 values of 4.7 and 4.8 mM, respectively. And MIN1 shows a combination of favorable biophysical and biological properties including its solubility, stability, nonreactivity, MCL-1 binding potency and selectivity, compatibility with and activity in a BAX-mediated liposomal release assay and relatively little to no toxicity in Bax-/-Bak-/- MEFs [1].
As an MCL-1 inhibitor, MIM1 selectively targets the BH3-binding groove of MCL-1, neutralizes its biochemical lockhold on apoptosis, and induces caspase activation and leukemia cell death in the

specific context of MCL-1 dependence.
The activity and specificity of MIM1 in cancer cells was dependable for assessing MCL-1 and BCL-XL dependence by employing murine BCRABL (p185)-transformed, Arf null, B-lineage acute lymphoblastic leukemia cells. Comparing to the effect of ABT-737 on p185+Arf-/-/Mcl-1-deleted B-ALL cells, MIM1 had the exact opposite effect, impacting the viability of the MCL-1-dependent cells (IC50, 4.2 mM), including dose-dependent induction of caspase 3/7 activity, but having no effect on the BCL-XL-dependent cells. A combination of MIM1 (IC50, 10.6 mM) and ABT-737 (IC50, 5.1 mM) resulted in synergistic cytotoxicity. Strikingly, when the MIM1/ABT-737 combination was applied to MCL-1-reconstituted p185+Arf-/-/Mcl-1-deleted B-ALL cells, the addition of ABT-737 had little effect [1].
MIM1 emerged as a potent and selective small molecule inhibitor of MCL-1 DNDC, capable of targeting the canonical BH3-binding point of MCL-1 and blocking MCL-1-mediated suppression of tBID-induced BAX activation in vitro. MIM1 may serve as a prototype for the development of next generation small molecules that effectively reduce the apoptotic threshold in cancers specifically driven by antiapoptotic MCL-1 [1].

***Reference**:*

[1]. Cohen NA, Stewart ML, Gavathiotis E, et al. A Competitive Stapled Peptide Screen Identifies a Selective Small Molecule that Overcomes MCL-1-Dependent Leukemia Cell Survival. Chemistry & Biology, 2012, 19(9): 1175-1186.

Protocol

Cell experiment:

Cell lines	p185+Arf−/−Mcl-1-deleted B-ALL cells
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.
Reacting conditions	IC50: 4.2 μM, 24 hours for impairing the cell viability rescued by MCL-1
Applications	MIM1 negatively impacted the viability of the MCL-1-dependent cells (p185+Arf−/−Mcl-1-deleted B-ALL cells) with IC50 value of 4.2 μM, including dose-dependent induction of caspase 3/7 activity, but having little to no effect on the BCL-XL-dependent cells. MIM1's cytotoxic effect on the MCL-1-dependent cells likewise corresponded to dose-dependent dissociation of the inhibitory MCL-1/BAK complex, as assessed by co-immunoprecipitation analysis.

***Reference**:*

[1] Cohen N A, Stewart M L, Gavathiotis E, et al. A competitive stapled peptide screen identifies a selective small molecule that overcomes MCL-1-dependent leukemia cell survival. Chemistry & biology, 2012, 19(9): 1175-1186.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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