

## Bovine Amnion-Alginate Sponge As A Modern Wound Dressing: A Literature Review On Bioactive Scaffold Integration For Chronic Wound Management

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### ABSTRACT

Chronic wounds, including diabetic foot ulcers, venous leg ulcers, and pressure sores, pose an increasing healthcare challenge owing to their ongoing inflammation, prolonged healing process, and elevated risk of infection. Conventional wound dressings often lack the bioactivity and structural versatility required to manage these complex conditions effectively. In response, bioengineered scaffolds that combine biological and physical functionalities have gained attention. This review focuses on the Bovine Amnion-Alginate Sponge (BAAS). This innovative composite wound dressing merges the biological potency of the bovine amniotic membrane (BAM) with the exudate-handling capabilities of alginate. BAM is rich in vascular endothelial growth factor (VEGF) and anti-inflammatory cytokines such as interleukin-10 (IL-10), which support angiogenesis, immune modulation, and tissue regeneration. Alginate, a polysaccharide obtained from brown algae, creates a hydrophilic gel when crosslinked with calcium, allowing it to sustain a moist environment for wounds while effectively absorbing surplus exudate. When integrated into a porous sponge structure, BAAS facilitates oxygen diffusion, cellular migration, and scaffold integrity—qualities essential for chronic wound management. Because the composite breaks down naturally, stays affordable, and can be applied without specialized equipment, it is especially useful in clinics with limited resources. While encouraging lab and early animal tests support its safety and usefulness, further living-animal studies and formal human trials are still needed to confirm BAASs healing power and fine-tune the recipe. Overall, BAAS appears to move wound care forward by offering a living, sturdy patch that helps stubborn sores finally close.

### 1. INTRODUCTION

Chronic wounds remain one of the most persistent challenges in modern healthcare, often characterized by delayed healing, prolonged inflammation, and high susceptibility to infection. Unlike acute wounds that follow a predictable healing trajectory, chronic wounds stall in the inflammatory phase, disrupting tissue regeneration and angiogenesis. Common etiologies include pressure ulcers, diabetic foot ulcers, and venous leg ulcers—all of which impose significant clinical and economic burdens globally. In the United States, the financial impact of managing chronic wounds ranges from \$28.1 billion to \$96.8 billion annually. This figure encompasses not only the direct costs associated with treatment but also the long-term care requirements and the quality-of-life challenges faced by those affected.<sup>1</sup>

These advanced wound dressings are crafted to protect the wound and play an active role in the healing process. Integrating natural biopolymers with biologically active membranes presents considerable therapeutic possibilities among the diverse bioengineered alternatives currently being explored.

The bovine amniotic membrane (BAM), a byproduct of the livestock industry, has emerged as a valuable biological scaffold due to its abundance of growth factors (e.g., vascular endothelial growth factor or VEGF) and anti-inflammatory cytokines (e.g., interleukin-10 or IL-10). These components are essential in modulating inflammation, promoting angiogenesis, and facilitating tissue regeneration—all critical for resolving chronic wounds<sup>2,3</sup>. Similarly, alginate—a polysaccharide derived from brown seaweed—has long been used in wound care for its hydrophilic gel-forming properties, which help maintain a moist wound environment and absorb excess exudate. When crosslinked with calcium chloride (CaCl<sub>2</sub>), alginate acquires improved structural integrity and water retention capacity.<sup>4</sup>

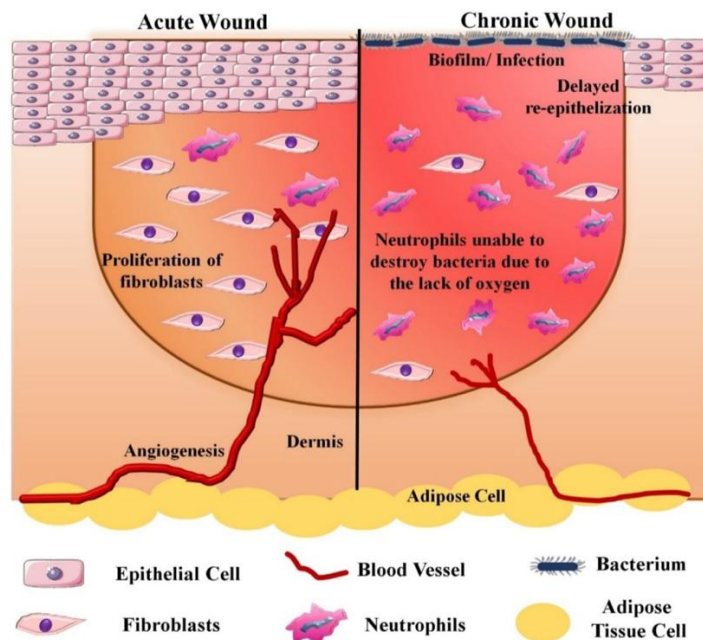
Integrating these two biomaterials into a composite construct—the Bovine Amnion-Alginate Sponge (BAAS)—represents an innovative approach to chronic wound management. BAAS points to saddle the regenerative capabilities of BAM and the liquid administration properties of alginate in a single, cost-effective dressing. Be that as it may, to reasonably legitimize the clinical interpretation of this novel detailing, a comprehensive assessment of its organic and physical properties is fundamental.

