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— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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(54) Title: POLYFUNCTIONAL COMPOUNDS AND GLASS-IONOMER CEMENT COMPOSITIONS AND METHODS FOR USING AS IMPLANT MATERIALS

(57) Abstract: Polyfunctional compounds and glass-ionomer cement compositions are described, useful in various dental, bone and orthopaedic repair, including augmentation and restoration.

POLYFUNCTIONAL COMPOUNDS AND GLASS-IONOMER CEMENT COMPOSITIONS AND METHODS FOR USING AS IMPLANT MATERIALS

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application Serial No. 61/045,112, filed April 15, 2008, and U.S. Provisional Application Serial No. 61/045,120, filed April 15, 2008, the disclosures of which are hereby incorporated herein by reference.

TECHNICAL FIELD

The invention described herein pertains to polyfunctional compounds and glass-ionomer cement compositions. In particular, the invention described herein pertains to polyfunctional compounds and glass-ionomer cement compositions and their use in various dental, bone and orthopaedic repair, including augmentation and restoration.

BACKGROUND

Glass-ionomer cements (GICs) have been successfully applied in dentistry for many decades (Smith, D.C., Development of Glass-Ionomer Cement Systems, Biomaterials, 19:467-478 (1998); Wilson, A.D., McLean, J.W., Glass-Ionomer Cements, Chicago, IL, Quintessence Publ. Co. (1988); Davidson, C.L., Mjör, I.A., Advances in Glass-Ionomer Cements, Chicago, IL, Quintessence Publ. Co. (1999); Wilson, A.D., Resin-Modified Glass-Ionomer Cement, Int. J. Prosthodont., 3:425-429 (1990)). Each of the foregoing publications, and subsequent publications cited herein are incorporated in their entirety by reference. GICs are generally water-based dental restoratives that harden following an acid-base reaction between calcium and/or aluminum cations released from a reactive glass and carboxyl anions pendent on polyacids. The success of these cements is attributed to the fact that they have unique and desirable properties such as direct adhesion to tooth structure and base metals (Hotz et al., Br. Dent. J., 142:41-47 (1977); Lacefield et al., J. Prosthet. Dent., 53:194-198 (1985)), anticariogenic properties due to release of fluoride (Forsten et al., Scand. J. Dent. Res., 85:503-4 (1977)), thermal compatibility with tooth enamel and dentin because of low coefficients of thermal expansion similar to that of tooth structure (Craig, R.G., Restorative Dental Materials, 10th ed., St. Louis, MO: Mosby-Year Book, Inc. (1997); McLean et al., Quintessence Int., 16:333-343 (1985)), minimized microleakage at the tooth-enamel interface due to low shrinkage, biological compatibility (Sasanaluckit et al., Biomaterials, 14:906-916 (1993)), and low cytotoxicity

(Nicholson et al., J. Biomater. Sci. Polym. Edn., 2(4):277-285 (1991); Hume et al., J. Dent. Res., 67(6):915-918 (1988)). The polymer backbones of GICs are generally prepared from polyacrylic acid homopolymers, poly(acrylic acid-co-itaconic acid) copolymers and/or poly(acrylic acid-co-maleic acid) copolymers (Nicholson, Biomaterials, 19:485-494 (1998)).

Even so, despite such advantages of GICs, and similarly for light-cured GICs (LCGICs), they may suffer from brittleness, low tensile and flexural strengths, and other mechanical property limitations, thus limiting the use of current conventional GICs for use only at certain low stress-bearing sites such as for example in the field of dentistry to Class III and Class V cavities. Much effort has been made to improve the mechanical strengths of GICs (Wilson, Int. J. Prosthodont., 3:425-429 (1990); Guggenberger et al., Biomaterials, 19:479-483 (1998); Mitra, J. Dent. Res., 70:72-74 (1991); Momoi et al., Dent. Mater. J., 14:109-119 (1995); Xie et al., J. M. S., Pure Appl. Chem., A35:1631-1650 (1998); Xie et al., J. Dent. Res., 72:385 (1993); Culbertson et al., J. Dent. Res., 76:317 (1997)). For example, light-cured GICs (LCGICs) are an improved resin-modified GIC (RMGIC) with reduced moisture sensitivity, improved mechanical strength, extended working time and ease of clinical handling. Another example is redox-initiated GICs, which have shown improvements in properties such as higher mechanical strength and controllable curing time (Xie et al., Eur. Polym. J., 40:343-351 (2004)). Another strategy involving resin-modified GICs is the incorporation of hydrophobic dimethacrylates or pendent (meth)acrylate moieties into the polyacid backbone in the GIC to make it less brittle and stronger (Xie et al., J. M. S. Pure Appl. Chem., A35(10):1631-1650 (1998); Xie et al., Eur. Polym. J., 40(2):343-351 (2004); Xie et al., Biomaterials, 25(10):1825-1830 (2004)). Another strategy is to directly increase molecular weight (MW) of the polyacid by either introducing amino acid derivatives or N-vinylpyrrolidone into the backbone of conventional poly(acrylic acid) homopolymer or poly(acrylic acid-co-itaconic acid) copolymer based GICs, which has been found to improve mechanical and bonding strength (Kao et al., Dent. Mater., 12:44-51 (1996); Kao et al., J. Dent. Res., 74:106 (1995); Xie et al., J. M. S. Pure Appl. Chem., A35(10):1615-1629 (1998)). However, especially in the case of linear polymers, increases in molecular weight are often accompanied by increases in viscosity, decreases in solubility, and decreases in workability.

The workability property is a characteristic that is considered when scientists, such as dentists, choose a material. It is appreciated for example that the dentist should be able to advantageously mix the cement easily just before the cement is placed into the cavity. Accordingly, a lower viscosity of the polyacid backbone in water is often a required feature to ensure such workability to the formulation while also attempting to maintain the mechanical strength. For example, certain GIC systems include tartaric acid to adjust working properties;

however, as a low molecular weight molecule, tartaric acid has been observed to correspondingly reduce mechanical strength (Xie et al., Dent. Mater., 21:739-748 (2005)). Similarly, N-vinyl pyrrolidone has been incorporated into the backbone of poly(acrylic acid-itaconic acid) based GICs for improved working properties; however, the mechanical strength did not show any significant improvement, possibly due to the presence of less carboxylic acid functional groups on the polymer backbone (Xie et al., J. M. S., Pure Appl. Chem., A35:615-1629 (1998)).

Moreover, it has been recently recognized that dental and orthopaedic implants are desirably bioactive (Ratner et al., Biomaterials Science, An Introduction to Materials in Medicine, 2nd Ed, San Diego, CA, Elsevier Academic Press, 2004). Such materials are generally referred to as bioactive GICs or bioactive glass (BAG) containing GICs. Accordingly, GICs have also been formulated in an attempt to stimulate bone growth (Kamitakahara et al., Biomaterials, 22:3191-3196 (2001)), to replace bone (Brook et al., Biomaterials, 19:565-71 (1998)) and to cap dentin for reduced hypersensitivity (Yli-Urpo et al., Biomaterials, 26:5934-5941 (2005)). In addition, BAG has been incorporated into certain GICs in an attempt to enhance these desired bioactivities (Biomaterials, 26:5934-5941 (2005); Dental Materials, 21:201-209 (2005)). Although such bioactive glass-containing GICs may exhibit bioactivity under simulated physiological conditions and may mineralize human dentin both in vitro and in vivo, it was reported that incorporating BAGs into GICs compromised the mechanical strength of the implant, limiting the utility of the products in dental clinics (Yli-Urpo et al., J. Biomater. Appl., 19:5-20 (2004)).

Therefore, a continuing need exists for providing GICs that have exhibited both high workability properties as well as high mechanical strengths.

SUMMARY OF THE INVENTION

Described herein are bioactive cement compositions prepared from glass-ionomer compositions. In one aspect, the glass includes a bioactive glass, and in another aspect the ionomer composition is a polyfunctional prepolymer that is curable, including light curable polyfunctional prepolymers. Compositions described herein exhibit strength properties that are suitable for preparing implant materials, such as bone and dental implant materials, such as for the repair and/or restoration of bones and teeth. In another aspect, the cement compositions described herein are suitable for use as high load bearing bone and dental implants. Also described herein are compositions that include one or more additional filler components.

Also described herein are the preparation and use of multifunctional core containing polycarboxylic acids. The multifunctional cores include a plurality of such polycarboxylic acids each connected to the core via sulfur through a sulfide bond. In one embodiment, the multifunctional core containing polycarboxylic acids are prepared via a chain-

transfer polymerization reaction using an initiating thiol, also referred to as mercaptyl, residue and one or more acrylic acids, such as acrylic acid, methacrylic acid, itaconic acid, and the like. In another embodiment, the multifunctional core containing polycarboxylic acids are used for preparing cements for a wide variety of applications, including but not limited to orthopaedic, bone, and dental applications, where the cements are used in the repair and/or restoration of defects in bones and teeth. In each of the foregoing embodiments, additional materials, such as fillers may also be included.

It has been discovered that polymers that include polyfunctional core molecules, such as star, hyperbranched, spherical, or dendritic shaped molecules, are useful as prostheses or implants in various tissue repair and/or restoration procedures. It has also been discovered that the monomers used to make such polymers, including those described herein may demonstrate low solution or melt viscosity, thus providing improved workability characteristics. It has also been discovered that cements may be prepared from such monomers and polymers prepared from the polyfunctional core molecules, and those cements may have improved mechanical strength properties over conventional cements. It has also been discovered that such cements may be mixed with bioactive materials, such as one or more bioactive glasses, and the resulting cement retains or shows improved workability characteristics, and retains or shows improved mechanical strength sufficient for use as implants in high load bearing sites.

In one illustrative embodiment, compositions are described herein for preparing implants. The compositions comprise one or more polymers and/or prepolymer oligomers. In one aspect, the compositions also comprise one or more bioactive glasses. In another aspect, such polymers and prepolymer oligomers include polyfunctional core molecules that may be used to initiate the preparation of a polymer or prepolymer. In one aspect, the polyfunctional core molecules may be used to initiate the preparation of a polymer or prepolymer through a thiol group. As used herein, polyfunctional core refers to those molecules that have a plurality of functional groups, such as, for example, thiol groups, that may be optionally used to initiate polymer chains, or which may be modified with oligomers or other prepolymers, each of which may be optionally used to initiate polymer chains.

In another illustrative embodiment, initiators are described that are prepared from a polyfunctional core molecule, where each of the functional groups present on the polyfunctional core molecule is covalently attached to another molecule that includes a functional group, such as, for example, a thiol group, capable of participating in a polymerization reaction with a plurality of acrylates. In another embodiment, polyfunctional prepolymers are described herein. Such polyfunctional prepolymers are prepared from polymer core initiators by polymerizing a plurality of acrylates to prepare a polyfunctional core polycarboxylic acid. In

another embodiment, such polyfunctional prepolymers having a plurality of carboxylic acids are further functionalized by adding crosslinkable groups, such as one or more acryloyl substituted groups as amides and/or esters of the polycarboxylic acids.

In another aspect, the compositions include one or more bioactive glasses. As used herein, bioactive glasses include materials that are bioinductive, bioconductive, bioerodable, bioresorptive, and/or biodegradable. In addition, bioactive glasses include materials that may attract, induce and/or promote the in-growth of tissue, such as bone or dental tissue. In addition, bioactive glasses include materials that may provide relief in the repairs involving deep dental cavity capping or bone restorations. Without being bound by theory, it is suggested that the bioactive glass cement systems described herein may facilitate or promote mineralization of calcium phosphate at or in the repair site.

In another embodiment, cements useful in the repair and/or restoration of tissues are described. Such cements may be prepared directly from the compositions of polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers. In one variation, the cements may be prepared directly from the compositions of polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers and the bioactive glasses described herein. In another variation, the cements may be prepared by co-polymerization of one or more co-monomers and the polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers described herein, either with or without bioactive glasses described herein. In another variation, the cements may be prepared by adding additional inorganic fillers, such as glasses, ceramics, biological tissues, and the like, to the compositions of polymerizing polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers, either with or without bioactive glasses described herein, with the optional inclusion of other co-monomers.

In another illustrative embodiment, processes for preparing polymer core initiators, polyfunctional prepolymers, and crosslinkable polyfunctional prepolymers are described herein, including polymerization performed using free-radical polymerization technologies such as atom-transfer radical polymerization (ATRP). Additional synthetic details are described by Matyjaszewski, K., Xia, J., "Atom Transfer Radical Polymerization," Chem. Rev., 101:2921-2990 (2001). In another illustrative embodiment, processes for preparing polymer core initiators, polyfunctional prepolymers, and crosslinkable polyfunctional prepolymers are described herein, including polymerization performed using sulfur-initiated polymerization technologies. In another embodiment, processes for preparing cements and cement compositions are described herein. The cement systems, optionally in the presence of one or more co-monomers, are curable by radiation, heat, and/or radical initiation. In one variation, the cement systems are curable with radiation.

In another embodiment, processes for preparing the polyfunctional core initiators, polyfunctional prepolymers, and implant polymers are described herein.

In another illustrative embodiment, methods for using the compositions of polyfunctional core initiators, polyfunctional prepolymers, and implant polymers described herein as cements for the repair and/or restoration of tissue are described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the effect of polymer/water (P/W) ratio (by weight) on compressive strength (CS) and diametral tensile strength (DTS) of the cements described herein: MW of the 6-arm poly(acrylic acid) = 15,272 Daltons; Filler = FUJI II LC; Grafting ratio = 50%; filler powder/liquid (P/L) ratio = 2.7. Specimens were conditioned in SBF at 37 °C for 24 h.

Figure 2 shows CS of FUJI II LC compared to illustrative cements described herein with and without BAG addition: For FUJI II LC cements, P/L ratio = 3.2 or 2.7; Filler = FUJI II LC or FUJI II LC + BAG. For illustrative cements described herein, MW of the 6-arm poly(acrylic acid) = 15,272 Daltons; Filler = FUJI II LC or FUJI II LC + BAG; Grafting ratio = 50%; P/L ratio = 2.7 or 2.5. P/W ratio = 70:30 or 75:25. All specimens were conditioned in simulated body fluid (SBF) at 37 °C for 24 h.

Figure 3 shows effect of aging in SBF on CS of illustrative cements: MW of the 6-arm poly(acrylic acid) = 15,272 Daltons; Filler = FUJI II LC or FUJI II LC + BAG; Grafting ratio = 50%; P/L ratio = 2.7 or 2.5. P/W ratio = 70:30 or 75:25. Specimens were conditioned in SBF at 37 °C for 24 h.

Figures 4(a) and 4(b) show the conversion and kinetic plot of the 4-arm poly(t-BA) derived from the FT-IR absorbance spectra. (X): Conversion (%) vs. time curve; (■): First-order kinetic plot of $\ln([M]_o/[M])$ vs. time. The 4-arm poly(t-BA) was prepared in dioxane via ATRP in the presence of the 4-arm BIBB, CuBr, and PMDETA. Linear regression of the First-order kinetic plot of $\ln([M]_o/[M])$ vs. time data yielded the following relationship:

$$f(x) = 0.722x - 0.0069; R^2 = 0.9886.$$

Figure 5 shows the yield compressive strength (YCS), ultimate compressive strength (UCS), and modulus (M) of Examples A-C including a polyfunctional core, compared to linear Example D: The compositions of Examples A-D are shown in Table 4; where the P/L ratio = 2.7. Each polymer solution was prepared by mixing a PAA with distilled water (1:1, by weight). Specimens were conditioned in distilled water at 37 °C for 24 h.

Figure 6 shows the compressive strength (CS) and diametral tensile strength (DTS) of illustrative cements described herein: Examples E-L refer to compositions as defined in Table 5; where M_n of each of the polymers = 18,066 Daltons; Filler = FUJI II LC; P/L ratio =

2.7. Specimens were conditioned in distilled water at 37 °C for 24 h.

Figure 7a shows the CS, DTS, and flexural strength (FS) of two selected illustrative cements described herein compared to FUJI II LC cement. For the illustrative cements described herein, MW of the polymer = 18,066; Filler = FUJI II LC; P/L ratio = 2.7. For FUJI II LC, P/L ratio = 3.2. Specimens were conditioned in distilled water at 37 °C for 24 h.

Figure 7b shows the CS, DTS and FS of Example M (EXPGIC) compared to FUJI II, FUJI II LC and VITREMER. For Example M: MW of the polymer = 18,066; filler = FUJI II LC; P/L ratio = 2.7. For FUJI II, FUJI II LC and VITREMER, P/L ratio = 2.7, 3.2, and 2.5, respectively. Specimens were conditioned in distilled water at 37 °C for 24 h.

Figure 8 shows the CS and DTS of the light-cured GM-crosslinked PAA-constructed Examples B-I: P/W ratio and grafting ratio are described in Table 5; Filler = FUJI II LC; P/L ratio = 2.7. Specimens were conditioned in distilled water at 37 °C for 24 h prior to testing.

Figure 9 shows the change in CS for Example M (EXPGIC), FUJI II, FUJI II LC and VITREMER in the course of aging in water. The h, d and w represent hour, day and week, respectively. Specimens were conditioned in distilled water at 37 °C prior to testing.

Figure 10 shows the cell viability comparison after culturing for 3 days with the eluates from selected cements. Eluates were obtained from the 3-day and 7-day incubation at a concentration of 80%. EXPGIC is Example M; NC is the negative control.

Figures 11(a) and 11(b) show cell viability (% survival) vs. cement eluate concentration: (a) Eluates obtained from a 3-day incubation; (b) Eluates obtained from a 7-day incubation. The cells were incubated with the medium containing different concentrations of the eluates at 37°C for 3 days before MTT testing. EXPGIC is Example M; NC is the negative control.

Figure 12. Effect of MW on strengths (CS and DTS) and viscosity: Molar ratio of poly(AA-co-IA) = 8:2; CTA = 4-arm CTA; Filler = FUJI II; P/L ratio = 2.7; P/W ratio = 50:50. Specimens were conditioned in distilled water at 37 °C for 24 h prior to testing.

Figure 13. Effect of P/W ratio on strengths (CS and DTS) and viscosity: Molar ratio of poly(AA-co-IA) = 8:2; CTA = 4-arm CTA; Filler = FUJI II; P/L ratio = 2.7. MW of poly(AA-co-IA) = 15K Daltons (calculated). Specimens were conditioned in distilled water at 37 °C for 24 h prior to testing.

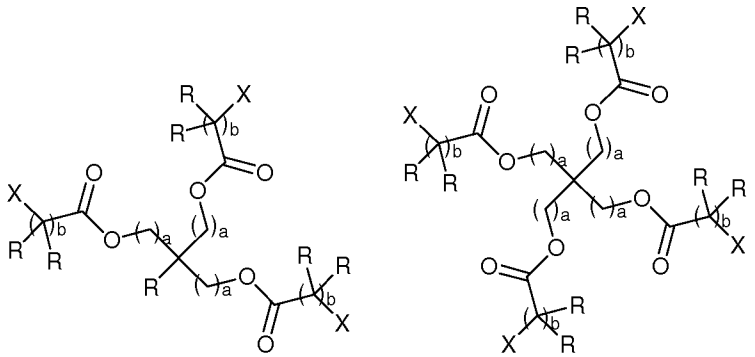
Figure 14. Effect of P/L ratio on strengths (CS and DTS): Molar ratio of poly(AA-co-IA) = 8:2; CTA = 4-arm CTA; Filler = FUJI II; P/W ratio = 50:50. MW of poly(AA-co-IA) = 15K Daltons (calculated). Specimens were conditioned in distilled water at 37 °C for 24 h prior to testing.

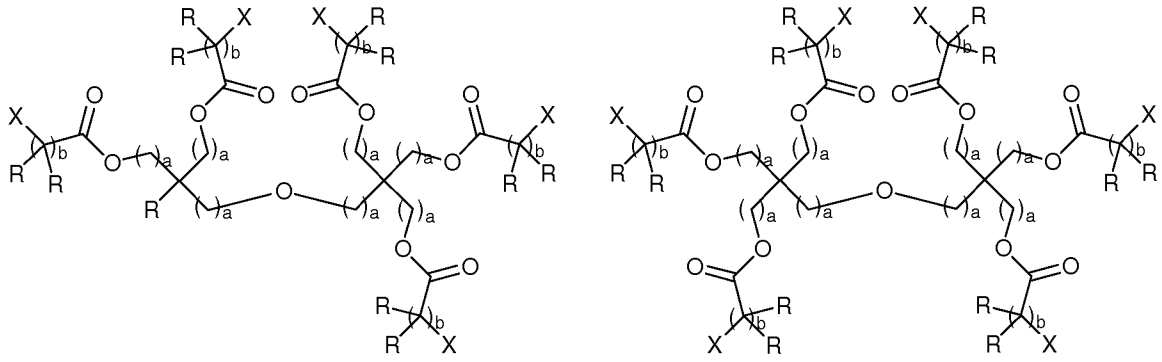
Figure 15. Effect of aging of the cements on CS: Molar ratio of poly(AA-co-IA) = 8:2; CTA = 4-arm CTA; Filler = FUJI II; P/L ratio = 3.3; P/W ratio = 50:50; MWs of poly(AA-co-IA) = 9K, 15K and 36K Daltons (calculated); Commercial FUJI II cement was used as control for comparison. Specimens were conditioned in distilled water at 37 ºC prior to testing.

DETAILED DESCRIPTION

In one embodiment, polymer core initiators are described herein. Such polymer core initiators may include from 3 to about 12 functional groups for polymerization. In one embodiment, the polymer core initiators may include 3, 4, 5, or 6 functional groups for polymerization. In one embodiment, the polymer core initiators are dendrimeric and may include from about 8 to about 12, or from about 10 to about 12 functional groups for polymerization. The functional groups may be leaving groups or electrophiles such as halo, alkoxy, acyloxy, sulfonyloxy, and the like, nucleophiles such as hydroxy, amino, carboxy, and the like, or radical initiators such as halo, stannyl, and the like. The functional groups may also be nucleophiles such as thiol groups, also referred to as mercaptyl groups. In one embodiment, the polymer core initiators are prepared as esters from polyhydroxy compounds and carboxylic acids, including mercapto carboxylic acids. Illustratively, the polyhydroxy compounds are poly(hydroxyalkyl) compounds including, but not limited to, trimethylolpropane (TMP), pentaerythritol (PE), dipentaerythritol (DPE), and the like. Illustratively, the carboxylic acids are omega halo or omega mercapto alkanoic acids, such as chloroacetic acid, 2-bromopropanoic acid, 3-iodopropanoic acid, 2-bromo-2-methylpropanoic acid, mercaptoacetic acid, 2-mercaptopropanoic acid, 3-mercaptopropanoic acid, 2-mercapto-2-methylpropanoic acid, and the like.

