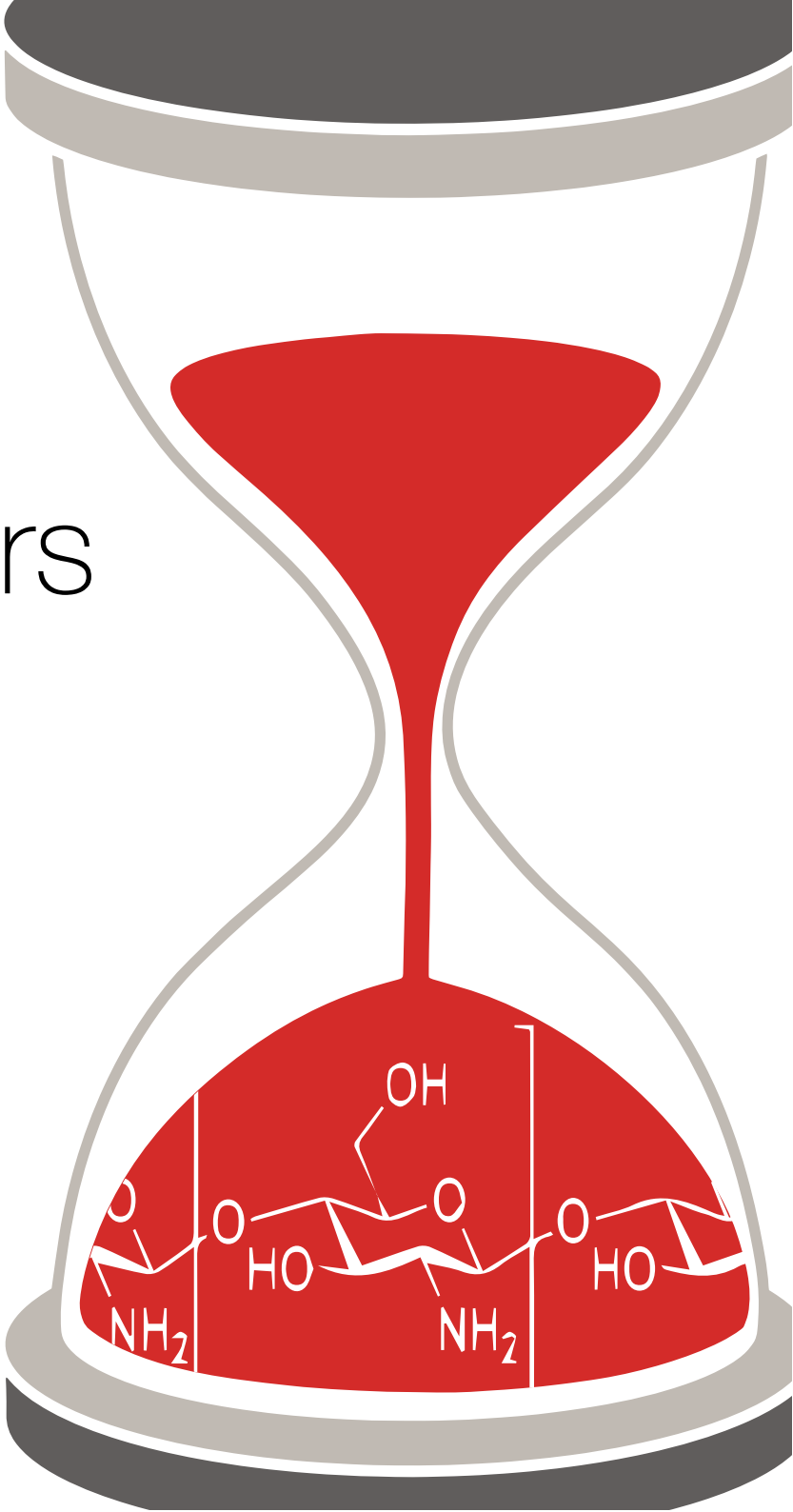
When
# time: matters

# science: matters




axiostat®
stops bleeding, instantly

Scientific Compendium


EMERGENCY | MILITARY | VASCULAR | DENTAL

axiostat®

*stops bleeding, instantly*

**ADVANCED HAEMOSTATIC DRESSING | STOPS SEVERE EXTERNAL BLEEDING | 100% CHITOSAN**

Award winning product Axiostat®, is a clinically validated sterile haemostatic dressing specifically designed to stop profuse bleeding, instantly. Axiostat® is based on a patented novel biomaterial - chitosan, which has been proven as an excellent haemostatic agent. Axiostat® is your solution to severe bleeding in Emergency Trauma, Interventional cardiology, Dental, Military bleeding situations.

Chitosan has been in use for medical applications since the beginning of the 21st century. Axio uses proprietary technology to filter & purify chitosan and the result is an end product without any variation in performance or safety features. Particularly, Axio technology uses low polydispersity, high molecular weight material and which is a pure, 100% chitosan, quick-acting Haemostat.

Axio products are constantly benchmarked with globally harmonised standards. Our products comply with ASTM standards and are made in GMP, ISO 13485 approved facilities.

**Device** Description

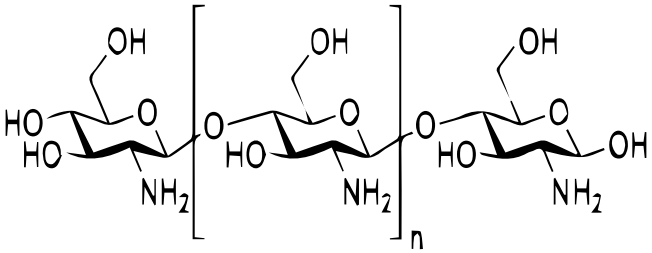
# Chitosan

Chitosan is a linear polysaccharide consisting of glucosamine and N-acetyl glucosamine chains and is derived mainly from shellfish. It has been used in many technical applications such as medical products, water purification, in cosmetics and as a fat-binding weight control product. Cationic nature of chitosan gives this polymer a mucoadhesive property which can be further activated for wound care applications.

