

Blood coagulation components in GtoPdb v.2025.3

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Abstract

Coagulation as a process is interpreted as a mechanism for reducing excessive blood loss through the generation of a gel-like clot local to the site of injury. The process involves the activation, adhesion (see [Integrins](#)), degranulation and aggregation of platelets, as well as proteins circulating in the plasma. The coagulation cascade involves multiple proteins being converted to more active forms from less active precursors (for example, prothrombin [Factor II] is converted to thrombin [Factor IIa]), typically through proteolysis (see [Proteases](#)). Listed here are the components of the coagulation cascade targeted by agents in current clinical usage or at an advanced level of development.

Contents

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Please note that the database version for the citations given in GtoPdb are to the most recent preceding version in which the family or its subfamilies and targets were substantially changed. The links below are to the current version. If you need to consult the cited version, rather than the most recent version, please contact the GtoPdb curators.

Database links

Blood coagulation components

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=853>

Enzymes

coagulation factor II, thrombin

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2362>

coagulation factor III, tissue factor

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=3192>

coagulation factor V

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2606>

coagulation factor VIII

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2607>

coagulation factor X

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2359>

coagulation factor XI

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2360>

antithrombin, antithrombin III (serpin family C member 1)

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2632>

References

1. AstraZeneca. AZ12971554. <http://openinnovation.astrazeneca.com/what-we-offer/compound/az12971554/>. Accessed on 12/09/2014.
2. Beck H, Mesch S, Vakalopoulos A, Pfaff N, Zimmermann S, Follmann M, Kersten E, Levilain G, Partikel K and Broehl AP *et al.* (2023) Substituted s-alaninate derivatives Patent number: [US20230391761A1](#). Assignee: Bayer AG. Priority date: 11/08/2023. Publication date: 07/12/2023.
3. Breij EC, de Goeij BE, Verploegen S, Schuurhuis DH, Amirkhosravi A, Francis J, Miller VB, Houtkamp M, Bleeker WK and Satijn D *et al.* (2014) An antibody-drug conjugate that targets tissue factor exhibits potent therapeutic activity against a broad range of solid tumors. *Cancer Res* **74**: 1214-26 [[PMID:24371232](#)]
4. Buneman P, Christie G, Davies JA, Dimitrellou R, Harding SD, Pawson AJ, Sharman JL and Wu Y. (2020) Why data citation isn't working, and what to do about it *Database* **2020** [[PMID:32367113](#)]
5. Cziraky MJ and Spinler SA. (1993) Low-molecular-weight heparins for the treatment of deep-vein thrombosis. *Clin Pharm* **12**: 892-9 [[PMID:8137606](#)]
6. Deinum J, Mattsson C, Inghardt T and Elg M. (2009) Biochemical and pharmacological effects of the direct thrombin inhibitor AR-H067637. *Thromb Haemost* **101**: 1051-9 [[PMID:19492147](#)]
7. Dilger AK, Pabbisetty KB, Corte JR, De Lucca I, Fang T, Yang W, Pinto DJP, Wang Y, Zhu Y and Mathur A *et al.* (2022) Discovery of Milvexian, a High-Affinity, Orally Bioavailable Inhibitor of Factor XIa in Clinical Studies for Antithrombotic Therapy. *J Med Chem* **65**: 1770-1785 [[PMID:34494428](#)]
8. Eriksson BI, Söderberg K, Widlund L, Wandeli B, Tengborn L and Risberg B. (1995) A comparative study of three low-molecular weight heparins (LMWH) and unfractionated heparin (UH) in healthy volunteers. *Thromb Haemost* **73**: 398-401 [[PMID:7667822](#)]