In one illustrative embodiment, the polymer core initiators are compounds of the formulae (Ia):



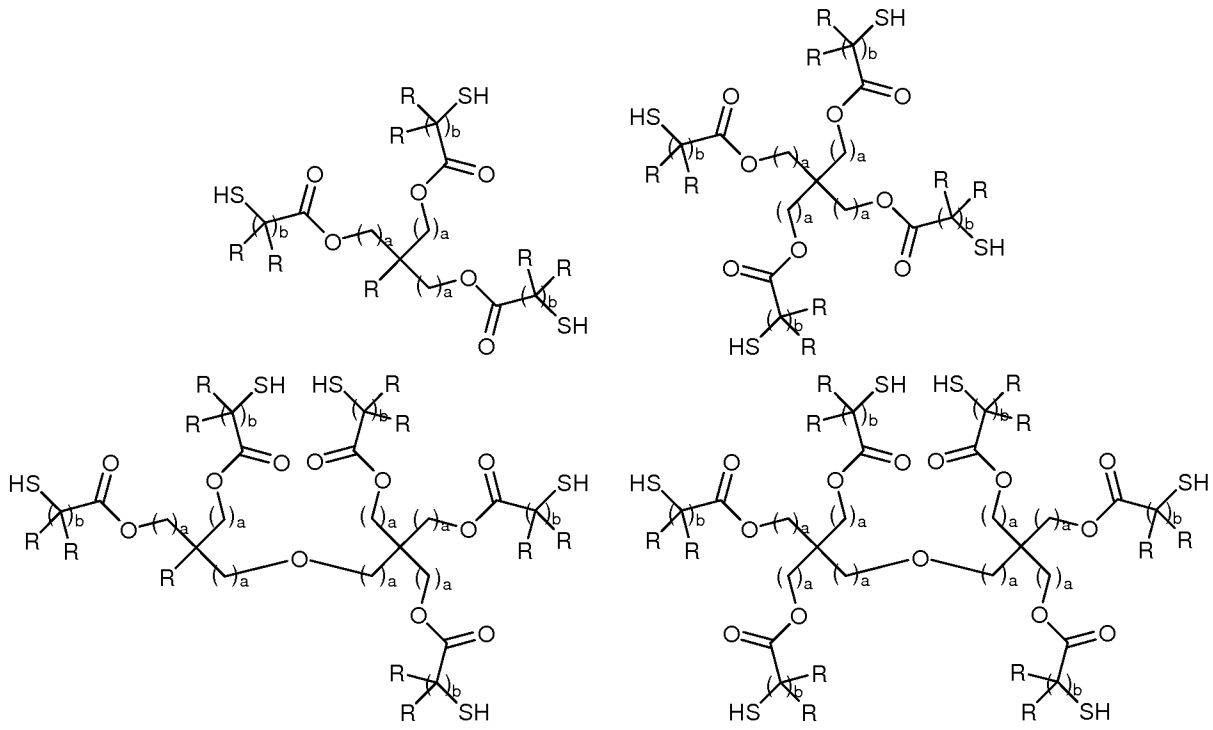


(Ia)

wherein in each instance, R is hydrogen or an independently selected alkyl group, a is an independently selected integer from 1 to about 4, b is an independently selected integer from 1 to about 4, and X is an independently selected leaving group, such as halo, acyloxy, sulfonyloxy, and the like.

In another embodiment, the polymer core initiators described herein are compounds of formulae (Ia) where a and b are each independently selected from 1 and 2. In another embodiment, the polymer core initiators described herein are compounds of formulae (Ia) where R is in each case independently selected from hydrogen or lower alkyl, such as methyl, ethyl, and the like. In another embodiment, the polymer core initiators described herein are compounds of formulae (Ia) where X is halo.

In one illustrative embodiment, the polymer core initiators are compounds of the formulae (Ib):



(Ib)

wherein in each instance R is hydrogen or an independently selected alkyl group; a is an

independently selected integer from 1 to about 4; and b is an independently selected integer from 1 to about 4.

In another embodiment, the polymer core initiators described herein are compounds of formulae (Ib) where a and b are each independently selected from 1 and 2. In another embodiment, the polymer core initiators described herein are compounds of formulae (Ib) where R is in each case independently selected from hydrogen or lower alkyl, such as methyl, ethyl, and the like.

It has been reported that polycarboxylic acids being used in current dental GICs are linear polymers and synthesized via conventional free radical polymerization. It is appreciated that one of the main reasons that different architectures of the polyacids for GIC applications have not been reported may be attributed to the fact that it is difficult to synthesize the polymers with different architectures by using conventional free-radical polymerization techniques. Atom-transfer radical polymerization (ATRP) is capable of making various architectures such as star polymers and block copolymers.

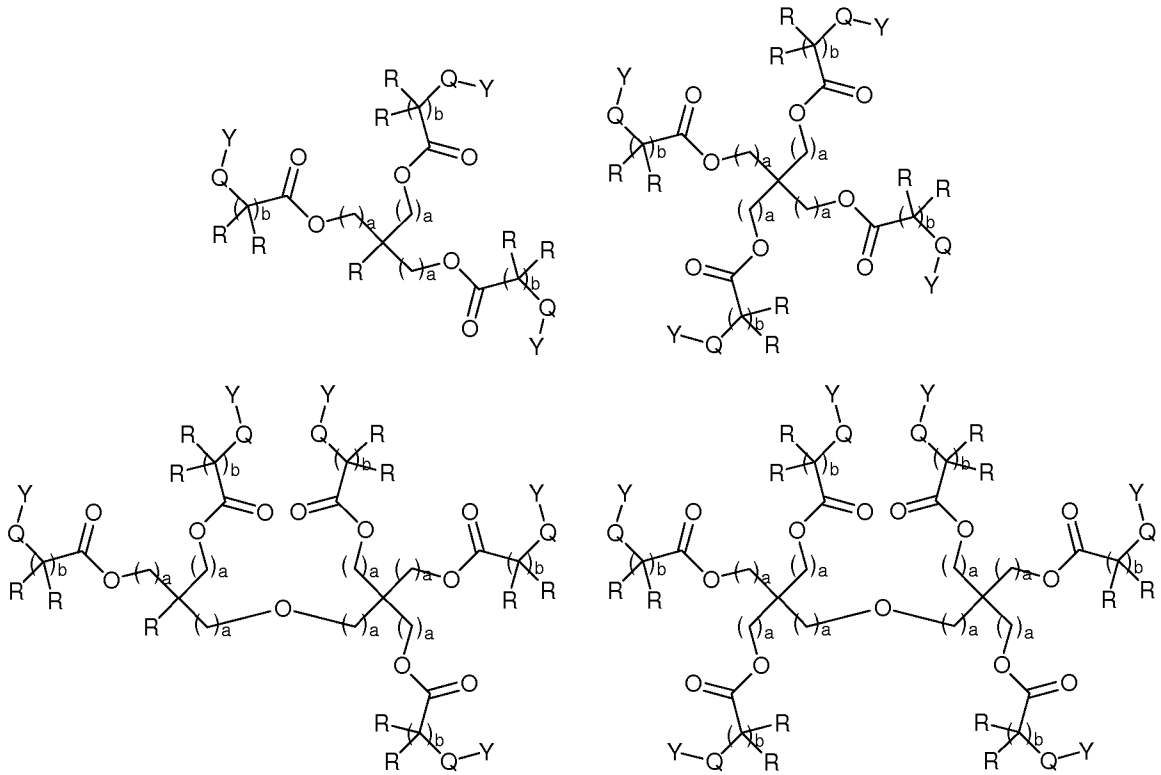
In another embodiment, polyfunctional core molecules are described herein. Without being bound by theory, it is suggested that such polyfunctional core molecules, and the prepolymer oligomers and polymers prepared therefrom may behave like solutions of spheres and therefore may exhibit fewer chain entanglements. It is further suggested that limiting chain entanglements in such prepolymer oligomers and/or polymers may be beneficial to polymer processing, as described by Bahadur, P., Sastry, N.V., "Principles of Polymer Science," Boca Raton, FL: CRC press, 2002; Huang, C.F., Lee, H.F., Kuo, S.W., Xu, H., Chang, F.C., "Star Polymers via Atom Transfer Radical Polymerization from Adamantine-Based Cores," Polymer, 45:2261-2269 (2004). Further, it has been discovered that the molecular weights of such monomers and polymers prepared from the polyfunctional core molecules described herein may be increased without a corresponding increase, or with proportionally less of a corresponding increase, in the viscosity of such polymers, and solutions thereof.

In one embodiment, the polyfunctional prepolymers are polymer core initiators further functionalized with polycarboxylic acids, such as poly(acrylic acid)s (PAA)s, and derivatives thereof. It is to be understood that as used herein, the term poly(acrylic acid) refers both to substituted and unsubstituted acrylic acids. Illustratively, PAAs include, but are not limited to, homo and co-polymers of acrylic acid, methacrylic acid, crotonic acid, maleic acid, fumaric acid, itaconic acid, citraconic acid, mesaconic acid, and the like. In addition, it is to be understood that as used herein, the acrylic acid starting materials that are used to prepare the PAAs described herein may be esters, amides, or acid salts. Illustratively, acrylic acid starting materials include methyl esters, ethyl esters, tert-butyl esters and the like. Further, acrylic acid

starting materials include amides, alkylamides, dialkylamides, dipeptides, and the like. Further, acrylic acid starting materials include monovalent and polyvalent cationic salts such as lithium, sodium, potassium, cesium, calcium, magnesium, and the like.

As used herein, the terms polymer and copolymer, such as referring to polycarboxylic acid Q may refer both individually and collectively to statistically distributed polymers, random polymers, grafting co-polymers, macromers, comb polymers, and block copolymers. In one embodiment, the polymer or copolymer included in the polyfunctional prepolymers described herein is a graft polymer. In one variation, the polymer or copolymer included in the polyfunctional prepolymers described herein is a comb polymer. In another variation, the polymer or copolymer included in the polyfunctional prepolymers described herein is a random polymer.

Illustratively, the polyfunctional prepolymer is a compound of the formulae (IIa):



(IIa)

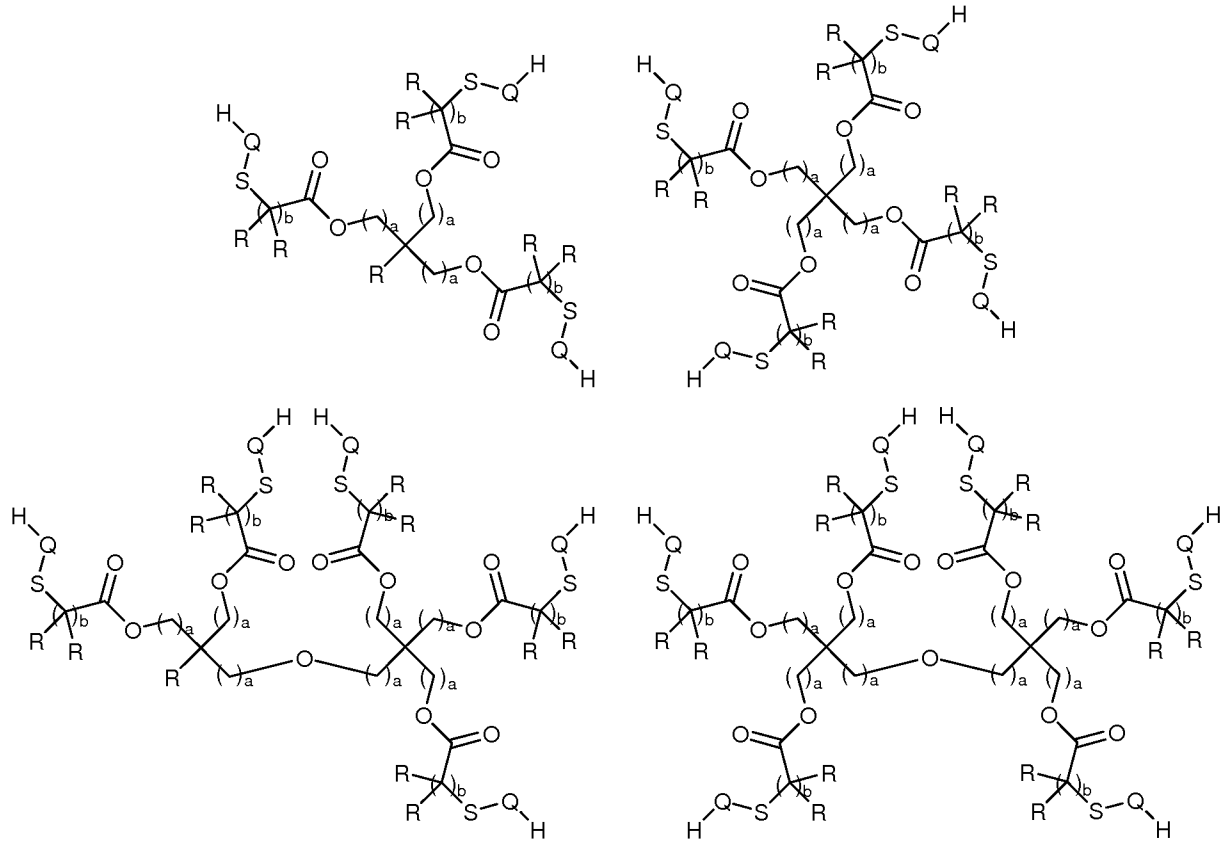
wherein in each instance R is hydrogen or an independently selected alkyl group; a is an independently selected integer from 1 to about 4; b is an independently selected integer from 1 to about 4; Q is an independently selected polymer, which may be a statistically distributed polymer, a random polymer, a grafting co-polymer, block copolymer, and the like, of one or more acrylic acids, or ester, amide, or salt derivatives thereof; and Y is an independently selected leaving group, such as halo, acyloxy, sulfonyloxy, and the like.

In one embodiment, each branch of the compounds of formula (IIa) illustratively

has a number average molecular weight in the range from about 750 to about 50,000, or in the range from about 750 to about 25,000. In another embodiment, each branch of the compounds of formula (IIa) illustratively has a weight average molecular weight in the range from about 900 to about 120,000.

In another embodiment, the polyfunctional prepolymers described herein are compounds of formulae (IIa) where a and b are each independently selected from 1 and 2. In another embodiment, the polyfunctional prepolymers described herein are compounds of formulae (IIa) where R is in each case independently selected from hydrogen or lower alkyl, such as C1-C4 alkyl, methyl, ethyl, and the like. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIa) where Y is halo. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIa) where Q is a homopolymer or copolymer of acrylic acid, methacrylic acid, maleic acid, and/or itaconic acid, or one or more carboxylic acid derivatives thereof. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIa) where Q is a homopolymer or copolymer of acrylic acid and/or methacrylic acid, or one or more carboxylic acid derivatives thereof. In one variation, Q is a homopolymer or copolymer of acrylic acid and/or methacrylic acid amides. In another variation, Q is a homopolymer or copolymer of acrylic acid and/or methacrylic acid esters.

Illustratively, the polyfunctional prepolymer is a compound of the formulae (IIb):



(IIb)

wherein in each instance R is hydrogen or an independently selected alkyl group; a is an independently selected integer from 1 to about 4; b is an independently selected integer from 1 to about 4; and Q is an independently selected polycarboxylic acid, said carboxylic acids selected from the group consisting of acrylic acids, and ester, amide, and salt derivatives thereof.

In one embodiment, each branch of the compounds of formula (IIb) illustratively has a number average molecular weight in the range from about 500 to about 100,000, or in the range from about 500 to about 50,000. In another embodiment, each branch of the compounds of formula (IIb) illustratively has a weight average molecular weight in the range from about 750 to about 150,000.

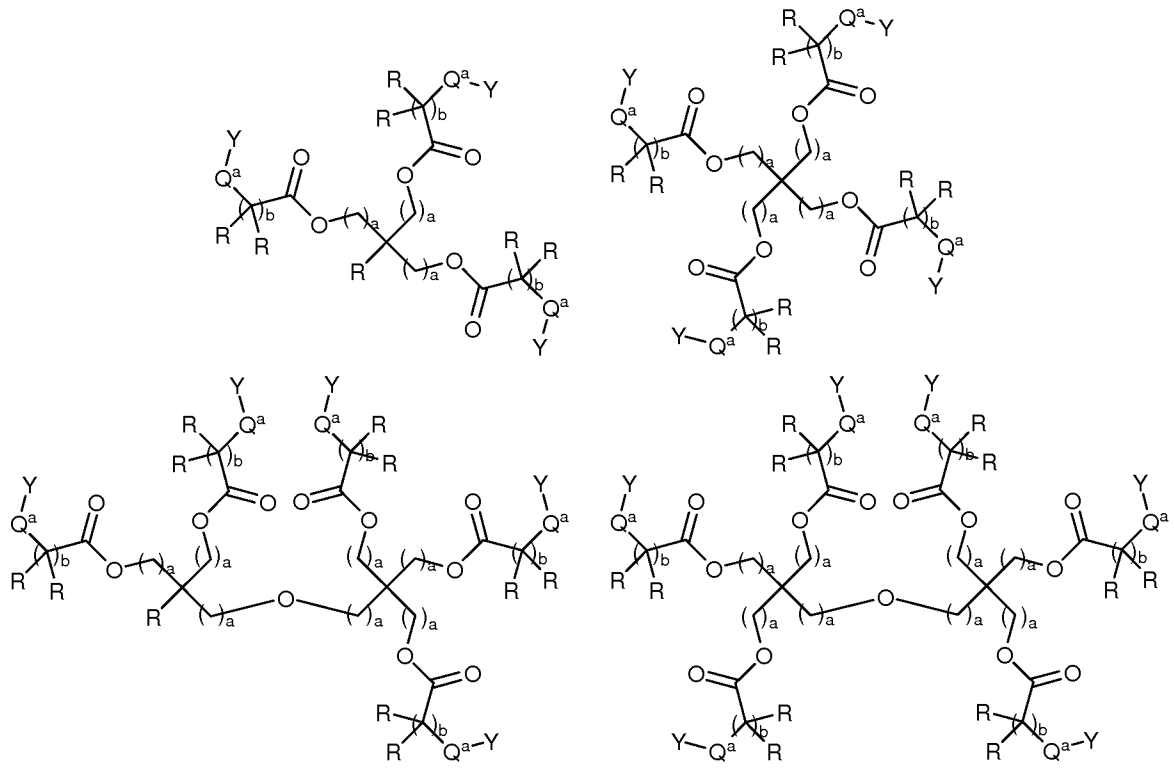
In another embodiment, the polyfunctional prepolymers described herein are compounds of formulae (IIb) where a and b are each independently selected from 1 and 2. In another embodiment, the polyfunctional prepolymers described herein are compounds of formulae (IIb) where R is in each case independently selected from hydrogen or lower alkyl, such as C1-C4 alkyl, methyl, ethyl, and the like. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIa) where Q is a homopolymer or copolymer of acrylic acid, methacrylic acid, maleic acid, and/or itaconic acid, or one or more carboxylic acid derivatives thereof. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIb) where Q is a homopolymer or copolymer of acrylic acid and/or methacrylic acid, or one or more carboxylic acid derivatives thereof. In one variation, Q is a homopolymer or copolymer of acrylic acid and/or methacrylic acid amides. In another variation, Q is a homopolymer or copolymer of acrylic acid and/or methacrylic acid esters.

In another embodiment, crosslinkable polyfunctional prepolymers are described herein. In one embodiment, the crosslinkable polyfunctional prepolymers are polyfunctional prepolymers further functionalized as acryloyloxy substituted alkyl esters or acryloyloxy substituted alkyl amides. In another embodiment, the crosslinkable polyfunctional prepolymers are polyfunctional prepolymers further functionalized as acryloylamino substituted alkyl esters or acryloylamino substituted alkyl amides. As described herein, acryloyl is understood to refer to substituted and unsubstituted acryloyls. Illustratively, acryloyls include, but are not limited to, acryloyl, methacryloyl, crotonoyl, maleoyl, fumaroyl, itaconoyl, citraconoyl, mesaconoyl, and the like. In one embodiment, the acryloyl is curable with radiation. In another embodiment, the acryloyl is curable under radical conditions, such as in the presence of heat and/or a radical initiator. In another embodiment, the acryloyl is a methacryloyl. In another embodiment, the substituted alkyl esters or substituted alkyl amides crosslinkable to the polyfunctional

prepolymers are prepared from acryloyloxy and acryloylamino alkylisocyanates, alkylepoxides, alkanols, alkylcarboxylic acids, and derivatives thereof, and the like.

It is appreciated that such crosslinkable groups may also include solubilizing groups, such as water solubilizing groups. Without being bound by theory, it is suggested that when such crosslinkable groups include water solubilizing groups, there is no longer, at least less of, a need to include conventional solubilizing monomers such as HEMA, and the like. However, it is understood that in certain configurations of the cement systems described herein, other monomers such as HEMA, and the like may be optionally added.

Illustratively, the crosslinkable polyfunctional prepolymer is a compound of the formulae (IIIa):

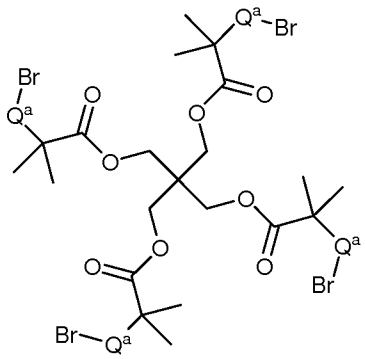


(IIIa)

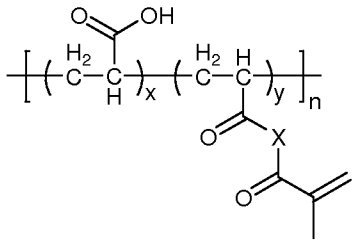
wherein in each instance R is hydrogen or an independently selected alkyl group; a is an independently selected integer from 1 to about 4; b is an independently selected integer from 1 to about 4; Q^a is an independently selected polymer, which may be a statistically distributed polymer, a random polymer, a grafting co-polymer, block copolymer, and the like, of one or more acrylic acids, or ester, amide, or salt derivatives thereof; and Y is an independently selected leaving group; providing that at least a portion of the acrylic acids forming the polymer Q^a includes one or more esters and/or amides of alcohols and/or amines each independently selected from the group consisting of acryloyloxyalkanols, acryloyloxyalkylamines, acryloylaminoalkanols, and acryloylaminoalkylamines, each of which is optionally substituted, such as with alkyl, hydroxy, halo, carboxyl, and the like.

In another embodiment, the crosslinking polyfunctional prepolymers described herein are compounds of formulae (IIIa) where a and b are each independently selected from 1 and 2. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIIa) where R is in each case independently selected from hydrogen or lower alkyl, such as methyl, ethyl, and the like. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIIa) where Y is halo. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIIa) where Q^a is a homopolymer or copolymer of acrylic acid, methacrylic acid, maleic acid, and/or itaconic acid, or one or more carboxylic acid derivatives thereof. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIIa) where Q^a is a homopolymer or copolymer of acrylic acid and/or methacrylic acid, or one or more carboxylic acid derivatives thereof. In one variation, Q^a is a homopolymer or copolymer of one or more acrylic acids, acrylic acid amides, methacrylic acids, and/or methacrylic acid amides. In another variation, Q^a is a homopolymer or copolymer of one or more acrylic acids, acrylic acid esters, methacrylic acids, and/or methacrylic acid esters. In another variation, Q^a includes a plurality of acryloyloxyalkanols as esters, such as esters of acryloyl and/or methacryloyl ethylene glycols. In another variation, Q^a includes a plurality of acryloyloxyalkanols as esters, such as esters of acryloyl and/or methacryloyl glycerols. In another variation, Q^a includes a plurality of acryloyloxyalkylamines as amides, such as amides of acryloyl and/or methacryloyl hydroxyethylamines. In another variation, Q^a includes a plurality of acryloylaminoalkylamines as amides, such as amides of acryloyl and/or methacryloyl ethylenediamines.

