

VITAGEL® BIBLIOGRAPHY

Clinical Publications:

1. Bochicchio G, Dunne J, Bochicchio K, Scalea T. ***The combination of platelet-enriched autologous plasma with bovine collagen and thrombin decreases the need for multiple blood transfusions in trauma patients with retroperitoneal bleeding.*** J Trauma. 2004;56:76-79.
Study Design:
 - Non-randomized, Prospective; 78 Patients
 - Patients undergoing immediate surgical exploration during which retroperitoneal bleeding was encountered**Test Materials:**
 - Gelfoam/Thrombin (Control); 40 Patients
 - CoStasis (Vitagel); 38 Patients
2. Bochicchio GV, Scalea TM: ***Acute caval perforation by an inferior vena cava filter in a multitrauma patient: Hemostatic control with a new surgical hemostat.*** J Trauma. 2001;51(5):991-993.
Study Design
 - Case Study
 - Trauma patient received IVC strut which migrated to cause multiple actively bleeding perforations**Test Materials:**
 - CoStasis (Vitagel); 1 Patient**Outcome Measures:**
 - Achievement of hemostasis**Results:**
 - Gelatinous plug immediately formed and hemostasis obtained
 - No further bleeding noted 24 hours later during re-exploration
3. Buncke GM, Sherman R. ***CoStasis provides superior control of diffuse bleeding at muscle-flap donor sites, compared to manual compression.*** J Recon Micro. 2000;16(7):557-561.
Study Design:
 - Randomized, Prospective; 47 Patients
 - Control of bleeding at donor site for surgical harvesting of large and medium size muscle flaps**Test Materials:**
 - Instat Collagen Sponge applied with manual pressure (Control); 25 Patients
 - CoStasis (Vitagel); 22 Patients**Outcome Measures:**
 - Hemostatic success (bleeding ceased within 10 minutes)
 - Time to controlled bleeding
 - Time to hemostasis

Results:

- 100% of the Vitagel group (22/22) reached hemostasis within 10 minutes (vs. 48% for the control group(12/25))
- Median time to controlled bleeding was 22 seconds for the Vitagel group (vs. greater than 600 seconds for the control group)
- Median time to complete hemostasis was 67 seconds for the Vitagel group (vs. greater than 600 seconds for the control group)
- 60% of the Vitagel group reached hemostasis within 2 minutes (vs. 5% in the control group)

4. Chapman WC, Clavien PA, Fung J, Khanna A and Bonham A. **Effective control of hepatic bleeding with a novel collagen-based composite combined with autologous plasma.** Arch Surg. 2000;135:1200-1204.

Study Design:

- Randomized, Prospective; 67 Patients
- Raw, diffusely bleeding liver sites exposed by hemi-hepatectomy or segmental resection

Test Materials:

- Instat collagen sponge applied with manual pressure (Control); 29 patients
- CoStasis (Vitagel); 38 patients

Outcome Measures:

- Hemostatic Success (bleeding ceased within 10 minutes)
- Time to complete hemostasis
- Time to controlled bleeding

Results:

- 100% of the Vitagel group (38/38) reached hemostasis within 10 minutes (vs. 69% of the control group (20/29))
- Median time to controlled bleeding was approximately 4 times longer for the control group (250 seconds vs. 62 seconds)
- Median time to complete hemostasis was 150 seconds in the Vitagel group vs. 360 seconds in the control group

5. Chapman WC, Wren SM, Lebovic GS, Malawar M, Sherman R and Block JE. **Effective management of bleeding during tumor resection with a collagen-based hemostatic agent.** Am Surg. 2002; 68(9):802-807.

Study Design:

- Randomized, Prospective; 53 patients
- Hemostatic control at the raw diffusely bleeding tumor bed after surgical tumor resection

Test Materials:

- Instat Collagen Sponge applied with manual pressure (Control); 30 Patients
- CoStasis (Vitagel); 23 Patients

Outcome Measures:

- Time to hemostasis

Results:

- 100% of the Vitagel group (23/23) reached hemostasis within 10 minutes (vs. 70% for the control group (21/30))
- Median time to complete hemostasis was 78 seconds for the Vitagel group (vs. 243 seconds for the control group)
- 80% of the Vitagel group reached hemostasis within 2 minutes (vs. 35% of the control group)

