

Scoping Review

Emerging Trends in Wound Management Using Alginatebased Dressings Functionalized with Metallic Nanoparticles: A Scoping Review



Davi Porfirio da Silva^{1,2,3}, Adriana dos Santos Silva⁴, José Vinicius Melo da Silva², Letícia Mirely de Melo Silva², José Joaquim da Silva Neto², Iramirton Figueredo Moreira³, Rossana Teotônio de Farias Moreira³ and Anielle Christine Almeida Silva^{1,4,5*}

¹Rede Nordeste de Biotecnologia, Chemistry Institute, Federal University of Alagoas, Maceió, Alagoas, Brazil; ²Wound Care Research Laboratory, School of Nursing, Federal University of Alagoas, Maceió, Alagoas, Brazil; ³Medical School, Federal University of Alagoas, Maceió, Alagoas, Brazil; ⁴Postgraduate Program in Materials, Technology Center, Federal University of Alagoas, Maceió, Alagoas, Brazil; ⁵Physics Institute, Federal University of Uberlândia, Uberlândia, Minas Gerais, Brazil

Received: June 12, 2025 | Revised: July 01, 2025 | Accepted: September 25, 2025 | Published online: November 14, 2025

Abstract

Nanobiotechnology has driven transformative advancements in healthcare, particularly in the development of innovative solutions for wound treatment, a persistent and costly global health concern. Among these advancements, the combination of biopolymers and metallic nanoparticles has attracted considerable interest due to their excellent biocompatibility and potent antimicrobial activity. This scoping review explores recent technological progress in wound care, with a focus on alginate-based dressings functionalized with metallic nanoparticles. Alginate, a highly versatile biopolymer, was frequently employed in diverse formats, including hydrogels, sponges, beads, films/membranes, and fibers, across the analyzed studies. Silver nanoparticles were the most extensively investigated agents, owing to their well-established efficacy and the development of strategies to mitigate associated risks. Other metallic nanoparticles were also reported, contributing to a growing body of evidence supporting their therapeutic relevance. The synergistic integration of alginate and metallic nanoparticles has shown promising potential to enhance the performance of wound dressings, representing a significant step forward in the design of next-generation materials for effective and targeted wound management.

Introduction

Nanobiotechnology has revolutionized healthcare by driving significant advancements in developing innovative solutions for the prevention and treatment of wounds. Wounds, particularly chronic and complex ones, remain a global public health challenge, causing substantial economic burdens and negative psychosocial impacts, including prolonged treatment costs and reduced quality of life for affected individuals. Omplex wounds, characterized

Keywords: Nanobiotechnology; Innovation; Alginate; Metallic nanoparticles; Wound care; Biocompatibility; Antimicrobial activity.

*Correspondence to: Anielle Christine Almeida Silva, Postgraduate Program in Biotechnology, Federal University of Alagoas, Maceió, Alagoas 57072-900, Brazil. ORCID: https://orcid.org/0000-0002-5274-156X. Tel: +82-3214-1779, E-mail: aniel-lechristineas@gmail.com

How to cite this article: da Silva DP, dos Santos Silva A, da Silva JéVM, de Melo Silva LiM, da Silva Neto JéJ, Moreira IF, *et al.* Emerging Trends in Wound Management Using Alginate-based Dressings Functionalized with Metallic Nanoparticles: A Scoping Review. *J Explor Res Pharmacol* 2025;10(4):e00029. doi: 10.14218/JERP. 2025.00029.

by impaired or delayed healing processes, require a multifaceted approach involving tissue debridement, infection control, moisture balance, and advanced dressings that create an optimal environment for tissue regeneration.⁴

The application of nanotechnology in wound care has emerged as a powerful tool for addressing these challenges. Nanomaterials, such as metallic nanoparticles (NPs), offer unique physicochemical properties, including a high surface area-to-volume ratio and tunable size, that enable enhanced interactions with biological systems. These properties provide a platform for developing innovative wound care products with superior functionality, such as targeted antimicrobial action, controlled drug release, and enhanced wound healing. However, nanotechnology also poses challenges, such as potential cytotoxicity, environmental persistence, and the need for precise synthesis and characterization methods. Despite these limitations, the significant potential of nanotechnology in optimizing wound treatment drives ongoing research and innovation.

Biopolymers, particularly alginate (ALG), have been extensively explored in this field due to their biocompatibility, biodeg-

radability, and ability to serve as platforms for bioactive dressing development.⁷ Alginate, a naturally derived hydrophilic polysaccharide, is especially valued for its gelling capacity and moisture retention properties, making it an ideal candidate for wound dressings. Its biodegradable, biocompatible, and bioadhesive characteristics further enhance its suitability for various forms, including hydrogels, microspheres, fibers, sponges, and membranes.^{8,9} The versatility of ALG has enabled the development of numerous commercially available wound care products.

Among these technologies, alginate-based hydrogels have garnered particular attention due to their cost-effectiveness, abundance, and adaptability. They are recognized for meeting the criteria of an ideal wound dressing, such as strong adherence to the wound surface, easy removal for cleaning, mechanical and thermal protection, moisture regulation, and the ability to deliver bioactive agents. However, traditional alginate dressings are limited in their antimicrobial efficacy and require functionalization with additional agents to address infection risks effectively.

Advances in nanobiotechnology have addressed these limitations by enabling the incorporation of metallic nanoparticles, such as silver nanoparticles (AgNPs), into alginate-based dressings. AgNPs have long been known for their potent antimicrobial properties, including antibacterial, antifungal, and antiviral activities, which are further enhanced at the nanoscale. Additionally, AgNPs offer anti-inflammatory and anticancer properties and have applications in biomedical device coatings, diagnostic imaging, and targeted drug delivery. In this versatility has led to their inclusion in various commercially available wound care products.

The antimicrobial mechanisms of AgNPs involve disrupting microbial cell membranes, generating reactive oxygen species, and interfering with essential cellular processes, such as protein synthesis and DNA replication. These properties make them effective against sensitive and multidrug-resistant microorganisms, offering a valuable tool for combating antibiotic resistance. However, their use is not without challenges. The potential cytotoxicity of AgNPs, mediated by mitochondrial respiratory chain disruption, reactive oxygen species overproduction, and adenosine triphosphate synthesis inhibition, raises concerns about their safety in clinical applications. Additionally, the environmental accumulation of metallic nanoparticles necessitates the development of sustainable synthesis and disposal strategies.

Despite these challenges, integrating alginate with metallic nanoparticles, particularly AgNPs, represents a promising innovation in wound care. This combination enhances the antimicrobial properties of alginate-based dressings and improves their ability to modulate the wound microenvironment and accelerate the healing process. The exploration of alternative metallic nanoparticles, such as gold (Au), zinc oxide (ZnO), and titanium dioxide (TiO₂), offers additional avenues for addressing the limitations of AgNPs while maintaining the advantages of nanotechnology in wound treatment. ^{16,17}

In this context, this scoping review aims to map and analyze the latest technological innovations in wound care involving alginate-based dressings functionalized with metallic nanoparticles. This approach seeks to provide insights into the benefits, limitations, and future potential of these advanced materials in addressing the complex challenges of wound management.

Methodology

Study design

This scoping review was conducted following the Joanna Briggs

Institute (JBI) methodological framework, ^{18–21} which provides a comprehensive approach to mapping the available evidence. The review was reported in accordance with the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) checklist, ^{22,23} and the research protocol was registered on the Open Science Framework platform.

Research question

The research question was developed using the "Population, Concept, Context" framework recommended by JBI, resulting in the following question: What are the technological innovations in wound care involving dressings developed with alginate and metallic nanoparticles?

