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Evaluation of a prepared sol-gel bioactive glass fiber-reinforced calcium phosphate cement

N. Nezafati[a,*], F. Moztarzadeh[a] and S. Hesaraki[b]

[a]*Faculty of Biomedical Engineering, Amirkabir University of Technology, No.424 Hafez Avenue, Tehran, Iran*
[b]*Ceramic Department, Materials and Energy Research Center, Tehran, Iran*

In this article 5-25 V% of a sol-gel bioglass fiber was incorporated into calcium phosphate bone cement to improve its mechanical properties. Compressive strength, work of fracture, elastic modulus and setting time of the cement were investigated as well as phase changes occurring during soaking the specimens in simulated body fluid (SBF). The cement microstructure was also observed by scanning electron microscope (SEM). The results showed that the compressive strength of the set cements without any fibers was 0.635 MPa which was optimally increased to 3.69 MPa by using 15% fibers and then decreased by further addition of the glass phase. In addition, both the work-of-fracture and elastic modulus of the cement were considerably increased when using the fibers in the cement composition. Setting time slightly decreased by using the fibers. A considerable content of the reactants in both fiber-free and fiber-containing cements were transformed to the apatite phase during soaking sample in SBF.

Key words: calcium phosphate, sol-gel, hydroxyapatite, bioglass, fiber.

Introduction

Calcium phosphate cements (CPCs) are types of biomaterials that have good biocompatibility and osteoconductivity and can be formed into different shapes. Among their applications are the surgery of head reconstruction, surgery of middle ear and spine and also they can be used as bone fillers. The most important properties of calcium phosphate cements are: the possibility of apatite-phase formation in the medium, the ability of forming, a choice of employment of biological factors in the cement composition for increasing the bone growth rate etc; but unfortunately their main restriction is poor mechanical properties, so their applications are just restricted to non-loading sites [1, 2]. Recently, many efforts have been made to improve this deficiency. One of these activities is the use of resorbable polymers in a cement matrix [3]. Xu and Quinn [3] used 25 vol.% resorbable polymer with diameter of 322 μm in a cement matrix. It was observed that the work-of-fracture and flexural resistance of cement were respectively increased 100 and 3 times greater than for unreinforced cements [3]. Another way is by using an injectable calcium phosphate containing growth factor β1 that is loaded with gelatin microparticles. This was injected in the femoral condyles of rabbits [4]. In another study [5], the mechanical strength of bone cement was increased by entering poly(lactic-co-glycolic acid) (PLGA) microparticles in the matrix of a calcium phosphate cement. In this research, which was done by Link and et al., the composite was tested under a mechanical test (push-out) after implantation in a rat cranial defect over 4 and 8 weeks. The result showed that the strength of the composite was increased significantly compared to cement without microparticles [5]. Fabrication of an injectable poly (propylene fumarate)/β-tricalcium phosphate paste composite was the next attempt to improve the mechanical properties of cement using its cross-linking characteristics [6]. Also Pan *et al*. [7] investigated the effect of chitosan fibers combined with gelatin on a calcium phosphate cement. It was shown that tensile strength of chitosan fiber composite was increased by 106 and 114 percent with the impregnation of gelatin at mass fractions of 5 and 10 percent. The optimal flexural strength enhancement was obtained when calcium phosphate cement (CPC) was reinforced with fibers at a volume fraction of 30 percent and a gelatin at mass fraction of 5 percent [7]. In other experiments, Santos and *et al.*,[8] studied the effect of the use of polyamide fibers on the mechanical properties of a calcium phosphate cement based on α-tricalcium phosphate as well as the mechanism involved in the increase of mechanical strength. The results demonstrate the possibility of the use of polymeric fibers to increase the mechanical strength and the need for coupling agents for the effective performance of the fibers as reinforcement in these materials [8].

Bioactive glass is a type of biomaterial that possesses the ability to bond to living tissues through the formation of a calcium phosphate-rich layer at their interfaces with living tissues [9]. Recently, glass fibers with a bioactive

*Corresponding author:
Tel : +982164542370
Fax: +982144849738
E-mail: n.nezafati@aut.ac.ir

composition have been prepared by a sol gel method and effective factors in the formation of fibers have been studied [10]. In this study, sol gel derived bioactive glass fibers were used to improve the mechanical properties of a calcium phosphate cement.