9. Eriksson BI, Wille-Jørgensen P, Kålebo P, Mouret P, Rosencher N, Bösch P, Baur M, Ekman S, Bach D and Lindbratt S *et al.* (1997) A comparison of recombinant hirudin with a low-molecular-weight heparin to prevent thromboembolic complications after total hip replacement. *N Engl J Med* **337**: 1329-35 [[PMID:9358126](#)]
10. Friedel HA and Balfour JA. (1994) Tinzaparin. A review of its pharmacology and clinical potential in the prevention and treatment of thromboembolic disorders. *Drugs* **48**: 638-60 [[PMID:7528134](#)]
11. Furugohri T, Isobe K, Honda Y, Kamisato-Matsumoto C, Sugiyama N, Nagahara T, Morishima Y and Shibano T. (2008) DU-176b, a potent and orally active factor Xa inhibitor: in vitro and in vivo pharmacological profiles. *J Thromb Haemost* **6**: 1542-9 [[PMID:18624979](#)]
12. Gailani D and Gruber A. (2016) Factor XI as a Therapeutic Target. *Arterioscler Thromb Vasc Biol* **36**: 1316-22 [[PMID:27174099](#)]
13. Galemme RA Jr., Fevig JM, Carini DJ, Cacciola J, Wells BL, Hillyer GL, Buriak J Jr., Rossi KA, Stouten PFW and Alexander RS *et al.* (1996) (N-acyl-N-alkyl)glycyl borolysine analogs: A new class of potent thrombin inhibitors. *Bioorg Med Chem Lett* **6**: 2913-2918
14. Gotti R, Parma B, Spelta F and Liverani L. (2013) Affinity capillary electrophoresis in binding study of antithrombin to heparin from different sources. *Talanta* **105**: 366-71 [[PMID:23598032](#)]
15. Guertin KR, Gardner CJ, Klein SI, Zulli AL, Czekaj M, Gong Y, Spada AP, Cheney DL, Maignan S and Guilloteau JP *et al.* (2002) Optimization of the beta-aminoester class of factor Xa inhibitors. Part 2: Identification of FXV673 as a potent and selective inhibitor with excellent In vivo anticoagulant activity. *Bioorg Med Chem Lett* **12**: 1671-4 [[PMID:12039587](#)]
16. Gustafsson D, Antonsson T, Bylund R, Eriksson U, Gyzander E, Nilsson I, Elg M, Mattsson C, Deinum J and Pehrsson S *et al.* (1998) Effects of melagatran, a new low-molecular-weight thrombin inhibitor, on thrombin and fibrinolytic enzymes. *Thromb Haemost* **79**: 110-8 [[PMID:9459334](#)]
17. Hara T, Yokoyama A, Ishihara H, Yokoyama Y, Nagahara T and Iwamoto M. (1994) DX-9065a, a new synthetic, potent anticoagulant and selective inhibitor for factor Xa. *Thromb Haemost* **71**: 314-9 [[PMID:8029795](#)]
18. Haeuël NH, Nar Jr., Priepke H, Ries U, Stassen JM and Wienen W. (2002) Structure-based design of novel potent nonpeptide thrombin inhibitors. *J Med Chem* **45**: 1757-66 [[PMID:11960487](#)]
19. Hayashi M, Hamada A, Okaya Y, Wakitani K and Aisaka K. (2001) Inhibitory effect of JTV-803, a new cyclic guanidine derivative, on factor Xa in vitro and in vivo. *Eur J Pharmacol* **428**: 163-8 [[PMID:11675032](#)]
20. Holmer E, Söderberg K, Bergqvist D and Lindahl U. (1986) Heparin and its low molecular weight derivatives: anticoagulant and antithrombotic properties. *Haemostasis* **16 Suppl 2**: 1-7 [[PMID:3744129](#)]
21. Jeko M, Tarumi T, Takeda M, Naito S, Nakabayashi T and Koike T. (2004) Synthetic selective inhibitors of coagulation factor Xa strongly inhibit thrombin generation without affecting initial thrombin forming time necessary for platelet activation in hemostasis. *J Thromb Haemost* **2**: 612-8 [[PMID:15102016](#)]
22. Iimiya M and Matsuo T. (1997) Inhibition of collagen-induced platelet aggregation by argatroban in patients with acute cerebral infarction. *Thromb Res* **88**: 245-50 [[PMID:9361377](#)]
23. Jimenez Nunez E, Ackerstaff J, Rohrig S, Hillisch A, Meier K, Heitmeier S, Tersteegen A, Stampfuss J, Ellerbrock P and Melbom D *et al.* (2017) Substituted oxopyridine derivatives Patent number: [WO2017005725A1](#). Assignee: Bayer Pharma. Priority date: 09/07/2015. Publication date: 12/01/2017.