Eligibility criteria

Studies were included if they addressed any stage of the development of dressings containing alginate and metallic nanoparticles; were available in full in the consulted databases or other sources; and were written in English, Portuguese, or Spanish, with no restrictions on publication year or methodological approach. Duplicate studies were removed and considered only once.

Search strategy

Descriptors were selected from the Health Sciences Descriptors and Medical Subject Headings. The final search expression was: ("Metal Nanoparticles" AND alginate) AND ("Wound Healing" OR "Wound Infection").

An initial calibration search was conducted in MEDLINE (via PubMed) to assess the sensitivity and specificity of the strategy. Once validated, the search was replicated in ScienceDirect, Web of Science, Scopus, LILACS, and SciELO. Additional studies were identified by screening the reference lists of included articles and through gray literature searches in Google Scholar (first 100 results). The search was completed on June 22, 2024.

Study selection

All retrieved references were imported into the Rayyan reference manager, where duplicates were removed. Two independent reviewers screened titles and abstracts, followed by full-text assessment according to the eligibility criteria. Discrepancies were resolved through discussion, with a third reviewer acting as arbitrator when necessary. The selection process is illustrated in Figure 1.

Data extraction and analysis

Data extraction was performed using a structured instrument developed by the authors in accordance with JBI guidelines. Extracted data included:

- Bibliographic details (author, year, journal, and country of origin based on the first author's affiliation);
- Methodological approach;
- Structural and functional components of the dressings;
- · Preparation methods, and
- Reported therapeutic outcomes.

The data analysis consisted of a qualitative descriptive synthesis. Studies were grouped into thematic categories—geographical research distribution, structural composition of dressings, functionalization strategies, fabrication techniques, and therapeutic performance. Patterns, technological trends, and knowledge gaps were identified through iterative comparison of study characteristics. The synthesis was supported by summary tables, infographics, and narrative integration of findings.

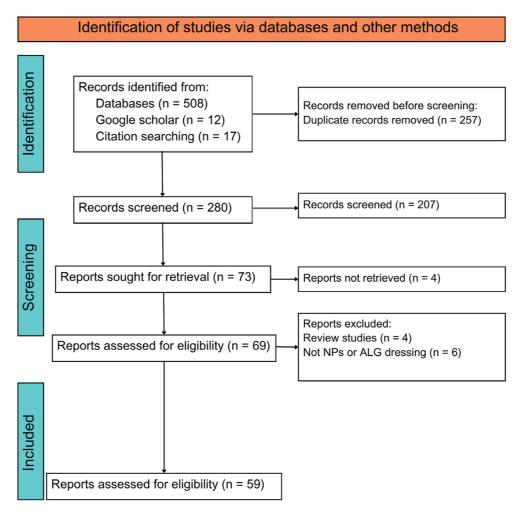


Fig. 1. PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) flow diagram of the study selection process. Flowchart illustrating the identification, screening, eligibility assessment, and inclusion of studies in accordance with PRISMA-ScR guide-lines. The diagram details the number of records retrieved from databases and other sources, duplicates removed, records screened by title/abstract, full-text articles assessed for eligibility, and final studies included in the review. ALG, alginate; NPs, nanoparticles.

Results

A total of 59 scientific articles met the inclusion criteria, covering studies conducted in Asia (66.1%), Europe (18.6%), Africa (10.2%), and the Americas (5.1%) between 2010 and 2024 (Fig. 2). Asia, particularly China, clearly dominates this field, reflecting its national investment in science, technology, and innovation as strategic pillars of development. This leadership is supported by robust research infrastructure, competitive funding, and international collaborations, combined with a growing domestic demand for advanced wound care solutions to address chronic wounds, diabetic ulcers, and age-related skin injuries. India also emerged as a strong contributor, prioritizing the development of cost-effective, biocompatible materials through environmentally friendly synthesis routes, often relying on indigenous algal species for alginate extraction. These initiatives align with policies aimed at positioning India as a hub for scalable biomedical technologies. In Europe, Italy and Serbia were notable, the former focusing on reinforcing alginate matrices with mechanical and bioactive enhancements, and the latter exploring antimicrobial applications of locally synthesized nanoparticles.

In Africa, Egypt adapted nanotechnology to local contexts by merging traditional medicinal knowledge with modern fabrication strategies. Meanwhile, the Americas produced comparatively fewer publications, though studies from Brazil and the United States offered important insights into antimicrobial alginate formulations for resource-limited healthcare environments. Taken together, this distribution underscores the emergence of a multipolar and collaborative scientific ecosystem in nanomedicine.

Across all studies, sodium alginate was the primary structural material, used either alone or in combination with natural or synthetic polymers such as chitosan, carboxymethyl chitosan, carboxymethyl cellulose, cellulose nanocrystals, gelatin, polyvinyl alcohol, polycaprolactone, or hyaluronic acid (Table 1).^{24–82} These combinations were reported to enhance stability, swelling behavior, tissue adhesion, and biodegradability, properties essential for effective wound healing.^{7–10} Among the functional agents, AgNPs were the most prevalent, appearing in more than 80% of the reviewed formulations. Their popularity is linked to broad-spectrum antimicrobial activity, low cytotoxicity at controlled doses, and prevention of biofilm formation.^{5,6,11} Other nanoparticles included ZnO (~18%), TiO₂ (~8%), FeO (~6%), CuO (~6%), PdNPs (~6%),

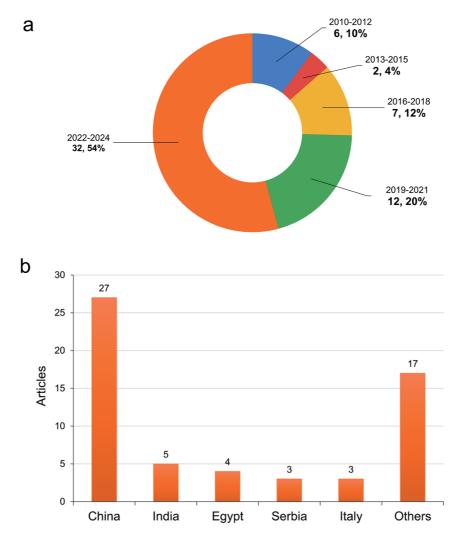


Fig. 2. Geographical and chronological distribution of the selected studies. (a) Donut chart illustrating the temporal evolution of research output between 2010 and 2024, showing a peak in publications from 2022 to 2024. (b) Bar chart comparing the number of publications among the top contributing countries/regions.

and Au (~4%). These alternatives offered additional benefits such as antioxidant activity, photothermal responsiveness, and catalytic effects. ^{11–13} Beyond metallic agents, natural bioactives like curcumin, tamanu oil, epigallocatechin gallate, honey, and essential oils were incorporated to further enhance anti-inflammatory and regenerative properties while addressing concerns over antimicrobial resistance.

The choice of fabrication method was closely linked to the intended structural and functional outcomes (Fig. 3). Ionic crosslinking with CaCl₂, CaCO₃, glutaraldehyde or glucono-delta-lactone was the most common, producing dressing with tunable stiffness and swelling properties. Freeze-drying generated porous sponges and scaffolds, with high absorptive capacity, while electrospinning produced nanofibers and membranes that mimic the extracellular matrix, thereby promoting cell adhesion, proliferation, and oxygen diffusion, whereas photocrosslinking stabilized hydrogel networks with photosensitive compounds, enabling precise control over morphology and mechanics.

The distribution of formulation types revealed a predominance of hydrogels, which accounted for more than 50% of the report-

ed systems. Microbeads, fibers, and discs represented over 30%, while films and membranes accounted for approximately 20%. Coating applications in wound dressings constituted about 10%. Regarding biological evaluations, most studies reported in vitro antimicrobial activity and included cytotoxicity assays. A smaller number involved *in vivo* animal models, and only a few presented preliminary clinical findings.

