Biomimetic Polymers as Drug-free Antibacterial Materials and Coatings

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INTRODUCTION: To tackle antibiotic resistance, a promising goal is to develop novel materials with intrinsic antibacterial functionality and able to prevent biofilm formation. To this aim, we explore the design of different polymers, mimicking antimicrobial peptides and honey respectively.

METHODS: AMP-MIMETIC POLYURETHANE (PUR) A liquid monomer was grafted from an amphiphilic printable polyurethane by heterophase polymerization. Next, the bis(trifluoromethanesulfonyl)imide anionic counter ions of the liquid monomer were mainly exchanged for hydrophilic bromide ions. Their characterization was conducted by ^{1}H, ^{13}C and ^{19}F NMR, Dynamic light scattering and zeta-potential measurements and cryo-TEM. MIC and MBC were determined by the broth microdilution method. Safranin staining was used to quantify biofilm biomass. L929, HaCaT and THP-1 were used for cytocompatibility evaluation by the multiplex assay.HONEY-LIKE HYDROGEL A hydrogel based on hyperbranched polyethylene diacrylate (HB PEGDA) and hyaluronic acid (HA-SH) was prepared by thiol-ene click chemistry. Glucose (G) and glucose oxidase (GO) were respectively added to HA-SH and HB PEGDA components. Rheological properties, water uptake and degradation of hydrogels were studied. Hydrogen peroxide (H_2O_2) release was measured and antimicrobial activity assessed.

RESULTS: The AMP-mimetic PUR was successfully synthesised as demonstrated by NMR spectra. The Cryo-TEM images of AMP-mimetic PUR aqueous solution, showed the formation of patchy colloidal particles, consisting of the self-organized mesophases formed by discrete nanodomains of charged ionic liquid moieties (fig.1). This polymer induces a rapid bactericidal effect on planktonic Gram-positive bacteria and it is able to prevent biofilm formation until 72 hours, and to disrupt Gram-positive mature biofilms with concentrations higher than 250 μg/mL against methicillin-sensitive S. aureus and MRSA, and above 31.25 μg/mL on Enterococcus faecalis and higher than 62.5 μg/mL in case of VRE. On L929 murine fibroblasts, HaCaT human keratinocytes and THP-1 monocyte-derived human macrophages, the cell viability was optimal in the presence of the lower concentrations that are active against bacteria.

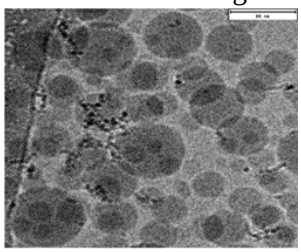

Fig. 1: Cryo-TEM image of AMP-mimetic PUR

The honey-like hydrogel produced antibacterial reactive H_2O_2, through the two components found in honey: GO within HB PEGDA and G in HA-SH. The hydrogel was able to produce 9.11 mmol H_2O_2 after 24 hours using 250 U/L GO and 2.5 % G. This amount caused a zone of inhibition as a measure of antibacterial activity against primarily gram-positive bacteria.

DISCUSSION & CONCLUSIONS: The AMP-mimetic PUR shows a positive selectivity index on all skin cell populations tested, indicating that they have a higher selectivity towards bacteria over mammalian eukaryotic cells. Honey mimetic hydrogels have the potential to be used as *in situ* forming antibacterial wound dressings.

ACKNOWLEDGEMENTS: HyMedPoly received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 643050.