Chitosan salts are used as a matrix or scaffold material as well as in non-parenteral delivery systems for challenging drugs.

## Characteristics of Chitosan

- Biocompatible
- Bioadhesive
- 100% Natural
- 0% Protein
- No exothermic reaction
- Easily broken down to glucosamine




**Active Ingredient** Information

# Chitosan as a Hemostatic Agent: Current State

European Journal of Medicine. Series B, 2015, Vol.(2), Is. 1

**[1] Maksym V. Pogorielov [2] Vitalii Z. Sikora**

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**Abstract:** Bleeding is the one of leading cause of death after civil and combat trauma and affective hemostasis is a key challenge for emergency medicine. Current review focused on modern topical hemostatic agents based on chitosan. This article prescribes mechanism of action of chitosan and its interaction with blood plasma, erythrocytes and platelets. Review classified all topical hemostatic agents and show advantage of chitosan-based dressing. Also it gives perspectives in hemostatic dressing research.

# Chitosan - Derivatives as hemostatic agents: Their Role in Tissue Regeneration

Regenerative Research 1(1) 2012 38-46

**Mercy HP[1], Halim AS*[1], Hussein AR[2]**

1) Reconstructive Sciences Unit, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.

2) Department of Hematology, School of Medical Sciences, Universiti Sains Malaysia 16150 Kubang Kerian, Kelantan, Malaysia.

**Abstract:** In a recent discovery in the field of tissue regeneration, chitosan, a natural polysaccharide, received attention as a hemostatic agent due to its character to function independently on platelets to achieve hemostasis. In our present review, we highlight the composition and chemical structure of chitosan and its application in the current medical breakthrough, its reactions on erythrocytes and platelets, and its use as a wound dressing to promote tissue regeneration.

# Mechanisms of Poly-N-Acetyl Glucosamine Polymer–Mediated Hemostasis: Platelet Interactions

The Journal of TRAUMA Injury, Infection, and Critical Care J Trauma. 2004;57:S13–S21.

**Hemant S. Thatte, PhD, Sofija Zagarins,**
**Shukri F. Khuri, MD, and Thomas H. Fischer, PhD**

**Background:** Investigations were performed to determine whether poly-N-acetyl glucosamine (p-GlcNAc) induces hemostasis by the activation of platelets.

**Methods:** Platelets were isolated from human blood, fixed in the presence poly-N-acetyl glucosamine fibers, and visualized with scanning electron microscopy. Platelet activation surface markers were measured by fluorescence multiphoton microscopy. Platelet aggregation in the presence of p-GlcNAc fibers and integrin receptor blockers was measured.

**Results:** Scanning electron microscopy indicated that contact of platelets with poly-N-acetyl glucosamine fibers resulted in platelet activation. Fluorescent microscopy showed that contact of platelets with the marine polymer increased intracellular levels of free calcium and resulted in surface exposure of platelet phosphatidylserine, P selectin, and the $\alpha_{IIb\beta3}$ integrin. Antibody inhibitors of the platelet $\alpha_{IIb\beta3}$ integrin inhibited p-GlcNAc to stimulate fibrin polymerization.

**Conclusion:** Poly-N-acetyl glucosamine fiber material promotes hemostasis by the activation of platelets.

# A Special Report on the Chitosan-based Hemostatic Dressing: Experience in Current Combat Operations

The Journal of TRAUMA Injury, Infection, and Critical Care J Trauma. 2006;60:655– 658.

**Ian Wedmore, MD, John G. McManus, MD, MCR,**
**Anthony E. Pusateri, PhD, and John B. Holcomb, MD**

**Background:** Hemorrhage remains a leading cause of death in both civilian and military trauma patients. The HemCon chitosan-based hemostatic dressing is approved by the US Food and Drug Administration (FDA) for haemorrhage control. Animal data have shown the HemCon dressing to reduce haemorrhage and improve survival. The purpose of this article is to report preliminary results of the hemostatic efficacy of the HemCon dressing used in the prehospital setting on combat casualties.

**Methods:** A request for case information on use of HemCon dressings in Operation Iraqi Freedom and Operation Enduring Freedom was sent to deployed Special Forces combat medics, physicians, and physician assistants.

**Results:** Sixty-eight uses of the HemCon dressing were reported and reviewed by two US Army physicians. Four of the 68 cases were determined duplicative resulting in a total of 64 combat uses. Dressings were utilized externally on the chest, groin, buttock, and abdomen in 25 cases; on extremities in 35 cases; and on neck or facial wounds in 4 cases. In 66% of cases, dressings were utilized following gauze failure and were 100% successful. In 62 (97%) of the cases, the use of the HemCon dressing resulted in cessation of bleeding or improvement in hemostasis. There were two reported dressing failures that occurred with blind application of bandages up into large cavitational injuries. Dressings were reported to be most useful on areas where tourniquets could not be applied to control bleeding. The dressings were reported to be most difficult to use in extremity injuries where they could not be placed easily onto or into the wounds. No complications or adverse events were reported.

**Conclusion**: This report on the field use of the HemCon dressing by medics suggests that it is a useful hemostatic dressing for prehospital combat casualties and supports further study to confirm efficacy.

