Tunable Biomimetic Hybrid Scaffold for Wound Healing and Skin Regeneration

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ABSTRACT

Skin has the ability to regenerate after traumatic injury. The injury triggers several regenerative processes during the overlapping haemostasis, inflammatory, proliferative, and maturation wound healing phases. Cases such as bleeding, infection, and in other cases, loss of major skin tissue delays and/or limit the action of the phases above to restore the damaged tissues. Treatment of some injury cases have traditionally focused on allograft and autograft. However, these approaches may take longer to incorporate into the patient's body, and could also be rejected by some patients and lastly the use of autograft results in the loss of tissue from one place to heal another. This gave rise to the tissue engineering field which includes the development of bioplatforms/devices/biomaterials suitable for the treatment of the cases mentioned above. These tissue engineering bioplatforms includes but not limited to hydrogels, gels, foams, nano/microparticles, scaffolds, sponges, fibres, and beads. The design of these bioplatforms ranges from natural/synthetic polymers, antibiotics, bioactives and peptides/proteins.

There has been great advancement in the tissue engineering field. However, there is still no bioplatform that meet the requirements for an ideal wound dressing. The current study outlines the properties of bioplatforms that can be controlled to improve the bioplatforms' translational performance as a wound dressing. To aid the biocompatibility and degradation of the wound dressings, natural polymers such as chitosan (CS) and alginate (Alg) were used along with natural phenolic agents such as transferulic acid (TFA) and tannic acid (TA). The properties of the bioplatforms were tunable by employing the partial crosslinking, freeze-drying, and lyophilization approach to fabricate particulate bioplatforms capable of forming an *in situ* interpolymer complex (IPC) hydrogel in the presence of fluids. The sodium tripolyphosphate and calcium chloride partial crosslinking approach enabled the incorporation of transferulic acid and also the *in situ* formation of IPC hydrogel.

Properties such as fluid absorption [(PC CS-Alg (4343.4%) and PC TFA-CS-Alg (3102%) in 24 hours)], degradation [(PC CS-Alg (78.2%) and PC TFA-CS-Alg (53.5%) in 14 days)], and mechanical properties [(rigidity of 2090 Pa, and 640 Pa for PC CS-Alg and PC TFA-CS-Alg, respectively)] were observed in this study. The Bioplatforms' performance such as the TFA encapsulation efficiency of 65.6% with a burst release of 57.5% in 8 hours to a total release of 67.3% in 3 days was also observed in the current study. These properties lead to translation performances such as non-toxic (cell viability > 90%) behaviour when the NIH 3T3 embryonic fibroblast cells were exposed to the bioplatforms for 3 days. Furthermore, the bioplatforms exhibited superior accelerated tissue remodelling and wound healing capabilities at the early stages of wound healing compared to the equivalent commercial product (Pharma-Algi®) and the control group. To elucidate the suitability of tuning bioplatform properties to translational performances, a self-assembling scaffold was developed from the natural polymers mentioned above, RGD peptide and TA.

Properties of the bioplatforms included the optimal swelling behaviour (absorbs fluid instantly), porosity (3-D architecture with an average pore size distribution of 168.4 μm^2), mechanical properties such as tensile strength of 0.0038 and 0.001725 MPa, compressive ultimate strength of 0.0571 and 0.07225 MPa, and storage modulus of 80.9 and 88.6 Pa for Alg-RGD-CS and Alg-RGD-CS-TA, respectively. These properties allowed for TA encapsulating efficiency 86% with a burst release of 57.12% in 24 hours, followed by gradual steady release of 8.45% per day up to 90% in 5 days. The Alg-RGD-CS scaffolds displayed high fluid uptake of 5240% in 24 hours vii compared to the 3716% absorbed by the Alg-RGD-CS-TA in 24 hours. These fluid uptake properties where superior to those observed on the particulate bioplatform and the comparative product.

Contrary to the particulate bioplatform degradation properties, the scaffolds exhibited low degradation extent (Alg-RGD-CS (33.68%) and Alg-RGD-CS-TA (16.53%) in 14 days). However, the decrease in the degradation extent from non-crosslinked to crosslinked bioplatforms was still observed. Similarly, for the partially-crosslinked bioplatforms the translational performances of the scaffolds were remarkable with a cytocompatible behaviour (cell viability > 80%) and accelerated wound closure at the early stages of wound healing. The scaffold and the particulate bioplatforms displayed desirable wound healing performances highlighted by the regeneration of scar-less skin tissues after 14 days of wound healing. The desirable features of the regenerated skin tissues attest to the effective tunable properties of bioplatforms translation to optimal performances as wound dressings and drug delivery systems.