In one illustrative embodiment, the light-curable polyfunctional prepolymer is a compound of the formula:



wherein Q^a is

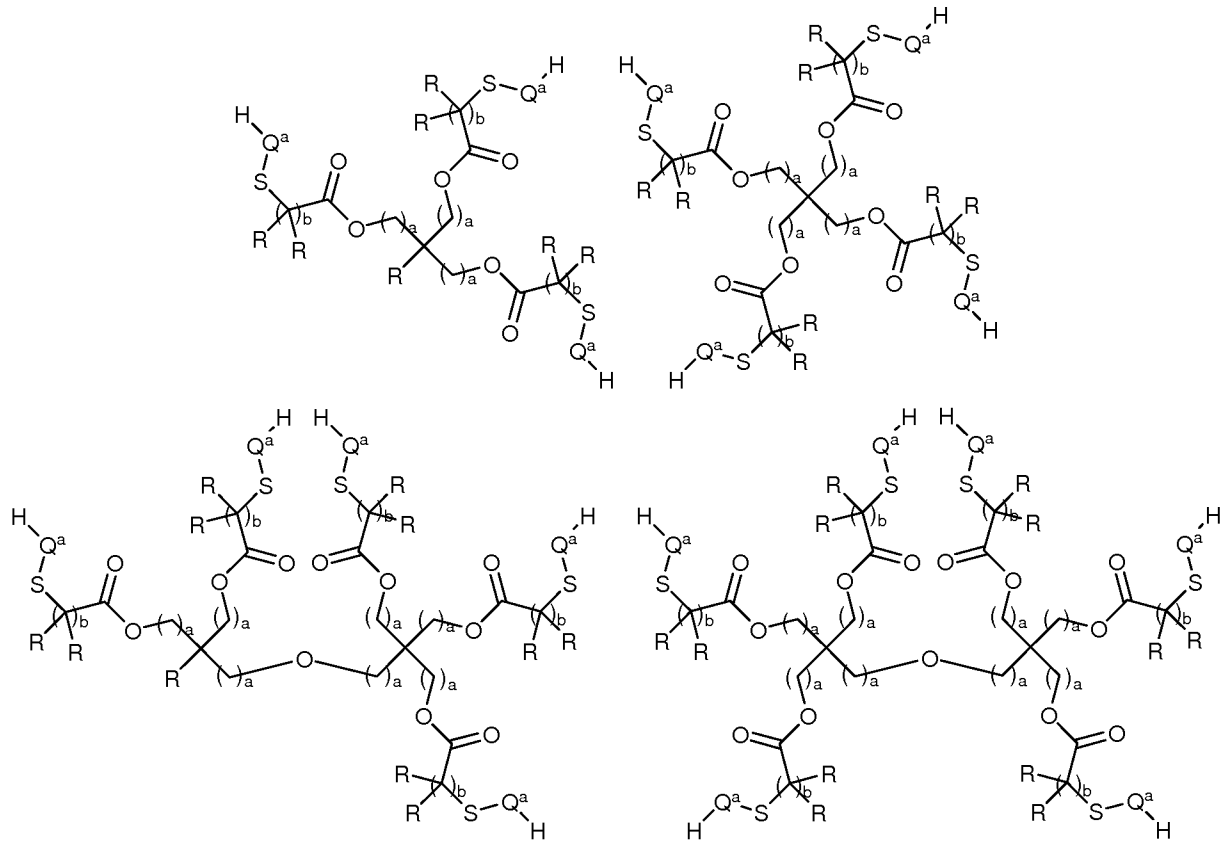


and;

wherein x and y are each independently selected in each instance from an integer in the range from 0 to about 5, and n is an integer independently selected in each instance in the range from 1 to about 1000. In another embodiment, x and y are each an independently selected integer in the range from 1 to about 4. In another embodiment, x, y, and n are each an independently selected integer in the range from 1 to about 4. In another embodiment, X is NH-CH_2-CH_2-O (IEM). In another embodiment, X is O-CH_2-CH(OH)-CH_2-O (GM).

In one embodiment of the compounds of formulae (IIIa), the portion of the acrylic acids forming the polymer Q^a that comprises esters or amides, or combinations thereof, of an alcohol or amine each independently selected from the group consisting of acryloyloxyalkanols, acryloyloxyalkylamines, acryloylaminoalkanols, and acryloylaminoalkylamines, each of which is optionally substituted, is about 5% to about 90%, about 20% to about 75%, or about 35% to about 60%.

Illustratively, the crosslinkable polyfunctional prepolymer is a compound of the formulae (IIIb):



(IIIb)

wherein in each instance R is hydrogen or an independently selected alkyl group; a is an independently selected integer from 1 to about 4; b is an independently selected integer from 1 to about 4; and Q is an independently selected polycarboxylic acid, said carboxylic acids selected from the group consisting of acrylic acids, and ester, amide, and salt derivatives thereof; providing that at least a portion of said polycarboxylic acid forming the polymer Q^a comprises esters or amides, or combinations thereof, of an alcohol or amine each independently selected from the group consisting of acryloyloxyalkanols, acryloyloxyalkylamines, acryloylaminoalkanols, and acryloylaminoalkylamines, each of which is optionally substituted.

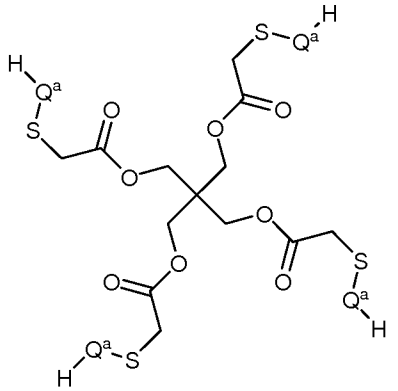
In another embodiment, the crosslinking polyfunctional prepolymers described herein are compounds of formulae (IIIb) where a and b are each independently selected from 1 and 2. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIIb) where R is in each case independently selected from hydrogen or lower alkyl, such as methyl, ethyl, and the like. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIIb) where Q^a is a homopolymer or copolymer of acrylic acid, methacrylic acid, maleic acid, and/or itaconic acid, or one or more carboxylic acid derivatives thereof. In another embodiment, the polyfunctional prepolymer described herein are compounds of formulae (IIIb) where Q^a is a homopolymer or copolymer of acrylic acid and/or methacrylic acid, or one or more carboxylic acid derivatives thereof. In one variation, Q^a is a homopolymer or copolymer of one or more acrylic acids, acrylic acid amides, methacrylic acids, and/or methacrylic acid amides. In another variation, Q^a is a homopolymer or copolymer of one or more acrylic acids, acrylic acid esters, methacrylic acids, and/or methacrylic acid esters. In another variation, Q^a includes a plurality of acryloyloxyalkanols as esters, such as esters of acryloyl and/or methacryloyl ethylene glycols. In another variation, Q^a includes a plurality of acryloyloxyalkanols as esters, such as esters of acryloyl and/or methacryloyl glycerols. In another variation, Q^a includes a plurality of acryloyloxyalkylamines as amides, such as amides of acryloyl and/or methacryloyl hydroxyethylamines. In another variation, Q^a includes a plurality of acryloylaminoalkylamines as amides, such as amides of acryloyl and/or methacryloyl ethylenediamines.

In one embodiment of the compounds of formulae (IIIb), the portion of the acrylic acids forming the polymer Q^a that comprises esters or amides, or combinations thereof, of an alcohol or amine each independently selected from the group consisting of acryloyloxyalkanols, acryloyloxyalkylamines, acryloylaminoalkanols, and acryloylaminoalkylamines, each of which is optionally substituted, is about 5% to about 90%, about 20% to about 75%, or about 35% to about 60%.

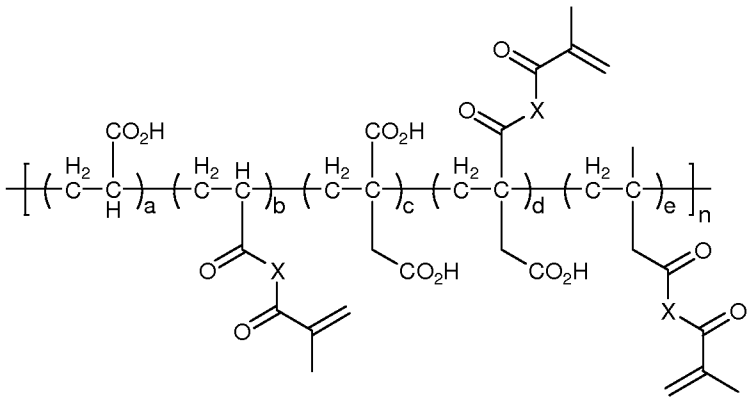
In one embodiment of the compounds of formulae (IIIb), the portion of the acrylic

acids forming the polymer Q that comprises esters or amides, or combinations thereof, of an alcohol or amine each independently selected from the group consisting of acryloyloxyalkanols, acryloyloxyalkylamines, acryloylaminoalkanols, and acryloylaminoalkylamines, each of which is optionally substituted, is about 5% to about 90%, about 20% to about 75%, or about 35% to about 60%.

In another illustrative embodiment, the light-curable polyfunctional prepolymer is a compound of the formula:



wherein Q^a is



and;

wherein a, b, c, d, and e are each independently selected in each instance from an integer in the range from 0 to about 5, and n is an integer independently selected in each instance in the range from 1 to about 1000. In another embodiment, a, b, c, d, and e are each an independently selected integer in the range from 1 to about 4. In another embodiment, a, b, c, d, e, and n are each an independently selected integer in the range from 1 to about 4. In another embodiment, X is NH-CH_2-CH_2-O (IEM). In another embodiment, X is O-CH_2-CH(OH)-CH_2-O (GM).

In another embodiment, the crosslinkable prepolymer has a lower viscosity, such as when measured in water, than a conventional cement composition. In one variation, the crosslinkable prepolymer has a lower viscosity to molecular weight ratio than a conventional cement composition. Without being bound by theory, it is suggested that such lower viscosity properties may improve the workability characteristics of cement compositions and cement systems prepared from such crosslinkable prepolymers. In addition, without being bound by

theory, it is suggested that such lower viscosity to molecular weight properties may provide cured cements that have higher strength properties, such as higher compressive strength, as compared to conventional cements with similar molecular weights.

As used herein, the terms polymer and copolymer, such as referring to polycarboxylic acid Q or crosslinkable polycarboxylic acid Q^a, may refer both individually and collectively to statistically distributed polymers, random polymers, grafting co-polymers, macromers, comb polymers, and block copolymers. In one embodiment, the polymer or copolymer included in the polyfunctional prepolymers described herein is a graft polymer. In one variation, the polymer or copolymer included in the polyfunctional prepolymers described herein is a comb polymer. In another variation, the polymer or copolymer included in the polyfunctional prepolymers described herein is a random polymer.

In another embodiment, the polymer or copolymer Q or Q^a included in the polyfunctional prepolymers described herein is of the formula:

$$-[(AA^1)x-(AA^2)y]z-$$

where AA^1 and AA^2 are illustrative acrylic acids, such as acrylic acid, methacrylic acid, itaconic acid, and the like, or illustrative crosslinkable acrylic acids, such as the foregoing further derivatized as amides and/or esters of acryloyloxyalkanols, acryloyloxyalkylamines, acryloylaminoalkanols, and acryloylaminoalkylamines, each of which is optionally substituted; and x, y, and z are each independently selected in each instance from integers in the range from 0 to about 3000. In another embodiment, the polymer or copolymer Q or Q^a included in the polyfunctional prepolymers described herein is of the formula:

$$-[(AA^1)x-(AA^2)y]z-$$

where x and y are in each instance independently selected integers in the range from 0 to about 5, and z is about 1000. It is to be understood that the above formulae include various combinations of polymer fragments. For example, the following formulae

$$-[(AA^1)x^a-(AA^2)y^a]z^a--[(AA^1)x^b-(AA^2)y^b]z^b-$$

$$-[(AA^1)x^a-(AA^2)y^a]z^a--[(AA^1)x^b-(AA^2)y^b]z^b--[(AA^1)x^c-(AA^2)y^c]z^c$$

$$-[(AA^1)x^a-(AA^2)y^a]z^a--[(AA^1)x^b-(AA^2)y^b]z^b--[(AA^1)x^c-(AA^2)y^c]z^c--[(AA^1)x^d-(AA^2)y^d]z^d$$

where each of x^a, x^b, x^c, and x^d are in each instance independently selected integers in the range from 0 to about 5, y^a, y^b, y^c, and y^d are in each instance independently selected integers in the range from 0 to about 5, and the sum of z^a, z^b, z^c, and z^d is in the range from about 5 to about 1000. It is understood that additional acrylic acids and/or crosslinkable acrylic acids, such as AA^3, AA^4, and the like may be included in the above formula to prepare the corresponding copolymers of three, four, and the like acrylic acids and/or crosslinkable acrylic acids.

In another embodiment, a novel glass-ionomer cement system composed of multi-

arm poly(carboxylic acid)s is described. In one variation, these polyacids are synthesized via a chain-transfer polymerization reaction using newly synthesized multi-arm chain-transfer agents.

In another embodiment, the cements formulated with the multi-arm polyacids described herein show significantly lower viscosities in water as compared to those formulated with their linear counterparts. It is appreciated that, due to the lower viscosities, the MW of the polyacids can be significantly increased for enhanced mechanical strengths while maintaining the ease of mixing and handling.

In another embodiment, the experimental cements show significantly improved compressive strengths as compared to FUJI II after aging in water for 3 months.

In another embodiment, the polyfunctional prepolymers are polycarboxylic acids. In one variation, the processes described herein may be performed on carboxylic acid monomers without the need for any protection of the free carboxylic acid groups. In one embodiment, the processes described herein include a thiol, also referred to as mercaptyl, chain transfer agent. The chain transfer agent is included in the polyfunctional core molecule and is used to build the subsequent polycarboxylic acid chain to prepare polyfunctional prepolymers described herein. In another embodiment, the polyfunctional prepolymers are compounds such as those described in co-filed and copending United States provisional patent application, titled "Bioactive light-curable glass-ionomer cements for dental and orthopaedic treatment," which is incorporated herein in its entirety by reference.

In another embodiment, the polyfunctional prepolymers are compounds such as those described in PCT international application publication WO 2007/103665, the disclosure of which is incorporated herein in its entirety by reference.

In another aspect, each of the crosslinkable polyfunctional prepolymers described herein, or a combination thereof, is combined with a bioactive glass to prepare a bioactive cement system. In one embodiment, the bioactive cement system is useful in dental applications, such as in repair and restoration. In another embodiment, the dental application includes use in treating high load bearing cavities, including Type I and Type II cavities. In another embodiment, the dental application includes root surface fillings. In one embodiment, the BAG is present in the cement systems herein in the range from about 10% to about 70% by weight.

In one illustrative embodiment, the BAG used herein may be selected from any of a number of known or conventional materials, including but not limited to bioactive glass S53P4, 45S5, 58S, S70C30, and the like. For example, bioactive glass S53P4, which is composed of SiO_2, Na_2O, CaO and P_2O_5, can be used for bone and dentin mineralization. It has been reported that the use of S53P4 in combination with conventional, such as linear, glass-ionomer cements for potential dentin mineralization results in materials that exhibit insufficient compressive

strength and hardness values to be clinically acceptable (Yli-Urpo et al., Biomaterials, 26:5934-5941 (2005); Yli-Urpo et al., Dent. Mater., 21:201–9 (2005)). Without being bound by theory, it is suggested that the reason for the low strength and hardness values of such cements may be the lack of formation of any or a sufficient number of chemical interactions or bonds between S53P4 and the GIC. Such a dearth or absence of chemical interactions or bonds may lead to a quick release of the bioactive glass, which is followed by a significant reduction in strength. In contrast, it is believed that the cement systems described herein may provide substantially higher mechanical strengths and hardness, and show a significant increase in strength during aging, as compared to commercial cements such as FUJI II LC.

In another illustrative embodiment, a bioactive cement system is described that also includes a filler compounds, such as but not limited to FUJI II LC filler. In another illustrative embodiment, a bioactive cement system is described that also includes water. In one aspect, the bioactive cement systems exhibit high mechanical strength and in vitro and/or in vivo bioactivity.

In another illustrative embodiment of in vivo bioactivity, the cement systems described herein induce or promote calcium phosphate or hydroxyapatite formation in simulated body fluid. In another illustrative embodiment of in vivo bioactivity, the cement systems described herein induce or promote the mineralization of bone or dentin, and the like.

Also described herein are processes for preparing cement systems containing crosslinkable polyfunctional prepolymers. Such systems are generated, for example, by initially determining and optimizing liquid formulations that contain the polymer and water and that may provide desirable compressive strength and diametral tensile strength, then mixing BAG with fillers and incorporating the mixed fillers into the optimal liquid formulations to provide cements having high strength and hardness characteristics. Without being bound by theory, such superior strength characteristics of the GIC systems herein may be attributable to the high content of carboxyl groups, high content of poly(acrylic acids), and/or high MW of poly(acrylic acid). Both high content of poly(acrylic acid) and carboxyl group may help build salt bridges between the metals, such as calcium, in BAGs and carboxyl groups pendent on the polycarboxylic acids. In contrast, FUJI II LC contains a substantial amount of hydroxyethylmethacrylate (HEMA) and dimethacrylate/oligomethacrylate which are unable to contribute to salt bridge formation, and thus the BAG may be released faster, resulting in a significant reduction in compressive strength.

In another embodiment, the BAG-containing cements herein exhibit higher values for yield strength (YS), modulus, ultimate compressive strength (UCS), diametral tensile strength (DTS) and Knoop hardness number (KNH) than those of BAG-containing commercial cements such as FUJI II LC cement. In yet another embodiment, the cement systems herein exhibit an

increase in CS upon aging. In another embodiment, the cement systems herein exhibit the effect of inducing mineralization of, for example, dentin surfaces upon aging.

Co-monomers of the polyfunctional prepolymers and crosslinking polyfunctional prepolymers are described herein. In one embodiment, the co-monomer is a hydroxy, amino, and/or carboxylic acid substituted alkyl amide or ester of an acrylate. As described herein, acrylate is understood to refer to substituted and unsubstituted acrylates. Illustratively, acrylates include, but are not limited to, acrylate, methacrylate, crotonate, maleate, fumarate, itaconate, citraconate, mesaconate, and the like. In variations of the embodiments described herein, such co-monomers are optionally added to polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers during curing to prepare polymers. It is appreciated that the addition of one or more co-monomers may increase the water solubility, hydrophilicity, and/or solvation of the polymers prepared from polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers. In addition, it is further appreciated that the addition of one or more co-monomers may increase the homogeneity of composites prepared from polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers, and fillers, such as glasses, ceramics, other inorganic materials, and the like. In one embodiment, the co-monomer is curable with radiation. In another embodiment, the co-monomer is curable under radical conditions, such as in the presence of heat and/or a radical initiator. Illustratively, the co-monomer is a hydroxyalkyl ester of methacrylate, or a carboxylalkylamide of methacrylate.

In another embodiment, GICs prepared from polyfunctional prepolymers and/or crosslinking polyfunctional prepolymers that do not include added co-monomers are described herein. It is appreciated that light-cured RMGICs described herein may have certain advantageous chemical and mechanical features, such as reduced moisture sensitivity, improved mechanical strengths, extended working time, ease of clinical handling, and the like. The advantages of such chemical and mechanical features are described by D. C. Smith, "Development of glass-ionomer cement systems," Biomaterials, 19:467-478 (1998); A. D. Wilson, "Resin-modified glass-ionomer cement," Int. J. Prosthodont., 3:425-429 (1990). It is also appreciated that light-cured RMGICs described herein may exhibit improved biocompatibility. Such advantages are described by J. W. Nicholson, J. H. Braybrook, and E. A. Wasson, "The biocompatibility of glass-poly(alkenoate) glass-ionomer cements: a review," J. Biomater. Sci. Polym. Edn., 2(4):277-285 (1991); W. R. Hume and G. J. Mount, "In vitro studies on the potential for pulpal cytotoxicity of glass-ionomer cements," J. Dent. Res., 67(6):915-918 (1988). Illustratively, it has been reported that RMGICs may generally be less biocompatible than conventional GICs, as described by C. A. de Souza Costa, J. Hebling, F. Garcia-Godoy, and C. T. Hanks, "In vitro cytotoxicity of five glass-ionomer cements," Biomaterials, 24:3853–3858

(2003); G. Leyhausen, M. Abtahi, M. Karbakhsch, A. Sapotnick, and W. Geustsen, "Biocompatibility of various light-curing and one conventional glass-ionomer cements," Biomaterials, 19:559-564 (1998). It has been suggested that one source of decreased biocompatibility may be attributed to the presence of 2-hydroxyethyl methacrylate (HEMA) in the co-monomer added to the conventional GIC. Unfortunately, it is also understood that the addition of HEMA may be responsible for the observed enhancement in water solubility of the methacrylate-containing polyacids. It is appreciated that residual HEMA from incomplete polymerization may leach from RMGICs such as VITREMER and COMPOGLASS, and exhibit cytotoxicity after contacting the dental pulp tissue and osteoblasts, further explaining why conventional GICs show less cytotoxicity to dental pulp or the other tissues. Each of the disclosures of the cited publications are incorporated herein by reference.

It is also suggested that conventional RMGICs require low MW amphiphilic molecules like HEMA. Accordingly, described herein are polyfunctional prepolymers crosslinkable to amphiphilic methacrylate functionalities. It is further suggested that such crosslinking onto the polyfunctional prepolymers may substitute for the HEMA-based hydrophobic methacrylate moieties incorporated into conventional RMGICs.

Syntheses of polymer core initiators are also described herein. Also described herein are syntheses of polyfunctional prepolymers. Also described herein are syntheses of crosslinkable polyfunctional prepolymers. In one embodiment, the crosslinkable polyfunctional prepolymers described herein may be prepared using a radical initiated polymerization process. Even so, it is understood that in certain configurations, conventional radical initiated polymerization to prepare polyfunctional prepolymers may be difficult to achieve. Accordingly, in one variation described herein are alternate syntheses of such compounds using atom-transfer radical polymerization (ATRP) processes and techniques.

In another embodiment, 4-arm PAA polyfunctional prepolymers are synthesized using ATRP. The 4-arm PAAs may also be modified by the addition of crosslinkable groups such as one or more of various substituted acrylate and methacrylate esters, such as 2-isocyanatoethyl methacrylate (IEM), glycidyl methacrylate (GM), 2-hydroxyethyl acrylate (HEA), 2-hydroxyethyl methacrylate (HEMA), and the like. The polyfunctional prepolymers and crosslinkable polyfunctional prepolymers described herein may also be formulated with co-monomers such as HEMA, in addition to water, and various optional polymerization initiators. In one variation, the polymerization of the polyfunctional prepolymers and crosslinkable polyfunctional prepolymers is initiated by radiation. In another variation, the polymerization of the polyfunctional prepolymers and crosslinkable polyfunctional prepolymers, with the optional addition of one or more co-monomers, is performed in the presence of one or more ceramic or

glass fillers, including but not limited to various forms of hydroxyapatite, commercially available ceramics, including FUJI II LC filler, and the like.

Light-cured, self-cured, and radical cured glass-ionomer cements (GICs) are described herein. In one embodiment, the GIC is prepared from one or more polyfunctional prepolymers. In another embodiment, the GIC is prepared from one or more crosslinkable polyfunctional prepolymers. In another embodiment, the GIC is prepared from one or more polyfunctional prepolymers and one or more crosslinkable polyfunctional prepolymers. In another embodiment, the GIC is prepared as described herein in the presence of one or more co-monomers. In one variation, the GIC is prepared from one or more crosslinkable polyfunctional prepolymers and one or more co-monomers. In another variation GIC is prepared from one or more crosslinkable polyfunctional prepolymers in the absence of any added co-monomers.

GICs are described herein that exhibit improved mechanical properties, illustratively improved mechanical strengths. In one embodiment, the cements described herein are evaluated for their mechanical properties. Mechanical properties include various mechanical strength parameters, including but not limited to compressive strength (CS), tensile strength (TS), toughness, modulus (M), and the like.

It is appreciated that polyfunctional prepolymers, crosslinkable polyfunctional prepolymers, and cements described herein may exhibit improved physical properties, workability properties, and mechanical properties than conventional prepolymers and cements. In one aspect, polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers described herein have a lower viscosity as compared to the corresponding linear counterpart, or conventional prepolymer. In one variation, the polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers described herein have a lower viscosity to molecular weight ratio as compared to the corresponding linear counterpart, or conventional prepolymer.

In another aspect, cements prepared from polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers described herein show higher mechanical strengths than corresponding conventional cements. For example, cements (LCGICs) prepared from both IEM-crosslinked PAAs and GM-crosslinked 4-arm PAAs show higher mechanical strengths than the cements prepared from the corresponding linear prepolymers. In addition, it is appreciated that the cements prepared from IEM-crosslinked PAAs may show higher CS and DTS than the corresponding cements prepared from GM-crosslinked PAAs. The IEM-crosslinked cements may show higher mechanical strengths than corresponding GM-crosslinked cements, possibly due to a hydrophobicity difference between the two corresponding polymers.

