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Revista FT | ISSN 1678-0817 | v. 30, n. 160, 2026 | DOI: 10.69849/yaj09497

Wounds treated with advanced biomaterials: strategies, evaluation, and therapeutic prospects

Feridas tratadas com biomateriais avançados: Estratégias, avaliação e perspectivas terapêuticas

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ABSTRACT

Bacterial cellulose (BC) has established as a remarkably versatile biomaterial. Excellent properties of BC laid the foundations for its application as a dressing in wound healing. Recent strategies include compounds loaded on to BC for the enhancement of its properties. We obtained BC from a fermentation process modified by the addition of Green Propolis and Usnic Acid to the culture medium and natural materials before the inoculation of bacteria. Here, we show some results of our investigation of this BC loaded biomaterial in the field of regenerative medicine. The great recovery and absence of adverse effects in cases here presented support its continuous investigation for the treatment of extreme conditions for wound healing.

Keywords: Bacterial cellulose, Biomaterials, Nanomedicine, wound healing, Green Propolis and Usnic acid.

RESUMO

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A celulose bacteriana (CB) tem se consolidado como um biomaterial notavelmente versátil. Suas excelentes propriedades estabeleceram as bases para sua aplicação como curativo no processo de cicatrização de feridas. Estratégias recentes incluem a incorporação de compostos à CB para potencializar suas propriedades. Neste estudo, obtivemos CB por meio de um processo de fermentação modificado pela adição de própolis verde e ácido úsnico ao meio de cultura e de materiais naturais antes da inoculação das bactérias. Apresentamos alguns resultados da investigação desse biomaterial enriquecido com CB no campo da medicina regenerativa. A excelente recuperação e a ausência de efeitos adversos nos casos aqui apresentados reforçam a importância de dar continuidade às investigações sobre seu uso no tratamento de condições extremas de cicatrização de feridas.

Palavras-chave: Celulose bacteriana, biomateriais, nanomedicina, cicatrização de feridas, própolis verde e ácido úsnico.

1. Introduction

Chronic and acute skin wounds, i.e. diabetic foot ulcers, venous leg ulcers and burns, affect more than 2 % of the global population and pose a significant burden on healthcare systems worldwide, often complicated by infections, poor vascularization, and prolonged inflammation.[1,2] These situations impose escalating socioeconomic costs due to the possibility of complications usually observed.[3]

The development of biomaterials that support tissue regeneration, while providing an optimal wound environment is critical, as conventional cotton gauze and hydrocolloids often fail to maintain an optimal moist microenvironment to recovering and preventing infection.

Bacterial cellulose (BC), a natural nano fibrillar biopolymer of β-1,4-glucan produced by certain strains of acetic-acid bacteria (*Komagataeibacter spp*, *Gluconacetobacter* spp.) has garnered attention due to its unique ribbon-like nanofiber network (3–8 nm), and high porosity that mimics native extracellular matrix, retains water, and shows mechanical strength comparable to collagen. [4] Unlike plant-derived cellulose, BC is non-toxicity and highly pure (i.e. lignin-free), it exhibits excellent biocompatibility and gas permeability, and also acts as a temporary extracellular matrix, which allow more control over cellular behavior during tissue healing, making it very suitable for biomedical use.[5,6]

Effective wound management requires dressings that control exudate, protect against microbial invasion and support tissue regeneration while avoiding possible infections due to the required time for complete healing. Traditional materials often fall short in balancing moisture and breathability, leading to treatment delay. Conversely, BC's ribbon-like nanofiber matrix (3–8 nm diameter) forms a highly porous hydrogel capable of retaining > 95 % water by weight, while permitting gas exchange, which prevents anaerobic conditions, as long as conforming to wound contours.[7]

Such multifunctional BC composites have demonstrated accelerated re-epithelialization,, reduced inflammation and enhanced collagen deposition in preclinical models, positioning BC as a next-generation wound-dressing platform.[8,9]

It's well known that timely wound care is important to prevent complications and reduce the time to healing, and disruption of wound care paradigms had led to modifications in the delivery of wound care.

This article outlines possible paths for the functionalization of BC with Green Propolis and Usnic Acid (BCGU), and evaluation as a relevant wound dressing material, demonstrating its potential to enhance re-epithelialization and tissue regeneration. [10,11] for very critical conditions in clinical practice.

