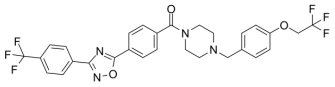
HP590

Cat. No.:	HY-151480
Molecular Formula:	$C_{29}H_{24}F_6N_4O_3$
Molecular Weight:	590.52
Target:	STAT; Apoptosis
Pathway:	JAK/STAT Signaling; Stem Cell/Wnt; Apoptosis
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 5 mg/mL (8.47 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6934 mL	8.4671 mL	16.9342 mL
	5 mM	0.3387 mL	1.6934 mL	3.3868 mL
	10 mM	---	---	---

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: ≥ 0.5 mg/mL (0.85 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 0.5 mg/mL (0.85 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

HP590 is an orally active, novel and potent STAT3 inhibitor (STAT3 luciferase activity: IC_{50}=27.8 nM; ATP inhibition: IC_{50}=24.7 nM). HP590 shows anti-proliferative activity to gastric cancer cells and induces apoptosis[1].

IC_{50} & Target

IC50: 27.8 nM (STAT3 luciferase activity)[1]

In Vitro

HP590 (0-40 μM; 72 h) shows anti-proliferative activities to MKN45, AGS, and MGC803 cells[1].
HP590 (0-40 nM; 0-24 h) inhibits STAT3 Tyr^{705} and Ser^{727} phosphorylation in GC cells, blocks the expression of STAT3 downstream genes (c-Myc and cyclin D1) in GC cells, reduces IL-6-mediated STAT3 nuclear translocation in MKN45 cells[1].
HP590 (5-20 nM; 48 h) induces gastric cancer cell apoptosis[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	MKN45, AGS, and MGC803 cells
Concentration:	0-40 μM
Incubation Time:	72 hours
Result:	Inhibited MKN45, AGS, and MGC803 cells with IC_{50}s of 9.3, 13.5, and 8.7 nM, respectively.

Apoptosis Analysis[1]

Cell Line:	MKN45 and AGS cells
Concentration:	5, 10, and 20 nM
Incubation Time:	48 hours
Result:	Induced apoptosis in MKN45 and AGS cells in a dose-dependent manner.

Western Blot Analysis[1]

Cell Line:	Gastric Cancer Cells
Concentration:	0-40 nM
Incubation Time:	0-24 h
Result:	Inhibited STAT3 p-Tyr^{705} and p-Ser^{727} in GC cells completely at 40 nM. Blocked the expression of STAT3 downstream genes, including c-Myc and cyclin D1, in a concentration-dependent and time-dependent manner. Showed the STAT3 p-Tyr^{705} stimulated by IL-6 in GC cell lines, but entirely suppressed by HP590 at 40 nM.

RT-PCR[1]

Cell Line:	MKN45 and AGS cells
Concentration:	10, 20, and 40 nM
Incubation Time:	48 hours
Result:	Suppressed the expression of STAT3 downstream genes (c-Myc and cyclin D1) at the mRNA level.

In Vivo

HP590 (oral administration; 25 and 50 mg/kg; once daily; 5 w) inhibits GC growth effectively by inhibiting the STAT3 activation and shows better tolerance in GC xenograft model[1].

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

Animal Model:	BALB/c-nude mice injected with GC cells[1]
Dosage:	25 and 50 mg/kg
Administration:	Oral administration; 25 and 50 mg/kg; once daily; 5 weeks
Result:	Inhibited MKN45 tumor growth in a concentration-dependent manner. Inhibited STAT3 phosphorylation at Tyr705 and Ser727 and reduced the expression of the downstream genes. Inhibited the expression of Ki67 (a proliferation marker).

	Showed no weight loss during HP590 treatment, and no apparent damage in the major organs of mice.

REFERENCES

[1]. He P, et al. Discovery of a Novel Potent STAT3 Inhibitor HP590 with Dual p-Tyr705/Ser727 Inhibitory Activity for Gastric Cancer Treatment. J Med Chem. 2022 Sep 14.

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