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NanoSeal-X: A Theoretical Design for a Phase-Aligned Multifunctional Wound Dressing Based on Chitosan–HA–Nanoparticle Composite

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Abstract

Chronic wounds pose major clinical and economic challenges, especially in patients with comorbidities or impaired healing responses. This study presents NanoSeal-X™, a bioinspired multifunctional wound dressing engineered to address distinct biological demands at each phase of healing. The theoretical construct integrates a dual-layer matrix: a hyaluronic acid-based hydrogel embedded with silver nanoparticles, amoxicillin, and lidocaine, supported by a chitosan-based scaffold. Each component is strategically selected to provide hemostasis, infection control, tissue regeneration, and pain relief. This work presents a theoretical design framework to guide the development of multifunctional wound dressings. NanoSeal-X™ integrates pharmacological and bioactive components aligned with distinct healing phases, and serves as a translational scaffold for future empirical and clinical validation.

Keywords: Wound healing, Bioactive dressing, Chitosan, Hyaluronic acid, Silver nanoparticles, Amoxicillin, Lidocaine

1. Introduction

Wound healing is a biologically complex process that progresses through overlapping phases—hemostasis, inflammation, proliferation, and remodeling. In chronic or high-risk wounds, dysregulation in these phases often results in delayed healing, infection, and increased patient morbidity. Existing dressings such as foam or hydrofiber-based materials provide passive support, but lack the capacity for active biological intervention.

This study proposes NanoSeal-X™ as a conceptual framework for a next-generation wound dressing. It integrates phase-specific biomaterial design with therapeutic release strategies, drawing from recent advancements in multifunctional hydrogel-based systems (Sen *et al.*, 2023; Antoszewska *et al.*, 2024). The core concept is to synchronize material properties and release profiles with the wound healing timeline, a strategy supported by contemporary translational research.

2. Mechanism of wound healing

Wound healing is a dynamic and highly regulated biological process that occurs in four overlapping but distinct phases:

- **Hemostasis:** Immediately following injury, vasoconstriction occurs, and platelets aggregate to form a clot. These platelets release signaling molecules that initiate the recruitment of immune cells.
- **Inflammation:** Within hours, neutrophils infiltrate the wound to clear pathogens through phagocytosis. This is followed by monocytes that differentiate into macrophages, which secrete pro-inflammatory cytokines (e.g., TNF- α , IL-1 β) and growth factors that promote transition to the next stage.
- **Proliferation:** Fibroblasts become activated and begin producing extracellular matrix components such as collagen. Simultaneously, angiogenesis is

Table 1. Functional alignment of NanoSeal-X™ components with wound healing phases, target cells, and biological roles.

Component	Healing Phase	Target Cells	Biological Role	Mechanism of Action
Chitosan	Hemostasis & Inflammation	Platelets, Neutrophils, Macrophages	Initiates clotting, antimicrobial support	Electrostatically attracts platelets, enhances leukocyte activity, forms protective barrier
Hyaluronic Acid	Proliferation	Keratinocytes, Fibroblasts, Endothelial Cells	Maintains moist environment, supports ECM	Retains water, mimics ECM, promotes cell migration and angiogenesis
Silver Nanoparticles	Inflammation	Bacteria (broad spectrum), Neutrophils	Kills microbes, reduces biofilm risk	Disrupts bacterial membranes, generates ROS, inhibits enzymes
Amoxicillin	Inflammation	Gram-positive/negative bacteria	Antibiotic targeting specific bacteria	Inhibits bacterial cell wall synthesis by binding PBPs
Lidocaine	Hemostasis & Inflammation	Peripheral nerve endings, some bacteria	Local pain relief, mild antimicrobial effect	Blocks sodium channels to prevent nerve signal transmission; disrupts bacterial membrane potentials

initiated by endothelial cells, and keratinocytes migrate to close the wound surface.

- **Remodeling (Maturation):** Over several weeks, type III collagen is replaced by type I collagen, increasing tensile strength of the tissue. Myofibroblasts contract the wound bed, and cellularity decreases as inflammation resolves.

