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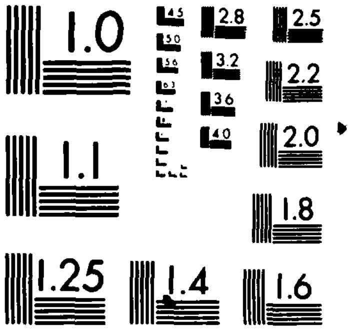

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DEVELOPMENT OF BIODEGRADABLE IMPLANTS FOR USE IN MAXILLOFACIAL SURGERY

Annual Technical Report
Year Five

to

US Army Medical Research and Development Command
Fort Detrick, Frederick, MD 21701-5012

Contract DAMD17-78-8059

SOUTHERN RESEARCH INSTITUTE
2000 Ninth Avenue South
P.O. Box 55305
Birmingham, AL 35255-5305

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I. SUMMARY

This report covers work performed during the fifth contract year on Project 4150, Contract DAMD17-78-8059, "Development of Biodegradable Implants for Use in Maxillofacial Surgery."

The objective of the project is to develop high-strength, bioabsorbable materials useful in the treatment and management of maxillofacial injuries. The specific goal for the current contract year has been the attainment of high-strength, high-modulus, biodegradable fibers for use in the reinforcement of biodegradable polymeric fracture-fixation plates. In studies conducted during the previous years of the project, composites fabricated from poly(DL-lactide) (DL-PLA) and commercially available, non-biodegradable ceramic or carbon fibers were shown to provide sufficient strength and rigidity for use in the repair of mandibular fractures in dogs. Our work during this period has been directed toward the examination of biodegradable ceramics and glasses for the production of biodegradable fibers for use in the construction of totally absorbable fixation-plate appliances.

Initially, we examined two bioabsorbable ceramic powders, β-tricalcium phosphate (β-TCP, whitlockite) and phosphate-free calcium aluminate (CaAl), as potential fiber-forming materials. Fibers of these materials were prepared by wet-spinning mixtures of the materials with two different polymeric binders. Ceramic loading, oxidative pretreatment, coupling agents, and sintering conditions were examined in an effort to improve spinnabililty and fiber properties. We were able to prepare only very weak fibers from both the calcium aluminate material and the β-TCP. The fibers produced from these materials were, in general, highly porous and fragile. Consequently, we turned our research efforts toward the evaluation of calcium metaphosphate (CMP), a bioabsorbable glass, as a fiber-forming material. Fibers of CMP were prepared by pulling from the melt and air quenching. Smooth, uniform fibers were obtained by this procedure. The strength and stiffness of fibers prepared from this material were comparable to those of commercially produced glass fibers. Composites fabricated from (DL-PLA) and CMP fiber exhibited strength and stiffness characteristics approaching those obtained with carbon or alumina-reinforced (DL-PLA) plates.

Optimization studies concentrating on continuous glass-fiber production, animal testing, and composite fabrication and evaluation will be required to achieve a totally biodegradable fixation system for use in mandibular fracture repair.

II. INTRODUCTION

The need for improved methods and materials for the management of severe maxillofacial wounds is well recognized in view of the substantial portion of these received by soldiers in recent conflicts. In its investigations of various approaches to improved surgical methods and patient care, the Army Institute of Dental Research (AIDR) has constantly sought better materials for use in the repair of jaw fractures.

Bone consists of a framework of collagenous fibers, a mineral matrix, which is primarily calcium hydroxyapatite, and a small amount of the polysaccharides. Even though a large portion of the volume of bone is water, bones are hard and tough. Although varying considerably in properties, depending on function, bones commonly have tensile strengths of 6,000 to 20,000 psi and values of modulus of elasticity of 1 to 3 x 10^6 psi. Metals are stronger and stiffer than bone. Most polymeric materials are as strong as bone but more deformable and require fiber reinforcement or crosslinking to equal the stiffness of bone.

