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# Effect of retardants on the heat release during setting of bone cement-type composites

**D. Pijocha*, G. Łój, W. Nocuń-Wczelik, A. Ślósarczyk**
Faculty of Materials Science and Ceramics, AGH-University of Science and Technology, Al. Mickiewicza 30, 30-059 Kraków, Poland
* Corresponding author: E-mail address: dav_p@o2.pl

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**Properties**

## ABSTRACT

**Purpose:** The aim of this work was to investigate the influence of retardants on the heat release during setting of the new hydroxyapatite (HA) - magnesium phosphate cement (MPC) - calcium sulphate hemihydrate (CSH) composites.
**Design/methodology/approach:** We used the calorimetric method to measure the temperature effect of setting reaction in these new composites. Microstructure observations by means of scanning electron microscopy was also performed.
**Findings:** The decrease in maximum temperature reached during hardening process with use of different retardants was confirmed.
**Research limitations/implications:** Biological evaluation and in vitro physico-chemical tests of the novel composites need to be done.
**Practical implications:** The highly exothermic setting reaction of cement composites based on MPC can be lowered to avoid harmful necrosis of the tissues surrounding the implant material.
**Originality/value:** Detailed studies on the heat release during setting of HA - MPC - CSH composites were performed for a first time, giving an opportunity to choose the best composition for further studies.
**Keywords:** Composites; Hydroxyapatite; Calorimetry; Microstructure

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## 1. Introduction

Calcium phosphates (CaPs) have been studied as bone repair materials since 1920 [1]. In the early 1980s, synthetic hydroxyapatite (HA) and β - tricalcium phosphate (β-TCP), became commercially available as implant materials largely due to the efforts of Jarcho et al. [2]. At present, also biphasic calcium phosphates (BCP) composed of HA and β-TCP are the most common materials from this group. The first studies on BCP reported by LeGeros et al. [3] demonstrate that the resorption rate of these ceramics may be controlled by manipulating the HA/ β-TCP ratios. CaPs biomaterials are applied in the form of powders, granules, porous and dense blocks. Synthetic CaPs are the alternatives to autogeneous bone for repair, substitution or augmentation. They can be potentially applied for regenerative medicine and tissue engineering. For many years they have been successfully used as coating of implants in orthopedic, cranio-

maxillofacial and dental surgery. These materials differ in composition and physical properties. Disadvantages of calcium phosphate ceramics are poor mechanical properties, especially brittleness, limiting their use to not loaded places in the skeletal system. Moreover their resorption rate is often not synchronized with a new bone formation [4].

Another form of CaPs are calcium phosphate cements (CPCs), firstly reported in 1986 by Brown and Chow [5]. From this time many CPCs were introduced to the medical products market. These materials are made of one or several CaPs powders and water or an aqueous solution. After mixing together, a paste is obtained that sets within a few minutes. CPCs are usually injectable and are proposed as a possible alternative to polymethacrylate (PMMA) cements. In contrary to the polymer derived bone cements they do not include potentially any harmful methyl methacrylate organic monomer and do not exhibit high temperature effect as well as polymerization shrinkage during setting [6]. CPCs belong to the second generation of bone substituting biomaterials and reveal excellent biological properties attributed to calcium phosphates in general, such as: biocompatibility, bioactivity, osteoconductivity and ability to set and harden within the living body. There are two basic products of the CPCs setting reaction: hydroxyapatite - $Ca_{10}(PO_4)_6(OH)_2$ and brushite - $CaHPO_4{\cdot}2H_2O$, which are formed depending on physicochemical conditions of environment at which the cements are obtained. When pH is acidic (pH < 4,2) main product of the setting reaction is brushite. In the other way (pH > 4,2) hydroxyapatite with a low crystallinity and high specific surface is formed [7].

