

Phosphate glasses and glass-ceramics for medical applications¹⁾

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Dedicated to Prof. Dr. Günther Heinz Frischat on the occasion of his 60th birthday

Modified calcium phosphate glass systems meet the requirements for the development of different biomaterials. Bioactive, long-term stable phosphate glass-ceramics and resorbable phosphate glasses were prepared in the systems $P_2O_5-CaO-Al_2O_3-Na_2O$ and $P_2O_5-CaO-MgO-Na_2O$. Due to their high thermal expansion coefficients the bioactive phosphate glass-ceramics are excellently suited for coating metals. Using a salt-sintering process, porous resorbable glasses can be obtained. The properties of glass-ceramic coatings on cobalt/chromium alloys and the production of porous resorbable phosphate invert glasses are described.

Phosphatgläser und -glaskeramiken für den Einsatz in der Medizin

Modifizierte Calciumphosphat-Glassysteme bieten sehr gute Voraussetzungen für die Entwicklung spezieller Biomaterialien für den Hartgewebeersatz. Bioaktive langzeitstabile Phosphatglaskeramiken können aus Gläsern des Ausgangssystems $P_2O_5-CaO-Al_2O_3-Na_2O$ hergestellt werden, während das System $P_2O_5-CaO-MgO-Na_2O$ die Grundlage für die Entwicklung in-vivo resorbierbarer Phosphatgläser bildet. Die langzeitstabilen Phosphatglaskeramiken eignen sich, besonders auf Grund sehr gut angepaßter thermischer Ausdehnungskoeffizienten, hervorragend zur Beschichtung von Cobalt/Chrom-Legierungen. Dabei entstehen stabile Werkstoffverbunde, die die mechanischen Eigenschaften des Metalls mit der Bioaktivität der Glaskeramik kombinieren. Die Resorbierbarkeit der Phosphatgläser aus dem System $P_2O_5-CaO-MgO-Na_2O$ läßt sich in einem breiten Bereich steuern. Zum besseren Einwachsen des Knochens und zur Vergrößerung der Oberfläche können diese Materialien porös gestaltet werden. Die Eigenschaften der Glaskeramik-Metall-Werkstoffverbunde sowie die Herstellung der porösen resorbierbaren Phosphatgläser werden dargestellt.

1. Introduction

Metals and alloys, plastic materials, ceramics, glasses and glass-ceramics are used as alloplastic implant materials for the substitution of human bone. The advantages of the metals consist in their good mechanical properties, however, their biological properties are controversial. In contrast, ceramics, glasses and glass-ceramics have opened up new possibilities in implantology. The chemical compositions of these materials can be adjusted to that of the mineralogical part of bone. Different silicate bioactive glasses and glass-ceramics have been described, for instance, in [1 to 4]. The impressive results of these investigations are known: the living bone grows together with the implant materials. The lack of sufficient strength can be compensated by the production of glass or glass-ceramic coatings on metals or by preparation of composites. However, besides the organic components human bone consists of crystalline and amorphous calcium phosphates, mainly hydroxyapatite $[Ca_{10}(PO_4)_6(OH)_2]$. Therefore, it is suitable to

investigate phosphate ceramics [5 to 7], phosphate glasses [8] and phosphate glass-ceramics [9] in view of their biological properties.

After the implantation of bioactive materials, the living bone forms a stable physicochemical bond to the implant. Such implants should possess a considerable stability against the chemical and biological attacks of the body fluid, because they are intended to remain in the living body. The presence of apatite promotes the good biological properties. On the other hand, often the regeneration of bony defects is favoured compared with bone substitution. Porous resorbable implants can support this regeneration, especially of spongy bone, by bridging large defects. The porosity of the implants acts as a guide rail for the bone growing in. The resorption of the implant materials begins simultaneously, and around one year or one and a half years later the defect is filled with new bone.

Figure 1 represents the different directions for the development of phosphatic materials provided for the use as bioactive long-term stable and resorbable bone implants, respectively. The development of these materials possessing well-defined biological properties is facilitated by knowledge of the glass structure. Usually, the structure of phosphate glasses is described by Q^n groups.