Active Ingredient Information

# Management of External Hemorrhage in Tactical Combat Casualty Care: Chitosan-Based Hemostatic Gauze Dressings

TCCC Guidelines – Change 13-05

**Brad L. Bennett, PhD, NREMT-P; Lanny F. Littlejohn, MD; Bijan S. Kheirabadi, PhD; Frank K. Butler, MD; Russ S. Kotwal, MD; Michael A. Dubick, PhD; Jeffrey A. Bailey, MD**

**Abstract:** Hemorrhage remains the leading cause of combat death and a major cause of death from potentially survivable injuries. Great strides have been made in controlling extremity hemorrhage with tourniquets, but not all injuries are amenable to tourniquet application. Topical hemostatic agents and dressings have also contributed to success in controlling extremity and compressible junctional hemorrhage, and their efficacy continues to increase as enhanced products are developed. Since the addition of Combat GauzeTM (Z-Medica Corporation, Wallingford, CT, USA; http://www.z-medica.com/) in April 2008 to the Tactical Combat Casualty Care (TCCC) Guidelines, there are consistent data from animal studies of severe hemorrhage that chitosan-based hemostatic gauze dressings developed for battlefield application are, at least, equally efficacious as Combat Gauze. Successful outcomes are also reported using newer chitosan-based dressings in civilian hospital-based surgical case reports and prehospital (battlefield) case reports and series. Additionally, there have been no noted complications or safety concerns in these cases or across many years of chitosan-based hemostatic dressing use in both the military and civilian prehospital sectors. Consequently, after a decade of clinical use, there is added benefit and a good safety record for using chitosan-based gauze dressings. For these reasons, many specific US military Special Operations Forces, NATO militaries, and emergency medical services (EMS) and law enforcement agencies have already implemented the widespread use of these new recommended chitosan-based hemostatic dressings. Based on the past battlefield success, this report proposes to keep Combat Gauze as the hemostatic dressing of choice along with the new addition of CeloxTM Gauze (Medtrade Products Ltd., Crewe, UK; http://www.celoxmedical.com/usa/products/celox-gauze/) and ChitoGauze® (HemCon Medical Technologies, Portland, OR, USA; http://www.hemcon.com/) to the TCCC Guidelines.

**Conclusion:** No current hemostatic agent or dressing has proven to be ideal for all trauma scenarios in normal and coagulopathic casualties. However, this review of animal studies and clinical case reports found that Celox Gauze and ChitoGauze are as efficacious as Combat Gauze. These chitosan-based dressings were not statistically different than Combat Gauze for most outcome measures. Many studies revealed that chitosan dressing had strong trends toward faster hemostasis onset, less total blood loss, less fluid resuscitation requirements, and, for the most important primary end point: enhanced survival. Even though neither chitosan-based dressing have been tested in the same USAISR safety model as conducted on Combat Gauze and WoundStat, the animal studies and clinical cases series suggest a very low risk of thromboembolic adverse effects. Preliminary data of external Celox Gauze long-term application (at least 48 hours and longer) suggest that it is effective and safe.

Field Data

# Topical haemostatic agents

Paper accepted 26 August 2008. Published online in Wiley InterScience (www.bjs.co.uk)
DOI: 10.1002/bjs.6357

**H. Seyednejad[1,3], M. Imani[3], T. Jamieson[1] and A. M. Seifalian[1,2]**

1) Division of Surgery and Interventional Science, University College London, and
2) Department of Surgery, Royal Free Hampstead NHS Trust Hospital,London, UK, and
3) Novel Drug Delivery Systems Department, Iran Polymer and Petrochemical Institute, Tehran, Iran

Correspondence to: Professor A. M. Seifalian, Academic division of Surgical and Interventional Sciences, University College London, London NW3 2PF, UK (e-mail: a.seifalian@ucl.ac.uk)

**Background:** A variety of local haemostatic agents is now available to stop troublesome bleeding. These agents are indicated for use during surgical interventions where conventional methods of haemostasis are not applicable because of the site of surgery or the degree of bleeding.

**Method:** A literature search using the PubMed and ISI Web of Knowledge databases identified relevant studies on topical haemostatic agents. Manufacturers' recommendations were also sought through commercial websites.

**Results and conclusion:** A significant body of evidence now exists to support the use of topical haemostatic agents in a wide variety of clinical situations. The advantages and disadvantages of many of these agents are highlighted.

Field Data

# Pre-hospital hemorrhagic control, effectiveness of Axiostat® dressing versus conventional method in acute hemorrhage due to trauma

**Mohamed Kabeer K. K, Subhash V.C. and Venugopalan.P.P**

Department of Emergency Medicine, Malabar Institute of Medical Science, Calicut, Kerala, INDIA.

**Abstract:** Trauma encompasses one of the leading causes of death and disability in the world and in India, where trauma care is still in its infancy, it accounts for almost 10% of deaths every year. Lack of adequate pre-hospital care (golden hour) and uncontrolled bleeding from wound site is stated as one of the prominent reasons of trauma related death. In this study we investigated the efficacy of a new hemostatic dressing (Axiostat®, Axio Biosolutions, INDIA), which is made from a natural biopolymer chitosan; as an initial hemorrhage controlling device in pre-hospital scenario in India where a good material to prevent early blood loss is absent. This prospective study was conducted with the help of 35 EMCTs (Emergency Medical Care Technicians). A total of 133 patients with scalp wound injury were identified for the study of which 29 patients were excluded because they did not meet the criteria. Of 104 victims, 47 (45.2%) victims were treated with Axiostat® and 57 victims (54.8%) with conventional dressing, cotton gauze. All subjects needed suturing as the victims included in the study were brought with open scalp wounds. Axiostat® dressing showed superior efficacy, compared to cotton gauze. The average time for hemostasis with cotton gauze dressing was about 18.56 ± 5.04 minutes and with Axiostat® it was found to be under 5 minutes (4.68 ± 1.04 min), confirming the hemostatic potential of the novel chitosan dressing when compared to traditional dressings. The findings from this study show that novel hemostatic dressings made out of chitosan has the potential to be used as first intervention in acute hemorrhage conditions especially in the pre-hospital scenario.