This literature review consolidates current knowledge on the functional components of BAAS and their individual and synergistic roles in wound healing. It aims to examine the rationale behind combining BAM and alginate, summarize empirical findings on porosity, VEGF, and IL-10 expression, water absorption, and retention capacities, and highlight why BAAS may fulfill the criteria for an ideal modern wound dressing. By investigating chronicled writing and later test results, this paper aims to establish BAAS's logical establishment and clinical pertinence in incessant wound care.

## 2. DISCUSSION

### Characteristics of an Ideal Wound Dressing for Chronic Wounds

Chronic wounds, such as diabetic foot ulcers, venous leg ulcers, and pressure ulcers, fail to progress through the ordinary stages of healing and regularly remain stuck within the inflammatory stage. These wounds are characterized by tireless contamination, high levels of exudate, tissue corruption, poor vascularization, and impaired cellular reactions (Figure 1). Therefore, wound dressings designed for chronic wounds must go beyond the conventional protective role to actively correct the hostile wound environment and stimulate regeneration.



**Figure 1. Schematic representation of acute versus chronic wound healing. In acute wounds, effective angiogenesis supports fibroblast proliferation, enhances neutrophil-mediated antimicrobial defense, and facilitates re-epithelialization. In contrast, chronic wounds are characterized by persistent bacterial infection, which impairs angiogenesis, disrupts fibroblast activity, and compromises the antimicrobial functions of neutrophils.<sup>5</sup>**

An ideal dressing for chronic wound care must maintain a moist but non-macerating environment, as excessive desiccation or exudation can impair epithelialization and increase infection risk. Moist wound environments have been shown to accelerate angiogenesis, collagen deposition, and keratinocyte migration—all critical in chronic wound resolution. Simultaneously, the dressing must effectively absorb exudate, which is often abundant and contains proteases and inflammatory cytokines that degrade the extracellular matrix and growth factors.

Due to the chronic inflammatory state, the dressing should ideally modulate the immune response, reducing pro-inflammatory cytokines like  $\text{TNF-}\alpha$  and IL-6 while supporting anti-inflammatory signals like IL-10. The ability to stimulate angiogenesis, particularly via growth factors such as vascular endothelial growth factor (VEGF), is essential to restore oxygen and nutrient delivery in ischemic wound beds<sup>6</sup>.

Mechanical and structural properties are equally important. The dressing must be biocompatible, non-toxic, and conformable to irregular wound topography. It should be non-adherent to newly formed tissue to avoid trauma during dressing changes,

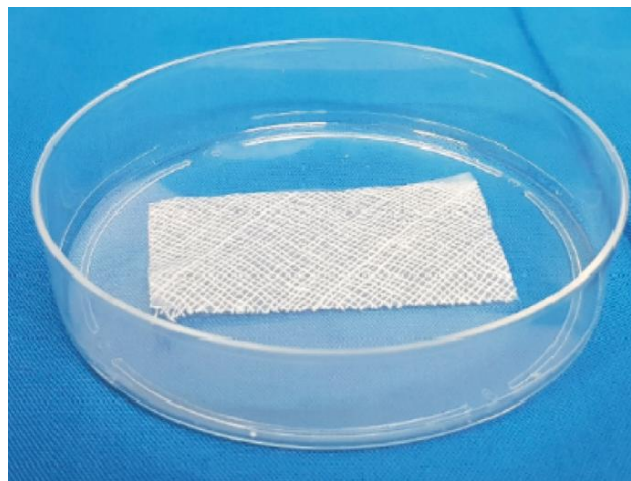
a frequent concern in long-term wound management. Biodegradability or painless removability further reduces tissue disturbance and enhances patient comfort.