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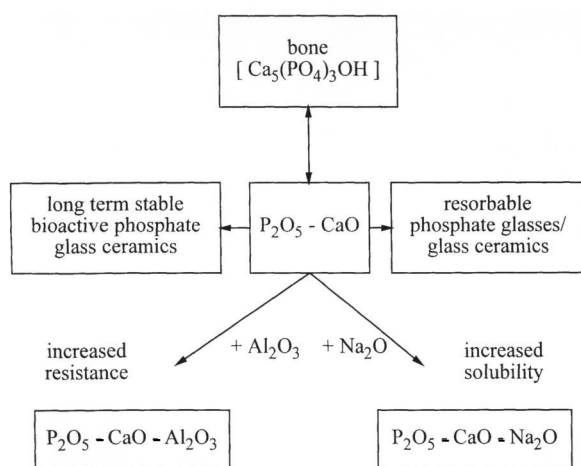


Figure 1. Base systems for the development of phosphate bio-materials.

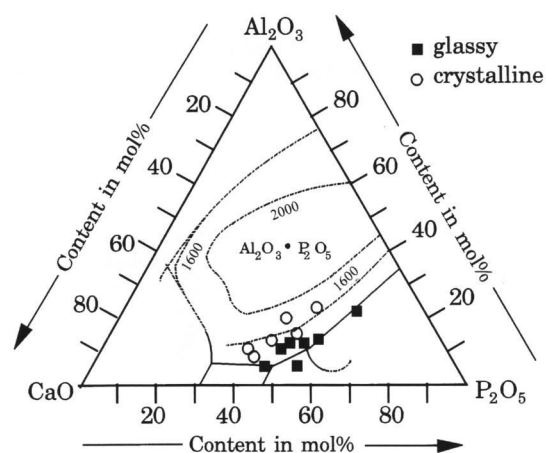


Figure 2. Investigated glasses and glassy-crystalline materials in the base system P_2O_5 -CaO- Al_2O_3 .

Q^n groups are PO_4 tetrahedra in which n is the number of bridging oxygen per PO_4 tetrahedron. Reliable information about the nature of phosphate building groups, the neighbouring cations and the ordering state of the materials can be obtained by ^{31}P MAS NMR investigations.

2. Bioactive phosphate glass-ceramics

Figure 2 shows the phase diagram of the ternary system P_2O_5 -CaO- Al_2O_3 . The calcium and aluminium contents of the melted glasses were selected as high as possible to promote the chemical stability of the glasses and the crystallization of apatite. The square points mark compositions forming glasses, the circular points mark compositions which crystallize spontaneously. The phase diagram is characterized by very high melting temperatures in the region around aluminium orthophosphate. Glass forming can be observed in compositions possessing more than 45 mol% P_2O_5 . ^{31}P MAS

NMR investigations showed that all glasses contain Q^2 and Q^1 groups exclusively. Therefore, the structure of these glasses can be described by a phosphate chain structure. Small amounts of phosphate rings cannot be excluded. Increasing contents of network modifying oxides result in a decreasing ratio Q^2 groups/ Q^1 groups, indicating shortened phosphate chains. However, the chain-like structure is retained. The subsequent annealing of these glasses results in the crystallization of aluminium orthophosphate, aluminium metaphosphate, calcium metaphosphate and calcium pyrophosphate. The crystallization of calcium orthophosphates, for instance of apatite, is inaccessible in glasses possessing chain structure. However, by addition of increasing amounts of Na_2O it was possible to crack the chain structures. The degree of condensation is strongly decreased and some glasses consist of ortho- and diphosphate groups exclusively. In these cases the glass formation is not determined by phosphate networks or by tangled phosphate chains but by interactions between the different cations. Similar effects in silicate glasses were described by Trap and Stevels [10]. Following their nomenclature, the glasses are called "phosphate invert glasses".

The subsequent annealing of these glasses results in the crystallization of apatite besides other crystalline phosphate phases. It can be controlled by the addition of nucleating agents, for instance iron oxide or zirconium oxide. In vitro and in vivo tests showed that these glass-ceramics are biocompatible, bioactive and stable for a long time [11 and 12].

