Published in final edited form as:

J Biomed Mater Res B Appl Biomater. 2012 October ; 100(7): 1764–1772. doi:10.1002/jbm.b.32743.

Microencapsulation of 2-octylcyanoacrylate tissue adhesive for self-healing acrylic bone cement

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Abstract

Here, we report the first phase of developing self-healing acrylic bone cement: the preparation and characterization of polyurethane (PUR) microcapsules containing a medical cyanoacrylate tissue adhesive. Capsules were prepared by interfacial polymerization of a toluene-2,4-diisocyanate-based polyurethane prepolymer with 1,4-butanediol to encapsulate 2-octylcyanoacrylate (OCA). Various capsule characteristics, including: resultant morphology, average size and size distribution, shell thickness, content and reactivity of encapsulated agent, and shelf life are investigated and their reliance on solvent type and amount, surfactant type and amount, temperature, pH, agitation rate, reaction time, and mode of addition of the oil phase to the aqueous phase are presented. Capsules had average diameters ranging from 74 to 222 μm and average shell thicknesses ranging from 1.5 to 6 μm . The capsule content was determined via thermogravimetric analysis and subsequent analysis of the capsules following up to 8 weeks storage revealed minimal loss of core contents. Mechanical testing of OCA-containing capsules showed individual capsules withstood compressive forces up to a few tenths of Newtons, and the contents released from crushed capsules generated tensile adhesive forces of a few Newtons. Capsules were successfully mixed into the poly(- methyl methacrylate) bone cement, surviving the mixing process, exposure to methyl methacrylate monomer, and the resulting exothermic matrix curing.

Keywords

self-healing; microencapsulation; bone cement; cyanoacrylate; biomaterial

INTRODUCTION

The terms “healing” and “biomaterials” are most commonly linked through the tissue response to the presence of an implant.¹ Ratner has coined the expression “biomaterials that heal” to describe biomaterials that actively promote wound healing as opposed to those aimed at passivity or inertness.² Although the biology and chemistry of healing have significant impacts on biomaterial performance, biological healing does not address the

physical repair of biomaterials that experience mechanical and chemical breakdown as they are subjected to loading and degradation effects *in vivo*. Developing synthetic biomaterials with the intrinsic ability to autonomously repair mechanical and chemical damage is particularly important for implants that replace tissues also capable of self-repair.^{3,4}

Self-healing materials are a rapidly emerging class of composites with applications intended for use in the civil, mechanical, electrical, and aerospace industries. These materials hold the potential for significantly extending material lifetimes by preventing and repairing failures caused by accumulated microdamage due to microcrack formation. To date, the majority of the research conducted on self-healing bulk materials has used composites, adhesives, and cements intended for traditional engineering applications.^{5–12} The most broadly reported self-healing scheme is that pioneered by White and Sottos et al. in which a polymer matrix is coembedded with a catalyst and microcapsules containing a reactive healing agent. Once encountered by a propagating microcrack, the capsule shell ruptures, releasing the healing agent into the crack plane and exposing it to the catalyst embedded in the matrix. *In situ* curing of the healing agent ensues, halting crack propagation.^{5–7,13–16}

The fixation of total joint replacements with acrylic bone cement is used in hundreds of thousands of patients each year.¹⁷ Poly(methyl methacrylate) (PMMA) bone cement is a space-filling matrix that forms mechanical interlocks between the stem of the implant and the surrounding bony tissue.^{18,19} Bone cement consists of two components: low molecular weight PMMA powder containing an initiator (e.g., benzoyl peroxide) and liquid methyl methacrylate monomer. Mixing the two components *in situ* forms a slurry that initiates polymerization yielding a workable dough that is applied to the implant and hardens into a solid mass after the implant is inserted into the bony tissue.¹⁸ Although broadly successful, cemented implants are subject to failure following prolonged exposure to the harsh environment of the body as well as the cyclic loading patterns seen *in vivo*. Microcrack formation and the generation of wear debris from both the articulating surfaces and the bone cement itself serve to accelerate wear that often leads to subsequent failure of the implant.^{17,20–24}