Nanoparticles were synthesized by chemical, physical, and increasingly by green methods, with synthesis routes strongly influencing size, morphology, and surface chemistry (Table 2, Fig. 4). ²⁴⁻⁸² As summarized in Table 2, AgNPs are typically produced via chemical reduction (Sodium borohydride, sodium citrate, trisodium citrate dimethyl formamide, carboxymethyl chitosan, ascorbic acid, epigallocatechin gallate, sodium alginate, lysozyme, tannic acid, sericin protein, LMWG 1,3:2,4-di(4-acylhydrazide)-benzylidenesorbitol (DBS-CONHNH₂), Tannic acid and Fe complexes (Ta/Fe), and d-glucose) yielding spherical, face-centered cubic structure, dotted structures, nanoclusters, and quasi-spherical structures ranging from 0,8-403 nm. ^{24-36,38-40,43-55,57,58,60-63,65,66,68,70-72,75,76} AuNPs synthesized through sodium citrate reduction exhibit uniform

Table 1. Compacted overview of references 24-82, highlighting main categories, methods, and designs of polymer-based biomaterials

	Structural components			
Group (Refs.)	Structural components (alginate association)	Functional components	Preparation	Dressings design
Alginate-based (25,29,30,33,42–44,47,51,54,55,63,65–67,72,73,75,77,79,80,82)	Alginate	NPs, Enzymes, Vitamins, Natural and synthetic compounds, Antibiot- ics, Laser irradiation	Water-soluble, Wet- spinning, Freeze- drying, Cross-linking, Water wash, Air-dried.	Hydrogel, Film, Sponge, Fibers, Beads, Discs, Sprayed gel, Scaffolds, Membrane, Wound dressing coating
Natural associations (24,28,31,36–38,40,41,45,46,48,49,56,58,60–62,64,78)	Chitosan, Cellulose, Gelatin, Natural gums, Hyaluronic Acid, Peptides and proteins	NPs, Proteins, Natural com- pound, Antibiotics, Metal organic framework materi- als, Photothermal treatment	Water-soluble, UV irradiation, Freeze-drying, Cross-linking, Water wash, Air-dried.	Hydrogel, Films, Sponge, Spheres, Wound dressing coating
Synthetic associations (26,27,35,39,52,53,5 9,69,70,71,74,76,81)	PCL, NIPAM, PVA, PVDF, DBS-CONHNH ₂ , PEG, PEGDA, Carbopol	NPs, Growth Factor Plasmid DNA, Hemin, Natural and synthetic compounds	Water-soluble, UV irradiation, Electrospinning, Cross-linking, Water wash, Air-dried.	Hydrogel, Films, Fibers, Scaffolds, Membrane, Discs, Beads
Hybrid natural—synthetic blends (32,34,50, 57,68)	Association of alginate, natural and syn- thetic polymers, and a plasticizing agent	NPs, coating agents, Antibiotics	Water-soluble, Mag- netic stirring, Overnight soaking, Casting tech- nique, Cross-linking.	Hydrogel, Films, Mem- brane, Dissolvable wound dressings

DBS-CONHNH₂, 1,3:2:4-di(4-acylhydrazide)-benzylidene sorbitol; NIPAM, poly(N-isopropyl acrylamide); NPs, nanoparticles; PCL, polycaprolactone; PEG, polyethylene glycol; PEG-DA, poly(ethylene glycol) diacrylate; PVA, polyvinyl alcohol; PVDF, polyvinylidene fluoride; UV, ultraviolet.

spherical morphologies (15–25 nm), ^{41,64} whereas CuNPs prepared via hydrothermal and one-pot synthesis form spherical or rod-like shapes of 50–300 nm. ^{56,77} ZnO nanoparticles produced via sol-gel,

co-precipitation, or hydrothermal approaches display diverse morphologies, including spheres, rods, hexagons, rectangles, and sheet-like, within 30–101 nm. 37,53,57,67,69,70,74,78,80

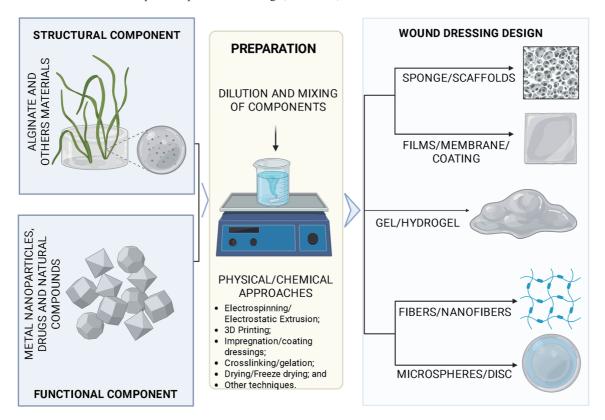


Fig. 3. Schematic representation of alginate-based dressing preparation incorporating metallic nanoparticles. Illustration of the main processing steps, including the selection of structural components (e.g., alginate, biopolymers), addition of functional agents (metallic nanoparticles), and fabrication methods (e.g., ionic crosslinking, electrospinning, freeze-drying) to obtain application-specific wound dressings.

Table 2. Summary of precursors, synthesis methods, sizes, and morphologies of nanoparticles reported in the literature

Nanopar- ticles	Precursor	Synthesis approach	Size range (nm)	Morphology	Refs
Ag	AgNO ₃ , Ag ₂ SO ₄	Photoreduction (ultraviolet light 365 nm), Chemical reduction (sodium borohydride, sodium citrate, trisodium citrate dimethyl formamide, carboxymethyl chitosan, ascorbic acid, epigallocatechin gallate, sodium alginate, lysozyme, tannic acid, sericin protein, LMWG 1,3:2,4-di(4-acylhydrazide)-benzylidenesorbitol (DBS-CONHNH ₂), Tannic acid and Fe complexes (Ta/Fe), and d-glucose), Electrochemical synthesis, Green synthesis	0.8 – 403	Spherical, face- centered cubic structure, dot- ted structures, nanoclusters, quasi-spherical	24–36,38–40, 43–55,57–58, 60–63,65,66,68, 70–72,75,76
Au	HAuCl ₄	Chemical reduction (sodium citrate)	15 – 25	Spherical	41,64
Cu	$Cu(NO_3)_2 \cdot xH_2O$	Hydrothermal, one-pot synthesis	50 – 300	Spherical, rod-shaped	56,74,77
ZnO	$ZnCl_2$, $Zn(OAc)_2$, $Zn(CH_3COO)_2$ · xH_2O	Sol-gel, hydrothermal meth- od, Co-precipitation	30 – 101	Spherical, rod- shaped, hexagonal and rectangular- shaped, sheet-like	37,53,57,67,69, 70,74,78,80
Fe_xO_x	FeSO ₄ ·7H ₂ O, Fe(acac) ₃	Solvathermal synthesis, sol-gel approach, chemical reduction (ethylene glycol)	5 - 64	Spherical, cubic shapes	70,80,81
TiO ₂	TiCl ₄ , Ti (Com- mercially plates), Ti(acac) ₂ OiPr ₂ , Ti(O-i-Pr) ₄	Green synthesis, Hydrothermal method	5 - 100	Nanoneedles	59,73,80,82
Pd	PdCl ₂	Green synthesis	~7 – 45	Spherical	42,55,79
Other (VOx, MgO, GeO _{2,} Al ₂ O ₃)	VO ₂ , MgCl ₂ , Ge(OEt) ₄ Al(O-i-Pr) ₃	Solvothermal method, chemical precipitation, sol-gel approach	10 – 200	Nanowires, rec- tangular and rod- shaped, spherical	43,70,80

Discussion

Recent advances in biomaterials for wound healing reveal that natural polysaccharides, synthetic polymers, and hybrid nanocomposites can be strategically combined to achieve multifunctional dressings. Alginate-based systems, often blended with chitosan, PEG, or protein-based polymers, have been functionalized with oxide metallic nanoparticles (AgO, ZnO, TiO₂, CuO, FeO) and others bioactive compounds to enhance antimicrobial activity, and tissue regeneration. Electrospun nanofibers, hydrogels, films, and 3D scaffolds have demonstrated controlled drug release, extracellular matrix-mimicking structure, and responsiveness to stimuli such as pH and temperature, showing superior healing outcomes compared to conventional dressings.

