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REVIEW ARTICLE

Mechanism and Clinical Efficacy of Spray-on Powder Systems for Hemostasis

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Abstract: Rapid control of non-compressible hemorrhage remains a critical challenge in both emergency medicine and surgical interventions. Traditional methods often fail to address complex wound geometries or high-pressure arterial bleeds in pre-hospital settings. Spray-on powder technologies have emerged as a transformative approach, utilizing high-surface-area microparticles to accelerate the natural coagulation cascade. These systems function through rapid moisture absorption, concentrating clotting factors, and providing a physical scaffold for platelet aggregation. Various formulations, including chitosan-based derivatives, inorganic minerals like zeolites or kaolin, and synthetic polymers, show significant potential in reducing time-to-hemostasis and improving survival rates in traumatic injury models. The delivery mechanism, typically involving pressurized aerosolization or manual bellows, ensures uniform coverage over irregular tissue surfaces, facilitating immediate interaction between the hemostatic agent and the wound bed. The state of current bioengineering techniques highlights the shift from passive dressings to active, micro-engineered interventions capable of stabilizing life-threatening bleeds within seconds. Future developments focus on improving the biocompatibility of these powders and integrating antimicrobial properties to mitigate infection risks during the critical "golden hour" of trauma care.

Keywords: Hemostasis; Hemostatic Powder; Coagulation Cascade; Chitosan; Trauma; Hemorrhage.

1. Introduction

Uncontrolled hemorrhage is one of the primary cause of preventable mortality in traumatic injury, representing a global health crisis that spans both civilian emergency response and frontline military operations. Statistics indicate that exsanguination is responsible for approximately 30% to 40% of all trauma-related deaths, with a significant portion occurring in the pre-hospital environment before definitive surgical care can be administered [1]. While the "golden hour" the critical window for life-saving intervention is well-recognized, the ability to achieve rapid vascular stabilization depends heavily on the tools available at the point of injury. In military contexts, the prevalence of high-energy penetrating trauma from explosive devices or ballistic fragments has increased the incidence of complex, multi-site bleeding that defies conventional management strategies.

The clinical disparity between extremity injuries and non-compressible hemorrhage is a fundamental driver of innovation in this field. While mechanical interventions like tourniquets and direct circumferential compression are highly effective for distal limb injuries, they are anatomically impossible to apply in junctional zones such as the axilla, groin, or supraclavicular regions, as well as within the abdominal and thoracic cavities [2]. These "non-compressible" areas host major vascular structures that, when compromised, result in rapid volumetric blood loss. The physiological environment in these zones is characterized by deep, irregular wound channels where the source of the bleed is often obscured by pooled blood or necrotic tissue, rendering standard pressure-based techniques insufficient. The limitations of traditional hemostatic agents have led to redundancy of passive materials. Current gold standards, which predominantly consist of gauzes impregnated with pro-coagulant minerals like kaolin or polysaccharides like chitosan, rely on the user's ability to pack the wound tightly and maintain continuous manual pressure for a minimum of three to five minutes [3]. In high-stress scenarios such as multi-casualty incidents or active combat providing sustained manual compression is often impractical or physically impossible for a single provider. Traditional gauzes frequently fail to achieve intimate contact with the bleeding vessel in deep or narrow wound tracts, as the density of the dressing material prevents it from conforming to the intricate micro-topography of a ragged injury. This lack of conformance creates "dead spaces" where blood continues to pool and

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bypass the hemostatic interface. The emergence of spray-on powder systems represents a fundamental shift in the logic of wound management, transitioning from "packing" to "coating" technologies. By delivering finely divided particles through a pressurized propellant or an air-driven manual mechanism, these systems leverage the physics of fluid dynamics to achieve a level of penetration into wound crevices that is otherwise inaccessible [4]. Unlike solid dressings, aerosolized powders act as a cloud of active agents that can navigate around anatomical obstructions, adhering to moist tissue surfaces and establishing a hemostatic barrier regardless of the wound's geometry. This kinetic delivery ensures that the active material reaches the actual site of vascular breach, providing a more reliable interface for the initiation of the clotting process.