Fracture fixation in maxillofacial surgery has traditionally been accomplished by the use of rigid, metallic fixation plates or cribs with metal bone screws used to attach the appliance to the surrounding bone. This method of fixation is less than satisfactory for two reasons: rigid fixation devices, which are of primary importance in the promotion of initial fracture union, may cause cortical bone to atrophy as the healing process progresses, and additional surgical procedures are required for removal after healing is complete, thus increasing surgical cost and patient inconvenience.

Ideally, fixation appliances should vary in stiffness as healing progresses, transferring an increasing proportion of the mastication forces to the mandibular bone as it becomes further ossified. This progressive load transfer ensures that the forming bone is strained and exercised. Both processes are necessary for the formation of healthy hard tissue that has properties commensurate with those of virgin bone. The development of variable-stiffness fixation devices is best accomplished by using a degradable polymer system with degradation products that are nontoxic and harmless to the host. A biodegradable material with properly tailored physical properties and degradation kinetics would ensure the development of strong, healthy bone and eliminate the need for surgical removal of the fixation device on completion of the healing process.

III. EXPERIMENTAL

Our major efforts during the last year were directed toward the development of biodegradable ceramic fibers for incorporation into and reinforcement of DL-PLA-based fracture-fixation appliances. Toward this end we examined the production of β-TCP and phosphate-free CaAl fibers by wet-spinning using two different polymeric resins as binders. As a portion of this phase of the work, we concentrated on the effects of ceramic-powder particle size, oxidative treatment prior to sintering, utilization of dispersing agents, and fiber diameter on the mechanical properties of sintered fibers. Subsequently, we examined the preparation of biodegradable glass fibers from CMP as a means of achieving reinforcement materials for DL-PLA plates.

A. Preparation of Fine-Particle Sized Ceramic Powder

During the previous year's effort, we determined that greater densification on sintering of ceramic articles, whether in pellet, rod, or fiber form, was achieved using powders of finer particle size. Greater densification and the associated reduction in void volume of formed articles resulted in products with greater strength and structural rigidity.

Additionally particles of finer size were required for the production of small-diameter ceramic filaments by the wet-spinning process. Consequently, we began preparing ceramic powders of fine particle size in our own laboratory. A Megapack high-energy vibratory mill(Dynatron; Cincinnati, OH) was used for particle-size reduction. The system employs the use of small-diameter steel balls vibrating at high frequencies for grinding of ceramic powders.

The procedure used to grind ceramic samples to fine particle sizes with this mill was: A slurry of TCP (or phosphate-free CaAl) in water was added to the vibratory mill, and the mill was activated and allowed to run for 4 h. During that time, samples were taken at periodic intervals and examined by scanning electron microscopy (SEM) to determine particle-size range. A milling time of 4 h was found to be sufficient to yield particles in the 1- to 2-µm range. At the end of that time, the slurry was removed from the mill and centrifuged for 30 min at 100 g. The supernatant was decanted, and dimethylacetamide was added to the centrifuge bottle; the contents were then agitated to resuspend the compacted ceramic powder. This process was repeated several times until all of the water was replaced by dimethylacetamide.

The vibratory milling technique allowed us to prepare slurries of ceramic powder in the appropriate polymer solvent both effectively and efficiently. Ceramic particles in this size range were appropriate for use in the wet-spinning of fine diameter filaments.

B. Wet-Spinning of Ceramic Fibers Using Polymeric Binders

During previous work on the project, we examined a number of methods for use in the production of ceramic fibers. Of the approaches examined, fiber production by wet-spinning proved to be the most successful method, and this approach was followed throughout the course of this project year. Simplistically speaking, fiber production by wet-spinning involves extruding a mixture of ceramic powder, binder, and solvent into a trough or bath containing a non-solvent for the binder. During extrusion into the non-solvent bath, the mixture coagulates to form a fiber or filament. The fibers or filaments are subsequently drawn from the coagulating bath using a series of water-flushed, heated godets to rinse and evaporate the remaining solvent. After passing through the rinsing and drying system, the fibers are taken up on a winding reel. The collected fibers are then soaked in distilled water to assure complete solvent removal and are, thereafter, dried in an air-circulating oven to produce the final dried fiber. For the production of fibers from both β-TCP and phosphate-free CaAl, it is necessary to sinter the dried fibers in an inert atmosphere maintained above 1150°C to achieve coalesence and densification of the ceramic particles.