There are several ways to overcome poor mechanical properties of the hardened cement. One of them is creating a composite which can combine excellent biological properties of calcium phosphates with good mechanical strength of the other cement component. Incorporating magnesium phosphate cement (MPC) powder into CPC is one of the solution proposed by Wu et al. [8]. Magnesium phosphate cement is used in industrial engineering. It exhibits desirable properties such as high early strength and fast setting rate [9]. Setting reaction of MPC includes acid-base reaction between MgO and acidic ammonium phosphate i.e. dihydrogen ammonium phosphate ($NH_4H_2PO_4$). The struvite phase ($NH_4MgPO_4{\cdot}6H_2O$) is the main product of this reaction and/or other magnesium phosphates such as schertelite: ($Mg(NH_4)_2H_2(PO_4)_2{\cdot}4H_2O$), $MgHPO_4$, $Mg_3(PO_4)_2{\cdot}0\text{-}4H_2O$. Higher temperature of the reaction medium favors formation of amorphous $MgHPO_4$ and $MgHPO_4{\cdot}3H_2O$ what can accelerate the degradation rate of the hardened cement *in vivo* [10]. Disadvantage of using MPC as a bone substitute material is its exothermal setting reaction which can cause necrosis of the living tissues. This effect can be avoided by introducing small amount of setting retardant, such as: sodium pyrophosphate ($Na_4P_2O_7{\cdot}10H_2O$), sodium borate ($Na_2B_4O_7{\cdot}10H_2O$), calcium sulfates: hemihydrate and dihydrate ($CaSO_4{\cdot}1/2H_2O$, $CaSO_4{\cdot}2H_2O$) [11]. Effect of retardant on setting of the MPC cement is still not fully known. Mestres et al. [12] used borax ($Na_2B_4O_7{\cdot}10H_2O$) as the retardant and obtained promising results (the temperature of the setting reaction ammonium containing MPC was reduced from 110°C to 42°C). Important fact is that increase in temperature during setting of MPC occurs before cement hardening in contrary to the PMMA cements, in which elevated temperature can be maintained for a longer periods of time [13]. The new generation of calcium - magnesium phosphate cements (CMPC) for bone tissue regeneration were developed by Wei et al. [14]. Incorporation of MPC into CPC resulted in hierarchically 3D structured scaffolds of micro/macroporous magnesium - calcium phosphate biomaterial.

Another implant material used in bone regeneration is calcium sulfate hemihydrate - $CaSO_4{\cdot}1/2H_2O$ (CSH) which was one of the first materials investigated as a substitute for bone grafts [15]. CSH sets in the presence of water and the product of the setting reaction is calcium sulfate dihydrate - $CaSO_4{\cdot}2H_2O$ (CSD). Their excellent biocompatibility is the most important advantage while a rapid resorption and low strength is highly disadvantageous. The dissolution rate of calcium sulfate has made it suitable as a carrier for drug release [16]. Addition of CSH powders to CPCs formulations may improve biodegradation properties of CPC cements. Ability to act as retardant in MPC setting reaction may be also useful in improving the properties of MPC based biomaterials [11].

In our studies we incorporated hydroxyapatite to MPC cement and added sodium pyrophosphate and CSH as retardants. CSH played also the role of the setting phase in this system. The novel composite type materials were obtained. The aim of this work was to investigate the exothermal behave or i.e. heat liberation and temperature evolution during setting reaction of biomaterials with different initial composition. The formation of microstructure after the exothermic setting was also studied.