**Conclusion:** Within the scope of this clinical trial which included only trauma cases that involved bleeding injuries to the scalp, we can conclude that the hemostatic dressing Axiostat® offers good hemostasis in prehospital scenario in India where an ideal hemostat to prevent early blood loss is lacking. On analyzing this study, it is evident that this dressing enables early hemostasis which prevents much blood loss and the wound becomes very clean on removal of dressing for later wound suturing when compared to normal cotton gauze. The Axiostat® is also very easy to apply on a bleeding wound with negligible side effects and having no allergic reactions. Hence, Axiostat® serves as a good hemorrhage controlling device in any prehospital health care systems especially in ambulances.

**References:**

1. Evans JA, van Wessem KJ, McDougall D, et al. Epidemiology of traumatic deaths: Comprehensive population-based assessment. World J Surg 2010;34:158–163.
2. World Health Organization: Injuries and Violence- The facts 2014. (http://www.who.int/violence_injury_prevention/media/news/2015/Injury_violence_facts_2014/en/).
3. World Health Organization: Global status report on road safety 2015. (http://www.who.int/violence_injury_prevention/road_safety_status/2015/en/).
4. Frederick BR, Katelyn JR, Brian WG. The golden hour in trauma: Dogma or medical folklore? Injury 2015; 46: 525-527.
5. Mohanan PV, Leo M, Ashish P. Toxicity and hemostatic potential of poly [ß-(1, 4)-2-amino-2- deoxy-D- glucosamine] based hemostatic material on albino rabbits, Tox Mech and Meth 2011, 21: 25-30.
6. Okamoto Y, Kawakami K, Miyatake K, Morimoto M, Shigemasa Y, Minami S. Analgesic effects of chitin and chitosan. Carbohydrate Polymers 2002; 49: 249–252.
7. Jones VJ. The use of cotton gauze: Will it ever change. Int Wound J 2006; 3:79–86.
8. Queen D, Orsted H, Sanada, H, Sussman G. A dressing history. Int. Wound J 2004;1:59–77.
9. Banks V, Bale S, Harding K, Harding EF. Evaluation of a new polyurethane foam dressing. J Wound Care. 1997;6: 266-269.
10. Thomas S, Loveless P. Comparative review of the properties of six semipermeable film dressings. Pharm J 1988; 240:785–787.
11. Paul W, and Sharma CP. Chitosan and alginate wound dressings: a short review. Trends Biomater. Artif. Organs 2004;18: 18-23.
12. Maryam K, Shahriar HE, Mohammad R, Mohammadreza T. Preparation and characterization of absorbable hemostat crosslinked gelatin sponges for surgical applications, Curr Appl Phy2011; 3:457-461.
13. Sirlak, Mustafa, et al. Comparative study of microfibrillar collagen hemostat (Colgel) and oxidized cellulose (Surgicel) in high transfusion-risk cardiac surgery. The Journal of thoracic and cardiovascular surgery 2003; 126: 666-670.
14. Pusateri AE, Holcomb JB, Kheirabadi BS, Alam HB, Wade CE, Ryan KL. Making sense of the preclinical literature on advanced hemostatic products. Journal of Trauma and Acute Care Surgery 2006; 60: 674-682.
15. Connolly RJ. Application of the poly-n- acetyl glucosamine-derived rapid deployment hemostat trauma dressing in severe/lethal swine hemorrhage trauma models. J Trauma 2004;57: S26-S28.
16. Arnaud F, Dione Parreño-Sadalan, Toshiki Tomori, Mariam Grace Delima, Kohsuke Teranishi, Walter Carr, George McNamee et al. Comparison of 10 hemostatic dressings in a groin transection model in swine. J Trauma 2009; 67: 848-855.
17. Granville-Chapman N, Jacobs MJ. Midwinter, Pre-hospital haemostatic dressings: A systematic review. Injury; 42: 447-459.
18. Joshipura MK, Shah HS, Patel PR, Divatiya PA, Desai PM. Trauma care systems in India – an overview. Injury 2003; 34: 686-692.
19. Zietlow JM, Zietlow SP, Morris DS, Berns KS, Jenkins DH. Prehospital Use of Hemostatic Bandages and Tourniquets: Translation from Military Experience to Implementation in Civilian Trauma Care. J Spec Oper Med 2015; 15: 48.

Clinical Studies

Pending Publication. Study done with Axiostat®

# Evaluating the effectiveness of Axiostat® hemostatic dressing material in patients on Oral Anti-Platelet Drugs

Department of Oral & Maxillofacial surgery KLE VK Institute of Dental Sciences, Belgaum, Karnataka, INDIA.

**Introduction:** The study was conducted to find out the efficacy of Axiostat® in controlling bleeding after tooth extraction. As profused bleeding during tooth extraction in particular with cardiac patients when they are on Blood thinners is a challenge for any dentist to control. Conventional method to stop bleeding using ordinary cotton usually takes more than 8-10mins.

**Method:** This prospective study was conducted on 40 cardiac patients who had underwent either Interventional procedures or open heart surgery. The selection criteria was such that 2 tooth extraction was performed for each patient. At one site, Axiostat® was used to achieve hemostasis and on the other site conventional method of using normal cotton/gauze was used.