Materials and Method

Production of sol-gel bioactive glass fiber

Sol gel derived bioactive glass fibers were produced as described previously [11]. Briefly, tetraethyl orthosilicate (TEOS, Merck, 8006581000) was added to a water-ethanol solution (pH = 1.5, adjusted with HCl) at a molar ratio of 2 : 1 for water/TEOS and 4 : 1 for ethanol/TEOS. The mixture was stirred for 1 h at room temperature. The prehydrolyzed ethyl phosphate (No.8211411000) was added to the silica sol, which was stirred for another 1 h. Calcium nitrate (No. 22384298) was then introduced to the sol and the mixture was stirred for an additional hour. The resultant sol was stirred at 50 rpm by concentrating the sol through solvent removal at 20 °C. The condensation process was terminated when the viscosity of the solution was sufficient for fiber pulling (until viscosities near 4-5 Pa-s were achieved). The fiber-shaped gel was produced by extruding the viscous gel through an insulin syringe with a barrel diameter of 1/2" or 12.7 mm (needle's inside diameter is 0.006" [0.1 mm]). Fibers were then dried for 24 hours at 70 °C. Finally they were then heated to 700 °C at an approximate rate of 3 $Kminute^{-1}$ and then sintered and stabilized at 700 °C for 24 h.

Calcium phosphate cement

Tetracalcium phosphate powder (TTCP, was synthesized) was synthesized by a combination of 1 mole of dicalcium phosphate dehydrate (DCPD, Merck, 2144) and 1 mole of calcium carbonate (Merck, 2069) after milling for 2 hours. Then, it was heated to 1500 °C (in an alumina crucible) at an approximate rate of 7 $Kminute^{-1}$ and maintained for 5 hours at the same temperature. After that, it was extracted immediately, cooled at a medium temperature and ground in a planetary mill to an average particle size of 12 μm (Fritsch particle sizer analysette 22). A mixture of DCPD (average particle size of 6 μm) and TTCP, in a molar ratio of 1 to 1, was used as the solid phase of the cement. The liquid phase was a solution of 6 wt% Na_2HPO_4. The cement paste was made by mixing the powder to the liquid phase at powder to liquid ratio of 3 g/ml.

Production of CPC/bioactive glass fiber composite

To prepare calcium phosphate/ glass fiber composites, the fibers were mixed with the cement powder at various weight ratios of 5, 15 and 25% (based on the whole weight of the powder and liquid) and then the liquid phase was added to the mixture to obtain a paste. Note that the weight of the glassy fibers was not considered in the Powder-to-Liquid (P/L) calculations.

Experimental Studies

Mechanical properties

To evaluate the compressive strength of the cements, a specimen of each composition was formed in Teflon mould (6 mm in diameter and 12 mm in height), stored in an incubator (100% humidity and 37 °C) for 24 hours and the compressive strengths of the wet samples were measured by a Zwick/Roell Universal Testing Machine apparatus with a crosshead speed of 1 mm/minute.

The following equations were used for the calculation of E (Young's modulus) and σ (ultimate tensile stress):

$$E = KL/A, \quad (1)$$

$$\sigma = F/A, \quad (2)$$

where: F = ultimate load, K = hardness , L = length of sample, A = average of surface area calculated from the following equation:

$$A = \pi/2 \times 1/4(d_1^2 + d_2^2), \quad (3)$$

where d_1 and d_2 are the diameters of the bases of the cylindrical samples.

The K value is calculated by the slope of the load-displacement curve at the fracture point.

The work-of-fracture (energy absorbed by the sample before the fracture) was obtained from the area under the load-displacement curve normalized by the specimen's cross-sectional area.

Setting time

The initial setting time of the samples was determined according to ASTM C266-89 standard using a Gillmore testing device. The Initial setting time is a time which a Gilmour needle with a weight of 113.4 g and a diameter of 2.13 mm does not have any marked effect on the surface of cement paste.

