A STUDY ON INJECTABLE BONE CEMENT

İbrahim Kapıcı[1], Feride Sermin Utku[2]

[1]Department of Biotechnology, Yeditepe University, Istanbul, Turkey

ibrahim.kapici@yeditepe.edu.tr

[2]Department of Biomedical Engineering, Yeditepe University, Istanbul, Turkey

sermin.utku@yeditepe.edu.tr

***Abstract*—Calcium phosphate materials are used as cements, composites and coatings in many medical and dental applications due to their similarity to bone both in composition and in osteoconductive and osteoactive properties. Injectable cement is used in hard tissue repair as an adjunct to internal fixation of fractures. In this study, we experimented with the production and characterization of Ca-P and silk based injectable calcium phosphate cement. HA, TCP, Na2HPO4 and polyamide solution were used to produce injectable bone cement. Mixing and solidification time was documented. The injectable cement material was characterized using XRD, SEM and FTIR. Characterization of samples indicated that a CHA-polymer based injectable cement with a setting time of 4 minutes and solidification time of 10 minutes was obtained. Further studies on cytotoxicity and biocompatibility as well as improvement on solidification time will be conducted.**

Keywords — injectable cement; CHA; bone replacement material. vertebraplasty

I. INTRODUCTION

Bone is a hard tissue that consists of 45% inorganic mineral salts, 25% water and 30% organic matter. The inorganic part of bone consists of calcium, magnesium, and phosphate. Therefore, calcium phosphate materials in different forms, such as cements, can be used in orthopedic and dental applications [1].

Calcium phosphate materials have been used in bone replacement, in the treatment of defects caused by surgical interventions on cancerous tissue in bone. In the repair of these defects, materials with similar composition to bone and with osteoinductive and osteoconductive properties are being used [2,3].

Injectable calcium phosphate cements (ICPC) are used in various orthopedic and dental applications, as an adjunct to internal fixation for treating fractures and repair of defects caused by oncological procedures, injury and osteoporosis. The main purpose of the cement is to fill voids in metaphyseal bone, thereby reducing the need for bone graft, but cements also may improve the holding strength around metal devices in osteoporotic bone. ICPC with conventional metal fixation in certain fractures of the distal radius, tibial plateau, proximal femur, calcaneus and in vertebroplasty has been shown to produce better stability, stiffness, and strength than metal fixation alone, as well as reduced time to full weight-bearing, rapid gain of strength and range of motion and improved stability [2,3].

The chemical properties and production and application methods of ICPC are completely different from acrylic cements, i.e. PMMA, which may lead to complications, such as necrosis, due to its exothermic polymerization process [4]. ICPC cements harden without generating high heat, develop compressive strength comparable to that of bone, and are remodeled slowly *in vivo*.

ICPC are produced by mixing powder and liquid components. Powder part is composed of various phosphate salts, such as amorphous calcium phosphate (ACP), tetra calcium phosphate (TTCP), di-calcium phosphate dehydrate (α-TCP) or mono-calcium phosphate monohydrate (MCPM). The liquid component consists of sodium phosphate solution. The two components are mixed to the consistency of a paste [3].

In this study, an ICPC was produced with the aim of biomimicking the organic and inorganic component of bone. Therefore, to place the collagen, a polyamide based polymer was used to complement the inorganic component, Ca-P in order to produce a bone replacement material with both components.

II. MATERIAL AND METHODS

In this study, Merck quality chemicals were used. HA was prepared in our laboratory according to Jalota et al. [5] using $NH_4H_2PO_4$ and $Ca(CH_3COO)_2$. Polyamide solution was prepared according to Du [6] by washing the polyamide fabric material in Na_2CO_3 in several washes and air-drying. It was solubilized using distilled H_2O, $CaCl_2$ and ethanol at a ratio of 1:8:2.

0.168 g of HA was weighted and crushed. 0.27 g of α-TCP was added and mixed. HA and α-TCP were mixed as the powder component of ICPC. As the liquid component, Na_2HPO_4 aqueous solution and polyamide solution were used. Various powder: polyamide solution: phosphate

solution ratios and phosphate concentration were experimented till the setting time and solidification time were reasonably reduced. The liquid mixture was added slowly to the powder mixture. The cement mixture was crushed for about three minutes to a smooth paste, placed in a syringe and injected. Mixing time and setting time were documented. ICPC was dried for 24 hours in a 60°C incubator and characterized using XRD, SEM and FT-IR.

III. RESULTS

Using the materials and methods stated above, a CHA based ICPC was prepared from HA, α–TCP, phosphate and polyamide and characterized morphologically and chemically.