Importantly, due to the chronic nature and prolonged treatment duration, the ideal dressing must be cost-effective and accessible, particularly in low-resource or tropical settings where wound infections are more prevalent<sup>7</sup>. Composite dressings integrating bioactive materials, such as natural growth factors and anti-inflammatory molecules, with moisture-regulating polymers have shown considerable promise in fulfilling these diverse clinical demands.

The Bovine Amnion-Alginate Sponge (BAAS) is an innovation designed with these principles. Its double composition targets natural incitement (through BAM) and liquid administration (by alginate), making it a solid candidate for compelling incessant wound treatment.

### **Biological Role of Bovine Amniotic Membrane (BAM)**

The bovine amniotic layer (BAM) shown in Figure 2 has earned critical consideration in regenerative medicine due to its rich content of bioactive molecules and auxiliary proteins. As the placenta's deepest layer, BAM comprises a basement membrane and stromal lattice containing a complex blend of developmental variables, cytokines, and extracellular matrix components that collectively support tissue repair.



**Figure 2. Bovine Amniotic Membrane<sup>8</sup>**

Vascular endothelial growth factor (VEGF) and interleukin-10 (IL-10) are its most valuable biological constituents. VEGF is pivotal in promoting angiogenesis, an essential process for restoring oxygen and nutrient supply to ischemic tissues, a hallmark of chronic wounds. Studies have shown that VEGF enhances endothelial cell proliferation, migration, and the formation of new capillaries, which are crucial for granulation tissue development and wound closure<sup>6</sup>. IL-10, on the other hand, acts as a potent anti-inflammatory cytokine that suppresses the expression of pro-inflammatory mediators like TNF- $\alpha$  and IL-6, shifting the wound environment from a chronic inflammatory state toward a regenerative one<sup>9</sup>.

The membrane, moreover, serves as a natural scaffold, giving basic proteins such as collagen, fibronectin, and laminin, which are necessary for cellular attachment, expansion, and movement. These components duplicate the work of the common extracellular matrix (ECM), empowering superior cell-material interaction during healing<sup>10</sup>.

Another critical advantage of BAM is its low immunogenicity. Through decellularization processes, antigenic cellular elements are removed while preserving key structural and functional proteins. This allows BAM to be safely applied across species with minimal risk of immune rejection<sup>11</sup>. Additionally, its biodegradability, biocompatibility, and availability as a livestock byproduct make BAM an attractive material, particularly in low-resource healthcare settings.

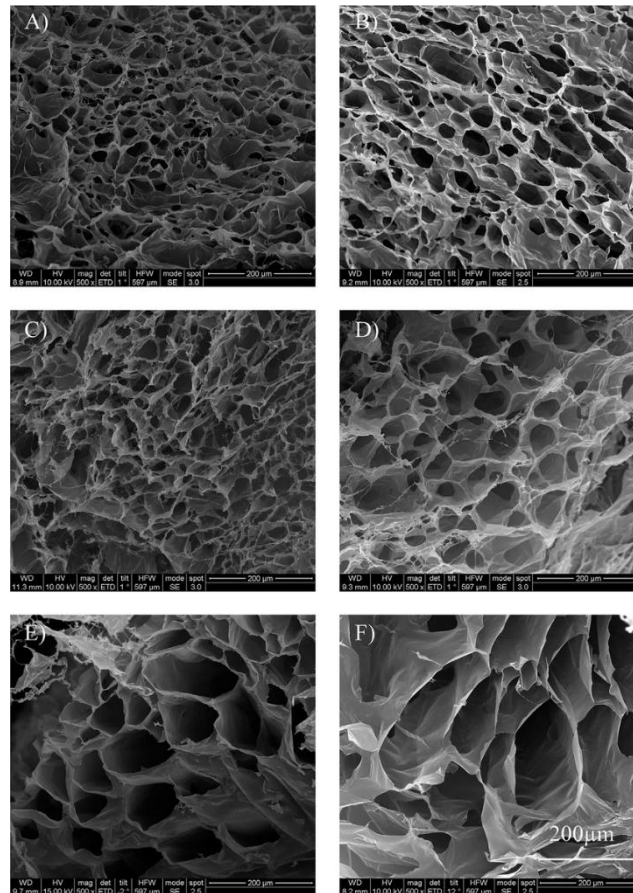
The cumulative evidence from previous studies supports the role of BAM as a bioactive and biocompatible wound healing material. Its incorporation into composite scaffolds, particularly when paired with hydrophilic polymers such as alginate, offers a promising route to enhance biological and mechanical wound dressing properties.

