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REVIEW

Review of Evidence Supporting the Arista™ Absorbable Powder Hemostat

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Background: Uncontrolled and diffuse bleeding is a dreaded event during open and laparoscopic surgery that may lead to postoperative complications, obstruction of the surgical field that reduces visualization, and prolonged operating times. Powder hemostats can be used to control bleeding and are easy to use, have a safe profile, and can achieve broad coverage area at a low cost.
Methods: A strategic literature search of peer-reviewed, English language studies was conducted to capture evidence on the clinical efficacy and safety of a Microporous Polysaccharide Hemosphere (MPH) based Hemostat (Arista™ Absorbable Hemostat (Arista™ AH)).
Results: Six preclinical studies were found which supported the use of MPH in various animal models of laparoscopic and open surgery, all of which demonstrated its safety and efficacy. Five single-arm and 11 comparative clinical studies similarly supported the efficacy and safety of MPH in various surgery types, including cardiac, renal, and dermatologic surgery.
Conclusion: Published evidence supports the safe and effective use of MPH across a variety of surgical settings.
Keywords: bleeding, hemostats, Arista™, surgery

Introduction

Uncontrolled and diffuse bleeding is a dreaded event during open and laparoscopic surgery and may lead to substantial morbidity and mortality.[1,2] Bleeding-related complications can be more common than thought, with one study reporting rates of up to 47.4% during cardiac surgery.[1] Further, uncontrolled bleeding can prolong hospital stay and result in significant additional medical interventions and costs.[3–5] Accordingly, effective hemostasis can improve surgical outcomes, reduce complications and the need for surgical re-intervention, and lower costs of medical care.[6,7]

The selection of optimal hemostatic agent depends on a variety of factors. These factors include surgery type, source and the extent of bleeding, as well as the patient's coagulation status and medical history.[8,9] Hemostats should meet basic clinical needs, which include efficacy, providing reliable and quick hemostasis, and having a preferable safety profile.[9–11] Additional considerations in hemostat selection include ease of storage, required preparation time/being ready on demand, and cost. For control of localized bleeding, application of direct pressure and thermal-based methods (eg, electrosurgery) are typically the methods of choice due to their simplicity.[11,12] However, these methods of hemostasis may not be effective in controlling diffuse bleeding, particularly when the site of bleeding is not visible.[8,13] Diffuse bleeding during surgery is associated with several complications, including reduction in core temperature, thrombocytopenia, and hypovolemic shock.[8] Further, diffuse bleeding can visually obstruct surgical field and thereby lead to longer operating times and increased risk of patient and staff injury.[8]

Given the unique challenges associated with diffuse bleeding, powder hemostats that can be easily and quickly applied over a large surface area provide advantages over other hemostat types in controlling diffuse bleeding in both open and laparoscopic surgery.[2,11,14] However, despite their frequent use in many surgical settings, there is a paucity of reviews focused specifically on powder hemostats for control of surgical bleeding, and factors influencing the selection of the optimal hemostat.

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The Microporous Polysaccharide Hemosphere (MPH) based hemostat (Arista™ Absorbable Hemostatic Particles (Arista™ AH), Becton, Dickinson and Company (BD), Franklin Lakes, NJ) was the first flowable powder hemostatic agent available on the market in the United States (US). This review will summarize the available clinical and preclinical evidence for MPH and evaluate its safety and efficacy versus other available powder hemostatic agents in controlling bleeding.[8]

Methods

A targeted literature review was conducted on April 30th, 2020 by an information specialist for English peer-reviewed articles evaluating the use of MPH and other powder hemostats in both preclinical and clinical settings. MEDLINE®, Embase, EMB Reviews, and Cochrane Central Register of Controlled Trials were searched for relevant articles. The goal was to find evidence demonstrating the safety and efficacy of MPH or other powder hemostats across surgery types. Search included key terms such as hemostatic agent, hemostasis, hemostatic technique, microporous or degradable.

Results

Overview of Powder Hemostats

Powder hemostats belong to the category of mechanical hemostats, which act as a molecular sieve through contact with the bleeding site and promote platelet aggregation.[8–10] These agents are used during surgery to control diffuse raw surface bleeding, hard to reach bleeding sites, oozing venous bleeding, bone bleeding, and needle-hole bleeding. Mechanical hemostats include agents derived from animal-based sources (collagen and gelatin), and those derived from plant sources (oxidized regenerative cellulose [ORC; Surgicel®] and MPH). Furthermore, mechanical hemostats are available in several forms including sponges, pads, foam, and powder.[8] In the US, MPH was the first flowable powder hemostat on the market and was approved for use in 2006. ORC was initially available as a fabric and has recently become available in the powder form. PerClot® is a modified starch powder hemostat that is available internationally and is expected to be submitted for approval for use in the US. Other powder hemostats that are available internationally include starch-based hemostats like 4DryField®, HaemoCer™, and StarSil®, and collagen-based Hemoblast™.