The efficacy of these innovative powders is derived from their multi-modal ability to manipulate the immediate physical and chemical environment of the hemorrhage. Upon contact with blood, these micro-particles act as highly efficient desiccants, rapidly absorbing the aqueous component of plasma and effectively concentrating the remaining platelets and endogenous clotting factors into a dense, pro-coagulant slurry [5]. This localized concentration effect significantly reduces the time required for the biochemical pathways to reach the threshold for fibrin formation. Additionally, many of these powders are engineered to provide direct chemical activation of the intrinsic or extrinsic pathways, bypassing the usual rate-limiting steps of the coagulation cascade. This review provides an account of the evolution of these materials, the specific biomechanical logic of their action, and the clinical data that supports their integration into modern trauma protocols.

2. Physiological Foundations of Hemostasis

The biological response to vascular injury involves a complex interplay of vascular constriction, platelet plug formation, and the activation of the coagulation cascade. Effective hemostatic powders are designed to augment one or more of these phases to achieve stability faster than the body's innate system.

2.1. The Coagulation Cascade and Secondary Hemostasis

The coagulation cascade is a series of enzymatic reactions divided into the intrinsic and extrinsic pathways, converging on the common pathway to convert fibrinogen into fibrin [6]. Most spray-on powders target the concentration of these essential proteins. When blood encounters a porous powder, the liquid component is absorbed, significantly increasing the local concentration of thrombin and fibrinogen [7]. This concentration effect effectively bypasses certain rate-limiting steps in the cascade, allowing for rapid fibrin polymerisation even in patients with diluted clotting factors due to massive fluid resuscitation [8].

2.2. Platelet Activation and Aggregation

Platelets serve as the primary cellular component of the initial clot. Certain spray-on materials, particularly those with a net positive charge like chitosan, interact directly with the negatively charged membranes of red blood cells and platelets [9]. This electrostatic attraction leads to the formation of a "mucoadhesive" plug that seals the vessel wall before the full fibrin mesh has matured [10]. The physical structure of the powder particles also provides a high-surface-area scaffold that encourages platelet adhesion and subsequent degranulation, releasing further pro-coagulant signals into the micro-environment [11].

3. Materials Science of Spray-on Hemostats

The choice of material dictates the speed of hemostasis and the long-term biological impact on the tissue. Materials are generally categorized into natural biopolymers, inorganic minerals, and synthetic composites.

3.1. Chitosan and Polysaccharide Derivatives

Chitosan, derived from the deacetylation of chitin, is one of the most researched materials for spray-on applications due to its inherent biocompatibility and hemostatic properties [12].

3.1.1. Electrostatic Interaction Mechanisms

The primary mechanism for chitosan-based powders is the "ionic bridge" formed between the polymer and blood components. Because blood cells carry a negative surface charge, the protonated amine groups on the chitosan chain create a rapid agglutination effect [13]. This process is independent of the classical coagulation cascade, making it particularly useful for patients on anticoagulant therapy, such as heparin or warfarin, where the chemical pathway is inhibited but the physical-ionic pathway remains functional [14].

Table 1. Classification of Hemostatic Powders by Origin and Mechanism

Material Category	Examples	Mechanism of Action	Surface Charge / Property
Natural Polysaccharides	Chitosan, Chitin, Starch	Electrostatic agglutination of RBCs; mucoadhesion	Highly Positive (Cationic)
Inorganic Minerals	Kaolin, Zeolite, Smectite	Factor XII activation; molecular sieving/dehydration	Highly Negative (Anionic)
Synthetic Polymers	Polyethylene Glycol (PEG), Cyanoacrylate	Chemical cross-linking; instant polymerization	Chemically Reactive
Biological Proteins	Thrombin, Fibrinogen, Collagen	Direct conversion of fibrinogen to fibrin	Bio-active Enzyme

3.1.2. Mucoadhesion

Beyond simple clotting, chitosan powders exhibit strong mucoadhesive properties, allowing the powder to stick to moist tissue surfaces and resist being washed away by high-pressure arterial flow [15]. This adherence is crucial for "spray-on" applications where the material must remain localized despite the force of the bleed. Over time, these polysaccharides are enzymatically degraded by lysozymes in the body, reducing the need for painful secondary debridement of the wound [16]

3.2. Inorganic Mineral-based Powders

Inorganic minerals represent a historically significant class of hemostatic agents. These materials typically function through physical adsorption and the activation of the intrinsic coagulation pathway via contact with negatively charged surfaces.

