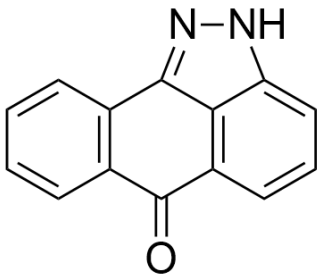
SP600125

Cat. No.:	HY-12041
CAS No.:	129-56-6
Molecular Formula:	$C_{14}H_8N_2O$
Molecular Weight:	220.23
Target:	JNK; Autophagy
Pathway:	MAPK/ERK Pathway; Autophagy
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 : ≥ 45 mg/mL (204.33 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	4.5407 mL	22.7035 mL	45.4071 mL
	5 mM	0.9081 mL	4.5407 mL	9.0814 mL
	10 mM	0.4541 mL	2.2704 mL	4.5407 mL

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

In Vivo

1. SP600125 is dissolved in 1% CMC-Na solution[5].

BIOLOGICAL ACTIVITY

Description

SP600125 is a reversible and ATP-competitive **JNK** inhibitor with **IC_{50}**s of 40, 40 and 90 nM for **JNK1**, **JNK2** and **JNK3**, respectively.

IC_{50} & Target

IC50: 40/40/90 nM (JNK1/2/3)[1]

In Vitro

SP600125 is an ATP-competitive inhibitor of JNK2 with a K_i value of 0.19±0.06 μM. SP600125 inhibits the phosphorylation of c-Jun with IC50 of 5 μM to 10 μM in Jurkat T cells. In $CD4^+$ cells, such as Th0 cells isolated from either human cord or peripheral blood, SP600125 blocks cell activation and differentiation and inhibits the expression of inflammatory genes COX-2, IL-2, IL-10, IFN-γ, and TNF-α, with IC_{50} of 5 μM to 12 μM[1]. In a mouse beta cells MIN6, SP600125 (20 μM) induces the phosphorylation of p38 MAPK and its downstream CREB-dependent promoter activation[2]. In HCT116 cells, SP600125 (20 μM) blocks the G2 phase to mitosis transition and induces

	endoreplication. This ability of SP600125 is independent of JNK inhibition, but due to its inhibition of CDK1-cyclin B activation upstream of Aurora A and Polo-like kinase 1[3].
In Vivo	Administration of SP600125 at 15 or 30 mg/kg i.v. significantly inhibits TNF-α serum levels, whereas oral administration dose-dependently blocks TNF-α expression with significant inhibition observed at 30 mg/kg per os[1]. SP600125 attenuates LPS-induced ALI in rats in vivo. The expression levels of TNF-α and IL-6 in the BALF in rats in the SP600125 group are significantly decreased[4].

PROTOCOL

Cell Assay [1]	Determination of mRNA half-life is performed essentially, except that $CD14^+$ cells are stimulated with (bacterial) lipopolysaccharide (LPS; 50 ng/mL) for 2 h before addition of actinomycin D (5 μg/mL). SP600125 (25 μM) or vehicle (0.5% DMSO vol/vol) is added immediately following the actinomycin D. Analysis is performed by using real-time reverse transcription (RT)-PCR. Total RNA is extracted with an RNeasy Mini kit. TNF mRNA is measured by real time RT-PCR, using a TNF Taqman probe. All data are normalized by using glyceraldehyde-3-phosphate dehydrogenase (GAPDH) expression. The TNF-α forward primer is 5′-CTGGCCCAGGCAGTCAGAT-3′ and the reverse primer is 5′-TATCTCTCAGCTCCACGCCATT-3′. The Taqman probe sequence is 5′-FAM-CCTGTAGCCCATGTTGTAGCAAACCCTCA-TAMRA-3′[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][4]	Mice[1] Female CD-1 mice (8-10 weeks of age) are dosed i.v. or per oswith SP600125 in PPCES vehicle (30% PEG-400/20% polypropylene glycol/15% Cremophor EL/5% ethanol/30% saline), final volume of 5 mL/kg, 15 min before i.v. injection with LPS in saline (0.5 mg/kg). At 90 min, a terminal bleed is obtained from the abdominal vena cava, and the serum is recovered. Samples are analyzed for mouse TNF-α by using an ELISA. Rats[4] A total of 40 male Wistar rats are randomly divided into four groups (n=10): the control group, LPS group, normal saline group (NS) and the SP600125 group. Acute lung injury (ALI) is induced via intratracheal injection of LPS. Briefly, the rats are anesthetized with pentobarbital sodium followed by intratracheal injection of 5 mg/kg LPS. The rats are then placed in a vertical position and rotated for 1 min to distribute the LPS in the lungs. Normal saline or SP600125 is administered via intraperitoneal injection (15 mg/kg) 10 min after the LPS injection. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **Sci Transl Med**. 2018 Jul 18;10(450). pii: eaaq1093.
- **Cell Syst**. 2018 Apr 25;6(4):424-443.e7.
- **Cell Death Differ**. 2017 Mar;24(3):492-499.
- **Elife**. 2016 Apr 11;5. pii: e14087.
- **J Autoimmun**. 2018 May;89:30-40.

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REFERENCES

[1]. Bennett BL, et al. SP600125, an anthrapyrazolone inhibitor of Jun N-terminal kinase. Proc Natl Acad Sci U S A, 2001, 98(24), 13681-13686.

[2]. Vaishnav D, et al. SP600125, an inhibitor of c-jun N-terminal kinase, activates CREB by a p38 MAPK-mediated pathway. Biochem Biophys Res Commun, 2003, 307(4), 855-860.

[3]. Kim JA, et al. SP600125 suppresses Cdk1 and induces endoreplication directly from G2 phase, independent of JNK inhibition. Oncogene, 2010, 29(11), 1702-1716.

[4]. Zheng Y, et al. JNK inhibitor SP600125 protects against lipopolysaccharide-induced acute lung injury via upregulation ofclaudin-4. Exp Ther Med. 2014 Jul;8(1):153-158.

[5]. Zhang H, et al. SP600125 Suppresses Keap1 Expression and Results in NRF2-mediated Prevention of Diabetic Nephropathy. J Mol Endocrinol. J Mol Endocrinol. 2018 Feb;60(2):145-157.

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