Powder hemostats can be easily dispersed over a large surface area and are therefore commonly used to control diffuse bleeding in open and laparoscopic surgeries.[13,15] Benefits of powder hemostats over other hemostat types (eg, flowables and sealants) include the following:

- Simple application that does not require a long-learning curve
- Control of bleeding at technically difficult-to-reach bleeding sites
- Control of bleeding over a large surface area and when the exact site of bleeding cannot be identified
- Compatible with autologous cell salvage machines
- Safe and well tolerated, without any known toxicity
- Effective in patients taking anticoagulants or anti-thrombotic medication
- Fast-acting and achieve rapid control of bleeding in high-risk patients
- Cost-effective

Although all powder hemostats offer benefits, these agents differ in terms of their characteristics, safety, efficacy, and ease of use. These characteristics are summarized in Table 1: Characteristics of mechanical hemostats approved for use in the US. The differentiating features of plant-based powder hemostats are discussed in the following section.[16]

Plant-Based Powder Hemostats

Plant-derived powder hemostats, which include starch-based (MPH) and cellulose-based (ORC) products, are commonly used as adjunctive hemostats due to their ease of use and efficacy.[16,19] Plant-derived hemostats may be beneficial in some surgical settings because they do not contain any animal- or human-derived components, which can cause adverse reactions in some patients.[20,21] Among plant-derived products, ORC, a cellulose-based hemostat, is well known and accepted because of its ease of use, and bactericidal properties*.[16] Although ORC is bactericidal against a wide range of

Table 1 Characteristics of Mechanical Hemostats Approved for Use in the US

Characteristic	MPH	ORC	Microfibrillar Collagen	Gelatin Matrix
Brand name	Arista™ AH	Surgicel®	Avitene™	Gelfoam® Surgifoam®
Available forms	Powder	Woven mesh or powder	Sponge or powder	Sponge or powder
Source	Plant		Bovine	Porcine
Mechanism of action	Absorbs water, concentrates platelets and blood proteins	Activates extrinsic coagulation cascade; provides scaffold for platelet aggregation and clot formation		Absorbs blood and fluid, matrix for clot formation, mechanical barrier
Absorption time	48 hours	1–2 weeks[a]	8–12 weeks	4–6 weeks
Storage	Room temperature			
Preparation before use	Not required			
Compatibility with autologous cell salvage machines	Yes	No		
Potential adverse events	None reported	Infection, abscess, foreign body reaction, granuloma formation	Infection, abscess, foreign body reaction, granuloma formation Systemic allergic reactions	Infection, abscess, foreign body reaction, granuloma formation
Other Considerations	Caution with use >50g in diabetic patients, as it may alter glucose level	Not to be used with topical thrombin Low pH has antimicrobial effect	None	Should not be placed in tight spaces due to risk of compression necrosis Can be moistened with thrombin

Notes: [a]There are rare reports of persistent material up to 15 months postoperatively. Vyas and Saha[17]
Abbreviations: AH, absorbable hemostat; MPH, microporous polysaccharide hemospheres; ORC, oxidized regenerative cellulose.

pathogenic microorganisms, it is not intended as a substitute for systemically administered therapeutic or prophylactic antimicrobial agents to control or to prevent postoperative infections.[22] However, despite its benefits, ORC may be associated with safety issues. For example, ORC is not fully absorbed for two to five weeks after surgery.[16] The material remaining at the surgical site may create granulation formation in the late post-operative period and result in foreign body reactions. Case studies have reported complications related to excess ORC at the surgical site, including adhesion formation and hematoma around ORC after cardiac surgery[23,24] and paraplegia following thoracic surgery.[25] Additionally, the low pH of ORC contributes to its anti-bactericidal properties.[26] However, the low pH also increases the inflammation of the surrounding tissue and has been reported to delay wound healing.[27] Further, studies have reported that excess ORC may interfere with postsurgical diagnostic investigations, given that commonly used imaging methods (eg, CT or nuclear magnetic resonance) cannot differentiate excess ORC from pathological growth.[28,29] The increased risk of complications associated with non-absorbed ORC is a known risk of the product and is included in the product's Instructions for Use.[30]

Starch Crystallinity as a Consideration in the Selection of Starch-Based Hemostats

Although all starch-based hemostats share certain features, they can be differentiated based on the unique properties of the starch they are derived from.[3,21,31] Starch is a semi-crystalline polymer consisting of amorphous (ie, non-crystalline) regions, which are easily degraded by amylases, and crystalline regions, which are degraded more slowly.[32] Therefore, starches with a higher

amount of crystallinity are not digested or resorbed as easily as those with less crystallinity.[33] Complications due to surgical gloves coated with starch powder are well documented and indicate an inflammatory response caused by the crystalline starch powder resulting in foreign body reactions, adhesion formation, and granulomatous reactions.[33–36] These concerns over inflammatory reactions have led several regulatory agencies to ban powdered surgical gloves.[37]

Although crystallinity of starch powder hemostats has not been well documented, one study showed that starch crystallinity was observed with PerClot®, HaemoCer™, and Starsil®, but not Arista™ AH.[35] Note that at the time of publication, PerClot®, HaemoCer™, and Starsil® are not available in the US. Starch crystallinity was evaluated by X-ray powder diffraction in non-degraded state and after 24-hour degradation with α-amylase using polarized light microscopy. As indicated in Nilsson and Gold, the crystalline granules were observed after exposure to in vitro amylase degradation for 24 hours, indicating that they are resistant to resorption.[35] These results were recently confirmed and expanded upon in a comparison of Arista™ AH and PerClot®.[38] In both an in vitro degradation assay and an in vivo preclinical model, Arista™ AH showed no crystallinity at any time point, no material detected by Day 3 and normal wound healing. In contrast, PerClot® PHS showed slow resorption and the local persistence out to the Day 28 endpoint of crystalline degradation products that were associated with the onset of chronic inflammation and an early foreign body response.