Because of its long history of use, lack of postpolymerization modifications, and need for improvement, the development of a self-healing PMMA bone cement is a very attractive option for the first self-healing biomaterial designed with the aforementioned embedded capsule and catalyst approach. However, none of the existing self-healing systems are suitable for *in vivo* deployment due to reagent toxicity and/or inability to cure under aqueous conditions. The production of a clinically acceptable PMMA-based acrylic bone cement containing a microencapsulated non-toxic healing agent is a logical starting point.

2-Octylcyanoacrylate (OCA) tissue adhesive is water-reactive, FDA-approved, and currently used in sutureless surgeries and external wound closure systems^{16,25} and is therefore a strong candidate for the biocompatible monomer healing agent in a self-healing biomaterial. By selecting OCA as the healing agent of interest, the aforementioned self-healing material design is simplified because no catalyst will need to be embedded within the material matrix; the released cyanoacrylate would be polymerized by ambient moisture permeating the bone cement matrix from the surrounding tissue.

Polyurethane (PUR) is widely used in biomaterials due to its blood compatibility and its ability to be engineered to have a wide range of mechanical properties through the selection of various soft and hard segments.^{26–29} PUR capsules have been previously generated via interfacial polymerization of a variety of isocyanates and polyols using numerous emulsion characteristics. Encapsulated agents include pesticides,^{30,31} oils and organic solvents,^{32–37} drugs and proteins such as ibuprofen, ovalbumin, and isoniazid,^{38–40} and various dyes.²⁸ Microcapsules of toluene-2,4-diisocyanate (TDI)-based PUR have been shown to be both robust and capable of containing a water-reactive monomer for self-healing applications,⁴¹ which we found attractive.

In this study we present the first phase of the development of a self-healing PMMA bone cement: the encapsulation of OCA within PUR microcapsules. The average capsule size and size distribution, capsule shell thickness, content and reactivity of encapsulated agent, and shelf life of these capsules were studied and preliminary experiments have been performed to incorporate these capsules into a bone cement matrix to assess their process survivability for future testing of a biocompatible self-healing composite.

EXPERIMENTAL

Materials

Unless otherwise specified, materials were obtained from commercial suppliers and used without further purification. OCA was generously donated by Ethicon, Raleigh, NC 27616. Acetone, methyl ethyl ketone (MEK), diethyl ketone (DEK), methyl isobutyl ketone (MIBK), and cyclohexanone (Sigma Aldrich) were used as solvents and TDI and 1,4-butanediol (1,4-BD) (Sigma Aldrich) were used to synthesize the polyurethane prepolymer (pPUR) following the protocol outlined by Yang et al.⁴¹ Pluronic F-68 (Sigma Aldrich) was used as a surfactant. Para-toluenesulfonic acid monohydrate (Sigma Aldrich, PTSA) was added to the organic phase as a monomer stabilizer. Commercially available bone cement (Biomet Cobalt G-HV High Contrast bone cement) was used in the preliminary bone cement matrix experiments.

Preparation of polyurethane prepolymer

A TDI prepolymer was prepared for use in the microencapsulation procedure by scaling up the protocol reported by Yang et al.⁴¹ Briefly, TDI (109.25 g) was dissolved in cyclohexanone (750 mL) in a three-necked round bottom flask. The mixture was suspended in an oil bath at 80°C and agitated with a magnetic stirrer. 1,4-BD (20.315 mL) was slowly added to the stirring TDI/cyclohexanone solution at a rate of 2 mL/min and then the flask was purged with N₂ and allowed to react for 24 h. Following this reaction time, the mixture was distilled at 100°C under vacuum for 4–5 h to remove the excess cyclohexanone, water, and TDI from the system. A viscous yellow pPUR remained in the flask following the completion of this process. Gel permeation chromatography analyses were performed with a Varian Prostar Model 210 pump, a Varian Prostar Model 320 UV/Vis detector set to 254 nm detection, a Wyatt Dawn EOS multiangle light scatterer, Wyatt QELS (quasi-electric light scattering), Wyatt Optilab DSP Interferometric Refractometer (RI), and a series of two Agilent Technology PL gel columns [7.5 × 300 mm², 1 79911GP-503 (10³ Å) and 1