1. Polymeric binders

As a consequence of the elevated temparture required for proper sintering of both of these materials, polymeric binders with superior thermal stability are required for use in the wet-spinning process. Although no resin yet produced is capable of withstanding these temperatures, we chose for examination three highly thermally stable resins which we felt might effectively bind the ceramic powders together in fiber form until preliminary sintering (lower temperature) was achieved. We investigated Barex 210 (Vistron Corp., Chemicals Division, Cleveland, OH), a terpolymer mostly composed of acrylonitrile; Polyacrylonitrile Type A (PAN-A) (Du Pont Wilmington, DE); and Ethocel #1 Standard (Dow Chemical Co., Midland, MI), an ethylcellulose material, as potential binders.

Polyacrylonitrile converts from a linear polymer to a ladder network upon heating in an oxidative environment. We felt that partial conversion of the linear resin to a ladder formation would increase the thermal stability of the resin and allow us to obtain a fiber with improved sintering characteristics. Ceramic fibers were prepared using both Barex 210 and Polyacrylonitrile Type A as binding materials.

2. Oxidative pretreatment

We prepared fibers containing 60 wt % TCP and 40 wt % Barex 210 resin by wet-spinning. Fibers containing 80 wt % TCP were prepared similarly. The coagulated fibers were soaked in tap water/isopropanol for 2 days to remove residual solvent (dimethylacetamide). The fibers were then dried in a vacuum oven for 24 h after removal from the soaking solution. Samples of the dried fibers were placed in an air-circulating oven maintained at 200 °C and removed at 30, 60, and 120 min to effect oxidative pretreatment. Untreated samples of the same fibers were used as controls. Treated and control fibers at both ceramic loadings were then sintered by heating to 1200 °C under a nitrogen purge. The samples were heated over a 4-h period and allowed to cool in the oven overnight. The pretreated fibers appeared coral. Although there were no obvious differences in fragility of samples pretreated for various times, the pretreated samples were in each case less fragile and more easily handled than the control fibers. Samples with the higher ceramic content were somewhat stronger than samples containing a lower ceramic loading.

We repeated the experiment using 250 °C as the oxidative pretreatment temperature. Samples subjected to treatment at this temperature and then sintered under the previously described conditions were weaker than samples that had been treated at 200 °C. Similar results were found when PAN-A was substituted for Barex 210 as a binding material. There was, however, no obvious improvement in sintering characteristics as a result of using the acrylonitrile homopolymer.

3. Dispersing agents

During some wet-spinning trials, we encountered problems with plugging of the in-line filter screen due to clumping of the ceramic particles. We examined the use of some commercially available dispersing agents for

BREAKING STRENGTH OF TRICALCIUM PHOSPHATE FIBERS

Average diameter mm	Breaking strength psi
0.559	169
0.508	353
0.356	69
0.124	419
0.122	477
0.074	1607

preventing clumping and elevating the ceramic loadings achievable with both binder materials. We obtained dispersing agents from Tenneco Chemicals (Piscataway, NJ) and Rohn and Haas (Philadelphia, PA) and evaluated them for compatibility with our systems. Tamol 960 and Tamol SN, both Rohm and Haas products, were incompatible with the solvent used for spinning-dope preparation. Nuosperse HOH and Nuosperse SN, both Tenneco products, were also incompatible. Kromosperse, another Tenneco product, was compatible, and this dispersing agent was used successfully in preventing clumping and improving spinnability.

As a further portion of our work on β-TCP, we examined the influence of fiber diameter on the tensile strength of filaments produced from this material. Spinning dope was prepared using dimethylsulfoxide (DMSO) as the solvent and PAN-A as the binder.

