Final Report

Project acronym: *SmartHyCAR*

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M-ERA.NET Call 20*16*

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Publishable project summary

The SmartHyCAR project aimed to design, prepare, and characterize a new multifunctional material, based on hyaluronic acid (**HA**), the dipeptide β-alanyl-L-histidine (carnosine, **CAR**) and/or the tripeptide glycil-L-histidyl-L-lysine (**GHK**), and copper ions (**Cu(II)**).
The hypothesis behind the project was to enhance, not just as additive effect but in a synergistic way, the properties of each single constituent of the multifunctional newly developed material. Specifically, HA, which is the main component of extracellular matrix, is considered one of the key players in the tissue regeneration process. Copper is a known potent angiogenic factor, and has antibacterial activity. The dipeptide CAR has antioxidant and anti-inflammatory action, as well as presents an inhibitory activity against the enzymatic degradation induced by the hyaluronidase enzyme on the HA chains. Moreover, CAR-Cu complexes mimic the activity of superoxide dismutase enzyme (SOD-like system) through the disproportion reaction of the superoxide radical anion. Finally, GHK-Cu complex is known to accelerate the wound healing and also exhibits anti-inflammatory activity.
The new formulation was demonstrated to exhibit improved performance as dressing for enhanced wound healing and scar reduction compared to other products already on the market.
The atmospheric plasma technology was integrated into the project activities concerning the following two approaches: i) the surface activation of the dressing substrates, for the grafting of a thin layer of the copper macrochelate with the new derivative (named **HyCAR-2**) of carnosine conjugated to the hyaluronic acid polymer via amino bonds (bottom-up chemical method), followed by post-coating discharge curing; ii) the plasma treatments of the solution mixtures of **HA + CAR + Cu** or **HA + GHK + CAR + Cu** (top-down physical method).
The new formulation of hydrogels was validated by pre-clinical *in vitro* and *in vivo* tests, and the set up for atmospheric plasma technology for the coating of dressings was defined both in lab and in industrially relevant environment.