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On calcium phosphate bio-cements

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Abstract

The prospect of clinical applications of bio-cements in bone implantation and tissue substitution implies strict requirements as regards material reliability and robustness. We suggest a technique to enhance the mechanical properties of bio-cements based on α-$Ca_3(PO_4)_2$. Various types of mechanical testing, including compressive deformation analysis, proved that the most robust bio-cement might be fabricated of α-TCP and 1% chitosan. The kinetics of transformation in experiments was considered in order to define the best selection of substance ratios and terms of stabilization. It is essential to increase the ultimate strength and other properties so that they are close to those of cortical bone and this was achieved with the additives chitosan and hydroxyapatite nanoparticles.

The general substance used in bone implantation and tissue substitution is titanium alloy [1], which is able to endure high stresses and is distinguished by its robustness. However, it has a number of downside features: it is pure resorbent, having low biocompatibility with bone tissue; considerable diversity in mechanical characteristics compared to bone tissues, which surround and hold the implant. To reduce these negative impacts, during the last decade calcium hydroxyapatite (HAp)—$Ca_{10}(PO_4)_6(OH)_2$ has been widely used.

This material has very similar physicochemical properties to bone [2] and can be used in the form of cement and ceramics [3]. The cement calcium phosphate nanocrystalline materials are more preferable than ceramics containing large crystallites, as they have better resorbence and adaptive properties to fill complex bone structures. The prospective application of bio-cements is also targeted at direct drug delivery into bone tissue [4]. Nevertheless their clinical adoption is hampered with the low mechanical strength, due to the high porosity (up to 50%). The bio-cement fracture stress normally reaches 60–80 MPa [5] compared to 300–400 MPa for ceramics.

To get better mechanical properties of bio-cements it is suggested that we synthesize them with chemical additives: HAp needle particles and 1% solution of chitosan (per 1 M of HCl). This would allow us to reduce porosity filling with HAp particles in either polymer substance.

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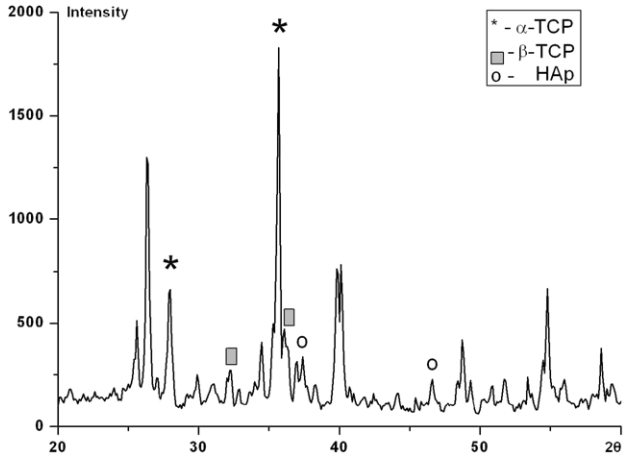

Figure 1. X-ray analysis of the base specimens.

1. Experiment

To make bio-cements we synthesized α-three calcium phosphate (TCP) powder. The 1:1 mixture of calcium carbonate $CaCO_3$ and pyrophosphate $Ca_2P_2O_7$ was annealed at $T = 1250\,^{\circ}C$ for 2 h in an air muffle furnace as the initial reagents to make α-TCP. The outcome samples contained α-phase and about 10% β-impurities. To make non-stoichiometric HAp the following reaction was performed:

$$3Ca_3(PO_4)_2 + H_2O \rightarrow Ca_9(HPO_4)(PO_4)_5OH.$$

As a liquid phase a water and chitosan 1%-solution was used in 1 M HCl. To synthesize bio-cements three additives were applied: water and TCP, chitosan and TCP, or TCP and HAp 1:9 mixture with water. Samples were pressed in forms having the same diameter and height—8 mm under 200 MPa pressure and normal temperature in 1 min intervals. Compressive strength tests were performed for various grades of cementation.

In order to scrutinize the kinetics of TCP–HAp conversion, the bio-cements were held in water at $T = 60\,^{\circ}C$ for up to 48 h. The grade of this conversion was defined with the ratio of the relevant x-ray peak ([001] and [002]) areas for apatite TCP and their Gaussian approximation. X-ray analysis was performed with the DRON-3 M diffractometer using Co Kα radiation. The registration for the phase analysis was executed at the angles $2\theta = 20°$–$60°$ with pace 0.1 and exposition 2 s. Powder microstructure studies were performed with a scanning electronic microscope LEO SUPRA 50VP on autoemission source. Mechanical compression was studied with Zwick/Roell Z100 testing equipment.

2. Results

As a basic method of non-stechiometric apatite formation, hydrolysis opposite to another acid-based cementation was used, because water utilization leads to a reduction in porosity and therefore to better mechanical strength properties. The diffraction analysis diagram (figure 1) shows the presence of the main synthesized substance α-TCP and about 10% of β-TCP impurities. The former are result under cooling conditions after annealing, as the β-TCP phase transition temperature is $1100\,^{\circ}C$ [6].