6. CoStasis: **A next generation hemostat with visible patient benefits.** Medco Forum. 2002;9(11).
- Anecdotal discussion of the benefits associated with the use of Vitagel in patients undergoing plastic surgery.
7. CoStasis Multi-center Collaborative Writing Committee. **A novel collagen-based composite offers effective hemostasis for multiple surgical indications: Results of a randomized controlled trial.** Surgery. 2001; 129(4): 445-450.
- Study Design:**
- Randomized, Prospective; 318 patients
 - Determination of safety and efficacy during general, hepatic, cardiac, and orthopedic surgeries
- Test Materials:**
- Instat Collagen Sponge applied with manual pressure (Control in general, hepatic, and orthopedic surgeries); 114 patients
 - Gauze and Sponges (Control in cardiac cases); 37 patients
 - CoStasis (Vitagel); 130 patients (general, hepatic, orthopedic) and 37 patients (cardiac)
- Outcome Measures:**
- Time to controlled bleeding (slight oozing)
 - Time to complete hemostasis – bleeding ceased within 10 minutes (general, hepatic, and orthopedic)
 - Time to complete hemostasis – bleeding ceased within 3 minutes (cardiac)
- Results:**
- General: Vitagel effective in 97% (77/79) of patients (vs. 65% (49/75) for the control)
 - Hepatic: Vitagel effective in 97% (38/39) of patients (vs. 70% (20/29) for the control)
 - Orthopedic: Vitagel effective in 83% (10/12) of patients (vs. 20% (2/10) for the control)
 - Cardiac: Vitagel effective in 76% (28/37) of patients (vs. 46% (17/37) for the control)
 - Median time to complete hemostasis was 75 seconds in the Vitagel group (vs. 252 seconds in the control group)
 - Median time to controlled bleeding was 42 seconds in the Vitagel group (vs. 150 seconds in the control group)
8. Dunne JR, Bochicchio GV, Scalea TM: **A novel approach to the treatment of gunshot injuries to the sacrum.** Amer Sur. 2003;69:91-94.
- Study Design:**
- Case Study – 2 Patients
 - Bleeding of sacrum calcenous bone due to a gunshot injury
- Test Materials:**
- Gelfoam/Thrombin; 2 Patients
 - Surgicel; 2 Patients
 - CoStasis (Vitagel); 2 Patients
- Outcome Measures:**
- Achievement of hemostasis
- Results:**
- The injury sites on both patients achieved hemostasis with the application of Vitagel. Hemostasis did not occur with the application of Gelfoam/Thrombin or Surgicel.

9. Jen A, Bhayani R, Ahn J. **CoStasis surgical hemostat in endoscopic sinus surgery**. San Diego, CA: American Academy of Otolaryngology – Head and Neck Surgery; Sept 22-25, 2002.

Study Design:

- Controlled, prospective; 40 patients
- Control of postoperative bleeding following septoplasty, turbinectomy, and endoscopic sinus surgery

Test Materials:

- Nasal packing (Control); 20 patients
- CoStasis (Vitagel); 20 patients

Outcome Measures:

- Control of postoperative bleeding
- Patient discomfort

Results:

- No postoperative bleeding complications in either group
- Vitagel treated patients had significantly decreased postoperative nasal congestion, pain, and discomfort compared to those who received nasal packing

10. Milkes DE, Friedland S, Lin OS, Reid TR, Soetikno RM. **A novel method to control severe upper GI bleeding from metastatic cancer with a hemostatic sealant: The CoStasis Surgical Hemostat**. *Gastrointestinal Endoscopy*. 2002;55(6):735-740.

Study Design:

- Case Study
- Severe bleeding in the GI tract following treatment for metastatic lung cancer

Test Materials:

- CoStasis (Vitagel); 2 patients

Outcome Measures:

- Control of bleeding in patients with metastatic lung cancer to the upper GI tract

Results:

- Case 1: CoStasis (Vitagel) achieved cessation of bleeding and long-term hemostatic control
- Case 2: CoStasis (Vitagel) provided short-term hemostatic control that enabled additional chemotherapy

11. Nelson PA, Powers JN, Estridge TD, Elder EA, Alea AD, Sidhu PK, Sehl LC, DeLustro FA: **Serological analysis of patients treated with a new surgical hemostat containing bovine proteins and autologous plasma**. *J Biomed Mater Res (Appl Biomater)*. 2001:710-719.

