Magnesium Phosphate Modified with 2-Hydroxyethyl Methacrylate as a Novel Representative of Dual-Setting Composite Bone Cements

Marcin Wekwejt[1], Maryia Khamenka[2], Justyna Kozłowska[3], Anna Ronowska[4] and Uwe Gbureck[5]
[1]Department of Biomaterials Technology, Gdańsk University of Technology, Poland
[2]Scientific Club 'Materials in Medicine', Advanced Materials Centre, Gdańsk University of Technology, Poland
[3]Deparment Of Biomaterials And Cosmetics Chemistry, Nicolaus Copernicus University, Poland
[4]Department of Laboratory Medicine, Medical University of Gdańsk, Poland
[5]Department for Functional Materials in Medicine and Dentistry, University of Würzburg, Germany

Statement of Purpose: Bone tissue has an innate regenerative potential and the ability to self-healing after defects. However, in some cases, the use of biomaterials dedicated to support bone regeneration is required. One particular group of synthetic bone substitute are bone cements. These materials usually consist of a powder and a liquid and their mixing initiates the reaction leading to the hardening of workable paste. Currently, two kinds of cement are used in clinical application: calcium phosphate cements and poly(methylmethacrylate) cements [1]. More recently, magnesium phosphate cements (MPC) were found to be an interesting alternative to traditional ceramic cements, due to properties such as: fast setting, high initial mechanical strength, favourable resorbability and greater osteogenic potential. Whereas, MPC cements also have a significant disadvantages, like: leachability of the paste, difficult injectability and high brittleness [2,3]. Therefore, further research on these cements are highly recommended. In this work, we proposed the novel cement formula based on MPC modified with 2-hydroxyethyl methacrylate (HEMA).

Methods: Tri-magnesium phosphate (TMP; $Mg_3(PO_4)_2$) was obtained by sintering mixture of $MgHPO_4 \cdot 3H_2O$ and $Mg(OH)_2$ (2:1 molar ratio, 1100°C/5 h), crushing, grounding and finally sieving (~11.2 μm). Then, this powder was mixed with 0.5 M di-ammonium hydrogen phosphate (~38.8 μm; 4:1 mass ratio). The cement liquids were water solutions of HEMA (15, 20, 25%) including 2.5 μl/mL N,N,N′,N′-tetramethylethylenediamine (TEMED). The hydrogel polymerization reaction was started by addining 2.5 μg/mL ammonium persulfate (APS) to solutions. Constant powder-to-liquid (P/L) ratio of 2.5 g/mL was applied in this study. The cement specimens were prepared by premixing HEMA solutions with APS activator for different premix times (2:30 or 4:00 min) and then added to cement powder and manually mixing until obtained a homogeneous paste. Next, the paste were transferred into silicone rubber molds and stored for 24 h at 37°C and > 90% humidity (water bath). As reference, the cement powder was mixed with destilled water and treated identically to the tested cements. The following properties were evaluated: setting time, microstructure (SEM microscopy), phase and chemical composition (XRD diffractometry, FTIR spectroscopy), compressive strength, degradation behaviour and porosity changes (immersion in the PBS solution for 18 days). Moreover, cytocompatibility of modified cements was evaluated on human osteoblast cell line (hFOB 1.19, ATCC) by the use of MTT assay after three days of culture.

Results: In this research, a novel dual-setting composite cement based on MPC and HEMA was efficiently developed. The addition of the hydrogel component significantly influenced the main properties of the magnesium phosphate cement resulting in shorter setting time, reduced initial porosity, improved mechanical strength, but also deterioration of the cellular response. The following properties were determined for modified cements: the setting time - 16-21 min (control ~22:33), initial porosity - 2.6-4.2% (control ~5%), final porosity - 6.5-11.5% (control ~7.2%), mass loss - 0.1-3.5% (control ~0.3%), compressive strength- 39.8-64.1 MPa (control ~50.1 MPa), Young Modulus – 2.1-3.2 GPa (control ~ 2.3 GPa) and hFOB cell viability - 22-54% (control 100%). In the SEM analysis, it was found that both HEMA content and premix time significantly influenced the formation of hydrogel agglomerates in the cement matix, which has a key impact on the differences in the tested properties. Based on XRD and FTIR evaluation, the polymerization reaction and cement crystallization were confirmed. Obtained cement mainly consisted of struvite, farringtonite and newberyite. The most effective improvement in the mechanical properties of modified cements was found for a longer premix time, however when there was higher HEMA concentration the effect was opposite. Evaluation of the PBS degradation process showed that cements obtained with a shorter premix time contribute to faster and more effective degradation of the matrix. The observed cytotoxic effect of cultured osteoblasts after HEMA addition into MPC was related to the polymer itself and was probably due to the use of TEMED as polymerization agent. Hence, despite obtaining favorable physical and mechanical properties of the developed cement, future research should focus on the selecting a different hydrogel additive or HEMA polymerization process. Based on results of this research, we found that the optimal composition of cement modification is 20% HEMA with 4 min of premix time and shows the most optimal effect on the cement properties.

References:

[1] Iaquinta MR. Int J Mol Sci. 2019;20:618.
[2] Brücker T. Materials. 2019;12:3819.
[3] Zhaoa Y. Materials & Design. 2021;200:109466.

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