4. β-TCP fibers

TCP powder prepared previously was wet sieved using No. 60 (250-μm) and No. 140 (160-μm) sieves. The fine particle cut was used to make the spinning dope. TCP was mixed with a solution of PAN-A in DMSO to make up the spinning composition. Care was taken to remove any entrapped air bubbles. The final spinning dope consisted of 7.4% TCP, 1.8% PAN-A, and 90.8% DMSO on a weight basis.

We prepared fibers by wet extrusion using a hypodermic syringe and hypodermic needles of various sizes. The needle sizes ranged from 15 G (1.37-mm ID) to 27 G (0.2 mm-ID). Distilled water at room temperature was used as the coagulating medium. The spinning dope was loaded into the syringe barrel, and the tip of the needle was placed below the surface of the coagulating fluid. Pressure was applied until a bead of coagulum formed at the needle's tip. The bead was grasped with a pair of tweezers and pressure was reapplied to the syringe barrel. Fibers were extruded for the length of the coagulating bath. Fibers prepared using the smaller diameter needles were considerably more difficult to extrude than fibers prepared using the larger needles. The extruded fibers were removed form the coagulating bath and placed in another water bath and allowed to soak to remove solvent. After soaking for a sufficient time, the fibers were removed from the bath with tweezers and placed on Teflon sheeting to dry in air overnight. The smaller fibers were easier to handle and exhibited more structural integrity. This was probably due to a higher residual solvent content in the larger fibers.

The fibers were then subjected to oxidative pretreatment to promote the formation of a ladder polymer and enhance the thermal stability of the binder matrix. Pretreatment was accomplished by placing the fibers in an air-circulating oven maintained at 200 °C for 30 min. Pyrex test tubes were used to contain the fibers during the pretreatment process. The fibers changed from white to tan during pretreatment.

After pretreatment the fibers were sintered in a Lindberg Hevi-Duty SB oven. The oven was maintained at 1200 °C and purged with nitrogen for the duration of the sintering cycle. The sintered fibers were light yellow. After sintering, some of the fibers shrank to less than 40% of their original diameter.

The fibers were tested for breaking strength on an Instron Model TMS Serial 72 testing machine. The fibers were prepared for testing by mounting on cardboard tabs. The finest fibers were attached to the tabs with paraffin, and the larger fibers were attached with sealing wax. After being tested, the samples were removed from the Instron, and the diameter at the fracture point was determined with a micrometer. The fracture surfaces were then examined by SEM. The test results are presented in the table. There is a dramatic effect of fiber diameter on tensile strength. As fiber diameter decreases, the strength increases. Such behavior is commonly found in the preparation of ceramic fibers. Results shown in the table reflect the average of test results for five specimens of each fiber diameter. One sample of the smallest diameter fiber had a tensile strength of 2500 psi. SEM photos showed voids and irregularities at the fracture surface of all specimens. In general, larger voids were associated with lower breaking strength, reflecting the stress-concentrating effects of the irregularities.

5. CaAL fibers

Fibers of phosphate-free calcium aluminate were prepared following the procedures used for β-TCP fiber production and using the same solvent and binder. After sintering, the fibers were so fragile that they could not be removed from the oven without breaking.

Calcium aluminate (Pfaltz & Bauer, Inc., Stamford, CT) was used to prepare the fibers. X-ray diffraction analysis revealed that the powder consisted of $CaAl_2O_4$ but also contained significant amounts of Al_2O_3 and $Ca_{12}Al_{14}O_{22}$. The CaAl was dry sieved through a No. 100 sieve (150-μm) to break up any clumps and remove any large particles.