**Results:** Axiostat® dressing showed superior efficacy, compared to cotton gauze. The average time for hemostasis with cotton gauze dressing was about 13.5 minutes and with Axiostat® it was found to be 1.13 minutes. The findings from this study shows that novel hemostatic dressings made out of chitosan has the potential to be used as first intervention in acute hemorrhage during tooth extraction.

**Conclusion:** Results of this study demonstrated utility of Axiostat® on extraction wounds was found satisfactory.

Total time taken to stop Bleeding was **1.13 minutes.**

Clinical Studies

# **SKIN** SENSITIZATION STUDY

**Introduction:** To determine the skin sensitization potential of the test item extracts using guinea pig maximization test (GPMT).

## Product Details:

| | |
|---|---|
| Test Item Name | Non Absorbable Haemostatic dressing (sterile) |
| Batch / Lot No. | 1039-014 |
| Manufacture Date | September 2015 |
| Expiry Date | August 2018 |
| Appearance | Chitosan sponge |
| Composition | Poly {β-(1,4) - 2 amino -2 deoxy -D Glucosamine} |
| Ingredients | Non-absorbable Chitosan |
| Solubility | Soluble in HCL, Acetic & Nitric acid |
| Stability | 37 °C |
| Condition | Sterile |

## Methods:

The method of administration is in line with the ISO 10993, Part-10 standard. For the induction phase intradermal injections and topical application was employed. The challenge phase was accomplished by topical applications.

**Results:** Chitosan-Non-absorbable Haemostatic Dressing (Sterile) is considered valid, as the control animals showed no skin reactions; and no significant loss of body weight. No mortality occurred in control group animals.

**Conclusion:** Axiostat® dressing does not induce any hyper sensitivity reactions in the body.


**References:**

1. Biological Evaluation of Medical Devices - Part 1, Evaluation and Testing within a Risk Management Process, ISO 10993-1:2009/Cor 1:2010(E).
2. Biological Evaluation of Medical Devices - Part 2, Animal Welfare Requirements, ISO 10993-2:2006(E).
3. Biological Evaluation of Medical Devices - Part 10, Tests for Irritation and Skin Sensitization, ISO 10993-10:2010(E).
4. Biological Evaluation of Medical Devices - Part 12, Sample Preparation and Reference Materials, ISO 10993-12:2012(E).


**Pre-clinical** Test Data

# CYTOTOXICITY TEST

**Introduction:** To evaluate whether or not the test item Non Absorbable Haemostatic dressing (sterile) induces cytotoxicity in Balb/c 3T3 cells using elution method.

## Product Details:

| | |
|---|---|
| Test Item Name | Non Absorbable Haemostatic dressing (sterile) |
| Batch / Lot No. | 1039-014 |
| Manufacture Date | September 2015 |
| Expiry Date | August 2018 |
| Appearance | Chitosan sponge, |
| Composition | Poly {β-(1,4) - 2 amino -2 deoxy -D Glucosamine} |
| Solubility | Soluble in HCL, Acetic & Nitric acid |
| Stability | 37 °C |
| Condition | Sterile |

## Methods:

**Rationale for assay method**

The NRU cytotoxicity assay procedure is a cell survival/viability chemo sensitivity assay based on the ability of viable cells to incorporate and bind neutral red dye. Specified in ISO 10993, Part-5 standard as an appropriate test to evaluate in vitro cytotoxicity of medical devices.

**Results:** Chitosan-Non-absorbable Haemostatic Dressing (Sterile) is considered as non-cytotoxic to Balb/c 3T3 cell lines, under the conditions of the test.

**Conclusion:** Axiostat® dressing does not have any toxic effect on the mammalian cells.

**References:**
1. Biological Evaluation of Medical Devices - Part 1, Evaluation and Testing within a Risk Management Process, ISO 10993-1:2009/Cor 1:2010(E).
2. Biological Evaluation of Medical Devices - Part 5, Tests for In vitro Cytotoxicity, ISO 10993-5:2009(E).
3. Biological Evaluation of Medical Devices - Part 12, Sample Preparation and Reference Materials, ISO 10993-12:2012(E).

**Pre-clinical** Test Data

# **ACUTE** SYSTEMIC TOXICITY TEST

**Introduction:** To determine the acute systemic toxicity potential of the test item Non Absorbable Haemostatic dressing (sterile) extracts in Swiss albino mice.

## Product Details:

| | |
|---|---|
| Test Item Name | Non Absorbable Haemostatic dressing (sterile) |
| Batch / Lot No. | 1039-014 |
| Manufacture Date | September 2015 |
| Expiry Date | August 2018 |
| Appearance | Chitosan sponge, |
| Composition | Poly {β-(1,4) - 2 amino -2 deoxy -D Glucosamine} |
| Solubility | Soluble in HCL, Acetic & Nitric acid |
| Stability | 37 °C |
| Condition | Sterile |

## Methods:

The extracts (Physiological saline and Cotton-seed oil) were administered without any dilution and the maximum dose volume used were 50 mL/Kg and 50 mL/Kg for IV and IP route, respectively. This is in line with the ISO 10993, Part-11 standard.

**Results:** Chitosan-Non-absorbable Haemostatic Dressing (Sterile) is considered valid, as the control animals showed no biological reactions; and no significant loss of body weight. No mortality or abnormal behaviour such as convulsion or prostration was occurred in control group animals.

**Conclusion:** Axiostat® dressing did not show any Systemic toxicity and hence meets the requirements of ISO 10993, Part-11:2006 (E).