3.2.1. Zeolites and Molecular Sieves

Zeolites are crystalline aluminosilicates characterized by a highly porous structure. When applied as a spray-on powder, zeolites act as molecular sieves that rapidly trap water molecules from the blood [17]. This selective dehydration concentrates platelets and clotting factors, such as Factor XII and prothrombin, at the site of injury [18]. While early formulations were associated with exothermic reactions that caused thermal tissue damage, modern micro-engineered zeolite powders have been modified to mitigate heat release while maintaining high absorbent capacity [19].

3.2.2. Kaolin and Smectite Clays

Kaolin is an aluminosilicate clay that directly activates the Hageman factor (Factor XII), initiating the intrinsic pathway of the coagulation cascade [20]. In a sprayable powder form, kaolin particles provide an expansive surface area for enzymatic assembly. Unlike biopolymers that rely on mucoadhesion, kaolin-based systems are primarily biochemical activators [21]. Smectite clays, such as bentonite, offer similar benefits but include superior swelling properties, which help in physically occluding smaller capillary bleeds through the formation of a viscous mineral paste upon contact with plasma [22].

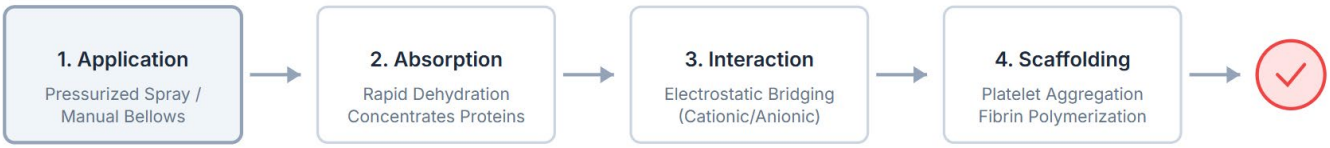

Figure 1. Biomechanical Pathway of Hemostatic Powders

3.3. Synthetic and Composite Formulations

To overcome the limitations of single-component materials, researchers have developed synthetic and hybrid powders that combine rapid action with improved safety profiles.

3.3.1. PEG-based and Cyanoacrylate Powders

Synthetic polymers like Polyethylene Glycol (PEG) and certain cyanoacrylates have been adapted into powder delivery systems. PEG-based powders often incorporate reactive groups that cross-link upon contact with the amine groups found in tissue proteins,

creating a robust synthetic seal [23]. Cyanoacrylate micro-powders, when aerosolized, polymerize instantly in the presence of moisture, providing an airtight and watertight barrier that is particularly effective for sealing air leaks in pulmonary surgery or stopping persistent oozing from highly vascular organs like the liver [24].

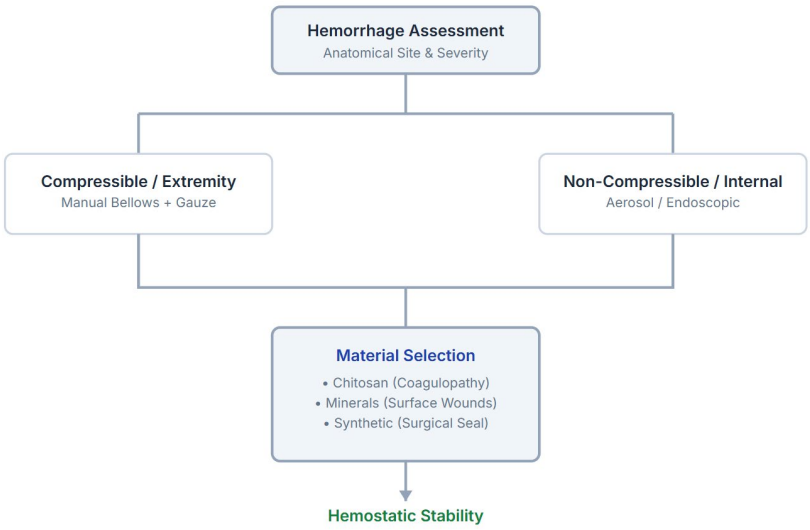

Figure 2. Decision-making Process for Hemostatic Powder Intervention.