24. Johnson PH, Sze P, Winant RC, Hudson D, Underhill P, Lazar JB, Olsen C and Almquist R. (1991) Structure-function and refolding studies of the thrombin-specific inhibitor hirudin. *Haemostasis* **21 Suppl 1**: 41-8 [PMID:1894196]
25. Kanji S, Devlin JW, Piekos KA and Racine E. (2001) Recombinant human activated protein C, drotrecogin alfa (activated): a novel therapy for severe sepsis. *Pharmacotherapy* **21**: 1389-402 [PMID:11714212]
26. Kapur S, Kupfer Y and Tessler S. (2001) Recombinant human activated protein C for severe sepsis. *N Engl J Med* **345**: 219-20; author reply 220-1 [PMID:11463021]
27. Kitazawa T, Esaki K, Tachibana T, Ishii S, Soeda T, Muto A, Kawabe Y, Igawa T, Tsunoda H and Nogami K *et al.*. (2017) Factor VIIIa-mimetic cofactor activity of a bispecific antibody to factors IX/Xa and X/Xa, emicizumab, depends on its ability to bridge the antigens. *Thromb Haemost* **117**: 1348-1357 [PMID:28451690]
28. Liu T, Hashizume K, Krieg E, Chen H, Mukaida Y, Thelen K, Friedrichs F, Willmann S, Schwes S and Solms A *et al.*. (2024) Pharmacokinetics, pharmacodynamics, and safety of fesomersen, a novel antisense inhibitor of factor XI, in healthy Chinese, Japanese, and Caucasian volunteers. *Clin Transl Sci* **17**: e13784 [PMID:38563414]
29. Lorentz CU, Tucker EI, Verbout NG, Shatzel JJ, Olson SR, Markway BD, Wallisch M, Ralle M, Hinds MT and McCarty OJT *et al.*. (2021) The contact activation inhibitor AB023 in heparin-free hemodialysis: results of a randomized phase 2 clinical trial. *Blood* **138**: 2173-2184 [PMID:34086880]
30. Macedo-Ribeiro S, Bode W, Huber R, Quinn-Allen MA, Kim SW, Ortel TL, Bourenkov GP, Bartunik HD, Stubbs MT and Kane WH *et al.*. (1999) Crystal structures of the membrane-binding C2 domain of human coagulation factor V. *Nature* **402**: 434-9 [PMID:10586886]
31. Manoharan J, Rana R, Kuenze G, Gupta D, Elwakiel A, Ambreen S, Wang H, Banerjee K, Zimmermann S and Singh K *et al.*. (2024) Tissue factor binds to and inhibits interferon- α receptor 1 signaling. *Immunity* **57**: 68-85.e11 [PMID:38141610]
32. Maryanoff BE and Costanzo MJ. (2008) Inhibitors of proteases and amide hydrolases that employ an alpha-ketoheterocycle as a key enabling functionality. *Bioorg Med Chem* **16**: 1562-95 [PMID:18053726]
33. Medicines and Healthcare products Regulatory Agency. Xigris 5 mg and 20 mg recall due to risk/benefit concerns <https://www.gov.uk/drug-device-alerts/drug-alert-xigris-5-mg-and-20-mg-recall-due-to-risk-benefit-concerns#:~:text=Immediate%20withdrawal%20of%20all%20distributed,Medical%20Information%20on%201256%20315000.&text=Any%20unused%20stock> Accessed on 31/07/2025.
34. Meijers JC, Tekelenburg WL, Bouma BN, Bertina RM and Rosendaal FR. (2000) High levels of coagulation factor XI as a risk factor for venous thrombosis. *N Engl J Med* **342**: 696-701 [PMID:10706899]
35. Nakase J, Toribatake Y, Moury Y, Seki H, Kitaoka K and Tomita K. (2009) Heparin versus danaproid for prevention of venous thromboembolism after hip surgery. *J Orthop Surg (Hong Kong)* **17**: 6-9 [PMID:19398784]
