R406

Cat. No.: HY-12067

CAS No.: 841290-81-1

Molecular Formula: $C_{28}H_{29}FN_6O_8S$

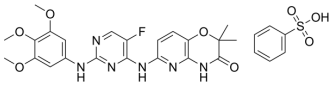
Molecular Weight: 629

Target: Syk; Apoptosis; FLT3

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 61 mg/mL (96.98 mM)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.5898 mL	7.9491 mL	15.8983 mL
	5 mM	0.3180 mL	1.5898 mL	3.1797 mL
	10 mM	0.1590 mL	0.7949 mL	1.5898 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 (3.97 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.97 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

R406 is an orally available and competitive Syk/FLT3 inhibitor for ATP binding with a K_i of 30 nM, potently inhibits Syk kinase activity in vitro with an IC_{50} of 41 nM, measured at an ATP concentration corresponding to its K_m value. R406 reduces immune complex-mediated inflammation[1]. R406 also inhibits Lyn (IC_{50}=63 nM) and Lck (IC_{50}=37 nM)[2].

IC_{50} & Target

Ki: 30 nM (Syk)[1]

IC50: 41 nM (Syk)[1]

FLT3[1]

IC50: 63 nM (Lyn), 37 nM (Lck)[2]

In Vitro

R406 inhibits adenosine A3 receptor (IC_{50}=0.081 μM), adenosine transporter (IC_{50}=1.84 μM), and monoamine transporter (IC_{50}=2.74 μM)[1].

?R406 inhibits Huh7 hepatocyte, A549 epithelial, and H1299 lung cancer lines with EC_{50}s of 15.1, 2.9 and 6.3 μM, respectively[1].

?R406 inhibits phosphorylation of Syk substrate LAT in mast cells and BLNK/SLP65 in B cells[1].

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

Western Blot Analysis[1]

Cell Line:	Cultured human mast cells (CHMC)
Concentration:	0.016, 0.08, 0.4, 2 μM
Incubation Time:	40 minutes
Result:	Inhibited all other kinases tested at 5 to 100 fold less potency than Syk as judged by phosphorylation of target proteins.

In Vivo

R406 (5 and 10 mg/kg) shows efficacy in the amelioration of the Arthus reaction and in reducing clinical symptoms in the collagen antibody-induced arthritis (CAIA) and K/BxN models of rheumatoid arthritis (RA). Immune complex (IC)-mediated inflammation is reduced by inhibition of Fc receptor signaling with R406[1].

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

Animal Model:	Female Balb/c mice (6-8 weeks) with CAIA[1]
Dosage:	5 and 10 mg/kg
Administration:	Administered orally, b.i.d, for 14 days, starting 4 hours after antibody challenge on day 0.
Result:	Reduced inflammation and swelling, and the arthritis progressed more slowly in treated animals than in vehicle controls.

Animal Model:	Female C57BL/6 mice with arthritis[1]
Dosage:	10 mg/kg
Administration:	Administered orally one hour before serum injection; b.i.d; for 13 days
Result:	Delayed the onset and reduced the severity of clinical arthritis. Paw thickening and clinical arthritis were reduced by approximately 50%.

CUSTOMER VALIDATION

- Cell. 2018 Oct 4;175(2):442-457.e23.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Nat Commun. 2022 Apr 19;13(1):2136.
- Arthritis Rheumatol. 2018 Sep;70(9):1419-1428.
- Theranostics. 2021 May 24;11(15):7308-7321.

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REFERENCES

[1]. Sylvia Braselmann, et al. R406, an orally available spleen tyrosine kinase inhibitor blocks fc receptor signaling and reduces immune complex-mediated inflammation. J Pharmacol Exp Ther. 2006 Dec;319(3):998-1008.

[2]. Hoon-Suk Cha , et al. A novel spleen tyrosine kinase inhibitor blocks c-Jun N-terminal kinase-mediated gene expression in synoviocytes. J Pharmacol Exp Ther. 2006 May;317(2):571-8.

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