3.3.2. Hybrid Bio-inorganic Composites

Hybrid systems attempt to leverage the ionic bonding of chitosan with the cascade activation of minerals like kaolin. These composites are engineered to provide a multi-modal approach: the mineral component initiates the clot, while the polymer component ensures the clot remains adhered to the wound wall [25]. Recent advancements include the incorporation of silver nanoparticles or localized antibiotics within the powder matrix to provide sustained antimicrobial activity without compromising the speed of hemostasis [26].

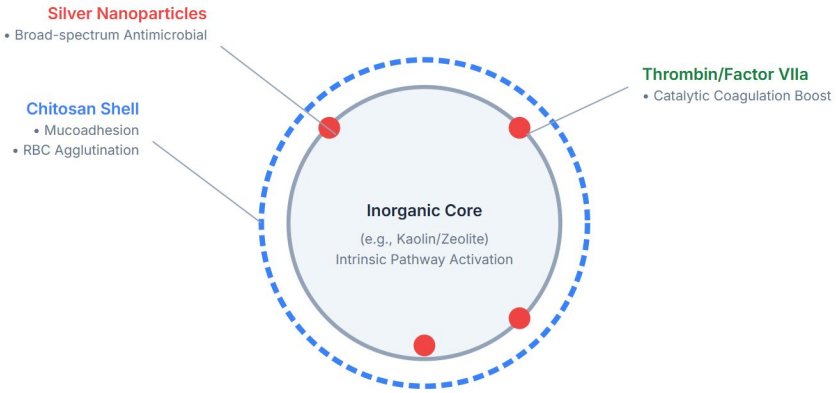

Figure 3. Structural Anatomy and Synergy of Hybrid Powders

Table 2. Hemostatic Materials and their Properties

Parameter	Chitosan-based Powders	Inorganic Mineral Powders	Synthetic PEG/Sealants
Onset of Action	2–5 Minutes	1–3 Minutes	< 1 Minute
Coagulation Dependency	Independent (Works with Anticoagulants)	Dependent (Requires Clotting Factors)	Independent (Mechanical Seal)
Tissue Adherence	High (Mucoadhesive)	Moderate (Forms Paste)	Very High (Covalent Bond)
Exothermic Reaction	None	Potential (in early Zeolites)	Minimal
Biodegradability	Excellent (Lysozyme degradation)	Poor (Requires debridement)	Variable (Hydrolytic)

4. Engineering of Spray-on Delivery Systems

The effectiveness of a hemostatic powder is heavily dependent on its delivery. A uniform, pressurized application is necessary to ensure the powder reaches the base of deep wounds and resists being displaced by active blood flow.

4.1. Aerosolization and Pressurized Propellants

Aerosol systems utilize medical-grade propellants to deliver hemostatic particles. This method provides a consistent flow rate and allows for a "dry" application that does not add excess fluid to the wound [27]. The kinetic energy of the aerosolized particles assists in their penetration through the blood layer to reach the damaged endothelium [28]. However, the use of pressurized gases requires careful regulation to avoid the risk of air embolism, especially when spraying near open venous structures in the thoracic or abdominal cavities [29].

4.2. Manual Bellows and Air-driven Dispensers

Manual delivery systems, such as bellows or squeeze-bulbs, offer a simplified, low-cost alternative for pre-hospital and military use. These systems rely on the user to generate the force required to expel the powder [30]. While less consistent than automated aerosols, manual dispensers are highly portable and eliminate the risks associated with pressurized propellants [31]. The design of the nozzle is critical in these devices; elongated, flexible tips allow surgeons to navigate around anatomical obstructions to reach junctional areas or posterior vessel walls [32].

4.3. Powder Particle Size and Morphology

The fluid dynamics of the spray are governed by the morphology of the powder. Particles are generally engineered to be between 10 and 100 micrometers [33].

