A 83-01

Cat. No.: HY-10432

CAS No.: 909910-43-6

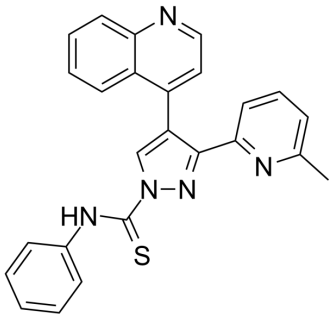
Molecular Formula: $C_{25}H_{19}N_5S$

Molecular Weight: 421.52

Target: ALK; TGF-β Receptor

Pathway: Protein Tyrosine Kinase/RTK; TGF-beta/Smad

Storage: -20°C, protect from light, stored under nitrogen
* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (98.86 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3724 mL	11.8618 mL	23.7237 mL
5 mM	0.4745 mL	2.3724 mL	4.7447 mL
10 mM	0.2372 mL	1.1862 mL	2.3724 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: ≥ 2.08 mg/mL (4.93 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.93 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.93 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

A 83-01 is a potent inhibitor of TGF-β type I receptor ALK5 kinase, type I nodal receptor ALK4 and type I nodal receptor ALK7, with IC_{50}s of 12 nM, 45 nM and 7.5 nM against the transcription induced by ALK5, ALK4 and ALK7, respectively[1].

IC_{50} & Target

ALK5	ALK4	ALK7
12 nM (IC_{50})	45 nM (IC_{50})	7.5 nM (IC_{50})

In Vitro

A 83-01 is a potent inhibitor of TGF-β type I receptor ALK5 kinase, ALK4 and ALK7, reduces the level of ALK-5-induced transcription with an IC_{50} of 12 nM in Mv1Lu cells, also blocks the ALK4-TD and ALK7-TD induced transcription with IC_{50}s of

	45 nM and 7.5 nM in R4-2 cells, and weakly suppresses that induced by constitutively active ALK-6, ALK-2, ALK-3, and ALK-1. A 83-01 (0.03-10 μM) potently prevents the growth-inhibitory effects of TGF-β, and completely inhibits the effect at 3 μM. A 83-01 (1-10 μM) inhibits TGF-β-induced Smad activation in HaCaT cells[1]. A 83-01 (1 μM) decreases cell motility, adhesion and invasion increased by TGF-β1 in HM-1 cells, but does not change cell proliferation[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	A 83-01 (50, 150 and 500 μg/mouse, i.p.) significantly improves survival of the mice without body weight or neurobehavioral appearances[2]. A 83-01 (0.5 mg/kg, i.p.) shows a significantly strong antitumor effect in mice bearing M109 cells[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	HM-1 cells are seeded into a 96-well plate and are incubated for 18 hr. A 83-01 (1 μM) or vehicle are then added for 12 hr followed by the addition of TGF-β1 (1 ng/mL) or vehicle for 60 hr. The number of viable cells in each well is examined using the WST-1 assay[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Female B6C3F1 mice used for the in vivo studies are maintained under specific pathogen-free conditions. To evaluate the effect of A 83-01 on the survival of mice bearing peritoneal dissemination, HM-1 cells (1×10^6) are injected into the abdominal cavity via the left flank of the mouse. Starting the next day, A 83-01 (150 μg/body) or vehicles (PBS with 0.5% DMSO) are injected into the abdominal cavity three times per week. Mice are euthanized before reaching the moribund state[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2020 Dec 4;370(6521):eaay2002.
- Sci Adv. 2021 Apr 14;7(16):eabb2213.
- Theranostics. 2021 Mar 14;11(11):5539-5552.
- FASEB J. 2020 Aug;34(8):11185-11199.
- Gynecol Oncol. 2019 Jun;153(3):639-650.

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REFERENCES

[1]. Tojo M, et al. The ALK-5 inhibitor A-83-01 inhibits Smad signaling and epithelial-to-mesenchymal transition by transforming growth factor-beta. Cancer Sci. 2005 Nov;96(11):791-800.

[2]. Yamamura S, et al. The activated transforming growth factor-beta signaling pathway in peritoneal metastases is a potential therapeutic target in ovarian cancer. Int J Cancer. 2012 Jan 1;130(1):20-8.

[3]. Taniguchi Y, et al. Enhanced antitumor efficacy of folate-linked liposomal Adriamycin with TGF-β type I receptor inhibitor. Cancer Sci. 2010 Oct;101(10):2207-13.

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

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