Development of 3D Bilayer Scaffolds for Tissue Regeneration in Pressure Ulcers



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Abstract:

The development of multifunctional three-dimensional (3D) scaffolds capable of promoting tissue regeneration while providing localized therapeutic delivery remains a major challenge in regenerative medicine. This is particularly relevant in chronic wounds such as pressure ulcers, where infection, poor vascularization, and impaired cellular response delay healing.

This study aimed to design and evaluate novel bilayer 3D scaffolds with antimicrobial and pro-regenerative properties for advanced wound healing applications. The scaffolds consist of an inner natural polymer-based layer composed of carboxymethyl chitosan (CMCh) combined with copper-doped bioactive glass nanoparticles and therapeutic ions (Sr^{2+}, Zn^{2+}, or Ga^{3+}), and an external synthetic polymer layer incorporating benzoyl peroxide (BPO) and gallium-loaded microspheres.

Three scaffold formulations were developed: CMChSrMicGaEUPBO, CMChZnMicGaEUPBO, and CMChGaMicGaEUPBO. Physicochemical characterization demonstrated suitable mechanical properties, flexibility, adhesion, swelling capacity, and controlled degradation profiles. Ion release studies confirmed sustained delivery of therapeutic ions (Ga^{3+}, Sr^{2+}, and Cu^{2+}), which are known to promote angiogenesis, cell proliferation, and antimicrobial activity.

Biological evaluation revealed high biocompatibility with keratinocytes and fibroblasts, alongside enhanced cell proliferation and migration, confirmed by scratch assays. Angiogenic potential was supported by in vitro and ex vivo models, showing increased vascularization. Gene expression studies (RT-PCR, RNA sequencing) indicated upregulation of key markers involved in tissue regeneration, including collagen synthesis (COL1A1, COL3A1), growth factors (EGF, FGF2), and extracellular matrix remodeling proteins.

Among the tested formulations, CMChSrMicGaEUPBO exhibited the most promising performance, with improved stability, hydrophilicity, and biological activity. Its antimicrobial effect is enhanced by the synergistic action of gallium ions and benzoyl peroxide, providing a non-antibiotic strategy that reduces the risk of bacterial resistance.

In conclusion, the developed bilayer scaffolds represent a promising platform for the treatment of pressure ulcers, combining structural support, controlled therapeutic ion release, angiogenic stimulation, and antimicrobial activity. This multifunctional approach positions these scaffolds as strong candidates for future clinical applications in tissue engineering and regenerative medicine.

Biography

Sofia Helena Harriet is a researcher in pharmaceutical technology and biomaterials at the University of Buenos Aires (UBA) and CONICET. Her work focuses on the development of advanced biomaterials for tissue engineering and regenerative medicine, particularly multifunctional scaffolds for complex wound healing. She has participated in national and international conferences and collaborates on interdisciplinary projects involving nanotechnology, drug delivery, and biomedical applications.