Microstructural studies

Fractured surfaces of the calcium phosphate cements were evaluated with a scanning electron microscope (Stereoscan S 360, Cambridge) before and after keeping in Ringer's solution. In this study, the morphology of the fibers was evaluated as well. The surfaces of the samples were coated by a thin layer of gold before the examination to avoid problems with charging.

X-ray analysis

Phase analysis has been accomplished by a Philips PW3710 diffractometer with a scan rate of 0.02(2θ/sec) and 2θ range of 10-50°. (Wavelength = 1/54 Å, anode: copper, filter: Ni, intensity of current: 30 mA, voltage: 40 kV). The phase composition of all samples (the cements containing fibers and without fibers) was studied after incubation for 24 hours and soaking in Ringer's solution for 7 days. The composition of Ringer's solution in 100 ml is shown in Table 1. Before the analysis of the soaked

Table 1. composition of Ringer's solution

quantity (g/l)	composition
0.860	NaCl
0.830	KCl
0.033	$CaCl_2,2H_2O$

Table 2. Initial setting time of CPCs.

% fibers in composite	0	5	15	25
Setting time (minute)	20 ± 1	19 ± 1	17 ± 2	15 ± 2

specimens, they were washed carefully with distilled water, dried at room temperature, crushed in an agate mortar and tested.

Results and Discussion

The initial setting time of the cements is presented in Table 2. The setting time of the fiber-free calcium phosphate cement (control) was about 20 minute, which was not significantly different to that of the composite with 5% glass fibers. By contrast, the setting time of the composites with 15% and 25% of glass fibers was lower than that of control.

The setting mechanism of CPC is based on acidic and basic reactions. This process is so complicated that it has not been identified completely but there are some hypotheses about setting phenomena of these cements. The main reason for the setting process of CPCs is the precipitation of different phases such as brushite, apatite or octacalcium phosphate in the cement paste [11]. In apatitic calcium phosphate cements, the presence of the initial crystals of apatite is due to the dissolution of tetracalcium phosphate particles and their hydrolysis to stoichiometric hydroxyl apatite (Eq. 4):

$$Ca_4(PO_4)_2 + H_2O \rightarrow Ca_{10}(PO_4)_6(OH)_2 + Ca(OH)_2 \quad (4)$$

In addition, the growth of apatite crystals is because of the acidic -basic reaction in Equation 5 [11]:

$$3Ca_4(PO_4)_2O + 6CaHPO_4 \rightarrow 2Ca_2(HPO_4)(PO_4)_5OH + H_2O \quad (5)$$

The setting process gradually continues and is completed after a lapse of time and cross-linking of ions, so as to cause cement its strength. There are different parameters, which affect the setting time of CPCs and consequently increase their strength, including the composition of material used in the liquid/solid phase, the powder-to-liquid ratio and particle size of the reactants [12]. In this study, the higher powder-to-liquid ratio of the fiber-containing cements (especially those with higher contents of fibers) suggested that this is the main reason for decreased initial setting time of composites.

Fig. 1 illustrates the load displacement curves for a calcium phosphate cement containing 15% fibers and an un-reinforced cement. The area below the curve is a measure

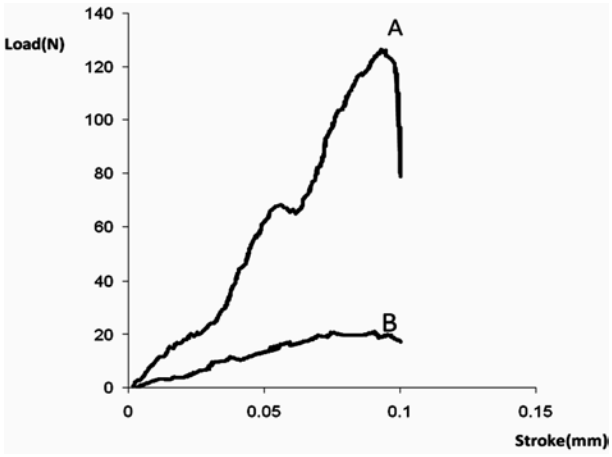

Fig. 1. Typical load-displacement curve for: A) bioactive glass-reinforced CPC (15 vol %) and B) unreinforced one.

of the fracture (the energy required to fracture the specimen, obtained from the area under the load-displacement curve normalized by the specimen's cross-sectional area). This fracture energy for the reinforced cement is higher than for the control cement (un-reinforced cement).