### **Alginate as a Functional Polymer in Chronic Wound Healing**

Unlike acute wounds, chronic wounds are characterized by determined aggravation, microbial colonization, tissue hypoxia, and excessive exudation. These conditions make an antagonistic microenvironment that slows down healing and regularly leads to recurrent disease and prolonged hospitalization. As a result, dressings for chronic wounds must protect the site and actively manage exudate, reduce inflammation, and support the regeneration process.

Alginate, a naturally derived polysaccharide from brown algae, has become a staple in treating chronic wounds due to its exceptional exudate-handling capacity and moisture-balancing properties. When in contact with calcium ions (commonly introduced through calcium chloride), alginate transforms into a hydrophilic gel capable of absorbing up to 20 times its weight in fluid<sup>4</sup>. This gel formation is crucial in chronic wounds, where excess exudate contains high levels of proteases and inflammatory mediators that can degrade growth factors and prevent re-epithelialization<sup>12</sup>.

Figure 3 illustrates alginate hydrogels' porous architecture and gel morphology under scanning electron microscopy (SEM), highlighting their high water-absorptive capacity and structural integrity after crosslinking with calcium ions.



**Figure 3. Scanning electron microscopy (SEM) images from the cross-section of alginate<sup>13</sup>**

Importantly, alginate dressings help maintain a moist wound environment — a key requirement for cell migration, angiogenesis, and autolytic debridement. At the same time, they prevent maceration of the surrounding skin, which is a common complication in chronic wounds with uncontrolled drainage<sup>14</sup>.

Chronic wounds often require frequent dressing changes, which can cause pain and trauma. Alginate's non-adherent nature minimizes tissue disruption during removal, preserving newly formed granulation tissue and improving patient comfort. Furthermore, alginate dressings can be tailored to deliver bioactive agents, including antimicrobials or cytokines, allowing for targeted therapy directly at the wound bed<sup>15</sup>.

Alginate is also biocompatible, biodegradable, and non-toxic. It is especially suitable for long-term use in patients with constant, non-healing wounds such as diabetic foot ulcers or pressure wounds. It is promptly accessible and moderately reasonable, supporting its role in high-resource and low-resource settings.

When combined with a biologically active component such as bovine amniotic membrane (BAM), alginate serves as a passive absorber and a structural framework that stabilizes the composite dressing. In the BAAS design, alginate contributes to the sponge's porosity, hydration retention, and ease of application, making it a functional cornerstone in the composite's performance for chronic wound healing.

#### **Bovine Amnion-Alginate Sponge (BAAS): Composite Scaffold Design**

The complexity of chronic wounds—characterized by persistent inflammation, poor vascularization, excessive exudate, and delayed epithelialization—requires wound dressings that provide biological stimulation and physical management. The

Bovine Amnion-Alginate Sponge (BAAS) was conceptualized as a hybrid scaffold to meet these multifactorial needs by combining the bioactive potential of bovine amniotic membrane (BAM) with the fluid-handling and structural advantages of alginate.

BAM serves as the biologically active core of the composite. As previously described, it is rich in key growth factors such as VEGF and anti-inflammatory cytokines like IL-10, critical for angiogenesis and immune modulation in chronic wounds<sup>6</sup>. In its native membrane form, BAM offers biological value but may lack mechanical strength or versatility in application. Processing BAM into a sponge structure improves its flexibility and coverage and enhances cellular infiltration and growth factor dispersion throughout the wound bed<sup>16</sup>.

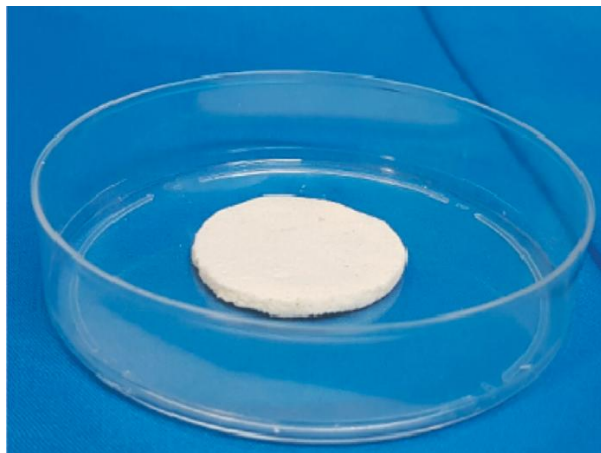
Alginate, on the other hand, contributes the physical matrix and moisture-regulating component. Once crosslinked with calcium chloride ( $\text{CaCl}_2$ ), alginate transforms into a stable hydrogel network capable of absorbing wound exudate, maintaining a moist wound environment, and preventing maceration. Its structural support allows the sponge to retain its integrity under moist conditions, making it suitable for highly exudative wounds<sup>4</sup>.

