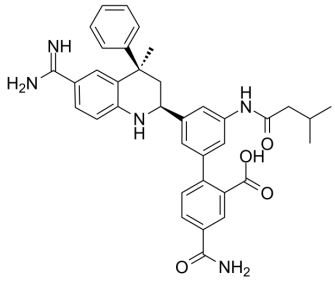
BMS-654457

Cat. No.:	HY-12631
CAS No.:	1004551-41-0
Molecular Formula:	$C_{36}H_{37}N_5O_4$
Molecular Weight:	603.71
Target:	Factor Xa
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	BMS-654457 is a small-molecule, reversible inhibitor of factor XIa (FXIa), binding with human and rabbit FXIa with K_is of 0.2 and 0.42 nM, respectively.
In Vitro	BMS-654457 shows comparable in vitro potency against FXIa in humans (Ki=0.2 nM) and in rabbits (Ki =0.42 nM), and was over 500-fold selective against coagulation-related proteases (thrombin, FXa and FVIIa) in these species[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BMS-654457 is effective in the prevention of arterial thrombosis in rabbits with limited effects on bleeding time. BMS-654457 is a promising antithrombotic therapy with a wide therapeutic window[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay	Platelet aggregation is measured in hirudin-treated rabbit platelet-rich plasma (PRP) with a platelet aggregometer. PRP is mixed with 2.5 μL of vehicle or BMS-654457 at 1 and 10 μM and incubated for 2 min at 37°C. Peak platelet aggregation is determined after the addition of 2.5 μL of the agonist (ADP at 10 μM, arachidonic acid at 250 μM and collagen at 10 μg/mL, final concentration)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rabbits[1] [1]BMS-654457 or vehicle (10 % N-N-dimethylacetamide:90 % of 5 % dextrose) is administered as a bolus plus sustaining IV infusion begun 30 min prior to each protocol. Treatment groups include BMS-654457 (mg/kg+mg/kg/h) at 0.011+0.008, 0.037+0.027, 0.11+0.08, 0.37+0.27 and 1.1 +0.8 or vehicle (n=6 per group). The plasma concentration that increased iCBF to EC_{50} was estimated for BMS654457[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Wong PC, et al. In vitro, antithrombotic and bleeding time studies of BMS-654457, a small-molecule, reversible and direct inhibitor of factor XIa. J Thromb Thrombolysis. 2015 Nov;40(4):416-23.

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