The spinning dope had a ceramic-to-binder ratio of 80:20 and consisted of 25% CaAl, 6% PAN-A, and 69% DMSO. Fibers were extruded from a hypodermic syringe and needle, as were the TCP fibers. Needle sizes 15 G through 25 G were used to form fibers. The 27-G needle proved to be too fine for the CaAl dope. The fibers were coagulated in a tap-water bath at ambient temperatures. The coagulated fibers were quite rigid and easier to handle than the TCP fibers at this stage. The fibers were dried at ambient conditions overnight. Oxidative pretreatment was performed in a circulating-air oven at 200 °C for 30 min. Prior to oxidation, the fibers were white. After oxidation the fibers turned brown. The fibers were then placed in an oven under a nitrogen purge, heated at 1200 °C, held for 1 h, and allowed to cool overnight. When the fibers were removed from the oven, they were found to be so fragile that they could not be removed without breaking.

C. Examination of Biodegradable Glasses for Fiber Production

Due to the relative lack of success in producing β-TCP and phosphate-free CaAl fibers with mechanical properties adequate for fixation-plate reinforcement, we investigated absorbable glasses as an alternative to ceramic materials for biodegradable-fiber production.

1. Bioglass fibers

As a preliminary step in this program, we investigated the fiber-forming properties of Bioglass, a partially biodegradable glass composed of ≈45% silicon dioxide. Various metallic oxides make up the rest of the material. We familiarized ourselves with the procedures for forming glass fibers from the molten state using this material while we awaited arrival of a shipment of CMP, a completely absorbable glass material.

We attempted to prepare fibers from the Bioglass by heating the material in a crucible until it became molten (≈900 °C) and withdrawing filaments with a stainless steel rod. We were successful in preparing fibers by this procedure, but there was considerable variation in both fiber diameter from sample to sample and uniformity of diameter throughout the length of a given sample. Samples of the glass fibers were mounted and tested in the same manner as the ceramic fibers. Breaking strength of the glass fibers varied from 9,000 to 50,000 psi. This variation was to be expected in view of the lack of uniformity from one sample to the next. However, the formation of fibers with high tensile strengths was most encouraging.

2. CMP fibers

We subsequently received our shipment of CMP and began examining the fiber-forming properties of this material. The apparatus for producing glass fibers consisted of a bench-top furnace with a maximum temperature of 1000 °C, an oxygen/natural-gas torch with a stand, a ring stand and clay triangle (to support a crucible), an alumina or platinum crucible, and a metal rod to pull fibers from the melt.

CMP was placed in a crucible and heated in a furnace at 1200 °C to achieve a molten state for fiber formation. Initially, we were unable to melt the material at this temperature. We felt that this was due to impurities in the material as it was supplied, and we searched the literature to find a purification method.

We found that US Patent No. 4,049,779 gave a process for making high-purity CMP for use in glass making. We followed this procedure to obtain CMP of sufficient purity for fiber formation. One liter of a 3-molar solution of phosphoric acid was prepared. One hundred grams of $CaCO_3$ was then slowly dissolved in the acid solution. Impurities were removed by precipitating with 2.5 g of ammonium 1-pyrrolidine dithiocarbamate dissolved in 50 mL of water. The resulting grey precipitate was then filtered out. The supernatant was concentrated by evaporation, and the pure CMP was precipitated. The precipitate was filtered out and washed with acetone to remove any residual phosphoric acid.

CMP produced by this method could be easily melted at 1000 °C, and fibers were readily prepared by pulling from the melt. The average initial breaking strength of fibers produced in this manner was 51,000 psi, with one sample exceeding 110,000 psi. The average diameter of these samples was 0.028 mm. Subsequent measurements of elastic modulus gave values averaging roughly 5×10^6 psi.

D. Evaluation of Biodegradable Composites

Composite samples were fabricated for preliminary evaluation using these fibers and DL-PLA. Fabrication procedures were the same as those procedures used earlier for composites that were not totally biodegradable. Three-point bending tests were conducted on these samples, and we found flexual moduli of 4 to 5 x 10^6 psi. These values compare favorably with the volues of strength and modulus, 15 to 50 x 10^3 psi and 1.5 to 5.8 x 10^6 psi, respectively, obtained with composites employing commercially available ceramic or carbon fibers for reinforcement.

