# TH-6

**Cat. No.:** HY-149029

**CAS No.:** 3031349-25-1

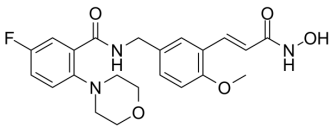
**Molecular Formula:** $C_{22}H_{24}FN_3O_5$

**Molecular Weight:** 429.44

**Target:** HDAC; Apoptosis; Reactive Oxygen Species

**Pathway:** Cell Cycle/DNA Damage; Epigenetics; Apoptosis; Immunology/Inflammation; Metabolic Enzyme/Protease; NF-κB

**Storage:** 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 50 mg/mL (116.43 mM; ultrasonic and warming and heat to 60°C)

| Preparing Stock Solutions | Mass / Solvent / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.3286 mL | 11.6431 mL | 23.2861 mL |
| | 5 mM | 0.4657 mL | 2.3286 mL | 4.6572 mL |
| | 10 mM | 0.2329 mL | 1.1643 mL | 2.3286 mL |

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

## BIOLOGICAL ACTIVITY

**Description**

TH-6 is a potent HDAC inhibitor with $IC_{50}$s of 0.115, 0.135, 0.242, 0.138, 2.120 μM for HDAC1, HDAC2, HDAC3, HDAC6, HDAC8, respectively. TH-6 inhibits cell migration and invasion. TH-6 induces apoptosis and cell cycle arrest at G2/M phase. TH-6 shows anti-tumor activity[1].

**$IC_{50}$ & Target**

| | | | |
|---|---|---|---|
| HDAC1<br>0.115 μM ($IC_{50}$) | HDAC2<br>0.135 μM ($IC_{50}$) | HDAC3<br>0.242 μM ($IC_{50}$) | HDAC6<br>0.138 μM ($IC_{50}$) |
| HDAC8<br>2.120 μM ($IC_{50}$) | | | |

**In Vitro**

TH-6 (0-2 μM) shows antiproliferative activities in cancer cell lines and normal human lung cells[1].
TH-6 (0-10 μM) inhibits tubulin polymerization with an $IC_{50}$ value of 4.06 μM[1].
TH-6 (0.03, 0.1, 0.3 1 μM; 24 h) increases the expression of Ac-α-Tubulin and AC-Histone H3 in HepG2 cells[1].
TH-6 (7.5, 15, 30 nM) induces apoptosis and cell cycle arrest at G2/M phase[1].
TH-6 (0-30 nM) decreases the MMP and increase ROS levels of HepG2 cells in a dose-dependent manner[1].
TH-6 (7.5, 15, 30 nM; 48 h) inhibits cell migration and invasion in MDA-MB-231 cells and suppress the migration of HUVECs in

a concentration-dependent manner[1].
TH-6 shows favorable liver microsomal stability in vitro with $t_{1/2}$ of 50.3 min[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

| | |
|---|---|
| Cell Line: | K562, GepG2, HCT-116, MDA-MB-231, H22, MCF-7, HFL-1 cells |
| Concentration: | 0-2 μM |
| Incubation Time: | |
| Result: | Showed antiproliferative activities with an $IC_{50}$ values of 18, 29, 28, 30, 26, 27, 134 nM for K562, GepG2, HCT-116, MDA-MB-231, H22, MCF-7, HFL-1 cells, respectively. |

Western Blot Analysis[1]

| | |
|---|---|
| Cell Line: | HepG2 cells |
| Concentration: | 0.03, 0.1, 0.3 1 μM |
| Incubation Time: | 24 h |
| Result: | Increased the intracellular levels of HDAC6 substrate acetyl-α-tubulin and the HDAC1/2/3 substrate acetyl-histone H3 in a dose-dependent manner. |

Cell Cycle Analysis[1]

| | |
|---|---|
| Cell Line: | HepG2 cells |
| Concentration: | 7.5, 15, 30 nM |
| Incubation Time: | |
| Result: | Induced cell cycle arrest at G2/M phase with decreased the expression of Cdc2, Cdc25c, and Cyclin B1 proteins in a dose dependent manner. |

Apoptosis Analysis[1]

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|---|---|
| Cell Line: | HepG2 cells |
| Concentration: | 7.5, 15, 30 nM |
| Incubation Time: | |
| Result: | Showed an accumulation of apoptotic cells from 27.04 to 50.54% and upregulated the expression of the pro-apoptotic protein (Bax and Bad) and downregulated the expression of the antiapoptotic protein (Bcl-2 and Bcl-xL) in a dose-dependent manner. |

**In Vivo**

TH-6 (10, 20 mg/kg; i.v.; daily for 21 days) shows anti-tumor activity in mouse[1].
TH-6 (20 mg/kg) shows antivascular activity and a good cardiovascular safety profile in mouse[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| | |
|---|---|
| Animal Model: | 4-5 weeks, 18-22 g female ICR mice (H22 allograft mouse model)[1] |
| Dosage: | 10, 20 mg/kg |
| Administration: | I.v.; daily for 21 days |

| | |
|---|---|
| Result: | Reduced tumor weights at day 21 by 82% and did not affect body weight during treatment, indicating the low toxicity. |

## REFERENCES

[1]. Zhu H, et al. Discovery of a Novel Vascular Disrupting Agent Inhibiting Tubulin Polymerization and HDACs with Potent Antitumor Effects. J Med Chem. 2022 Aug 4.



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