In another embodiment, the effects of grafting ratio, polymer/water (P/W) ratio, filler powder/polymer liquid (P/L) ratio, and aging on strengths are described for LCGICs

prepared from polyfunctional prepolymers and/or crosslinkable polyfunctional prepolymers that are not polymerized or cured with any co-monomer. In one embodiment, the 4-arm PAA polymer may exhibit a lower viscosity compared to the corresponding linear counterpart synthesized via conventional free-radical polymerization. For such monomer-free cements, increasing P/W ratio may increase both CS and DTS; increasing grafting ratio may increase CS; and increasing P/L ratio may increase CS. Also for such monomer-free cements, aging may allow the ultimate CS (MPa) to increase over time. It is appreciated that monomer-free LCGICs may have the advantage of lower cytotoxicity to dental tissue due to the absence of monomers, such as HEMA, that may remain in some polymerized cements and leach into tissues.

In another embodiment, kits are described herein. The kit may include one or more polyfunctional prepolymers and/or one or more crosslinkable polyfunctional prepolymers. The kit may also include other formulating materials, including but not limited to co-monomers, initiators, and fillers. The kit may also include a container adapted for mixing the various components of the cement prior to application, implantation, or introduction into the treatment site. The kit also includes instructions for preparing the cement system from the various components, and optionally instructions for application, implantation, or introduction into the treatment site.

In another embodiment, methods for repairing, and/or restoring tissue are described herein. Illustrative tissues that may be repaired or restored include but are not limited to dental tissues, bone tissues, and cartilage tissues. The polyfunctional prepolymers, crosslinkable polyfunctional prepolymers, and cements described herein may be used as replacement materials for conventional GICs. In one embodiment of the methods, a curable composition including one or more of the polyfunctional prepolymers and/or one or more crosslinkable polyfunctional prepolymers is placed in the defect, and cured. Curing may take place by initiating with radiation, and/or a chemical reagent, such as a radical initiator. The polyfunctional prepolymers, crosslinkable polyfunctional prepolymers, and cements described herein may also be used in conjunction with other prosthetic materials in the repair or restoration of the tissue.

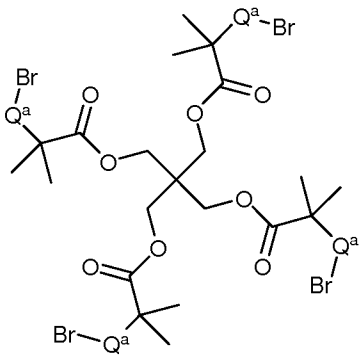
ILLUSTRATIVE EXAMPLES

The following illustrative examples describe particular embodiments of the invention. However, these examples are illustrative only, and should not be construed to limit the scope of either the specification or the claims.

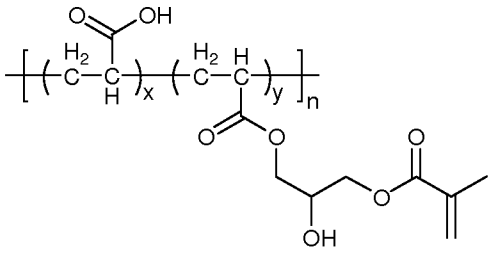
Materials: Trimethylolpropane (TMP), pentaerythritol (PE), triethylamine (TEA), dipentaerythritol (DPA), mercaptoacetic acid, 2-mercaptoethanol, p-toluenesulfonic acid monohydrate, sodium bicarbonate ($NaHCO_3$), sodium chloride (NaCl), acrylic acid (AA),

itaconic acid (IA), 2-bromoisobutyryl bromide (BIBB), cuprous bromide (CuBr), N,N,N',N',N''-pentamethyldiethylenetriamine (PMDETA), dl-camphoroquinone (CQ), diphenyliodonium chloride (DC), 2,2'-azobisisobutyronitrile (AIBN), 4,4'-azobis(4-cyanovaleric acid) (ACVA), dibutyltin dilaurate (DBTL), triphenylstilbine (TPS), pyridine (C_5H_5N), tert-butyl acrylate (t-BA), methacryloyl chloride, beta-alanine (BA), 2-hydroxyethyl methacrylate (HEMA), 2-isocyanatoethyl methacrylate (IEM), glycidyl methacrylate (GM), anhydrous magnesium sulfate ($MgSO_4$), sodium hydroxide (NaOH), hydrochloric acid (HCl, 37%), toluene, diethyl ether (Et_2O), tetrahydrofuran (THF), methanol (MeOH), deuterated methyl sulfoxide (DMSO-d_6), and ethyl acetate (EtOAc) were used as received from commercial suppliers.

EXAMPLE 1: The following light-curable 6-arm star-shape poly(acrylic acid) was synthesized as described by Xie et al., Dent. Mater., 23:395-403 (2007):



wherein Q^a is



and;

wherein x, y, and n are as described herein.

In this illustrative example, the MW of the 6-arm poly(acrylic acid) = 15,272 Daltons. The water used herein was distilled and deionized. The simulated body fluid (SBF) was prepared following published protocols (Kamitakahara et al., Biomaterials, 22:3191-3196 (2001); Forsback et al., Acta Odontol. Scand., 62:14-20 (2004)). Reagent grade NaCl, $NaHCO_3$, KCl, $K_2HPO_4.3H_2O$, $MgCl_2.6H_2O$, $CaCl_2.2H_2O$ and Na_2SO_4 were dissolved in water, and the resulting solution was buffered at physiological pH 7.4 and 37 °C with tris(hydroxymethyl)aminomethane and hydrochloric acid. The ion concentrations of the SBF (Na^+ 142.0, K^+ 5.0, Mg^{2+} 1.5, Ca^{2+} 2.5, Cl^- 147.8, HCO_3^- 4.2, HPO_4^{2-} 1.0, SO_4^{2-} 0.5 mM) were nearly equal to those of human plasma (Cho et al., J. Am. Cream Soc., 78:1769-74 (1995)). Light-cured FUJI II LC kit and FUJI II LC glass powders were supplied by GC America Inc

(Alsip, IL). Bioactive glass filler (BAG, S53P4), in which SiO_2 = 53%, Na_2O = 23%, CaO = 20% and P_2O_5 = 4% and particle size ≤ 50 μm, was purchased from Vivoxid Ltd., Turku, Finland.

EXAMPLE 2: Formulation and Preparation of Specimens. Synthesis and characterization of the light-curable 6-arm star-shape poly(acrylic acid) polymer was done as described in the literature (Xie et al., Dent. Mater., 23:395-403 (2007)). The cements were formulated with a two-component system (liquid and powder). The liquid was formulated with the light-curable 6-arm star shape poly(acrylic acid), water, 0.9% camphorquinone (CQ, photo-initiator, by weight), 1.8% diphenyliodonium chloride (DC, activator) and 0.05% hydroquinone (HQ, stabilizer). The polymer/water ratios (by weight) are shown in Table 1. FUJI II LC glass powder was either used alone or mixed with BAG to formulate the cements. The BAG fillers were mixed into FUJI II LC powders in three ratios (by weight): 10%, 15% and 20%. The detailed formulations are shown in Table 1. FUJI II LC cement with a P/L ratio of 3.2, where the P/L ratio was applied per manufacturer's recommendation, was used as control.

Table 1. Materials and formulations used in the study

Code	Liquid formulation[1]	BAG % (by weight)[2]	P/L ratio (by weight)[3]
FIILC(3.2)	N/A	0	3.2
FIILC(2.7)	N/A	0	2.7
FIILC(3.2)10	N/A	10	3.2
FIILC(2.7)10	N/A	10	2.7
FIILC(2.7)15	N/A	15	2.7
FIILC(2.7)20	N/A	20	2.7
EXP(2.7)	70/30	0	2.7
EXP(2.5)	75/25	0	2.5
EXP(2.7)10	70/30	10	2.7
EXP(2.7)15	70/30	15	2.7
EXP(2.7)20	70/30	20	2.7
EXP(2.5)10	75/25	10	2.5
EXP(2.5)15	75/25	15	2.5

[1]Liquid formulation: N/A = not available; Liquid for EXP = 6-arm star-shape poly(acrylic acid) vs. water (by weight); [2]BAG was mixed with Fuji II LC filler; 0 = only Fuji II LC filler was used; [3]P/L ratio = a total amount of glass filler powder vs. polymer liquid.

Glass-ionomer specimens were fabricated at room temperature according to published protocols (Xie et al., Dent. Mater.,23:395-403 (2007); Xie et al., Dent. Mater., 23:994-1003 (2007)). The cylindrical specimens were prepared in glass tubing with dimensions of 4 mm in diameter by 8 mm in length for compressive strength (CS) and 4 mm in diameter by 2 mm in length for diametral tensile strength (DTS) tests. The disk specimens with dimensions of 4 mm in diameter by 2 mm in thickness were prepared in glass ring covered with transparent plastic sheets on both sides for hardness test. All the specimens were exposed to blue light (EXAKT 520 Blue Light Polymerization Unit, 9W/71, GmbH, Germany) for 1 min, then were conditioned in 100% humidity for 15 min, removed from the mold and conditioned in SBF at 37 ℃ for 24 h prior to testing, unless specified.

EXAMPLE 3: Dentin Disk and Bonding Preparation. Extracted human third molars were cleaned with hand instruments to remove the soft tissue. Each tooth was cut along its horizontal axis just below the dentin-enamel junction using a water-cooled low speed diamond saw. The 1-mm-thick disk prepared from each tooth was cleaned with 0.5% NaOCl at room temperature for 5 min, followed by washing with distilled and deionized water and 70% ethanol for 20 min. The prepared dentin disk was either immersed with one cured cylindrical GIC specimen in SBF or directly bonded to one cylindrical GIC specimen (Lucas et al., Biomaterials, 24:3787–3794 (2003)) followed by immersion in SBF, prior to testing or examination.

EXAMPLE 4: Strength Measurements. Strength measurement testing of specimens was performed on a screw-driven mechanical tester (QTest QT/10, MTS Systems Corp., Eden Prairie, MN), with a crosshead speed of 1 mm/min for CS and DTS measurements. The sample sizes were n = 6-8 for each test. CS was calculated using the equation: $CS = P/\pi r^2$, where P = the load at fracture and r = the radius of the cylinder. DTS was determined from the relationship $DTS = 2P/\pi dt$, where P = the load at fracture, d = the diameter of the cylinder and t = the thickness of the cylinder.

EXAMPLE 5: Scanning Electron Microscopic (SEM) Analysis. The surface of the dentin specimen from selected groups was observed over a magnification of 1500x with a scanning electron microscope (Model XL-30CP, Philips Electronics N.V., The Netherlands) to examine in vitro mineralizations. The specimens were vacuum sputter-coated with gold-palladium (Au-Pd), and a vacuum was used for dehydration of the coated specimens before SEM analysis.

EXAMPLE 6: Statistical Analysis. One-way analysis of variance (ANOVA) with the post hoc Tukey-Kramer multiple range test was used to determine significant differences of strengths among the materials. A level of $\alpha = 0.05$ was used for statistical significance.

EXAMPLE 7: Evaluation of Mechanical Strengths of the Cements. Figure 1

shows the effect of polymer/water (P/W) ratio (by weight) on CS and DTS, after the cements were conditioned in SBF for 24h. FUJI II LC glass fillers without BAG were mixed with the star-shape polymer liquid at different P/W ratios. The strengths (MPa) were in the decreasing order: (CS) 75/25 (277.9 ± 12) > 70/30 (270.3 ± 7.2) > 60/40 (187.7 ± 4.5) > 50/50 (113.1 ± 4.4), and (DTS) 75/25 (59.2 ± 7.8) > 70/30 (54.3 ± 6.1) > 60/40 (34.1 ± 2.9) > 50/50 (17.1 ± 2.0), where there were no significant differences in both CS and DTS between 75/25 and 70/30 ($p > 0.05$).

Figure 2 shows the CS of experimental and FUJI II LC cements with and without BAG after being conditioned in SBF for 24h. The CS (MPa) was in the decreasing order: (1) For FUJI II LC cement, FIILC3.2 (212.7 ± 15) > FIILC3.2 (10) (127.0 ± 1.5) > FIILC2.7 (10) (98.9 ± 2.8) > FIILC2.7 (15) (35.3 ± 3.7) > FIILC2.7 (20) (0) ($p < 0.05$); (2) For experimental cement, EXP2.5 (270.5 ± 6.1) ≈ EXP2.7 (270.3 ± 7.2) > EXP2.5 (10) (239.2 ± 3.9) ≈ EXP2.7 (10) (234.9 ± 4.5) > EXP2.5 (15) (196.9 ± 3.8) > EXP2.7 (15) (164.1 ± 6.4) > EXP2.7 (20) (85.5 ± 6.5), where there were no significant differences between EXP2.5 and EXP2.7 and between EXP2.5 (10) and EXP2.7 (10) ($p > 0.05$).

Table 2 shows the mean values and standard deviations of yield compressive strength (YS), modulus, ultimate compressive strength (UCS), DTS and Knoop hardness number (KHN) of FUJI II LC and the experimental cements with and without BAG after being conditioned in SBF for 24h. For FUJI II LC cement, almost all the measured properties were in the same decreasing order: FIILC3.2 > FIILC3.2 (10) > FIILC2.7 (10). For experimental cement, all the measured properties except for KHN were in the same decreasing order: EXP2.7 ≈ EXP2.5 > EXP2.7 (10) > EXP2.5 (15) > EXP2.7 (15). The decreasing order for KHN was EXP2.5 > EXP2.7 > EXP2.7 (10) > EXP2.5 (15) > EXP2.7 (15).

Table 2. Mechanical property comparison

Material	YS[1] [MPa]	Modulus [GPa]	UCS[2] [MPa]	DTS[3] [MPa]	KNH[4]
FIILC (3.2)	120.9(10)[a, 5]	5.33 (0.09)[c]	212.7 (15)[e]	31.1 (2.1)[g]	23.7 (0.9)
FIILC(3.2)10	30.1 (9.1)	2.01 (0.07)	127.0 (1.5)	21.0 (1.9)	13.1 (3.3)[i]
FIILC(2.7)10	20.7 (1.5)	1.31 (0.07)	98.9 (2.8)	15.3 (0.9)	13.8 (2.3)[i]
EXP(2.7)	192.9 (9.1)[b]	8.23 (0.13)[d]	270.3 (7.2)[f]	54.3 (6.1)[h]	47.6 (3.0)[j]
EXP(2.7)10	136.1 (8.0)	7.09 (0.15)	234.9 (4.5)	51.3 (3.3)[h]	45.0 (5.1)[j]
EXP(2.7)15	62.2 (1.5)	3.20 (0.45)	129.0 (6.4)	29.0 (2.9)[g]	19.1 (1.5)
EXP(2.5)	196.3 (6.3)[b]	8.14 (0.12)[d]	270.5 (6.1)[f]	56.2 (4.5)[h]	56.4 (1.6)
EXP(2.5)15	108.3 (2.3)[a]	5.31 (0.21)[c]	196.9 (3.8)[e]	37.5 (2.1)	40.0 (2.5)

[1]YS = CS at yield; [2]UCS = ultimate CS; [3]DTS = diametral tensile strength; [4]KHN = Knoop hardness number; [5]Entries are mean values with standard deviations in parentheses and the mean values with the same superscript letter were not significantly different ($p > 0.05$). Specimens were conditioned in SBF at 37 °C for 24 h.

Figure 3 shows the effect of the experimental cement aging in SBF on CS. The experimental cements with and without BAG were conditioned in SBF for up to 3 months. The data were collected at 1 h, 1 day, 1 week, 1 month and 3 months for CS evaluation. The results indicate that all the cements showed a pattern of increased CS over time. Table 3 shows the details of strength changes of the experimental cements in the course of aging on behalf of YS, modulus and UCS. All the YS, modulus and UCS data showed an increased pattern.

Table 3. YS, modulus, UCS in the course of aging

Material	1 h	1 d	1 w	1 m
		YS[1] (MPa)		
EXP(2.7)	68.0 (6.2)[a, 5]	192.8 (9.1)[f]	247.3 (6.3)[A]	249.3 (1.8)[k,A]
EXP(2.5)	76.6 (3.6)[a]	196.3 (6.3)[f]	228.5 (2.4)	242.4 (0.2)[k]
EXP(2.7)10	N/A[2]	136.1 (8.0)	178.8 (7.6)[B]	177.5 (2.5)[B]
EXP(2.7)15	N/A	62.2 (1.5)	43.8 (3.1)[C]	45.8 (2.3)[C]
EXP(2.5)15	N/A	108.3 (2.3)	137.9 (2.0)[D]	150.2 (9.3)[D]
		Modulus (GPa)		
EXP(2.7)	4.68 (0.06)[b]	8.24 (0.13)[g]	9.10 (0.09)	9.56 (0.14)
EXP(2.5)	4.57 (0.20)[b]	8.14 (0.12)[g]	8.76 (0.14)	9.08 (0.10)
EXP(2.7)10	1.54 (0.02)	7.09 (0.15)	7.84 (0.21)[E]	7.83 (0.25)[E]
EXP(2.7)15	1.16 (0.03)[c]	3.20 (0.46)	1.91 (0.22)[F]	2.03 (0.19)[F]
EXP(2.5)15	1.17 (0.03)[c]	5.31 (0.21)	5.71 (0.31)	6.33 (0.32)
		UCS[3] (MPa)		
EXP(2.7)	194.5 (9.2)[d]	270.3 (7.2)[h,G]	290.4 (12)[i,G,H]	300.6 (6.3)[m,H]
EXP(2.5)	210.1 (0.4)[d]	270.5 (6.1)[h,I]	274.4 (9.8)[i, j,I,J]	287.1 (2.9)[m,J]
EXP(2.7)10	132.1 (5.8)[e]	234.9 (4.5)[K]	252.6 (10.3)[j,L]	247.4 (9.0)[n,K,L]
EXP(2.7)15	104.4 (2.5)	129.0 (6.4)[M]	131.5 (1.3)[M]	133.2 (4.9)[M]
EXP(2.5)15	119.0 (1.3)[e]	196.9 (3.8)[N]	204.5 (5.6)[N,O]	224.8 (11)[n,O]

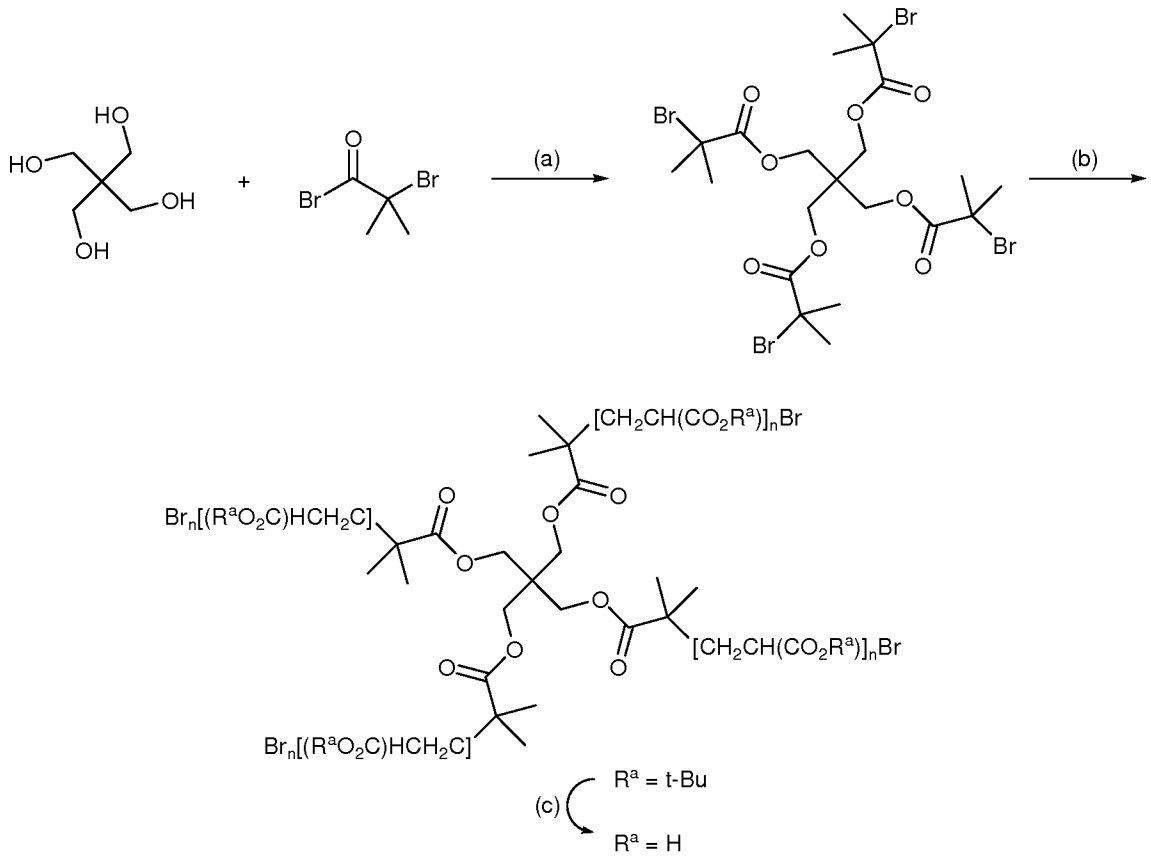
[1]YS = CS at yield; [2]N/A = not measurable; [3]UCS = ultimate CS; [5]Entries are mean values with standard deviations in parentheses and the mean values with the same superscript letter were not significantly different ($p > 0.05$). Specimens were conditioned in SBF at 37 °C prior to testing.

EXAMPLE 8: Evaluation of Dentin Surface. After being conditioned in SBF for two weeks, the dentin surfaces, either directly bonded to the BAG-containing experimental cements or immersed in SBF with the BAG-containing experimental cements, were examined by SEM. The photographs of dentin surfaces after being treated with the BAG-containing experimental cements in SBF, in comparison with those of the dentin surface after being immersed in SBF alone without any BAG or BAG-containing cement, reveal the following. The photographs of the dentin surfaces detached from the BAG-containing experimental cements EXP2.7 (10), EXP2.7 (15) and EXP2.5 (15), after being immersed in SBF, clearly show calcium phosphate crystals on the surface, except for the blocked dentin tubules. Furthermore, the photographs of the dentin surfaces treated with both EXP2.7 (15) and EXP2.5 (15) cements had more crystals than those treated with the EXP2.7 (10) cement. Photographs of the dentin surfaces after being immersed in SBF with the BAG-containing experimental cements EXP2.7 (10), EXP2.7 (15) and EXP2.5 (15) show that all of the dentin tubules were blocked, but no surface crystals could be observed.

EXAMPLE 9. Synthesis of the 4-Arm Pentaerythritol tetrakis(2-Bromoisobutyrate) Initiator. To a reactor charged with 100 ml (0.72 mole) of TEA, 15 g (0.11 mole) of pentaerythritol and 200 ml of THF, a mixture of 100 ml (0.81 mole) of BIBB in 25 ml of THF was added dropwise with stirring at room temperature. After addition was completed, additional one hour was added to complete the reaction. The solution was washed with 5% NaOH and 1% HCl and then extracted with ethyl acetate. The extract was dried with anhydrous $MgSO_4$, concentrated in vacuo and crystallized. The final product was re-crystallized from diethyl ether. The schematic diagram for the 4-arm initiator synthesis is shown in Scheme 1a. Additional synthetic details are described by Wang, X., Zhang, H., Zhong, G., Wang, X., "Synthesis and Characterization of Four-Armed Star Mesogen-Jacketed Liquid Crystal Polymer," Polymer, 45(11):3637-3642 (2004).

Schemes 1(a)-1(c) describe illustrative syntheses: (a) Synthesis of the 4-arm PAA: (1) Synthesis of the 4-arm BIBB initiator; (2) Synthesis of the 4-arm poly(t-BA) via ATRP; and (3) Hydrolysis of the 4-arm poly(t-BA); (b) Crosslinking either IEM or GM onto the 4-arm PAA; (c) Chemical structure of HEMA.