79911GP-504 (10^4 Å)] in tetrahydrofuran at 22°C. Molecular weights were calculated using a dn/dc value of 0.108 mL/g calculated from solutions of known concentration using the dn/dc calibration mode of the Wyatt Technology ASTRA software version 5.3.2.16. The polydispersity index of the prepolymer was found to be 1.23, which was comparable to the value of 1.33 reported by Yang et al.⁴¹

Preparation of microcapsules

At room temperature, Pluronic F-68 surfactant (1.84 g) was dissolved in deionized water (90 mL) in a 250-mL beaker. The solution was agitated for 1 h with a digital mixer (VWR PowerMax Elite Dual-Speed Mixer) before beginning the encapsulation procedure. The aqueous phase was suspended in a hot water bath and heated to 40°C before the addition of the organic phase and chain extender.

To prepare the organic solutions, the pPUR (3 g) was dissolved in MEK (10 mL) at room temperature. OCA (4 mL) was dissolved in MIBK (8 mL) separate from the pPUR solution. PTSA (1%) was dissolved in the MIBK phase to further stabilize the OCA monomer. The pPUR and OCA solutions were added simultaneously to the aqueous phase but not mixed prior to this addition. After the organic and aqueous phases were combined, 1,4-BD (3 mL) chain extender was added dropwise to the stirring mixture via a syringe to form the segmented PUR shell material consisting of hard TDI-based segments and soft 1,4-BD segments. After a reaction time of 2 h, the agitator was switched off, the suspension of microcapsules rinsed with deionized water, and vacuum filtered.

Characterization of microcapsules

Capsule morphology, size, and shell thickness—A vacuum sputter coater (Denton Desk IV) was used to deposit a 10 nm layer of gold onto the microcapsule samples for scanning electron microscope (SEM) imaging. The surface morphology of the capsules was examined and average capsule diameters and shell thicknesses were also measured.

Characterization of capsule content and reactivity—Following the vacuum filtering and drying of the capsules, samples were taken and examined under a stereoscope (Bausch & Lomb). Capsules were sliced open with a scalpel and release of their liquid contents observed. Capsules were then crushed between two glass coverslips to qualitatively assess their bonding ability.

Thermogravimetric analysis (TGA; TA Instruments Q500 v6.7) was used to quantitatively analyze the capsule contents as well as the shelf life of the capsules. Small amounts (<10 mg) of each sample were heated from 25 to 650°C at a rate of 10°C/min under N₂ environment until all the material was vaporized. Comparisons were made between the decomposition rates of pure PUR shell, pure OCA healing agent, pure MIBK solvent, and capsules containing healing agent fabricated under various conditions to approximate the content of the capsules. Samples were also tested after various storage times to assess capsule shelf life.

Compression testing of microcapsules—The compressive strength of single microcapsules was measured using a dynamic mechanical analyzer (DMA; TA Instruments RSA-G2 solid analyzer). This approach was adapted from a procedure described elsewhere^{41,42} that used a single capsule compression apparatus to examine the mechanical response of microcapsules. A single capsule was placed on the lower DMA compression plate and the presence of a single capsule on the testing plate was verified by performing sample loading under a stereoscope. Displacement of the upper DMA plate was applied at a constant rate of 5 $\mu\text{m/s}$ until shell compressive failure was observed.