Advantages of Arista™ AH Absorbable Hemostatic Particles

Arista™ AH consists of Microporous Polysaccharide Hemospheres (MPH), which are derived from purified potato starch and are currently used as an absorbable hemostatic agent. MPH is delivered as a flowable powder engineered to rapidly dehydrate blood, enhancing clotting on contact. MPH provides hemostasis by absorbing water and low-molecular weight compounds from the blood to concentrate blood solids, creating a scaffold for the formation of fibrin clot.[39,40] The clot formed by the swelling of MPH beads, platelets, and clotting proteins is more resilient than a naturally formed clot. Preclinical studies show that the MPH-enhanced clot is enzymatically broken down within 12 hours of application, leaving no residue in the surgical field.[40] Clinical studies show that MPH is absorbed from the surgical field 24–48 hours postoperatively.[41,42] Notably, the MPH mechanism of action does not depend upon the patient's coagulation status, making it suitable for patients on anti-coagulation therapy across a variety of surgical settings.

The MPH particles in Arista™ AH are made through the reaction of purified starch and epichlorohydrin and were developed to provide a biocompatible, purified starch composition.[43]

In the US, Arista™ AH is indicated in most surgical procedures as an adjunctive hemostatic device to assist when control of capillary, venous, and arteriolar bleeding by pressure, ligature, and other conventional procedures are ineffective or impractical, or when added hemostasis is necessary.

Preclinical studies have shown that the properties and mechanisms of action of Arista™ AH are associated with several benefits:

- Due to fast absorption (within 24 hours), Arista™ AH does not interfere with imaging[43]
- It is associated with a minimal, if any inflammatory response[44]
- The starch in the proprietary MPH technology does not exhibit starch crystallinity[45]
- Arista™ AH powder is ready on demand to address diffuse surgical bleeding, with no preparation needed as an adjunct to conventional hemostasis[42]
- Arista™ AH provides broad area coverage on rough surfaces and hard-to-reach areas when adjunctive hemostasis is required[2]
- Complete hemostasis is achieved within minutes[46,47]
- It is not associated with adhesion formation[48–50]
- Safety and efficacy have been demonstrated across a variety of surgical areas, including general surgery, obstetrics/gynecology, urology, cardiac, and orthopedic surgery[2,39,41,51–65]

However, it should be noted that some of this data was generated in preclinical models and may not correlate to performance in humans. Preclinical and clinical evidence supporting the use of MPH in a variety of surgical settings are detailed in the following sections.

Preclinical Evidence of MPH

Studies in animal models generally show that MPH effectively achieves hemostasis with minimal complications in both laparoscopic and open surgeries. These studies, which consist of single-arm and comparative studies, are summarized in Tables 2 and 3.

Two single-arm studies of MPH, both in porcine models of laparoscopic surgery, demonstrated that MPH provides effective and safe hemostasis, with complete hemostasis being achieved with a single application of MPH.[46,47] Studies

Table 2 Summary of Preclinical Studies of Arista™ AH

Reference	Study Objective/Surgery Type/Animal Model	Experimental Groups	Key Results
Single-arm studies of Arista™ AH			
• Murat et al (2006)[42]	• Evaluate the efficacy of Arista™ AH for parenchymal hemostasis during laparoscopic partial nephrectomy in the porcine model • Laparoscopic partial nephrectomy	• Arista™ AH	• Hemostasis was achieved after one Arista™ AH application in 8/12 kidneys • In 3 kidneys, a small amount of Arista™ AH (1 g) was required for minor residual bleeding • In 1 kidney, an additional 2.0 g of Arista™ AH was required • After one week, no residual Arista™ AH was found • In 2/6 chronic phase kidneys, small urinomas (<2 cm in greatest diameter) were found at necropsy; these were the only post-operative complications
• Humphreys et al (2008[a])[43]	• Evaluate Arista™ AH in intracorporeal laparoscopic splenic injury • Pigs	• Arista™ AH	• Arista™ AH successfully achieved hemostasis for all splenic injuries except in 1 case, where a 12-mm lesion transected the splenic artery • Mean time to hemostasis (s): - 5-mm injuries: 165.3 ± 45.7 - 12-mm injuries: 200.7 ± 106.5 • Number of Arista™ AH applications: 1.3 ± 0.5 in both groups • Estimated blood loss (g): - 5-mm injuries: 12.0 ± 4.6 - 12-mm injuries: 17.7 ± 9.1
Studies comparing Arista™ AH to control			
• Benlier et al (2007)[63]	• Evaluate the effects of Arista™ AH on tissue toxicity/vessel damage, patency rates, and anastomotic time in vascular anastomosis • Vascular surgery • Rats	• Arista™ AH • Control: conventional interrupted suture technique	• Duration of clamping was significantly shorter in the Arista™ AH than in the control group ($P < 0.001$) • All the vessels were patent at 1 hr and 24 hrs after the release of clamps • Thrombus formation was observed in two vessels on Day 28 in the control group, but the difference was not significant between groups • The Arista™ AH group showed qualitatively less perivascular foreign-body giant cell reactions than the control group • There was no evidence of vascular mural fibrinoid necrosis, indicating that Arista™ AH was nontoxic to the vessel walls

(*Continued*)

Table 2 (Continued).