**References:**

1. Biological Evaluation of Medical Devices - Part 1, Evaluation and Testing within a Risk Management Process, ISO 10993-1:2009/Cor 1:2010(E).
2. Biological Evaluation of Medical Devices - Part 2, Animal Welfare Requirements, ISO 10993-2:2006(E).
3. Biological Evaluation of Medical Devices - Part 11, Tests for Systemic Toxicity, ISO 10993-11:2006(E).
4. Biological Evaluation of Medical Devices - Part 12, Sample Preparation and Reference Materials, ISO 10993-12:2012(E).


**Pre-clinical** Test Data

# INTRACUTANEOUS REACTIVITY TEST

**Introduction:** To determine the irritation potential of the test item extracts following intracutaneous injection into New Zealand white rabbits.

## Product Details:

| | |
|---|---|
| Test Item Name | Non Absorbable Haemostatic dressing (sterile) |
| Batch / Lot No. | 1039-014 |
| Manufacture Date | September 2015 |
| Expiry Date | August 2018 |
| Appearance | Chitosan sponge |
| Composition | Poly {β-(1,4) - 2 amino -2 deoxy -D Glucosamine} |
| Ingredients | Non-absorbable Chitosan |
| Solubility | Soluble in HCL, Acetic & Nitric acid |
| Stability | 37 °C |
| Condition | Sterile |

## Methods:

The extracts (Physiological saline and Cottonseed oil) were administered intracutaneously without any dilution and the dose volume used was 0.2 mL per injection. This is in line with the ISO 10993, Part-10 standard.

**Results:** Chitosan-Non-absorbable Haemostatic Dressing (Sterile) is considered valid, as the control animals showed no skin reactions; and no significant loss of body weight. No toxicity or mortality occurred in control group animals.

**Conclusion:** Axiostat® dressing did not show any intracutaneous reactivity and meets the requirements of ISO 10993, Part-10:2010(E).

**References:**


1. Biological Evaluation of Medical Devices - Part 1, Evaluation and Testing within a Risk Management Process, ISO 10993-1:2009/Cor 1:2010(E).
2. Biological Evaluation of Medical Devices - Part 2, Animal Welfare Requirements, ISO 10993-2:2006(E).
3. Biological Evaluation of Medical Devices - Part 10, Tests for Irritation and Skin Sensitization, ISO 10993-10:2010(E).
4. Biological Evaluation of Medical Devices - Part 12, Sample Preparation and Reference Materials, ISO 10993-12:2012(E).


**Pre-clinical** Test Data

# Toxicity and hemostatic potential of poly [ß-(1,4)-2-amino-2-deoxy-D-glucosamine] based hemostatic material on albino rabbits

Toxicology Mechanisms and Methods, 2011; 21(1): 25–30

**PV Mohanan [1], Leo Mavely [2], and Ashish Pandya [2]**

1) Toxicology Division, Biomedical Technology Wing, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Poojapura, Thiruvananthapuram, Kerela, India, and
2) Axio Biosolutions Pvt. Ltd, 411-A, Smita Towers, Ahmedabad - 380052, India

**Abstract:** The present study was designed to evaluate the hemostatic potential of poly [ß-(1,4)-2-amino-2-deoxy-D-glucosamine]- based hemostatic dressing material on albino rabbits. In vitro cytotoxicity study of poly [ß-(1,4)-2-amino-2-deoxy-D-glucosamine]- based hemostatic dressing samples was carried out with L929 cells, the cytotoxic potential was evaluated at the end of 24 h. The skin irriation was carried out in albino rabbits. Extract of the material was applied topically and irritation response was evaluated up to 72 h. The hemostatic study was initiated in rabits after feneral anesthesia with a mixture of ketamine and xylazine. Using a sharp surgical blade, a 1.0 cm longitudinal incision was made on the right (test) and left (control) marginal ear arteries. Through the resultant jet spray of blood, the right 1.0 cm long wound was immediately covered with a 2X2 cm2 piece of test material poly [ß-(1,4)-2-amino-2-deoxy-D-glucosamine] of known weight (w1). Similarly the left wound (1.0cm length) was covered with commercially-available bandage (control) of known weight (w2). Direct pressure was applied for 2 min and then the samples were removed and weighed immediately (w3 for test and w4 for control) after hemostasis. Blood loss (w3-w1 for the test and w4-w2 for control) was calculated from the materials weight before and after absorbing blood. The result of the study indicated that the indigenously developed material has local biological activity in the form of hemostatic action and, together with its ability to activate macrophages, resulted in wound healing applications.

Hence the present study concluded that the poly [ß-(1,4)-2-amino-2-deoxy-D-glucosamine] - based hemostatic dressing material is non-toxic, non-skin irritant, and has better hemostatic potential than a commercially available material with enhanced hemostatic capabilities for various wound dressing.

***Keywords:*** *Haemostatic; wound healing; skin irritation; cytotoxicity; SEM*

ISSN 1537-6516 print/ISSN 1537-6524 online © 2011 Informa Healthcare USA, Inc.
DOI: 10.3109/15376516.2010.529185

Pre-clinical Data

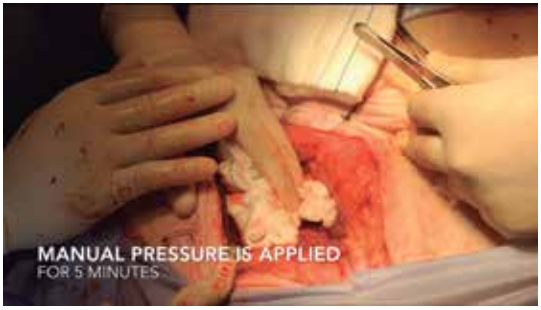
# Control of Arterial Bleeding using Axiostat® dressing on Swine Model

Two adult white swines were selected to study the efficacy of Axiostat® haemostatic dressing in controling arterial bleeding compared to cotton gauze. The study was based on US Army protocol for worst case scenario bleeding.

