Bone ingrowth 를 위한 생분해성 bone cement (I): 제조 및 물리적 성질

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Partially biodegradable bone cement for bone ingrowth (I): Preparation and physical properties

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Introduction

The longevity of cemented total hip replacement, namely total hip arthroplasty, is one of the goals to bioengineers and scientists. It depends on the integrity of the cement *per se* and interfaces of the metallic stem/cement, cement/bone, and stress/strain transmission and its distribution.[1]

The problems at the bone/cement interface cannot be easily overcome since these problems arise from the intrinsic properties of the bone cement as well as extrinsic factors such as cementing technique. The toxicity of the monomer, inherent weakness of the cement as a material due to the unfavorable inclusion of the pores, and blood tissue debris mixed during surgery can contribute to the problem of loosening at the bone/cement interface.[2]

The bone/cement interface strength may be enhanced by growing bone into the cement after fixation. Bone cement can be used for immediate fixation yet provide tissue ingrowth space later by incorporating resorbable particles such as inorganic bone particles. Some studies indicate that the concept can be used effectively, at least in rabbit and canine models.[3,4] However, the bone ingrowth is limited because the pores are not continuous. So, making continuous open pores allow bone ingrowth to cement more deeply.

In this study, we proposed that copolymerization of bone cement with biodegradable polymer, such as poly lactic acid, can make continuous open pore in the cement mantle. It may give stronger interfacial strength between cement and bone.

Materials and Methods

Synthesis of poly-L-(lactic acid) (PLLA)

Poly-L-(lactic acid) (PLLA) was prepared by bulk polymerization with lactic acid monomer. (PURAC PF90, PURAC Biochem, Gorinchem, Holland) Schematic diagram of polymerization condition and structure of PLLA is shown in Fig. 1.

Three different types of molecular weight of PLLA were synthesized. Those are 500, 1500, 3000 g/mol. The molecular weight was checked by gel permeation chromatography (GPC). Also the structure of the poly-L-lactic acid was observed by ^{1}H and ^{13}C nuclear magnetic resonance (NMR).

Synthesis of vinyl-PLLA (v-PLLA)

Vinyl-PLLA was synthesized by the method shown in Fig. 2. Ten percent PLLA solution was prepared by dissolving 100 g of the prepared PLLA in 900 g of chloroform. Purified methacryloyl chloride was dropped slowly into the 10% PLLA solution at 0 °C under N_2 atmosphere. After the reaction, chloroform in the solution was removed by rotary evaporator. The final product was obtained in the form of powder. The structure of the final product was confirmed by ^{1}H and ^{13}C NMR.

Preparation of v-PLLA incorporated bone cement

Orthopedic bone cement kit (CMW, CMW Laboratory Dentsply, Exter, England) was used for this study. The kit consists of two parts. One part is 40 g of bone cement powder (PMMA) and the other part is 20.72 g of bone cement liquid (MMA). The v-PLLA powder was mixed with the powder of bone cement by 30 wt%. For group A, the mixture (cement powder + v-PLLA) and liquid bone cement was mixed in a 2:1 ratio thoroughly for about 15 seconds. For group B, the same process was applied except PLLA powder was added (cement powder + v-PLLA + PLLA particles) to the powder mixture by 20 wt%. The size of PLLA powder particles was 100~300 μm. When the powder part and liquid part mixed together, it went to dough state. The dough state of the mixture was poured into the prepared mold for fabricating specimens. The specimens were cured for a week at room temperature.

Characterization of the specimens

The specimens were prepared according to standard D 638M-93 of the American Society for Testing and Materials (ASTM) for tensile test. The mechanical properties of the prepared specimens were measured by tensile test by an Instron hydraulically controlled materials testing machine (Instron model 8511, Canton, Massachusetts). A constant cross-head speed of 0.01 mm/sec was applied to the specimen.

In vitro simulation for biodegradation test of the prepared bone cement was investigated in the phosphate buffered saline (PBS) solution (pH=7.4) in a shaking incubator at 60 °C for 1 to 4 weeks. The test was done with specimens of PLLA itself (Mn=1500 g/mol), v-PLLA incorporated bone cement, and v-PLLA incorporated bone cement mixed with PLLA particles. The weight of all samples was measured before the test and remeasured the weight in completely dried condition after the test.

