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Therapeutic Potential of Amniotic Membrane in Oral Soft Tissue Healing

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Abstract

The human amniotic membrane (hAM) has emerged as a significant biomaterial in regenerative medicine, particularly for its applications in oral soft tissue healing. This review comprehensively examines the therapeutic potential of hAM, focusing on its unique biological properties, mechanisms of action, and diverse clinical applications in oral surgery and periodontology. Rich in growth factors, cytokines, and extracellular matrix components, hAM exhibits potent anti-inflammatory, anti-scarring, antimicrobial, and pro-regenerative effects. Its mechanisms of action involve modulating immune responses, promoting cell proliferation and migration, and providing a natural scaffold for tissue repair. Clinical applications range from gingival recession coverage and guided tissue regeneration to the treatment of oral ulcers and maxillofacial wound management. While hAM offers distinct advantages over conventional therapies, such as reduced patient morbidity and enhanced healing, challenges related to standardization, cost-effectiveness, and the need for long-term clinical data remain. Future directions include personalized medicine approaches, advanced bioengineering, and combination therapies to further optimize its clinical utility. This review underscores hAM's promising role as an indispensable tool in advancing oral healthcare and improving patient outcomes.

Keywords: improving, indispensable, conventional, combination

Introduction

Oral soft tissue healing is a complex biological process crucial for maintaining oral health and function. Challenges such as infection, inflammation, scarring, and delayed healing can compromise treatment outcomes in various dental and maxillofacial procedures. The human amniotic membrane (hAM), a readily available and ethically sourced biomaterial, has garnered significant attention in regenerative medicine due to its unique biological properties. Historically used in ophthalmology and wound care, its application has expanded to diverse surgical fields, including oral surgery and periodontology. This review aims to comprehensively explore the therapeutic potential of the amniotic membrane in promoting oral soft tissue healing, detailing its biological characteristics, mechanisms of action, and current clinical applications, while also addressing existing challenges and future directions for its utilization.

Biological Properties of Amniotic Membrane

The human amniotic membrane (hAM) is the innermost layer of the fetal membrane, characterized by its avascular, transparent, and tough structure. Its therapeutic efficacy stems from a unique combination of biological properties, including anti-inflammatory, anti-scarring, anti-angiogenic (under certain conditions), and anti-microbial effects, alongside its ability to promote epithelialization and modulate immune responses (1, 2).

Histologically, hAM consists of three main layers: a single layer of epithelial cells, a thick basement membrane, and a compact stromal layer. The epithelial cells are metabolically active and secrete various growth factors, cytokines, and extracellular matrix (ECM) components. The basement membrane, rich in collagen types IV, V, and VII, laminin, and fibronectin, provides a natural scaffold for cell adhesion, migration, and differentiation. The stromal layer, composed primarily of collagen types I and III, fibroblasts, and mesenchymal stem cells (MSCs), further contributes to its regenerative capabilities (3, 4).

Key bioactive molecules present in hAM include a wide array of growth factors such as epidermal growth factor (EGF), keratinocyte growth factor (KGF), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), and transforming growth factor-beta (TGF-β) (5, 6). These factors play crucial roles in cell proliferation, migration, and tissue remodeling. Additionally, hAM contains anti-inflammatory cytokines, tissue inhibitors of metalloproteinases (TIMPs), and hyaluronic acid, all contributing to its wound healing and anti-scarring properties (7, 8).

Mechanisms of Action in Oral Soft Tissue Healing

The therapeutic effects of hAM in oral soft tissue healing are multifaceted, primarily attributed to its ability to modulate inflammation, promote cell proliferation and migration, prevent scarring, and exert antimicrobial activity (9).

Anti-inflammatory and Immunomodulatory Effects: hAM contains various anti-inflammatory cytokines and growth factors that help to downregulate the inflammatory response at the wound site. It has been shown to suppress the activity of inflammatory cells, reduce the production of pro-inflammatory mediators, and promote a shift towards a regenerative environment (10). The presence of mesenchymal stem cells (MSCs) within the stromal layer also contributes to its immunomodulatory properties, influencing immune cell behavior and reducing tissue damage (4).