E. Preparation of Crosslinkable Biodegradable Polymers

The lack of success in preparing ceramic fibers with high tensile strength and modulus prompted us to re-examine cross linkable biodegradable resins as an alternative means of achieving initially strong and rigid fixation plates. We approached the preparation of a readily crosslinkable polymer of DL-lactide by two different methods. The first method involved the preparation of copolymers of DL-lactide with glycidyl methacrylate. If successful, these copolymers would contain pendant acrylic unsaturation. The second method involved the preparation of DL-PLA with reactive hydroxyl end groups. If this procedure were successful, it should then be possible to prepare crosslinked polymer though the addition of poly-functional hydroxyl-terminated materials using difunctional isocyantes or other materials or end linking reagents.

1. Synthesis of poly(DL-lactide-co-glycidyl methacrylate)

The most versatile method of crosslinking polymeric materials is by free radical addition. Systems utilizing this method of crosslinking have extreme versatility in that they can be compounded, preformed into a variety of shapes by various processing methods, stored for long periods, and finally cured over a broad range of temperatures very rapidly. To crosslink a material by this technique, it is desirable to have unsaturation present either in the polymer backbone or pendant to it.

Very few materials are available that can be incorporated into the cationic addition reaction leading to DL-PLA. One material that we have identified as a possible candidate is glycidyl methacrylate. Glycidyl methacrylate has two different available reactive sites. There is acrylic unsaturation and an epoxide ring. Under certain conditions, it is possible to polymerize epoxides and cyclic ethers by ring-opening cationic polymerization techniques. Because DL-PLA is prepared by cationic ring-opening techniques, it might be feasible to prepare copolymers of these two materials if the proper reaction conditions can be determined.

In our first experiment (B469-3), we charged 45.5 g of DL-lactide to a dried 300 mL, three-neck, round-bottom flask. The flask was fitted with a stirrer and a gas-inlet tube. The flask was connected to a nitrogen purge and was lowered into an oil bath at 140 °C. After the monomer had completely melted, 4.5 g of glycidyl methacrylate was added to the molten lactide with a syringe. The monomer mixture was stirred, and 19 μL (0.025 g) of stannous octoate was introduced as a catalyst. The polymerizate became too viscous to stir within 5 min after introduction of the catalyst. Heating was continued for a total reaction time of 2 h, and the flask was removed from the oil bath. The polymer was allowed to cool under nitrogen. The polymer was then dissolved in methylene chloride and precipitated into methanol. The precipitate was removed and dried under vacuum. A small quantity of the dried sample was mixed with a small quantity of azobisisobutyronitrile in a petri dish and heated on the surface of a hot plate. The crosslinking reaction was apparent in that the material initially became molten and then solidified to an infusible mass. A small portion of the crosslinked material was then placed into a vial containing methylene chloride. After standing overnight, the sample did not redissolve. This was further evidence that crosslinking had occurred.

Samples of the initial polymer were submitted for infrared (IR) and nuclear magnetic resonance (NMR) spectroscopy. We hope to be able to obtain meaningful information regarding the molecular structure of the sample from these analyses. Additional experimental work can be planned once more information on the polymer structure is obtained.

2. Synthesis of hydroxyl-terminated DL-PLA

If DL-PLA can be synthesized with reactive functional end groups such as hydroxyl, crosslinking would also be possible by reaction with other polyfunctional materials like polyfunctional isocyanates. Based on an assumed cationic reaction mechanism for DL-PLA initiated with glycols, it is feasible that we should be able to prepare DL-PLA with terminal reactive hydroxyl functional groups.

During this reporting period, we prepared 100 g of a DL-PLA diol with theoretical molecular weight of 2000 by initiation with ethylene glycol. The polymerization was the same as that described above except that 97 g of DL-lactide and 3 g of ethylene glycol were charged to a predried 300-mL, round-bottom flask. The flask was heated for 30 min under a nitrogen purge in an oil bath at 140 °C to melt the lactide prior to adding 38 μL (0.05 g) of stannous octoate catalyst. The reaction was allowed to continue an additional 2 h at 140 °C. The flask was then removed from the oil bath and allowed to cool under nitrogen. The polymer (Sample B469-9) was dissolved in methylene chloride and held for later crosslinking trials.