Adhesion testing of crushed microcapsules—Microcapsules containing OCA were crushed between two aluminum plates (8 mm diameter) using a Tinius Olsen 1000 Universal Testing Machine. The contents were allowed to cure at room temperature for 1.5 h, thus gluing the plates together. The detachment force necessary to break the bond between the upper and lower plates was recorded. The adhesive forces measured for Loctite Super Glue (ethyl 2-cyanoacrylate), monomer OCA, monomer OCA dissolved in MIBK, crushed empty capsules, and crushed empty capsules manually mixed with OCA were used as negative and positive controls.

Incorporation of capsules into a PMMA matrix—Biomet Cobalt G-HV High Contrast bone cement kits were obtained from the Duke University Medical Center. The powder component of the bone cement (10 g) was mixed with the liquid monomer (4.7 g) according to the manufacturer's instructions. PUR capsules (1 g) were added to the PMMA dough and vigorously stirred to disperse the capsules within the matrix material. The cement dough was shaped into small disks and cured for 1 h. Small samples of the resulting composites were broken from the polymerized disks and analyzed under a stereoscope as well as via SEM to visualize the embedded capsules and estimate the fraction that remained intact.

RESULTS

Reaction conditions

Organic solvents—Numerous solvents have been used in PUR microcapsule formation to encapsulate drugs, pesticides, oils, organic solvents, and various dyes.^{35,36,41,43} Several organic solvents were considered for the organic phase. The majority of these solvents were eliminated either because they failed to dissolve the pPUR (octanol, valeric acid, hexane, cyclohexane, butanol, toluene, dichloromethane, ethyl acetate, xylene, and ethyl ether) and/or had toxicity concerns (chlorobenzene, cyclohexanone, and tetrahydrofuran). Acetone and acetic acid were eliminated for being too miscible with water. Following these broad solvent eliminations, only MEK, DEK, and MIBK remained from the original group of potential solvents. MIBK was selected as the solvent for OCA and PTSA because its solubility in water is lower than that of MEK and DEK. However, the pPUR was not soluble in DEK or MIBK; therefore, MEK was selected as the solvent for pPUR.

Surfactants—Several emulsifying surfactants were also considered.^{38–40} Tergitol NP-10, Myrj 52, Brij 52, Tween 20, Tween 65, sodium dodecyl sulfate, and poly(styrene-*co*-maleic

anhydride) were eliminated because they were unable to create a stable emulsion, resulting in a solid mass of polymer. Poly(vinyl alcohol) resulted in the formation of capsules, but was eliminated because it appeared to react with the OCA monomer. Gum arabic was eliminated because it resulted in the formation of both capsules and solid spheres. Pluronic F-68 was selected because it consistently yielded spherical capsules of uniform size, density, and smooth surface morphology.

Temperature—Reactions performed at room temperature (25°C) and 40°C produced capsules with similar spherical morphology and smooth capsule characteristics, however, increased temperature resulted in decreased average diameter and narrower capsule size distribution ($342 \pm 99 \mu\text{m}$ at 25°C vs. $220 \pm 74 \mu\text{m}$ at 40°C at 500 rpm agitation rate). Reactions performed at 70°C yielded a polymer mass within the reaction vessel rather than capsules. A reaction temperature of 40°C was selected because smaller capsules are more ideal when considering the effects of their inclusion on the mechanical properties of the matrix. Furthermore, the increased temperature should serve to enhance the rate of interfacial polymerization.

Controlling reactivity of OCA—The reactivity of the OCA was reduced by adding 1% PTSA to the organic phase. PTSA dissociates into H^+ and a tosylate anion that is stable with the OCA monomer and should not initiate anionic polymerization. The addition of PTSA eliminated the formation of residual polymer seen on the blades of the agitator, enhanced the adhesion of capsules crushed between two glass slides, and resulted in capsules that were 15–25% smaller than those made without PTSA.

To minimize interactions between the OCA and the pPUR before encapsulation, separate organic pPUR and OCA solutions were prepared and added to the aqueous phase simultaneously at the same rate using 25-mL pipettes. This mode of addition resulted in increased uniformity of the size, shape, and surface morphology of resulting capsules.

