

# Protégé Biomedical, LLC

Protégé Biomedical, LLC is a medical device company with a unique line of hemostatic device products. The company was formed to develop patented discoveries into novel hemostatic products for human use that stop bleeding faster, safer, and in a cost-effective manner to meet market needs.

## Coagulants for External and Surgical Applications

Protégé's first product has been used successfully in a variety of large and small animals to stop bleeding from external wounds, deep wounds involving arterial lacerations, and internal surgical wounds. It allows healing of wounds without the need to remove the product from the wound site after bleeding has stopped. Development of various Protégé products for human use is currently under way.

## Overview of Protégé Technology

The product technology is a proprietary, specifically processed, mixture of the minerals Mullite and aluminum sulfate. This composition yields a multi-action process that includes the 1) recruitment of cells (flocculation), 2) immediate initiation of the Factor XII coagulation cascade, 3) vessel constriction and 4) plasma absorption that collectively accelerates the clotting of blood to rapidly stop bleeding from wounds. It works on minor surface wounds and deep cuts or puncture wounds, including those that involve arterial lacerations.

The technology confers many of the characteristics of an ideal coagulant, including:

1. Rapid and convenient application
2. Quick clotting action
3. Biocompatibility
4. Film formation (helps protect the wound site)
5. Effectiveness in liquid
6. Localized action
7. Vaso-constriction
8. Complete cessation of bleeding

**Table 1:** Comparison to Competitive Products

Protégé Product Technology Versus Other Hemostasis Products							
Product Name	Description	Biocompatible <sup>1</sup>	Quick Acting <sup>2</sup>	Large Wounds	Effective in Liquid	Localized Action	Physical Form (at)
<b>Protégé Biomedical:</b> -Fermata™ (humans) -ClotIt® (animals)	Factor XII activation, flocculation	Yes	< 10s	Yes	Yes	Yes	Powder
<b>Z-Medica:</b> -Quik-Clot™	Factor XII activation, absorption of blood	Yes	> 60s	Yes	No	Yes	Impregnated gauze pad
<b>Bard Davol:</b> -Arista™ -Hemablock™	Blood absorption, viscosity increase	Yes	> 60s	Yes	No	Yes	Powder
<b>GimBorn:</b> -KwikStop Styptic Powder	Vaso-constriction	No	< 10s (temporary)	No	No	Yes	Powder

<sup>1</sup> Biocompatible means: doesn't harm tissue, non-toxic, non-irritating.  
<sup>2</sup> Times listed are taken from experiments described on the next page.



## How Protégé Biomedical's Technology Works

Protégé products work by acting on both the biochemical (soluble factors) and cellular parts of the hemostasis system. The Mullite component activates soluble Factor XII of the intrinsic coagulation pathway. The aluminum sulfate causes an ionic attraction flocculation (clumping together) of the blood cells bringing the platelets into closer than normal proximity. Since an early step in coagulation is the formation of platelet aggregates, which requires platelets to be close to each other, the flocculation of platelets by Protégé's technology means the overall effect is to accelerate the formation of a clot and greatly decrease the clotting time.

## Independent Laboratory Studies

### Impedance Aggregometry

A study was performed by an independent laboratory to evaluate the efficacy of Protégé Biomedical's technology versus some of the most commonly used hemostatic products. The effects of Protégé's components, individually and in combination, on blood clot formation were studied using impedance aggregometry (IA). IA measures clot formation by following the change in impedance of a blood sample over time, after treatment with hemostatic agent. As a clot forms and more mass is added to it by way of recruiting more platelets and red blood cells (RBCs), the impedance of the blood sample increases. The faster the increase in impedance, the more rapid the clot is forming. Also, the higher the final impedance of the sample, the more massive and greater the strength of the clot.

**Figure 1:** Progression of clot formation over time with four different hemostatic formulations. Impedance of a blood sample was followed over time from just before to 90 seconds after adding hemostatic agent. The results are plotted as degree of clotting (vertical axis) vs. time (seconds). The degree of clotting is a percentage of the maximum Protégé value. The **black arrow** points to the time of addition of the hemostatic agent(s) while the **red arrow** points to the impedance value at which a solid clot was achieved. The term "solid clot" refers to a clot that could not be shaken out of the impedance cuvette except by vigorous shaking. Such shaking resulted in the removal of the clot as a single large mass.