Study Design:

- Prospective, Randomized; 176 patients
- Assessment of immune response of CoStasis-treated patients and control patients
- Comparison with immunological results previously reported

Test Materials:

- Instat Collagen sponge (non-cardiac), tamponade and/or cautery (cardiac); 84 patients
- CoStasis (Vitagel); 92 patients

Outcome Measures:

- Presence of antibodies to bovine collagen, bovine thrombin, and bovine FV/Va (relation to adverse events)
- Purity comparison between commercially available thrombins

Results:

- Antibody response with CoStasis group were similar to reported literature for all antigens screened and were not associated with any adverse reactions
- Thrombin present in CoStasis has greater purity and lower bovine FVa and FXa than other commercially available thrombin.

12. Sherman R, Chapman WC, Hannon G, Block JE. **Control of bone bleeding at the sternum and iliac crest donor sites using a collagen-based composite combined with autologous plasma: results of a randomized controlled trial.** Orthopedics. 2001;24(2):137-141.

Study Design:

- Prospective, Randomized; 83 patients
- Control of bleeding at the sternal edge site following sternotomy and the iliac crest donor site following bone graft harvest

Test Materials:

- Electrocautery (control); 28 patients (sternal)
- Manual compression with collagen sponge (control); 6 patients (sternal) & 7 patients (iliac crest)
- DynaStat (Vitagel); 30 patients (sternal) & 12 patients (iliac crest)

Outcome Measures:

- Time to controlled bleeding (slight oozing)
- Time to complete hemostasis

Results:

- 83% of the Vitagel group (25/30) achieved hemostasis within 3 minutes (vs. 44% for the control groups (15/34)) at the sternal sites
- 83% of the Vitagel group (10/12) achieved hemostasis within 10 minutes (vs. 29% for the control groups (2/7)) at the iliac crest sites
- Average time to controlled bleeding at the sternal edge was 3 times longer for the control patients (125 seconds vs. 43 seconds)
- Median time to controlled bleeding in the ilium was 42 seconds for the Vitagel group (vs. >600 seconds for the control group)

13. Thibodeaux KT, Lorio MP, Block JE. **Intraoperative hemostasis during spinal reconstructive procedures.** Orthopedics. 2003;26(4):413-414.

Study Design:

- Non-randomized, Prospective; 19 patients
- Patients undergoing spinal reconstructive procedures in the thoracolumbar region where intraoperative bleeding was expected to be significant

Test Materials:

- Manual compression with gauze and sponges (control); 9 patients
- CoStasis (Vitagel); 10 patients

Outcome Measures:

- Time to hemostasis (immediate or not)
- Total volume of operative blood loss
- Operative Duration

Results:

- All Vitagel subjects (10/10) achieved immediate hemostasis vs. none of the control group (0/9)
- Average perioperative blood loss was twice as great in the control group (1322 mL) vs. the Vitagel group (685 mL)

14. Turley K. ***Aortic homograft root replacement for failed freehand homograft aortic valve: effectiveness of a collagen/thrombin/plasma composite hemostat in the setting of technically complicated homograft root anastomosis.*** 1999.
Available at <http://www.hsforum.com/vol2/issue2/1999-0120.html>.

Study Design:

- Case Study – 1 patient
- Patient required aortic homograft root replacement

Test Materials:

- Tissue Glue
- Gelfoam/Thrombin
- Surgicel
- CoStasis (Vitagel)

Outcome Measures:

- Hemostasis at the anastomosis site (coagulopathic patient, heparinized and on bypass for 469 minutes)

Results:

- Vitagel effectively allowed the anastomosis site to achieve hemostasis. Vitagel was on trial and used on a “compassionate use basis” after tissue glue, Gelfoam/thrombin, and Surgicel were ineffective. Patient was successfully weaned from bypass without incident.

Preclinical Publications:

15. Prior JJ, Powers N, DeLustro F. ***Efficacy of a novel hemostatic agent in animal models of impaired hemostasis.*** J Biomed Mat Res. 2000;53:252-257.