Reference	Study Objective/Surgery Type/Animal Model	Experimental Groups	Key Results
• Humphreys et al (2008[b])[37]	• Determine the effectiveness of Arista™ AH in the intracorporeal laparoscopic environment for trocar injury to the renal parenchyma • Laparoscopic renal surgery • Pigs	• Arista™ AH • Control: compression	• Mean time to hemostasis was significantly shorter in the Arista™ AH than in the control group for both 5 mm and 12 mm lesions (P = 0.005) • Mean number of Arista applications: - 5-mm lesions: 1.0 ± 0.0 - 12-mm lesions: 1.7 ± 0.5 • Mean blood loss until hemorrhage stopped was not different between the Arista™ AH and control groups
• Egeli et al (2012)[64]	• Investigate the effects of Arista™ AH on lymphovascular drainage and delay in wound healing, which may lead to seroma formation • Mastectomy • Rats	• Arista™ AH • No hemostat	• Mean seroma volume was significantly lower in the Arista™ group than in the control group (P = 0.001) • Increase in fibrous tissue was greater in the control than in the Arista™ AH group (P = 0.032) • Mean albumin and LDH levels, and WBC count were significantly higher in the control group (P = 0.03 for all parameters)
• Offodile et al (2017)[18]	• Evaluate the effect of Arista™ AH on tissue survival • Skin flap • Rats	• Arista™ AH • No hemostat	• Arista™ AH group had a significantly larger mean area of necrosis at the distal flap than the control group

Abbreviations: AH, absorbable hemostat; LDH, lactate dehydrogenase; WBC, white blood cells.

Table 3 Comparative Animal Studies of Arista™ AH versus Surgicel®

Reference	Study Objective/Surgery Type/ Animal Model	Experimental Groups	Key Results
Studies comparing Arista™ AH to Surgicel® and other plant-based topical hemostats			
• Hoffmann et al (2009)[66]	• Examine the impact of Arista and Surgicel® on intraperitoneal and cecal adhesion formation • Abdominal surgery • Rats	• Arista™ AH • Surgicel® • Control: no treatment	• Mean total adhesion score was significantly lower with Arista™ AH and Surgicel® compared with control (P < 0.05 for both comparisons) • Only Arista™ AH was completely resorbed on day 7 in all animals
• Emmez et al (2010)[67]	• Compare the effectiveness and safety of Surgicel® and Arista™ AH • Neurosurgery • Rats	• Arista™ AH • Surgicel® • Control: cotton irrigated with isotonic saline	• There were no significant differences in hemorrhage, inflammation, pericellular edema, or neuronal degeneration between groups • Hemostatic agent was visible in all specimens in the Surgicel® group, but not in the Arista™ AH or control groups • MRI revealed no significant differences in edema volume between Arista™ AH and Surgicel® groups • Edema volume was significantly larger in the control group compared to Arista™ AH or Surgicel® groups (P < 0.001)

(*Continued*)

Table 3 (Continued).