3. Synthesis of polyfunctional lactide adducts

The hydroxyl-terminated DL-PLA described in Section 2 above should be crosslinkable by reaction of the end groups with polyfunctional isocyanates providing the material is hydroxyl terminated. A convenient method of preparing a polyfunctional isocyanate compound is to react an excess of a diisocyanate with a polyhydroxylated material such as a carbohydrate or a carbohydrate/lactide adduct. We felt it desirable to attempt synthesis of a carbohydrate/lactide adduct for this purpose to assure absorbable biodegradation products.

During this reporting period, we prepared the addition product of erythritol, a quadrafunctional carbohydrate, with DL-lactide (B469-11). The reaction was carried out in the same manner as described above for the preparation of the hydroxyl-terminated DL-PLA. A total of 50 g of material was prepared by reacting 41.3-g DL-lactide with 8.7 g of DL-erythritol in the presence of 19 L (0.025μg) of stannous octoate at 140 °C for 2 h. The product was an amber amorphous gum. It was dissolved in methylene chloride and stored for later experimental trials as a crosslinking agent. Work on the synthesis of crosslinked resins was discontinued once we initiated our experimental work on biodegradable glasses.

IV. CONCLUSIONS AND RECOMMENDATIONS

During the past project year, we have demonstrated the feasibility of wet-spinning bioabsorbable ceramic fibers, producing of biodegradable glass fibers by pulling from the molten state, and utilitzing of biodegradable glass fibers for the fabrication of totally bioabsorbable fracture-fixation plates. We found that neither β-tricalcium phospate or phosphate-free calcium aluminate formed fibers of sufficient strength and stiffness for use in fixation-plate reinforcement. Calcium metaphosphate, however, was readily prepared in fiber form and was adequate for use in composite fabrication. Composites prepared using this material were comparable in strength and rigidity to fixation plates prepared previously using commercially produced ceramic and carbon fibers. It is our opinion that biodegradable glass fibers offer significant promise over biodegradable ceramic fibers for the reinforcement of DL-PLA plates. The most notable problem associated with the production and in vivo use of biodegradable ceramic fibers lies in the area of densification. Densification of wet-spun fibers is difficult to achieve and, without this densification, it would be impossible to obtain fibers with the strength and modulus required for use in fracture-fixation appliance reinforcement. However, high densification of ceramic materials of this type also leads to degradation times far in excess of those times required for a biodegradable mandibular crib or fixation plate. Densification and absorption are not problems with calcium metaphosphate glass fibers.

Preliminary evidence indicates that DL-PLA plates reinforced with calcium metaphosphate glass fibers will, with optimization, provide totally biodegradable fracture-fixation plates suitable for use in the repair of mandibular fractures. Further work is needed, however, in evaluating the biocompatibility of the glass fibers and the composites fabricated therefrom. Additional in vitro and in vivo work is needed to identify clearly the degradation rates and reduction of mechanical properties of the devices due to this degradation. More clinical work is needed to demonstrate the efficiency of the composite plates for use in the repair of experimental fractures in an animal model. With further effort in these areas, we feel that we will be able to fabricate and provide to the Army totally biodegradable fracture-fixation appliances suitable for use in maxillofacial surgery.

V. ACKNOWLEDGMENT

Mr. Joseph J. Forbes, Associate Engineer, and Mr. James P. English, Senior Chemist, have been instrumental in carrying out various phases of the experimental work. Mr. W. Curtis Stoner assisted in the preparation of ceramic fibers.

Submitted by:

Robert A. Casper
Robert A. Casper
Head, Biomaterials Section

Approved by:

Richard L. Dunn
Richard L. Dunn
Head, Polymer Division
Principal Investigator

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