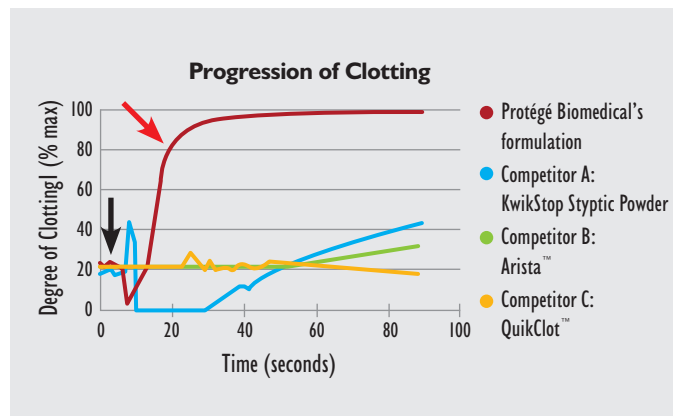
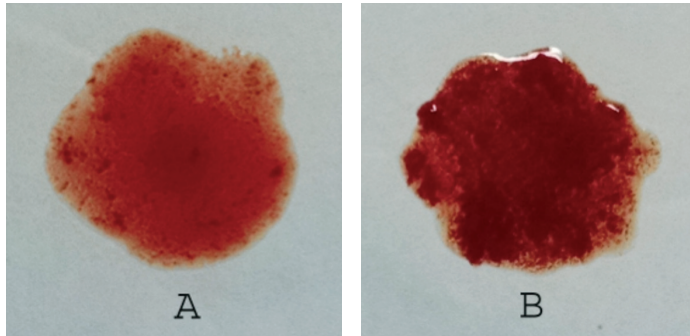


Figure 1 demonstrates that Protégé Biomedical's formulation begins clotting within a couple of seconds after contacting the blood and forms a solid clot within 15 seconds. Clot mass continues to increase along with the impedance for up to about 90 seconds. The Styptic, Quick-Clot™, and Arista™ all require a much longer time to initiate a clot (25 to 50 seconds) and do not reach the same degree of clotting as Protégé's formulation, with the Styptic and Arista™ reaching degrees of clotting of 40% and 30% respectively, within the time frame of this study. The response of Arista™ is unsurprising since it employs a different mechanism of action that does not involve flocculation or strong activation of soluble clotting factors. This is the reason for the claim that Arista™ **controls** bleeding as contrasted with Protégé's formulation which **stops** bleeding. In any case, it is immediately apparent that in our experimental system the dual action of Protégé's formulation initiates clotting sooner, and more rapidly completes clotting, compared to any of the other hemostatic agents tested. Protégé is successfully able to stop the bleeding where others are slowing. Protégé also produces a denser and stronger clot than the other coagulants.

## Flocculation

**Figure 2:** Effect of aluminum sulfate on whole blood is flocculation (clumping) of blood cells (A). Effects of the combination of aluminum sulfate and mullite (Protégé) is first flocculation followed by clotting (B). The initial phase of Protégé Biomedical's technology is flocculation which brings blood cells (platelets, RBCs & WBCs) in close proximity followed by the rapid activation of the intrinsic coagulation pathway. Activation of the intrinsic coagulation pathway results in the formation of thrombin which in turn activates platelets and leads to the generation of fibrin, all of which are involved in the formation of the final clot. The speed of this process directly effects the speed at which a clot is formed. The combination of flocculation and activation results in a very rapid generation of a stable clot.

### Factor XII



## Summary

Protégé Biomedical's formulation, mechanism of action, and flexible format gives it characteristics that make it superior to competitive products, specifically:

1. Speed of clotting – lowers blood loss and decreases total procedural time leading to better outcomes.
2. Cessation of bleeding – bleeding stops and does not recur, because of the density and strength of the clot.
3. Effectiveness in liquid – effect not diluted out, works when there is a lot of blood or other fluid at the site.
4. Film formation – provides a barrier, helping to protect the wound.
5. The multi-action and efficacy of Protégé Biomedical's formulation in liquid allows a broader range of applications, allowing the development of multiple product configurations for a larger range of internal and external indications.

## Conclusion

Protégé Biomedical's formulation stops bleeding fast, forming a solid clot within 15 seconds. The proprietary mixture of the mineral mullite and aluminum sulfate are biocompatible and effective for wounds of all sizes, from minor surface cuts to deep lacerations or puncture wounds. The multi-action mechanism of action that includes flocculation (cell recruitment), immediate initiation of the coagulation cascade, vessel constriction, and plasma absorption results in a unique and highly efficacious product that is indicated for a broad range of medical applications. Clinical evidence demonstrates that Protégé technology is superior to competitive products; The mineral compound, combined with flocculation of platelets by Protégé technology accelerates the formation of the clot and greatly decreases the clotting time, forming a complete and solid clot within 15 seconds, 5 times faster and a much greater degree of efficacy than other hemostasis products. In addition, it produces a denser and stronger clot than the other coagulants, to aid in optimal healing.

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