Arterial puncture was made on the femoral artery of swines and was allowed to bleed for 45 seconds. Axiostat was applied with pressure through a pool of blood. Haemostasis was observed after 5 minutes of using Axiostat. However, cotton gauze could'nt control bleeding even after 15 minutes.

After achieving haemostasis, Axiostat was easily extracted through saline irrigation.







Data on file.

Pre-clinical Data

**Doctor/Technician:**
Sakariya Samuel
Apollo Hospital, Bangalore

**Patient History:**

**54 year old female**
**Angioplasty**

Total time to achieve haemostasis **6** minutes

Interventional Cardiology Procedure - Radial
Heparin dosage – 9000 U
Estimated time of procedure: 1-3 hours
Sheath size: 7F
Usage of secondary dressing: No

**Patient outcome with Axiostat®:**

| | |
|---|---|
| Ease of Application | Easy |
| Ease of Removal | Excellent |
| Adherence to wound | Good |
| Conformability of dressing | Excellent |

**Summary:**

Results of this case study demonstrated utility of Axiostat® on Vascular interventional procedure and found satisfactory. Total time taken to achieve Haemostasis was **6 mins.**

Data on file.

Case Study

**Doctor/Technician:**
Dr.Girish.B. Navasundi
Apollo Hospital, Bangalore

**Patient History:**

**64 year old male**
**Angioplasty**

Total time to achieve haemostasis **5** minutes

Interventional Cardiology procedure - Femoral
Heparin dosage – 8000 U
Estimated time of procedure: <1Hour
Sheath size: 7F
Usage of secondary dressing: No

**Patient outcome with Axiostat®:**

| | |
|---|---|
| Ease of Application | Good |
| Ease of Removal | Good |
| Adherence to wound | Good |
| Conformability of dressing | Good |

**Summary:**

Results of this case study demonstrated utility of Axiostat® on Vascular interventional procedure and found satisfactory. Total time taken to achieve Haemostasis was **5 mins.**

Data on file.

Case Study

**Doctor/Technician:**
Dr. Seema
Care Hospital, Namapally

**Patient History:**

**55 year old male**

Total time to achieve haemostasis **3** minutes

Type of wound: Arterial Bleeding
Type of bleeding: Severe
Wound location and description:
Deep glass cut injury on left arm

**Patient outcome with Axiostat®:**

Time of observing rebleeding: after 30 mins of applying Axiostat

Rebleeding observed during removal: No

**Summary:**

Results of this case study demonstrated utility of Axiostat® on arterial bleeding was found satisfactory. Total time taken to achieve Haemostasis was **3 mins.**

Data on file.

Case Study

**Doctor/Technician:**
Dr. Gaurav Patel
SCL Hospital, Ahmedabad

**Patient History:**

**45 year old male**

Total time to achieve haemostasis **2.5** minutes

Type of wound: Puncture
Type of bleeding: Moderate to Severe
Wound location and description:
On face

**Patient outcome with Axiostat®:**

Time of observing rebleeding: after 15 mins of applying Axiostat

Rebleeding observed during removal: No

**Summary:**

Results of this case study demonstrated utility of Axiostat® on puncture wound was found satisfactory. Total time taken to achieve Haemostasis was **2.5 mins.**

Data on file.

Case Study

# **Neck** Trauma

At **11:40 AM,** the victim was brought in with a severe lacerations on her chin & neck and was treated with multiple Axiostat® dressings.
**Bleeding** was stopped within **3 minutes** and at **11:45 AM**, the dressing was removed for further treatment.

The lacerations required 75 external and 25 internal stitches.

# **Head** Trauma

The victim was brought in with a profusely bleeding head injury and was treated with Axiostat® at **8:38 AM**.

At **8:45 AM,** the bleeding was controlled and the patient was taken for secondary dressing.

**Case** Study

# **Knee** Trauma

The victim was brought in with a profusely bleeding knee injury and was treated with Axiostat® at **10:35 AM.**

Wound after removal of Axiostat® using saline at **11:00 AM.**

# **Access site** Bleeding

Axiostat® Vascular dressing used to control arterial bleeding quickly at radial access site post removal of sheath during cathlab procedure.

**Case** Study

# Testimonials

***Dr. T S Srinath Kumar***
*President-SEMI*
*Consultant Emergency Department*

***Narayana Mazumdar-Shaw***
***Medical Center,*** *Bangalore, India*

*Axiostat® is a product which we used during trauma cases (laceration) and it has considerably reduced the bleeding per se. Thereby reduced the secondary insult to the patient and maintaining hemodynamic stability by reducing excess blood loss from the wound. I would like to recommend this product in trauma cases for external bleeding control.*

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***Bhavesh Chavan***
*Senior Cathlab Technologist*

***Bhakti Vedanta Hospital***
***& Research Institute,*** *Mumbai, India*

*This is to state that, I had the opportunity of using the Axiostat® hemostatic pad in the Department of Cardiology in our hospital for the interventional cardiology procedures. The Axiostat® Pad is a great help in stopping severe femoral bleeding within minutes of application. It is also observed that by using Axiostat® the loss of blood is minimal, thereby saving the time of technicians & supporting staff. I would recommend use of Axiostat® in all interventional procedures.*