Effect of agitation rate

The average diameters of the microcapsules were measured for a range of agitation rates (impellor speed of 350–1100 rpm) while all other reaction conditions were held constant. Figure 1(A) is a double-y plot of microcapsule diameter and shell thickness as a function of agitation rate. Similar results were also reported for urea-formaldehyde capsules containing dicyclopentadiene⁴⁴ and PUR capsules containing isophorone diisocyanate.⁴¹ Increasing agitation rate from 350 to 1100 rpm decreased the average capsule diameter from 222 ± 56 to $74 \pm 19 \mu\text{m}$, and decreased the capsule shell thickness from 6.3 ± 2.6 to $1.6 \pm 0.5 \mu\text{m}$, although both appeared to reach asymptotes with increasing agitation rate (numbers given as average $\pm$ one standard deviation of at least 200 diameter and 15 shell thickness measurements). Figure 1(B) is an SEM image of microcapsules made at 700 rpm. The ratio of shell thickness to shell diameter also remained remarkably consistent from 350 to 1100 rpm, ranging from 0.01 to 0.02.

Capsule thermal properties

TGA was used to determine the composition of the OCA-containing PUR microcapsules by comparing the thermal properties of the intact microcapsules made at various agitation rates with samples of the pure OCA monomer, pure MIBK solvent, and pure PUR shell wall material. Figure 2(A,B) presents the weight loss and derivative of weight loss for these samples at increasing temperatures. MIBK and OCA showed sharp vaporization curves, with samples completely vaporized by 78°C and 255°C, respectively. The pure PUR shell wall material and OCA-containing microcapsules demonstrated more prolonged and multiphased vaporization curves. The pure shell material rapidly loses about 50% of its weight between 200 and 325°C, whereas the remainder was lost more gradually between 325 and 650°C. These two distinct phases may be attributed to the degradation of the PUR soft (1,4-BD) and hard (TDI) segments, respectively.

The TGA graphs of the weight loss and derivative weight loss of OCA-containing microcapsules fabricated at agitation rates ranging from 350 to 1100 rpm are also shown in Figure 2(A,B). Note that these traces exhibit the same multiphasic behavior of the pure shell material, but are initiated at lower temperatures due to the presence of core OCA material. The weight percentages of the core and shell components in the various capsule types were estimated based on analysis of the TGA data as described previously.⁴¹ Figure 3 shows the weight percentages of MIBK, OCA, and PUR shell for the intact capsules as a function of agitation rate. The OCA content in the core decreased from 58% in capsules made at 350 rpm to 46% in capsules made at 1100 rpm, while the shell content increased correspondingly from 37 to 47%. Note, the presence of MIBK was consistently less than 7% in capsules made at all agitation rates.

Figure 4 shows the TGA curves of OCA-containing microcapsules made at 700 rpm that were stored at room temperature for up to 8 weeks in sealed glass scintillation vials. A 4.9% reduction in the core content was observed over a 14-day storage period with a total reduction of 6.6% seen following 56 days of storage.

Capsule mechanical properties

Stress-strain curves of individual OCA-filled microcapsules compressed at constant rate of 5 $\mu\text{m/s}$ are shown in Figure 5. For all samples, the load increased monotonically in response to a constant compression rate until reaching failure at a maximum load. The inset is an SEM image of a typical compression-failed microcapsule postfracture. The largest and thickest walled microcapsules showed the greatest malleability, and the thinnest shelled capsules demonstrated the lowest compressive strength. Normalizing the DMA data shown in Figure 5 to microcapsule equatorial cross-sectional area yields the compressive strengths listed in Table I. As both the shell and liquid contents contribute to the mechanical properties of the capsules, variations in the percent fill of the capsules could play a significant role in the maximum loads that can be borne by those capsules and account for some of the observed variability. An increase in microcapsule stiffness with increasing compression rate used during testing was also observed (data not shown), possibly due to viscous contributions from the fluid-filled core. A decrease in the strain at failure was also observed in capsules fabricated at higher agitation rates.

