SELENIUM CONTAINING HYDROXYAPATITE GRANULES AS DRUG CARRIERS FOR RISEDRONATE

KOLMAS JOANNA*, PAJOR KAMIL, PAJCHEL ŁUKASZ, OLĘDZKA EWA, SOBCZAK MARCIN

DEPARTMENT OF INORGANIC AND ANALYTICAL CHEMISTRY, FACULTY OF PHARMACY, MEDICAL UNIVERSITY OF WARSAW
*E-MAIL: JOANNA.KOLMAS@WUM.EDU.PL

[ENGINEERING OF BIOMATERIALS 138 (2016) 70]

Introduction

Substituted hydroxyapatites have many applications from optoelectronics to biomaterials for regenerative medicine and dentistry [1]. It is known that partial ionic substitutions may change physicochemical, biological or mechanical properties of apatites. Selenium is an essential microelement playing a significant role in many metabolic processes [2]. Its anticancerogenic activity and beneficial impact on the inflammatory response of osteoblasts in the metastasis of certain bone tumours have been reported. Risedronate sodium is a drug from the group of bisphosphonates. It slows bone loss and is commonly used in osteoporosis and Paget's disease treatment [3]. It inhibits bone metastasis and can be used in certain bone tumours treatment.

In this work, we prepared selenite (SeO_3^{2-}) enriched hydroxyapatite to produce porous granules for risedronate release.

Materials and Methods

SeO_3^{2-}-containing hydroxyapatite (Se-HA) was synthesized by the standard wet method [4]. The obtained precipitates were aged, centrifuged, washed and dried at 130°C. The powders were physicochemically studied by using powder X-ray diffractometry (PXRD), infrared spectroscopy (FT-IR), atomic absorption spectrometry (AAS). The powder was then granulated with the use of 4% alginate sodium aqueous solution and hydrogen ammonium carbonate (0-5 wt. %). The hydroxyapatite/alginate ratios were optimized. During the granules formation, a solution of risedronate sodium was added into the alginate solution. After that, the dense suspension was squeezed out into small spherical drops by a syringe needle and added to 1.5% solution of $CaCl_2$. These alginate/apatite granules were washed with water and dried in air at 40°C for 24h.

Solid-state MAS NMR (^{13}C, ^{31}P, ^{1}H) was used for structural analysis of Se-HA and porous composite granules.

Results and Discussion

PXRD diffractograms have shown that the initial powders are nanocrystalline hydroxyapatites without other crystalline phases. The obtained crystallites are plate-like shaped. Selenium content was calculated as 7.5 wt%. Selenite ions are located in the crystalline core and in the hydrated surface layer. The porous beads size and the pore microstructure characteristics were analysed with scanning electron microscopy (SEM; FIG. 1). ^{31}P MAS NMR was used for specific surface area estimation (SSA_{Se-HA}= 150 m^2/g). In ^{31}P CP MAS spectra the characteristic signals from hydroxyapatite (at ca. 3.2 ppm) and from risedronate (a broad signal at ca. 19 ppm) are visible. The risedronate present in the granules reacted with calcium cations. In ^{13}C CP MAS NMR spectra we can observe the signals from alginates and risedronate.

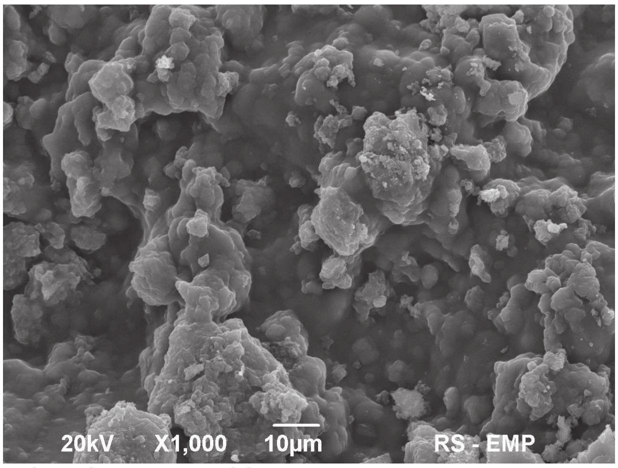

FIG. 1. SEM image of SeHA/alginate granules.

Conclusions

Nanocrystalline hydroxyapatite doped with selenite ions was successfully prepared and used for porous granules production. The composite beads contained risedronate adsorbed on the apatitic crystals in amount detectable in NMR experiments. Future studies will focus on evaluation of drug release and biological tests.

Acknowledgments

This work was supported by the research program (Project NCN-2011/03/D/ST5/05793) of the National Center of Science, Poland.

References

[1] J.H. Shepherd, D.V. Shepherd, S.M. Best, J. Mater. Sci. Mater. Med. 23 (2012) 2335-47.
[2] M.P. Rayman, Lancet 356 (2000) 233-241.
[3] R. Moreno-Reyes et al., J. Bone Miner. Res. 16 (2001) 1556-1563.
[4] J. Kolmas et al., Mater. Sci. Eng. 39 C (2014) 134-142.