Some mechanical properties of the cements reinforced with bioactive fibers are compared to a cement sample without fibers (control) in Table 3.

The compressive strength, Young's modulus and work-of-fracture values of cements containing 5 and 15% fibers were considerably higher than that of the un-reinforced cement, while the values of a composite with 25% fibers were significantly lower than that of control. It can be seen that larger amount of the fibers mix not only increase the mechanical properties of CPC but also act as defect sites in the cement microstructure decreasing its mechanical characteristics. The mechanical strength of calcium phosphate cements is highly dependent on the particle size of the powder [13]. The degree of crystallinity of the apatite crystals also affects this property so that decreasing the crystal size causes more entanglement and density in the crystalline structure and thus the strength will increase. In this study CPC with a known reactant particle size was used. The mechanisms which increase the work-of-fracture and prevent flaw growth, by adding fibers, have been suggested as follows: (1) fibers bridging the crack resist its further

Table 3. Some mechanical properties of reinforced cements compared to the control sample

	Ultimate stress (MPa)	Young's Modulus (MPa)	Work-of-fracture (kJm^{-2})
A (5%fibers)	1.53 ± 0.01	129.73 ± 2.14	0.18 ± 0.02
B (15%fibers)	3.69 ± 0.07	144.61 ± 0.51	0.54 ± 0.01
C (25%fibers)	0.89 ± 0.01	123.42 ± 3.50	0.12 ± 0.01
Control sample (without fibers)	0.63 ± 0.01	97.21 ± 0.23	0.09 ± 0.01

opening and propagation; (2) multiple cracking of the matrix consuming the applied work in creating new surfaces; and (3) frictional sliding and stretching of fibers during pullout [14]. Factors such as the type and shape of the fibers can also affect the work-of-fracture and strength of ceramic composites reinforced by fibers such as glass fibers. This means that factor(s) which cause(s) an increase composite strength would has/have positive effects on work-of-fracture.

Fig. 2 shows XRD patterns of the control (unreinforced cement) and a CPC composite with 15% bioactive glass fibers, before and after soaking in Ringer's solution. For both formulations, a considerable amount of the reactant phase in the cement composition is observed before putting the cement in Ringer's solution. The apatite phase is also observed in the compositions (apatite is the product of the setting reaction). But after 7 days of keeping the samples in Ringer's solution, almost all the reactants were converted to the product phase. The large width of the peak (relative to the apatite phase) indicates a very low crystallinity of this phase (a nearly amorphous-like phase). It is seen that glass fibers never prevent the conversion of reactant materials (TTCP and DCPD) to apatite. The patterns of other composites were very similar to that presented here.

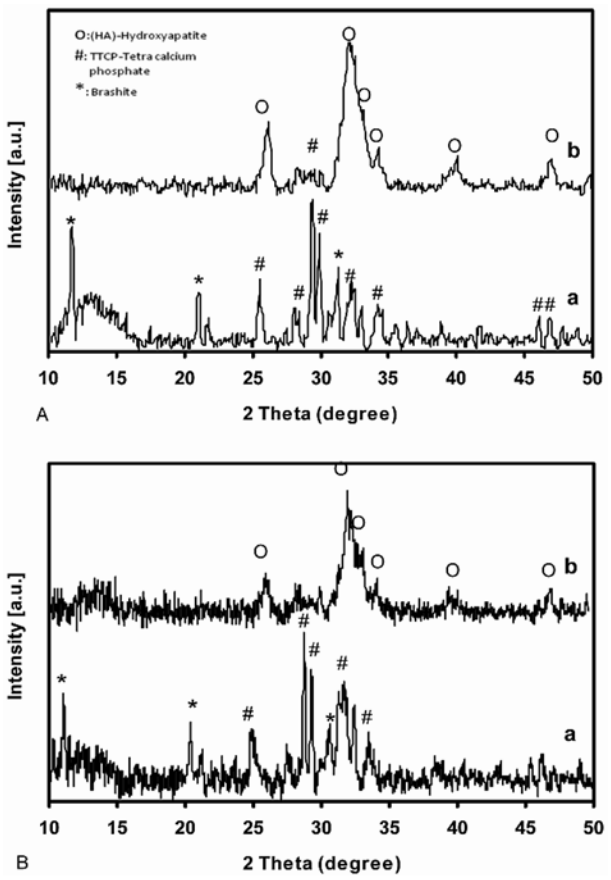

Fig. 2. XRD patterns of A) Fiber- free CPC and B) CPC with 15% bioactive glass fiber: a) before soaking in Ringer's solution, b) after soaking in Ringer's solution for 7 days.