To quantify the adhesive properties of the encapsulated healing agent, capsules fabricated at 700 rpm were crushed between two aluminum plates. The detachment force necessary to separate the bonded upper and lower plates is presented in Table II for microcapsules along with values for the pure adhesive positive controls and empty capsule negative controls. Crushed empty microcapsules showed no detachment force, whereas crushed OCA-containing microcapsules exhibited nearly the same detachment force as crushed empty capsules manually mixed with adhesive, but considerably less detachment force than the adhesives alone.

Incorporation of capsules into a PMMA matrix

OCA-filled microcapsules fabricated at 500 rpm were added to Biomet Cobalt G-HV High Contrast bone cement and mixed, cast, cured, and fractured as described above. Figure 6(A) shows an SEM image of intact microcapsules distributed throughout the PMMA matrix. The crack plane of a PMMA specimen containing 30 wt % capsules is shown in Figure 6(B); capsules fractured by the damage event are clearly visible in this plane as well as in Figure 6(C), a magnified SEM image of a ruptured microcapsule. A scan of fractured planes indicates that roughly 40% of the capsules remained intact following the damage event.

DISCUSSION

The OCA-containing PUR capsules described here represent a new embedded catalyst-free self-healing system with biomedical applications. The optimization of the encapsulation protocol relied on the identification of the proper emulsion conditions with respect to variables such as solvent, surfactant, and temperature. The primary concerns were improper solvent miscibility, insufficient stability of the o/w interface, interaction between the OCA and other emulsion components, and reaction temperature. Although a number of options were considered and investigated, the final conditions using MEK and MIBK as solvents, Pluronic-F68 as the surfactant, and a reaction temperature of 40°C were selected.

The average diameter of the microcapsules was influenced by various factors including the fluid mechanics associated with the mixing apparatus, viscosity of the emulsion, the characteristics of the surfactant used, the agitation rate, and the temperature of the emulsion.⁴¹ As the agitation rate was increased, the oil phase was emulsified into smaller droplets on its introduction to the aqueous phase. Variability in capsule contents was observed although most can be attributed to variations in solvent content. Capsules were all tested day 1 postfabrication and were thoroughly dried before all TGA procedures were performed so losses in weight at less than 78°C are most likely due to loss of MIBK rather than loss of surface moisture; the change in weight between 78 and 100°C was minimal in capsules made at all agitation rates, suggesting little to no water is present in or on the capsules at day 1. Differences in the shell content of the capsules determined from TGA (Figure 3) correlated with the small variations in the ratio of shell thickness to capsule diameter for capsules made at higher agitation rates; that is, the slightly higher t/d values for capsules made at 900 and 1100 rpm (0.02 vs. 0.01) indicate that a larger weight percent of those capsules is composed of shell material.

It is interesting to note that at 110°C, the upper end of the PMMA polymerization exotherm,⁴⁵ there is little mass loss seen in capsules with low MIBK content (500 and 900 rpm), indicating that capsules will survive the temperatures associated with matrix polymerization [Figure 2(A)]. This observation was later supported by the successful incorporation of the capsules into a PMMA matrix (Figure 6). However, temperature is not the only factor that will come into play when assessing the process survivability of the capsules¹⁶ and these observations merely confirm the feasibility of the material design concept.

