Alfimeprase is a metalloproteinase that degrades fibrin and fibrinogen in a plasmin-independent fashion. In the circulation, alfimeprase is rapidly inhibited by α_2-macroglobulin. Consequently, the drug must be delivered via a catheter directly into the thrombus. Studies of alfimeprase for treatment of peripheral arterial occlusion or for restoration of flow in blocked central venous catheters were stopped due to lack of efficacy. The disappointing results with desmoteplase and alfimeprase highlight the challenges of introducing new fibrinolytic drugs.

CONCLUSIONS AND FUTURE DIRECTIONS

Thrombosis involves a complex interplay among the vessel wall, platelets, the coagulation system, and the fibrinolytic pathways. Activation of coagulation also triggers inflammatory pathways that may exacerbate thrombosis. A better understanding of the biochemistry of blood coagulation and advances in structure-based drug design have identified new targets and resulted in the development of novel antithrombotic drugs. Well-designed clinical trials have provided detailed information on which drugs to use and when to use them. Despite these advances, however, thromboembolic disorders remain a major cause of morbidity and mortality. Therefore, the search for better targets and more potent antiplatelet, anticoagulant, and fibrinolytic drugs continues.