Fig. 3 shows a typical SEM micrograph of a bioactive glass fiber produced by extruding the gel composition. Fiber diameters are less than 100 mm and their lengths are more than 7 times their diameters. Fig. 4 shows that the glass fibers were incorporated into the matrix. A dispersed particle of a glass phase (which is probably due to crushing of the glass fibers) is also observed. Fig. 5 shows the typical morphology of apatite crystals in the microstructure of a CPC/ bioactive glass fiber

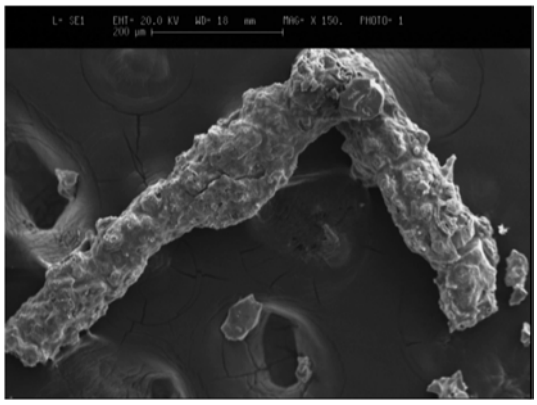

Fig. 3. SEM micrograph of a sol gel derived bioglass fiber.

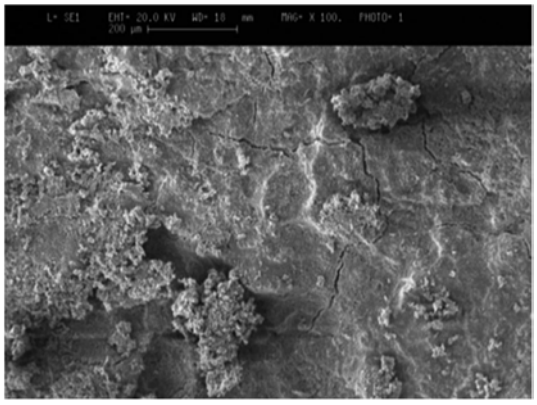

Fig. 4. SEM image of a CPC/ bioactive glass fiber composite illustrating pull-out of glass fibers in the CPC matrix.

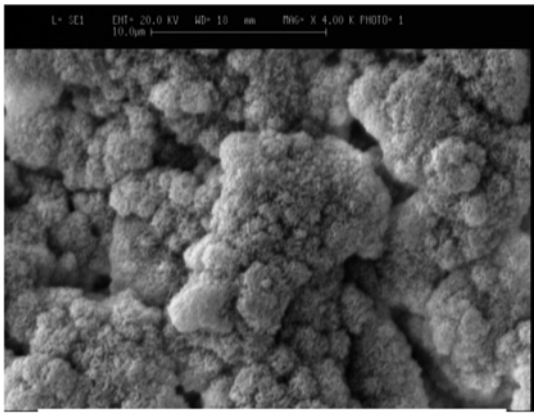

Fig. 5. Typical morphology of apatite crystals in the microstructure of a CPC/bioactive glass fiber composite soaked in Ringer's solution for 7 days.

composite soaked in Ringer's solution. The presence of tiny crystals of apatite in a microporous structure is observed in this figure. No fibers are observed in the microstructure of the cement at this magnification.

Conclusions

CPC with improved mechanical properties could be produced by incorporating sol-gel derived bioactive glass fibers. The optimum amount of the fibers which successfully improved the compressive strength, modulus and toughness of the CPC was 15 wt% based on the total weight of the cement powder and liquid. Using bioactive glass fibers did not influence the bioactivity of the cement through the conversion rate of the reactants into the apatite phase during soaking the samples in Ringer's solution.

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