Results and Discussion

PLLA was synthesized without any catalyst for this study. The relationship of polymerization time vs. molecular weight of PLLA is shown in Fig. 3. Structure of the synthesized PLLA was identified by NMR spectroscopy. The molecular weight of obtained PLLA for this study was 1500 g/mol checked by GPC.

Structure of the synthesized v-PLLA was identified by ^{1}H, ^{13}C NMR spectroscopy as shown in Figs. 4 and 5. The NMR spectra of v-PLLA show that the vinyl group was introduced successfully to the PLLA. According to the spectra, yield of v-PLLA was about 80% by ^{1}H NMR.

We supposed that the vinyl-PLLA could be copolymerized with MMA monomer in the liquid part of the bone cement. However, we could not checked that v-PLLA was copolymerized with MMA or not. But, a fact that no solvent was found for the v-PLLA incorporated bone cement specimen would be an indirect evidence of copolymerization. It may elucidate that the v-PLLA and MMA were possibly copolymerized together and cross-linking would be occurred.

The results of mechanical test are summarized in Table 1. The average tensile strength of control specimens (~33.05 MPa) in this study was within the average tensile strength of the bone cement ranged from 21.7 to 34.8 MPa in general.[5] The tensile strength of group A (~24.4 MPa) is also within the average tensile strength of the bone cement. However, group B showed lower tensile strength due to the addition of PLLA powder. Compared with Lui's study, the tensile strength of experimental specimen (~15.7 MPa) showed same value of group B of this study as shown in Table 1. So, possibly PLLA powder added specimen could be used in clinical application. Tensile strength of bone particle impregnated bone cement was decreased, while Young's modulus was slightly increased as same way as this study.

Results of *in vitro* biodegradability simulation test were shown in Figs. 6, 7 and 8. In Fig. 6, PLLA itself showed very fast degradation. This may be due to very low molecular weight (Mn=1500 g/mol) of PLLA. However, the group A (Fig. 7), the specimens supposed to be copolymer of v-PLLA and PMMA, showed very little amount of degradation of PLLA compared to the group B (Fig. 8). It can be inferred that the mixed PLLA powder near the surface of the bone cement (group B) can be more dissolved out in ease than the copolymerized PLLA in the cement mantle by PBS solution. The other possible factor is that the degradation rate can be accelerated by dissolving PLLA particles at the surface of the specimen. That is the PBS solution can penetrate easily into the cement mantle after the PLLA particles at the surface dissolved out.

We suspect that the bone could be grow into the pores where the copolymerized PLLA resorbed out because of the pore size. The bone ingrowth can be occurred in the pore size of 100-350 μm. So, the PLLA particles were impregnated in the copolymer of PLLA and MMA bone cement. We will investigate the morphology of pores in the cement mantle of copolymerized cement as well as PLLA particle impregnated copolymerized bone cement by SEM study.

Conclusion

We investigated the PLLA incorporated bone cement (we called biodegradable bone cement). The mechanical property of biodegradable cement looks good compared with the other studies. The PLLA powder impregnated biodegradable bone cement has lower tensile strength. However, it showed possibilities to develop the biodegradable bone cement. Degradation of the copolymerized PLLA in bone cement was very lower than that of impregnated PLLA particles in PBS solution.

The remained work to do is to find the optimized condition of PLLA and v-PLLA to increase mechanical properties and degradation rate.

Table 1. Summary of tensile test.

Specimens	Tensile strength (MPa)	Young's modulus (GPa)
Control	33.05 ± 6.07	1.6 ± 0.4
Group A	24.4 ± 2.4	1.72 ± 0.14
Group B	15.7 ± 3.4	
†Liu's Group		
Control	23.6 ± 1.9	1.9 ± 0.04
Experimental	15.7 ± 1.0	2.84 ± 0.46

†Reference from "Bone-particle-impregnated bone cement in vitro study

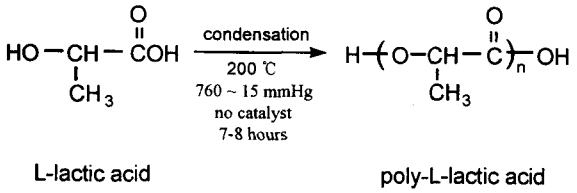

Fig. 1. Polymerization process for PLLA.

