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Fabrication and biocompatibility of monodisperse PLGA/MgO-alginate core-shell microspheres via a microfluidic capillary device for in-situ bone regeneration

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INTRODUCTION

Osteoporosis is disease that mainly affects elder people over age of 50 around the world. The use of bisphosphonates (BPs) is the common drug treatment for Osteoporosis. However, long-term medication of BPs reported to be likely associated with atypical bone fractures recently. Other biological agents eg. bone morphogenetic proteins (BMP-2) and insulin-like growth factors, are costly, easily deactivated by enzymes and rapidly degraded. Our previous studies proposed that magnesium ions in specific concentration can stimulate bone regeneration in vivo[1]. Therefore, this study aims at designing a drug delivery system by using a FDA approved polymer namely poly(lactic-co-glycolic acid) (PLGA) , alginate and magnesium oxide in order to constantly deliver magnesium ions for in situ bone regeneration.

EXPERIMENTAL METHODS

The PLGA/MgO (w:w=1:0.25) and PLGA/MgO-alginate core-shell microspheres were fabricated by the technique of microfluidics. PLGA was dissolved in dichloromethane (DCM). Afterwards, MgO nanoparticles were suspended to DCM solution that defined as inner phase(oil phase). The mix solution flowed through the capillary. 3% polyvinyl alcohol(PVA) solution was defined as outer phase(water phase) to shear the inner phase to form PLGA/MgO droplets, followed by drying overnight.

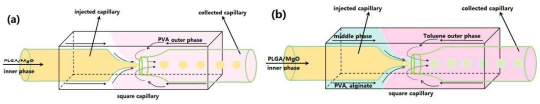

Fig.1 Schematic diagrams of (a)PLGA/MgO single emulsion droplets and (b) PLGA/MgO-alginate double emulsion droplets fabricated by the microfluidic technique

RESULTS AND DISCUSSION

Narrow size distribution and smooth surfaces were obtained from the microfluidic PLGA-based microspheres. Moreover, homogenous magnesium distribution and inner porous structures were observed from the inner part of microspheres by employing the cryostat sections method, which played an impact on drug release kinetics of PLGA/MgO and PLGA/MgO-alginate core-shell microspheres in vitro. For PLGA/MgO-alginate core-shell microspheres, they achieved high drug content, encapsulation efficiency and reduced initial burst release of magnesium ions resulting from the homogenous alginate shells set as physical barriers. The profiles of magnesium ions release kinetics in vitro revealed the parabolic release pattern and near-sigmoid release pattern for PLGA/MgO and PLGA/MgO-alginate core-shell microspheres respectively, indicating disparate drug release kinetics mechanisms. Furthermore, the PLGA-based microspheres were injected into the defects at the lateral epicondyle of rats created by a hand driller to investigate the real-time new bone formation in vivo.

The results showed that PLGA/MgO-alginate core-shell microspheres group exhibited apparent new bone formation at post-surgery week 2 and achieved most new bone volumes among these groups due to the sustain release of magnesium ions for stimulation of local bone formation.

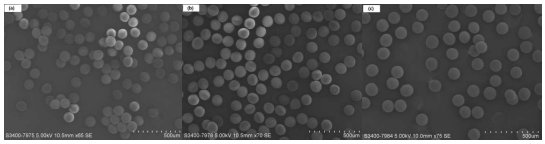

Fig. 2 The morphology of (a)PLGA microspheres,(b) PLGA/MgO microspheres and (c)PLGA/MgO-alginate core-shell microspheres observed by SEM

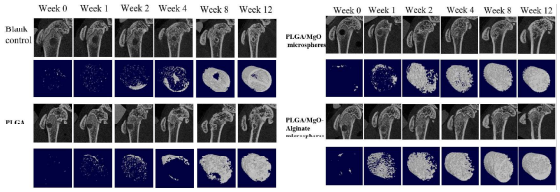

Fig. 3 Micro-CT images and 3D models of PLGA-based microspheres after post-surgery at various time points.

CONCLUSION

The microfluidic technique via a microfluidic capillary device provided good templates for fabrication of monodisperse PLGA/MgO and PLGA/MgO-alginate core-shell microspheres with narrow size distribution and smooth surfaces. Constant magnesium ions release from the PLGA/MgO-alginate core-shell microspheres showed great potentials in controlled drug release for in-situ bone regeneration.

REFERENCES

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ACKNOWLEDGMENTS

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