Proceedings of the 8th World Congress on Recent Advances in Nanotechnology (RAN'23)
Lisbon, Portugal – March 23 – 25, 2023
Paper No. NDDTE 132
DOI: 10.11159/nddte23.132

Quercetin Delivery Systems for the Treatment of Burn Wounds

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Introduction

Extensive burns are difficult to treat, as they are characterised by a prolonged inflammation phase, which inhibits cell proliferation and tissue remodelling, and as a result. alters wound healing [1]. Quercetin (QE), which has antioxidant anti-inflammatory, and antimicrobial properties, can prevent prolonged inflammation and fibrosis and thus reduce scarring [2]. It is known that dressings ensuring a suitable aqueous environment can accelerate the healing of burn wounds. The purpose of this work was to manufacture and characterise the properties of lauric acid (LAU) microparticles (MPs) as QE delivery systems for the treatment of burn wounds. The MPs were suspended in a polysaccharide matrix to obtain dressing prototypes for the treatment of burn wounds.

Materials and Methods

MPs were manufactured from LAU by an oil-in-water emulsification. As oil phase, LAU with addition of 5%, 10% or 20% QE was prepared at 65 °C and homogenised using an ultrasonic probe for 60 s at 30% amplitude. The oil phase was poured into water phase supplemented with 10% polyvinyl alcohol (PVA) at 65 °C and mixed using vortex for 90 s. The prepared emulsion was poured into liquid nitrogen to form MPs. The MPs were centrifuged, washed, frozen, and stored at -20 °C prior to further use. The morphology and size of the particles were evaluated by optical microscopy. The encapsulation efficiency of QE in MPs was assessed by Folin-Ciocalteu reaction. Hydrogels were prepared as previously described [3]. Briefly, gellan gum (GG) was dissolved in ultrapure water at 90 °C, then equal volumes of crosslinking agent (1% $CaCl_2$) and aqueous suspension of lipid MPs loaded with 10 mg/ml QE were added, mixed in vortex, and cooled down. The samples were then frozen for 24 h, freeze-dried for 48 h and stored at -20 °C. The dressing prototypes were characterised by optical and scanning electron microscopy (SEM). Swelling and mass changes as a function of incubation in PBS, as well as *in vitro* cytotoxicity on L929 fibroblasts, were tested.

Results and Discussion

MPs were successfully manufactured with 50% efficiency. The particles were round and homogeneous with diameters in the range of 0.5 to 10 μm. The presence of QE did not influence the shape of the MPs. The size of QE loaded MPs was slightly larger than unloaded. However, the fraction 0.5 – 4 μm still represented the highest percentage of all particles. The encapsulation efficiency was the highest for the samples with addition of 5% QE and decreased for those with higher concentrations of loaded QE, i.e. 10% or 20%. The dressing prototypes were highly porous with a high swelling capacity of >1500% and were found to be cytocompatible with L929 cells.

Conclusions

In conclusion, QE carriers in the form of lipid MPs for the treatment of burn wounds have been successfully manufactured. Prolonged QE release, and thus an increased anti-inflammatory efficacy, was provided by inclusion of QE-loaded lipid microparticles in the GG matrix. We believe that the developed materials are promising for burn healing applications. Further studies will include examination of the QE release kinetics and more advanced *in vitro* studies with primary fibroblasts and keratinocytes.

Acknowledgments

This study was financed by the Program "Excellence Initiative – Research University" and from subsidy (No 16.16.160.557) for the AGH University of Science and Technology.

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