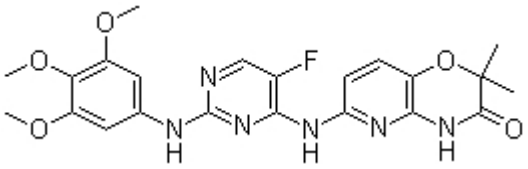
Product Introduction

R406 (free base)

R406 (free base) is a potent **Syk** inhibitor with **IC50** of 41 nM, strongly inhibits Syk but not Lyn, 5-fold less potent to Flt3. Phase 2.

Technical Data:

Molecular Weight (MW):	470.45	
Formula:	C22H23FN6O5	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 21 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	841290-80-0	

Biological Activity

R406 is an ATP-competitive inhibitor of Syk with a Ki value of 30 nM. R406 selectively inhibits Syk-dependent signaling with EC50 values ranging from 33 nM to 171 nM, more potently than Syk-independent pathways in different cells. [1] R406 inhibits cellular proliferation of a large panel of diffuse large B-cell lymphoma (DLBCL) cell lines at EC50 values ranging from 0.8 μM to 8.1 μM. R406 treatment (1 μM or 4 μM) induces the activation of caspases 9 and 3, but not caspase 8, leading to significant apoptosis of the majority of DLBCL cell lines. Pretreatment of R406 completely blocks the

phosphorylation of SYK525/526 and the SYK-dependent phosphorylation of BLNK in R406-sensitive DLBCLs following B-cell receptor (BCR) crosslinking. [2] R406 potently decreases MMP-9 mRNA levels by 2.8- and 4.3-fold lower than controls after 24 and 48 hours treatment, respectively, and reduces the invasive capacity of the RL cells. [3]

R406 has shown efficacy in a number of animal models of immune disorders. Oral administration of R406 in mice with immune complex-mediated inflammation significantly inhibits the cutaneous reverse passive Arthus reaction by approximately 72% and 86% at 1 mg/kg and 5 mg/kg, respectively, compared with the control. R406 treatment at 10 mg/kg significantly reduces inflammation and swelling, decreases the progressive arthritis to a lower level in the passive anticollagen antibody-challenged mice, and delays the onset and reduces paw thickening and clinical arthritis by approximately 50% in the K/BxN serum transfer mice model. [1]

References

[1] Braselmann S, et al. J Pharmacol Exp Ther, 2006, 319(3), 998-1008.
[2] Chen L, et al. Blood, 2008, 111(4), 2230-2237.
[3] Fruchon S, et al. Leukemia, 2011, 1-11.

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