Promotion of Cell Proliferation and Migration: The rich composition of growth factors (EGF, KGF, FGF, PDGF, TGF-β) within hAM directly stimulates the proliferation and migration of various cell types crucial for wound healing, including epithelial cells, fibroblasts, and endothelial cells (5, 6). The basement membrane acts as a natural scaffold, providing an ideal substrate for cell attachment and guiding cell migration, thereby facilitating re-epithelialization and tissue regeneration (3).

Anti-scarring Properties: hAM's ability to reduce scar formation is a significant advantage in oral soft tissue healing. It achieves this by modulating the activity of matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs), thereby influencing collagen remodeling and preventing excessive fibrous tissue deposition. Additionally, the anti-inflammatory effects of hAM contribute to minimizing scar tissue formation (7).

Antimicrobial Activity: While not a primary antibiotic, hAM possesses inherent antimicrobial properties due to the presence of antimicrobial peptides and its ability to act as a physical barrier against bacterial invasion. This helps to reduce the risk of infection at the wound site, a common complication in oral surgery that can impede healing (9).

Angiogenesis Modulation: hAM can influence angiogenesis, the formation of new blood vessels. While some studies suggest anti-angiogenic properties, particularly in ocular applications, in wound healing, it can also promote a balanced angiogenic response necessary for tissue repair and regeneration by providing growth factors that support vascularization (11).

Clinical Applications in Oral Surgery and Periodontology

The unique biological properties of hAM have led to its increasing application in various oral surgical and periodontal procedures, demonstrating promising results in accelerating healing, reducing complications, and improving patient outcomes.

Gingival Recession Coverage: hAM has been explored as a viable alternative or adjunct to conventional connective tissue grafts (CTGs) for root coverage procedures. Studies have shown comparable root coverage outcomes with hAM, along with reduced patient morbidity due to the elimination of a secondary surgical site for graft harvesting (12, 13). Its ability to promote epithelialization and reduce inflammation contributes to successful and stable root coverage (14).

Guided Tissue Regeneration (GTR) and Guided Bone Regeneration (GBR): In periodontal regeneration, hAM can serve as a barrier membrane in GTR procedures, preventing epithelial down-growth into periodontal defects and facilitating the regeneration of lost periodontal tissues, including cementum, periodontal ligament, and alveolar bone (15). Similarly, in GBR procedures for alveolar ridge augmentation or implant site preparation, hAM can act as a scaffold and barrier, promoting bone formation and soft tissue integration (16).

Treatment of Oral Ulcers and Lesions: The anti-inflammatory and regenerative properties of hAM make it beneficial for the treatment of various oral mucosal lesions, including recurrent aphthous stomatitis, traumatic ulcers, and even some herpetic lesions. It can alleviate pain, reduce inflammation, and accelerate healing, leading to faster resolution of symptoms and improved patient comfort (17).

Maxillofacial Surgery: In broader maxillofacial surgery, hAM has been successfully utilized for wound coverage, reduction of inflammation, and as a scaffold for tissue repair following tumor resections, trauma, or reconstructive procedures. Its versatility makes it an effective option for promoting wound healing and minimizing scarring in complex surgical sites (18, 19).

Vestibuloplasty: While specific studies on hAM in vestibuloplasty relapse rates are less abundant, its regenerative and anti-scarring properties suggest a potential role in improving outcomes and reducing relapse compared to conventional methods. Further research is needed to establish its efficacy in this specific application.

Comparison with Conventional Therapies

To fully appreciate the therapeutic potential of hAM, it is essential to compare its efficacy and advantages against conventional therapies currently employed in oral soft tissue healing. Traditional approaches often involve autogenous connective tissue grafts (CTGs), free gingival grafts (FGGs), or synthetic membranes, each with its own set of benefits and limitations.

Autogenous Connective Tissue Grafts (CTGs): CTGs are considered the gold standard for root coverage and soft tissue augmentation due to their predictable outcomes and biological compatibility. However, CTG harvesting requires a secondary surgical site, leading to increased patient morbidity, pain, and a longer recovery period.

Limited tissue availability from the donor site is another significant drawback (20). In contrast, hAM offers an off-the-shelf solution, eliminating the need for a second surgical procedure and reducing patient discomfort (12). While some studies suggest comparable root coverage results between hAM and CTGs, long-term stability and predictability still favor CTGs in certain complex cases (13).