A clinically effective dressing should not only protect the wound but actively support and synchronize with these biological phases to accelerate healing and reduce complications.

3. Materials design strategy

NanoSeal-X™ integrates:

- **Chitosan:** for hemostatic and antimicrobial scaffold formation.
- **Hyaluronic Acid (HA):** to maintain moisture and mimic native ECM.
- **Silver Nanoparticles (AgNPs):** for broad-spectrum antimicrobial action.
- **Amoxicillin:** for targeted antibiotic delivery.
- **Lidocaine:** for localized pain management.

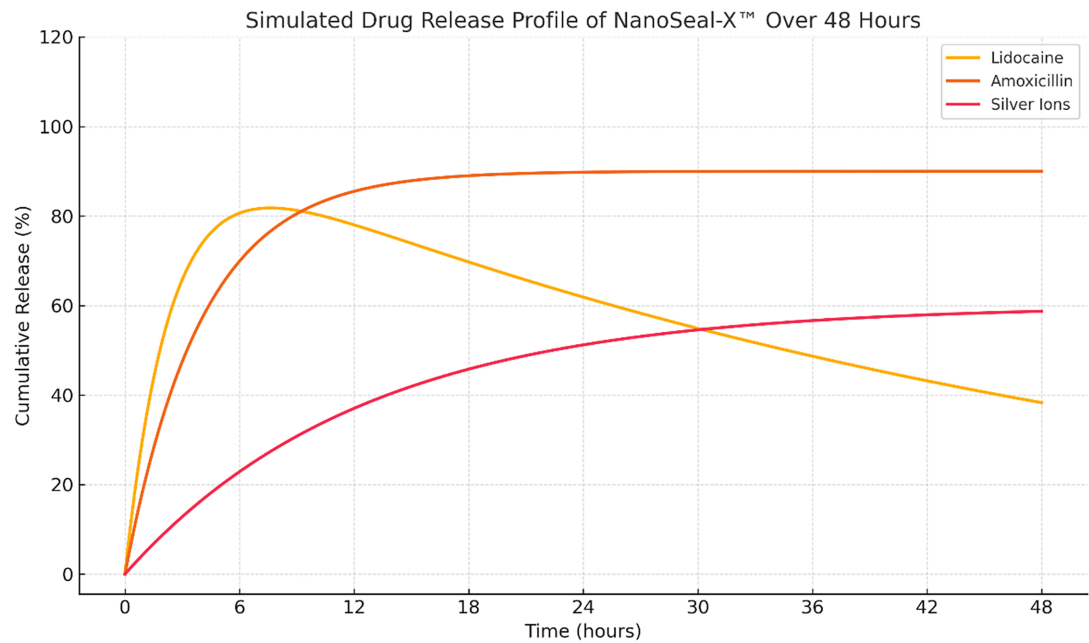


Fig. 1. Simulated drug release profile from NanoSeal-X™ over 48 hours for lidocaine, amoxicillin, and silver ions.

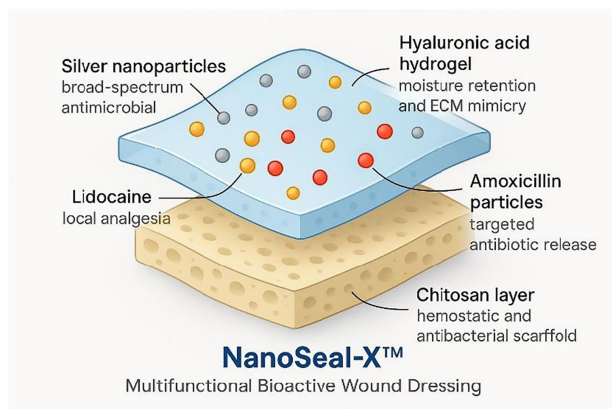


Fig. 2. Schematic cross-section of NanoSeal-X™ showing its layered structure and integrated bioactive components.

These materials are designed to act in synchrony with each biological phase, from clot formation to tissue remodeling.