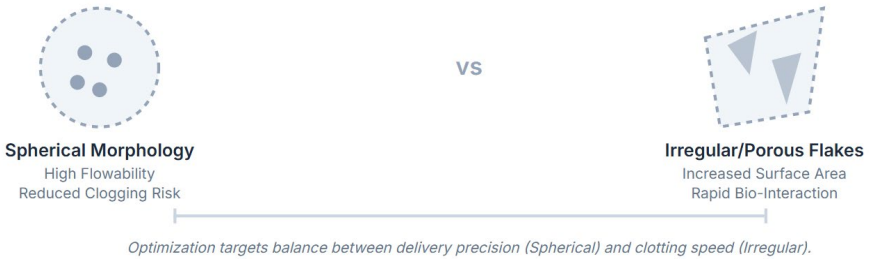

Figure 4. Impact of Particle Microstructure on Functional Outcomes.

Particles that are too fine may become airborne and pose an inhalation risk to the medical provider, while particles that are too large may not achieve the necessary surface area-to-volume ratio for rapid moisture absorption [34]. Spherical morphologies are often preferred for their flowability, preventing clogging within the delivery device and ensuring a predictable spray pattern [35].

Table 3. Technical Specifications of Spray-on Delivery Systems

Delivery Mode	Driving Mechanism	Optimal Particle Size	Primary Advantage	Main Limitation
Aerosol Canister	Compressed Gas (CO_2/Nitrogen)	20–50 µm	Consistent flow; deep penetration	Risk of air embolism
Manual Bellows	Atmospheric Air (Compression)	50–100 µm	Portable; no specialized gas	Variable pressure/dosage
Endoscopic Catheter	Air Pump / Channel Flush	10–40 µm	Non-invasive; targeted internal use	Frequent nozzle clogging
Laparoscopic Sprayer	Pressurized CO_2	30–60 µm	Precise application in MIS	Requires specialized hardware

5. Clinical Applications and Efficacy Profiles

The transition of spray-on powders from experimental models to clinical practice is defined by their performance in high-stakes environments, such as battlefield medicine and complex surgical suites.

5.1. Traumatic Hemorrhage and Pre-hospital Care

In trauma management, the ability to control hemorrhage during the "golden hour" is the primary determinant of survival. Spray-on powders offer an advantage in treating junctional wounds areas such as the groin, axilla, or neck where standard tourniquets cannot be applied [36].

5.1.1. Penetrating and Fragment Injuries

For narrow, deep wound tracts caused by shrapnel or ballistic trauma, traditional gauze packing is often insufficient and difficult to perform under fire. High-pressure spray systems can propel hemostatic particles deep into the wound cavity, ensuring contact with the severed vessel [37]. Studies in porcine models of lethal femoral artery injury have demonstrated that spray-on chitosan powders can achieve stable hemostasis in under three minutes, significantly reducing the volume of blood loss compared to standard pressure dressings [38].

5.1.2. Non-compressible Torso Hemorrhage

Internal bleeding within the abdominal or thoracic cavities presents a unique challenge as manual pressure is impossible. Recent developments in laparoscopic sprayers allow for the application of hemostatic powders during minimally invasive procedures or emergency laparotomies [39]. These systems are particularly effective for "weeping" hemorrhage from parenchymal organs like the spleen or liver, where the diffuse nature of the bleed makes suturing or clipping impractical [40].

5.2. Surgical Hemostasis

Beyond trauma, spray-on powders serve as essential adjuncts in elective and emergency surgeries where traditional mechanical or thermal hemostasis is insufficient.

Table 4. Clinical Efficacy of Hemostatic agents in various Injury Models

Clinical Indication	Study Type	Hemostatic Agent	Outcome Metric	Reference
Lethal Femoral Bleed	Porcine (Swine)	Chitosan Powder	100% Survival at 3 hours	[38]
Upper GI Bleeding	Human Clinical Trial	Mineral Powder	96% Initial Hemostasis	[41]
Liver Parenchymal Tear	Murine (Rat)	Cyanoacrylate	45-second TTH (Time to Hemostasis)	[24]
Splenic Trauma	Porcine (Swine)	Zeolite	Reduced blood loss by 60%	[17]
Arterial Anastomosis	Human Case Series	PEG-based Spray	Zero post-op re-bleeding	[43]

5.2.1. Gastrointestinal Endoscopy

One of the most successful clinical applications of hemostatic powder is in the management of upper gastrointestinal bleeding. Endoscopic delivery catheters allow for the non-contact application of mineral or polysaccharide powders to bleeding ulcers or post-polypectomy sites [41]. The powder forms a mechanical barrier over the lesion, which is particularly beneficial for patients with diffuse neoplastic bleeding where a single source cannot be identified [42].