To be implemented successfully, these capsules must retain their self-healing capability for a significant percentage of the lifetime of the implant. Even though TGA data showed a 4.9% decrease in core content over 2 weeks of storage time, this could be partially attributed to the diffusion and subsequent evaporation of MIBK through the capsule shell. At day 14, only 0.4% of capsule weight was lost prior to 78°C, bolstering the hypothesis that solvent evaporation is the main cause in the decrease of capsule core content during that time frame. Testing of the capsules after 56 days dry storage indicates minimal change in the capsules over that time as a majority of the MIBK evaporated during the first 2 weeks of storage. The rightward shift in the TGA curve over time could be explained by slow polymerization of the encapsulated OCA monomer by infiltrating moisture. In a previous study, Yang et al.⁴¹ reported a loss in core contents of 7.9 and 8.6 wt % of PUR capsules containing isophorone diisocyanate following 3 and 6 months storage. The decreases presented here are comparable to these rates of mass loss. Future TGA analysis will be performed to determine if the loss of core material continues to be marginal over longer storage times. Shelf life studies following capsule storage in water, an environment more relevant for this application, are also underway.

Other groups have reported single microcapsule compression testing using a modified load frame^{41,42} to gather information on the mechanical properties of the shell material. In this study, compression testing showed the larger microcapsules to be more malleable; the compressive stress also decreased with decreasing shell thickness. The strain at failure decreased with increasing agitation rate and increasing PUR content, suggesting the OCA core contributes to the malleability of the capsules. Loads born by smaller microcapsules made at 900 and 1100 rpm were very similar (Figure 5) as expected given the similarities between the average diameters and shell thicknesses of microcapsules made at these rates.

Bulk PUR elastomers typically show MPa strengths and stiffnesses;⁴⁶ however, there is some uncertainty in the literature about how to calculate single microcapsule strength and stiffness. When normalized to equatorial shell cross-sectional area only, as reported previously,⁴¹ our microcapsules showed GPa strengths and stiffnesses, which are extremely high for an elastomer such as 1,4-BD-extended TDI. When normalized to the full equatorial cross-sectional area of the shell plus the core, the microspheres showed both MPa strengths and stiffnesses that are consistent with bulk elastomers. This makes sense as both the OCA core material and the shell contribute to microcapsule mechanical properties.

Detachment force studies were conducted to provide a quantitative measure of the adhesive capability of crushed OCA-containing microcapsules. Pure OCA tissue adhesive exhibited a

detachment force of $\approx 100\text{ N}$ that was 20% that of pure Loctite Super Glue, indicating that OCA is a weaker adhesive. Dissolving OCA in MIBK, as used in the encapsulation process, weakened the average detachment force to $\approx 40\text{ N}$. Crushed OCA-containing microcapsules and crushed empty microcapsules mixed with OCA or Loctite Super Glue exhibited detachment forces of 4–8 N. As expected, crushed empty microcapsules exhibited no detachment force.

The OCA-containing microcapsules clearly possessed bonding capability, albeit much weaker than the pure adhesive. Samples of crushed OCA-containing microcapsules removed from between the aluminum plates were composite patties of bonded microcapsule fragments. This same patty formation was observed with crushed empty microcapsules manually mixed with OCA or Loctite Super Glue; however, crushing of empty capsules resulted in an unbonded powder of broken PUR shell fragments. This indicates that the released or added adhesive was more effective in forming a composite of shell fragments and polymerized OCA than it was in bonding the aluminum plates together. It should be noted, however, that compression testing and detachment force testing are considerably different measures of microcapsule functionality and not necessarily a good indicator of how microcapsules may perform in halting the progression of microcracks within the PMMA matrix.

The next phases of this project will focus on (1) optimizing the microcapsule preparation protocol and investigating the effects of capsule inclusion on the bulk mechanical properties of PMMA, (2) characterizing the fracture toughness and self-healing functionality of the system, and (3) investigating the biocompatibility of the microcapsule-embedded bone cement compared with commercial formulations.