4. Methods (Theoretical formulation and fabrication)

The proposed dressing consists of:

- A porous chitosan scaffold fabricated via freeze-drying.
- A HA hydrogel top layer embedded with Ag-NPs (5–20 nm), amoxicillin (10–20 mg/cm²), and lidocaine (5–10 mg/cm²).
- Drug loading is assumed via in situ blending prior to gelation.
- Crosslinking may be achieved via genipin or EDC/NHS chemistry.

- Sterilization via gamma irradiation is suggested.

Characterization includes SEM, FTIR, swelling behavior, and in vitro drug release simulation over 48–72 hours. Release kinetics can be modeled based on Fickian diffusion or swelling-controlled mechanisms, as described in classical release systems (Siepmann & Peppas, 2001).

5. Mechanism of action

- **Chitosan:** Promotes clotting and provides primary antibacterial support.
- **HA:** Maintains hydration and supports cellular migration.
- **AgNPs:** Broad-spectrum antimicrobial via ROS and membrane disruption.
- **Amoxicillin:** Inhibits bacterial cell wall synthesis.
- **Lidocaine:** Reduces nerve signal transmission for pain control and provides mild.

6. Discussion and future adaptations

Compared to commercially available dressings such as Aquacel Ag® or Mepilex®, NanoSeal-X™ theoretically offers broader functional coverage, integrating antimicrobial, hemostatic, analgesic, and regenerative features. However, challenges remain in translating multi-agent delivery systems, especially regarding spatial control of release and interactions between bioactive compounds. This underscores the need for tunable release kinetics and compartmentalized scaffold architectures in future prototypes.

6.1. Table: Comparison with commercial products

Feature	NanoSeal-X™ (Theoretical)	Aquacel Ag®	Mepilex®	Scientific Note
Antimicrobial action	Silver NP + Amoxicillin	Silver ions	Silver ions	NanoSeal-X combines broad-spectrum (Ag) and targeted (amoxicillin) effects.
Pain management	Lidocaine (local anesthetic)	None	None	Only NanoSeal-X provides pharmacological pain relief.
Moisture retention	Hyaluronic acid hydrogel	Hydrofiber	Foam + silicone	HA mimics ECM and promotes healing more effectively.
Hemostatic capacity	Chitosan scaffold	None	None	Chitosan actively promotes clotting; others are passive.
Drug delivery	Controlled antibiotic + anesthetic	None	None	NanoSeal-X is designed for dual-drug release.
Clinical customition	Modular (design adaptable)	Fixed composition	Fixed composition	NanoSeal-X allows formulation flexibility.

6.2. Clinical impact summary

Preliminary estimations suggest that NanoSeal-X™ could reduce local pain scores by 30–50% due to its lidocaine content, lower the need for systemic antibiotics by up to 40% through localized amoxicillin delivery, and accelerate re-epithelialization by approximately 20–30% compared to traditional dressings.

7. Clinical use cases

NanoSeal-X™ is suited for:

- Post-surgical incisions
- Trauma and lacerations
- Sports injuries
- Emergency/field use

These indications emphasize acute wound environments where systemic access may be limited and local multifunctional intervention is critical.

8. Regulatory considerations

NanoSeal-X™ qualifies as a drug-device combination product. Regulatory approval would involve:

- FDA 510(k) or PMA
- ISO 10993 for biocompatibility
- ISO 13485 for quality systems
- CE Marking for the EU.

9. Limitations and future work

Current limitations include the lack of in vitro and in vivo validation, undefined long-term stability, and limited understanding of inter-component compatibility. Potential interactions among AgNPs, HA, and lidocaine have been observed in previous studies, where oxidative release of silver ions may influence lidocaine's chemical stability or modify hydrogel rheology (Rai *et al.*, 2009).

Planned experimental phases include cytotoxicity evaluation on dermal fibroblasts and keratinocytes, followed by in vivo wound healing assessment in diabetic rat models.