Scheme 1(a)



(a) TEA/THF; (b) tert-butyl acrylate, CuBr/PMDETA (via ATRP); (c) hydrolysis with 37% HCl.

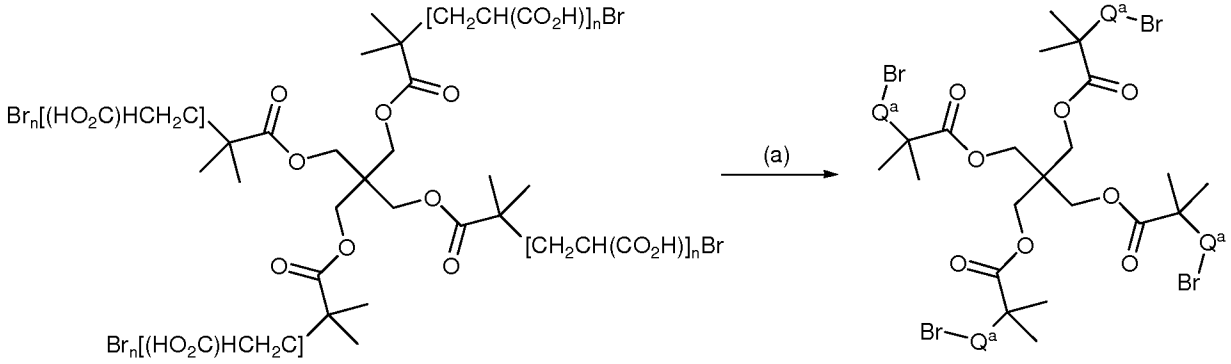
In Scheme 1(a), n is in each instance an independently selected integer, which when selected collectively corresponds to an average molecular weight (M_n) of the polymer in

the range from about 1,000 to about 50,000. Illustratively, the integers n are values that collectively correspond to an average molecular weight (M_n) of the polymer in the range from about 5,000 to about 30,000, or in the range from about 9,000 to about 22,000. In addition, it is to be understood that the preparation described in Scheme 1(b) may be used for other polymer core initiators and for other acrylates, by changing the starting compounds to those desired.

EXAMPLE 10. Synthesis of the 4-Arm Poly(acrylic Acid) via ATRP. To a flask containing dioxane (5.0 g or 0.056 mole), 4-arm initiator (1% by mole), PMDETA (3%, ligand) and t-BA (5.0 g or 0.04 mole) were charged. The CuBr (3%) was incorporated under N_2 purging after the above solution was degassed and nitrogen-purged by three freeze-thaw cycles. The solution was then heated to 120 °C to initiate the ATRP. FT-IR was used to monitor the reaction. After the polymerization was completed, the poly(t-BA) polymer was precipitated from water. CuBr and PMDETA were removed by re-precipitated from dioxane/water. The colorless polymer was then hydrolyzed in a mixed solvent of dioxane and HCl (37%) (dioxane/HCl = 1/3) under refluxed condition for 6-18 h, depending on the molecular weight of the polymer. The hydrolyzed poly(acrylic acid) was dialyzed against water until the pH in water became neutral. The purified 4-arm poly(acrylic acid) (PAA) was obtained after freeze-dried. The reaction scheme for PAA synthesis via ATRP is described in Scheme 1a. Three 4-arm PAA polymers with the same feed t-BA were synthesized at the initiator concentration of 0.5, 1.0, and 1.5%, respectively. Additional synthetic details are described by Ibrahim, K., Lofgren, B., Seppala, J., "Synthesis of tertiary-Butyl Acrylate Polymers and Preparation of Diblock Copolymers Using Atom Transfer Radical Polymerization," Eur. Polym. J., 39:2005-2010 (2003); Davis, K.A., Charleux, B., Matyjaszewski, K., "Preparation of block copolymers of polystyrene and poly(t-butyl acrylate) of various molecular weights and architectures by atom transfer radical polymerization," J. Polym. Sci. A, Polym. Chem., 38:2274-2283 (2000).

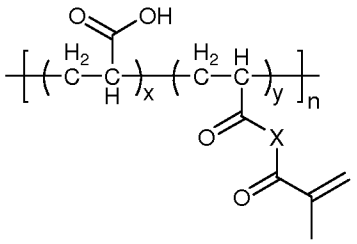
EXAMPLE 11. Synthesis of the IEM-Crosslinked 4-Arm PAA. To a three-neck flask containing PAA (4.1g or 0.057 mole), THF (18 ml), BHT (0.1%, by weight), TPS (0.1%) and DBTL (2%), a mixture of IEM (3.1 g or 0.02 mole for 35% grafting or 4.4 g or 0.029 mole for 50% grafting) and 3.7 ml of THF was added dropwise at 40 °C under a nitrogen blanket. FT-IR spectroscopy was used to monitor the reaction. The polymer crosslinked with IEM was recovered by precipitation from diethyl ether, followed by drying in a vacuum oven at 23 °C. The scheme for synthesis of the IEM-crosslinked PAA is described in Scheme 1b. Additional synthetic details are described by Xie, D., Chung, I.-D., Wu, W., Lemons, J., Puckett, A., Mays, J., "An amino acid modified and non-HEMA containing glass-ionomer cement," Biomaterials, 25(10):1825-1830 (2004).

Scheme 1(b)



(a) IEM or GM; catalyst.

wherein Q^a is



;

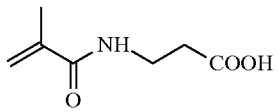
X is NH-CH_2-CH_2-O (IEM) or O-CH_2-CH(OH)-CH_2-O (GM); and wherein x, y, and n are as described herein. an independently selected integer in the range from 1 to about 4. In another embodiment,

In Scheme 1(b), n is in each instance an independently selected integer, which when selected collectively corresponds to an average molecular weight (M_n) of the polymer in the range from about 1,000 to about 50,000. Illustratively, the integers n are values that collectively correspond to an average molecular weight (M_n) of the polymer in the range from about 5,000 to about 30,000, or in the range from about 9,000 to about 22,000. Also in Scheme 1(b), x and y are integers, each of which is in each instance independently selected. It is therefore to be understood that the structures shown in Scheme 1(b) correspond to a variety of arrangements of the PAA and crosslinked PAA fragments. In one illustrative aspect, the values of each x, y, and n are such that a random polymeric chain results, or a statistically distributed polymeric chain results, where for example, the values of x and y in each case are small, such as less than 10, or less than 5. In another illustrative aspect, the values of each x, y, and n are such that the PAA and crosslinked PAA fragments form a graft polymer or block copolymer, where for example, the values of x and y in each case are large, such as greater than 10, or greater than 20. In another illustrative aspect, the values of each x, y, and n are diverse such that the PAA and crosslinked PAA fragments form random sections adjacent to block copolymeric sections. In addition, it is to be understood that the preparation described in Scheme 1(b) may be used for other polymer core initiators, for other acrylates, and for other crosslinking molecules by changing the starting compounds to those desired. It is therefore further appreciated that the

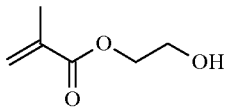
nature of these numerous possible polymeric chain arrangements will vary with the selection of the polymer core initiators, the acrylates, and the crosslinking molecules.

EXAMPLE 12. Synthesis of the GM-Crosslinked 4-Arm PAA. To a three-neck flask containing PAA (4.1 g or 0.057 mole), THF (18 ml) and BHT (0.5% by weight), a mixture of GM (2.8 g or 0.02 mole for 35% grafting or 4.0 g or 0.029 mole for 50% grafting), THF (21 ml), and pyridine (1% of GM, by weight) was added dropwise. Under a nitrogen blanket, the reaction was initiated and run at 60 °C for 5 h and then kept at room temperature overnight. FT-IR spectroscopy was used to monitor the reaction. The polymer crosslinked with GM was recovered by precipitation from diethyl ether, followed by drying in a vacuum oven at 23 °C. The scheme for synthesis of the GM-crosslinked PAA is also described in Scheme 1b.

COMPARATIVE EXAMPLE. Synthesis of Methacryloyl beta-Alanine (MBA). To a reactor containing beta-alanine (BA) and NaOH (NaOH/BA = 2:1, by mole) aqueous solution, methacryloyl chloride equivalent to BA (by mole) was added at 5 °C. After completion of the reaction, the solution was acidified to pH = 2 with HCl (37%) and extracted three times with ethyl acetate. The extract was dried with anhydrous $MgSO_4$ and concentrated using a rotary evaporator to obtain white crystals. The chemical structure of MBA is shown in Scheme 1c. Additional synthetic details are described by Xie, D., Faddah, M., Park, J.G., "Novel amino acid modified zinc polycarboxylates for improved dental cements," Dent. Mater., 21:739-748 (2005).



MBA



HEMA

Scheme 1(c)

COMPARATIVE EXAMPLE. Synthesis of the Linear PAA via Conventional Free-Radical Polymerization. To a flask containing AIBN and THF, a mixture of AA and THF was added dropwise. Under a nitrogen blanket, the reaction was initiated and run at 62 °C for 10 h. After the reaction was completed, the PAA was purified by precipitation using ether and drying in a vacuum oven. Additional synthetic details are described by Xie, D., Faddah, M., Park, J.G., "Novel amino acid modified zinc polycarboxylates for improved dental cements," Dent. Mater., 21:739-748 (2005).

EXAMPLE 13. Characterization of the Initiator and Polymers. The synthesized 4-arm initiator was characterized by melting point identification, FT-IR spectroscopy and nuclear magnetic resonance (NMR) spectroscopy. The 4-arm polymers were characterized by FT-IR, NMR and vapor pressure osmometry. Both IEM-crosslinked and GM-crosslinked polymers were identified by FT-IR and NMR spectroscopy. The melting point was measured using a digital melting point apparatus (Electrothermal IA9000 Series, Electrothermal Engineering Ltd., Essex,

United Kingdom). FT-IR spectra were obtained on a FT-IR spectrometer (Mattson Research Series FT/IR 1000, Madison, WI). ^{1}H NMR spectra were obtained on an ARX-300 NMR Spectrometer using deuterated methyl sulfoxide (DMSO-d_6) as a solvent. The number average molecular weight (M_n) was determined using a vapor pressure osmometer (K-7000, ICON Scientific, Inc., North Potomac, MD). The viscosity of the liquid formulated with the polymer and distilled water (50:50, by weight) was determined at 25 and 40 °C using a programmable cone/plate viscometer (RVDV-II + CP, Brookfield Eng. Lab. Inc., Middleboro, MA).

EXAMPLE 14. Formulation and Preparation of Specimens for Strength Tests. (A) Self-cured specimens. A two-component system (liquid and powder) was used to formulate the self-cured cements, as described by Kao, E.C., Culbertson, B.M., Xie, D., "Preparation of glass-ionomer cement using N-acryloyl-substituted amino acid monomers: evaluation of physical properties," Dent. Mater., 12:44-51 (1996). The liquid was prepared by simply mixing either 4-arm PAA or linear PAA with distilled water (50:50, by weight). FUJI II glass powder was used for making cements. The powder/liquid (P/L) was 2.7/1 (by weight, as recommended by the manufacturer). (B) Photo-cured specimens. The light-cured cements were also formulated with a two-component system (liquid and powder), as described by Xie, D., Chung, I.-D., Wu, W., Lemons, J., Puckett, A., Mays, J., "An amino acid modified and non-HEMA containing glass-ionomer cement," Biomaterials, 25(10):1825-1830 (2004). The liquid was formulated with either IEM-crosslinked or GM-crosslinked polymer, water, 0.7% CQ (photo-initiator, by weight), 1.4% DC (activator) and 0.05% HQ (stabilizer). FUJI II LC glass powder was used to formulate the cements with a powder/liquid (P/L) ratio of 2.7. FUJI II LC kit with a P/L ratio of 3.2 (recommended by manufacturer) was used as control.

Specimens were fabricated at room temperature according to these published protocols. Briefly, the cylindrical specimens were prepared in glass tubing with dimensions of 4 mm diameter by 8 mm length for compressive strength (CS) and 4 mm diameter by 2 mm length for diametral tensile strength (DTS) tests. A split Teflon mold with dimensions of 3 mm in width × 3 mm in thickness × 25 mm in length was used to make rectangular specimens for flexural strength (FS) test. A transparent plastic window was used on top of the split mold for light exposure. Specimens were removed from the mold after 15 min in 100% humidity, and conditioned in distilled water at 37 °C for 24 h. Light-cured specimens were exposed to blue light (EXAKT 520 Blue Light Polymerization Unit, 9W/71, GmbH, Germany) for 1 min before conditioned in 100% humidity.

EXAMPLE 15. Strength Measurements. Testing of specimens was performed on a screw-driven mechanical tester (QTest QT/10, MTS Systems Corp., Eden Prairie, MN), with a crosshead speed of 1 mm/min for CS, DTS and FS measurements. The CS and DTS tests

measurements were done as described in Example 4. The FS test was performed in three-point bending, with a span of 20 mm between supports. FS was obtained using the expression FS = $3Pl/2bd^2$, where P = the load at fracture, l = the distance between the two supports, b = the breadth of the specimen, and d = the depth of the specimen.

EXAMPLE 16. Characterization of the Synthesized Initiator and Polymers. The purified 4-arm BIBB initiator was white crystal (yield = 45%) with melting point of 135-136 °C. The IR spectra for BIBB and 4-arm BIBB showed the following characteristic peaks: (1) BIBB (cm^{-1}): carbonyl: 1808 and 1767 (C=O stretching, strong) and 944 (C=O bending); C-Br: 848, 626 and 599 (C-Br bending); CH_3: 1459, 1371 and 1112 (CH_3 bending) and 2975-2950 (weak C-H stretching). (2) 4-arm BIBB: carbonyl: 1738 (C=O stretching, strong) and 1271 (C-O-C stretching); C-Br: 1164 (C-Br bending); CH_3: 1390, 1372, 1106 and 984 (CH_3 bending) and 2976-2933 (C-H stretching). The significant shift of the carbonyl group from two peaks at 1808 and 1767 to one peak at 1738 and disappearance of 944 and 848 peaks strongly confirmed the formation of the 4-arm BIBB.

The FT-IR spectra for t-BA, 4-arm poly(t-BA), 4-arm PAA, IEM-crosslinked 4-arm PAA and GM-crosslinked 4-arm PAA showed the following. The t-BA shows multiple peaks in its spectrum. Among them, 1722 and 1636 are two most characteristic peaks associated with carbonyl and carbon-carbon double bond, respectively. In contrast, disappearance of the peak at 1636 cm^{-1} in the spectrum for the 4-arm poly(t-BA) confirmed the completion of polymerization. After hydrolysis of the 4-arm poly(t-BA), a broad and significant peak at 3600-2300 cm^{-1} and a strong but wider peak at 1714 cm^{-1} could be observed as compared to poly(t-BA). The former is the typical peak for hydroxyl group on carboxylic acids (OH stretching) whereas the latter is the characteristic peak for carbonyl stretching on PAA. In contrast, the IEM-crosslinked 4-arm PAA shows four typical peaks: 3600-2400 cm^{-1} (OH stretching on COOH); 1717 (carbonyl, C=O stretching on COO and CONH, where both carbonyl peaks were overlapped); 1636 (C=C bending); and 1553 (amide II, CONH). For the GM-crosslinked PAA, four characteristic peaks are: 3600-2400 cm^{-1} (OH stretching on COOH); 3434 (OH on crosslinked methacrylate); 1716 (C=O stretching on COO); and 1636 (C=C bending). It was apparent that a peak at 3434 cm^{-1} on the GM-crosslinked 4-arm PAA and a peak at 1553 cm^{-1} on the IEM-crosslinked 4-arm polymer identified the difference between these two polymers. A peak at 1636 cm^{-1} identified the difference between the 4-arm PAA and IEM/GM-crosslinked 4-arm PAA.

The ^1H NMR spectra for the 4-arm BIBB, 4-arm PAA, IEM-crosslinked 4-arm PAA and GM-crosslinked 4-arm PAA showed the following. The chemical shifts of the 4-arm BIBB initiator were found as follows (ppm): a: 4.3 (CH_2) and b: 1.9 (CH_3). The chemical shifts

of the 4-arm PAA were (ppm): a: 12.25 (COOH); b: 3.4 (CH_2); c: 2.25 (CH); d: 1.8 and 1.55 (CH_2); and e: 1.1 (CH_3). A single peak at 2.50 (between b and c) was the chemical shift for solvent DMSO. All the spectra contained this peak. The typical chemical shifts for the IEM-crosslinked 4-arm PAA were (ppm): a: 12.25 (COOH), b: 7.9 (CONH), and c: 6.15 and 5.75 ($C=CH_2$). Characteristic chemical shifts at 7.9, and 5.75 and 6.15 identified the difference between 4-arm PAA and IEM-crosslinked 4-arm PAA. The typical chemical shifts for the GM-crosslinked 4-arm PAA were: a: 12.30 (COOH), b: 5.70 and 6.10 ($C=CH_2$), and c: 3.25 (OH). The chemical shift for COOH on GM-crosslinked 4-arm PAA was weak but broad. The characteristic chemical shifts at 3.25, 5.70 and 6.10 identified the difference between the 4-arm PAA and GM-crosslinked 4-arm PAA.

EXAMPLE 17. Synthesis and Hydrolysis of the 4-Arm poly(t-BA). Figure 4 shows a semi-logarithmic plot of the ATRP of t-BA in dioxane (a) and a kinetic plot of monomer to polymer conversion versus time (b). The polymerization was initiated by the 4-arm BIBB, catalyzed by CuBr-PMDETA complex and run at 120 °C. The plot of $\ln([M]_0/[M])$ versus time (Figure 4(a)), where $[M]_0$ = the initial concentration of the monomer and [M] = the monomer concentration at any time, is almost linear. Without being bound by theory, it is believed that the polymerization propagation was constant throughout the reaction or, in other words, a constant concentration of growing radicals reflects a first-order kinetics. From the kinetic plot of monomer to polymer conversion versus time (Figure 4(b)), it appears that the monomer conversion increased with time. The reaction in dioxane took 3 h to reach a 90% conversion and 5 h to reach a 97% conversion. In order to demonstrate that the t-BA was polymerized only by ATRP but not by heat-initiated conventional free-radical polymerization, a parallel experiment without any initiator involved was conducted under the same condition. It was found that no polymer was generated within 8 h. Without being bound by theory, it is believed that the poly(t-BA) was polymerized by the ATRP reaction.

The 4-arm PAA was prepared by hydrolysis of the poly(t-BA) in a mixed solvent of dioxane and aqueous HCl (37%) for 8-12 h under refluxed condition, followed by dialysis against water until the pH reached neutral. Additional synthetic details are described by L. Stanislawski, X. Daniau, A. Lauti A., and M. Goldberg, "Factors responsible for pulp cell cytotoxicity induced by resin-modified glass ionomer cements," J. Biomed. Mater. Res., 48(3):277-88 (1999). It was observed that the higher the MW of the 4-arm poly(t-BA) the longer was the time needed for hydrolysis. In the case of the poly(t-BA) with MW of 15,701, it took about eight hours to complete the hydrolysis. For the poly(t-BA) with MW of 21,651, however, eighteen hours were required for completing the hydrolysis. Without being bound by theory, it is believed that this is probably due to the bulky long chains from the 4-arm poly(t-BA).

The molecular weights (MWs) of the synthesized 4-arm PAA via ATRP and linear PAA via conventional free-radical polymerization were characterized using VPO as shown in Table 4. Table 4 shows the MW, conversion and viscosity of the three 4-arm PAAs and one linear PAA. The MWs of the 4-arm PAAs synthesized via ATRP were 15,701, 18,066 and 21,651 Daltons whereas the MW of the linear PAA synthesized via conventional free-radical polymerization was 9,704. The conversions of the monomer to polymer were determined using FT-IR spectra and they were all greater than 97%. The viscosities were measured using a cone & plate viscometer and shown in Table 4. At 25 °C, the viscosities of the two 4-arm PAAs (MW = 15,701 and 18,066) were 48.2 and 148.6 (cp) but the solutions of the other 4-arm PAA (MW = 21,651) and the linear PAA (MW = 9,704) were too viscous to be measured for their viscosities. At 40 °C, the viscosities of both 4-arm PAA (MW = 21,651) and linear PAA could be measured but they were much higher than the other two 4-arm PAAs. It is observed that the 4-arm PAA even with a MW of 18,066 showed a lower viscosity value than the linear PAA (not measurable), although the latter's MW was only 9,704. It appears that increasing MW increased the viscosity of polymer aqueous solution, and that the star-shape structure of the 4-arm PAA may contribute to a lower viscosity as compared to the linear PAA, even though the linear polymer had a lower MW. Without being bound by theory, it is believed that these results suggest that the more spherical nature of the multifunctional core molecule in the 4-arm PAA improves viscosity even at high molecular weight.

Table 4. Conversion, MW and viscosity of synthesized polymers.

Example	Polymer	Conversion [1] (%)	MW [2] (Dalton)	Viscosity [3] (cp)	Viscosity [4] (cp)
A	4-arm PAA	99.4	15,701	49.2	11.2
B	4-arm PAA	97.5	18,066	148.6	67.3
C	4-arm PAA	97.0	21,651	NM[5]	980
D	Linear PAA [6]	99.9	9,704	NM[5]	1890

[1]Conversion (%) was measured from FT-IR spectra; [2]MW (number average) was determined in DMF via a vapor pressure osmometer; [3]Viscosity of the aqueous polymer solution (PAA:distilled water = 1:1, by weight) was measured using a cone & plate viscometer at 25 °C. [4]Viscosity was measured using a cone & plate viscometer at 40 °C. [5]NM stands for the viscosity that was not measurable at the given temperature due to gel formation. Specimens were conditioned in distilled water at 37 °C for 24 h; [6]Linear PAA was synthesized via conventional free-radical polymerization using 1% AIBN as initiator.

EXAMPLE 18. Synthesis of the IEM-Crosslinked and GM-Crosslinked 4-Arm PAAs. The reaction between IEM and carboxylic acid on PAA took only two hours to complete. Disappearance of the isocyanate group at 2250 cm^{-1} by FT-IR monitoring confirmed the completion of the reaction. The reaction between GM and carboxylic acid on PAA took about fourteen hours to complete. Disappearance of the epoxy group on GM at 761 cm^{-1} confirmed the completion of the crosslinking reaction. The completion of the crosslinking for both reactions was also confirmed by the fact that yields were greater than 95%.

EXAMPLE 19. Selection of the 4-Arm PAA for Methacrylate Crosslinking. In this study, three 4-arm PAA polymers A, B and C with MW of 15,701, 18,066 and 21,651, respectively, were synthesized. The viscosities of these polymers in water (50/50, by weight) were also determined at 25 °C and 40 °C, respectively. The values (cp) at 25 °C were in the order of C (too high, not measurable) > B (148.6) > A (49.2), corresponding to their decreased MW. The viscosities at 40 °C (elevated temperature) showed that C was much higher than both B and A. The compressive strengths (CS) of the corresponding cements formulated with FUJI II glass fillers are shown in Figure 5. The cement B with MW of 18,066 showed the highest yield CS (YCS, 190.0 MPa), ultimate CS (UCS, 212.2 MPa) and modulus (M, 8.33 GPa), followed by the A (160.9, 184.1 and 8.11) and the C (157.1, 176.9 and 7.74). Due to its suitable viscosity and highest CS, the polymer B was selected for methacrylate crosslinking. For comparison, the CS of the linear PAA-composed cement D (liquid viscosity at 25 °C = not measurable and at 40 °C = 1350 cp) was also determined. The CS values for D were 167 MPa in YCS, 183 MPa in UCS and 7.04 GPa in M. It was observed that making the specimens from both C and D was very difficult because of their high solution viscosities. Without being bound by thoery, it is believed that the higher viscosities of both C and D is attributable to strong hydrogen bonding.