CONCLUSIONS

This study is the first report of encapsulated OCA with adhesive capability, which supports the feasibility of our self-healing biomaterial design. OCA-containing PUR microcapsules possessing regular, spherical morphology were created via interfacial polymerization of a TDI-based pPUR with a small chain diol. Capsules with average diameters ranging from approximately 75 to 220 μm were made at agitation rates of 350–1100 rpm. Average capsule diameter and shell thickness both decreased with increasing agitation rate; however, a consistent wall thickness to diameter ratio of 0.01–0.02 was observed throughout. Core content comprised more than half of the microcapsule volume at all agitation rates with little weight loss after 8 weeks of storage. Individual capsule compression tests showed that larger microcapsules were more malleable and microcapsule strength was influenced by shell thickness. Crushed OCA-containing capsules possessed bonding capability that was diminished due to the presence of capsule debris that interfered with the ability of the glue to bond between the two testing surfaces.

Acknowledgments

Contract grant sponsor: NIH; contract grant numbers: T32-GM8555 (ABWB), R21 EB 013874-01 (WMR)

The authors thank Ethicon, Inc. for the generous donation of OCA, use of their TGA, and conversations with Dr. William Daunch, Dr. Ibraheem Badejo, Andrés Rivera, and Errol Purkett. The authors also gratefully recognize the contributions of Duke University colleagues Dr. Stephen Craig, Dr. James Ogle, and Zachary Kean for polymer synthesis, Ashley Black Ramirez for GPC analysis, and Matthew Novak for assistance with TGA data analysis.

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FIGURE 1.

(A) Increasing agitation rate results in decreasing average capsule diameter and average shell thickness; (B) smooth surface morphology of microcapsules made at 700 rpm is clearly visible under SEM. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIGURE 2.

TGA results provide thermal degradation behaviors of capsules made under various conditions. The weight loss curves of capsules as well as pure samples of MIBK, OCA, and PUR shell material are shown in (A). Derivatives of the TGA data for capsules, MIBK, OCA, and PUR shell material are presented in (B). All experiments were conducted at a heating rate of 10°C/min under N₂. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIGURE 3.

TGA data analysis was used to determine the various weight fractions of the components of the microcapsules.

FIGURE 4.

TGA weight loss curves of microcapsules made at 700 rpm following 56 days of storage.

[Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIGURE 5.

Stress–strain curves of microcapsules fabricated at various agitation rates. All compressions performed at a rate of 5 $\mu\text{m/s}$. Following capsule shell failure, the capsule was removed from the lower DMA compression plate, transferred to carbon tape on an SEM stage, gold-coated, and then imaged. (Inset) An SEM image of a capsule post-DMA testing where the failure plane is clearly visible; the original capsule diameter was 180 μm . [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

FIGURE 6.

(A) An SEM image of PMMA bone cement containing intact microcapsules, (B) a PMMA fracture plane in which ruptured capsules are visible, and (C) a magnified image of a fractured microcapsule within the damage plane of the matrix.

TABLE IMechanical Properties of Single Capsules (Data Presented as Average $\pm$ One Standard Deviation)

Agitation Rate (rpm)	t (μm)	σ_{max} (MPa)	ϵ at Failure (%)
500	2.88 ± 1.5	13.63 ± 1.44	20.8 ± 0.2
700	1.42 ± 0.3	6.71 ± 0.79	10.4 ± 3.1
900	1.65 ± 0.5	9.38 ± 1.95	10.6 ± 0.9
1100	1.60 ± 0.5	8.33 ± 2.25	8.1 ± 0.8

TABLE II

Detachment Forces Required to Separate Aluminum Plates Bonded by Various Cyanoacrylates (Data Presented as Average $\pm$ Standard Deviation)

Material	Detachment Force (N)
Adhesives	
Loctite Super Glue	546 $\pm$ 112
Pure OCA	108 $\pm$ 18
OCA dissolved in MIBK	40.8 $\pm$ 1.7
Crushed Microcapsules	
Empty microcapsules	0 $\pm$ 0
Empty microcapsules + Loctite Super Glue	7.6 $\pm$ 1.4
Empty microcapsules + OCA	5.1 $\pm$ 0.4
OCA-containing microcapsules	4.4 $\pm$ 0.8