5.2.2. Cardiovascular and Thoracic Surgery

In cardiac surgery, persistent needle-hole bleeding from prosthetic grafts or anastomotic sites can lead to significant post-operative complications. Sprayable synthetic powders, such as PEG-based sealants, provide an immediate waterproof seal that resists the high pressures of the arterial system [43]. In thoracic surgery, these powders are utilized to seal alveolar air leaks, reducing the duration of chest tube drainage and hospital stay [44].

6. Safety, Biocompatibility, and Metabolic Clearance

The long-term physiological impact of hemostatic powders is as critical as their immediate efficacy. An ideal agent must be effectively cleared by the body without inducing systemic toxicity or excessive inflammation.

6.1. Inflammatory Response and Tissue Healing

All foreign materials introduced into a wound elicit some degree of inflammatory response. Inorganic minerals, if not thoroughly debrided, can lead to granuloma formation or delayed wound healing [45]. In contrast, biodegradable polymers like chitosan or starch-based powders are typically resorbed within days to weeks through enzymatic pathways, leaving minimal histological evidence of their presence [46].

Table 5. Safety Profiles and Metabolic Fate of Selected Materials

Material	Systemic Absorption Risk	Local Inflammatory Response	Metabolic Clearance Pathway
Chitosan	Negligible	Low/Transient	Enzymatic (Lysozyme/Chitinase)
Kaolin	Low (if localized)	Moderate (Granuloma risk)	Phagocytosis (Insoluble)
PEG	Minimal	Very Low	Renal Excretion (Hydrolysis)
Starch	Moderate (Micro-particles)	Minimal	Amylase Degradation
Cyanoacrylate	Negligible	Moderate (Heat release)	Sloughing/Slow Degradation

6.2. Risk of Systemic Embolization

A significant concern with aerosolized or fine-particle powders is the potential for material to enter the venous circulation, leading to pulmonary or systemic embolization. This risk is highest when applying powders under high pressure directly into large, open venous voids [47]. Engineering controls, such as larger particle sizes and regulated delivery pressures, are essential to mitigate these risks. Clinical guidelines recommend maintaining a specific distance between the spray nozzle and the tissue surface to prevent the forced entry of gas or particles into the vasculature [48].

7. Next Generation Hemostats

The next generation of spray-on hemostats is moving toward "smart" materials that respond to the wound environment or provide multi-functional therapeutic benefits.

7.1. Stimuli-Responsive and Bio-Active Systems

Research is currently focused on powders that undergo phase transitions such as turning from a powder to a hydrogel upon contact with blood [49]. This change increases the cohesive strength of the clot and improves its resistance to displacement. Additionally, the incorporation of pro-coagulant enzymes like thrombin or snake venom-derived proteins into the powder matrix can further accelerate the clotting process in coagulopathic patients [50].

7.2. Digital and Robotic Delivery

As robotic-assisted surgery becomes more prevalent, the integration of automated spray systems into robotic platforms is anticipated. These systems could use computer vision to identify bleeding points and apply a precise dose of hemostatic powder with sub-millimeter accuracy, minimizing material waste and maximizing efficacy [50].

8. Conclusion

Spray-on hemostatic powders represent a significant advancement in the management of acute hemorrhage. These systems provide a versatile solution for wounds that are otherwise difficult to treat by combining the rapid biochemical activation of the coagulation cascade with the physical benefits of high-surface-area microparticles. While material selection ranging from natural polysaccharides to inorganic minerals dictates the specific mechanism of action, the engineering of the delivery device is equally paramount to ensure effective tissue coverage. As formulations become more biocompatible and delivery methods more precise, these innovative tools will continue to play an indispensable role in reducing trauma-related mortality and improving surgical outcomes.

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