Takinib

Cat. No.: HY-103490

CAS No.: 1111556-37-6

Molecular Formula: $C_{18}H_{18}N_4O_2$

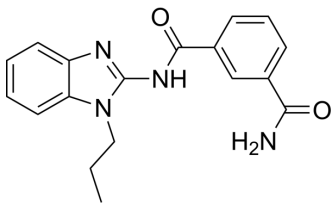
Molecular Weight: 322.36

Target: MAP3K; Apoptosis

Pathway: MAPK/ERK Pathway; 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 : 50 mg/mL (155.11 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1021 mL	15.5106 mL	31.0212 mL
	5 mM	0.6204 mL	3.1021 mL	6.2042 mL
	10 mM	0.3102 mL	1.5511 mL	3.1021 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 (7.76 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (7.76 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Takinib (EDHS-206) is an orally active and selective TAK1 inhibitor (IC_{50}=9.5 nM), more than 1.5 log more potent than the second and third ranked targets, IRAK4 (120 nM) and IRAK1 (390 nM), respectively. Takinib is an inhibitor of autophosphorylated TAK1 that non-competitively binds within the ATP binding pocket. Takinib induces apoptosis following TNFα stimulation in cell models of rheumatoid arthritis and metastatic breast cancer. Takinib is also a P. falciparum protein kinase 9 (*Pf*PK9) inhibitor ($K_{D(app)}$ of 0.46 μM)[1][2][3].

IC_{50} & Target				
	TAK1 9.5 nM (IC_{50})	IRAK4 120 nM (IC_{50})	IRAK1 390 nM (IC_{50})	GCK 430 nM (IC_{50})
	CLK2	MINK1		

	430 nM (IC_{50})	1.9 μM (IC_{50})

In Vitro

Takinib (10-10000 nM; 24 hours) induces apoptosis following TNF-α stimulation in MDA-MB-231 cells[1].
?Takinib (10 μM; 0-1 hours) reduces phosphorylation of IKK and p65[1].
?Takinib serves as a chemical starting point for the development of PfPK9 ($K_{D(app)}$ of 0.46 μM) inhibitors for malaria[3].
?Takinib (2 hours; 0.1-20 μM; human RASFs) induces phosphorylation of TAK1$^{Thr184/187}$, STAT3^{Tyr705} and STAT3^{Ser727} in IL-1 β-treated (10 ng/mL; 30 min) RASFs[4].

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

Western Blot Analysis[1]

Cell Line:	Breast cancer cell line MDA-MB-231
Concentration:	10 μM
Incubation Time:	5, 15, 30, 60 minutes
Result:	IKK and p65 were maximally phosphorylated at 15 minutes, which indicated activation of the NF-κB pathway, while p38 phosphorylation peaks at 30 minutes.

Western Blot Analysis[4]

Cell Line:	IL-1β-treated (10 ng/mL; 30 min) RASFs
Concentration:	0.1-20 μM
Incubation Time:	2 hours
Result:	Induced phosphorylation of TAK1$^{Thr184/187}$, STAT3^{Tyr705} and STAT3^{Ser727}.

In Vivo

Takinib (50 mg/kg; intraperitoneally; daily from days 18-36) reduces the clinical score in type II collagen-induced arthritis (CIA) mouse model of rheumatoid arthritis[4].
?Takinib (50 mg/kg; oral gavage; daily until 17 days) slows tumor growth in the Hodgkin lymphoma xenograft NSG mice[5].

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

Animal Model:	Male DBA/1 mice (CIA arthritis model)[4]
Dosage:	50 mg/kg
Administration:	Intraperitoneally; daily from days 18-36
Result:	Showed a reduction in clinical arthritic score compared to vehicle control.

Animal Model:	Female NSG mice (8 weeks old)[5]
Dosage:	50 mg/kg
Administration:	Oral gavage; daily until 17 days
Result:	Slowed tumor growth and reduced tumor size/weight.

CUSTOMER VALIDATION

- ACS Cent Sci. 2018 Aug 22;4(8):982-995.

- EMBO J. 2021 Sep 2;e108028.
- Clin Transl Med. 2022 Jun;12(6):e850.
- J Cell Biol. 2018 Aug 6;217(8):2727-2742.
- Elife. 2022 Jun 28;11:e78044.

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REFERENCES

[1]. Totzke J, et al. Takinib, a Selective TAK1 Inhibitor, Broadens the Therapeutic Efficacy of TNF-α Inhibition for Cancer and Autoimmune Disease. Cell Chem Biol. 2017 Aug 17;24(8):1029-1039.

[2]. Scarneo SA, et.al. Pharmacological inhibition of TAK1, with the selective inhibitor takinib, alleviates clinical manifestation of arthritis in CIA mice. Arthritis Res Ther. 2019 Dec 17;21(1):292.

[3]. Raphemot R, et al. Plasmodium PK9 Inhibitors Promote Growth of Liver-Stage Parasites. Cell Chem Biol. 2019 Mar 21;26(3):411-419.e7.

[4]. Panipinto PM, et.al. Takinib Inhibits Inflammation in Human Rheumatoid Arthritis Synovial Fibroblasts by Targeting the Janus Kinase-Signal Transducer and Activator of Transcription 3 (JAK/STAT3) Pathway. Int J Mol Sci. 2021;22(22):12580. Published 2021 Nov 22.

[5]. Song Z,et.al. Essential role of the linear ubiquitin chain assembly complex and TAK1 kinase in A20 mutant Hodgkin lymphoma. Proc Natl Acad Sci U S A. 2020 Nov 17;117(46):28980-28991.

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