Reference	Study Objective/Surgery Type/ Animal Model	Experimental Groups	Key Results
• Ereth et al (2008[a])[65]	• Compare the safety and efficacy of commonly used agents with Arista in a neurosurgical model • Neurosurgery • Rats	• Arista™ AH • Surgicel® • Control: no hemostat	• Complete hemostasis was achieved after 1 min in the majority of lesions treated with a hemostatic agent • All rats in the Surgicel® group had residual material upon examination • None of the rats with Arista™ AH had any residue as early as 6 hours after application • The amount of residual material was significantly greater with Surgicel® compared with Arista™ on Days 3 and 7 ($P < 0.001$) • Arista™ AH was the only agent that was not associated with inflammation (granuloma) at any time point after surgery
• MacDonald et al (2017)[19]	• Compare the efficacy of powder hemostats • Liver punch biopsy and liver abrasion • Pigs	• Arista™ AH • Surgicel® absorbable powder • PerClot®[b]	• Effective hemostasis was achieved in all cases in the Arista™ AH and Surgicel® groups • The proportion of cases that achieved effective hemostasis was significantly higher with Arista™ AH and Surgicel® than with PerClot® • Hemostatic efficacy (ie, complete hemostasis achieved within 10 minutes) was significantly better with Surgicel® than with Arista™ AH or PerClot® • Time to hemostasis was significantly shorter with Surgicel® than with Arista™ or PerClot®
Studies comparing Arista™ AH to animal-based hemostats			
• Singh et al (2019)[41]	• Compare bovine-derived gelatin hemostatic powder to Arista™ AH • Sinus surgery • Pigs	• Arista™ AH • Bovine-derived gelatin	• Immediate hemostatic success (ie, hemostasis within 2 minutes of application) was achieved in 88% of gelatin-treated lesions and 65% of Arista™ AH -treated lesions • Gelatin powder achieved significantly greater hemostatic success compared with Arista™ AH (OR 15.18; 95% CI 7.37–31.27; $P < 0.001$)
• Ereth et al (2009)[68]	• Determine if the use of Arista™ AH in abdominal surgical incisions reduces infection • Abdominal surgery • Rats	• Arista™ AH • Gelatin matrix (Gelfoam®) • Control: no hemostat	• The gelatin matrix group had greater median bacterial count in the incisions and more clinical infections than the control and Arista groups ($P < 0.0001$) at 72 hrs. after E. coli instillation • There were no differences in bacterial count between the Arista™ AH and control groups
• Antisdel et al (2008)[69]	• Evaluate the effects of Arista™ AH on healing and intact sinus mucosa • Sinus surgery • Rabbits	• Arista™ AH • FloSeal®	• In Arista™ AH-treated sinuses, the epithelium in the mucosa-intact rabbits was not different from untreated intact rabbit maxillary sinus mucosa • No foreign material or foreign body reaction was noted • FloSeal® treated stripped mucosa showed disrupted and disorganized epithelial regrowth with sparse cilia, with foreign body material on both sides of the epithelium • In FloSeal®-treated mucosa-of intact sinuses, abnormal and metaplastic epithelium with a large decrease of cilia was observed • Moderate submucosal fibrosis with loss of serous glands, osteoneogenesis, and chronic inflammation of the lamina propria • Residual FloSeal® was observed intraluminally

(*Continued*)

Table 3 (Continued).

Reference	Study Objective/Surgery Type/ Animal Model	Experimental Groups	Key Results
• Ereth et al (2008[b])[70]	• Evaluate the effects of Arista™ AH and other hemostatic agents on bone healing and regeneration • Cranial surgery • Rabbits	• Arista™ AH • Microfibrillar collagen • Bone wax • Control: no hemostat	• Bone healing score was significantly higher with Arista™ AH than with microfibrillar collagen ($P < 0.05$); there were no significant differences between Arista™ AH, control, and bone wax • Histomorphometry analysis showed that at 7 weeks, 2 defects in the control group and 1 in Arista™ AH group were completely healed, whereas no defect in the microfibrillar collagen or bone wax groups healed completely

Notes: [a]Other agents were also evaluated in the study, however, data are only presented for hemostatic agents available in the US. [b]PerClot® is expected to be approved in the US in 2023.
Abbreviations: AH, absorbable hemostat; CI, confidence interval; MRI, magnetic resonance imaging; OR, odds ratio.

that evaluated MPH versus control (no hemostat applied) also show that MPH provides effective hemostasis in a variety/multitude of surgical settings. A study in a rat model of vascular anastomosis showed that MPH significantly reduced the duration of clamping and qualitatively reduced perivascular foreign body reactions compared with control.[67] The study also showed that MPH did not affect vessel patency after anastomosis and did not cause toxicity to the vessel walls. Another study in a porcine model of laparoscopic renal surgery showed that MPH significantly reduced the time to hemostasis compared to control treatment (ie, compression alone), regardless of lesion size.[40] In a rat model of mastectomy, MPH significantly reduced seroma volume, amount of fibrous tissue, as well as albumin, lactate dehydrogenase (LDH) levels, and white blood cell count, indicating that MPH may reduce seroma volume after mastectomy.[66]

Animal studies that compared plant-based MPH (starch) to ORC (cellulose) and animal-based hemostats (ie, gelatin, thrombin, and collagen) are summarized in Table 3. These studies show that MPH is the only agent that is completely cleared from the surgical site within 24 hours of application.[71] Studies that compared MPH with ORC reported no significant differences in the amount of hemorrhage or edema volume between the two agents.[71,72] A study that evaluated the two agents in a rat model of abdominal surgery showed that MPH was associated with significantly lower adhesion scores than controls, whereas this difference was not seen with ORC.[73] Another study using a rat model for neurosurgery compared MPH, ORC Avitene®, and FloSeal®. This study showed that MPH was the only agent that was not associated with granulomatous formation at any point after surgery.[71] Finally, a study using a porcine model for hepatic surgery showed that both MPH and ORC achieved effective hemostasis in all cases. However, in this study, time to hemostasis was better with ORC.[19]

Clinical Evidence for MPH

Published clinical evidence for MPH supports the findings of the animal studies. Single-arm studies, which include three prospective, observational studies, and three case studies are summarized in Table 4. Case studies show that MPH provides adequate control of bleeding in cardiac and cranial surgeries.[51,52,55] Two prospective, observational studies of patients undergoing sinus surgery have also demonstrated MPH effectively controls bleeding and achieves hemostasis in as little as 30–45 seconds after application.[53,54] In both studies, MPH was well tolerated and no patients developed allergic reactions or systemic complications. Additionally, MPH was rapidly cleared from the surgical site and was undetectable one week after surgery.[53] Although not indicated in the US for use in neurosurgery, one neurosurgery study showed that MPH provided effective hemostasis, which was achieved in approximately one minute of application.[41] Additionally, MPH was undetectable at the surgical site one day postoperatively, indicating that it is rapidly absorbed in neural tissue.