2. Materials and Methods

2.1. Study design

This study is a retrospective case series evaluating the clinical application of a functionalized bacterial cellulose biomaterial. A total of nine patients (n = 8) presenting with diverse wound etiologies were selectively treated and monitored. The cohort presented an age range from 1 month to 101 years and encompassed the following etiologies: sacral pressure ulcer (n = 1), Stevens-Johnson Syndrome/Staphylococcal Scalded Skin Syndrome (n = 2), diabetic foot ulcer (n = 1), sharp traumatic laceration (n = 1), second-degree burns (n = 2), and neonatal extravasation injuries (n = 2). Patients were followed clinically until complete wound healing or discharge. Wound progression and structural changes were assessed by direct clinical visual inspection during follow-up. Digital planimetry software was not utilized in this series. To isolate the therapeutic contribution of the biomaterial, standard concomitant care protocols were maintained under specialized supervision at Al Qassimi Hospital. For the sacral pressure sore and diabetic foot ulcer, pressure offloading and targeted debridement were performed. The Stevens-Johnson Syndrome (SJS) and Staphylococcal Scalded Skin Syndrome (4S) cases received intensive supportive management, strict fluid resuscitation, and critical care monitoring in the Intensive Care Unit (ICU). Burn management involved immediate blister removal followed by standard topical hygiene. Neonatal extravasation injuries required surgical debridement of necrotic tissue performed by the pediatric surgery team, along with systemic antibiotic therapy and peripheral cannula management for vital blood product transfusions.

2.2. Bionanocomposite Preparation (BCGU / Nanoskin® ACT)

The advanced wound dressing consists of a bacterial cellulose (BC) matrix functionalized with 2% usnic acid and 1% green propolis. During the manufacturing protocol, the active compounds are loaded into the matrix with an addition timing of 10 minutes to ensure homogeneous incorporation. The final clinical product (commercially designated as Nanoskin® ACT) is sterilized via gamma radiation. In specific clinical presentations, it was used in combination with supporting formulations of the same platform, such as Nanoskin® Biogel Activator, Biogel Spray, or Intense Care Oil.

BC was synthesized using *Acetobacter xylinus* (ATCC 53582) cultivated in Hestrin-Schramm (HS) medium (glucose 20 g/L, yeast extract 5 g/L, peptone 5 g/L, citric acid 1.15 g/L, Na2HPO4 2.7 g/L) under static conditions at 30 °C for 7–10 days. The pellicles formed at the air–liquid interface were harvested, washed in distilled water, and treated with 0.1 M NaOH at 80 °C to remove bacterial residues, followed by extensive rinsing to neutral pH.

Besides, BC natural membranes of Nanoskin® have green própolis and usnic acid which is effective antibacterial agent and immunogenic substance. When it is linked in cellular receptors, it increases immune body response. Such natural membranes change ECM synthesis of new vessels, granulation tissue and epithelialization that are produced in patient skin.[12,13]

2.3 *In Vivo* Clinical Evaluation

The study was approved by the Institutional Ethics Committee of Al Qassimi Hospital (Sharjah, UAE) and was conducted in accordance with the ethical principles of the Declaration of Helsinki[6] Informed consent was obtained from all patients and/or legal guardians. Full-thickness or partial-thickness wounds of various etiologies were treated with the BC membranes functionalized with Usnic Acid and Green Propolis, changed every 3 days. Wound closure was monitored by digital planimetry on specific days, Secondary gauze dressings were used when needed.

The primary clinical endpoint evaluated was complete wound closure, defined as full re-epithelialization with skin regeneration and absence of drainage. Secondary endpoints included infection control (monitored via clinical signs of inflammation and exudate qualitative assessment), pain management, and the incidence of local or systemic adverse events during the follow-up period.

