**////Title: Template-driven Electrospinning: A Smart Manufacturing Approach to Treating Skin Injuries**

**////Stand-first**:

Human skin acts as an important line of defence against the external environment. To preserve this important function, the regeneration of injured skin is critical. Scientists are now able to artificially replicate aspects of the complex microenvironment in which human skin stem cells reside thanks to the technological advances in the field of biomaterial devices. Dr Ilida Ortega Asencio, from the University of Sheffield, UK, and her team have developed a new approach in which electrospun patches with defined microenvironments can be functionalised with key compounds to aid the formation of new blood vessels in injured skin.

**////Body text:**

Skin injuries, particularly the most severe, can lead to extensive structural damage to the capillaries, which are critical in providing the skin with nutrients and oxygen, and in preserving tissue function. The formation of new blood vessels is known as angiogenesis and this process plays a key role in the progression of wound healing.

Dr Ilida Ortega Asencio and her team from the University of Sheffield, UK, use a state-of-the-art technique known as electrospinning to fabricate fibrous and intricate three-dimensional shapes that can resemble the stem cell microenvironments in which skin cells reside in native skin. The team has also worked to introduce angiogenic compounds that promote the formation of new blood vessels into these constructs to study their vascularisation potential. Vascularisation is a key but complex process in skin tissue engineering, allowing the determination of the biological function.

Dr Ortega Asencio is an expert in the manufacturing, characterisation and *in vitro* testing of biomaterial devices for tissue engineering applications. In particular, her group has achieved many impressive feats in the manufacturing of biomaterial devices for hard and soft tissue engineering.

Recently, Dr Ortega Asencio and her team published an article describing how smart drug delivery materials can be used to regenerate injured skin. The first step toward this aim was the production of scaffolds made of fibrous polycaprolactone a polymer commonly used in the biomedical field. The fibrous scaffolds were provided with extra biological value via the inclusion of bioactive compounds that have been studied before for their potential effects in supporting angiogenesis: 2-deoxy-D-ribose estradiol and aloe vera.

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Electrospinning is a manufacturing technique that uses an electric field to draw charged polymer threads into ultrafine fibres with diameters in the order of several to a few hundred nanometres. The team compared two different approaches in the production and optimisation of the fibrous scaffolds.

The first approach involved the formation of random electrospun scaffolds where the polycaprolactone polymer was delivered to a collector template via syringes with caps connected to a voltage supply. Different controlled flow rates and voltages were used for the different solutions and optimised for each angiogenic compound.

The fabrication of topographically controlled electrospun scaffolds was carried out by combining electrospinning with three-dimensional printed templates which were used as collectors. As with the random electrospun scaffold membranes, the flow rate and voltage used for the different solutions of bioactive compounds were controlled.

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Dr Ortega Asencio confirmed that human skin cell lines have a dose-dependent response to the bioactive compounds and that their inclusion has the potential to improve cell viability and have an impact on the expression of collagen and other relevant protein markers; importantly, some of the compounds were able to enhance blood vessel formation.

The team evaluated and compared the different strategies employed to micro-fabricate the bio-functional scaffolds and optimise the delivery of angiogenic agents 2-deoxy-D-ribose, estradiol and aloe vera. The researchers point out, however, that more research is needed to fully characterise the new developed biofunctional scaffolds, particularly the topographically controlled ones so that the angiogenic capabilities can be fully understood.

No significant changes in the mechanical or thermal properties of the polycaprolactone scaffolds loaded with 2-deoxy-D-ribose, estradiol or aloe vera were found. However, when measured, the topographically controlled electrospun scaffolds had higher diameters than the random spun scaffolds. This change in diameter was accompanied by increased hydrophobicity relating to water contact and propensity for rapid cell attachment, an aspect that is critical for most tissue engineering applications.

Consistent with previous research, the researchers found increased cell metabolic activity and proliferation when using 2-deoxy-D-ribose, further confirming its applicability and versatility in tissue engineering. No such beneficial effects were found for estradiol. Aloe vera had beneficial effects at low doses, but consistent with prior research, had negative effects at higher doses.

An interesting and attractive approach that was not tested in the current study is the potential for delivering two angiogenic agents via the same scaffold. Dr Ortega Asencio and the team note that this will be explored in future work as they further develop the topographically controlled electrospun scaffold methodology and its associated capabilities.

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To summarise, Dr Ortega Asencio and her colleagues provide new and encouraging evidence that Aloe Vera, as well as estradiol and 2-deoxy-ribose, can be loaded and delivered via bioengineered polycaprolactone scaffolds to induce blood vessel formation in injured human skin tissue. The artificial scaffolds produced by the team have the potential to be used in the development of complex wound healing devices, such as smart wound dressings that enable cellular infiltration and encourage skin regeneration.

This SciPod is a summary of the paper ‘Delivery of Bioactive Compounds to Improve Skin Cell Responses on Microfabricated Electrospun Microenvironments’, from the journal Bioengineering. DOI: https://doi.org/10.3390/bioengineering8080105

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