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Hemostatic Sponges for Trauma Management: A Comparative Review of Chitosan, Gelatin, and Kaolin-Based Materials

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Abstract. Uncontrolled hemorrhage remains one of the leading causes of trauma-related mortality, and traditional methods such as compression or ligation are often insufficient in complex or large-area bleeding scenarios. In response, hemostatic sponges have emerged as promising materials due to their strong fluid absorption, compressibility, and potential for bioactive functionalization. This review focuses on three representative types of hemostatic sponges—chitosan-, gelatin-, and kaolin-based systems. Relevant studies were collected and analyzed to summarize their structural features, hemostatic mechanisms, biological properties, and reported clinical performance. The comparison highlights both the advantages, such as biocompatibility, antibacterial potential, and clot-promoting activity, and the limitations, including solubility issues, mechanical weakness, or lack of biodegradability. Overall, this review provides a comprehensive evaluation of current sponge-based hemostatic materials. It concludes that the rational combination of natural polymers with inorganic components, as well as structural optimization, could significantly improve their performance. These insights offer guidance for the design of next-generation hemostatic sponges with enhanced safety, multifunctionality, and clinical applicability.

Keywords: Hemostasis, Hemostatic sponges, Chitosan, Gelatin, Kaolin, Biomaterial

1. Introduction

Hemorrhage, particularly acute and uncontrolled bleeding, remains a major contributor to trauma-related mortality. Examples include subarachnoid hemorrhage, intracranial hemorrhage, and obstetric hemorrhage. Moreover, excessive bleeding can cause other adverse symptoms and even death [1-3]. While traditional hemostatic strategies (e.g., direct compression or ligation) are effective in certain contexts, their limitations become evident in situations involving massive bleeding, irregular wound surfaces, or limited access to immediate medical intervention [4-5]. The mechanism of hemostasis contains primary and secondary processes: Upon vascular injury, an immediate vasoconstrictive response is initiated to reduce blood flow at the site of damage. Concurrently, the exposure of subendothelial matrix components—particularly collagen—triggers platelet adhesion. The adherent platelets undergo activation and the release of procoagulant mediators, which serve to amplify platelet recruitment and aggregation. This results in the formation of a primary platelet plug.

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Subsequently, the coagulation cascade is activated through either the intrinsic or extrinsic pathway, ultimately converging on the activation of prothrombin to thrombin. Thrombin cleaves soluble fibrinogen into insoluble fibrin monomers, which spontaneously polymerize to form a fibrillar network. This fibrin meshwork interlaces with the platelet plug, stabilizing the clot and restoring vascular integrity [5-6].

These clinical demands have driven the development of advanced hemostatic materials that can promote rapid clotting, provide mechanical support, and integrate effectively with biological tissues. Among various hemostatic strategies, hemostasis sponge represents a promising class of materials, characterized by several advantages. These include efficient fluid absorption that facilitates platelet aggregation, compressibility that enables physical hemostasis, and the potential for antibacterial and self-healing functionalities through rational material design and incorporation of bioactive components [7]. Up till now, many kinds of hemostasis sponges have been invented. Chitosan hemostatic sponges, as a type of polysaccharide-based hemostatic sponge, are typically prepared using chitosan as the base material, crosslinked with other substances. This is attributed to chitosan's biocompatibility, antibacterial properties, and structurally engineered porous framework [7-8]. Gelatin, a natural polymer derived from collagen, is considered another effective hemostatic material due to its excellent biocompatibility, strong water-absorbing capacity, and intrinsic ability to promote coagulation [9]. However, since it lacks intrinsic antibacterial properties, gelatin is often combined with antimicrobial components (e.g., ZnO and AgNPs) to effectively prevent wound-related infections [10-12]. Additionally, many sponges use kaolin as a base material, and different substrates are cross-linked to achieve of hemostasis sponges based on three representative materials, focusing on their structural characteristics, hemostatic mechanisms, and material-specific advantages. Considering the high risk of mortality from uncontrolled hemorrhage, the development of safe and multifunctional hemostatic sponges is of great clinical importance. By comparing chitosan-, gelatin-, and kaolin-based sponges, this review aims to clarify their strengths and weaknesses and provide guidance for designing next-generation hemostatic materials with better clinical applicability.