Study Design:

- Pre-Clinical Study; Adult New Zealand White Rabbits
- Evaluate hemostatic performance in conditions mimicking patients with normal coagulation (no treatment) and significantly compromised coagulation (aspirin treated and heparin treated)

Test Materials:

- Instat Collagen sponge
- Fibrin Sealant (unidentified)
- CoStasis (Vitagel)
- No hemostat

Outcome Measures:

- Platelet aggregation percentage before and after anticoagulation treatment
- Mean time to hemostasis
- Mean blood loss

Results:

- Under normal coagulation: Vitagel achieved hemostasis significantly faster than the other hemostatic groups. Blood loss was also significantly less in the Vitagel group.
- Under aspirin anticoagulation: Vitagel achieved hemostasis significantly faster than the other hemostatic groups. Blood loss was also significantly less in the Vitagel group. There was no difference in time to hemostasis in the Vitagel groups between untreated and aspirin treated rabbits.
- Under heparin anticoagulation: Vitagel achieved hemostasis faster than the other hemostatic groups. Blood loss was also less in the Vitagel group.

16. Prior JJ, Wallace DG, Harner A, Powers N. ***A sprayable hemostat containing fibrillar collagen, bovine thrombin, and autologous plasma.*** Ann Thorac Surg.1999;68:479-485.

Study Design:

- Preclinical Study; Adult New Zealand White Rabbits
- Evaluation of in vivo hemostatic performance in a bleeding rabbit kidney and spleen model

Test Materials:

- Instat collagen sponge
- Investigational fibrin sealant (unidentified)
- Tisseel
- CoStasis (Vitagel)

Outcome Measures:

- Hemostatic performance under normal conditions
- Hemostatic performance with depleted fibrinogen
- Hemostatic performance with depleted platelets
- Platelet aggregating properties

Results:

- Vitagel under normal conditions had the fastest mean and median times to hemostasis of the four materials tested in both the spleen and kidney.
- Vitagel was the only material to achieve complete hemostasis in 100% of the sites in under 2 minutes.
- Vitagel was found to be effective when either platelets or fibrinogen were depleted by 50%.
- Collagen shown to have a fibrillar structure and the ability to aggregate platelets.

17. Turner AS, Parker D, Egbert B, Maroney M, Armstrong R, Powers N. ***Evaluation of a novel hemostatic device in an ovine parenchymal organ bleeding model of normal and impaired hemostasis.***

J Biomed Mat Res. 2002;63:37-47.

Study Design:

- Preclinical Study; Sheep
- Control of bleeding from parenchymal organ injuries under normal and impaired hemostatic conditions

Test Materials:

- Investigational Fibrin Sealant 1 (unidentified); Control of bleeding under normal conditions
- Investigational Fibrin Sealant 2 (unidentified); Control of bleeding under impaired conditions
- Collagen sponge (unidentified); Control of bleeding under normal conditions
- CoStasis (Vitagel); Control of bleeding under normal and impaired conditions

Outcome Measures:

- Time to hemostasis
- Total Blood Loss

Results:

- In all surgical sites combined, under normal conditions, Vitagel had significantly faster times to hemostasis than the other materials tested.
- In all surgical sites combined, under normal conditions, the collagen sponge had 32% higher average blood loss and Investigational Fibrin Sealant 1 had 44% higher average blood loss compared to Vitagel.
- In animals treated with heparin, in all surgical sites, the mean time to hemostasis was comparable between Vitagel and Investigational Fibrin Sealant 2.
- Vitagel blood loss was not increased in heparin treated animals, unlike Investigation Fibrin Sealant 2 which experienced a significant increase.
- Vitagel treated sites demonstrated higher levels of tissue repair (lower inflammation, more extensive tissue repair, and less residual implant material) compared to the fibrin sealant or the collagen sponge treated sites.

White Papers:

18. Berkman EF. ***The effect of unilateral application of a local hemostatic agent in a bilateral total knee arthroplasty.***

Study Design:

- Case Study – 1 Patient
- Patient undergoing bilateral Total Knee Arthroplasty

Test Materials:

- No treatment (control) – left knee
- Vitagel - right knee

Outcome Measures:

- Ecchymosis
- Swelling
- Active bleeding
- Infection

Results:

- Vitagel treated knee experienced decreased postoperative ecchymosis and swelling in comparison to the untreated knee.