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Mechanical modulation of human plasma-based skin scaffold via reactive multi-arm polyethylene glycols

Rocío Corrales[1*], Michael Sikorski[1], Marta García[1], Diego Velasco[1, 2], José Luis Jorcano[1, 3]

[1] Department of Bioengineering and Aerospace, Universidad Carlos III de Madrid, Leganés (Madrid), Spain
[2] Instituto de Investigación Sanitaria de la Fundación Jiménez Díaz, Madrid, Spain
[3] Regenerative Medicine Unit and Epithelial Biomedicine Division, CIEMAT, Madrid, Spain
*coor.rocio@gmail.com

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Introduction: Autologous human plasma-based dermo-epidermal skin equivalents have been designed over the past decade to treat burns and surgical wounds [1]; however, poor mechanical properties including fragility during handling, high degradation rates, and shrinking during culture and implantation persist and demand creative solutions. The described research project aims to improve the material properties of these scaffolds through mechanical modulation using versatile polyethylene glycols (PEGs). Amine reactive multi-arm PEG platforms have previously been investigated as tissue adhesives, surgical sealants, and hemostatic agents, and have demonstrated excellent strength as network gels. The incorporation of a biologically reactive biodegradable PEG network into this clinically relevant skin scaffold should improve the aforementioned mechanical deficiencies and demonstrate new methods of scaffold preparation, processing, and handling.

Methods: A method was developed to modulate the material properties of autologous human plasma-based hydrogel scaffolds by incorporating a matrix of biodegradable multi-arm PEGs. Amine reactive succinimidyl glutarate terminated 4-arm PEG (4SG-PEG) and amine terminated 4-arm PEG (4A-PEG) reacted covalently with fibrinogen, plasma proteins, and each other to form a PEG-fibrin network hydrogel. Mechanical behaviour of the new scaffolds was assessed by mass swelling, protein release, and gelation time. Regarding cell viability, human fibroblast and keratinocyte's proliferation were assessed by Alamar Blue and MTS assays respectively.

Results: Increasing PEG content delayed gelation time, possibly caused by competitive covalent and non-competitive physical inhibition with normal fibrin formation. The capacity of each gel to swell was increased as a function of PEG content, and increased PEG network helped reduce protein leeching. Elasticity and ease of handling also improved as PEG content was increased. Regarding cell viability, human fibroblast and keratinocyte's proliferation were assessed by Alamar Blue and MTS assays respectively. Results indicated a slight decrease in fibroblast proliferation as crosslinking increased, and suggested a decrease in keratinocyte adhesion to the scaffold when PEG was present. However, biocompatibility was demonstrated.

Conclusions: Reactive multi-arm polyethylene glycols have shown to modulate the physical behaviour of a human plasma-based biological skin scaffold while having only mild effects on the viability of fibroblasts and keratinocytes. The addition of biodegradable and biocompatible synthetic materials (i.e. PEGs) to clinically relevant biological scaffolds warrants further investigation as an approach to improve material properties.

References

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