Z-Medica Corporation is proud to be the leader in the rapidly growing area of products that stop moderate to severe bleeding. First to market with the original QuikClot® brand hemostatic agent, the company continues to develop new products, technologies and delivery mechanisms that make a difference wherever bleeding presents a problem. Our products make a difference around the world: from the battlefields of Iraq and Afghanistan, to the tactical law enforcement officer in Los Angeles, to the mass casualty preparedness teams in New York, to a mother in Illinois whose son's life was saved by QuikClot® 1st Response™ brand. Our technology has come a long way since its introduction in 2002, and along the way it has saved many lives.

HOW QUIKCLOT® BRAND PRODUCTS WORK TO STOP BLEEDING

Z-Medica provides products based on two separate platform technologies. While the two technologies are similar and overlap in their mechanisms of action, it makes sense to discuss each separately. This paper will address the **Kaolinite Based Products.**

Kaolinite is a white alumina silicate clay material that has a long history of uses in many applications, including ceramic, construction and medicine. Kaolin has been known for decades to activate blood clotting *in vitro*. The concept that blood and plasma develop clotting properties when exposed to glass or related materials has been known for about 50-60 years.[1,2] This process can take place even when calcium and platelets are absent.

In 1958 Dr. Margolis from Oxford, England published a paper titled "The Kaolin Clotting Time".[3] In this study he developed a system to diagnose plasma clotting defects by using recalcified plasma where the contact surface and the number of platelets were kept constant. In his study, Dr. Margolis quickly recognized that instead of relying on the walls of glass tubes as the activating surface, he could get the same activation effect by adding kaolin to the process.

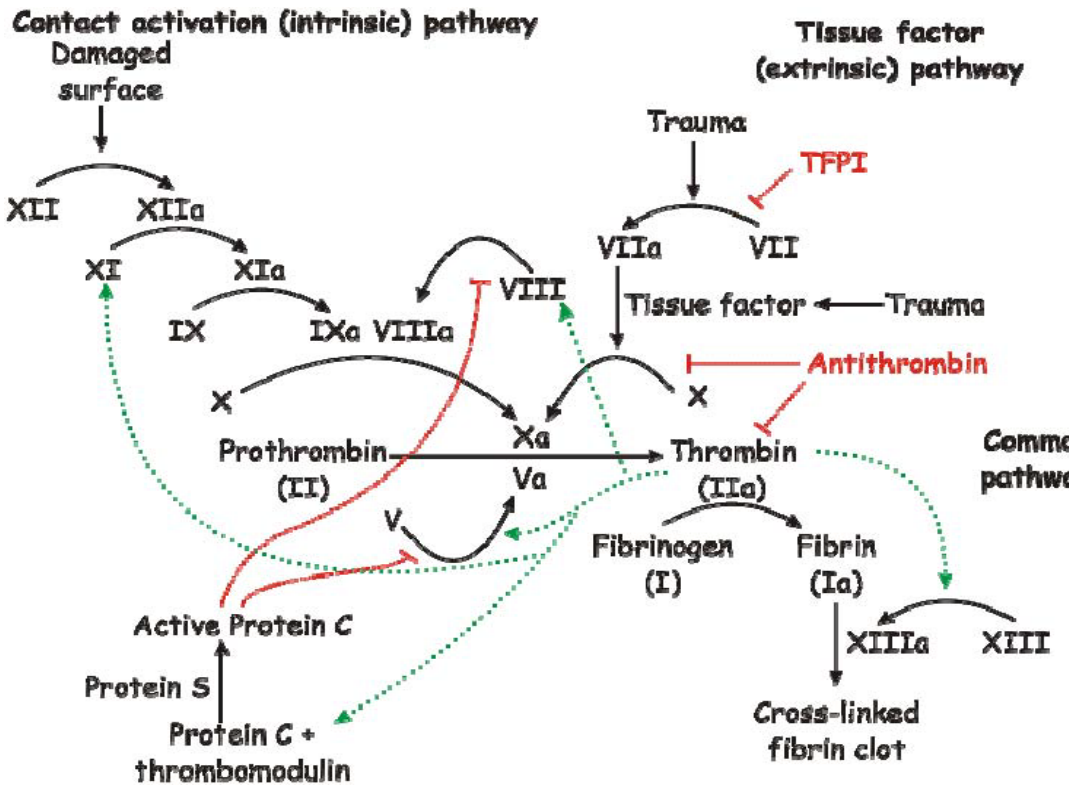
Further studies[4,5] discovered that exposure of human plasma to kaolin (or glass-like substances) initiates a group of reactions known as contact activation phase which include the activation of the intrinsic blood coagulation sequence, the kinin-forming pathway, the plasma fibrinolytic system and the generation of permeability factors.

Human plasma deficient in factor XII (Hageman factor), factor XI, prekallikrein and high molecular weight kininogen (HMK) lacks normal contact activation reactions. Therefore, interaction among these proteins is fundamentally important to contact clotting

The overall reaction can be simplified as follows:

- Contact between kaolin and Factor XII initiates the process.
- This reaction leads to the transformation of Factor XII, Factor XI and prekallikrein to their activated forms.
- The activation of Factor XII to factor XIIa is highly dependent on the presence of HMK and kaolin since both these compounds increase the susceptibility of Factor XII to plasma kallikrein.
- In addition, Factor XII can activate prekallikrein even without kaolin, but kaolin presence markedly enhance the rate of activation.[6-8]

- The activation of both Factor XI and XII will lead to the rest of the coagulation cascade as indicated in the picture.



In conclusion, HMK accelerates the surface-mediated activation of Factor XII by increasing the susceptibility of Factor XII to plasma kallikrein and the affinity of Factor XIIa to prekallikrein. Kaolin activates these processes by concentrating and organizing the different components on its negatively charged surface.

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