Nano-enabled stimuli-responsive scaffolds for delivery of targeted antimicrobial systems to treat Staphylococcus aureus-mediated infections and restore skin homeostasis

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Skin infections have a significant impact on human health, especially when they cause disability and disfigurement. Treatments using antibiotics not only select for antimicrobial resistance (AMR), a global healthcare treat and heavy economic burden, but also disrupt the protective skin microbiome promoting new or recurrent infections. In TARDIS, we took advantage of the expertise of the consortium to engineer **novel nano-enabled hydrogel scaffolds containing targeted bio-based bactericides for effective treatment of *S. aureus*-mediated infections and restoring of the skin physiological functions**. SINTEF produced marine-derived extracts from the side-stream fish industry, as oils and peptides, with antimicrobial properties which were nanoformulated by UPC together with the flavonoid luteolin from extracted leaf olive trees identified by MAR. Due to the specific interaction of luteolin with bacterial cell-to-cell communication receptor the produced delivery nanosystems (NSs) have the ability to kill only *S. aureus*, when used in mixed cultures with Gram-negative *E. coli*. SoU further incorporated the targeted NSs into biocompatible scaffolds able to respond at specific stage of infection (e.g., higher pH and temperature). ADSSC developed a skin model using skin from donors following plastic surgery as ex vivo model to assess TARDIS NSs safety to the skin host and microbiome. TARDIS novelties have been published in peer-reviewed journals and presented at conferences. The project has also contributed to the formation of students on the initial steps of their research career. Two workshops have been organised to establish interaction with different stakeholders, such as academia and industry. TARDIS results demonstrate the capacity of biobased-targeted NSs to reach and attack only the pathogen of interest, being an efficient therapeutic approach for managing *S. aureus* infections, avoiding the use of antibiotics and preventing AMR development.