





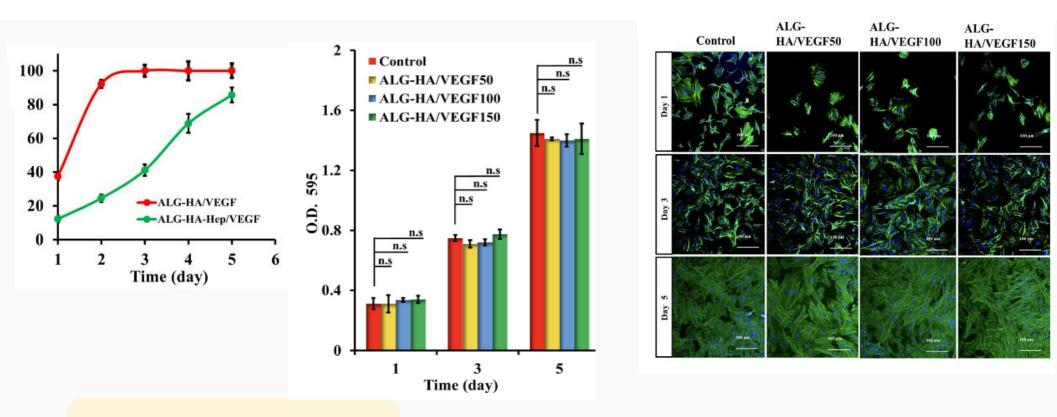
Controlled slow release of vascular endothelial growth factor (VEGF) in alginate and hyaluronic acid bead system to promote wound healing in punch-induced wound rat model

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Introduction

- Background
 - Wound Healing Challenges: Angiogenesis is crucial for wound repair but often delayed, leading to poor outcomes.
 - VEGF: Stimulates blood vessel formation, essential for tissue regeneration.
- Objective
 - Develop a controlled-release bead system with alginate (ALG) and hyaluronic acid (HA).
 - Test its efficacy in accelerating wound healing in a rat model.
- Key Components
 - Materials: ALG, HA, VEGF, Heparin.
 - Method: Crosslinked beads for gradual VEGF release to promote



In Vivo Results

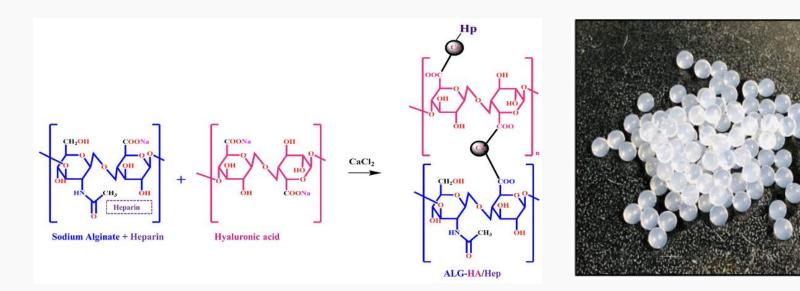
- Wound Healing Efficacy
 - Significant Wound Closure: After 14 days, the wounds treated with VEGF-loaded ALG-HA beads showed approximately 70%

vascularization.

Materials and Methods

Beads Fabrication

- *Materials:* Sodium alginate (ALG) and hyaluronic acid (HA) were combined in an 80:20 ratio.
- Crosslinking Process: Beads were formed by crosslinking with calcium chloride (CaCl₂), and heparin was incorporated to bind VEGF for controlled release.
- **VEGF Loading:** VEGF was encapsulated into the beads, allowing for sustained release during wound healing studies.
- In Vitro Studies
 - **Biocompatibility:** The biocompatibility of the VEGF-loaded beads was tested using calf pulmonary artery endothelial (CPAE) cells to ensure no cytotoxicity and to observe cell proliferation.
- In Vivo Studies
 - **Rat Model:** An 8mm punch wound was created on rats, and the VEGF-loaded beads were implanted to test wound healing efficacy over 7 and 14 days.



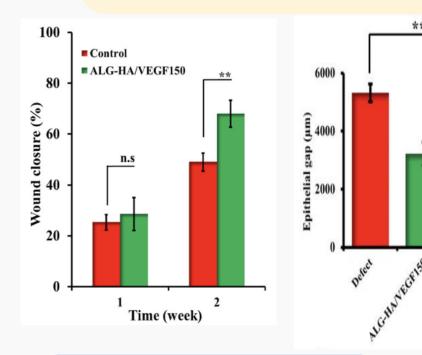
In Vitro Results

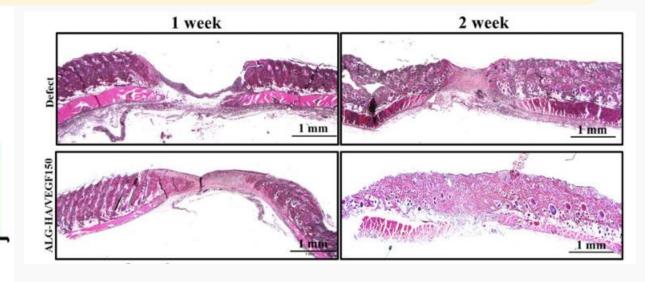
- closure, compared to 50% in the control group.
- *Key Finding:* The sustained release of VEGF enhanced wound healing, accelerating tissue repair and reducing the epithelial gap in the treated wounds.

Histological Analysis

- **Enhanced Vascularization:** Histological studies revealed significantly improved vascularization in the treatment group, indicating better blood supply to the wound area.
- **Collagen and Fibronectin Development:** Immunohistochemistry showed increased collagen type-1 and fibronectin expression in the treated wounds, supporting tissue regeneration.

The VEGF-loaded beads not only promoted faster wound closure but also enhanced tissue quality through improved vascularization and extracellular matrix formation.





Conclusion

- **Key Findings**: The controlled VEGF release from ALG-HA beads significantly enhanced wound healing, promoting faster closure, better vascularization, and increased collagen and fibronectin deposition.
- **Mechanism**: Sustained VEGF release stimulated angiogenesis, supporting tissue regeneration and wound recovery.

- VEGF Release Profile
 - **Sustained Release:** The ALG-HA/heparin beads showed a controlled release of VEGF over 5 days, compared to a burst release in the ALG-HA-only beads.
 - *Key Finding:* The heparin crosslinking effectively extended the VEGF release period, promoting sustained bioactivity.
- Biocompatibility and Cell Migration
 - **Biocompatibility:** CPAE cells cultured with VEGF-loaded beads demonstrated high viability, confirming that the beads were non-toxic.
 - Cell Proliferation: Increased optical density (OD) in the MTT assay indicated enhanced cell proliferation with higher concentrations of VEGF (150 ng/mL) in the ALG-HA/heparin beads.

The VEGF-loaded beads not only **support cell growth** but also **promote endothelial cell proliferation**, essential for angiogenesis and wound healing.

Clinical Implications

• Suitable for treating chronic wounds or surgical recovery, offering a biodegradable and biocompatible solution.

Future Directions

- **Optimization**: Fine-tuning VEGF release for different wound types.
- Next Steps: Expanding to human clinical trials to assess safety and efficacy.