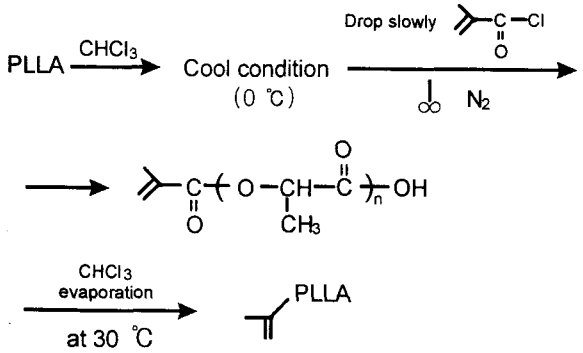

Fig. 2. Process for synthesis of vinyl-PLLA.

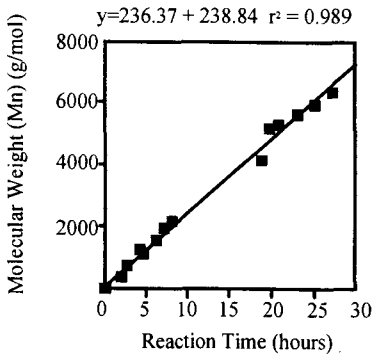

Fig. 3. Plot for molecular weight vs. reaction of PLLA.

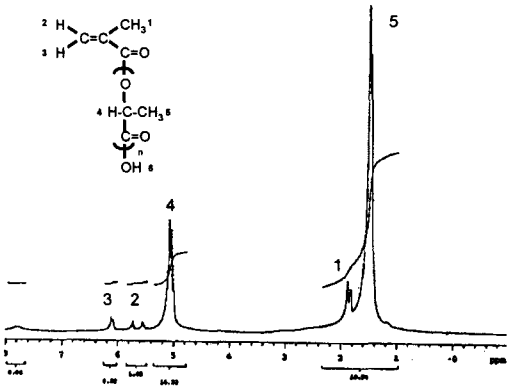

Fig. 4. ^{1}H NMR spectrum of vinyl-PLLA.

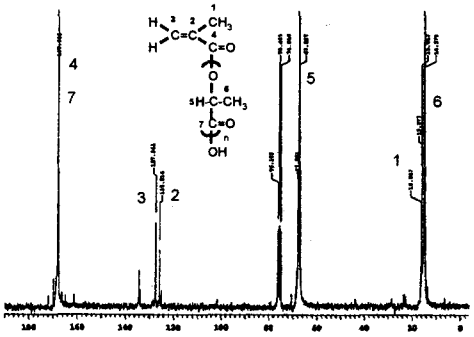

Fig. 5. ^{13}C NMR spectrum of vinyl-PLLA.

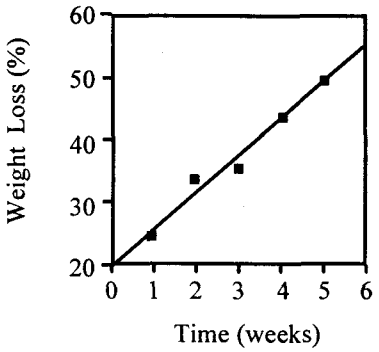

Fig. 6. Plot for weight loss vs. time of PLLA in PBS solution.

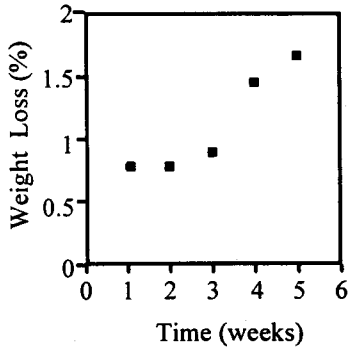

Fig. 7. Plot for weight loss vs. time of PLLA copolymerized bone cement in PBS solution.

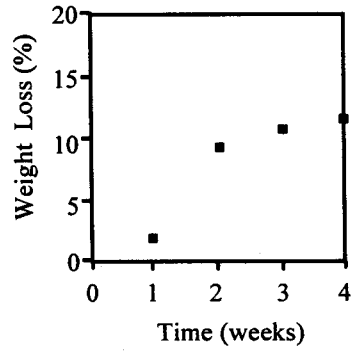

Fig. 8. Plot for weight loss vs. time of PLLA particle impregnated copolymerized bone cement in PBS solution.

References

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