

Editorial

Thrombin: a crucial enzyme involving the blood coagulation

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Thrombin is a multifunctional serine protease formed from prothrombin and plays a central role in hemostasis by converting fibrinogen, a soluble protein in the blood into fibrin, an insoluble protein forming a mesh-like network of clots to stop bleeding. Thrombin also activates factor XIII to form factor XIIIa which catalyzes the cross-linkage of fibrin to form a mature clot.^{1,2} Thrombin helps to modulate downstream anticoagulants and the fibrinolytic pathway whenever coagulation is activated.³ Thrombin also affects on other cells including platelet activation, inflammatory cell chemotaxis, stimulation of endothelial cells changes as well as production of cytokines.⁴ Thrombin signaling is mediated by protease-activated receptor 1 (PAR-1), PAR-3 and PAR-4 which is expressed by platelets, endothelial cells, leucocytes and smooth muscle cells.⁵ Thrombin cleavage of PAR-1 or PAR-4 on platelets results in platelet activation, platelet aggregation and adhesion to endothelium.⁶ Thrombin activation of PAR-1 on endothelial cells leads to the release of von Willebrand factor and the expression of adhesion molecules including E-selectin, P-selectin, intracellular cell adhesion molecule-1 and vascular cell adhesion molecule -1 promoting adhesion, rolling, attachment and activation of platelets and leucocytes.^{7,8} Endothelial cell activation by thrombin also results in increased expression of cytokines, chemokines and gene related to hemostasis such as tissue factor and plasminogen activator inhibitor-1. Finally, thrombin activation results in increased permeability of endothelial cell monolayer, alteration of vascular tone and vascular remodeling.⁶

Human thrombin is commercially manufactured by chromatographic purification of prothrombin from cryo-poor plasma followed by activation with calcium chloride. Human thrombin is topically applied as an aid to hemostasis whenever oozing bleed and minor bleeding from capillaries and small venules are accessible and control of bleeding by standard surgical technique (such as suture, ligature or cautery) is ineffective or impractical.^{9,10} Another topical adhesive, called fibrin glue or fibrin sealant, imitates the final stage of coagulation. The glue consists of a solution of fibrinogen which is activated by adding thrombin and calcium chloride.¹¹ The resultant clot aids hemostasis and tissue sealing and is completely absorbed during wound healing without foreign body reaction or extensive fibrosis. Fibrinogen can be prepared from a single unit preparation of fresh frozen plasma or cryoprecipitate mixed with tranexamic acid in a 4:1 ratio.¹² An equal volume of fibrinogen and thrombin from two separate syringes will be applied to the operation site simultaneously. Then fibrin glue will form immediately as a local hemostasis which can be used in various surgeries such as cardiovascular, ear, nose, throat, neurosurgeries, orthopedic and dental procedures.¹³ At present, fibrin glue is commercially available but the price is high. For cost saving, different concentrations of thrombin have been evaluated revealing that concentrations of thrombin at 100, 250 and 500 IU/mL are suitable for providing local hemostasis to patients undergoing dental procedures, general and orthopedics surgeries, urological and neurological procedures, respectively.¹⁴

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Recently, the National Blood Centre, Thai Red Cross Society is able to prepare thrombin solution for services. Patients receiving various surgeries will benefit from an affordable fibrin glue product as an additional local hemostasis.

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