Abstract 810

BONE-TARGETING DELIVERY OF ALENDRONATE FOR THE TREATMENT OF OSTEOPOROSIS.

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BACKGROUND & AIMS: Osteoporosis is a major health burden. Current therapeutic treatments have disadvantages such as systemic side effect and low bioavailability. Bone-targeting drug delivery system are designed to improve the therapeutic effect of drugs and minimize the potential toxic side effects. We fabricated a novel drug nanocarrier for bone-targeting alendronate delivery using glycol chitosan (GC)-poly(lactide-co-glycolide) (PLGA) and PLGA-alendronate conjugates.

MATERIALS & METHODS: Chitosan-based nanoparticles were prepared with GC-PLGA and PLGA-alendronate conjugate by nanoprecipitation. Alendronate sodium, a commonly used bisphosphonate drug for osteoporosis therapy, serves as both a bone-targeting ligand and a loading drug. The size of the nanoparticles was determined by dynamic light scattering (DLS) measurement. The morphology of the GC-PLGA/PLGA-alendronate nanoparticles was examined by scanning electron microscopy (SEM). Drug release profile, cytotoxicity and cellular uptake were evaluated in vitro. Bone-targeting potential was assessed by hydroxyapatite binding assay and an ex vivo porcine bone model.

RESULTS: The conjugation of GC-PLGA and PLGA-alendronate was confirmed by Fourier-transform Infrared Spectroscopy (FTIR) and nuclear magnetic resonance (NMR) analysis. The prepared nanoparticles are highly aqueous dispersible with an average size range from 90 to 130 nm based on various polymer ratio. Morphological characterization (SEM) revealed that the nanoparticles are spherical in shape. In vitro tests demonstrated sustained drug release of alendronate, good biocompatibility and intracellular uptake of nanoparticles. Hydroxyapatite affinity test and ex vivo porcine bone model confirmed the bone-targeting potential.

CONCLUSION: The bone-targeting GC-PLGA nanoparticles may be a drug delivery system for the treatment of osteoporosis. Further study of biodistribution is warranted.

References

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Abstract 812

FUCOIDAN HYDROGELS SIGNIFICANTLY ALLEVIATE OXIDATIVE STRESS AND ENHANCE THE ENDOCRINE FUNCTION OF ENCAPSULATED BETA CELLS

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Background: Oxidative stress is a major factor limiting encapsulated islet efficacy. Fucoidans (marine polysaccharide) possess strong anti-oxidant properties (1) but its effects on islet encapsulation is unknown. We assessed the feasibility of fucoidan hydrogels (Fucogel) for islet encapsulation to improve viability and function.

Methods: Fucogel prepared by blending fucoidan with alginate and fucoidan microcapsules made using a droplet generator. Total antioxidant capacity (TAC) and viscoelastic properties of Fucogel assessed. Ability of Fucogel to alleviate oxidative stress determined using transduced INS1E cells. Human, rat and neonatal pig islets encapsulated in Fucogel and viability, ATP and insulin secretion assessed. Fucogel potential to protect islets against cytokine and H2O2 induced oxidative damage assessed.

Results: The TAC of Fucogel was ~35-fold higher compared to alginate hydrogel. Both alginate and Fucogel had similar viscoelastic properties with no differences in their hydrogel mesh sizes. Fucogel significantly alleviated intracellular oxidative stress in transduced INS1E compared to alginate. Viability and ATP levels of human islets in Fucogel at days 1 and 5 were significantly higher compared to those in alginate. Human islets in Fucogel functioned better in response to high glucose with a ~2-fold higher stimulation index compared to alginate. Similar results were seen with rat and neonatal pig islets encapsulated in Fucogel. Exposure to proinflammatory cytokines or H2O2 dramatically rescued human islets in Fucogel with significantly higher viability, ATP and stimulation index compared to those encapsulated in alginate.

Conclusion: Fucoidan hydrogels possess strong antioxidant property, significantly alleviate oxidative stress and enhance encapsulated islet viability and function.

Keywords: Fucoidan hydrogel; Microencapsulation; Oxidative stress

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Abstract 813

INFLUENCE OF STATINS ON CARTILAGE HOMEOSTASIS AFTER TRAUMATIC LOADING AND DURING CHONDROGENIC DIFFERENTIATION

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As inhibitors of HMG-CoA-reductase, statins are widely used as cholesterol-lowering drugs. Due to the anti-inflammatory effects, statin therapy has also been discussed for osteoarthritic disease. Therefore, we investigated the potential therapeutic effects of fluvastatin (hydrophile) and simvastatin (lipophile) after ex vivo cartilage trauma. Macroscopically intact human cartilage was obtained with consent of donors undergoing total knee joint replacement (n = 11). Cartilage explants were subjected to a blunt trauma (0.59 J)