## 2. Materials and methods

Initial powders were produced by mixing MPC cement with HA powder raw and calcined at 800°C in the air (both were obtained in UST-AGH Cracow). Sodium pyrophosphate (Chempur, Polska) or calcium sulfate hemihydrate (Across, USA) were applied as the setting process retardants at various proportions (Table 1). MPC was prepared by mixing equimolar amounts of crystalline $NH_4H_2PO_4$ (POCH, Poland) with MgO. Magnesium oxide was obtained by calcination of basic magnesium carbonate: $4MgCO_3{\cdot}Mg(OH)_2{\cdot}5H_2O$ (POCH, Poland) at the temperature around 1300°C. The resulting powder was sieved using the sieve of mesh size below 0.1 mm. $NH_4H_2PO_4$ was ground in a mortar, then sieved (mesh size of a sieve: 0.1 mm). HA was synthesized by wet method using CaO and $H_3PO_4$ as reactants. Some part of HA prepared was calcined at 800°C in the air atmosphere, then sieved (mesh size of a sieve: 0.1 mm). Distilled water has been used as setting liquid. The exothermic setting process was studied by calorimetric method - a very useful as a tool giving an overall continuous view on the hydration process; it is also very helpful as the more practical parameters of material are concerned (potential degradation because of thermal stresses, heat flux to the surrounding materials) [17]. The heat release was measured using 8g. powder samples and the corresponding amount of water mixed together for 30 seconds before the measurement, except of the HM sample due to rapid setting reaction. HM sample was mixed with water for only 15 seconds. The calorimeter constructed in the Department of Building Materials, Faculty of Material Science and Ceramics AGH, according to the recommendation of the PN EN 196-9:2010 standard for common and special cements, was

adapted for this purpose. The measurements were carried out in isothermal conditions giving the temperature vs. time plots, accompanying the reactions occurring in the mixtures. The temperature was scanned with the 10 s. interval. In order to evaluate the total heat evolved in calorimeter the calibration was done using the gypsum hemihydrate. Microstructure of the hardened bodies was investigated by scanning electron microscopy (Nova 200 Nanosem of FEI company) at the magnifications of 2000 and 10000.

## 3. Results and discussion

In the Table 1 compositions of powder phases of studied materials as well as L/P (liquid to powder ratios applied during pastes preparation) are presented together with maximum temperature during setting reaction and time at which maximum temperature was reached.

The calorimetric curves shown in Figs. 1-2 exhibit an initial exothermic peak within the first minutes of reaction, attributed to the complex processes occurring as a consequence of mixing, wetting, dissolution, nucleation and growth of reaction products.

As it can be easily seen the rise of temperature reflecting the heat evolution, equivalent to the kinetics and heat of particular processes in the HM samples mixed with set retardants is significantly modified. The maximum temperature significantly falls down and the temperature peak shifts, as it is listed in Table 1. The temperature vs. time plots become more or less broadened and flattened; it means that the processes are slowed down. This retarding effect is more visible for the $HM_{piro}$ sample, subsequently in the H3k and H2s one. Among the other compositions of samples the H1s, H2k and H1k the temperature rise is on the level 30-35°C and the process is more or less spread in time; only the peak for H2s appears earlier. A mild effect of initial thermal treatment of hydroxyapatite on maximum setting temperature was concluded.

Table 1.
Powder compositions and maximum temperature obtained during setting of HA-MPC-CSH composite type cements

| Symbol | Powder composition [wt. %] | L/P ratio [ml/g] | Maximum temperature [°C] | Time at which maximum temperature was reached |
|---|---|---|---|---|
| **H1s** | $HA_{raw}$ - 46<br>MPC - 46<br>Pyrophosphate - 8 | 0.40 | 56.35 | 10 min. |
| **H2s** | $HA_{raw}$ - 57<br>MPC - 37<br>Pyrophosphate - 6 | 0.50 | 52.15 | 8 min. |
| **H3s** | $HA_{raw}$ - 68<br>MPC - 28<br>Pyrophosphate - 4 | 0.60 | 42.90 | 9 min. 30 s. |
| **H1k** | $HA_{calcined}$ - 46<br>MPC - 46<br>Pyrophosphate - 8 | 0.50 | 51.30 | 11 min. 20 s |
| **H2k** | $HA_{calcined}$ - 57<br>MPC - 37<br>Pyrophosphate - 6 | 0.60 | 52.70 | 9 min. 30 s. |
| **H3k** | $HA_{calcined}$ - 68<br>MPC - 28<br>Pyrophosphate - 4 | 0.70 | 42.35 | 13 min. |
| **HC** | $HA_{raw}$ - 40<br>CSH - 60 | 0.54 | 25.50 | 2 min. 40 s. |
| **HCM1** | $HA_{raw}$ - 40<br>MPC - 15<br>CSH - 45 | 0.52 | 36.50 | 16 min. 20 s. |
| **HCM2** | $HA_{raw}$ - 40<br>MPC - 30<br>CSH - 30 | 0.42 | 32.55 | 15 min. 20 s. |
| **HCM3** | $HA_{raw}$ - 40<br>MPC - 45<br>CSH - 15 | 0.48 | 46.95 | 13 min. 40 s. |
| **HM** | $HA_{raw}$ - 40<br>MPC - 60 | 0.26 | 88.10 | 7 min. |
| **$HM_{piro}$** | $HA_{raw}$ - 45<br>MPC - 55<br>Pyrophosphate - 10 | 0.26 | 37.50 | 13 min. 20 s. |