The integration of BAM and alginate into a porous, sponge-like construct addresses several critical issues in chronic wound care:

- Porosity and structure: The sponge format provides an interconnected pore network that promotes oxygen and nutrient diffusion, supports neovascularization, and facilitates cellular migration<sup>17</sup>.
- Moisture balance: The hydrophilic nature of alginate ensures fluid regulation, while BAM contributes additional water-binding and bioactive functions.
- Handling and adaptability: BAAS conforms to wound geometry, is easy to apply and remove, and is suitable for large or irregular wounds, particularly in outpatient or rural settings.

Various studies have emphasized the clinical value of such composite scaffolds, especially when tailored for chronic wounds. The combination of biochemical cues (from BAM) and mechanical performance (from alginate) mirrors the multi-layered functions of human skin, making BAAS, as shown in Figure 4, a promising candidate for translational wound therapy<sup>18</sup>.

Moreover, BAM and alginate are biodegradable, biocompatible, and cost-effective, supporting the development of scalable and accessible wound care solutions in low- to middle-income countries with high chronic wound burdens.



**Figure 4. Bovine Amniotic Sponge<sup>8</sup>**

### Clinical Implications and Future Research Directions

The clinical burden of chronic wounds continues to escalate globally, particularly among patients with diabetes, peripheral vascular disease, or immobility. In low- and middle-income countries, including Indonesia, the situation is further exacerbated by limited access to advanced wound care products, high infection rates, and prolonged healing durations. Against this backdrop, the Bovine Amnion-Alginate Sponge (BAAS) emerges as a practical and scientifically grounded innovation, offering a biologically active, structurally supportive, and economically feasible solution.

From a clinical perspective, BAAS addresses many core challenges in chronic wound care:

- Its moisture-retentive and exudate-absorbing properties are suited for heavily draining wounds, reducing the frequency of dressing changes and improving patient comfort<sup>18</sup>.
- The bioactive components of BAM, especially VEGF and IL-10, align with therapeutic goals in chronic wound

resolution: promoting angiogenesis and modulating persistent inflammation<sup>6</sup>.

- The sponge form factor ensures good wound-bed contact, adaptability to irregular wound shapes, and ease of handling — crucial attributes in outpatient or home-care settings<sup>16</sup>.

Furthermore, the composite design enables the possibility of drug-loading or cell-seeding, opening pathways for the sponge to serve as a platform for regenerative therapies in the future<sup>15</sup>.

Despite these promising attributes, several research gaps remain. Most existing studies—including foundational research on BAAS—are preclinical or in vitro, and clinical translation requires robust in vivo animal studies followed by controlled clinical trials. Key areas needing further investigation include:

- Long-term safety and immunogenicity of the BAM component in human subjects.
- Optimal BAM-to-alginate ratios for specific wound types and healing phases.
- Scalability and sterilization techniques to preserve biological activity while meeting regulatory standards<sup>19</sup>.
- Cost-effectiveness analysis compared to existing bioactive dressings in diverse healthcare systems.

Furthermore, studies on combination treatments, such as coordinating antimicrobials or stem cells into the BAAS matrix, may advance its adequacy, particularly for tainted or ischemic wounds<sup>20</sup>.

BAAS represents a bridge between biological relevance and clinical practicality as the field moves toward personalized and regenerative wound care. Its modularity, biocompatibility, and affordability position it as a strong candidate for widespread implementation, pending the necessary translational and clinical validation.

### 3. CONCLUSION

Chronic wounds represent a persistent clinical challenge due to their complex pathophysiology and resistance to conventional treatment approaches. As explored in this review, the Bovine Amnion-Alginate Sponge (BAAS) offers a promising solution that integrates the bioactivity of bovine amniotic membrane with alginate's structural and moisture-balancing properties. BAM contributes critical biological cues—such as VEGF and IL-10—to promote angiogenesis and modulate inflammation, while alginate ensures exudate control and scaffold integrity in moist environments.

The sponge format further enhances cellular infiltration and wound bed contact, making BAAS an adaptable and practical dressing, especially for irregular or deep chronic wounds. Its affordability and reliance on readily available biomaterials make it a viable option in resource-limited settings.

While current preclinical evidence is encouraging, further in vivo and clinical trials are essential to validate BAAS's therapeutic efficacy, safety, and cost-effectiveness. With continued development and translational research, BAAS has the potential to become a cornerstone in the management of chronic wounds.

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