Multifunctional Sr,Mg doped mesoporous bioactive glass nanoparticles

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INTRODUCTION: Recently, mesoporous bioactive glass particles (MBGs) doped with therapeutical ions have emerged as a promising biomaterial with ability to simultaneously deliver drugs and ions, leading to synergistic outcomes. Sr and Mg ions are widely investigated in ion-doping approach of bioceramics and bioactive glasses due to their ability to stimulate osteogenesis and angiogenesis. The co-doping of MBGs with Sr and Mg might lead to accelerated bone regeneration, however the presence of dopant ions can also influence the mesoporosity of MBGNs, and thus affect bioactivity and drug release behaviour. The objective of this study was to investigate the influence of Sr,Mg co-doping on the textural properties, drug delivery, as well as pro-osteogenic and pro-angiogenic potential of MBGs.

EXPERIMENTAL: A modified micro-emulsion assisted sol-gel synthesis coupled with ultra-sonication was used to obtain Sr,Mg-MBGs. Mesoporosity was assessed by the N_2 adsorption (Micromeritics ASAP 2020, Norcross) and HR-TEM (FEI Talos F200X) analysis. Morphology of the particles and bioactivity was determined by FESEM (Tescan Mira 3 XMU). Ibuprofen was used as a model drug for analysis of drug delivery properties performed by the dialysis tubing diffusion method in PBS (pH 7.4). UV-VIS spectrophotometer (Shimadzu, UV-1800) and a simultaneous DSC-TGA instrument (SDT Q-600, TA Instruments) were employed to quantify amount of drug loaded and drug release rate.

Indirect assays were used to determine biocompatibility, and potential pro-osteogenic and pro-angiogenic properties of MBGs using human bone marrow-derived mesenchymal stem cells in 2D and endothelial cells EA.hy926 in 0.5 % collagen 3D models. Dissolution extracts were prepared by dispersing 1 mg/ml MBGs in DMEM without any supplements for 24 h. Resazurin reduction assay was used at days 1, 3 and 7 of cultivation for measuring cellular metabolic activity (n=3). To evaluate calcium deposition, and detect alkaline phosphatase (ALP) activity Alizarin red S (ARS) staining and colorimetric p-nitrophenyl phosphate assay were performed at day 7 of cultivation, respectively. Fluorescence staining with phalloidin and DAPI was done to visualize the morphology and spreading of EA.hy926 cells at day 3 and day 7.

RESULTS AND DISCUSSION: Results showed that ion-doping influenced the mesoporosity of MBGs changing the pore shape from worm-like to radial dendritic, which resulted in increased pore volume with smaller pore size. As a results, the drug-loading capacity of SrMg-MBGs was slightly reduced, while the drug release rate was somewhat increased. After 7 days of immersion in the SBF the surface of particles had rough appearance due to dissolution of glass and precipitation of nanocrystals on the surface, accompanied by formation of needle-like crystals characteristic of hydroxy-carbonate apatite. After 14 days, the surface of was completely covered in thick layer of the apatite crystals confirming the bioactive nature of the SrMg-MBGs. The biological evaluation assays showed that Sr,Mg-MBGNs has ability to slightly induce human bone marrow-derived mesenchymal stem cells osteogenic potential due to the improvement in ALP production and calcium deposition, and to stimulate the proliferation of endothelial cells in 3D models.

CONCLUSIONS: The study demonstrates that Sr,Mg-doped MBGs can be considered as a promising multifunctional biomaterial for application in biomedicine.

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