The cement - type samples with calcined HA (H1k, H2k, H3k) revealed a little lower setting temperature then corresponding samples based on raw HA (H1s, H2s, H3s) – Table 1. A better comparison can be derived from the total heat evolved plots (Fig. 2). The estimated results of the heat evolved values after 1 h storage in the calorimeter (approximately - the heat of reaction with water) can be ordered according to the following sequence: HM (ca. 520 J/g) → H1s (420 J/g) → H2k (380 J/g) → H1k (325 J/g) → H2s (280 J/g) → H3k (265 J/g) → H3s (260 J/g) → $HM_{piro}$ (250 J/g). In case of the series of samples modified with calcium sulfate hemihydrate the retarding action of the additive is more visible as one can see in Figs. 3 and 4. The maximum temperature rise is very low, especially for the HC sample, as well as for HCM1 and HCM2. The peaks are very broad and flat. The sequence of estimated hydration effects after 1h process are as follows: HM (ca. 520 J/g) → HCM3 (370 J/g) → HCM1 (225 J/g) → HCM2 (200 J/g) → HC (90 J/g).

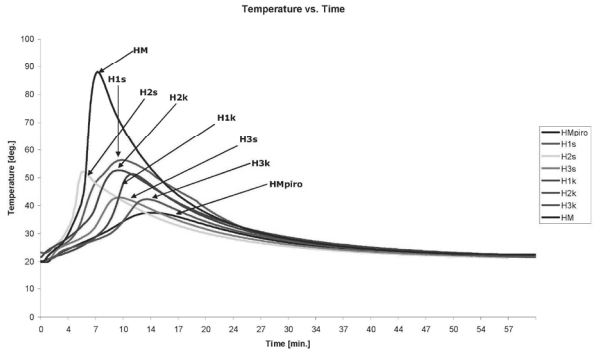


Fig. 1. Temperature evolution during 60 minutes of measurement. Composites with added sodium pyrophosphate as a retardant (HM - fast setting material)

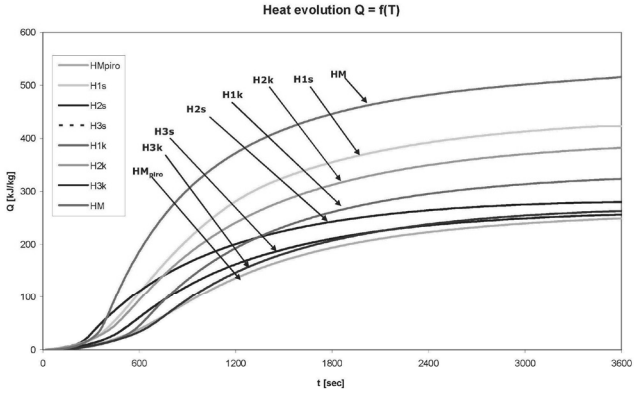


Fig. 2. Heat evolution during 60 minutes of measurement. Composites with added sodium pyrophosphate as a retardant (HM - fast setting material)