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# Testimonials

**Dr. Shailendra Trivedi**
*Director Cardiology*

**Medanta Super-Speciality Hospital,**
*Indore, India*

*Axiostat® Haemostatic pad is novel device to get control of bleeding post sheath removal specially from Femoral arterial puncture site. I have used the device successfully in my patients undergoing diagnostic and/ or therapeutic Femoral cannulation.*

---

**Dr. Avinash A Gutte**
*Associate Professor*

**GMC And Sir J. J. Hospital,**
*Mumbai, India*

*This is to certify that the product of AXIO BIOSOLUTIONS named "Axiostat® V55" was used on 20/07/2015 in our department and the results was found satisfactory within the expected time.*

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**Dhiraj Yadav**
*Cathlab Technologist*

**Bhakti Vedanta Hospital & Research Institute,** *Mumbai, India*

*This is to state that, I had the opportunity of using the Axiostat® hemostatic pad in the Department of Cardiology in our hospital for the interventional cardiology procedures. The Axiostat® Pad is a great help in stopping severe femoral bleeding within minutes of application. It is also observed that by using Axiostat® the loss of blood is minimal, thereby saving the time of technicians & supporting staff. I would recommend use of Axiostat® in all interventional procedures.*

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**Q: What is Axiostat®?**
**A:** Axiostat® is a sterile, non-absorbable haemostatic dressing intended to control profuse bleeding within minutes of application by providing an active mechanical barrier to the wound site.

Axiostat® stops moderate to severe bleeding due to cuts, abrasions, lacerations, venous/arterial punctures and more. Mechanism of action is such that Axiostat® is an extremely positive dressing that becomes very sticky in the presence of negatively charged blood and thus seals the wound area.

**Q: Why Axiostat®?**
**A:** Conventional interventions as applying manual pressure, Cotton gauze etc. takes more than 10-15 minutes to stop profuse bleeding and in majority of cases they are incapable of controlling profuse bleeding. Axiostat® helps stabilize the patient immediately and also helps save time for caregiver to focus on severe injuries. Use of Axiostat® reduces blood loss, and thus the demand for blood transfusion products such as red blood cells or plasma

**Q: Is Axiostat® easy to use?**
**A:** Axiostat® comes in sterile multi-layered pouches/blisters which can be easily opened using one hand. Axiostat® can be directly applied onto bleeding with palm pressure. It doesn't require pre-mixing or preparation prior to use.

**Q: How easy is it to remove Axiostat®?**
**A:** Axiostat® can be removed using saline or water irrigation. It will turn into a gel that can be easily peeled away without causing any trauma to the wound. This is one major advantage in using Axiostat® as it can be completely removed from wound without dislodging the already formed clot.

**Q: What precautions need to be taken while using Axiostat®?**
**A:** Axiostat® has a higher affinity to blood and may stick to gloves if not dry. Axiostat® also needs adequate blood to wet & be activate to aid in quick control of bleeding.

**Q: What is Axiostat® made of?**
**A:** Axiostat® is made of a naturally occurring polymer known as Chitosan (Poly [β-(1,4)-2-amino- 2-deoxy- D-glucosamine],) which is a biocompatible polysaccharide extracted from endoskeleton of cephalopods like squid. They are rigorously processed and purified prior to fabricating into dressing and is terminally sterilized using Gamma irradiation.

**Q: Can Axiostat® be left behind in the body?**
**A:** No. Axiostat® is a non-absorbable dressing and is not an Implant. It should be removed prior to wound closure using water/saline.

# Frequently Asked Questions

**Q: Can Axiostat® cause allergies?**
**A:** There have been no known allergic reactions from the use of Axiostat® since 2011. Chitosan used in Axiostat® does not contain any protein or allergic components.

**Q: How long can Axiostat® be kept on the wound?**
**A:** Axiostat® can be kept on wound up to 48 hours.

**Q: Is secondary dressing required after using Axiostat®?**
**A:** Secondary dressing such as cotton gauze may be used to keep Axiostat® dry and in position. Axiostat® sticks to bleeding wound quickly and it eliminates the need for any other dressings.

**Q: Will Axiostat® work on patients with bleeding disorders or who are on blood thinning drugs?**
**A:** Axiostat® works independently of natural clotting mechanism and is based on adhesive property due to charge density of blood components. Hence we would expect the dressing to work on patients with bleeding tendency due to drugs or any disorder, we have not conducted any clinical studies to demonstrate efficacy.

**Q: How do I justify the additional cost of using Axiostat® in my current procedure?**
**A:** Using Axiostat® may seem like an additional cost at the onset but that cost is considered negligible, even negated, in the long run.

In an environment where critical care is being administered like an Emergency Room or Trauma Center, time becomes of prime importance. Any extra time spent in stoppage of bleeding with one patient is time that could be utilized with another patient in need of immediate attention.
Stoppage of bleeding can also minimize the need for transfusion products, thereby reducing the risk of complications and additional cost.
Overhead costs are also reduced when the turnaround time is decreased. Whether it is in emergency care or in a Cathlab, the shorter the procedure, the faster the bed can be turned around for the next patient. This translates directly into increased revenue as a result of additional patients served.

**Q: How is V35/V25 different from your current product V55?**
**A:** V35/V25 has been customized based on feedback & creative input received from CathLab surgeons and technicians from across the country. These variants have been designed with efficiency, application and economics in mind.

**Q: How does Axiostat® stop bleeding at the blood vessel level when it is applied topically at the skin level?**
**A:** Axiostat® works at the mechanical, electrostatic & biological level to effectively create a clot plug at an accelerate rate that cannot be matched by a non-active material such as cotton gauze. The haemostasis achieved is total and extends all the way to the blood vessel level.

# Frequently Asked Questions

# Axio

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