EXAMPLE 20. COMPARATIVE EXAMPLE. Crosslinking of IEM or GM onto the 4-Arm PAA for Light-Curable GICs. To overcome the low solubility of IEM-crosslinked PAA in water, amphiphilic comonomers such as HEMA or amino acid derivatives, may be incorporated, as described by Xie, D., Chung, I.-D., Wu, W., Lemons, J., Puckett, A., Mays, J., "An amino acid modified and non-HEMA containing glass-ionomer cement," Biomaterials, 25(10):1825-1830 (2004); Xie, D., Faddah, M., Park, J.G., "Novel amino acid modified zinc polycarboxylates for improved dental cements," Dent. Mater., 21:739-748 (2005). In this study, both HEMA and MBA were used as a comonomer for comparison. Regarding GM crosslinking, it is appreciated that using this reagent for GIC modifications has not been reported so far. By looking at the IR spectrum of the crosslinked chemical structure, each GM molecule produces one extra hydroxyl group when epoxy group on GM reacts with carboxyl group on PAA. It is understood that, unlike IEM-crosslinking, these hydroxyl groups should make the GM-crosslinked PAA less hydrophobic or at a minimum they should not change the original hydrophilicity of the PAA much.

Table 5 shows the effects of different comonomer and grafting agent on compressive properties. Codes E, F, G and H stand for the cements crosslinked with 35%, 35%, 50%, and 50% GM and mixed with HEMA, MBA, HEMA and MBA, respectively. By comparing E and F, the MBA, acid-containing comonomer, exhibited significantly high YCS, M and UCS. It appears that both YCS and M increased even more significantly. Without being

bound by theory, it is believed that this increase can be attributed to formation of salt-bridges contributed by MBA, and it is appreciated that salt-bridges often make the cements more brittle and it is also appreciated that brittle materials are high in yield strength and modulus. The same principle may be applied to G and H. By comparing E and G or F and H, a higher grafting ratio gave higher UCS but not necessarily YCS and M.

In the case of IEM-crosslinking I, J, K and L, the trend was pretty similar to that for the GM-crosslinked cements. As shown in Table 5, J was much higher in YCS, modulus and UCS than I whereas L was much higher than K. For the HEMA-containing cements, the 50% IEM-crosslinked cement (K) was statistically the same in YCS and UCS as the 35% IEM-crosslinked cement (Ia) but was lower in M. A similar result was found to the MBA-containing cements (L and J). However, by comparing the GM- and IEG-crosslinked cements, it was apparent that all the IEM-crosslinked cements were higher in YCS, modulus and UCS than corresponding GM-crosslinked cements. For example, the 50% IEM-crosslinked cement with MBA (175.1 MPa in YCS, 6.5 GPa in modulus and 257 MPa in UCS) was 22%, 20% and 21% higher than corresponding the 50% GM-crosslinked cement with MBA (144.1, 5.4 and 213.2). Without being bound by theory, it is believed that this difference may be attributed to the difference between IEM and GM-crosslinked cements, because the former contains more hydrophobic IEM-crosslinked 4-arm PAA whereas the latter contains more hydrophilic GM-crosslinked 4-arm PAA due to the extra hydroxyl groups, andthese hydroxyl groups can keep more water around, which make the cements relatively weaker in strength because the cement somehow behaves like a hydrogel material. It has been reported that polymeric hydrogel materials often show lower mechanical strengths due to their hydrophilic nature, as described by Ratner, B.D., Hoffman, A.S., Schoen, F.J., Lemons, J.E., Biomaterials Science, An Introduction to Materials in Medicine, San Diego, CA: Academic Press, 1996. Figure 6 shows both UCS and DTS values of the cements discussed above. Not only CS but also DTS showed the same trends in mechanical strengths to these cements. The order of DTS (MPa) was: L (58.9 ± 7.2) > J (46.7 ± 2.7) > I (33.9 ± 6.4) > K (31.3 ± 1.9) > H (26.5 ± 3.6) > F (24.7 ± 3.8) > G (23.5 ± 4.4) > E (22.1 ± 1.2). Both CS (257.1 ± 18 MPa) and DTS (58.9 ± 7.2 MPa) of the 50% IEM-crosslinked cement with MBA as comonomer was the highest among all the cements.

Table 5. Effects of comonomer and crosslinking type on compressive properties

Example	Comonomer	Graft Type	Grafting Ratio	YCS [MPa][1]	Modulus [GPa]	UCS [MPa][2]
E	HEMA	GM	35%	54.2 (2.1)[3, a]	2.29 (0.18)[e]	137.3 (6.8)[g]
F	MBA	GM	35%	134.9 (6.6)[b]	6.10 (0.21)[f]	184.1 (7.9)[h]
G	HEMA	GM	50%	53.0 (3.7)[a]	2.65 (0.25)[e]	157.4 (4.4)[g, i]
H	MBA	GM	50%	144.1 (8.2)[b]	5.40 (0.37)	213.2 (15)
I	HEMA	IEM	35%	68.1 (4.2)[c]	3.12 (0.32)	166.7 (12)[i, j]
J	MBA	IEM	35%	173.5 (1.1)[d]	7.10 (0.07)	249.5 (1.8)[k]
K	HEMA	IEM	50%	66.8 (7.5)[a, c]	2.63 (0.20)[e]	175.2 (10)[h, j]
L	MBA	IEM	50%	175.1 (4.9)[d]	6.50 (0.54)[f]	257.1 (18)[k]

[1]YCS = CS at yield; [2]UCS = ultimate CS; [3]Entries are mean values with standard deviations in parentheses and the mean values with the same superscript letter were not significantly different ($p > 0.05$). Specimens were conditioned in distilled water at 37 °C for 24 h.

EXAMPLE 21. COMPARATIVE EXAMPLE. Mechanical Strength Comparison Among the Cements Described Herein and Commercial FUJI II LC. The CS, DTS and FS of illustrative Examples were compared with those of commercial FUJI II LC cement. The results in Figure 7a show that the IEM-crosslinked cement exhibited significantly higher FS, DTS, and CS than FUJI II LC. The GM-crosslinked cement exhibited significantly higher FS and statistically similar DTS and CS compared to FUJI II LC. In addition, Figure 7b shows the CS, DTS and FS values for Example M (GM-crosslinked 4-arm PAA) compared to commercial FUJI II, FUJI II LC, and VITREMER cements. The observed strengths (MPa) for the cements are shown in Table 6. Example M refers to a cement with a P/L ratio of 2.7/1, GM-grafting ratio =50% and P/W=75/25 (see, Xie, D., Yang, Y., Zhao, J., Park, J-G., Zhang, J.-T., "A Novel Comonomer-Free Light Cured Glass-Ionomer Cement for Reduced Cytotoxicity and Enhanced Mechanical Strengths," Dental Materials, 23(8):994-1003 (2007)).

Table 6. FS, DTS, and CS for Examples compared to commercial cements.

Example	FS (MPa)	DTS (MPa)	CS (MPa)
IEM-crosslinked	93.9 ± 11	58.9 ± 7.2	257.1 ± 18
GM-crosslinked	74.7 ± 12	24.4 ± 3.6	213.3 ± 15
Example M	90.8 ± 5.5	50.2 ± 0.5	272.9 ± 8.4
FUJI II	25.1 ± 4.8	21.6 ± 0.1 [(b)]	235.6 ± 4.4 [(a)]
FUJI II LC	55.8 ± 4.1 [(c)]	31.2 ± 2.2	212.7 ± 12 [(a)]
VITREMER	57.8 ± 6.9 [(c)]	25.6 ± 0.6 [(b)]	148 ± 0.6

[(a)] Not significantly different ($p > 0.05$); [(b)] Not significantly different ($p > 0.05$); [(c)] Not significantly different ($p > 0.05$).

The light-curable 4-arm star-shape PAA was synthesized via ATRP and showed a lower viscosity as compared to the corresponding linear counterpart that was synthesized via conventional free-radical polymerization. Without being bound by theory, it is suggested that the spherical nature of the 4-arm star-shape PAA may account for the difference in observed viscosity. Both GM-crosslinked and IEM-crosslinked variants of the 4-arm PAA-constructed

LCGICs showed significantly high mechanical strengths than conventional cements. It was also observed that the MBA-containing cement variants exhibited much higher CS than the HEMA-containing cement variants. Without being bound by theory, it is also suggested that a salt-bridge contribution of the MBA may account for the improved CS. The IEM-crosslinked cement variants showed much higher mechanical strengths than the GM-crosslinked cement variants. Without being bound by theory, it is also suggested that a hydrophobicity difference between the two corresponding polymers may account for the improved mechanical strengths. The selected cements described herein showed 13% improvement in CS, 178% improvement in DTS, and/or 123% improvement in FS over the conventional cement prepared from FUJI II LC.

The results in Table 7 show that the polyfunctional core molecules and prepolymer compounds described herein, including poly(acrylic acid) crosslinked with pendent methacrylate to formulate the LCGIC improves the mechanical strengths and wear resistance of the GICs. The 4-arm star poly(acrylic acid) Example was improved by 48% in CS, 76% in DTS, 95% in FS and 60% in FT higher than FUJI II LC cement. The Example also showed higher wear-resistance (97.5 $\mu m^3 cycle^{-1}$) than FUJI II LC (11525 $\mu m^3 cycle^{-1}$). Although the Example was 5% lower in CS, 20% higher in DTS, 20% lower in FS and 15% lower in FT than Filtek P60 posterior composite resin, it showed surprisingly improved (97.5 $\mu m^3 cycle^{-1}$) wear-resistance than Filtek P60 (545 $\mu m^3 cycle^{-1}$). These results indicate that it is feasible to make glass-ionomer cements to become a restorative with wear-resistance and mechanical strengths comparable to current posterior composite resins.

Table 7. CS, DTS, FS, FT and wear of 4-arm, FUJI II LC and FiltekP60

Example[1]	CS [MPa]	DTS [MPa]	FS [MPa]	FT [$MPa \cdot m^{-1/2}$]	Wear (volume loss)
4-arm	323.3 (11)	61.7 (5.3)	103.5 (0.7)	1.45 (0.05)	0.039 (0.01)
FUJI II LC	219.1 (1.7)	34.9 (2.9)	53.0 (2.8)	0.91 (0.03)	4.61 (0.44)
P-60	349.1 (18)	43.9 (4.2)	157.6 (2.6)	1.71 (0.07)	0.218 (0.05)

14-arm: The 4-arm star-shape poly(acrylic acid)-composed LCGIC, where Filler = FUJI II LC filler, Grafting ratio = 50%, P/W ratio = 75/25, and P/L ratio = 2.7; FUJI II LC: FUJI II LC LCGIC, where P/L ratio = 3.2; P-60: Filtek P60 posterior composite resin; All the specimens were light cured for 1-2 min. The 4-arm and FUJI II LC GICs for CS, DTS, FS, and FT tests were conditioned in distilled water at 37 °C for 1 week prior to testing. The 4-arm and FUJI II LC for wear-resistance were tested on a three-body machine after 24 h storage in water at 37 °C. All the cured specimens for P-60 were tested after 1 h under dry conditions. The wear cycle = 400,000.

EXAMPLE 22. Synthesis of the GM-Crosslinked 4-Arm PAA. The reaction between GM and carboxylic acid on PAA took about fourteen hours to complete. Disappearance of the epoxy group on GM at 761cm^{-1} in the FT-IR spectrum confirmed the completion of the crosslinking reaction. The completion of the crosslinking of GM was also confirmed by the fact that the yield was greater than 95%.

METHOD EXAMPLE. Significance of Crosslinking of GM onto the 4-Arm

PAA. It is believed that the main difference between RMGICs and conventional GICs is their liquid composition as described by A. D. Wilson, "Resin-modified glass-ionomer cement," Int. J. Prosthodont., 3:425-429 (1990). The liquid in RMGICs is composed of HEMA, photo-initiators, water, and a poly(alkenoic acid) having pendent in situ polymerizable methacrylate on its backbone or a mixture of poly(alkenoic acid) and methacrylate-containing monomer/oligomer. The liquid in conventional GICs consists of only hydrophilic poly(alkenoic acid) and water. Due to introduction of hydrophobic methacrylate functionality, amphiphilic monomers such as HEMA have to be incorporated into the RMGIC liquid formulation to enhance the solubility of the hydrophobic poly(alkenoic acid) in water. It is appreciated that, without these amphiphilic small molecules like HEMA, it is difficult to formulate RMGICs by using current technologies. It has been reported that crosslinking GM onto the poly(alkenoic acid) backbone can increase water-solubility of the polyacid because of introduction of hydroxyl groups as compared to 2-isocyanatoethyl methacrylate (IEM)-crosslinked poly(alkenoic acid), as described by D. Xie, J. G. Park, and M. Faddah, J. Biomater. Sci. Polym. Edn., 17:303-322 (2006); S. B. Mitra, J. Dent. Res., 70:72-74 (1991); D. Xie, B. M. Culbertson, and W. M. Johnston, J. M. S., Pure Appl. Chem., A35(10):1631-1650 (1998); D. Xie, I.-D. Chung, W. Wu, J. Lemons, A. Puckett, and J. Mays, "An amino acid modified and non-HEMA containing glass-ionomer cement," Biomaterials, 25(10):1825-1830 (2004). The IR spectrum of the GM-crosslinked 4-arm PAA indicates that each GM molecule produces one extra hydroxyl group when the epoxy group on GM reacts with the carboxyl group on PAA. It is appreciated that, unlike IEM-crosslinking, these hydroxyl groups may make the GM-crosslinked PAA less hydrophobic or at least not increase the hydrophilicity of the PAA. It is also appreciated however that additional hydroxyl groups have the potential to reduce the mechanical strength and increase the viscosity due to their ability to absorb water and serve as a hydrogel. In contrast, those same hydrogen bonds make a contribution to hydrogen bond formation, thus increasing viscosity.

METHOD EXAMPLE. Effects of Polymer/Water Ratio and Grafting Ratio on Compressive Properties. To study the effects of P/W ratio (by weight) and grafting ratio (by mole) on strengths, seven liquid solutions (C to I) based on the 4-arm PAA crosslinked with GM and one liquid solution (B*) based on the linear PAA crosslinked with GM were formulated. Three P/W ratios including 50/50, 60/40 and 75/25 and three grafting ratios including 35%, 50% and 70% were studied. Table 8 and Figure 8 show the results of CS and DTS of the cements prepared from the above formulations. The cements C, D and E represent the 35% GM-crosslinked 4-arm PAAs with the P/W ratio at 50/50, 60/40 and 75/25. It is observed that increasing P/W ratio significantly increased yield compressive strength (YCS), modulus (M) and ultimate compressive strength (UCS), indicating that a higher polymer concentration may

enhance the mechanical strength of the relatively hydrophilic GM-crosslinked PAA cement. The cement C showed the lowest YCS (47.5 MPa), M (2.65 GPa) and UCS (68.5 MPa), suggesting that at 50/50, the hydrophilic characteristic of the GM-crosslinked PAA prevails and the cement behaves like a hydrogel. However, increasing polymer content in water overcomes that property exhibited by the hydroxyl groups from the GM-crosslinked PAA and makes the cement stronger.

METHOD EXAMPLE. The effect of grafting ratio on the strength was studied by changing the grafting ratio from 35% to 70%. It was observed that at P/W = 60/40 increasing grafting ratio significantly increased YCS and UCS but not necessarily M. However, at 75/25, increasing grafting ratio did significantly increase the CS values from 35% to 50% but did not significantly change the CS when the ratio reached 70%. However, there was no statistical difference between the 50% and 70% GM-crosslinked cements at 75/25. The highest strength values were observed as falling between the 50% and 70% GM-crosslinked 4-arm PAA cements at P/W ratio = 75/25, a shown in Table 8. These results support the feasibility of eliminating low MW comonomers in RMGIC formulations, which may improve the biocompatibility of conventional light-cured GICs. In contrast, the linear PAA (B*) that was synthesized via conventional free-radical polymerization showed much lower strengths (YCS = 105.4 MPa, M = 5.43 GPa and UCS = 124.5) than those for corresponding 4-arm PAA cement (G, 170.3, 6.62 and 245.8). The data from DTS showed the similar trend to those from CS. The order of DTS (MPa) was: I (39.5 ± 4.6) > G (29.3 ± 2.4) > H (29.1 ± 4.5) > F (21.3 ± 2.0) > E (18.4 ± 2.2) > D (17.3 ± 2.2) > N (14.4 ± 2.0). Both CS (256.0 MPa) and DTS (39.5 MPa) of the 70% GM-crosslinked cement at a P/W ratio of 75/25 were the highest among all the GM-crosslinked 4-arm PAA-constructed cements.

Table 8. Effects of polymer/water ratio and GM grafting ratio on compressive properties

Example	P/W Ratio	Grafting Ratio	YCS [MPa][1]	Modulus [GPa]	UCS [MPa][2]	Viscosity[3]
C	50/50	35%	47.5 (8.2)[3]	2.65 (0.82)	68.5 (7.2)	75.6
D	60/40	35%	81.8 (6.0)	5.00 (0.25)[b,c]	124.8 (9.4)[e]	275.2
E	75/25	35%	143.2 (2.7)	6.43 (0.18)[d]	166.8 (9.9)[f]	3323
F	60/40	50%	91.9 (4.2)	4.85 (0.18)[b]	146.5 (6.9)	171.5
G	75/25	50%	202.3 (7.2)	6.84 (0.45)[d]	272.9 (8.5)[g]	1764
H	60/40	70%	105.5 (7.9)[a]	5.19 (0.25)[c]	159.7 (7.6)[f]	206.4
I	75/25	70%	197.2 (11)	6.67 (0.18)[d]	286.8 (12)[g]	2094
B*[4]	75/25	50%	105.4 (7.7)[a]	5.43 (0.34)[c]	126.5 (7.7)[e]	6830

[1]YCS = CS at yield; [2]UCS = ultimate CS; [3]Entries are mean values with standard deviations in parentheses and the mean values with the same superscript letter were not significantly different ($p > 0.05$). [4]B* = linear PAA, which was synthesized via conventional free-radical polymerization and crosslinked with GM. Specimens were conditioned in distilled water at 37 °C for 24 h.

METHOD EXAMPLE. Effect of Glass Powder/Polymer Liquid Ratio on Compressive Properties. It is appreciated that the glass powder/polymer liquid (P/L) ratio is an

important parameter in formulating GICs. It is also appreciated that a higher P/L ratio may result in higher mechanical strengths, especially CS, but it may also shorten working time. It is also appreciated that working time is less of an issue for a light-curable GIC system, and therefore a higher P/L ratio may be used in LCGICs, such as the filler FUJI II LC (3.2). The effect of three P/L ratios (2.2, 2.7 and 3.0) on CS is shown in Table 9. A significant increase in YCS, M and UCS was observed when the P/L ratio was increased from 2.2 to 2.7 but not from 2.7 to 3.0. No statistical difference in YCS, M and UCS was found between 2.7 and 3.0. A formulation with a P/L ratio of 2.7/1 for the Examples was used to make experimental cements derived from GM-crosslinked 4-arm PAA.

Table 9. Effects of P/L ratio and aging on compressive properties

Parameter	YCS [MPa][1]	UCS [MPa][2]	Modulus [GPa]
	Effect of P/L ratio[4]		
2.2	144.2 (1.3)[3]	204.7 (1.8)	5.86 (0.30)
2.7	202.3 (7.2)	272.9(8.5)	6.89 (0.45)[c]
2.7	164.0 (1.1)[a]	256.0 (5.8)[b]	6.89 (0.33)[c]
3.0	179.4 (1.9)	244.2 (2.1)	6.94 (0.21)[c]
3.0	170.4 (2.1)[a]	244.2 (2.1)[b]	6.94 (0.21)[c]
	Effect of aging[5]		
1 h	78.1 (2.8)	209.2 (6.5)	2.59 (0.02)
1 d	164.0 (1.1)	256.0 (5.8)	6.89 (0.33)
1 w	252.9 (3.1)	329.7 (11)	8.12 (0.29)

[1]YCS = CS at yield; [2]UCS = ultimate CS; [3]Entries are mean values with standard deviations in parentheses and the mean values with the same superscript letter were not significantly different ($p > 0.05$); [4]Grafting ratio = 70% and P/W ratio = 75/25; Specimens were conditioned in distilled water at 37 °C for 24 h; [5]Grafting ratio = 70%, P/W ratio = 75/25 and P/L ratio = 2.7. Specimens were conditioned in distilled water at 37 °C prior to testing.

METHOD EXAMPLE. Aging. It has been reported that GICs increase their strengths with time due to the continuing formation of salt-bridges, as described by C. L. Davidson, and I. A. Mjör, "Advances in glass-ionomer cements," Quintessence Publ. Co., Chicago, IL, 1999. The optimal 70% GM-crosslinked 4-arm PAA cement was conditioned at 37 °C in distilled water for 1 h, 1 day and 1 week, followed by CS determinations. As shown in Table 9, the compressive strengths were significantly increased from 78.1 to 252.9 MPa in YCS, 2.59 to 8.12 GPa in M, and 209.2 to 329.7 MPa in UCS within one week.

Comparison between the experimental cement and commercial control. The FS of the optimal experimental cement was measured and compared to the measured CS, DTS and FS of commercial FUJI II LC cement. The strengths of both cements were determined after conditioning in distilled water at 37 °C for 24 h. The CS, DTS and FS of illustrative cements described herein were compared to FUJI II LC. For the illustrative cements, GM grafting ratio = 70%; P/W ratio = 75/25; P/L ratio = 2.7; For FUJI II LC, P/L ratio = 3.2. The light-cured cement described herein showed significantly higher CS (256.0 ± 5.8 MPa), DTS (39.5 ± 4.6 MPa) and

FS (98.4 ± 5.0 MPa) as compared to corresponding 228.2 ± 6.4, 21.2 ± 1.1 and 44.2 ± 3.4 for FUJI II LC.

METHOD EXAMPLE. Mechanical Strength Comparison. The mechanical strength (CS, DTS and FS) between Example M and commercial FUJI II (conventional GIC), FUJI II LC (light-cured GIC) and VITREMER (light-cured GIC) (Figure 9). Table 10 shows the details of strength changes of these cements in the course of aging, including yield compressive strength (YS), modulus (M), and ultimate compressive strength (UCS). Example M showed significantly higher CS, DTS and FS as compared to the tested commercial cements as shown in Table 9. Higher mechanical strengths is exhibited by Example M. Without being bound by theory, it is suggested that because Example M has a comonomer-free and pendent hydroxyl group-containing system, the polymer liquid contains highly concentrated GM-crosslinked star-shape poly(AA) in water, which provides not only a large quantity of carboxyl groups for salt-bridge formations but also a substantial amount of carbon-carbon double bond for covalent crosslinks. In contrast, both FUJI II LC and VITREMER contain HEMA and/or other low MW methacrylate comonomers. The effect of aging on Example M, FUJI II, FUJI II LC and VITREMER on CS over a period of two weeks is shown in Figure 9. As shown in Figure 9, they have a lower strength as compared to Example M. FUJI II showed relatively higher CS but lower DT and FS as compared to FUJI II LC and VITREMER. Conventional GICs do not produce any covalent crosslinks except for salt-bridges (ionic bonds) when they are set.

Table 10. YS, modulus, UCS in the course of aging.