In recent years, hybrid and smart systems have expanded the potential of alginate-based dressings. Dual-drug nanofibers, photothermal hydrogels, and electroactive composites were frequently reported as strategies to achieve multifunctionality. These dressings can respond to stimuli such as pH, temperature, or light, aligning with the concept of personalized wound care. For example, Zhao *et al.*²⁴ developed an electroactive hydrogel of oxidized sodium alginate and carboxymethyl chitosan embedded with AgNPs, which promoted fibroblast proliferation, angiogenesis, and collagen deposition while exerting anti-inflammatory effects. Wang *et al.*²⁷ introduced a thermosensitive ALG-EDA/NIPAM-co-HEMIN formulation with AgNPs that transitioned into a hydrogel at body temperature, showing strong antibacterial activity against *E. coli*

and *S. aureus* and stimulating collagen synthesis in diabetic mice. Likewise, pH-responsive hydrogels based on carboxyethyl chitosan/oxidized alginate with AgNPs demonstrated effective hemostasis, broad antimicrobial activity, and biocompatibility.⁶¹

The most extensively studied systems (Table 1) were valued for their tunable rheology, moisture retention, and ability to maintain a pro-healing environment. Yet, conventional ionically crosslinked hydrogels often lack stability under physiological conditions. ⁸³ Recent modifications, such as incorporating oxidized alginate with amine-rich polymers (e.g., gelatin, chitosan), have enabled covalent crosslinking via Schiff bases, improving durability and resistance to premature degradation. ⁴ Electrospun nanofibers, often loaded with AgNPs and phytochemicals, mimicked extracellular matrix properties and provided high porosity for drug release. These systems showed antimicrobial, hemostatic, and regenerative activity. ^{25,26,39,43,54,67} Comparative studies reported superior healing outcomes in animal models compared to commercial dressings. ⁸⁴

Porous sponges combined strong absorptive capacity with adaptability to irregular wounds. So Calcium alginate/lysozyme/AgNP sponges and chitosan/alginate sponges with sericin-AgNPs and curcumin promoted angiogenesis, 33,40 reduced inflammation, and controlled infections. Films offered wound protection and controlled release of active agents. 37,38,45,46,49,54,59,82 Alginate membranes with hyaluronic acid and AgNPs accelerated healing while preventing biofilm formation. The only Brazilian study identified tested sodium alginate films esterified with poly(3-hydroxybutyrate) and PEG, loaded with AgNPs, which showed promis-

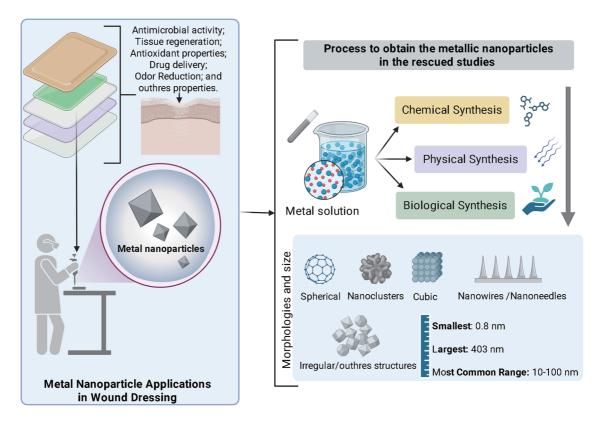


Fig. 4. Applications of metallic nanoparticles in the development of alginate-based wound dressings. Graphical representation of the roles of metallic nanoparticles (e.g., antimicrobial action, antioxidant effect, photothermal activity) and their integration into various wound dressing formats to enhance therapeutic performance.

ing preclinical results.⁶⁸ Alginate coatings improved textile-based dressings. Nonwoven fabrics coated with alginate and AgNPs (sometimes with essential oils) displayed synergistic antimicrobial activity and enhanced healing.^{63,65}

Smaller nanoparticles generally exhibit greater antimicrobial potency but also carry higher cytotoxicity risks. 86,87 AgNPs remain the most extensively studied, although cost, long-term safety, and potential resistance remain concerns. 88 Green synthesis strategies, often employing plant extracts or microbial systems, 40,46,54 are increasingly favored due to reduced toxicity and environmental impact, 89 though scalability and reproducibility continue to be challenging. Other oxide metallic nanoparticles, including MgO, TiO₂, VO, FeO, CuO, ZnO, Al₂O₃, GeO, Pd, and Au NPs, have been explored, but clinical translation is limited by insufficient biosafety data. 16,90

Consistently, physicochemical attributes such as size, shape, and surface chemistry determine biological performance. 91-93 For instance, ultra-small AgNPs (<1 nm) demonstrate potent antibacterial activity without detectable cytotoxicity, 58 whereas anisotropic AuNPs show higher cytotoxicity than their spherical counterparts. 93 Despite substantial progress, challenges remain: ionically crosslinked hydrogels are unstable under physiological conditions, AgNPs dominate the field despite cost and toxicity concerns, and alternative metallic nanoparticles require systematic toxicological evaluation for safe clinical translation.

The next stage of development for alginate—nanoparticle wound dressings will depend on refining synthesis and functionalization strategies to meet the complex demands of modern wound care. Technologies such as 3D printing and stimuli-responsive platforms

(Fig. 4) hold strong potential for personalized and adaptive therapies, while advances in standardization, regulation, and clinical validation will be critical to ensure their safe and effective application in patients.

Future directions

Despite advances in alginate—metallic nanoparticle dressings, critical gaps hinder clinical translation. Most studies are limited to *in vitro* assays, with few *in vivo* evaluations and only minimal clinical data. Long-term biocompatibility, degradation kinetics, and immunological consequences of these composites remain poorly understood, particularly regarding the fate of metallic degradation products in chronic wound environments.

Variability in synthesis methods, nanoparticle characterization, and biological testing complicates reproducibility and data comparability. Establishing standardized fabrication protocols, reporting guidelines, and performance criteria is essential to ensure reliable benchmarking and accelerate translation from laboratory research to clinical application.

Multi-component dressings combining different nanoparticles or natural bioactives show synergistic antimicrobial and regenerative effects, yet the underlying molecular mechanisms and optimal formulations remain unclear. Stimuli-responsive dressings offer innovative functionality, but their stability and predictable performance under dynamic wound conditions have not been fully demonstrated, highlighting the need for systematic *in vivo* studies.

Green synthesis approaches are gaining attention due to lower

toxicity and environmental impact, but scalability and life-cycle assessments are limited. Addressing these challenges will require interdisciplinary collaboration, integration of regulatory frameworks from early development stages, and adoption of advanced fabrication strategies such as 3D printing to create safe, sustainable, and clinically effective next-generation wound care platforms.

Conclusions

Alginate-based dressings functionalized with metallic nanoparticles represent a promising advancement in wound management, combining biocompatibility with enhanced antimicrobial and regenerative properties. AgNPs remain the most explored due to their efficacy and commercial availability; however, concerns regarding cost, cytotoxicity, resistance, and uncontrolled ion release necessitate safer, more sustainable approaches. Strategies such as green synthesis, smart-release systems responsive to pH or temperature, and composite formulations with structural enhancers show strong potential to address these limitations. The exploration of alternative nanoparticles (e.g., TiO2, ZnO, Cu, Au) offers new opportunities but requires rigorous validation to ensure biosafety and clinical applicability. Future progress will rely on integrating innovative synthesis, precise dosage control, and advanced fabrication techniques such as 3D printing, alongside robust regulatory frameworks. These combined efforts can pave the way for nextgeneration wound dressings that are effective, safe, and tailored to patient-specific needs.

