上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：R406 (free base)
产品别名：R406 free base

生物活性：

Description

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. IC50 value: 41 nM [1] Target: Syk in vitro: R406 is a potent inhibitor of immunoglobulin E (IgE)- and IgG-mediated activation of Fc receptor signaling. R406 inhibits the anti-IgE-induced production and release of LTC4 and cytokines and chemokines, including TNFα, IL-8, and GM-CSF. R406 inhibits phosphorylation of Syk substrate linker for activation of T cells in mast cells and B-cell linker protein/SLP65 in B cells. R406 binds to the ATP binding pocket of Syk and inhibits its kinase activity as an ATP-competitive inhibitor with Ki of 30 nM. R406 blocks Syk-dependent FcR-mediated activation of monocytes/macrophages and neutrophils and Bcr-mediated activation of B lymphocytes [1]. R406 significantly induces chronic lymphocytic leukemia (CLL) cell apoptosis in nurselike cells cocultures and blocks CCL3 and CCL4 secretion by CLL cells in response to B-cell antigen receptor (Bcr) triggering [2]. R406 is a potent inhibitor of platelet signaling and functions initiated by FcγRIIA cross-linking by specific antibodies or by sera from HIT patients [3]. in vivo: R406 reduces cutaneous reverse passive Arthus reaction by approximately 86% at 5 mg/kg in prophylactic treated mice. R406 also shows efficacy in inhibiting paw inflammation in antibody-induced arthritis mouse models [1]. R406 does not adversely affect macrophage or neutrophil function in innate immune responses and has minimal functional immunotoxicity notwithstanding its lymphocytopenic effect [4].

Solvent&Solubility

In Vitro:

DMSO : ≥ 10 mg/mL (21.26 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1256 mL	10.6281 mL	21.2562 mL
	5 mM	0.4251 mL	2.1256 mL	4.2512 mL
	10 mM	0.2126 mL	1.0628 mL	2.1256 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 0.5 mg/mL (1.06 mM); Clear solution

此方案可获得 ≥ 0.5 mg/mL (1.06 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 5.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 0.5 mg/mL (1.06 mM); Clear solution 此方案可获得 ≥ 0.5 mg/mL (1.06 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 5.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Braselmann S, 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, 319(3), 998-1008. [2]. Quiroga MP, et al. B-cell antigen receptor signaling enhances chronic lymphocytic leukemia cell migration and survival: specific targeting with a novel spleen tyrosine kinase inhibitor, R406. Blood, 2009, 114(5), 1029-1037. [3]. Lhermusier T, et al. The Syk-kinase inhibitor R406 impairs platelet activation and monocyte tissue factor expression triggered by heparin-PF4 complex directed antibodies. J Thromb Haemost, 2011, 9(10), 2067-2076. [4]. Zhu Y, et al. Immunotoxicity assessment for the novel Spleen tyrosine kinase inhibitor R406. Toxicol Appl Pharmacol, 2007, 221(3), 268-277.