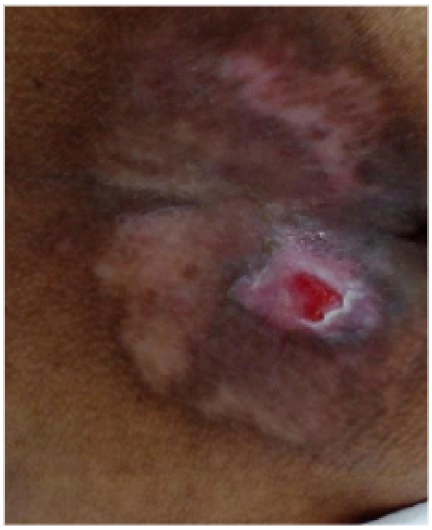
3) Results and Discussion

Bacterial cellulose (BC) has emerged as a premier biopolymer for wound management due to its high purity, exceptional water-holding capacity, and biocompatibility, which collectively mimic the native extracellular matrix. Recent translational reviews have highlighted how the highly porous nanofibrous network of BC not only maintains an optimal moist healing environment but also serves as an ideal scaffolding matrix for incorporating bioactive agents—such as antimicrobial compounds, essential oils, and phytotherapeutic extracts—to actively combat biofilms and accelerate re-epithelialization [14]. Furthermore, advanced engineering of BC nanocomposites has shifted the paradigm from passive physical barriers to smart, responsive therapeutic platforms capable of modulating the chronic wound microenvironment, regulating exudate levels, and promoting angiogenesis [15]. Clinical and pre-clinical evaluations underscore that the chemical functionalization of BC matrices successfully overcomes the native polymer's lack of inherent antimicrobial activity, establishing these bio-nanocomposites as versatile solutions for complex, non-healing, and infected wound etiologies [16].BCGU membrane was applied for wound healing in some patients showing extensive and very difficult clinical conditions. Here we show some application cases and their outcomes.

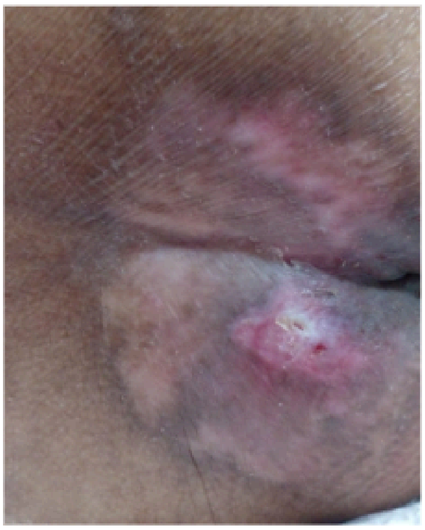
Figure 1. Case 1 (Sacral Pressure Sore): A 101-year-old bedridden female patient with a history of Type II diabetes mellitus, prior cerebrovascular accident (CVA, PEG-dependent), epilepsy, hypothyroidism, and dyslipidemia presented with a severe sacral bed sore. Treatment with Nanoskin® ACT combined with Nanoskin® Biogel Activator was initiated on 14/05/2025 and ended on 08/06/2025.

Initial (0^{th} day)

5^{th} day

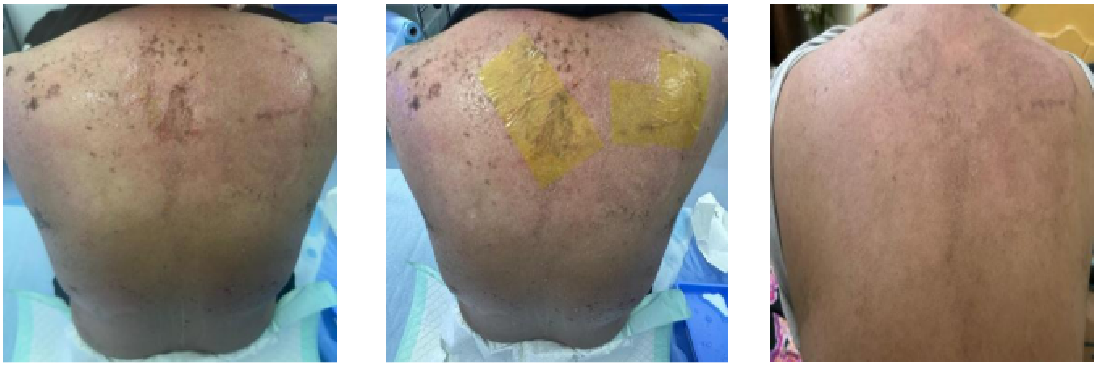


16^{th} day



25^{th} day

Figure 2. A 32-year-old female patient with known allergies to allopurinol and azithromycin developed Stevens-Johnson Syndrome (SJS). The condition manifested as a rapidly progressing acute cutaneous drug reaction secondary to allopurinol introduction for gout treatment. Symptoms advanced from initial facial/upper limb erythema to generalized blisters, cracked lips, and extensive epidermal detachment at the dermal-epidermal junction. Application of Nanoskin® ACT was used to manage the extensive areas of denuded skin. with drug-induced Stevens-Johnson syndrome (SJS) presented with fever, sore throat, body rash, generalized erythema with new blisters on face, trunk, upper limbs and thighs. SJS is a severe, often drug-induced mucocutaneous reaction within the spectrum of epidermal necrolysis, with high morbidity and mortality.[17] After 3 dressing applications, complete re-epithelialization was achieved with minimal scarring. In contrast, standard supportive care and conventional wound management for SJS is typically describing in literature by requiring 12–16 weeks for re-epithelialization in mild-to-moderate cases.[18]



Initial (0^{th} day) Middle (4^{th} day) Final (8^{th} day)