Microporous hardened materials with visible crystalline phases were obtained. The results of microstructure observations of the HM material based on HA and MPC are presented in Figures 5-7. The crystals of magnesium phosphates (point 1 on Fig. 5) and calcium phosphates (point 2 on Fig. 6) are homogeneously distributed in the body. The surface of the sample with addition of 10 wt.% of sodium pyrophosphate is cracked (Fig. 6). EDS studies (Fig. 7) indicate on sodium separation. Differences in $Na^+$ concentration near the surface (point 1 on Fig. 7) and inside the sample (point 2 on Fig. 7) were found. During setting diffusion of $Na^+$ to the surface occurs. The layer formed on the surface shrinks faster during the hardening process causing tensile stresses, what leads to the surface destruction. In the three-phase material HA - MPC - CSH (HCM2 - Fig. 8) except magnesium phosphates and calcium phosphates, calcium sulfate dihydrate (CSD) crystals are also seen (Fig. 8). The microstructure formed as a result of high temperature setting reaction (Fig. 5) reveals better densification then microstructure obtained from low temperature setting (Fig. 8).

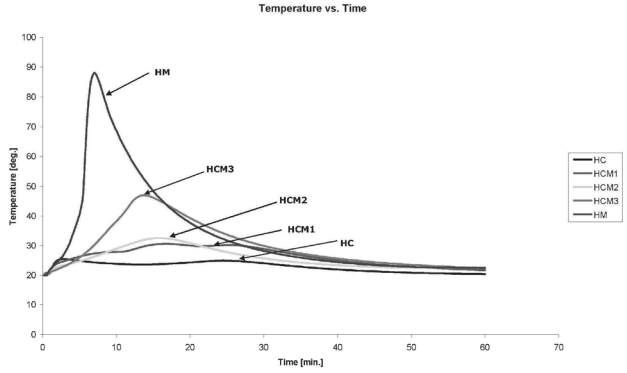


Fig. 3. Temperature evolution during 60 minutes of measurement. Composites with added calcium sulfate hemihydrate as a retardant (HM and HC - fast and slow setting materials)

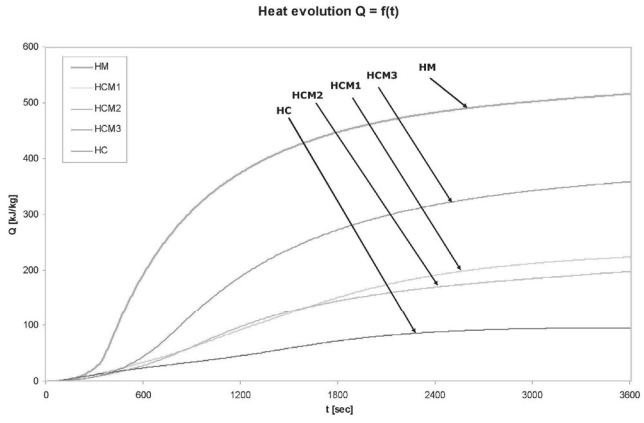


Fig. 4. Heat evolution during 60 minutes of measurement. Composites with added calcium sulfate hemihydrate as a retardant (HM and HC - fast and slow setting materials)

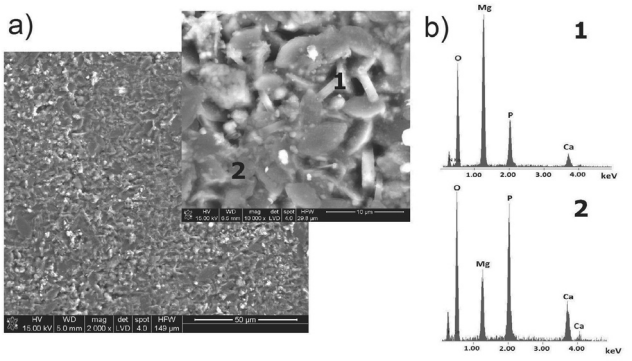


Fig. 5. SEM images of the surface of HM material after setting and hardening for 24 hours (a) and EDS analysis in microareas (b)

