IPA-3

Cat. No.: HY-15663

CAS No.: 42521-82-4

Molecular Formula: $C_{20}H_{14}O_2S_2$

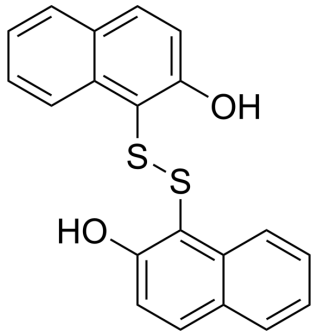
Molecular Weight: 350.45

Target: PAK

Pathway: Cell Cycle/DNA Damage; Cytoskeleton

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 : 41.67 mg/mL (118.90 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8535 mL	14.2674 mL	28.5347 mL
5 mM	0.5707 mL	2.8535 mL	5.7069 mL
10 mM	0.2853 mL	1.4267 mL	2.8535 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: 2.5 mg/mL (7.13 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (7.13 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

IPA-3 is a selective non-ATP competitive PAK1 inhibitor with IC_{50} of 2.5 μM, and shows no inhibition to group II PAKs (PAKs 4-6).

IC_{50} & Target

PAK1
2.5 μM (IC_{50})

In Vitro

IPA-3 inhibits Pak1 activation in part by binding covalently to the regulatory domain of Pak1. IPA-3 binds Pak1 covalently in

a time- and temperature-dependent manner. IPA-3 prevents binding of the Pak1 activator Cdc42. IPA-3 binds directly to the Pak1 autoregulatory domain. IPA-3 reversibly inhibits PMA-induced membrane ruffling in cells[1]. IPA-3 (2 μM, 5 μM or 20 μM) reduces cell spreading in human primary Schwann and schwannoma cells. IPA-3 treatment significantly reduces the number of adherent Schwann and schwannoma cells in a dose-dependent manner[2]. IPA-3 is a non ATP-competitive, allosteric inhibitor of p21-activated kinase 1 (Pak1). PIR3.5 is the control compound of IPA-3. IPA-3 prevents Cdc42-stimulated Pak1 autophosphorylation on Thr423. IPA-3 also prevents sphingosine-dependent Pak1 autophosphorylation. IPA-3 does not target exposed cysteine residues on Pak1. The disulfide bond of IPA-3 is critical for inhibition of Pak1 and in vitro reduction by the reducing agent dithiothreitol (DTT) abolishes Pak1 inhibition by IPA-3. IPA-3 inhibits activation of Pak1 by diverse activators, but does not inhibit preactivated Pak1. IPA-3 inhibits PDGF-stimulated Pak activation in mouse embryonic fibroblasts[3].

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

PROTOCOL

Kinase Assay [1]

Pak1 (150 nM final) is pre-incubated with MBP (8.3 μM), indicated proteins, and IPA-3 or DMSO in Kinase buffer for 20 minutes at 4°C. Cdc42-GTPγS (3.2 μM) is then added and the reaction is pre-equilibrated 10 minutes at 30°C. Kinase reactions are started by the addition of ATP (to 30 μM) containing [^{32}P]ATP and are incubated 10 min and analyzed by SDS-PAGE and autoradiography.

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Cell Assay [2]

Human primary schwannoma cells are grown on 96 well plates for 2 days. Cells are left untreated or treated with 5 μM IPA-3, 20 μM IPA-3 or 20 μM PIR-3.5 for 24 hours. The MTS-solution is left on the cells for 3 hours, before the absorbance at 490 nm is measured. The experiments are conducted three times and mean and standard error of the mean is calculated with Excel.

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

CUSTOMER VALIDATION

- Cell Rep. 2022 Nov 15;41(7):111636.
- Front Immunol. 2021 Aug 2;12:686846.
- Front Immunol. 02 August 2021.
- Comput Struct Biotec. 2021;19:1933-1943.
- J Virol. 2022 Dec 21;96(24):e0144622.

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REFERENCES

[1]. Viaud J, et al. An allosteric kinase inhibitor binds the p21-activated kinase autoregulatory domain covalently. Mol Cancer Ther. 2009 Sep;8(9):2559-65.

[2]. Flaiz C, et al. PAK kinase regulates Rac GTPase and is a potential target in human schwannomas. Exp Neurol. 2009 Jul;218(1):137-44.

[3]. Deacon SW, et al. An isoform-selective, small-molecule inhibitor targets the autoregulatory mechanism of p21-activated kinase. Chem Biol. 2008 Apr;15(4):322-31

Caution: Product has not been fully validated for medical applications. For research use only.

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