Figure 3. Case 3 (Diabetic Foot Ulcer): A 64-year-old patient with comorbidities including type 2 diabetes, hyperlipidemia, hypertension, and hypothyroidism presented with a 1.5 x 0.5 cm traumatic ulcer on the medial aspect of the left big toe caused by footwear friction. The lesion was treated successfully with Nanoskin® ACT. With standard care (debridement, offloading, and conventional dressings), neuropathic diabetic foot ulcers heal in a mean of approximately 50–78 days, while neuroischemic ulcers may take more than hundred.[19]

0^{th} day 14^{th} day

Figure 4. Cases 5 (Second-Degree Burns). A female patient (aged 29) presented with circumferential second-degree burns on the right wrist caused by boiling liquids (coffee and water, respectively). Following mechanical blister removal, the lesions were managed with Nanoskin® Biogel Spray, ACT, and Intense Care Oil. Here, a circumferential wrist burn healed completely within one month using Nanoskin® ACT biogel spray as adjunct. Standard treatment with 1% silver sulfadiazine for partial-thickness (second-degree) burns results in mean healing times of 19–24 days.[20,21]

0th day

4th day

12th day

15th day

Figure 5. Cases 6 and 7 (Neonatal Extravasation Injuries). An extreme preterm female infant born at 23 weeks and 3 days gestation (birth weight 720g, corrected age 38 weeks and 1 day) required prolonged NCU support (106 days) for multiple complications, including bronchopulmonary dysplasia, patent ductus arteriosus, and necrotizing enterocolitis. Due to mandatory peripheral cannulation for blood transfusions and therapeutics, the patient sustained device-related pressure sores on the right wrist and multiple extravasation injuries on the right leg, left leg, and left wrist. Following surgical debridement of necrotic tissue on the left wrist by pediatric surgery, the affected areas were treated with Nanoskin® ACT. First application on the right hand wound occurred on 11/06/2025, achieving complete healing and skin regeneration by 15/07/2025, with stable outcomes confirmed at follow-up on 27/07/2025.. A) left leg; B) right hand. In both cases, the membrane remained adherent and dry, requiring only secondary gauze. Conservative management of neonatal extravasation injuries typically demands 13–29 days (mean 13 days) or up to 7.5 weeks in more extensive lesions.[22,23]

B) Extravasation injury in the right hand

Figure 6. Case 8 (Pediatric). A 19-month-old male infant presented with a severe acute dermatosis initially mimicking a semi-SJS condition post-fever. Upon expert evaluation, the condition was diagnosed as Staphylococcal Scalded Skin Syndrome. The patient was immediately admitted to the ICU for systemic stabilization and advanced dressing application. Because of fever, developed to semi Steven John's case, first diagnosed with *Staphylococcal* Scalded Skin Syndrome 4S DD 26/01/2025 evening, and on 27/01/2025 went to Hospital and immeditaely admitted to Intensive Care Unit, where the treatment started on 01/02/2025 and finished on 09/02/2025. It healed fast with no scar, contractures, and keloids. Also, no pain on application and after application.

4. Conclusion

This study our BCGU as a robust, adaptable platform for wound healing dressings. Its intrinsic nanofibrillar matrix provides mechanical protection and moisture balance, while facile post-processing enables loading with antimicrobials, antioxidants or growth factors that further accelerate tissue repair. Functionalized BCGU outperformed a market hydrocolloid by enhancing wound closure, reducing inflammation and fostering collagen maturation. [24,25] Ongoing researches should focus on scalable bioreactor production, GMP-compliant purification and controlled-release strategies tailored to specific wound etiologies (diabetic, burn, radiation). Given its favorable safety record and mounting clinical evidence, BC-based dressings are poised to transition from bench to bedside, addressing a critical unmet need in time-extended wound management in clinical scenario as showed here.

Future researches should ultimately enable tailored BC-based therapies across diverse wound types. The in vivo studies confirm its efficacy in accelerating wound closure and reducing inflammatory response. Future directions of BC will include functionalization with antimicrobial and angiogenic agents to further enhance its therapeutic performance.

In conclusion, bacterial cellulose nanocomposite membranes with BCGU (Nanoskin®) combine excellent biocompatibility, optimal moisture management, and bioactive properties that support the healing process in both acute and chronic human wounds. This case series provides preliminary clinical evidence that the composite is a safe, effective, and versatile advanced biomaterial suitable for translation into routine wound-care protocols. Future work will focus on large-scale GMP production and well-designed randomized controlled trials to establish comparative efficacy against standard market hydrocolloids and evaluate microscopic tissue parameters such as inflammation reduction and collagen maturation

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