TPCA-1

Cat. No.: HY-10074

CAS No.: 507475-17-4

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

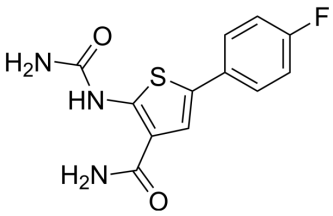
Molecular Weight: 279.29

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	1 year
	-20°C	6 months



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 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. 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. 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 (5×10^6)

	[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

- Signal Transduct Target Ther. 2021 Apr 24;6(1):167.
- Cell Mol Immunol. 2023 Aug 17.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- ACS Nano. 2015 Dec 22;9(12):11800-11.
- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2996-3005.

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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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