2. Hemostatic sponges

2.1. Chitosan hemostatic sponge

Chitosan, its oligosaccharides, and derivatives have demonstrated considerable potential as therapeutic materials due to their antimicrobial activity, anti-inflammatory effects, and inherent biological viscosity. As a polysaccharide, chitosan can be enzymatically degraded in vivo into non-toxic byproducts, which enhance its biocompatibility and safety for biomedical applications. Moreover, the presence of three reactive functional groups on the chitosan backbone enables diverse chemical modifications, allowing the generation of novel derivatives with tailored physicochemical and biological properties. These polymers exhibit varying levels of antimicrobial activity against different microorganisms, which are influenced by multiple factors such as molecular weight, degree of acetylation, and environmental pH. Studies have shown that, in acidic media, the antibacterial efficacy of chitosan increases with higher molecular weight. In contrast, under neutral conditions, this trend is reversed, with higher molecular weight associated with reduced antimicrobial activity. Notably, the correlation between molecular weight and antimicrobial efficacy differs between chitosan and its oligosaccharide derivatives, and the underlying mechanisms governing these differences remain unclear to date. In addition, while chitosan itself possesses anti-inflammatory properties, chitooligosaccharides have been reported to exert pro-inflammatory effects. Regarding

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acetylation, a lower degree of acetylation is generally associated with enhanced antimicrobial performance [13].

Recent advances have highlighted chitosan-based materials as promising candidates for the development of hemostatic sponges. A hemostatic sponge was developed by combining chitosan with hydroxypropyl methylcellulose (HPMC) using a blending and freeze-drying strategy. The resulting material exhibited excellent flexibility, high porosity, and a coagulation-promoting chemical structure. Moreover, it effectively induced red blood cell and platelet adhesion, thereby exhibiting rapid hemostatic efficacy [14]. In another study, a composite sponge was fabricated by coupling chitosan to alginate and fucoidan. The resulting material exhibited favorable elasticity and significantly promoted wound healing, particularly by enhancing epidermal regeneration, collagen deposition within the dermis, and even hair follicle neogenesis [15]. In addition, chitosan has also been combined with cellulose and tannic acid to construct a bio-composite sponge. This material exhibited excellent blood absorption capacity, contributing to its superior procoagulant performance. It also exerted strong antioxidant activity and effective antibacterial activity against Staphylococcus aureus and Escherichia coli [16]. Furthermore, another chitosan-based hemostasis sponge constructed by immobilizing peptides onto a chitosan–graphene matrix also exhibited excellent fluid absorption capacity. This material effectively activated platelets and triggered the coagulation cascade, demonstrating outstanding hemostatic performance. Moreover, it showed good biocompatibility, indicating a favorable safety profile for clinical biomedical applications [17].

2.2. Gelatin hemostasis sponge

Gelatin is a natural biopolymer extracted from collagen, featuring excellent biocompatibility, biodegradability, and low immunogenicity, making it a promising candidate for various biomedical applications [18]. According to reports, as a partial hydrolysate of collagen, gelatin retains an amino acid composition similar to the extracellular matrix (ECM), predominantly consisting of glycine, proline, and hydroxyproline. This enables it to closely mimic the natural ECM structure, thereby enhancing compatibility with cells and host tissues [19-20]. Additionally, gelatin contains Arg-Gly-Asp (RGD) motifs and matrix metalloproteinase (MMP)-sensitive sites, which are crucial for promoting cell adhesion, migration, and differentiation, while facilitating enzymatic degradation and remodeling in vivo [21]. Its lower content of aromatic amino acids (e.g., tyrosine and tryptophan) compared to collagen reduces the likelihood of forming antigenic epitopes, thus minimizing immunogenic responses [22]. Nevertheless, gelatin lacks inherent antimicrobial activity and often requires the incorporation of functional additives or other polymers to achieve infection resistance [23]. In addition to these biological advantages, gelatin is capable of forming physical cross-links naturally, which makes it a favorable base matrix for constructing novel composite hemostatic sponges by incorporating other functional agents. However, the physical cross-linked networks formed by gelatin are thermally unstable under physiological conditions. Therefore, it is often necessary to introduce chemical cross-linking strategies to enhance the structural stability and performance of gelatin-based materials in practical applications [24].