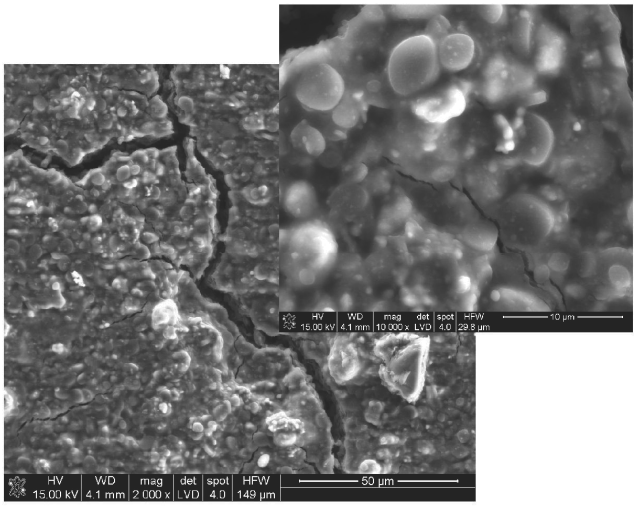


Fig. 6. SEM images of the surface of $HM_{piro}$ material after setting and hardening for 24 hours

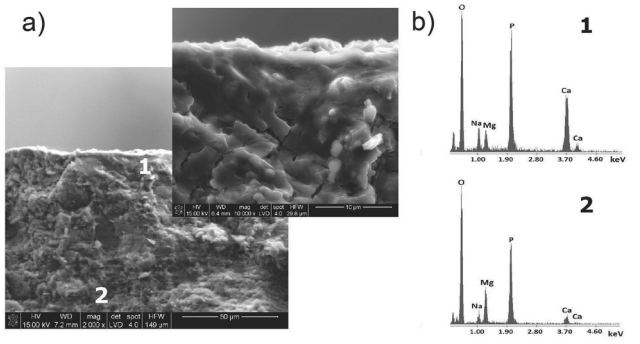


Fig. 7. SEM images of the cross section of $HM_{piro}$ material near the surface after setting and hardening for 24 hours (a) and EDS analysis in microareas (b)

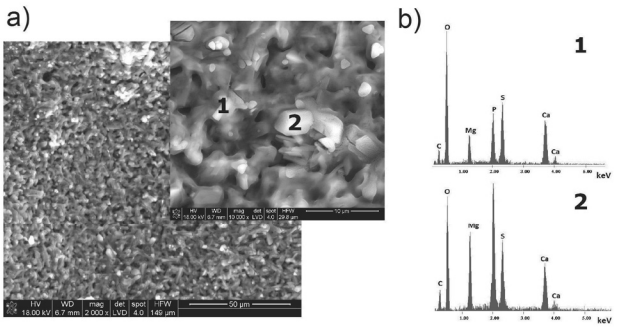


Fig. 8. SEM images of the surface of HCM2 material after setting and hardening for 24 hours (a) and EDS analysis in microareas (b)

## 4. Conclusions

The studied materials belong to the new generation of cement - type bone substitutes. Their solid phase is composed of two or three powders: hydroxyapatite - HA (raw or calcined), magnesium phosphate cement - MPC and calcium sulfate hemihydrate - CSH or sodium pyrophosphate - $Na_4P_2O_7 \cdot 10H_2O$. The CSH component plays a double role: it acts as a retardant and as a setting material in the system. As an alternative retardant sodium pyrophosphate was used.

The effectiveness of both investigated retardants was confirmed. The maximum temperature of setting reaction was reduced significantly i. e. from $88.10^0$C to 32.5°C-37.5°C. These achievements are very important for bone substitutes since high temperature has a harmful necrotic influence on living tissues. The studied composites HA - MPC - CSH have opened up new horizons for orthopedic and dental applications of bioceramics. Further studies on biological evaluation of the obtained composites are necessary.

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