Acknowledgments

None.

Funding

This study received financial support from the Research Support Foundation of the State of Alagoas (FAPEAL), the Coordination for the Improvement of Higher Education Personnel (CAPES), the Northeast Biotechnology Network (Rede Nordeste de Biotecnologia – RENORBIO), and the National Council for Scientific and Technological Development (CNPq). Productivity Grant No. 309813/2023-9 (ACAS).

Conflict of interest

The authors declare no conflict of interest.

Author contributions

Conceptualization (DPS, ACAS), methodology (ASS, JJSN), investigation (DPS, LMMS), formal analysis (JVMS), data curation (DPS, ASS), validation (LMMS, IFM), resources (JJSN, IFM, RTFM), visualization (DPS), writing – original draft preparation (DPS), writing – review & editing (ASS, JVMS, LMMS, JJSN, IFM, RTFM, ACAS), supervision (RTFM, ACAS), project administration (ACAS), and funding acquisition (ACAS). All authors have read and approved the final version of the manuscript.

References

Jiang T, Li Q, Qiu J, Chen J, Du S, Xu X, et al. Nanobiotechnology: Applications in Chronic Wound Healing. Int J Nanomedicine

- $2022; 17: 3125 3145.\ doi: 10.2147/IJN. S372211, \ PMID: 35898438.$
- [2] Graves N, Phillips CJ, Harding K. A narrative review of the epidemiology and economics of chronic wounds. Br J Dermatol 2022;187(2):141–148. doi:10.1111/bjd.20692, PMID:34549421.
- [3] Olsson M, Järbrink K, Divakar U, Bajpai R, Upton Z, Schmidtchen A, et al. The humanistic and economic burden of chronic wounds: A systematic review. Wound Repair Regen 2019;27(1):114–125. doi:10.1111/wrr.12683, PMID:30362646.
- [4] Bowers S, Franco E. Chronic Wounds: Evaluation and Management. Am Fam Physician 2020;101(3):159–166. PMID:32003952.
- [5] Parvin N, Joo SW, Mandal TK. Nanomaterial-Based Strategies to Combat Antibiotic Resistance: Mechanisms and Applications. Antibiotics (Basel) 2025;14(2):207. doi:10.3390/antibiotics14020207, PMID:40001450.
- [6] Tenchov R, Hughes KJ, Ganesan M, Iyer KA, Ralhan K, Lotti Diaz LM, Bird RE, Ivanov JM, Zhou QA. Transforming Medicine: Cutting-Edge Applications of Nanoscale Materials in Drug Delivery. ACS Nano 2025;19(4):4011–4038. doi:10.1021/acsnano.4c09566, PMID:39823199.
- [7] Abourehab MAS, Rajendran RR, Singh A, Pramanik S, Shrivastav P, Ansari MJ, et al. Alginate as a Promising Biopolymer in Drug Delivery and Wound Healing: A Review of the State-of-the-Art. Int J Mol Sci 2022;23(16):9035. doi:10.3390/ijms23169035, PMID:36012297.
- [8] Zhang H, Cheng J, Ao Q. Preparation of Alginate-Based Biomaterials and Their Applications in Biomedicine. Mar Drugs 2021;19(5):264. doi:10.3390/md19050264, PMID:34068547.
- [9] Cao Y, Cong H, Yu B, Shen Y. A review on the synthesis and development of alginate hydrogels for wound therapy. J Mater Chem B 2023;11(13):2801–2829. doi:10.1039/d2tb02808e, PMID:36916313.
- [10] Barbu A, Neamtu B, Zăhan M, Iancu GM, Bacila C, Mireşan V. Current Trends in Advanced Alginate-Based Wound Dressings for Chronic Wounds. J Pers Med 2021;11(9):890. doi:10.3390/jpm11090890, PMID:34575668.
- [11] Jiang H, Li L, Li Z, Chu X. Metal-based nanoparticles in antibacterial application in biomedical field: Current development and potential mechanisms. Biomed Microdevices 2024;26(1):12. doi:10.1007/ s10544-023-00686-8, PMID:38261085.
- [12] d'Amora M, Schmidt TJN, Konstantinidou S, Raffa V, De Angelis F, Tantussi F. Effects of Metal Oxide Nanoparticles in Zebrafish. Oxid Med Cell Longev 2022;2022:3313016. doi:10.1155/2022/3313016, PMID:35154565.
- [13] Alavi M, Kamarasu P, McClements DJ, Moore MD. Metal and metal oxide-based antiviral nanoparticles: Properties, mechanisms of action, and applications. Adv Colloid Interface Sci 2022;306:102726. doi:10.1016/j.cis.2022.102726, PMID:35785596.
- [14] Jaros SW, Król J, Bażanów B, Poradowski D, Chrószcz A, Nesterov DS, et al. Antiviral, Antibacterial, Antifungal, and Cytotoxic Silver(I) BioMOF Assembled from 1,3,5-Triaza-7-Phoshaadamantane and Pyromellitic Acid. Molecules 2020;25(9):2119. doi:10.3390/molecules25092119, PMID:32369972.
- [15] Lee SH, Jun BH. Silver Nanoparticles: Synthesis and Application for Nanomedicine. Int J Mol Sci 2019;20(4):865. doi:10.3390/ ijms20040865, PMID:30781560.
- [16] Choudhary A, Singh S, Ravichandiran V. Toxicity, preparation methods and applications of silver nanoparticles: an update. Toxicol Mech Methods 2022;32(9):650–661. doi:10.1080/15376516.2022.206425 7. PMID:35403559.
- [17] Bruna T, Maldonado-Bravo F, Jara P, Caro N. Silver Nanoparticles and Their Antibacterial Applications. Int J Mol Sci 2021;22(13):7202. doi:10.3390/ijms22137202, PMID:34281254.
- [18] Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil H. Scoping Reviews (2020). Aromataris E, Lockwood C, Porritt K, Pilla B, Jordan Z, editors. JBI Manual for Evidence Synthesis. JBI 2024. doi:10.46658/JBIMES-24-09.
- [19] Peters MDJ, Marnie C, Tricco AC, Pollock D, Munn Z, Alexander L, et al. Updated methodological guidance for the conduct of scoping reviews. JBI Evid Synth 2020;18(10):2119–2126. doi:10.11124/ JBIES-20-00167, PMID:33038124.
- [20] Khalil H, Peters MD, Tricco AC, Pollock D, Alexander L, McInerney P, et al. Conducting high quality scoping reviews-challenges and solutions. J Clin Epidemiol 2021;130:156–160. doi:10.1016/j.jcline-