Based on these favorable characteristics, gelatin is widely regarded as a promising base material for the development of hemostatic sponges. For instance, according to Zhu et al., a hemostatic sponge fabricated by cross-linking aminated gelatin with dialdehyde starch exhibited excellent biocompatibility and hemostatic efficacy. This performance was attributed to its hydrophilic nature and highly porous surface morphology, which not only facilitate rapid absorption of blood fluid but also enhance electrostatic interactions that accelerate the coagulation cascade [25]. Xie et al. created an ultralight three-dimensional gelatin sponge composed of nanofibers by using a conjugated

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electrospinning strategy. This sponge exhibited a unique high surface area and exceptional liquid absorption capacity. Moreover, it demonstrated excellent biocompatibility without inducing cytotoxic effects. Upon bleeding, the nanofibrous architecture significantly promoted platelet plug formation, resulting in rapid and effective hemostasis [26]. Due to the lack of inherent antimicrobial properties, gelatin-based sponges often require the incorporation of additional components when applied to traumatic wounds. In this regard, Wang et al. reported the development of a gelatin–tannic acid–Siberian polyglycan nanofibrous sponge fabricated via electrospinning technology. This composite sponge exhibited excellent water absorption capacity, biocompatibility, antimicrobial activity, and hemostatic efficiency. Moreover, it facilitated cell adhesion and, with the assistance of the polysaccharide component, demonstrated superior wound healing performance [27-28].

2.3. Kaolin hemostasis sponge

Kaolin is an aluminosilicate mineral that has been utilized as a hemostatic agent due to its ability to promote blood coagulation without causing harm to human tissues [29]. Due to its negatively charged surface, kaolin can activate coagulation factor XII upon contact with blood, thereby initiating the intrinsic pathway of the coagulation cascade. Additionally, kaolin accelerates fibrin formation, facilitating the development of stable blood clots at the site of injury [30]. In addition, kaolin exhibits inherent analgesic and anti-inflammatory properties that may help mitigate edema and discomfort during wound treatment [31]. Its chemically inert nature also minimizes the risk of skin irritation or allergic reactions, making it suitable for use in a wide range of clinical applications [32].

Following its adoption by the U.S. military in 2008, ongoing efforts have led to the continuous development of kaolin-based hemostatic dressings [29]. In one study, a kaolin–graphene composite sponge was synthesized via a hydrothermal process. This composite material demonstrated rapid plasma absorption and effective blood cell aggregation, thereby facilitating coagulation. In addition, it exhibited favorable biocompatibility and safety profiles [29]. A composite sponge composed of carboxymethyl chitosan, sodium alginate, and kaolin has also attracted attention for its outstanding hemostatic performance. This sponge exhibited excellent hemostatic performance both in vitro and in vivo. It achieves rapid hemostasis and exhibits strong clotting capacity without causing harm to surrounding tissues, highlighting its clinical potential [33]. Another example is a polyurethane-based sponge loaded with kaolin, tannic acid, and tranexamic acid, which exerts hemostatic effects through multiple coagulation pathways. In addition to its effective hemostatic activity, this composite material is non-cytotoxic toward human dermal fibroblasts and demonstrates inherent antibacterial properties, further supporting its potential for safe clinical application [34]. Besides, a composite sponge composed of chitosan, carboxylated hemicellulose, and kaolin has been developed, featuring a directionally aligned groove-like porous structure. This material demonstrates excellent physical properties, including superior water absorption and compressive resilience. In addition, it exhibits notable antibacterial activity and protein adsorption capacity, while maintaining good biocompatibility. These characteristics make it particularly suitable for managing deep and large-area hemorrhages [35].

