Kinase Assay:[1] The activity of Rivaroxaban against purified serine proteases is measured using chromogenic or fluorogenic substrates in 96-well microtiter plates. The enzymes are incubated with Rivaroxaban or its solvent, dimethyl sulfoxide (DMSO), for 10 minutes. 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 minutes. Enzymatic activity is analyzed in the following buffers (final concentrations): human FXa (0.5 mM), rabbit FXa (2 mM), 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 mM), or plasmin (3.2 mM) in 0.1 mM Tris–HCl, pH 8.0, and 20 mM CaCl₂; chromozym TH (200 μM), chromozym plasmin (500 μM), or chromozym trypsin (500 μM) with FXa (1 mM) or APC (10 mM) in 50 mM phosphate buffer pH 7.4, 150 mM NaCl; and S 2366 (150 or 500 μM) with FVa (1 nM) and tissue factor (3 nM) in 50 mM Tris–HCl buffer, pH 8.0, 100 mM NaCl, 5 mM CaCl₂ and 0.3% BSA, H-D-Phe-Pro-Arg-Glu-aminol-1-naphthyl-hexahydrobenzofurazan-2-sulfonamide.H₂O (100 μM) and measured for 3 hours. The FⅢa/FX assay, comprising FIXaβ (8.8 mM) and FX (8.5 mM) in 50 mM Tris–HCl buffer, pH 7.4, 100 mM NaCl, 5 mM CaCl₂ and 0.1% BSA, is started by the addition of L-1100 (50 μM) and measured for 60 minutes. The inhibitory constant (Kᵢ) against FXa is calculated according to the Cheng–Prusoff equation. The IC₅₀ is the amount of inhibitor required to diminish the initial velocity of the control by 50%.

Cell Assay:[2] Cell Lines Caco-2, wild-type, and P-gp-overexpressing LLC-PK1
Concentrations 0 - 100 μM
Incubation Time 2 hours

IC₅₀ of 0.7 nM. Rivaroxaban (Xarelto, BAY 59-7939) is a direct inhibitor of Factor Xa with Kᵢ and IC₅₀ of 0.4 nM and 0.7 nM respectively.

In vitro Rivaroxaban is an oral, direct inhibitor of Factor Xa (FXa), being developed for the prevention and treatment of arterial and venous thrombosis with a Kᵢ of 0.4 nM. Rivaroxaban also inhibits prothrombinase activity with IC₅₀ of 2.1 nM. Rivaroxaban also shows a similar affinity to purified human and rabbit FXa (IC₅₀ 0.7 mM and 0.8 mM respectively), but a lesser potency against purified rat FXa (IC₅₀ 3.4 mM). Endogenous human and rabbit FXa in plasma is inhibited to a similar extent by Rivaroxaban (IC₅₀ 21 nM and 21 mM respectively), while 14-fold higher concentrations are required in rat plasma (IC₅₀ 290 nM). [1] Rivaroxaban exhibits high permeability and polarized transport across Caco-2 cells as a substrate of the P-gp, but exhibits no inhibitory effect on P-gp-mediated drug transport up to concentrations of 100 μM in vitro. [2]

In vivo Rivaroxaban reduces venous thrombosis in a dose dependent manner (ED₅₀ 0.1 mg/kg i.v.) in a rat venous stasis model. Rivaroxaban reduces arterial thrombus formation in an arteriovenous (AV) shunt in rats (ED₅₀ 5.0 mg/kg p.o.) and rabbits (ED₅₀ 0.6 mg/kg p.o.). [1] Plasma pharmacokinetics of Rivaroxaban are linear across the investigated dose range (1-10 mg/kg in rats, 0.3-3 mg/kg in dogs). Plasma clearance is low: 0.4 L/kg in rats and 0.3 L/kg in dogs; the volume of distribution (Vₚ) is moderate: 0.3 L/kg in rats, and 0.4 L/kg in dogs. The elimination half-life after oral administration is short in both species (0.9-2.3 hours). [3]

Clinical Trials Rivaroxaban is currently being tested in Phase II clinical trials in patients with cardiovascular disease.

Return Policy Selleck Chemicals wishes you the best possible online shopping experience with our 365 day unconditional Return Policy. If you are not satisfied with your purchase, either for protocol related or product related problems, you may return any item(s) within 365 days from the original purchase date. Please see the following instructions when you return products.

1. All requests for returns should be communicated to Selleck Chemicals prior to shipping. Any items returned to Selleck Chemicals should be in the original packaging and in the same condition as originally purchased.
2. When returning purchased goods, please inform us of the purchase order number or package tracking number.
3. Return shipping is absolutely FREE. This offer is only valid for products purchased directly from Selleck and its authorized distributors.
4. Once your return request is received and approved, your refund will be processed or automatically applied to your credit card within 7 days. Please note that depending on your credit card company, it may take additional 2-10 business days for us to post the refund to your account.

Toll Free: (877) 796-6397 -- USA and Canada only --
Fax: +1-713-796-9816
Orders: +1-832-582-8158
sales@selleckchem.com
Tech Support: +1-832-582-8158
Ext 3
Monday–Friday 9:00 AM–5:00 PM (Central Time)
tech@selleckchem.com
We will contact you within one business day.

Website: www.selleckchem.com
METHODS

the respective final test concentrations (final DMSO concentration is always 1%). For inhibitor studies, the inhibitor is added at the appropriate concentration. After 2 hour incubation at 37 °C, samples are taken from both compartments and, after the addition of ammonium acetate buffer and acetonitrile, are analyzed by LC-MS/MS.

Animal Study:[1]

Animal Models
Fasted, male Wistar rats (HsdCpb/WU) and fasted, female New Zealand White rabbits (Esd:NZW).

Formulation
Rivaroxaban dissolves in polyethylene glycol/H2O/glycerol (996 g/100 g/60 g) and is given by i.v. Rivaroxaban dissolved in solutol/ethanol/H2O [40%/10%/50% (v/v/v)] and is given by p.o.

Doses
≤0.3 mg/kg for i.v. and ≤3 mg/kg for p.o.

Administration
Administered via i.v. or p.o.

References

PLEASE KEEP THE PRODUCT UNDER -20°C FOR LONG-TERM STORAGE.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE

Specific storage and handling information for each product is indicated on the product datasheet. Most Selleck products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality, but save your shipping charges by using the most economical storage conditions for an overnight shipment. Upon receipt of the product, follow the storage recommendations on the product datasheet.