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产品名称：5-R-Rivaroxaban
产品别名：5-R-利伐沙班

生物活性：

Description	5-R-Rivaroxaban is (R)-enantiomer of Rivaroxaban. Rivaroxaban (BAY 59-7939) is a highly potent and selective, direct Factor Xa (FXa) inhibitor, achieving a strong gain in anti-FXa potency (IC_{50} 0.7 nM; K_i 0.4 nM).
IC_{50} & Target	FXa[1]
In Vitro	Rivaroxaban (BAY 59-7939) is an oral, direct Factor Xa (FXa) inhibitor in development for the prevention and treatment of arterial and venous thrombosis. Rivaroxaban competitively inhibits human FXa (Ki 0.4 nM) with >10 000-fold greater selectivity than for other serine proteases; it also inhibits prothrombinase activity (IC50 2.1 nM). Rivaroxaban inhibits endogenous FXa more potently in human and rabbit plasma (IC50 21 nM) than rat plasma (IC50 290 nM). It demonstrates anticoagulant effects in human plasma, doubling prothrombin time (PT) and activates partial thromboplastin time at 0.23 and 0.69 μM, respectively[2].
In Vivo	Rivaroxaban (BAY 59-7939) is a potent and selective, direct FXa inhibitor with excellent in vivo activity and good oral bioavailability[1]. Rivaroxaban (BAY 59-7939), administered by i.v. bolus before thrombus induction, reduces thrombus formation (ED50 0.1 mg/kg), inhibits FXa, and prolongs PT dose dependently. PT and FXa are affected slightly at the ED50 (1.8-fold increase and 32% inhibition, respectively). At 0.3 mg/kg (dose leading to almost complete inhibition of thrombus formation), Rivaroxaban moderately prolongs PT (3.2±0.5-fold) and inhibits FXa activity (65±3%)[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 33.33 mg/mL (76.47 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2942 mL	11.4710 mL	22.9421 mL
	5 mM	0.4588 mL	2.2942 mL	4.5884 mL
	10 mM	0.2294 mL	1.1471 mL	2.2942 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: 2.5 mg/mL (5.74 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.74 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

	以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.5 mg/mL (5.74 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.74 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Roehrig S, et al. Discovery of the novel antithrombotic agent 5-chloro-N-({(5S)-2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]-1,3-oxazolidin-5-yl}methyl)thiophene- 2-carboxamide (BAY 59-7939): an oral, direct factor Xa inhibitor. J Med Chem. 2005 Sep 22;48(19) [2]. Perzborn E, et al. In vitro and in vivo studies of the novel antithrombotic agent BAY 59-7939--an oral, direct Factor Xa inhibitor. J Thromb Haemost. 2005 Mar;3(3):514-21.

实验参考：

Animal Administration	Rats[2] Fasted, male Wistar rats (HsdCpb:WU) are used. Rat venous stasis model Thrombus formation is induced in anesthetized rats (n=10 per dose group), with minor modifications. The abdominal vena cava is exposed and two loose sutures (8-10 mm apart) are placed below the left renal venous branch. Rivaroxaban dissolved in polyethylene glycol/H_2O/glycerol (996 g/100 g/60 g), or vehicle is given by intravenous (i.v.) bolus injection into a tail vein 15 min before thrombus induction. Thromboplastin (0.5 mg/kg) is injected into a femoral vein and, after 15 s, the proximal and distal sutures are tied. Fifteen minutes later, the ligated segment is removed, the thrombus withdrawn and weighed. Blood samples are obtained by cardiac puncture immediately before thrombus removal.
Kinase Assay	The activity of Rivaroxaban (BAY 59-7939) against purified serine proteases is measured using chromogenic or fluorogenic substrates in 96-well microtiter plates at 25°C. The enzymes are incubated with Rivaroxaban or its solvent, DMSO, for 10 min. The reactions are initiated by the addition of the substrate, and the color or fluorescence is monitored continuously at 405 nm using a Spectra Rainbow Thermo Reader, or at 630/465 nm using a SPECTRAfluor plus, respectively, for 20 min. Enzymatic activity is analyzed in the following buffers (final concentrations): human FXa (0.5 nM), rabbit FXa (2 nM), rat FXa (10 nM), or urokinase (4 nM) in 50 mM Tris-HCl buffer, pH 8.3, 150 mM NaCl, and 0.1% bovine serum albumin (BSA); Pefachrome FXa (50-800 μM) or chromozym U (250 μM) with thrombin (0.69 nM), trypsin (2.2 nM), or plasmin (3.2 nM) in 0.1 μM Tris-HCl, pH 8.0, and 20 mM $CaCl_2$; chromozym TH (200 μM), chromozym plasmin (500 μM), or chromozymtrypsin (500 μM) with FXIa (1 nM) or APC (10 nM) in 50mM phosphate buffer, pH 7.4, 150 mM NaCl; and S 2366 (150 or 500 μM) with FVIIa (1 nM) and tissue factor (3 nM) in 50 mM Tris-HCl buffer,pH 8.0, 100 mM NaCl, 5 mM $CaCl_2$ and 0.3% BSA, H-D-Phe-Pro-Arg-6-amino-1-naphthalene-benzylsulfon-amide H_2O (100 μM) and measured for 3 h. The FIXab/FX assay, comprising FIXab (8.8 nM) and FX (9.5 nM) in 50 mM Tris-HCl buffer, pH 7.4, 100 mM NaCl, 5 mM $CaCl_2$ and 0.1% BSA, is started by the addition of I-1100 (50 μM), and measured for 60 min. The inhibitory constant (K_i) against FXa is calculated according to the

	Cheng-Prusoff equation ($K_i=IC_{50}/1+[S]/K_m$), where [S] is the substrate concentration, and K_m is the Michaelis-Menten constant. K_m is determined from a Lineweaver-Burk plot. The IC_{50} is the amount of inhibitor required to diminish the initial velocity of the control by 50%[2].
References	[1]. Roehrig S, et al. Discovery of the novel antithrombotic agent 5-chloro-N-({(5S)-2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]-1,3-oxazolidin-5-yl}methyl)thiophene- 2-carboxamide (BAY 59-7939): an oral, direct factor Xa inhibitor. J Med Chem. 2005 Sep 22;48(19) [2]. Perzborn E, et al. In vitro and in vivo studies of the novel antithrombotic agent BAY 59-7939--an oral, direct Factor Xa inhibitor. J Thromb Haemost. 2005 Mar;3(3):514-21.