

Evaluation of the potential of fucoidan-based microparticles for diabetes treatment

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INTRODUCTION: Marine organisms have in their constitution materials with a wide range of properties and characteristics inspiring their application within the biomedical field. One important example is fucoidan (Fu), an underexploited sulfated polysaccharide extracted from the cell wall of the brown seaweeds, with high solubility in water¹. Fucoidan is composed of L-fucose and glucuronic acid including sulfate groups and has important bioactive properties such as antioxidative, anticoagulant, anticancer and in the reduction of blood glucose^{1,2}. In this work, the biomedical potential of fucoidan was assessed by processing modified fucoidan (MFu) into microparticles by photocrosslinking using superhydrophobic surfaces and visible light^{3,4}. Biological performance on the developed constructs using human pancreatic beta cells is currently under investigation.

METHODS: To design the materials structures, fucoidan was modified by methacrylation reaction³. Briefly, Fu aqueous solution 4% w/v was mixed with methacrylated anhydride (MA) in volume of 12% v/v at 50°C to react for 6h. Further, MFu particles with and without insulin (0.5% w/v) were produced by pipetting a solution of 5% MFu v/v with triethanolamine and eosin-y (photoinitiators) onto superhydrophobic surfaces⁴ (Fig. 1A) and then photocrosslinking using visible light⁴. MFu and developed particles were characterized using ¹HNMR, turbidimetry and SEM to assess their chemistry and morphology, respectively. Moreover, the insulin release was evaluated in phosphate buffered saline (PBS) solution at pH 7 and simulated intestinal fluid (SIF) at pH 5. The ability of the developed materials to support adhesion and proliferation of cells was assessed by suspension culture of human pancreatic cells 1.1B4 (3.5×10^5 cells/ml) in contact with MFu microparticles during up to 7 days.

RESULTS: The chemical modification performed on Fu was confirmed by the presence of vinyl and additional methyl peaks in the ¹HNMR of modified fucoidan, not present in Fu spectrum. Methacrylated fucoidan was obtained with a methacrylation degree of 17%. The produced fucoidan particles have round shape and average diameter of 1.53 μ m (Fig. 1B). The insulin release in PBS and SIF demonstrate that the particles can release insulin in a sustained manner under the studied period. It seems that the insulin release is slower for SIF (pH5, Fig. 1C), than for PBS. The biological tests regarding the culture of pancreatic beta cells demonstrate that cells show a round-like shape and tend to form pseudo-islets during the culture period studied (Fig. 1D).

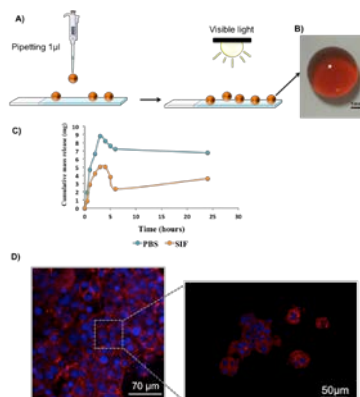


Fig. 1: A) Scheme of modified fucoidan particles production, B) modified fucoidan-particles, C) insulin release profile and D) confocal microscopy images of 1.1B4 cells seeded onto MFu after 7 days in culture; staining of actin (red) and nuclei (blue).

DISCUSSION & CONCLUSIONS: This work demonstrates the successful production of fucoidan-based-microparticles through the methacrylation of fucoidan, using visible light and superhydrophobic surfaces. The covalent crosslinking methacrylated fucoidan through visible light represents a promising method to obtain biocompatible fucoidan particles with a uniform round shape. The obtained insulin release profiles are sensitive to different pH (pH7 and pH5), mimicking the normal physiological pathway for insulin release. Furthermore, the results suggest these systems could be used for treatment of type I diabetes mellitus as they sustain beta cells viability and proliferation. The response also suggested, that the MFu particles could be a good candidate as drug delivery vehicles for the diabetes mellitus treatment.

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