- pi.2020.10.009, PMID:33122034.
- [21] Peters MDJ, Godfrey C, McInerney P, Khalil H, Larsen P, Marnie C, et al. Best practice guidance and reporting items for the development of scoping review protocols. JBI Evid Synth 2022;20(4):953–968. doi:10.11124/JBIES-21-00242, PMID:35102103.
- [22] Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med 2018;169(7):467–473. doi:10.7326/ M18-0850, PMID:30178033.
- [23] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi:10.1136/bmj. n71, PMID:33782057.
- [24] Zhao L, Feng Z, Lyu Y, Yang J, Lin L, Bai H, et al. Electroactive injectable hydrogel based on oxidized sodium alginate and carboxymethyl chitosan for wound healing. Int J Biol Macromol 2023;230:123231. doi:10.1016/j.ijbiomac.2023.123231, PMID:36641017.
- [25] Neibert K, Gopishetty V, Grigoryev A, Tokarev I, Al-Hajaj N, Vorstenbosch J, et al. Wound-healing with mechanically robust and biodegradable hydrogel fibers loaded with silver nanoparticles. Adv Healthc Mater 2012;1(5):621–630. doi:10.1002/adhm.201200075, PMID:23184797.
- [26] Hu WW, Lin YT. Alginate/polycaprolactone composite fibers as multifunctional wound dressings. Carbohydr Polym 2022;289:119440. doi:10.1016/j.carbpol.2022.119440, PMID:35483853.
- [27] Wang YY, Addisu KD, Gebrie HT, Darge HF, Wu TY, Hong ZX, et al. Multifunctional thermosensitive hydrogel based on alginate and P(NIPAM-co-HEMIN) composites for accelerated diabetic wound healing. Int J Biol Macromol 2023;241:124540. doi:10.1016/j.ijbio-mac.2023.124540, PMID:37085062.
- [28] Montaser AS, Jlassi K, Ramadan MA, Sleem AA, Attia MF. Alginate, gelatin, and carboxymethyl cellulose coated nonwoven fabrics containing antimicrobial AgNPs for skin wound healing in rats. Int J Biol Macromol 2021;173:203–210. doi:10.1016/j.ijbiomac.2021.01.123, PMID:33484799.
- [29] Hu Q, Nie Y, Xiang J, Xie J, Si H, Li D, et al. Injectable sodium alginate hydrogel loaded with plant polyphenol-functionalized silver nanoparticles for bacteria-infected wound healing. Int J Biol Macromol 2023;234:123691. doi:10.1016/j.ijbiomac.2023.123691, PMID:3680 6769.
- [30] Bîrcă AC, Gherasim O, Niculescu AG, Grumezescu AM, Vasile BŞ, Mihaiescu DE, et al. Infection-Free and Enhanced Wound Healing Potential of Alginate Gels Incorporating Silver and Tannylated Calcium Peroxide Nanoparticles. Int J Mol Sci 2024;25(10):5196. doi:10.3390/ijms25105196, PMID:38791232.
- [31] Ma L, Tan Y, Chen X, Ran Y, Tong Q, Tang L, et al. Injectable oxidized alginate/carboxylmethyl chitosan hydrogels functionalized with nanoparticles for wound repair. Carbohydr Polym 2022;293:119733. doi:10.1016/j.carbpol.2022.119733, PMID:35798428.
- [32] Chen K, Wang F, Liu S, Wu X, Xu L, Zhang D. In situ reduction of silver nanoparticles by sodium alginate to obtain silver-loaded composite wound dressing with enhanced mechanical and antimicrobial property. Int J Biol Macromol 2020;148:501–509. doi:10.1016/j.ijbiomac.2020.01.156, PMID:31958554.
- [33] Chen LL, Shi WP, Zhou YQ, Zhang TD, Lin WJ, Guo WH, et al. Highefficiency antibacterial calcium alginate/lysozyme/AgNPs composite sponge for wound healing. Int J Biol Macromol 2024;256(Pt 1):128370. doi:10.1016/j.ijbiomac.2023.128370, PMID:38000594.
- [34] Tarusha L, Paoletti S, Travan A, Marsich E. Alginate membranes loaded with hyaluronic acid and silver nanoparticles to foster tissue healing and to control bacterial contamination of non-healing wounds. J Mater Sci Mater Med 2018;29(3):22. doi:10.1007/s10856-018-6027-7, PMID:29396683.
- [35] Liu K, Dai L, Li C. A lignocellulose-based nanocomposite hydrogel with pH-sensitive and potent antibacterial activity for wound healing. Int J Biol Macromol 2021;191:1249–1254. doi:10.1016/j.ijbiomac.2021.10.006, PMID:34634323.
- [36] Ma W, Dong W, Zhao S, Du T, Wang Y, Yao J, et al. An injectable adhesive antibacterial hydrogel wound dressing for infected skin wounds. Biomater Adv 2022;134:112584. doi:10.1016/j.msec.2021.112584, PMID:35525738.

- [37] Gong CP, Luo Y, Pan YY. Novel synthesized zinc oxide nanoparticles loaded alginate-chitosan biofilm to enhanced wound site activity and anti-septic abilities for the management of complicated abdominal wound dehiscence. J Photochem Photobiol B 2019;192:124–130. doi:10.1016/j.jphotobiol.2019.01.019, PMID:30735953.
- [38] Gómez Chabala LF, Cuartas CEE, López MEL. Release Behavior and Antibacterial Activity of Chitosan/Alginate Blends with Aloe vera and Silver Nanoparticles. Mar Drugs 2017;15(10):328. doi:10.3390/ md15100328, PMID:29064431.
- [39] Tran TPA, Luong AH, Lin WC. Characterizations of Centrifugal Electrospun Polyvinyl Alcohol/Sodium Alginate/Tamanu Oil/Silver Nanoparticles Wound Dressing. IEEE Trans Nanobioscience 2024;23(2):368– 377. doi:10.1109/TNB.2024.3371224, PMID:38427547.
- [40] Jiang M, Li S, Ming P, Guo Y, Yuan L, Jiang X, et al. Rational design of porous structure-based sodium alginate/chitosan sponges loaded with green synthesized hybrid antibacterial agents for infected wound healing. Int J Biol Macromol 2023;237:123944. doi:10.1016/j. ijbiomac.2023.123944, PMID:36898466.
- [41] Liang L, Li X, Tan Z, Liu M, Qiu Y, Yu Q, et al. Injectable spontaneously formed asymmetric adhesive hydrogel with controllable removal for wound healing. J Mater Chem B 2023;11(45):10845–10858. doi:10.1039/d3tb02014b, PMID:37937417.
- [42] Luo Y, Zhou X, Liu C, Lu R, Jia M, Li P, et al. Scavenging ROS and inflammation produced during treatment to enhance the wound repair efficacy of photothermal injectable hydrogel. Biomater Adv 2022;141:213096. doi:10.1016/j.bioadv.2022.213096, PMID:36067644.
- [43] Huang L, Yu L, Yin X, Lin Y, Xu Y, Niu Y. Silver nanoparticles with vanadium oxide nanowires loaded into electrospun dressings for efficient healing of bacterium-infected wounds. J Colloid Interface Sci 2022;622:117–125. doi:10.1016/j.jcis.2022.04.026, PMID:35490615.
- [44] Montaser AS, Abdel-Mohsen AM, Ramadan MA, Sleem AA, Sahffie NM, Jancar J, et al. Preparation and characterization of alginate/silver/nicotinamide nanocomposites for treating diabetic wounds. Int J Biol Macromol 2016;92:739–747. doi:10.1016/j.ijbiomac.2016.07.050. PMID:27431797.
- [45] Das M, Sethy C, Kundu CN, Tripathy J. Synergetic reinforcing effect of graphene oxide and nanosilver on carboxymethyl cellulose/sodium alginate nanocomposite films: Assessment of physicochemical and antibacterial properties. Int J Biol Macromol 2023;239:124185. doi:10.1016/j.ijbiomac.2023.124185, PMID:36977443.
- [46] Murugaiah H, Teh CL, Loh KC, Mohamad Yahya AR, Md Noh NA, Abu Bakar NHH, et al. Study of Antibacterial and Anticancer Properties of bioAgNPs Synthesized Using Streptomyces sp. PBD-311B and the Application of bioAgNP-CNC/Alg as an Antibacterial Hydrogel Film against P. aeruginosa USM-AR2 and MRSA. Molecules 2021;26(21):6414. doi:10.3390/molecules26216414, PMID:34770823.
- [47] Wang T, Li Y, Liu Y, Xu Z, Wen M, Zhang L, et al. Highly biocompatible Ag nanocluster-reinforced wound dressing with long-term and synergistic bactericidal activity. J Colloid Interface Sci 2023;633:851–865. doi:10.1016/j.jcis.2022.11.139, PMID:36495807.
- [48] Tao G, Cai R, Wang Y, Zuo H, He H. Fabrication of antibacterial sericin based hydrogel as an injectable and mouldable wound dressing. Mater Sci Eng C Mater Biol Appl 2021;119:111597. doi:10.1016/j. msec.2020.111597, PMID:33321641.
- [49] Marie Arockianathan P, Sekar S, Sankar S, Kumaran B, Sastry TP. Evaluation of biocomposite films containing alginate and sago starch impregnated with silver nano particles. Carbohydr Polym 2012;90(1):717–724. doi:10.1016/j.carbpol.2012.06.003, PMID:24751098.
- [50] Mekkawy AI, El-Mokhtar MA, Nafady NA, Yousef N, Hamad MA, El-Shanawany SM, et al. In vitro and in vivo evaluation of biologically synthesized silver nanoparticles for topical applications: effect of surface coating and loading into hydrogels. Int J Nanomedicine 2017;12:759–777. doi:10.2147/IJN.S124294, PMID:28176951.
- [51] Wang C, Huang X, Deng W, Chang C, Hang R, Tang B. A nano-silver composite based on the ion-exchange response for the intelligent anti-bacterial applications. Mater Sci Eng C Mater Biol Appl 2014;41:134–141. doi:10.1016/j.msec.2014.04.044, PMID:24907746.
- [52] Piras CC, Mahon CS, Smith DK. Self-Assembled Supramolecular Hybrid Hydrogel Beads Loaded with Silver Nanoparticles for Antimicrobial Applications. Chemistry 2020;26(38):8452–8457. doi:10.1002/chem.202001349, PMID:32294272.