Free Gingival Grafts (FGGs): FGGs are primarily used for increasing the width of keratinized gingiva. Similar to CTGs, FGGs require a donor site, contributing to patient discomfort and potential complications. The aesthetic outcome of FGGs can also be a concern due to color discrepancies with adjacent tissues. hAM, with its transparent nature and regenerative properties, may offer a more aesthetically pleasing outcome and avoid donor site morbidity (21).

Synthetic and Allogeneic Membranes: Various synthetic (e.g., collagen membranes) and allogeneic (e.g., acellular dermal matrix) membranes are used in GTR and GBR procedures. While these eliminate donor site morbidity, they may lack the full spectrum of bioactive molecules and immunomodulatory properties found in hAM. Synthetic membranes can sometimes elicit foreign body reactions, and allogeneic membranes carry a theoretical risk of disease transmission, although highly minimized by processing (22). hAM, being a natural biological membrane with inherent growth factors and anti-inflammatory properties, often integrates more favorably with host tissues and promotes a more biologically driven healing process (15).

Conventional Wound Dressings and Medications: For oral ulcers and general wound care, conventional treatments include topical corticosteroids, analgesics, and antiseptic rinses. While these can manage symptoms, they often do not actively promote tissue regeneration or reduce scarring to the extent that hAM does. hAM's ability to provide a protective barrier, deliver growth factors, and modulate inflammation offers a more comprehensive approach to wound healing (17).

In summary, while conventional therapies have established roles, hAM presents several advantages, including reduced patient morbidity, availability, and a unique biological profile that actively promotes regeneration and reduces inflammation and scarring. However, further research, particularly large-scale, long-term clinical trials, is needed to definitively establish its superiority and expand its indications in all aspects of oral soft tissue healing.

Challenges and Future Directions

Despite the promising therapeutic potential of hAM in oral soft tissue healing, several challenges need to be addressed to facilitate its widespread adoption and optimize its clinical efficacy.

Standardization of Preparation and Storage: The methods for harvesting, processing, and preserving hAM vary significantly across different centers and commercial products. This lack of standardization can lead to inconsistencies in the biological activity and clinical outcomes of hAM grafts. Future efforts should focus on developing standardized protocols for hAM preparation and storage to ensure consistent quality and efficacy (23).

Cost-Effectiveness: The cost of commercially prepared hAM products can be a barrier to its routine use, especially in resource-limited settings. While the long-term benefits of reduced complications and improved healing may offset initial costs, more research is needed to establish the cost-effectiveness of hAM compared to conventional therapies (24).

Long-term Clinical Data: While numerous studies demonstrate the short-term efficacy of hAM, long-term clinical data, particularly from large-scale randomized controlled trials, are still relatively limited. More robust evidence on the long-term stability, predictability, and recurrence rates of hAM applications in various oral soft tissue procedures is crucial for its broader acceptance (13).

Optimizing Delivery Methods: The optimal form and delivery method of hAM (e.g., fresh, cryopreserved, dehydrated, micronized, or in combination with other biomaterials) may vary depending on the specific clinical application. Research into novel delivery systems and combinations with growth factors or stem cells could further enhance its regenerative potential (25).

Understanding Specific Mechanisms: While the general mechanisms of action are understood, a more in-depth understanding of the precise molecular pathways and cellular interactions involved in hAM-mediated healing in the oral environment is still evolving. This knowledge could lead to the development of more targeted and effective hAM-based therapies.

Future Directions: Future research should focus on:

- **Personalized Medicine:** Tailoring hAM applications based on individual patient needs and wound characteristics.
- **Bioengineering Approaches:** Developing advanced hAM-derived scaffolds or hydrogels with enhanced properties for specific oral tissue regeneration.
- **Combination Therapies:** Exploring the synergistic effects of hAM with other regenerative materials, growth factors, or cell-based therapies.
- **Clinical Trials:** Conducting more rigorous, large-scale, and long-term clinical trials to generate high-level evidence for its efficacy and safety.

