IMT1

Cat. No.: HY-134539

CAS No.: 2304621-31-4

Molecular Formula: $C_{21}H_{21}NO_4$

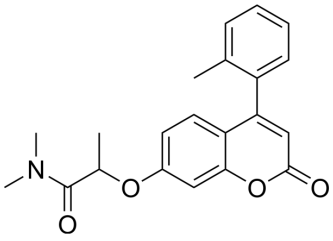
Molecular Weight: 351.4

Target: Mitochondrial Metabolism; DNA/RNA Synthesis; Oxidative Phosphorylation

Pathway: Metabolic Enzyme/Protease; Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (142.29 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8458 mL	14.2288 mL	28.4576 mL
5 mM	0.5692 mL	2.8458 mL	5.6915 mL
10 mM	0.2846 mL	1.4229 mL	2.8458 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.11 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.11 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

IMT1 is a first-in-class specific and noncompetitive human mitochondrial RNA polymerase (POLRMT) inhibitor. IMT1 causes a conformational change of POLRMT, which blocks substrate binding and transcription in a dose-dependent way in vitro. IMT1 reduces deoxynucleoside triphosphate levels and citric acid cycle intermediates, resulting in a marked depletion of cellular amino acid levels. IMT1 has the potential for mitochondrial transcription disorders related diseases[1].

In Vitro

IMT1 (0.00001-10 μM; 0-168 h) has a dose-dependent decrease in cell viability in A2780, A549 and HeLa cells. IMT1 shows a strong decrease in cell viability in about one third of the cancer cell lines, 89 cancer cell lines and primary cells (IMR90 lung

fibroblasts and human peripheral blood mononuclear cells (PBMCs)), whereas primary cells remained unresponsive[1].
?IMT1 (0.01-10 μM; for 24-200 h) causes a dose-dependent decrease in the levels of mitochondrial transcripts and gradual depletion of mtDNA in HeLa cells. There is a dose-dependent decrease in the levels of subunits (NDUFB8, UQCRC2 and COXI) of respiratory chain complexes I, III and IV[1].
?IMT1 reveals a time-dependent and marked increase in the levels of mono- and diphosphate nucleotides that results in a considerable increase in the AMP/ATP ratio and levels of phosphorylated AMPK in A2780 cells[1].
?IMT1 severely impairs mtDNA gene expression in A2780 cells that express wild-type POLRMT, whereas cells that express mutant POLRMT (L796Q or L816Q) are resistant[1].
?POLRMT is essential for mtDNA transcription and biogenesis of the oxidative phosphorylation (OXPHOS) system[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	A2780, A549 and HeLa cells
Concentration:	0.00001-10 μM
Incubation Time:	0-168 hours
Result:	Had a dose-dependent decrease in cell viability in A2780, A549 and HeLa cells, but had not cytotoxic to human PBMCs or pooled primary human hepatocytes.

CUSTOMER VALIDATION

- Nature. 2023 Mar;615(7952):490-498.
- Nat Commun. 2023 Feb 16;14(1):872.
- Theranostics. 2023 May 29;13(10):3330-3345.

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REFERENCES

[1]. Nina A Bonekamp, et al. Small-molecule inhibitors of human mitochondrial DNA transcription. Nature. 2020 Dec;588(7839):712-716.

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