HA was prepared in the laboratory and its crystal structure was confirmed by XRD analysis (Fig. 1). The peaks that are unique to HA were observed around 22º, 26º, 28º, 31º, 32º, 33º and 34º 2Theta. Crystallinity of the samples was high, thus, sharp peaks were obtained at these positions. The FT-IR spectrum for HA (Fig. 2) displayed phosphate peaks at 559, 598, 1000-1200 cm^{-1}, a carbonate peak at 1417 cm^{-1} and a very distinct and sharp hydroxide peak at 3640 cm^{-1}. The morphological structure for HA displayed a homogenous powder, with HA nanocrystals as displayed in the SEM image (Fig. 3).

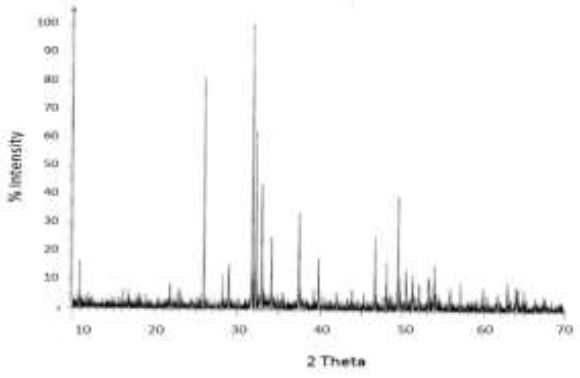

Figure 1. The XRD spectrum for HA produced in the laboratory according to [5].

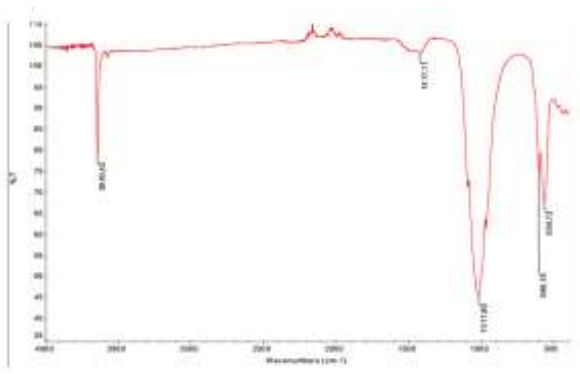

Figure 2. The FT-IR spectrum for HA produced in the laboratory according to [5].

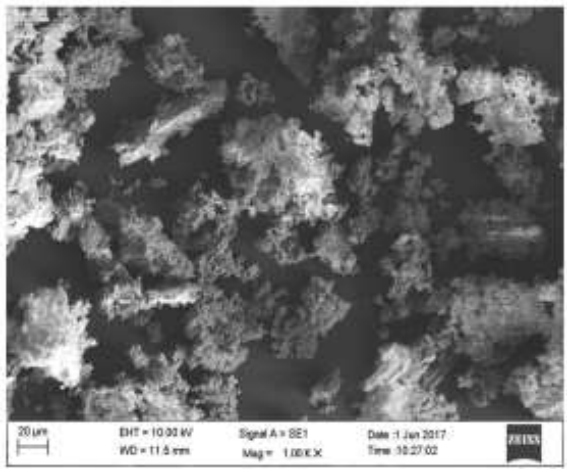

Figure 3. The SEM image for HA produced in the laboratory according to [5].

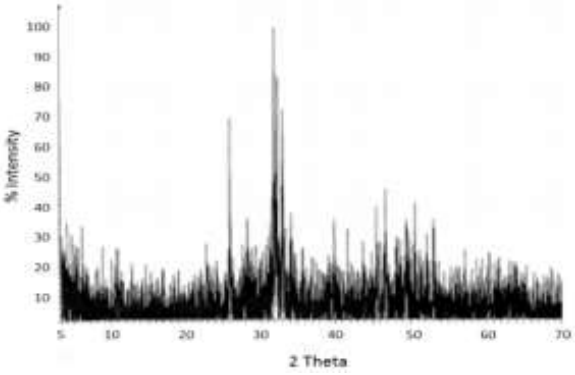

Figure 4. The XRD spectrum for ICPC.

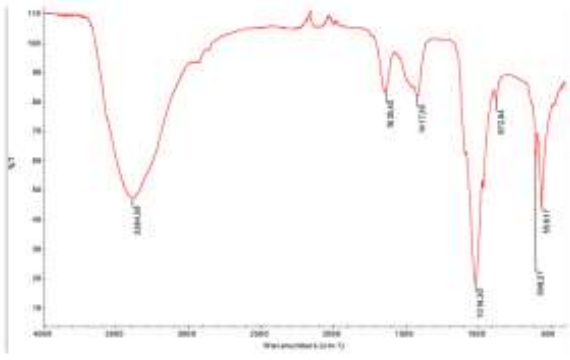

Figure 5. The FT-IR spectrum for ICPC.

