

BATROXOBIN VS THROMBIN

Thrombin and batroxobin are equivalent enzymes. Both act on the fibrinogen molecule, removing fibrinopeptides, hence inducing fibrin polymerization and gelation of PRP. Thrombin is the fibrinogen converting enzyme naturally occurring in mammals, while batroxobin is a purified enzyme from snake venom.

Thrombin has been described as a potential inducer of bovine-human cross-reacting antibodies to coagulation factor V and XI (Zehnder JL & Leung LLK. Blood 1990;76:2011-2016); this effect has never been observed using batroxobin.

Thrombin catalyzes the release of both fibrinopeptide A and B, while batroxobin removes only fibrinopeptide A (Hantgan R et al. Thromb Haemost 1980;44:119-124). Thrombin is active on several coagulation factors, which are not affected by batroxobin.

Thrombin activates platelets, while batroxobin does not affect the platelet function (Niewiarowski S et al. Am J Physiol 1980;229:737-745 Hantgan RR et al, Blood 1985, 65: 1299-1311) (**see figures 1 and 2**).

Thrombin is inhibited by heparin, while batroxobin is not (Stocker K et al. Toxicon 1982;20:265-273). ***This propriety is particularly useful when harvesting precursor cells-containing bone-marrow blood, which is usually harvested using heparin-citrate anticoagulant solution. Batroxobin is unique fibrinogen cleaving enzyme able to induce fast gelation of bone marrow-harvested blood samples.***

Batroxobin has been topically used for about 60 years because of its haemostatic properties. Batroxobin is still widely used in some countries as defibrinogenating agent to be infused *in vivo*, such as in emergency care for patients with acute non-hemorrhagic stroke. No safety-related issues were reported.

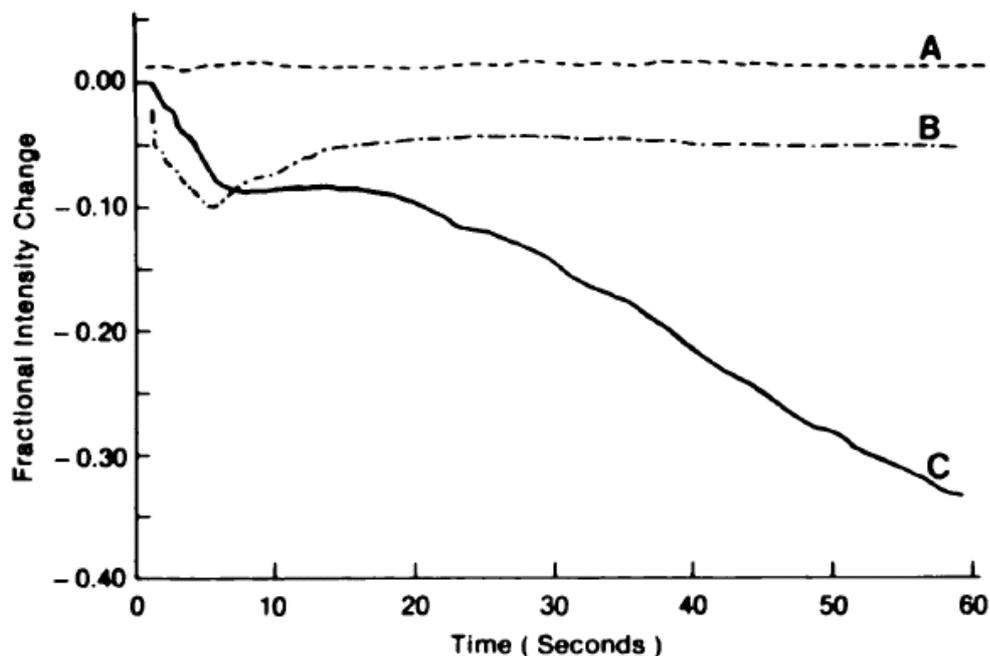


Figure 1. Platelet aggregation induced by A) batroxobin 0.7 U/mL; B) ACD 0.09 mmol/L; C) thrombin 0.2 U/mL (from Hantgan RR et al, Blood 1985, 65: 1299-1311)