36. Ngo JC, Huang M, Roth DA, Furie BC and Furie B. (2008) Crystal structure of human factor VIII: implications for the formation of the factor IXa-factor VIIIa complex. *Structure* **16**: 597-606 [PMID:18400180]
37. Oelschlager C, Römisch J, Staubitz A, Stauss H, Leithäuser B, Tillmanns H and Hölschermann H. (2002) Antithrombin III inhibits nuclear factor kappaB activation in human monocytes and vascular endothelial cells. *Blood* **99**: 4015-20 [PMID:12010802]
38. Paolucci F, Claviès MC, Donat F and Necciari J. (2002) Fondaparinux sodium mechanism of action: identification of specific binding to purified and human plasma-derived proteins. *Clin Pharmacokinet* **41 Suppl 2**: 11-8 [PMID:12383040]
39. Perzborn E, Strassburger J, Wilmen A, Pohlmann J, Roehrig S, Schlemmer KH and Straub A. (2005) In vitro and in vivo studies of the novel antithrombotic agent BAY 59-7939--an oral, direct Factor Xa inhibitor. *J Thromb Haemost* **3**: 514-21 [PMID:15748242]
40. Pinto DJ, Smallheer JM, Cheney DL, Knabb RM and Wexler RR. (2010) Factor Xa inhibitors: next-generation antithrombotic agents. *J Med Chem* **53**: 6243-74 [PMID:20503967]
41. Pinto DJP, Orwat MJ, Smith 2nd LM, Quan ML, Lam PYS, Rossi KA, Apedo A, Bozarth JM, Wu Y and Zheng JJ *et al.*. (2017) Discovery of a Parenteral Small Molecule Coagulation Factor XIa Inhibitor Clinical Candidate (BMS-962212). *J Med Chem* **60**: 9703-9723 [PMID:29077405]
42. Pollack Jr CV, Kurz MA and Hayward NJ. (2020) EP-7041, a Factor XIa Inhibitor as a Potential Antithrombotic Strategy in Extracorporeal Membrane Oxygenation: A Brief Report. *Crit Care Explor* **2**: e0196 [PMID:32984829]
43. Qiu X, Zhou J, Wang W, Zhao Z, Tang L and Sun S. (2019) Effect of a new inhibitor of factor Xa zifaxaban, on thrombosis in the inferior vena cava in rabbits. *J Thromb Thrombolysis* **47**: 80-86 [PMID:30298304]
44. Salomon O, Steinberg DM, Koren-Morag N, Tanne D and Seligsohn U. (2008) Reduced incidence of ischemic stroke in patients with severe factor XI deficiency. *Blood* **111**: 4113-7 [PMID:18268095]
45. Schaefer M, Buchmueller A, Dittmer F, Straßburger J and Wilmen A. (2019) Allosteric Inhibition as a New Mode of Action for BAY 1213790, a Neutralizing Antibody Targeting the Activated Form of Coagulation Factor XI. *J Mol Biol* **431**: 4817-4833 [PMID:31655039]
46. Seidel H and Kolde HJ. (2018) Monitoring of Argatroban and Lepirudin: What is the Input of Laboratory Values in "Real Life"? *Clin Appl Thromb Hemost* **24**: 287-294 [PMID:28320219]
47. Setyono-Han B, Stürzebecher J, Schmalix WA, Muehlenweg B, Sieuwerts AM, Timmermans M, Magdolen V, Schmitt M, Klijn JG and Foekens JA. (2005) Suppression of rat breast cancer metastasis and reduction of primary tumour growth by the small synthetic urokinase inhibitor WX-UK1. *Thromb Haemost* **93**: 779-86 [PMID:15841327]
48. Smits NC, Kobayashi T, Srivastava PK, Skopelja S, Ivy JA, Elwood DJ, Stan RV, Tsongalis GJ, Sellke FW and Gross PL *et al.*. (2017) HS3ST1 genotype regulates antithrombin's inflammomodulatory tone and associates with atherosclerosis. *Matrix Biol* **63**: 69-90 [PMID:28126521]