The TCP to HAp conversion is essentially improved with thermostabilization in water, as the temperature raising accelerates HAp formation in the TCP dissolution. Also, mechanical

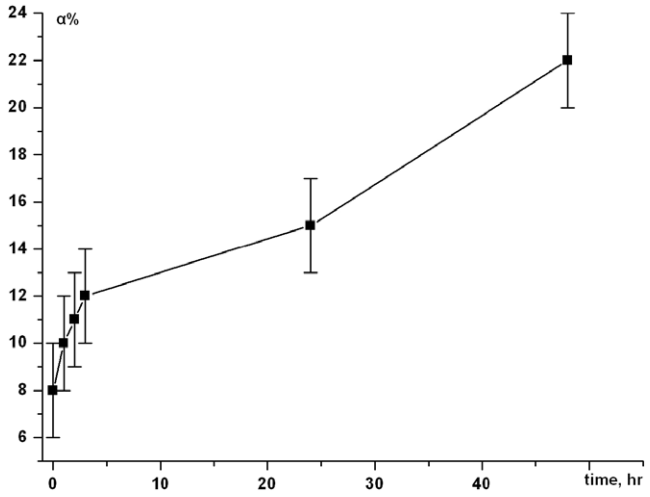

Figure 2. TCP–HAp transformation grade kinetics.

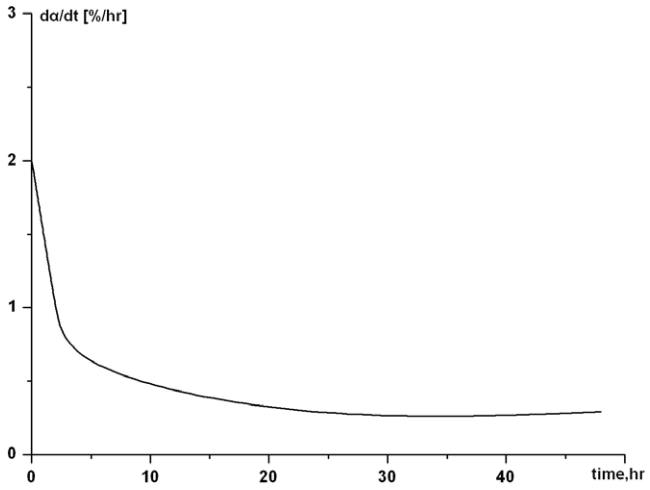

Figure 3. TCP–HAp transformation rate kinetics.

strength enhancement is achieved with the HAp needle crystallites filling the bio-cements pores. Specimens thermostabilized during various time intervals were studied with XRD spectrum to define their phase and mass composition. The ratio of the relevant x-ray peak areas with a Gaussian approximation allowed us to determine the transformation grade. The relevant graphs for grades and rates of transformation depending on time of water stabilization are shown in figures 2 and 3.

The 3:1 maximum of TCP to HAp transformation was achieved in 48 h. Further processing has a low rate, as this rate exponentially falls in time (figure 3). On the other hand, the HAp crystallites growth declines during thermostabilization, because increasing the substance surface layer results in worse diffusion.

As the first kind of phase transition, the novel phase HAp nuclei growth on TCP crystal might be separated into three stages according to the kinetics. The first stage is a novel phase nuclei growth.

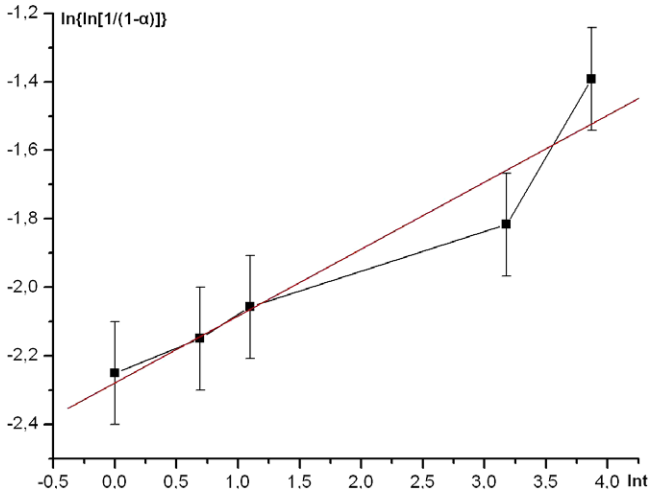

Figure 4. The logarithmic dependence $\ln(1/(1-\alpha))$ on time.

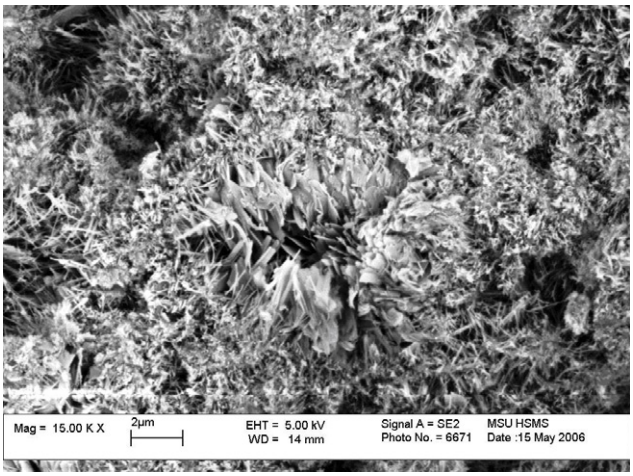

Figure 5. Bio-cements synthesized from chitosan and TCP (microphotograph).