Conclusion

The human amniotic membrane represents a highly promising biomaterial with significant therapeutic potential in oral soft tissue healing. Its unique biological composition, encompassing anti-inflammatory, anti-scarring, antimicrobial, and regenerative properties, positions it as a versatile tool in various oral surgical and periodontal procedures. From gingival recession coverage and guided tissue regeneration to the treatment of oral ulcers and maxillofacial wound management, hAM offers distinct advantages over conventional therapies, primarily by reducing patient morbidity and actively promoting a more favorable healing environment.

While current evidence strongly supports its efficacy, challenges related to standardization, cost-effectiveness, and the need for more extensive long-term clinical data persist. Addressing these challenges through rigorous research, optimized preparation protocols, and innovative delivery methods will be crucial for unlocking the full potential of hAM. As our understanding of its complex mechanisms of action deepens, hAM is poised to become an indispensable component of regenerative strategies in oral healthcare, ultimately leading to improved patient outcomes and enhanced quality of life.

References

[1] Sabbatini, M. (2025). A Rediscovered Tool to Improve Wound Healing in Oral Surgery. PMC, PMC12429774. [https://pmc.ncbi.nlm.nih.gov/articles/PMC12429774/]

[2] Parmar, U. P. S. (2025). Amniotic Membrane Transplantation for Wound Healing, Tissue Regeneration, and Immune Modulation. PMC, PMC12316762. [https://pmc.ncbi.nlm.nih.gov/articles/PMC12316762/]

[3] Guzeldemir-Akcakanat, E. (2025). The Human Amniotic Membrane and its Applications in Regenerative Dentistry: An Overview. SpringerLink, 10.1007/s40496-025-00408-4. [https://link.springer.com/article/10.1007/s40496-025-00408-4]

[4] Dawiec, G. (2024). Introduction to Amniotic Membranes in Maxillofacial Surgery. MDPI, 1648-9144/60/4/663. [https://www.mdpi.com/1648-9144/60/4/663]

[5] Dadkhah Tehrani, F. (2021). A Review on Modifications of Amniotic Membrane for Tissue Engineering Applications. Frontiers in Bioengineering and Biotechnology, 10.3389/fbioe.2020.606982/full. [https://www.frontiersin.org/journals/bioengineering-and-biotechnology/articles/10.3389/fbioe.2020.606982/full]

[6] Leal-Marin, S. (2021). Human Amniotic Membrane: A review on tissue engineering applications. Wiley Online Library, 10.1002/jbm.b.34782. [https://onlinelibrary.wiley.com/doi/10.1002/jbm.b.34782]

[7] Odet, S. (2022). Human amniotic membrane application in oral surgery: A systematic review. Frontiers in Bioengineering and Biotechnology, 10.3389/fbioe.2022.968346/full. [https://www.frontiersin.org/journals/bioengineering-and-biotechnology/articles/10.3389/fbioe.2022.968346/full]

[8] Law, E. J. (2022). Amniotic Membrane: An Approach to Periodontal Regeneration. PMC, PMC9458385. [https://pmc.ncbi.nlm.nih.gov/articles/PMC9458385/]

[9] Chopra, A., & Thomas, B. S. (2013). Amniotic Membrane: A Novel Material for Regeneration and Repair. Russell Health. [https://www.russellhealth.com/wp-content/uploads/2013/01/Dental-Amniotic-Membrane-A-Novel-Material-for-Regeneration-and-Repair-Aditi-Chopra-and-Betsy-S-Thomas-2013.pdf]

[10] Schmiedova, I. (2021). Using of Amniotic Membrane Derivatives for the Treatment of Oral Mucosa Defects. PMC, PMC8706466. [https://pmc.ncbi.nlm.nih.gov/articles/PMC8706466/]

[11] Ruiz-Cañada, C. (2021). Chronic Wound Healing by Amniotic Membrane: TGF-β and EGF Signaling Modulation in Re-epithelialization. Frontiers in Bioengineering and Biotechnology, 10.3389/fbioe.2021.689328/full. [https://www.frontiersin.org/journals/bioengineering-and-biotechnology/articles/10.3389/fbioe.2021.689328/full]