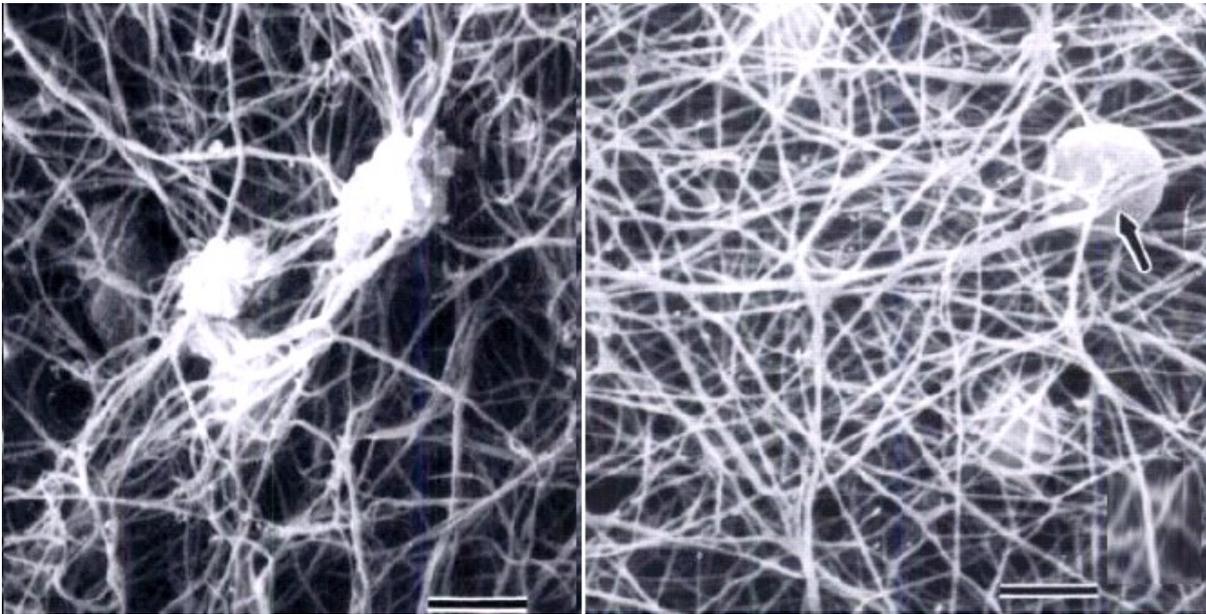


Figure 2. Thrombin-clotted fibrin clotted (thrombin 0.2 U/mL) and consequent platelet aggregation (left), batroxobin-clotted thrombin (batroxobin 0.7 U/mL) without platelet aggregation (right) (from Hantgan RR et al, Blood 1985, 65: 1299-1311)

These differences provide batroxobin with several advantages over thrombin in the production of autologous **platelet-gel**.

PLATELTEX® PROVIDES RAPID AND REPRODUCIBLE GELATION TIME

Platelet-rich plasma is converted in PRP-gel through induction of clot formation. In any other marketed device clotting is induced by addition of calcium or calcium plus thrombin. Thrombin may be either bovine, human, or autologous.

If calcium is used alone (not combined with clotting enzyme) clotting occurs slowly at 37C° taking more or less half an hour. Gelation time also depends on the amount of the autologous thrombin in the PRP sample.

Bovine thrombin has risks associated with its bovine origin. Furthermore, immunization to coagulation factor V is likely to occur. Marketed human thrombin is very expensive, taking also into account that, once opened, safety recommendations prescribe that a vial should not be used again for other patients.

PLATELTEX® provides pretitred (5 BU) batroxobin and calcium. Batroxobin is heparin insensitive and provide rapid and reproducible complete gelation in a few minutes (8-10 minutes). Gelation time is not dependent upon the concentration of autologous thrombin, fibrinogen, and platelets within the PRP sample. Furthermore, batroxobin provides slower and more controlled release of growth factors since platelets does not become activated during the clotting phase. Batroxobin and calcium provide formation of a stable and easy-to-handle gel in a mean time of 8 minutes. All of this is important in medical and surgical practice which needs well scheduled working time and maximization of growth factor activity.