Example	1 h	1 d	1 w	2 w
	YS[1] (MPa)			
M[4]	81.7 (0.9)[a,3]	202.3 (7.2)[c]	274.1 (2.1)[A]	278.5 (11)[A]
FUJI II	95.1 (0.8)[b]	199.9 (2.7)[c]	200.1 (3.0)[B]	204.2 (10)[B]
FUJI II LC	87.8 (2.3)[a,b]	120.9 (10)	125.7 (7.0)[C]	141.5 (9.4)[C]
VITREMER	32.2 (2.4)	87.3 (0.7)	104.9 (5.8)[D]	101.7 (7.3)[D]
	Modulus (GPa)			
M	4.18 (0.19)	6.84 (0.45)	8.73 (0.05)[E]	8.87 (0.23)[E]
FUJI II	6.98 (0.05)	9.06 (0.07)	9.52 (0.13)[F]	9.62 (0.04)[F]
FUJI II LC	3.62 (0.16)	5.33 (0.09)[d,G]	5.40 (0.28)[f,G]	5.64 (0.15)[g]
VITREMER	2.07 (0.09)	4.99 (0.17)[d]	5.38 (0.17)[f]	5.78 (0.31)[g]
	UCS[2] (MPa)			
M	217.5 (4.0)	272.9 (8.5)	334.9 (5.4)[H]	335.2 (4.5)[H]
FUJI II	152.0 (0.3)	235.6 (4.4)[e,I]	252.0 (7.4)[I]	251.4 (6.9)[I]
FUJI II LC	181.5 (12)	212.7 (15)[e,J]	219.1 (1.7)[J]	208.6 (11)[J]
VITREMER	88.9 (4.5)	148.1 (0.6)[K]	153.5 (2.3)[K]	150.8 (1.6)[K]

[1]YS = CS at yield; [2]UCS = ultimate CS; [3]Entries are mean values with standard deviations in parentheses and the mean values with the same superscript letter were not significantly different ($p > 0.05$); [4]Grafting ratio = 50%, P/W ratio = 75/25 and P/L ratio = 2.7. Specimens were conditioned in distilled water at 37 °C prior to testing.

METHOD EXAMPLE. In Vitro Cytotoxicity. The *in vitro* cytotoxicity of

Example M was studied using Balb/c 3T3 mouse fibroblast cells. It has been reported that RMGICs are more cytotoxic than conventional GICs (see, Leyhausen, G., Abtahi, M., Karbakhsch, M., Sapotnick, A., Geustsen, W., "Biocompatibility of various light-curing and one conventional glass-ionomer cements," Biomaterials, 19:559-564 (1998)). It has been suggested that certain leachable material, such as HEMA and incorporated photo-initiators and activators from RMGICs, which have been shown to cause adverse effects on cell viability and thus caused cytotoxicity (Geurtsen, W., Spahl, W., Leyhausen, G., "Residual monomer/additive release and variability in cytotoxicity of light-curing glass-ionomer cements and compomers," J. Dent. Res., 77(12):2012-9 (1998)), may be the cause. However, it is appreciated that glass-ionomers generally are considered to be inert materials as compared to dental composite resins. Unpolymerized monomers my also be responsible for pulp cell cytotoxicity (Stanislawski, L., Daniau, X., Lauti, A., Goldberg, M., "Factors responsible for pulp cell cytotoxicity induced by resin-modified glass ionomer cements," J. Biomed. Mater. Res., 8(3):277-88 (1999)). RMGICs have been shown to cause the highest cytophatic effects on odontoblast cell line (MDPC-23) (de Souza Costa, C.A., Hebling, J., Garcia-Godoy, F., Hanks, C.T., "In vitro cytotoxicity of five glass-ionomer cements," Biomaterials, 24:3853-3858 (2003)).

In vitro cell culture studies have been used as screening tests for evaluation of dental materials. Balb/c 3T3 mouse fibroblast cell lines were used to examine the *in vitro* cytotoxicity of Example M and compared it with those for commercial FUJI II, FUJI II LC and VITREMER, with the help of MTT assay. Example M was not expected to show any significant cytotoxicity and its *in vitro* cytotoxicity was expected to be as low as that of those conventional GICs because that example does not contain any comonomers in its formulation. Figure 10 shows the cell viability after the cells were cultured with the eluates of Example M, FUJI II, FUJI II LC, VITREMER, and blank, i.e., negative control (NC). The viability (%) was in the decreasing order: (1) for the 3-day eluate, NC (99.4 ± 1.9) > Example M (86.1 ± 1.9) > FUJI II (83.4 ± 2.6) > FUJI II LC (70.5 ± 6.7) > VITREMER (55.8 ± 3.2), where Example M and FUJI II were not significantly different from each other ($p > 0.05$); (2) for the 7-day eluate, NC (98.1 ± 6.7) > Example M (93.4 ± 0.8) > FUJI II (86.1 ± 3.3) > VITREMER (43.6 ± 6.6) > FUJI II LC (31.7 ± 7.8), where NC, Example M and FUJI II were not significantly different from each other ($p > 0.05$). Figure 11a and Figure 11b show the cell viability vs. eluate concentration at the 3-day and 7-day extractions, respectively.

Optical photomicrographs were obtained that showed the cell morphology and density after culturing for with the following cement eluates: NC, Example M, FUJI II, FUJI II LC and VITREMER.

From Figure 10, except for NC, Example M showed the highest cell viability after

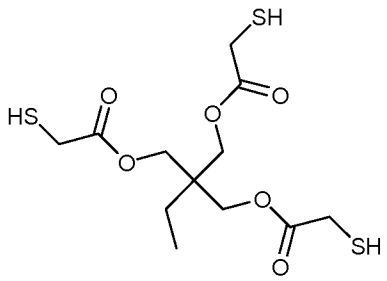
cell exposure to both 3-day and 7-day eluates. VITREMER showed the lowest viability to the 3-day eluate whereas FUJI II LC showed the lowest viability to the 7-day eluate. This may be attributed to the fact that Example M contains no comonomers before polymerization and thus no leachables (unreacted monomers) should be expected. Likewise, FUJI II showed very little cytotoxicity because it is a conventional GIC, which does not contain any leachable monomers or other additives such as photo-initiators and activators (Wilson, A.D., McLean, J.W., "Glass-ionomer cements," Chicago, IL, Quintessence Publ Co., 1988; Davidson C.L., Mjör. I.A., "Advances in glass-ionomer cements," Chicago, IL, Quintessence Publ. Co., 1999). VITREMER cement was reported to be the most cytotoxic among several tested cements including FUJI II LC (de Souza Costa, C.A., Hebling, J., Garcia-Godoy, F., Hanks, C.T., "In vitro cytotoxicity of five glass-ionomer cements," Biomaterials, 24:3853-3858 (2003); Stanislawski, L., Daniau, X., Lauti, A., Goldberg, M., "Factors responsible for pulp cell cytotoxicity induced by resin-modified glass ionomer cements," J. Biomed. Mater. Res., 48(3):277-88 (1999); Geurtsen, W., Spahl, W., Leyhausen, G., "Residual monomer/additive release and variability in cytotoxicity of light-curing glass-ionomer cements and compomers," J. Dent. Res., 77(12):2012-2019 (1998)), which has been attributed mainly to the photo-activator, diphenyliodonium chloride and partially to the comonomer, HEMA.

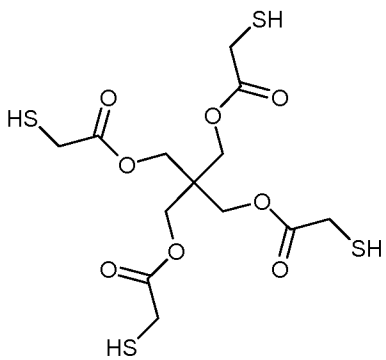
In the case of FUJI II LC, it was believed that this cement is much less *in vitro* cytotoxic than VITREMER because there is no diphenyliodonium chloride in the formulation of FUJI II LC, although FUJI II LC contains HEMA (Geurtsen, W., Spahl, W., Leyhausen, G., "Residual monomer/additive release and variability in cytotoxicity of light-curing glass-ionomer cements and compomers," J. Dent. Res., 77(12):2012-2019 (1998)). However, the present study showed that FUJI II LC was more cytotoxic than VITREMER after the cells were cultured with the 7-day eluate, even though VITREMER showed a strong cytotoxicity to the cells for the 3-day eluate. Without being bound by theory, this new finding suggests that the cytotoxic elutes from FUJI II LC may require more time to leach out of the specimens, as compared to the other LCGICs including VITREMER. Indeed, FUJI II LC had been reported to contain a substantial amount of HEMA in its liquid formulation by gas chromatography.

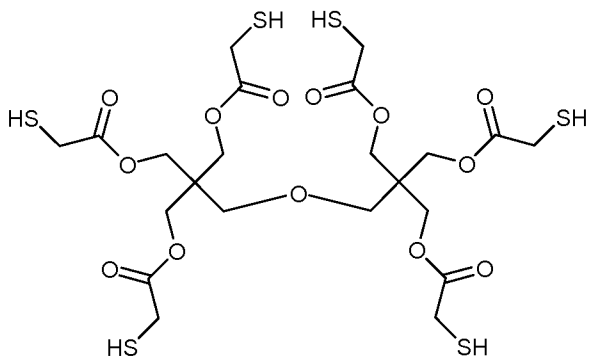
Additionally, the cytotoxicity of the materials was dose-dependent (see Figure 11a and 11b) (Stanislawski, L., Daniau, X., Lauti, A., Goldberg, M., "Factors responsible for pulp cell cytotoxicity induced by resin-modified glass ionomer cements," J. Biomed. Mater. Res., 48(3):277-88 (1999). The eluate concentration at 80% showed the highest cytotoxicity. Regarding the cell morphology and density, the optical photomicrographs showed that NC, Example M and FUJI II exhibit very high cell density and the cells almost grew full of a cell well. In contrast, there were very few cells in both cell wells containing FUJI II LC and

VITREMER, indicating that most cells died due to the cytotoxicity of the sample eluates. The cell morphology and density for the 3-day eluate were similar to those for the 7-day eluate.

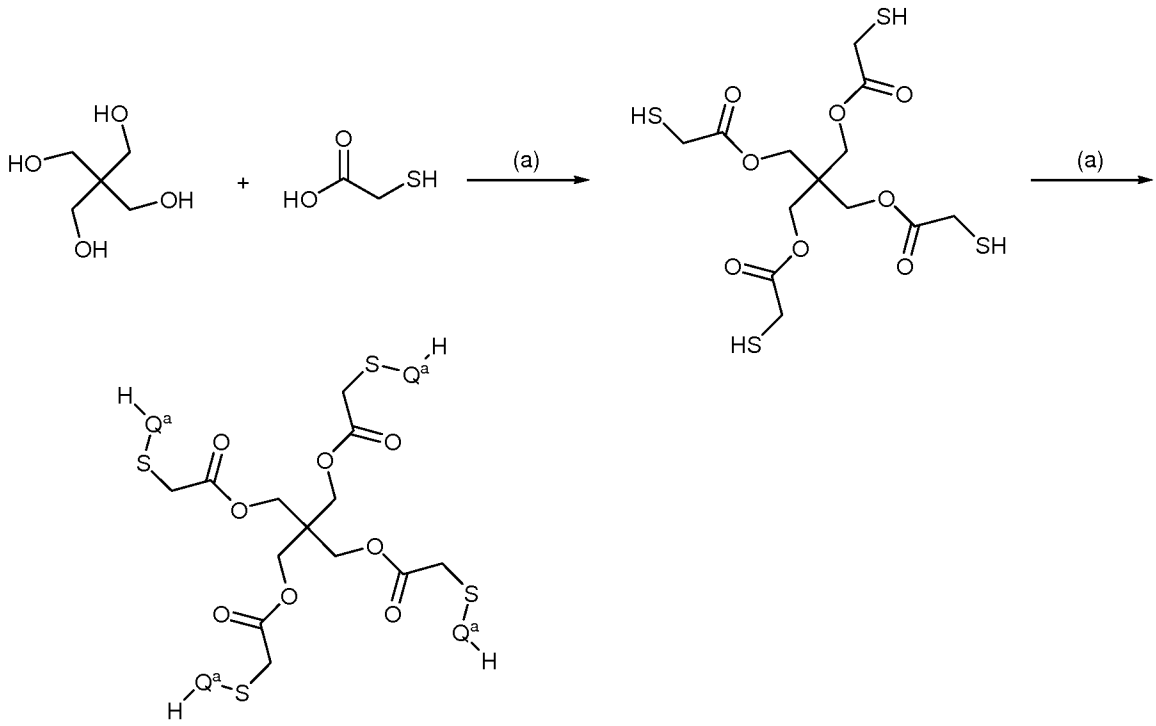
EXAMPLE 23. Synthesis of 4-Arm Chain-Transfer Agent. 4-Arm chain-transfer agent (CTA), pentaerythritol tetra(mercaptoacetate), was prepared as described by Mayadunne et al., Tetrahedron Letters, 43:6811-6814 (2002). To a flask equipped with a thermometer, condenser and Dean Stark trap for collecting water, a mixture of pentaerythritol (11.1 g, 0.0815 mol), mercaptoacetic acid (45 g, 0.4885 mol) and p-toluenesulfonic acid monohydrate (1.5 g, 7.88 mmol) in toluene (50 ml) was added. After refluxing in toluene for 3.5 h, the mixture was poured into saturated $NaHCO_3$ solution followed by extracting with ethyl acetate. After washing with 10% HCl and saturated NaCl solution, the extract was dried with anhydrous $MgSO_4$. The final product was obtained by completely removing ethyl acetate. The 3-arm trimethylolpropane tri(mercaptoacetate) and 6-arm dipentaerythritol hexa(mercaptoacetate) were synthesized similarly. The yields were greater than 95% for all three CTAs. Illustrative CTAs, 1-arm, 3-arm, 4-arm, and 6-arm, respectively, described herein are as follows:



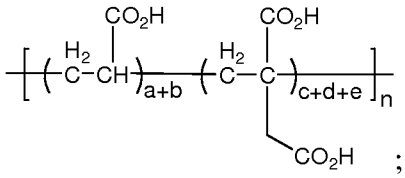




EXAMPLE 24. Synthesis of Polymers. Poly(AA-co-IA) copolymer was synthesized using a free-radical polymerization, as follows:

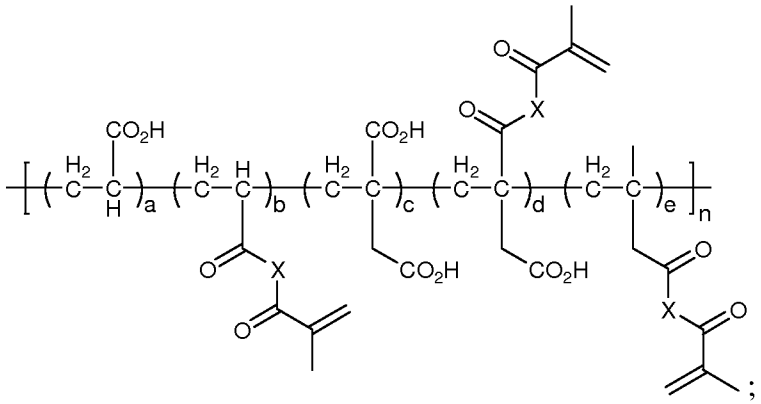


wherein Q^a is



where a, b, c, d, e, and n are as described herein.

To a round-bottom flask, a mixture of AA (5.2 g, 0.072 mol), IA (2.34 g, 0.018 mol), ACVA (0.025 g, 0.09 mmol), 4-arm CTA (0.218 g, 0.503 mmol) and distilled water (7.5 ml) was added. After being degassed and nitrogen-purged three times via a freeze-thaw cycle, the solution was heated to 70 ºC and kept at that temperature for 17 h. The molar feed ratio (AA/IA = 8:2 by mole) was used as described by Xie et al., J. Biomater. Appl., 21:147-165 (2006). The polymers with different molecular weights (MW) were prepared by changing the amount of CTA used. The final products were freeze-dried, ground, and stored prior to use. The yields were greater than 96% for all the polymers synthesized in the study. It is to be understood that the compounds illustrated in this example may be, as described herein, converted into the corresponding crosslinkable polyfunctional prepolymers described herein, where Q^a is



where X is illustratively NH-CH_2-CH_2-O (IEM) or O-CH_2-CH(OH)-CH_2-O (GM); and a, b, c, d, e, and n are as described herein.

EXAMPLE 25. Characterization of Monomers and Polymers. The synthesized chain-transfer agents were characterized by FT-IR and NMR spectroscopy. The polymers were characterized by FT-IR and gel permeation chromatography (GPC). FT-IR spectra were obtained on a FT-IR spectrometer (Mattson Research Series FT/IR 1000, Madison, WI). ^{1}H NMR spectra were obtained on a NMR spectrometer (Varian-Inova narrow-bore 500 MHz NMR, Varian, Inc., Palo Alto, CA) using deuterated methyl sulfoxide as a solvent. For determination of molecular weight, the polymers were treated with diazomethane, which was generated from DIAZALD reacted with potassium hydroxide (KOH) in water/ethanol solution at 65 °C, to obtain partially esterified products, having solubility in THF for molecular weight estimation. Molecular weights were estimated on a Waters GPC unit (Model 410 differential refractometer, Waters Inc., Milford, MA), using standard GPC techniques and polystyrene standards. THF was used as a solvent.

EXAMPLE 26. Viscosity Determination. The viscosity of the liquid formulated with the polymer and distilled water was determined at 23 °C using a programmable cone/plate viscometer (RVDV-II + CP, Brookfield Eng. Lab. Inc., Middleboro, MA).

EXAMPLE 27. Formulation and Preparation of Specimens for Strength Tests. A two-component system (liquid and powder) was used to formulate the cements. The liquid was prepared by simply dissolving the polymer in distilled water. The powder was FUJI II glass powder for conventional GIC. Specimens were prepared under the same conditions unless specified: powder/liquid ratio (P/L, by weight) = 2.7/1 (as recommended by the manufacturer) and polymer/water ratio (P/W, by weight) = 50/50. Specimens were fabricated at room temperature according to the protocol published by Wu et al., Eur. Polym. J., 39:959-968 (2003). The cylindrical specimens were prepared in glass tubing with dimensions of 4 mm diameter by 8 mm length for compressive strength (CS) and 4 mm diameter by 2 mm length for diametral tensile strength (DTS) tests. Specimens were removed from the mold after 15 minutes in 100%

humidity, and conditioned in distilled water at 37 ºC for 24 h prior to testing.

EXAMPLE 28. The synthesized chain-transfer agents (CTA) and polymer were characterized using FT-IR and ^{1}H NMR spectrometers. The FT-IR spectra for 2-mercaptoethanol (1-arm CTA), 3-arm CTA, 4-arm CTA and 6-arm CTA had the following characteristic peaks (cm^{-1}): (1) 1-Arm CTA: 3367 (O-H stretching) and 1637 (O-H deformation) for hydroxyl group; 2933, 2555, 1462, 1292 and 757 (stretching and deformation) for thiol group; 2968 and 2874 (C-H stretching) for methylene group. (2) 3-Arm CTA: 2937, 2567, 1465, 1277 and 755 (stretching and deformation) for thiol group; 1735 (C=O stretching) for carbonyl group; 2967, 2884, 1408, 1147 and 1017 (C-H stretching and deformation) for methylene group; 1388, 1053 and 784 (C-H stretching and deformation) for methyl group. (3) 4-Arm CTA: 2937, 2566, 1469, 1273 and 755 (stretching and deformation) for thiol group; 1736 (C=O stretching) for carbonyl group; 2962, 2900, 1407, 1145 and 1022 (C-H stretching and deformation) for methylene group. (4) 6-arm CTA: 2930, 2566, 1467, 1276 and 755 (stretching and deformation) for thiol group; 1735 (C=O stretching) for carbonyl group; 2962, 2904, 1405, 1147 and 1018 (C-H stretching and deformation) for methylene group. The significant and strong peaks at 1735 or 1736 for carbonyl and 1273 or 1276 for thiol groups confirmed the formation of the 3-, 4- and 6-arm CTAs.

The FT-IR spectra for 4-arm CTA, AA, IA and 4-arm poly(AA-co-IA) showed the following characteristic peaks: (1) 4-Arm CTA: 2937, 2566, 1469, 1273 and 755 (stretching and deformation) for thiol group; 1736 (C=O stretching) for carbonyl group; 2962, 2900, 1407, 1145 and 1022 (C-H stretching and deformation) for methylene group. (2) AA: 3600-2400 (O-H stretching), 1727 (C=O stretching), and 1617, 1299, 1189 as well as 931 (O-H and C-O deformation and stretching) for carboxyl group; 1635 (C=C bending) and 1440, 1412, 1189, 1060, 984 as well as 812 (C=C deformation) for C=C group. (3) IA: 3600-2400 (O-H stretching), 1702 (C=O stretching), and 1628, 1309, 915, 734 as well as 626 (O-H and C-O deformation and stretching) for carboxyl group; 1633 (C=C bending) and 1436, 1412, 1216, 1066, 986 as well as 817 (C=C deformation) for C=C group; 2930, 2620, 1392, 1168 and 943 (C-H stretching and deformation) for methylene group. (4) Poly(AA-co-IA): 3600-2400 (very broad O-H stretching), 1716 (C=O stretching) and 1628, 1402, 1258, 1025 as well as 808 (O-H and C-O deformation and stretching) for carboxyl group; 2949, 2586, 1454, 1168 and 943 (C-H stretching and deformation) for methylene group. Formation of the very broad peak at 3600-2400 for associated carboxyl groups from poly(AA-co-IA) and disappearances of the peaks at 1635 or 1633, 1436, 1412, 1216, 1066, 986 and 817 for C=C group confirmed the formation of poly(AA-co-IA) copolymer.

EXAMPLE 29. The ^{1}H NMR spectra for mercaptoacetic acid, pentaerythritol, 4-arm CTA and 4-arm poly(AA-co-IA) showed the following chemical shifts (ppm): (1)

Mercaptoacetic acid: a: 7.58 (COOH); b: 3.56 (CH_2); and c: 3.87 (S-H). (2) Pentaerythritol: a: 4.22 (CH_2) and b: 3.36 (O-H). (3) 4-Arm CTA: a: 4.18 (CH_2); b: 3.35 (S-H); and c: 2.94 (CH_2). (4) 4-Arm poly(AA-co-IA): a: 12.25 (COOH). For mercaptoacetic acid, pentaerythritol and the synthesized 4-arm CTA, the corresponding ^1H NMR spectra confirmed their structures. For the 4-arm poly(AA-co-IA), its typical carboxylic acid (COOH) peak was observed at 12.25 ppm.

EXAMPLE 30. The molecular weights of the synthesized polymers and the viscosities of the polymer aqueous solutions were determined using GPC and a viscometer, respectively. Table 1 shows the theoretical MWs, measured number average MW (Mn), measured weight average MW (Mw), MW distribution (PDI) of the synthesized polymers and viscosity values of the polymers in water (50/50, by weight). In the case of the 4-arm CTA, the measured Mn was quite similar to the calculated MW, except for 15K and 18K. The measured Mw shows the trend of consistency with the calculated MW. The PDI values were between 1.33 and 1.93. The viscosities (38.6 to 1439.5 cp) of these polymers were directly proportional to the measured Mw (7541 to 65130), i.e., the higher the MW the higher the viscosity. The effect of arm number was also compared in Table 1. The 4-arm star polymer (18K) showed a relatively lower viscosity as compared to the 3-arm polymer (18K) under the similar MW and so did the 6-arm (18K) polymer. It seems that the more arms that the polymer has, the lower the viscosity that the polymer exhibits. To demonstrate the star (or spherical) effect, we synthesized three linear polymers with the corresponding theoretical MWs of 9K, 18K and 36K using mercaptoethanol (1-arm CTA) as chain transfer agent for comparison. Apparently all the measured Mn values of the linear polymers were much higher than their corresponding calculated MWs, indicating that the synthesis of the linear polymers is more easily out of control as compared to that for the star polymers. Further, the linear polymers show much higher viscosity values (529, 1660 and 3737 cp) than their corresponding 4-arm star counterparts (87, 243 and 1439 cp), indicating a lower viscosity characteristic of the star-shape polymers.

