# TPCA-1

**Cat. No.:** HY-10074

**CAS No.:** 507475-17-4

**Molecular Formula:** $C_{12}H_{10}FN_3O_2S$

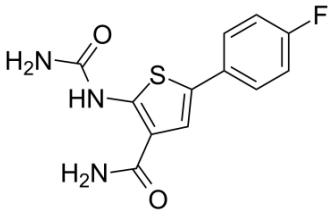
**Molecular Weight:** 279.29

**Target:** IKK; STAT; Apoptosis

**Pathway:** NF-κB; JAK/STAT Signaling; Stem Cell/Wnt; Apoptosis

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 6 months |
| | -20°C | 1 month |




## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : ≥ 100 mg/mL (358.05 mM)

* "≥" means soluble, but saturation unknown.

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| 1 mM | 3.5805 mL | 17.9025 mL | 35.8051 mL |
| 5 mM | 0.7161 mL | 3.5805 mL | 7.1610 mL |
| 10 mM | 0.3581 mL | 1.7903 mL | 3.5805 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: ≥ 7.5 mg/mL (26.85 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 7.5 mg/mL (26.85 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 7.5 mg/mL (26.85 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

TPCA-1 is a potent and selective inhibitor of IKK-2 with $IC_{50}$ of 17.9 nM. TPCA-1 is an effective inhibitor of STAT3 phosphorylation, DNA binding, and transactivation.

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

| | |
|---|---|
| IKK-2<br>17.9 nM ($IC_{50}$) | STAT3 |

**In Vitro**

TPCA-1 inhibits lipopolysaccharide-induced human monocyte production of TNF-α, IL-6, and IL-8 with an $IC_{50}$ of 170 to 320 nM[1][2].

TPCA-1 (0-2 μM) inhibits STAT3 phosphorylation and transactivation induced by cytokines and nonreceptor tyrosine kinase in dose- and time-dependent manner. TPCA-1 completely inhibits STAT3 phosphorylation without changing total STAT3 levels[3].

TPCA-1 increased sensitivity to ZD1839 in both TKI sensitive cells and insensitive cells[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

| | |
|---|---|
| Cell Line: | human peripheral blood monocytes stimulated with LPS. |
| Concentration: | 0-10 μM. |
| Incubation Time: | ~24 hours. |
| Result: | TPCA-1 Inhibits LPS-Induced TNF-α, IL-6, and IL-8 production by human monocytes. |

Cell Viability Assay[3]

| | |
|---|---|
| Cell Line: | HCC827 and H1975 cells. |
| Concentration: | 0-10 μM. |
| Incubation Time: | 0.5-2 hours. |
| Result: | Suppressed proliferation of HCC827 and H1975 cells.<br>Led to a $G_2$-M cell-cycle arrest in HCC827 but not A549. |

Western Blot Analysis[3]

| | |
|---|---|
| Cell Line: | HEK-293T cell lines. |
| Concentration: | 0-2 μM (before IL-2 or IFN-α treatment). |
| Incubation Time: | 0.5-2 hours. |
| Result: | Inhibited STAT3 phosphorylation and transactivation induced by cytokines and nonreceptor tyrosine kinase in dose- and time-dependent manner. |

**In Vivo**

TPCA-1 (3, 10, or 20 mg/kg, i.p.) results in a dose-dependent reduction in the severity of murine collagen-induced arthritis (CIA)[2].

TPCA-1(10 mg/kg, i.p. daily) inhibits growth of NSCLC with EGFR mutation and potentiates antitumor effect of ZD1839 in xenograft models[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| | |
|---|---|
| Animal Model: | 10-12 weeks old male DBA/1 OlaHsd mice[2]. |
| Dosage: | 3, 10, or 20 mg/kg. |
| Administration: | I.P., b.i.d, from days 1 to 47. |
| Result: | Reduced the severity and delays the onset of CIA.<br>Attenuated ex vivo antigen-induced T cell proliferation in CIA. |

| | |
|---|---|
| Animal Model: | Six-week-old BALB/c female nude mice injected subcutaneously with HCC827 cells ($5\times10^6$) |

| | |
|---|---|
| | [3]. |
| Dosage: | 10 mg/kg. |
| Administration: | Intraperitoneally daily. |
| Result: | The tumor weight inhibition rate of TPCA-1, ZD1839, and their combination are 0.419($E_{TPCA-1}$), 0.680($E_{ZD1839}$), and 0.837($E_{observed}$), respectively. |

## CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- ACS Nano. 2015 Dec 22;9(12):11800-11.
- Signal Transduct Target Ther. 2021 Apr 24;6(1):167.
- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2996-3005.
- Cell Death Dis. 2018 Apr 27;9(5):500.

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## REFERENCES

[1]. Sachse F, et al. IKK-2 inhibitor TPCA-1 represses nasal epithelial inflammation in vitro.Rhinology. 2011 Jun;49(2):168-73.

[2]. Podolin PL, et al. Attenuation of murine collagen-induced arthritis by a novel, potent, selective small molecule inhibitor of IkappaB Kinase 2, TPCA-1 (2-[(aminocarbonyl)amino]-5-(4-fluorophenyl)-3-thiophenecarboxamide), occurs via reduction of proinflamm

[3]. Nan J, et al. TPCA-1 is a direct dual inhibitor of STAT3 and NF-κB and regresses mutant EGFR-associated human non-small cell lung cancers. Mol Cancer Ther. 2014 Mar;13(3):617-29.



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