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BIOMATERIAL-BASED MICRONEEDLES FOR ABNORMAL SCARS TREATMENT

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Abnormal scars, also known as pathological scars, refer to a variety of skin formations that deviate from the typical healing process after injury. These scars may include keloids, hypertrophic scars, or scars resulting from conditions like acne or burns [1]. Recent research has highlighted the potential of drug-free microneedles (MN) in reducing scar growth by inhibiting skin fibroblast proliferation [2]. This effect, known as the contact inhibition effect, is achieved by disrupting the mechanical communication between fibroblasts and the extracellular matrix [3].
The objectives of the present work are i) the development of novel composite biomaterials consisting of whey protein isolate (WPI, Milei GmbH, DE), and chitosan (CS, Sigma Aldrich, I) or trimethyl chitosan (TMC, ChitoLytic, CAN) and ii) the design and production of composite biomaterial-based MN that employ a mechanotherapeutic approach to treat abnormal scars.
For the development of the composite biomaterials different complexes were prepared by mixing 4% w/w WPI aqueous solution and 4% w/w CS solution in 0.5 M acetic acid or 4% w/w TMC aqueous solution according to 1:1 weight ratio. The influence of WPI denaturation (70°C for 20 min) on complexes formation was investigated. Rheological, turbidimetric, dynamic and electrophoretic light scattering, SEM analyses were performed to characterize the complexes. Moreover, *in vitro* biocompatibility on NHDF cells and antioxidant activity were also evaluated.
MN patches consisting of the complexes were fabricated via a two-step centrifugation casting method. Three different female molds of polydimethylsiloxane (PDMS) (Micropoint Technologies Pte Ltd., SGP) containing pyramidal cavities with base diameter of 200 µm were used: i) 15×15 arrays, 600 µm depth; ii) 10×10 arrays, 600 µm depth; iii) 10×10 arrays, 800 µm depth. Briefly, complex aqueous dispersions were sonicated for 10 min to remove the trapped air. A fixed volume of the dispersion (150 µl or 200 µl for 10x10 and 15x15 arrays, respectively) was placed on the PDMS mold. Then the mold was centrifuged at 5900 rpm for 5 min. After the centrifugation step, 150 µl or 200 µl for 10x10 and 15x15 arrays, respectively, was added to the PDMS mold to form the patch backing layer. The filled molds were dried at room temperature for about 6 hours. Finally, the microneedle array was gently peeled out of the mold. The MN patches were characterized for morphology and mechanical strength. Insertion studies were also performed on model membranes. For the *in vitro* performance studies, a fibroblast-populated collagen lattice system (FPCL) model was used to investigate if MN were able to reduce collagen matrix contraction, modifying its viscoelastic properties.
The formation of CS-TMC:WPI complexes was significantly affected by WPI denaturation. All complexes were characterized by *in vitro* biocompatibility and antioxidant properties. MN showed a well-defined structure with a pyramidal morphology, evidenced by SEM analysis. The fracture force for all the MN prepared exceeded 0.058 N, that is the minimum average penetration force for normal skin. Preliminary results pointed out that MN inhibited FPCL contraction with a significant change in its viscoelastic properties. *In vivo* studies on animal model are on-going to evaluate the biocompatibility of the obtained composite biomaterial-based MN.

References:

[1] Y. Chen, et al., Polymers 2022, 14, 4436.
[2] D. Yeo, et al., Eur. J. Med. 2017, 22, 28.
[3] Q. Zhang, et al., ACS Nano 2022, 16, 10163-10178

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