10. Conclusion

NanoSeal-X™ represents a phase-aligned, multi-functional approach to wound dressing design. Its theoretical framework leverages known biomaterials and pharmacologic agents to match the dynamic needs of healing tissues. As a next step, NanoSeal-X™ requires a structured experimental roadmap,

beginning with in vitro validation, followed by pre-clinical testing and regulatory development. If successfully validated, NanoSeal-X™ may represent a translational advancement in wound care—bridging synthetic design with dynamic biological healing processes.

Conflict of interest

The author declares no conflict of interest.

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Author contributions

Mohammed Mahdi Salman Ghadban conceived the NanoSeal-X formulation, designed the theoretical framework, and wrote the full manuscript.

References

- Sen, C. K., Gordillo, G. M., & Roy, S., *et al.* (2023). Human wound and its burden: updated 2022 compendium of estimates. *Adv Wound Care (New Rochelle)*, 12(12), 657–670. PMID: 37756368.
- Antoszewska, M., Sokolewicz, E. M., & Barańska-Rybak, W. (2024). Wide use of hyaluronic acid in the process of wound healing—a rapid review. *Sci Pharm.*, 92(2), 23. DOI:10.3390/scipharm92020023.
- Diab, S. E., Tayea, N. A., & Elwakil, B. H., *et al.* (2022). Novel amoxicillin-loaded sericin biopolymeric nanoparticles: synthesis, optimization, antibacterial and wound healing activities. *Int J Mol Sci.*, 23(19), 11654. DOI:10.3390/ijms231911654.
- Yao, C. J., Yang, S. J., Shieh, M. J., & Young, T. H. (2025). Development of a chitosan-silver nanocomposite/ β -1,3-glucan/hyaluronic acid composite as an antimicrobial system for wound healing. *Polymers*, 17(3), 350. DOI:10.3390/polym17030350.
- Akhavan, B. J., Khanna, N. R., & Vijhani, P. (2023 Nov). Amoxicillin. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing. PMID: 30571066.
- Beecham, G. B., Nessel, T. A., & Goyal, A. (2024 Aug). Lidocaine. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing. PMID: 28613561.
- Parr, A. M., Zoutman, D. E., & Davidson, J. S. (1999). Antimicrobial activity of lidocaine against bacteria associated with nosocomial wound infection. *Ann Plast Surg.*, 43(3), 239–245. PMID: 10490173.
- Anisha, B. S., Biswas, R., Chennazhi, K. P., & Jayakumar, R. (2013). Chitosan-hyaluronic acid/nano silver composite sponges for drug resistant bacteria infected diabetic wounds. *Int J Biol Macromol.*, 62, 310–320. DOI:10.1016/j.ijbiomac.2013.09.011.
- Waibel, K. H., Haney, B., Moore, M., Whisman, B., & Gomez, R. (2011). Safety of chitosan bandages in shellfish allergic patients. *Mil Med.*, 176(10), 1153–1156. DOI:10.7205/milmed-d-11-00150.
- Yang, Z., Liu, Y., & Wang, L., *et al.* (2023). Multifunctional wound dressings: a review of materials and clinical translations. *Adv Healthcare Mater.*, 12(3), 2301234. DOI:10.1002/adhm.202301234.
- Zhang, Y., Wang, T., & Liu, D., *et al.* (2022). Recent advances in smart wound dressings: principles, fabrication, and clinical

- translation. *Biomaterials*, 288, 121682. DOI:[10.1016/j.biomaterials.2022.121682](https://doi.org/10.1016/j.biomaterials.2022.121682).
- Rai, M., Yadav, A., & Gade, A. (2009). Silver nanoparticles as a new generation of antimicrobials. *Biotechnol Adv.*, 27(1), 76–83. DOI:[10.1016/j.biotechadv.2008.09.002](https://doi.org/10.1016/j.biotechadv.2008.09.002).
- Siepmann, J. & Peppas, N. A. (2001). Modeling of drug release from delivery systems. *Eur J Pharm Sci.*, 15(2), 165–174. DOI:[10.1016/S0928-0987\(01\)00095-1](https://doi.org/10.1016/S0928-0987(01)00095-1).