The disadvantage of these glass-ceramics is their low mechanical strength. The bending strength amounts to around 45 MPa for the glasses and around 80 MPa for the glass-ceramics. This is insufficient to apply the materials as bulk materials. However, these materials possess a high thermal expansion coefficient, α , similar to that of cobalt/chromium alloys (phosphate glass-ceramic $\alpha = (14 \text{ to } 18) \cdot 10^{-6} K^{-1}$, cobalt/chromium $\alpha = (15 \text{ to } 18) \cdot 10^{-6} K^{-1}$). Therefore, a good connection between the alloy and the glass-ceramics could be expected by using thermal coating techniques. To produce phosphate glass-ceramic coatings on cobalt/chromium alloys, a simple sintering procedure was used, but plasma spraying is also possible. The shearing strength values measured at sintered layers amount to around 30 MPa. The results of long-term mechanical strength measurements of a sintered glass-ceramic layer on a cobalt/chromium alloy are as follows: $10 \cdot 10^6$ bending cycles were fixed as the limiting value. It was reached by applying a bending tension of 320 MPa, approximately corresponding to the basic value of the used alloy (340 MPa) [13].

The described results were the base of further animal experiments. Pins of cobalt/chromium alloy coated with phosphate glass-ceramic by sintering were implanted into the pelvic bone of pigs. The scanning electron micrograph (figure 3) shows a microtome section of an implant 32 weeks after operation. The integration of the

implant into the bone is good, and the obtained results are similar to that of pure glass-ceramic implants. The glass-ceramic layer of this sample possesses many bubbles and so far it is not exemplary. However, in the right side of the implant a crack is detectable caused by the preparation of the microtome section. This crack passes through the glass-ceramic layer exclusively, but never through the interface metal/glass-ceramic, indicating an excellent mechanical behaviour of the coated implants in the living body.

3. Resorbable porous phosphate glasses

After it was found that in modified calcium phosphate systems the preparation of phosphate invert glasses is possible, the development of resorbable phosphate glasses possessing a comparable structure was intended in the P_2O_5 -CaO- Na_2O system. The implantation of these resorbable glasses into the living bone should promote the complete resorption process.

Figure 4 shows the phase diagram of the ternary system P_2O_5 -CaO- Na_2O . Square points mark compositions forming glasses, circular points mark compositions crystallizing spontaneously. Glass formation can be observed in compositions possessing more than 36 mol% P_2O_5 . Some of the glasses were investigated by ^{31}P MAS NMR. The lines of two kinds of Q^n groups could be observed: Q^2 groups mainly influenced by sodium ions and Q^1 groups influenced by sodium and calcium ions. Their contents differ clearly with the P_2O_5 quantity. Increasing P_2O_5 contents promote the building of long phosphate chains. Decreasing P_2O_5 contents promote short chains. The intended phosphate invert glass structure is not available in the ternary system P_2O_5 -CaO- Na_2O . The further increase of the CaO content results in spontaneous crystallization. Glasses containing high contents of sodium oxide react with moisture.

Investigations of Murthy et al. [14] showed that the combination of the binary systems Li_2O - P_2O_5 , Na_2O - P_2O_5 , K_2O - P_2O_5 results in a considerable extension of the glass forming area compared with that of the pure binary systems. However, because of the strong increase of the solubility, the content of alkaline oxides could not be increased in the here investigated glasses. Therefore, the diagonal relationship lithium/manganese in the periodic table was used and MgO was added. The obtained glasses were investigated by ^{31}P MAS NMR spectroscopy [15]. Corresponding to the decreasing P_2O_5 content (caused by increasing MgO content), the fraction of Q^2 groups decreases in favour of Q^1 groups. Below 33 mol% P_2O_5 also the fraction of Q^1 groups decreases in favour of 'isolated' orthophosphate groups and the glasses possess invert glass structure. In vitro investigations of these glasses showed excellent results in view of the intended controlled solubility.

