

LOVENOX® MOA Video

OVERVIEW

Lovenox® is a low molecular weight heparin with anti-thrombotic properties. It acts primarily on the coagulation factor Xa, and also, but to a lesser degree, on thrombin (factor IIa). Centered at the convergence of the intrinsic and extrinsic coagulation pathways, factor Xa transforms prothrombin into thrombin. Limiting this pivotal coagulation factor (Xa) Lovenox inhibits the subsequent step in the cascade, the explosive generation of thrombin. Lovenox also acts on thrombin, which is crucial for the formation of fibrin, an essential component of clots. Additional anti-thrombin activity of Lovenox limits the amplification of the coagulation cascade by thrombin. Lovenox joins with antithrombin III (ATIII) to form a complex which subsequently undergoes a conformational change.

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ANTI-FACTOR Xa

The Lovenox-ATIII complex inhibits factor Xa, thus preventing the formation of the XA/Va complex, and subsequently, preventing the conversion of prothrombin to thrombin by the Xa/Va complex.

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ANTI-FACTOR IIa

The Lovenox-ATIII complex prevents thrombin from converting fibrinogen to fibrin. The Lovenox-ATIII complex also prevents thrombin's amplification effect on the activation of platelets. Factor XI is activated by XIIa. However, an alternative pathway to the activation of XI is thrombin. The Lovenox-ATIII complex prevents thrombin's activation of factor XI. In addition, the Lovenox-ATIII complex prevents thrombin's amplification effect on the activation of factor VIII. Lovenox-ATIII also prevents thrombin's amplification effect on the activation of factor V. The Lovenox-ATIII complex also prevents thrombin's amplification effects on factor XIII, thus preventing stabilization of the clot.

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LOVENOX® Clotting Cascade Video

OVERVIEW

Clotting begins with some abnormalities in the blood or blood vessel. Subsequently, a sequential cascade of enzymatic reactions in the blood clotting factors is triggered. Platelets adhere to the surface and become activated. In this clotting cascade, the activated form of one blood factor catalyzes the activation of the next, and so on. There are two pathways in the cascade: the intrinsic and extrinsic, which unite at the common pathway. The process ends with the formation of a fibrin mesh that stabilizes the platelet plug over the damaged area.

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EXTRINSIC PATHWAY

The extrinsic pathway of the clotting cascade begins when trauma exposes a membrane lipoprotein called tissue factor (TF) which then attaches to factor VII. Factor VII becomes activated. The TF-VIIa complex then activates factor X. With the activation of factor X to Xa, the extrinsic pathway ends and the common pathway begins.

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INTRINSIC PATHWAY

The intrinsic pathway is initiated when collagen in the damaged wall is exposed to blood, triggering the activation of clotting factors. One of the first factors that is activated in the blood is factor XII. Activated factor XII (XIIa) then activates factor XI. Factor XIa then activates factor IX. Factor IXa combines with factor VIIIa to form a complex called the Tenase complex, which activates factor X. With the activation of factor X to Xa, the intrinsic pathway ends and the common pathway begins.

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COMMON PATHWAY

The extrinsic and intrinsic pathways converge to a common pathway after the activation of factor X. Activated factor X (Xa) and activated factor V (Va) form a complex which converts prothrombin (II) to thrombin (IIa). Next, thrombin converts fibrinogen to fibrin which creates a mesh-like web of

threads around the platelets. In addition to platelets, red blood cells may be trapped in the mesh. As these processes continue, the clot continues to grow.

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AMPLIFICATION

Although traditionally viewed as a cascade, recent studies have shown the intrinsic and extrinsic pathways to be more of a network, with numerous interactions between them. A number of positive feedback loops exist which serve to amplify the coagulation process. Primarily, thrombin amplifies the activation of several factors, including factors XI, VIII, V and XIII, as well as activating platelets.

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