Studies comparing MPH with untreated controls generally show that use of MPH significantly improves clinical outcomes in a variety of surgery types, including cardiac, nasal, general, and orthopedic surgeries. These studies are summarized in Table 5. In a retrospective study of 240 patients undergoing cardiothoracic surgery, MPH significantly

Table 4 Single-Arm Clinical Studies of Arista™ AH

Reference	Study Design (N)	Surgery Type	Key Results
Bruckner and Loebe (2012[a])[48]	• Case study • N = 2	• Cardiac	• Surgical field bleeding improved after application of Arista™ AH
Bruckner and Loebe (2012[b])[49]	• Case study • N = 1	• Cardiac	• Arista™ AH provided effective local control of diffuse bleeding
Galarza et al (2011)[52]	• Case series • N = 10	• Cranial	• Effective hemostasis was achieved in ≤2 min after Arista™ AH application in 8/10 patients • There were no allergic reactions or systemic complications • There were no cases of cerebral hematoma, swelling, or infection
Phillips (2013)[51]	• Prospective, observational • N = 155	• Sinus	• Arista™ AH was well-tolerated and no allergic reactions were observed • None of the patients required secondary intervention for obstructive synechiae • Nursing personnel noted improvements in patient satisfaction and reduced post-operative bleeding
Sindwani (2009)[50]	• Prospective, observational • N = 65	• Sinus	• Hemostasis was obtained in ~30–45 s after Arista™ AH application • There was no significant postoperative bleeding that required an ER visit, hospital admission, or nasal packing or cautery • No Arista™ AH was detected in any of the sinus cavities at the one-week debridement • Synechiae formation was noted in 8/65 of patients; only 2 were grade 2 and required lysis

Abbreviations: AH, absorbable hemostat; ER, emergency room.

Table 5 Comparative Clinical Studies of Arista™ AH

Reference	Study Design; N; Comparators	Surgery Type	Key Results
Studies comparing Arista™ AH to untreated control			
Bruckner et al (2014)[2]	• Retrospective; • N = 240 • n = 103 Arista™ AH • n = 137 Control • Control patients received another hemostatic agent (FloSeal®, Gelfoam® with thrombin, or Surgicel®)	• Cardiothoracic	• Hemostasis time was significantly shorter in the Arista™ AH than in the control group ($P = 0.02$) • Arista™ AH significantly reduced postoperative chest tube output in the first 48 hrs. (<0.001), and the red blood cell transfusion volume ($P < 0.001$) • The length of ICU stay was numerically lower in the Arista™ AH (8 days) than in the control group (9 days; $P = 0.08$) • There were no significant differences in 30-day mortality or postoperative complications between the groups
Reynbakh et al (2018)[53]	• Retrospective • N = 283 • n = 77 Arista™ AH • n = 206 Control • Method of hemostasis in the control group not specified	• Cardiac	• Arista™ AH was associated with a significantly lower complication rate compared to control ($P < 0.05$) • The rate of hematoma was lower in the Arista™ AH (0.4%) than in the control (0.8%) group • The rate of infection was lower in the Arista™ AH (0%) than in the control (3.4%) group

(*Continued*)

Table 5 (Continued).

Reference	Study Design; N; Comparators	Surgery Type	Key Results
Antisdel et al (2009)[54]	• Randomized, controlled, single-blinded • n = 40 Arista™ AH • n = 40 Untreated control • Contralateral side served as a non-treated control	• Sinus	• Bleeding score on post-operative day 1 was significantly lower in the Arista™ AH than in the control group ($P < 0.0001$) • Patient-reported scores for bleeding were not significantly different between the groups ($P > 0.05$) • There were no significant differences in pain, obstruction, or nasal discharge between Arista™ AH-treated and control sides
Antisdel et al (2011)[55]	• Randomized, controlled, double-blind • n = 40 Arista™ AH • n = 40 Control • Contralateral side served as a non-treated control	• Sinus	• There was no significant difference in synechiae formation, or the frequency or degree of debridement between the Arista™-treated and control sides • No residual material was noted on either the Arista™ AH-treated or control sides • The presence and degree of infection and extent of edema were similar between the two groups
Suarez-Kelly et al (2019)[36]	• Prospective, randomized, single-blinded • N = 42 • n = 21 Arista™ AH • n = 21 Untreated	• General (mastectomy)	• There were no significant differences between Arista™ AH and control groups in mean time until drain removal, drain output, number of clinic visits, or postoperative complications
Nunez-Nateras et al (2013)[56]	• Retrospective • N = 30 • n = 10 Arista™ AH • n = 20 Control • Method of hemostasis for the control group was not specified	• Prostatectomy	• The change in hemoglobin after 24 hrs. was lower in the Arista™ AH group, but the difference was not statistically significant • 2 patients in the control group had urinary extravasation that required prolonged catheterization • There were no significant differences between groups in prostate size, post-operative Gleason sum, negative margins, proportion of patients requiring transfusion, or duration of catheterization • OR time was shorter in the Arista™ AH group, but was not sig. diff. (P = 0.038)
Gilbert et al (2016)[57]	• Prospective randomized • N = 88 • n = 88 Arista™ AH • n = 88 Untreated control (contralateral side)	• Prostatectomy with pelvic lymph node dissection	• Fewer lymphoceles were found on the Arista™ AH-treated side (5.7%) than the control side (10.2%), although the difference was not statistically significant
Gleason et al (2019)[58]	• Case-control retrospective chart review • N = 147 • n = 93 Arista™ AH • n = 54 Untreated control	• Orthopedic	• There were no differences in the rate of superficial infections or hematomas between the groups • Expected surgical blood loss was significantly higher in the Arista™ AH group (P = 0.0004) • There were no significant differences in the reduction in hemoglobin levels between pre-operative levels and post-operative Day 2 between the Arista™ AH and control groups (P = 0.604) • There were no differences in transfusion rates between the groups (P = 0.844)