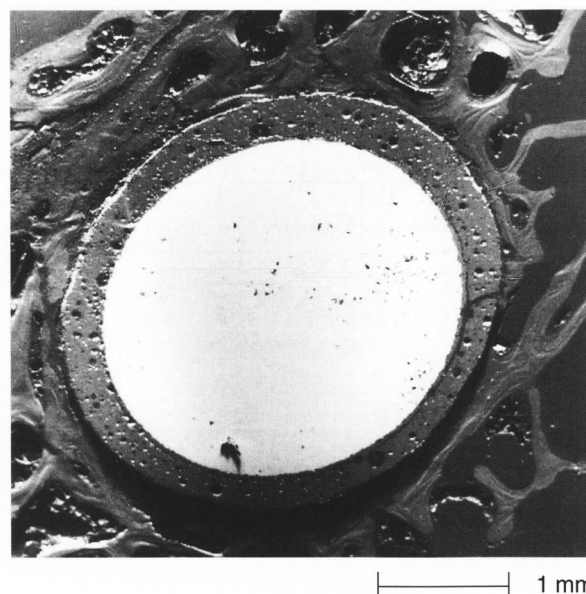


Figure 3. Scanning electron micrograph of a metal implant coated with bioactive phosphate glass-ceramic, 32 weeks after operation, pelvic bone of pig.

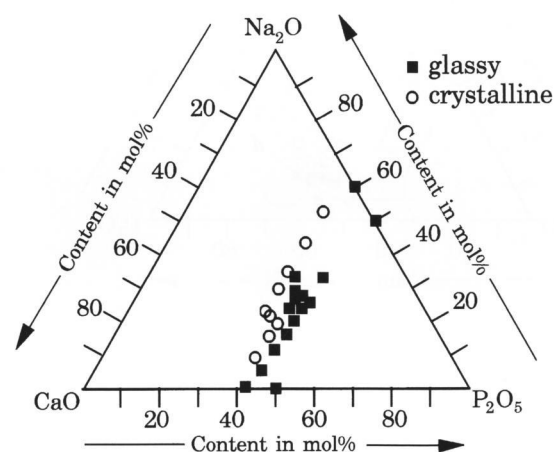


Figure 4. Investigated glasses and glassy-crystalline materials in the base system P_2O_5 -CaO- Na_2O .

The porous textures of the glasses were obtained by a sintering process. Mixtures of common salt (grain size 250 to 315 μm) and glass powders (grain size around 10 μm) were sintered at temperatures above T_g . After sintering the salty phase was dissolved by water. The diameters of the pores caused by dissolution vary between 150 and 400 μm (figure 5) and the total porosity ranges from 40 to 75% depending on the glass to salt ratio of the sintered mixture (table 1). Around 15% of the porosity are caused by the sintering process. The diameters of these pores range from about 1 to 60 μm .

Suitable porous resorbable phosphate invert glasses possessing a total porosity of around 65% were implanted into the tibia of guinea pigs and into the pelvic bone of pigs. First results show that bony cells grow into

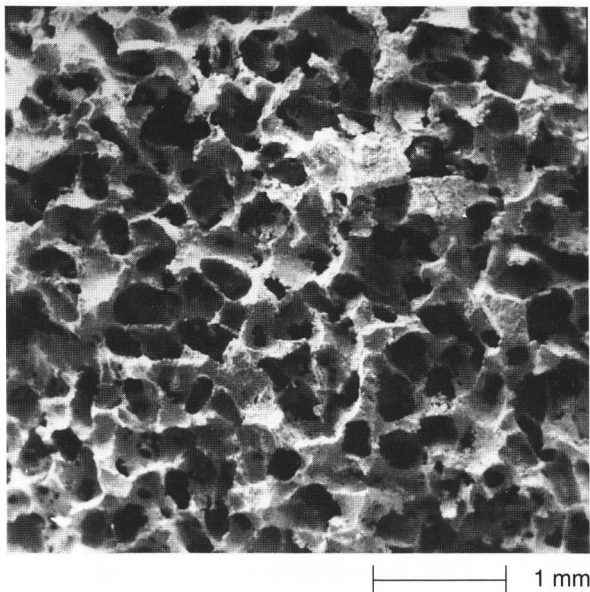


Figure 5. Scanning electron micrograph of a porous resorbable phosphate invert glass.

Table 1. Porosity and pore volume of porous resorbable phosphate invert glasses

sample	NaCl content in vol. %	porosity in vol% (open pores)	pore volume in mm ³ /g
A1	33.3	46	312
A2	35.7	50	370
A3	40.0	56	473
A4	45.5	61	565
A5	50.0	65	680
A6	54.5	71	924
A7	56.5	71	918
A8	58.3	72	975
A9	60.0	74	1032

the porous texture of the implants and the pores are filled with young bony cells only a few weeks later. Further animal experiments have to be conducted especially in view of the exact resorption term of the materials.

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