49. Stone GW, McLaurin BT, Cox DA, Bertrand ME, Lincoff AM, Moses JW, White HD, Pocock SJ, Ware JH and Feit F *et al.*. (2006) Bivalirudin for patients with acute coronary syndromes. *N Engl J Med* **355**: 2203-16 [PMID:17124018]
50. van Boven HH and Lane DA. (1997) Antithrombin and its inherited deficiency states. *Semin Hematol* **34**: 188-204 [PMID:9241705]
51. Van Huis CA, Casimiro-Garcia A, Bigge CF, Cody WL, Dudley DA, Filipski KJ, Heemstra RJ, Kohrt JT, Leadley Jr RJ and Narasimhan LS *et al.*. (2009) Exploration of 4,4-disubstituted pyrrolidine-1,2-dicarboxamides as potent, orally active Factor Xa inhibitors with extended duration of action. *Bioorg Med Chem* **17**: 2501-11 [PMID:19231206]
52. Walenga JM, Jeske WP, Samama MM, Frapaise FX, Bick RL and Fareed J. (2002) Fondaparinux: a synthetic heparin pentasaccharide as a new antithrombotic agent. *Expert Opin Investig Drugs* **11**: 397-407 [PMID:11866668]
53. Warkentin TE, Greinacher A, Craven S, Dewar L, Sheppard JA and Oforu FA. (2005) Differences in the clinically effective molar concentrations of four direct thrombin inhibitors explain their variable prothrombin time prolongation. *Thromb Haemost* **94**: 958-64 [PMID:16363236]
54. Weitz JI and Chan NC. (2019) MAA868 locks factor XIa in a zymogen-like state. *Blood* **133**: 1393-1394 [PMID:30923107]
55. Wienen W, Stassen J-M, Priepke H, Ries UJ and Haeucl N. (2007) In-vitro profile and ex-vivo anticoagulant activity of the direct thrombin inhibitor dabigatran and its orally active prodrug, dabigatran etexilate *Thrombosis and Haemostasis* **98**: 155-162
56. Witting JI, Bourdon P, Breznjak DV, Maraganore JM and Fenton 2nd JW. (1992) Thrombin-specific inhibition by and slow cleavage of hirulog-1. *Biochem J* **283 (Pt 3)**: 737-43 [PMID:1290488]
57. Wong PC, Crain EJ, Xin B, Wexler RR, Lam PY, Pinto DJ, Luetgen JM and Knabb RM. (2008) Apixaban, an oral, direct and highly selective factor Xa inhibitor: in vitro, antithrombotic and antihemostatic studies. *J Thromb Haemost* **6**: 820-9 [PMID:18315548]
58. Xu G, Liu Z, Wang X, Lu T, Desjarlais RL, Thieu T, Zhang J, Devine ZH, Du F and Li Q *et al.*. (2022) Discovery of Potent and Orally Bioavailable Pyridine N-Oxide-Based Factor XIa Inhibitors through Exploiting Nonclassical Interactions. *J Med Chem* **65**: 10419-10440 [PMID:35862732]
59. Yamauchi T, Umeda F, Inoguchi T and Nawata H. (1989) Antithrombin III stimulates prostacyclin production by cultured aortic endothelial cells. *Biochem Biophys Res Commun* **163**: 1404-11 [PMID:2675842]
60. Yi BA, Freedholm D, Widener N, Wang X, Simard E, Cullen C, Al-Saady NM, Lepor NE, Coulter S and Lovern M *et al.*. (2022) Pharmacokinetics and pharmacodynamics of Abelacimab (MAA868), a novel dual inhibitor of Factor XI and Factor XIa. *J Thromb Haemost* **20**: 307-315 [PMID:34714969]
61. Zhang P, Huang W, Wang L, Bao L, Jia ZJ, Bauer SM, Goldman EA, Probst GD, Song Y and Su T *et al.*. (2009) Discovery of betrixaban (PRT054021), N-(5-chloropyridin-2-yl)-2-(4-(N,N-dimethylcarbamimidoyl)benzamido)-5-methoxybenzamide, a highly potent, selective, and orally efficacious factor Xa inhibitor. *Bioorg Med Chem Lett* **19**: 2179-85 [PMID:19297154]