(*Continued*)

Table 5 (Continued).

Reference	Study Design; N; Comparators	Surgery Type	Key Results
Studies comparing Arista™ AH to other hemostats			
Bard Davol Inc (2015)[39]	• Prospective, multi-center, randomized, non-inferiority, controlled • N = 288 • n = 145 Arista™ AH • n = 143 absorbable gelatin sponge with or without Thrombin	• General • Orthopedic • Cardiac	• Complete hemostasis within 5 min (3 min for cardiac surgery): - Arista™ AH: 90.3% - Gelatin sponge: 80.4% - P < 0.0001 • Complete hemostasis in 1 min: - Arista™ AH: 50.3% - Gelatin sponge: 32.9% • Complete hemostasis in 3 min: - Arista™ AH: 85.5% - Gelatin sponge: 72.0% • P = 0.003 (overall time to hemostasis) • Time to hemostasis, median (min) - Arista™ AH: 1.0 - Gelatin sponge: 2.0 - P = 0.002
Palacios et al (2013)[59]	• Retrospective • N = 23 • n = 12 Arista™ AH • n = 11 FloSeal® (contralateral side)	• Renal	• There were no significant differences between Arista™ AH and FloSeal® in the cool ischemia time, intra-operative blood loss, duration of hospital stay, or postoperative complications
Antisdel et al (2016)[60]	• Prospective, double-blind • N = 48 • n per group not reported • Arista™ AH • Sinufoam™ (CMC foam/gel) • Nexfoam® (starch wafer)	• Sinus	• There were no significant differences between groups in patient-reported symptoms • There were no significant differences in synechiae formation, debridement requirement, mucosal edema, or infection between the groups • There was more crusting and granulation the Sinufoam™ group, although the difference was not statistically significant

Abbreviations: AH, absorbable hemostat; CMC, carboxymethyl cellulose; ICU, intensive care unit; MPH, microporous polysaccharide hemospheres.

reduced hemostasis time, postoperative chest tube output in the first 48 hours, and the need for postoperative blood transfusion.[2] In another retrospective study of patients undergoing cardiac surgery, MPH was associated with a significantly lower rate of complications including hematoma and infections compared with control.[56] A randomized, controlled study of 40 patients undergoing nasal surgery reported that MPH significantly reduced postoperative bleeding compared with control, with no differences in the rate of infections, edema, synechiae formation, pain, obstruction, or nasal discharge between the groups.[57,58] In a retrospective study of patients undergoing robot-assisted prostatectomy, operating room time was shorter in the MPH group than in the control group.[59]

Two studies did not show differences in clinical outcomes between MPH and control treatment. In a study of patients undergoing mastectomy, there were no significant differences between the MPH and control groups in the duration or quantity of serosanguinous drainage or postoperative complications.[39] In a retrospective chart review of patients undergoing primary total knee arthroplasty, there were no differences in the rate of hematomas or infections between the MPH and control groups.[61]

Comparative studies of MPH versus other hemostats are limited, with considerable variability among published studies in terms of study design, surgery type, and reported outcomes. Currently, ongoing studies are being performed to better compare Arista to other hemostatic agents. The safety and effectiveness of MPH compared with those of a gelatin sponge with or without thrombin were evaluated in a prospective, multi-center, multi-specialty, randomized, non-

inferiority, controlled study.[42] The study included 288 patients undergoing general (n = 144), orthopedic (n = 72), or cardiac (n = 72) surgery. The proportion of patients who achieved complete hemostasis of the first treated lesion with 5 minutes (3 minutes for cardiac surgery; primary endpoint), was significantly higher in the MPH group (90.3%) than in the gelatin sponge group (80.4%; $P < 0.0001$). The time to achieve complete hemostasis was significantly different between the MPH and gelatin sponge groups ($P = 0.003$). The proportion of patients who achieved complete hemostasis within one minute was higher in the MPH group (50.3%) compared with the gelatin sponge group (32.9%).