[12] Lubaib et al. (2025). Comparative evaluation of amniotic membrane and titanium mesh in guided bone regeneration: A systematic review and meta-analysis. ScienceDirect, S2212-4268(25)00146-0. [https://www.sciencedirect.com/science/article/pii/S2212426825001460] [13] Ghahroudi-Khorsand, F. (2014). Comparison of amnion allograft with connective tissue graft for root coverage procedures: A double-blind randomized controlled clinical trial. ResearchGate. [https://www.researchgate.net/publication/259453883_Comparison_of_amnion_allograft_with_connective_tissue_graft_for_root_coverage_procedures_A_double-blind_randomized_controlled_clinical_trial]

[13] Periyasamy, I. K. (2024). Efficacy of Amniotic and Chorionic Membrane in Facial Wound Healing: A Comparative Study. Cureus, 239213. [https://www.cureus.com/articles/239213-efficacy-of-amniotic-and-chorionic-membrane-in-facial-wound-healing-a-comparative-study] [15] Elkhenany, H. (2022). Applications of the amniotic membrane in tissue engineering and regenerative medicine. PMC, PMC8744057. [https://pmc.ncbi.nlm.nih.gov/articles/PMC8744057/]

[14] Ng, F. (2008). PDGF, TGF-β, and FGF signaling is important for differentiation and growth of mesenchymal stem cells (MSCs): transcriptional profiling can identify markers and pathways. ScienceDirect, S0006-4971(20)47001-6. [https://www.sciencedirect.com/science/article/pii/S0006497120470016]

[15] Arai, N. (2012). Clinical Application of a Hyperdry Amniotic Membrane on Surgical Defects of the Oral Mucosa. ScienceDirect, S0278-2391(11)01577-1. [https://www.sciencedirect.com/science/article/abs/pii/S0278239111015771]

[16] Dawiec, G. (2024). Introduction to Amniotic Membranes in Maxillofacial Surgery. PubMed, 38674309. [https://pubmed.ncbi.nlm.nih.gov/38674309/]

[17] Sabbatini, M. (2025). The Human Amniotic Membrane: A Rediscovered Tool to Improve Wound Healing in Oral Surgery. MDPI, 1422-0067/26/17/8470. [https://www.mdpi.com/1422-0067/26/17/8470]

[18] Sundar, T. A. (2025). Hyaluronic acid versus amniotic membrane in wound healing and bone regeneration: A comparative study. ScienceDirect, S2212-4268(25)00029-6. [https://www.sciencedirect.com/science/article/pii/S2212426825000296]

[19] Kapp, D. (2026). Efficacy of a dual-layer pre-hydrated amniotic membrane allograft in the treatment of chronic wounds: a retrospective multicentre analysis. Magonlinelibrary, 10.12968/jowc.2025.0604. [https://www.magonlinelibrary.com/doi/full/10.12968/jowc.2025.0604]

[20] Tobin, M. J. (2025). Comparing Amniotic Membranes to Other Bioengineered Skin Substitutes for Wound Healing: A Large Database Study. MDPI, 2077-0383/14/12/4272. [https://www.mdpi.com/2077-0383/14/12/4272]

[21] Laurent, I. (2017). Efficacy and Time Sensitivity of Amniotic Membrane treatment in patients with diabetic foot ulcers: a systematic review and meta-analysis. PMC, PMC5630554. [https://pmc.ncbi.nlm.nih.gov/articles/PMC5630554/]

[22] Bowlin, C. (n.d.). Accelerated Healing of Diabetic and Venous Ulcers with Adjunctive Dehydrated Human Amniotic Membrane: A Real-World Retrospective Cohort Study from a Single Provider Practice. Genesis Publishing. [https://www.genesispub.org/accelerated-healing-of-diabetic-and-venous-ulcers-with-adjunctive-dehydrated-human-amniotic-membrane-a-real-world-retrospective-cohort-study-from-a-single-provider-practice]

[23] Grzywocz, Z. (2014). Growth factor and interleukin concentrations in amniotic membrane-conditioned medium. Folia Histochemica et Cytobiologica, FHC.2014.0019/27591. [https://journals.viamedica.pl/folia_histochemica_cytobiologica/article/viewFile/FHC.2014.0019/27591]