- [53] Gill SZ, Niazi MBK, Malik US, Jahan Z, Andleep S, Ahmed T. Development and characterization of SA/PEG hydrogel membranes with Ag/ZnO nanoparticles for enhanced wound dressing. Mater Chem Phys 2024;317:129170. doi:10.1016/j.matchemphys.2024.129170.
- [54] Stojkovska J, Petrovic P, Jancic I, Milenkovic MT, Obradovic B. Novel nano-composite hydrogels with honey effective against multi-resistant clinical strains of Acinetobacter baumannii and Pseudomonas aeruginosa. Appl Microbiol Biotechnol 2019;103(20):8529–8543. doi:10.1007/s00253-019-10055-2, PMID:31396680.
- [55] Shan J, Li X, Huang Z, Kong B, Wang H, Ren L. In Situ Sprayed Difunctional Gel Avoiding Microenvironments Limitations to Treat Pressure Ulcers. Macromol Biosci 2023;23(5):e2300006. doi:10.1002/mabi.202300006, PMID:36951403.
- [56] Wang Y, Qi W, Mao Z, Wang J, Zhao RC, Chen H. rPDAs doped antibacterial MOF-hydrogel: bio-inspired synergistic whole-process wound healing. Mater Today Nano 2023;23:100363. doi:10.1016/j.mtnano.2023.100363.
- [57] Ndlovu SP, Fonkui TY, Kumar P, Choonara YE, Ndinteh DT, Aderibigbe BA. Dissolvable zinc oxide nanoparticle-loaded wound dressing with preferential exudate absorption and hemostatic features. Polym Bull 2023;80(7):7491–7518. doi:10.1007/s00289-022-04358-0.
- [58] Catanzano O, D'Esposito V, Pulcrano G, Maiolino S, Ambrosio MR, Esposito M, et al. Ultrasmall silver nanoparticles loaded in alginatehyaluronic acid hybrid hydrogels for treating infected wounds. Int J Polym Mater Polym Biomater 2017;66(12):626–634. doi:10.1080/00 914037.2016.1252358.
- [59] Ibrahim MA, Nasr GM, Ahmed RM, Kelany NA. Physical characterization, biocompatibility, and antimicrobial activity of polyvinyl alcohol/sodium alginate blend doped with TiO(2) nanoparticles for wound dressing applications. Sci Rep 2024;14(1):5391. doi:10.1038/s41598-024-55818-8, PMID:38443415.
- [60] Zhang H, Peng M, Cheng T, Zhao P, Qiu L, Zhou J, et al. Silver nanoparticles-doped collagen-alginate antimicrobial biocomposite as potential wound dressing. J Mater Sci 2018;53(21):14944–14952. doi:10.1007/s10853-018-2710-9.
- [61] Khadem E, Kharaziha M, Salehi S. Colorimetric pH-responsive and hemostatic hydrogel-based bioadhesives containing functionalized silver nanoparticles. Mater Today Bio 2023;20:100650. doi:10.1016/j.mtbio.2023.100650, PMID:37206880.
- [62] Wang N, Guang S, Xu H. Litchi-like silver nanoparticles immobilized in microspheres for effective bacteriostasis, rapid hemostasis, and wound healing. Mater Today Chem 2023;29:101462. doi:10.1016/j. mtchem.2023.101462.
- [63] Vasile BS, Birca AC, Musat MC, Holban AM. Wound Dressings Coated with Silver Nanoparticles and Essential Oils for The Management of Wound Infections. Materials (Basel) 2020;13(7):1682. doi:10.3390/ ma13071682, PMID:32260273.
- [64] Deng Z, Li M, Hu Y, He Y, Tao B, Yuan Z, et al. Injectable biomimetic hydrogels encapsulating Gold/metal-organic frameworks nanocomposites for enhanced antibacterial and wound healing activity under visible light actuation. Chem Eng J 2021;420:129668. doi:10.1016/j. cej.2021.129668.
- [65] Brindhadevi K, Elesawy BH, Elfasakhany A, Badruddin IA, Kamangar S. Wound dressings coated with silver nanoparticles and essential oil of Labdanum. Appl Nanosci 2023;13(2):1345–1354. doi:10.1007/s13204-021-02040-x.
- [66] Lin YH, Dai NT, Hong PD. Combination of high efficiency nanosilver and alginate for wound infection control. Int J Nanotechnol 2013;10(10-11):905–915. doi:10.1504/IJNT.2013.058118.
- [67] Dodero A, Scarfi S, Pozzolini M, Vicini S, Alloisio M, Castellano M. Alginate-Based Electrospun Membranes Containing ZnO Nanoparticles as Potential Wound Healing Patches: Biological, Mechanical, and Physicochemical Characterization. ACS Appl Mater Interfaces 2020;12(3):3371–3381. doi:10.1021/acsami.9b17597, PMID:31876405.
- [68] Silva MRPD, Matos RS, Monteiro MDS, Santos SB, Filho HDF, Andrade GRS, et al. Exploiting the Physicochemical and Antimicrobial Properties of PHB/PEG and PHB/PEG/ALG-e Blends Loaded with Ag Nanoparticles. Materials (Basel) 2022;15(21):7544. doi:10.3390/ma15217544, PMID:36363134.
- [69] Liang J, Zeng H, Qiao L, Jiang H, Ye Q, Wang Z, et al. 3D Printed Pi-