Then (the second stage) the aggregate growth is seen, but the quantity stays constant. It decreases the grade of the solid solution over-saturation. Such effects are well-studied experimentally. The decay of over-saturated solutions follows the empirical Abraham equation: $(N(t) - N_{\mathrm{E}})/(N(0) - N_{\mathrm{E}}) = \exp(-kt^n)$, where $N(t)$ is the monomer concentration; N_{E} is the equilibrium monomer concentration; k and n are experimental constants.

The logarithmic dependence $\ln(1/(1-\alpha))$ on time—t is shown on figure 4, where α is the transformation grade. The parameter $n \approx 2.11$ might be found out from the above equation as the slope of a curve of the linear approximation.

Following Ham [7], studies on the crystallites growth of various geometries depend on the parameter n ($n = 3/2$ for permanent eccentric isolations and $n = 2$ for disc isolations, which can be seen in microphotographs (figure 5)). Besides, for spherical crystallites $n = 3$, when their growth is limited with reactions of particles attaching to the surface, as was shown by Turnbull [8].

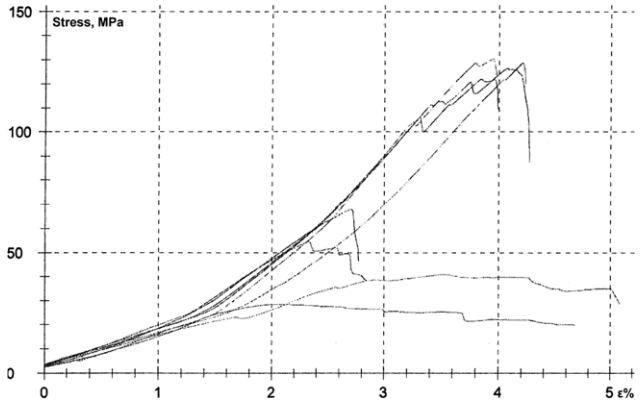

Figure 6. Compressive strength against deformation for 1%-chitosan samples.

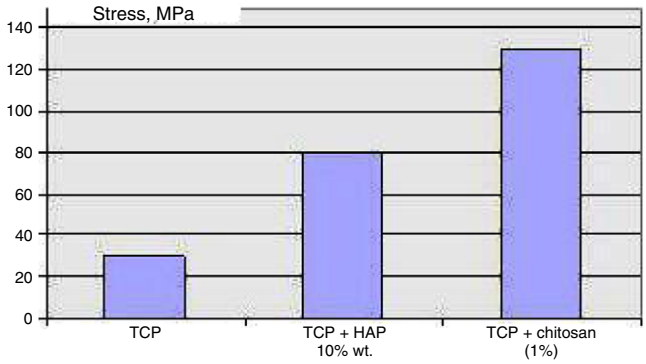

Figure 7. Compressive strength.
(This figure is in colour only in the electronic version)

Table 1. Data of micro hardness measurements.

No.	TCP Average load (MPa)	TCP and 1% chitosan Average load (MPa)	TCP and 10% HAp Average load (MPa)
1	6.87	16.61	12.98
2	6.95	16.90	9.32
3	4.98	14.96	14.90

The third and final stage aggregates the dissolution of small particles and the growth of large ones. Particularly, during TCP to HAp transformation the formation of the layer of plate crystallites slows down diffusion and the rate of reaction. The microphotographs of bio-cements (figure 5) synthesized from TCP and 1% chitosan demonstrate bulky aggregates sized a few microns, consisting of nanosized particles.

The data of micro hardness measurements, however divergent they are, provide evidence that the best results have been obtained with TCP and chitosan mixtures (table 1, figure 6).

To verify this conclusion, further mechanical compression experiments were performed and their results were combined in a summary diagram (figure 7).

3. Conclusions

We demonstrated a technique to synthesize bio-cements, based on α-Ca3 (PO4)2. X-ray analysis confirmed the presence of the following bio-cement phases: HAp, α- and β-TCP (90% wt targeted phase, because of the phosphorus loss in high temperature annealing). The compressive deformation analysis proved that the most robust bio-cement might be fabricated of α-TCP and 1% chitosan.

The kinetics of bio-cement transformation in the experiments confirmed the best choice to be a 3:1 TCP–HAp limit ratio with thermoconditioning for 48 h. Moreover, using additives like hydroxyapatite nanopowder [9] or chitosan will increase the ultimate strength up to 130 MPa, which is similar to the value for cortical bones. Further research based on novel nanomechanical modelling of porous materials [9] will allow us shortly to synthesize modified bio-cements, matching the natural bone tissue for clinical applications.

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