A retrospective study of patients undergoing partial nephrectomy surgery also compared MPH to FloSeal®, a gelatin/thrombin-based hemostatic matrix.[62] Both agents effectively achieved hemostasis, with no differences between the groups in the cool ischemia time, intra-operative blood loss, duration of hospital stay, or postoperative complications. A prospective, double-blind study of patients undergoing sinus surgery compared MPH with Sinufoam™, a carboxylmethyl cellulose-based foam/gel and Nexfoam®, a starch-based sponge hemostat.[63]

Comparative clinical evidence shows that there were no significant differences between MPH and FloSeal® in renal surgery or nasal dressings in sinus surgery, indicating that MPH is equally effective in these surgical settings.[62,63] However, it should be noted that these studies enrolled a relatively small number of participants (N = 23–48) and therefore the results may not have reached statistical significance. Therefore, further studies are needed to further evaluate the comparative efficacy of MPH and other hemostats.

Economic Benefits of Using an Effective Topical Hemostatic Agent

Evidence shows that selection of optimal hemostatic agents can lead to cost savings, resulting from reduced surgery time, reduced need for surgical re-interventions, fewer blood transfusions, and fewer post-operative complications.[6,7,17,68,74,75] Cost savings associated with these outcomes can be substantial, with one study showing that, for a US hospital that performed 245 cardiac surgeries annually, the improved outcomes associated with a topical hemostat corresponded to a net annualized saving of $1,532,896.[68] Another study that evaluated cost savings associated with the use of hemostats in spine surgery in the US estimated hospital savings of $2445 per surgery.[74] Additionally, a study that evaluated economic benefits of a topical hemostat from the perspective of the National Health Service in the United Kingdom (UK) showed overall net savings to the NHS of £178,283 ($228,078 USD) per 100 cardiac surgery patients who experience intraoperative bleeding requiring hemostatic therapy.[17]

Taken collectively, results of these studies indicate that selection of the appropriate hemostatic agent can provide substantial cost savings for hospitals as a result of improved clinical outcomes.

Discussion

As detailed in this review, MPH is a safe and effective hemostatic agent in various types of surgical procedures. Although all powder hemostats are efficacious at achieving hemostasis, MPH has a well-established safety profile and therefore addresses some of the limitations associated with other hemostats. For example, ORC has been associated with foreign body reactions, adhesion formation, and hematoma.[23,24] In contrast, animal studies show that MPH reduced adhesion formation compared to the control[73] and is not associated with foreign body reactions[67] or granuloma formation.[71]

Fast absorption time is a key benefit of MPH over other powder hemostats. This feature is particularly important when postoperative imaging is required, as residual material associated with some hemostats may interfere with diagnostic imaging and cause incorrect diagnoses such as abscesses or hematomas.[28,29] Additionally, MPH is the only starch-based powder hemostat that has been shown not to exhibit starch crystallinity, which decreases the risk of adhesion formation and granulomatous reactions. Accordingly, MPH has a well-documented safety profile and is not associated with foreign body reactions or allergic reactions.

Overall, preclinical and clinical evidence indicates that MPH is a safe and effective powder hemostat and provides solutions in a multitude of bleeding situations and surgical settings. A summary of published clinical evidence for MPH is provided in Tables 2–5. Notably, in two studies, MPH was associated with a shorter OR time compared with control (although statistical significance was not reached in one of the studies). Although comparative clinical evidence evaluating MPH versus ORC is limited, published studies generally show that MPH is associated with equally low rates of complications, including hematoma and infection, as other topical hemostats. However, additional studies with larger numbers of participants are ongoing to determine the benefits of MPH versus other powder hemostats.

Although there are few studies that evaluated the economic value of MPH, its clinical benefits, including reduced surgery duration, reduced need for re-interventions, fewer blood transfusions, and reduced rate of complications, can provide significant economic benefits. The rapid absorption of MPH may provide further economic benefits over hemostats that do not get rapidly absorbed from the surgical site. For example, residual ORC can interfere with diagnostic imaging, with residual hemostat appearing as a pathological condition and therefore necessitate further investigation and medical interventions.[28,29] Therefore, hemostats that are completely absorbed by the tissue may be advantageous in terms of reducing the costs of additional medical procedures.

While the benefits of MPH have been established in the literature and discussed in this review, it should be noted that there are some limitations listed in the product Instructions for Use.[39] Due to its primary component being potato starch, it is recommended that no more than 50g of MPH be used in patients with diabetes, though this is not unique to MPH and is similar to other starch-based hemostats. Also, the safety and effectiveness has not been fully established in neurosurgical and ophthalmic procedures.

Finally, potential economic or surgical benefits of MPH may result from a reduced need for specialized storage, which reduces preparation time and potential costs.[42,69] A survey of 200 US registered nurses reported that hemostatic agents that require mixing or preparation prior to application (ie, Floseal®, Thrombin, Tissel®, Sugiflo®, Gelfoam® Plus, and Vitagel®) required two to six minutes of preparation time.[69] Therefore, agents that are ready on demand, such as MPH, may save costs as a result of reduced nursing time, as well as a reduction in wasted product (ie, product that is mixed but unused).

Conclusions

In summary, published preclinical and clinical evidence supports the use of MPH as a topical hemostatic agent in a variety of surgical settings. Use of MPH may be particularly beneficial in situations where fast absorption of the hemostat is desired, such as cases that require post-operative imaging. More trials and ongoing studies will continue to better define the benefits of MPH.

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