- ezoelectric Wound Dressing with Dual Piezoelectric Response Models for Scar-Prevention Wound Healing. ACS Appl Mater Interfaces 2022;14(27):30507–30522. doi:10.1021/acsami.2c04168, PMID:357 68948
- [70] Nqoro X, Adeyemi SA, Ubanako P, Ndinteh DT, Kumar P, Choonara YE, et al. A Topical Alginate-Based Wound Gel Fixated with Metal-Based Nanoparticles and Tranexamic Acid as a Hemostatic Wound Healing System. BioNanoScience 2023;13(4):2400–2417. doi:10.1007/s12668-023-01208-9.
- [71] Kong F, Fan C, Yang Y, Lee BH, Wei K. 5-hydroxymethylfurfural-embedded poly (vinyl alcohol)/sodium alginate hybrid hydrogels accelerate wound healing. Int J Biol Macromol 2019;138:933–949. doi:10.1016/j.ijbiomac.2019.07.152, PMID:31351961.
- [72] Seo SY, Lee GH, Lee SG, Jung SY, Lim JO, Choi JH. Alginate-based composite sponge containing silver nanoparticles synthesized in situ. Carbohydr Polym 2012;90(1):109–115. doi:10.1016/j.carbpol.2012.05.002, PMID:24751017.
- [73] Rani VVD, Ramachandran R, Chennazhi KP, Tamura H, Nair SV, Jayakumar R. Fabrication of alginate/nanoTiO2 needle composite scaffolds for tissue engineering applications. Carbohydr Polym 2011;83(2):858–864. doi:10.1016/j.carbpol.2010.08.065.
- [74] Hia EM, Jang SR, Maharjan B, Park J, Park CH. Cu-MSNs and ZnO nanoparticles incorporated poly(ethylene glycol) diacrylate/sodium alginate double network hydrogel for simultaneous enhancement of osteogenic differentiation. Colloids Surf B Biointerfaces 2024;236:113804. doi:10.1016/j.colsurfb.2024.113804, PMID:38428209.
- [75] Jovanović Ž, Stojkovska J, Obradović B, Mišković-Stanković V. Alginate hydrogel microbeads incorporated with Ag nanoparticles obtained by electrochemical method. Mater Chem Phys 2012;133(1):182– 189. doi:10.1016/j.matchemphys.2012.01.005.
- [76] Obradovic B, Stojkovska J, Jovanovic Z, Miskovic-Stankovic V. Novel alginate based nanocomposite hydrogels with incorporated silver nanoparticles. J Mater Sci Mater Med 2012;23(1):99–107. doi:10.1007/ s10856-011-4522-1, PMID:22203513.
- [77] Li S, Wang X, Chen J, Guo J, Yuan M, Wan G, et al. Calcium ion crosslinked sodium alginate hydrogels containing deferoxamine and copper nanoparticles for diabetic wound healing. Int J Biol Macromol 2022;202:657–670. doi:10.1016/j.ijbiomac.2022.01.080, PMID:350 66024.
- [78] Raguvaran R, Manuja BK, Chopra M, Thakur R, Anand T, Kalia A, et al. Sodium alginate and gum acacia hydrogels of ZnO nanoparticles show wound healing effect on fibroblast cells. Int J Biol Macromol 2017;96:185–191. doi:10.1016/j.ijbiomac.2016.12.009, PMID:2793
- [79] Hamid LL, Hassan MH, Obaid AS. Construction of Sodium alginate/ palladium Nanoparticles SA/Pd NPs Aerogel for in vitro and in vivo Antibacterial and Wound Healing Applications. J Clust Sci 2024;35(6):2069–80. doi:10.1007/s10876-024-02643-8.
- [80] Kędzierska M, Hammi N, Kolodziejczyk-Czepas J, Katir N, Bryszewska M, Milowska K, et al. Glassy-like Metal Oxide Particles Embedded on Micrometer Thicker Alginate Films as Promising Wound Healing Nanomaterials. Int J Mol Sci 2022;23(10):5585. doi:10.3390/ijms23105585, PMID:35628396.
- [81] Nqoro X, Adeyemi SA, Ubanako P, Ndinteh DT, Kumar P, Choonara YE, et al. Wound healing potential of sodium alginate-based topical gels loaded with a combination of essential oils, iron oxide nanoparticles and tranexamic acid. Polym Bull 2024;81(4):3459–78. doi:10.1007/s00289-023-04879-2.
- [82] Bargavi P, Balakumar S, Raghunandhakumar S. Multi-functional bandage - bioactive glass/metal oxides/alginate composites based regenerative membrane facilitating re-epithelialization in diabetic wounds with sustained drug delivery and anti-bactericidal efficacy. Int J Biol Macromol 2024;262(Pt 2):130054. doi:10.1016/j.ijbiomac. 2024.130054. PMID:38342258.
- [83] Tomić SL, Babić Radić MM, Vuković JS, Filipović VV, Nikodinovic-Runic J, Vukomanović M. Alginate-Based Hydrogels and Scaffolds for Biomedical Applications. Mar Drugs 2023;21(3):177. doi:10.3390/md21030177. PMID:36976226.
- [84] Stojkovska J, Djurdjevic Z, Jancic I, Bufan B, Milenkovic M, Jankovic R, et al. Comparative in vivo evaluation of novel formulations based on alginate and silver nanoparticles for wound treatments. J Biomater Appl

- 2018;32(9):1197–1211. doi:10.1177/0885328218759564, PMID:294 63162.
- [85] Zhang M, Zhao X. Alginate hydrogel dressings for advanced wound management. Int J Biol Macromol 2020;162:1414–1428. doi:10.1016/j.ijbiomac.2020.07.311, PMID:32777428.
- [86] Wang L, Hu C, Shao L. The antimicrobial activity of nanoparticles: present situation and prospects for the future. Int J Nanomedicine 2017;12:1227–1249. doi:10.2147/IJN.S121956, PMID:28243086.
- [87] Ridolfo R, Tavakoli S, Junnuthula V, Williams DS, Urtti A, van Hest JCM. Exploring the Impact of Morphology on the Properties of Biodegradable Nanoparticles and Their Diffusion in Complex Biological Medium. Biomacromolecules 2021;22(1):126–133. doi:10.1021/acs. biomac.0c00726, PMID:32510218.
- [88] Nqakala ZB, Sibuyi NRS, Fadaka AO, Meyer M, Onani MO, Madie-he AM. Advances in Nanotechnology towards Development of Silver Nanoparticle-Based Wound-Healing Agents. Int J Mol Sci 2021;22(20):11272. doi:10.3390/ijms222011272, PMID:34681930.
- [89] Mousavi SM, Hashemi SA, Ghasemi Y, Atapour A, Amani AM, Savar Dashtaki A, et al. Green synthesis of silver nanoparticles toward bio

- and medical applications: review study. Artif Cells Nanomed Biotechnol 2018;46(sup3):S855–S872. doi:10.1080/21691401.2018.151776 9, PMID:30328732.
- [90] Medici S, Peana M, Pelucelli A, Zoroddu MA. An updated overview on metal nanoparticles toxicity. Semin Cancer Biol 2021;76:17–26. doi:10.1016/j.semcancer.2021.06.020, PMID:34182143.
- [91] Mohanta YK, Mishra AK, Panda J, Chakrabartty I, Sarma B, Panda SK, et al. Promising applications of phyto-fabricated silver nanoparticles: Recent trends in biomedicine. Biochem Biophys Res Commun 2023;688:149126. doi:10.1016/j.bbrc.2023.149126, PMID:379 51153.
- [92] Jo DH, Kim JH, Lee TG, Kim JH. Size, surface charge, and shape determine therapeutic effects of nanoparticles on brain and retinal diseases. Nanomedicine 2015;11(7):1603–1611. doi:10.1016/j. nano.2015.04.015, PMID:25989200.
- [93] Wu H, Tang L, Dong H, Zhi M, Guo L, Hong X, et al. Shape and Size Dependence of Pharmacokinetics, Biodistribution, and Toxicity of Gold Nanoparticles. Mol Pharm 2025;22(1):196–208. doi:10.1021/ acs.molpharmaceut.4c00832, PMID:39589203.