Fabrication of Calcium Phosphate-Calcium Sulfate Injectable Bone Substitute Using Chitosan and Citric Acid

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Introduction: The injectable systems can mold to the shape of the bone cavity and set in-situ when injected. Such systems should shorten the surgical operation time, reduce the damaging effects of large muscle retraction decrease the size of the scars and diminish the post operating pain. It also allows the patient to achieve rapid recovery in a cost-effective manner. In this study, we investigated the effect of calcium sulfate hemihydrate (CSH) on the calcium phosphate based injectable bone cement. The solution of citric acid and chitosan was used as the liquid phase and the powder component was consisted of tetracalcium phosphate(TTCP)-dicalcium phosphate(DCPA)-CSH. The setting behavior and compressive strength were measured depending on the amount of CSH addition.

Methods: The liquid phase was an aqueous solution of chitosan (Sigma, Iceland) and citric. The mass fraction of chitosan and citric acid were 2% and 20%, respectively. The powder component was a mixture of TTCP, DCPA and CSH. TTCP was synthesized by solid state reaction method. TTCP and DCPA powders were mixed at a molar ratio of 1:1 to obtain the calcium phosphate cement (CPC) powder. Four different percentages of CSH powders were added to this CPC powder ranging from 0-30wt.%. Depending on the CSH content, four types of cement were named as IBS-0 to IBS-30. The liquid and solid components were mixed manually with a spatula and the liquid-to-powder (L/P) ratio was 1:0.41 (ml:g). Setting times of these cements were measured according to the ISO 9917 standard for dental silicophosphate cement [1]. The injectability was calculated using the following equation [2]: Inj% = (Paste weight expelled from the syringe)/(total pasteweight before injecting)…………. (1)
The compressive strengths were measured using a computer controlled Universal Testing Machine (R & B, Korea) after incubated at 37°C and 100% relative humidity at time intervals of 1, 3, 7, 14 and 28 days.

Results/Discussion: Chitosan was cross-linked by citric acid and the viscosity of the liquid phase increased. Usually, calcium phosphate cement containing carboxylic acid hardens rapidly, with an insoluble matrix by chelation. The hardening of the present cement was occurred by several reactions such as the chelate reaction between citric acid and calcium in the powder component and the transformation reaction of the components of the cements to HAp. TTCP and DCPA were transformed according to the following reaction: $6CaHP0_4 + 6Ca_4(P0_4)_20 \text{ -+ } 3Ca_{10}(P0_4)6(OH)_2$ (2)
In our investigation, setting time has increased significantly at 10 wt% CSH addition and it successively decreased at 20 and 30 wt% CSH. At 10 wt% CSH, the chelate reaction was retarded by the CSD due to the interaction with citric acid which in turn increased the setting time. On the other hand, at 20 or 30 wt% CSH, the cement became supersaturated that accelerated the setting reaction and promoted the reaction as mentioned in equation (2). Retardation was dominant in the former (10% CSH) while supersaturation was the dominant in later (20 & 30% CSH). As the CSH content increased the injectability also increased. No cement had shown filter-pressing phenomenon in which the liquid alone was pushed out keeping the major portion of powder inside the syringe. HAp conversion has been enhanced with the addition of CSD and as the amount of CSD increased the intensity of the HAp peak also increased (Fig. 1). On the contrary, the relative intensity of TTCP peaks decreased. The compressive strength of this system improved with the addition of CSH and after 28 day incubation, IBS-20 showed maximum strength. For all four types of cement, the strength increased as the incubation period increased. This was due to the fiber like crystallization of HAp which appeared more in CSH added cements.

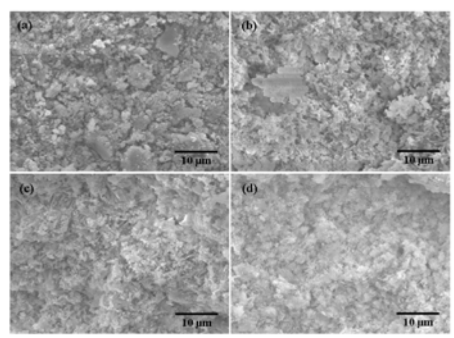

Fig. 1: SEM images of fracture surfaces of (a) IBS-0 incubated 14d, (b) IBS-0 incubated 28d, (c) IBS-20 incubated 14d and (d) IBS-20 incubated 28d at 37ºC 100% humidity.

Conclusion: The setting time was anomalously increased at 10 wt%CSH and began to decrease gradually as the content of CSH increased. The injectability retained almost 100% up to 20 min for IBS-20 and IBS-30. In terms of microstructure, fiber like apatite formed in all four types of cements after incubation. This apatite possibly increased the compressive strength of the cements.

Reference: 1. ISO 9917-1, 2003. Dentistry-water-based cements—part 1: powder/liquid acid–base cements, ISO, Geneva, Switzerland.
2. Bohner, M. Biomaterials 2004;25:741–749.