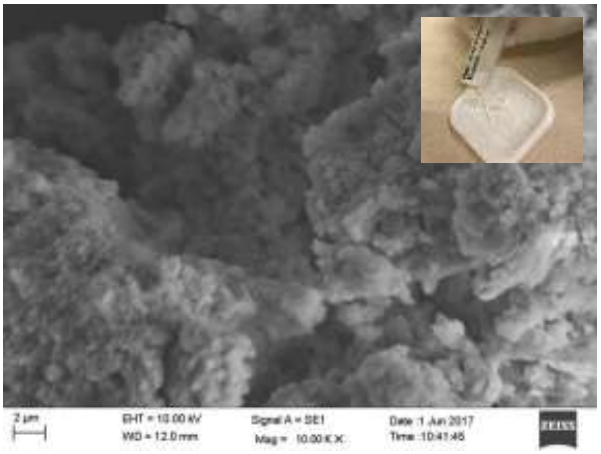

Figure 6. The SEM image for ICPC made of liquid component containing polyamide solution. Inset shows ICPC ejection.

With the addition of liquid component to powder, a mixture with a gel-like consistency was formed. The setting time was found to be 4 min. during which, the reactants were vigorously mixed using a mortar and pestle. The solidification time for the cement was found to be 10 min. The solidification process continued in the 60°C incubator for another 24 hours and completely dried.

The XRD spectrum of the ICPC (Fig. 4) displayed a poorly crystalline structure which contained the typical expected peaks of CHA as stated above. However, the XRD spectrum was much noisier than HA, probably due to the polymeric component of the cement. CHA formation with characteristic peaks was observed. The FT-IR spectrum for the ICPC (Fig. 5) displayed the typical, above stated phosphate peaks, carbonate peaks at 875 and 1417 cm^{-1}, and a carboxyl peak at 1635 cm^{-1}. The hydroxide peak was observed as a wide band stretching from 2800 to 3600 cm^{-1}. The ICPC obtained was a cream-colored, plastic-like, hard-to-crush powder. The SEM image of the ICPC displayed rather uniformly organized nanocrystals (Fig. 6).

IV. DISCUSSION

The main aim of this study was to produce an ICPC for hard tissue repair with a polymeric material, i.e. polyamide as a replacement for collagen in calcium phosphate bone cements. Various types of Ca-P and Calcium Sulphate (Ca-S) based injectable cements have been developed and marketed over the years. Recently, premixed ICPC that are stable in the package have been developed to ensure proper mixture and injection in time. These cements may have slightly lower strength, thus they have been reinforced mainly with chitosan based polymers, which have lower rate of solubility. In this study, a macroporous, three-dimensional Ca-P-polyamide cement as a bone replacement material was developed for use in treatment of traumas, such as bone fractures and bone loss as very common medical problems. Highly biocompatible polyamide component offered here as a better substitute for the organic portion of bone acts as an element to increase bone strength and integrity and a regulator of bone formation due its low rate of degradation. Therefore, the use of polyamide reinforced ICPC is a novel contribution in this field.

The effect of polyamide and phosphate solution ratio as well as the polyamide content on the texture and consistency of the paste-like, set and solidified ICPC were investigated. In order to adjust the stiffness and solidification time of the cement, with the amount of HA and α-TCP kept constant, the volume of polyamide and water as well as the amount of Na_2HPO_4 were changed. The reaction of these chemicals releases water [4]; thus, with extensive and vigorous mixing of reactants till completion, the amount of water released as the end-product was increased, thus increasing the setting time while easing the mixing process. Thus, the water content had to be controlled carefully. By increasing polyamide to phosphate solution ratio, setting time could be decreased.

With incubation at 60°C, water contained in the injectable cement was evaporated and further dried. Increasing the concentration of Na_2HPO_4 lead to reduction of setting time for ICPC. Thus, solidification time for ICPC was further reduced to form a more solid injectable cement. This may imply that ICPC can be produced with a high elastic modulus to be used as a weight-bearing material. Thus, the polymer-inorganic composite obtained in this study may be further strengthened to be used in weight-bearing applications.

V. CONCLUSION

The aim of this project was the production of ICPC for hard tissue repair. HA, α-TCP, phosphate solution and polyamide were used to obtain an ICPC. XRD, FT-IR and SEM results confirmed the production of a CHA based ICPC. In the future, further research on the mechanical properties, chemical stability and degradation properties of cement will be conducted.

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