3. Challenges and future perspectives

Despite the promising hemostatic performance exhibited by chitosan-, gelatin-, and kaolin-based sponge materials, several limitations remain that hinder their clinical translation and long-term application.

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Chitosan-Based Materials: Chitosan possesses intrinsic hemostatic and antibacterial properties, but its application is limited by poor water solubility at physiological pH and low molecular weight, which results in its inability to effectively combine with plasma, and limited mechanical strength when used alone. Thus, the hemostatic sponge containing only chitosan will not exhibit a good hemostatic effect [35-36]. Moreover, the blood-absorption capacity and antibacterial properties of non-functionalized chitosan hemostatic sponges are limited [37].

Gelatin-Based Materials: Gelatin is a widely used natural polymer due to its excellent biocompatibility and film-forming capability. However, due to its excellent water absorption capacity, it can absorb approximately 45 times its own weight in blood, which may cause compressive injury in confined spaces (such as near the spinal cord or nerves), potentially leading to delayed neurological complications [38-39]. Gelatin-based materials have also been reported to induce various adverse effects, including allergic reactions, granuloma formation, and foreign body responses. Besides, prior to their complete resorption, these hemostatic agents may provoke localized inflammatory reactions in surrounding tissues [40]. Non-reinforced gelatin sponges tend to slip on moist or contoured wound surfaces, which compromises their hemostatic efficiency [41].

Kaolin-Based Materials: Kaolin, an inorganic clay mineral, is non-biodegradable in the human body and must be completely removed after achieving hemostasis post-implantation [42]. Under high-pressure arterial bleeding conditions, the intense and continuous blood flow can rapidly displace these materials from the wound site, significantly impairing their hemostatic performance. Moreover, maintaining effective hemostasis while ensuring adequate adherence to wet tissue surfaces and preserving biocompatibility remains a significant challenge for their clinical application [43]. In addition, to date, no literature has reported any intrinsic antibacterial properties or tissue regeneration-promoting capabilities associated with kaolin. In most cases, it must be combined with additional antimicrobial agents, bioactive components, or functional carriers to enhance its efficacy in infection control and wound healing.

Future Perspectives: To overcome the current limitations of chitosan-, gelatin-, and kaolin-based hemostatic sponges, future research should focus on the development of multifunctional and clinically adaptable materials. Combining natural polymers with inorganic components—for example, chitosan or gelatin with kaolin—can improve both hemostatic performance and biocompatibility. Structural modifications such as optimized porosity, directional alignment, or shape-memory properties may enhance fluid absorption, conformability to wound surfaces, and stability under complex bleeding conditions. In addition, efforts to introduce bioresorbable or stimuli-responsive elements into kaolin-based systems may alleviate their non-degradability. Incorporating antimicrobial agents, growth factors, or other bioactive compounds could further broaden the functional scope of hemostatic sponges, facilitating infection control and wound healing. Moving forward, establishing standardized evaluation models and scalable manufacturing strategies will be essential to facilitate clinical translation and broader clinical application of advanced hemostatic materials.

4. Conclusion

This review discussed hemostatic sponges based on chitosan, gelatin, and kaolin, summarizing their structures, hemostatic mechanisms, and main advantages and drawbacks. It answered the central question raised in the introduction by showing that while these sponges can accelerate hemostasis and provide additional functions, they still face challenges such as solubility, mechanical weakness, or poor degradability. However, it is limited by relying only on published literature without original experimental validation, and the reference scope may not fully represent the latest progress. Future

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work will involve expanding the range of references, performing experimental evaluations, and further optimizing the design of multifunctional sponges. In particular, our research will focus on developing composite materials that integrate hemostatic, antibacterial, and regenerative properties to enhance their clinical applicability.

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