Table 1. MWs and viscosities of the synthesized poly(AA-co-IA) polyacids

Polymer[1]	CTA[2]	MW_{theo}[3]	M_n[4]	M_w[5]	PDI[6]	Viscosity (cp)[7]
4-arm (4.5K)	4-arm	4932	4929	7541	1.53	38.6
4-arm (9K)	4-arm	9432	7942	12152	1.53	87.2
4-arm (12K)	4-arm	12432	10995	16933	1.54	126.9
4-arm (15K)	4-arm	15432	11822	22816	1.93	181.7
4-arm (18K)	4-arm	18432	31548	41959	1.33	243.2
4-arm (36K)	4-arm	36432	39473	65130	1.65	1439.5
3-arm (18K)	3-arm	18356	27407	37822	1.38	439.5
6-arm (18K)	6-arm	18698	21940	30935	1.41	237.6
Linear (9K)	1-arm	9078	28827	42664	1.48	529.3
Linear (18K)	1-arm	18078	38817	58614	1.51	1660.5
Linear (36K)	1-arm	36078	65330	114982	1.76	3737.5
Fuji II	N/A[8]	N/A	N/A	N/A	N/A	375.0

[1]Polymer = poly(AA-co-IA) with a molar ratio of 8:2; 4.5K, 9K, 12K, 15K, 18K and 36K represent the calculated or expected MW; [2]CTA = multi-arm chain-transfer agent used; [3]MW_{theo} = calculated MW; [4]M_n = number average MW measured by GPC; [5]M_w = weight number average MW measured by GPC; [6]PDI = MW distribution determined by GPC; [7]Viscosity of the polymer aqueous solution [poly(AA-co-IA):distilled water = 1:1, by weight] was measured using a cone & plate viscometer at 23 °C; [8]N/A stands for not available.

EXAMPLE 31. Formulation and Property Determination. To formulate a desired GIC, several important parameters needed to be considered. These parameters include MW of polymer, water content in formulation (polymer/water or P/W ratio), glass powder/liquid (P/L) ratio, etc. The effects of arm number of CTA, MW of the formed polymer, P/W ratio, P/L ratio and aging were evaluated. Table 2 shows the effect of arm number of CTA on compressive properties and viscosity. The linear polymer showed the lowest YS, modulus, UCS and highest viscosity, the 6-arm star polymer showed the highest YS and lowest viscosity, and the 4-arm star polymer showed the highest modulus and UCS. No significant differences were found in YS and UCS among all the four polymers. No statistically significant differences were found in modulus between the linear and 3-arm star polymers, between the 4-arm and 6-arm star polymers, and among the 3-arm, 4-arm and 6-arm star polymers. All the star-polymers showed much lower viscosities than the linear polymers, suggesting that we can increase MW of star-polymers to improve the mechanical strength of the cement while still keeping a relatively low viscosity for easy mixing and handling. It has been reported that the higher the MW the higher the mechanical strengths, as has been described by Wilson et al., J. Dent. Res., 68:89-94 (1989).

Table 2. Effect of CTA with different arms on compressive properties and viscosity

CTA[1]	Polymer[2]	YS[3] [MPa]	Modulus [GPa]	UCS[4] [MPa]	Viscosity[5] (cp)
1-arm	linear	166.3 (4.4)[a,6]	8.03 (0.13)[b]	199.9 (5.3)[e]	1660
3-arm	3-arm star	171.5 (11)[a]	8.13 (0.13)[b,c]	204.7 (9.9)[e]	440
4-arm	4-arm star	179.2 (6.4)[a]	8.43 (0.07)[c,d]	214.4 (7.2)[e]	243
6-arm	6-arm star	186.9 (13)[a]	8.30 (0.08)[c,d]	210.4 (9.9)[e]	237

[1]CTA = chain-transfer agent; [2]Polymer = poly(AA-co-IA) with a molar ratio of 8:2 and MW = 18K (calculated); [3]YS = CS at yield; [4]UCS = ultimate CS; [5]Viscosity of the polymer aqueous solution [poly(AA-co-IA):distilled water = 1:1, by weight] was measured using a cone & plate viscometer at 23 °C. [6]Entries are mean values with standard deviations in parentheses and the mean values with the same superscript letter were not significantly different ($p > 0.05$). All the specimens were conditioned in distilled water at 37 °C for 24 h.

EXAMPLE 32. Figure 12 shows the effects of MW and viscosity of the 4-arm star polymer on mechanical strengths of the cements. The viscosity values (cp) were in the decreasing order of 36K (1439.5) > 18K (243.2) > 15K (181.7) > 12K (126.9) > 9K (87.2) > 4.5K (38.6). Both CS (MPa) and DTS (MPa) were in the decreasing order of 15K (225.7 ± 5.6) > 36K (214.9 ± 2.5) > 18K (214.4 ± 7.2) > 9K (212.8 ± 8.1) > 12K (210.2 ± 5.6) > 4.5K (184.7 ± 2.5) for CS and 36K (29.6 ± 2.1) > 18K (25.4 ± 0.7) > 15K (23.8 ± 0.6) > 9K (23.6 ± 1.6) > 12K (23.5 ± 2.0) > 4.5K (19.8 ± 0.3) for DTS. There were no statistically significant differences in CS among all the polymers with different MWs and in DTS among all the polymers ($p > 0.05$) except for 36K, although the viscosity and MW values of the polymers were significantly different from one another. It seems that the polymer with MW of 15K gave the optimal CS and DTS and a reasonably low viscosity.

EXAMPLE 33. Figure 13 shows the effect of P/W ratio on strengths and viscosity. Both CS (MPa) and DTS (MPa) were in the decreasing order of 50/50 (225.7 ± 5.6) > 60/40 (205.1 ± 8.3) > 70/30 (139.1 ± 6.9) > 40/60 (130.4 ± 2.4) for CS and 60/40 (27.8 ± 1.4) > 50/50 (23.8 ± 0.5) > 70/30 (20.7 ± 1.1) > 40/60 (17.8 ± 1.6) for DTS. There were no statistically significant differences between 40/60 and 70/30 for CS, and between 50/50 and 70/30 and between 40/60 and 70/30 for DTS ($p > 0.05$). The viscosity values (cp) were in the decreasing order of 70/30 (20640) > 60/40 (1252) > 50/50 (181.7) > 40/60 (31.8). Increasing P/W ratio dramatically increased the viscosity but significantly decreased CS. The 50/50 showed the highest CS and second to the highest DTS. The 60/40 showed the highest DTS whereas the 40/60 showed the lowest CS and DTS. It has been reported that, in general, higher content of polymer leads to higher strengths (Xie et al., Dent. Mater., 23:994-1003 (2007)); however, it is appreciated that too much polymer can cause difficulty in mixing, which in turn leads to a reduction of strengths. From the results, the 50/50 appears to be the optimal P/W ratio among all

the P/W ratios studied based on both strength and viscosity.

EXAMPLE 34. Figure 14 shows the effect of P/L ratio on strengths. Both CS (MPa) and DTS (MPa) were in the decreasing order of 3.3 (248.8 ± 7.2) > 3.6 (248.3 ± 6.7) > 3.0 (235.2 ± 5.3) > 2.7 (225.6 ± 5.6) > 2.4 (200.7 ± 7.4) for CS and 3.3 (31.3 ± 1.3) > 3.6 (30.2 ± 1.7) > 3.0 (28.8 ± 1.0) > 2.7 (23.8 ± 0.6) > 2.4 (18.9 ± 0.5) for DTS. It appears that there were no statistically significant differences between 2.7 and 3.0 and among 3.0, 3.3 and 3.6 for CS and among 3.0, 3.3 and 3.6 for DTS ($p > 0.05$). Increasing P/L ratio seemed to increase both CS and DTS. The 3.3 appeared to show the highest CS and DTS whereas the 2.4 appeared to show the lowest CS and DTS. It is appreciated that, in creating composites, synergetic properties are often anticipated when the two components are combined, and that, in general, the proportion or ratio of these components in the mixture can significantly influence the properties of the formed composite. It is appreciated that more glass powder in the system often results in higher compression resistance, and that too much glass can lead to difficult handling, like the effect of very high polymer content. Without being bound by theory, it is believed that that is why there was no significant increase in strengths when P/L ratio = 3.6. During cement preparation, difficulties in mixing were encountered when a high P/L ratio (3.6) was used. However, unlike other polymer systems such as those reported by Crisp et al., J. Dent., 4:287-290 (1976), the P/L ratio in this new star polymer system can easily reach 3.3 without causing significant mixing difficulties. Without being bound by theory, it is believed this may be attributed to the characteristic of star shape of the polymers. It was found that a P/L ratio of 3.3 was optimal because it demonstrated both good mechanical strength and acceptable handling characteristics.

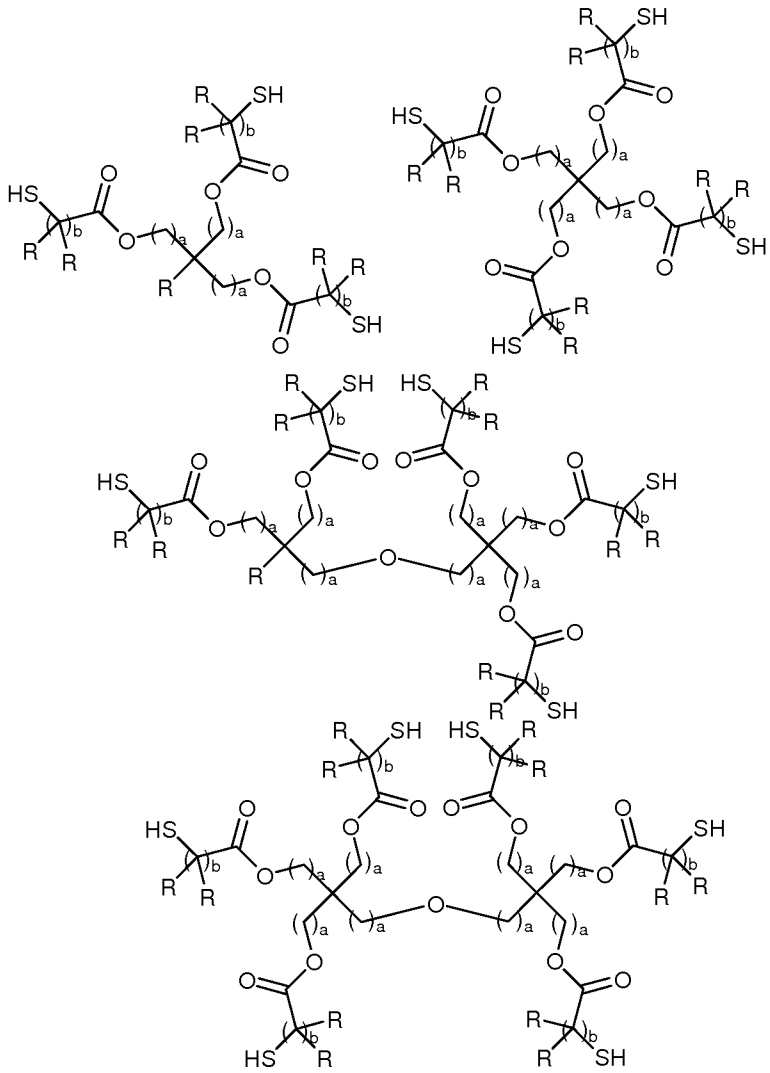
EXAMPLE 35. Figure 15 shows the effect of aging on CS. It has been reported that GICs increase their strengths in water with time due to constant salt-bridge formations (Cattani-Lorente et al., Dent. Mater., 10:37-44 (1994); Pearson et al., Biomaterials, 12:658-660 (1991)). The CS values of the 4-arm star polymer-composed cements with MWs of 9K, 15K and 36K were measured after being conditioned in water for 1 h, 1 day, 1 week, 1 month and 3 month. It is apparent that all the cements showed a significant increase (40 to 57%) in CS from 1 hr to 1 day. After that a slower increase (1.6%, 6% and 13% for 9K, 15K and 36K) in CS was noticed during a week. Finally, the cements with 9K, 15K and 36K showed 62%, 64% and 79% increase in CS from 1 hr to 3 months, respectively, with the final values of 270.1, 293.3 and 326.4 MPa. The cement with a MW of 36K increased CS the most, followed by the cements with 15K and 9K, indicating that the higher the MW of the polymer the more the CS increment of the cements. It is appreciated that this result is consistent with those reported in the dental literature. To compare this new system with control FUJI II cement, the aging of FUJI II cement was also tested. The result (Figure 15) shows that FUJI II exhibited 55% and 7% increases in CS from 1 h

to 1 day and from 1 day to 1 week, respectively. After that no changes were observed. The total CS increase of FUJI II was 68% during a 3-month aging period. The experimental cements (9K, 15K and 36K) showed 6% (270.1), 15% (293.3) and 28% (326.4) in CS higher than FUJI II (255.1) after aged in water for 3 months.

The foregoing examples are set forth as illustrative embodiments of the invention described herein. However, it is to be understood that such examples are not to be construed as limiting the invention as otherwise described herein. Variations and combinations of the features described herein are contemplated. For example, such variations as applied to the invention are also found in the cited documents, the disclosures of which are incorporated herein by reference.

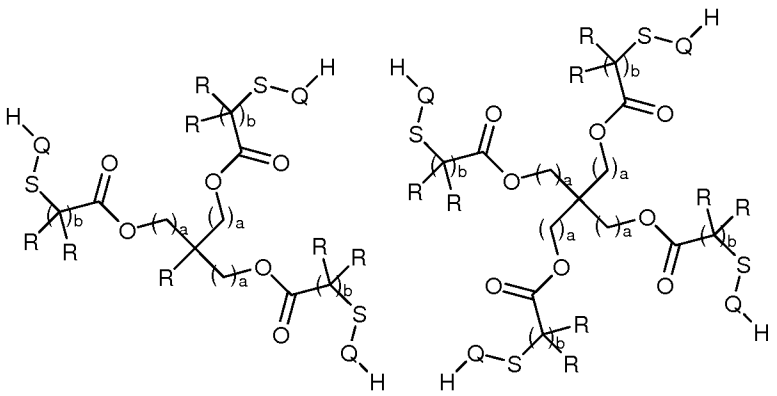
WHAT IS CLAIMED IS:

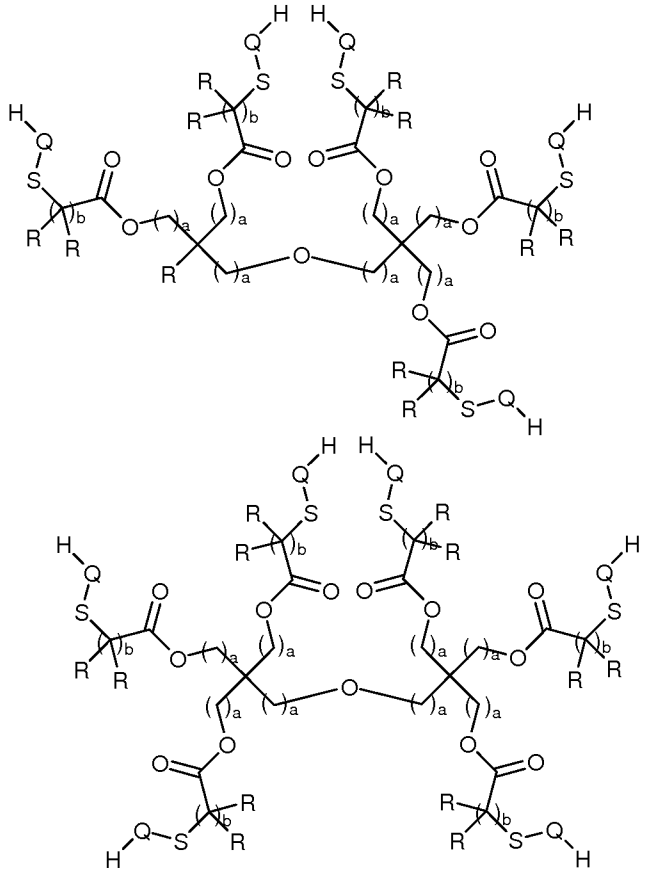
1. A polymer core initiator of the formula:



wherein in each instance R is hydrogen or an independently selected alkyl group; a is an independently selected integer from 1 to about 4; and b is an independently selected integer from 1 to about 4.

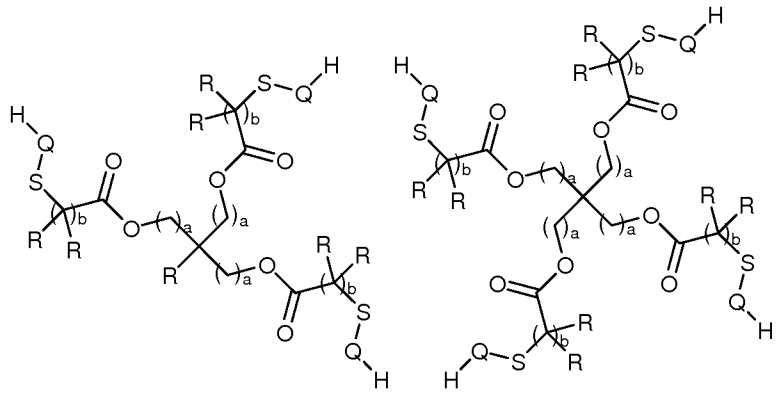
2. A polyfunctional prepolymer of the formula:

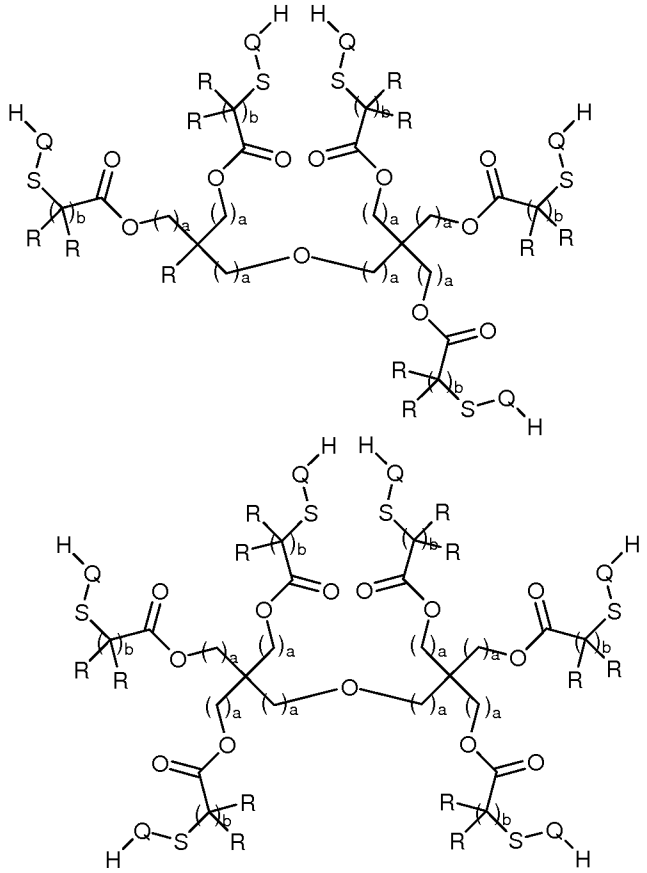




wherein in each instance R is hydrogen or an independently selected alkyl group; a is an independently selected integer from 1 to about 4; b is an independently selected integer from 1 to about 4; and Q is an independently selected polycarboxylic acid, said carboxylic acids selected from the group consisting of acrylic acids, and ester, amide, and salt derivatives thereof.

3. A cross-linkable polyfunctional prepolymer of the formula:





wherein in each instance R is hydrogen or an independently selected alkyl group; a is an independently selected integer from 1 to about 4; b is an independently selected integer from 1 to about 4; and Q is an independently selected polycarboxylic acid, said carboxylic acids selected from the group consisting of acrylic acids, and ester, amide, and salt derivatives thereof.

providing that at least a portion of said acrylic acids forming the polymer Q comprises esters or amides, or combinations thereof, of an alcohol or amine each independently selected from the group consisting of acryloyloxyalkanols, acryloyloxyalkylamines, acryloylaminoalkanols, and acryloylaminoalkylamines, each of which is optionally substituted.

4. The polyfunctional prepolymer of claim 2 or 3 wherein Q is a copolymer of one or more carboxylic acids selected from the group consisting of acrylic acid, methacrylic acid, and itaconic acid.

5. The polyfunctional prepolymer of claim 2 or 3 wherein Q is a block copolymer of one or more carboxylic acids selected from the group consisting of acrylic acid, methacrylic acid, and itaconic acid.

6. The polyfunctional prepolymer of claim 3 wherein the portion of said acrylic acids forming the polymer Q comprises esters or amides, or combinations thereof, of an alcohol or amine each independently selected from the group consisting of 2-isocyanatoethyl methacrylate, 2-hydroxyethyl methacrylate, and glycidyl methacrylate, and combinations thereof.

7. The polyfunctional prepolymer of claim 3 wherein the portion of said

acrylic acids forming the polymer Q comprises amides of 2-isocyanatoethyl methacrylate.

8. The polyfunctional prepolymer of claim 3 wherein the portion of said acrylic acids forming the polymer Q comprises esters of glycidyl methacrylate.

9. The polyfunctional prepolymer of claim 6 wherein the portion is about 10% to about 80% of Q.

10. The polyfunctional prepolymer of claim 6 wherein the portion is about 30% to about 60% of Q.

11. A kit comprising the polyfunctional prepolymer of claim 3.

12. The kit of claim 11 further comprising one or more acrylate co-monomers.

13. The kit of claim 12 wherein at least one co-monomer is selected from the group consisting of 2-isocyanatoethyl methacrylate, 2-hydroxyethyl methacrylate, glycidyl methacrylate, and combinations thereof.

14. The kit of claim 12 wherein at least one co-monomer is selected from the group consisting of 2-hydroxyethyl methacrylate, glycidyl methacrylate, and combinations thereof.

15. The kit of claim 12 wherein at least one co-monomer is glycidyl methacrylate.

16. A cement system comprising the polyfunctional prepolymer of claim 3.

17. The cement system of claim 16 further comprising one or more acrylate co-monomers.

18. The cement system of claim 17 wherein at least one co-monomer is selected from the group consisting of 2-isocyanatoethyl methacrylate, 2-hydroxyethyl methacrylate, glycidyl methacrylate, and combinations thereof.

19. The cement system of claim 17 wherein at least one co-monomer is selected from the group consisting of 2-hydroxyethyl methacrylate, glycidyl methacrylate, and combinations thereof.

20. The cement system of claim 17 wherein at least one co-monomer is glycidyl methacrylate.

21. The cement system composition of any one of claims 16 to 20 further comprising an inorganic filler.

22. The cement system composition of any one of claims 16 to 20 further comprising a radical initiator.

23. A method for repairing or restoring a defect in a mammalian tissue comprising the step of placing the cement system of any one of claims 16 to 20 in the defect, and curing the curable polymer composition.

24. The method of claim 23 wherein the cement system further comprises an inorganic filler.

25. method of claim 23 wherein the cement system further comprises a radical initiator.

26. The method of claim 23 wherein the curing step includes curing with radiation.

27. The method of claim 23 wherein the curing step includes curing with a radical initiator.

28. A process for preparing a dental implant polymer, the process comprising the steps of:

(a) providing a polyfunctional polymer core initiator, where the initiator includes a plurality of thiol groups; and

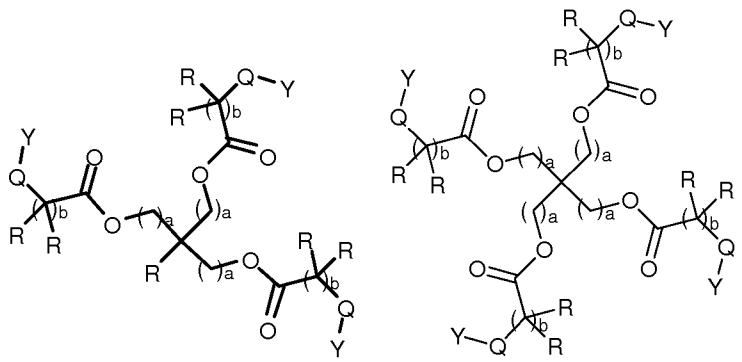
(b) reacting said thiol groups in a polymerization reaction with one or more acrylic acid monomers.

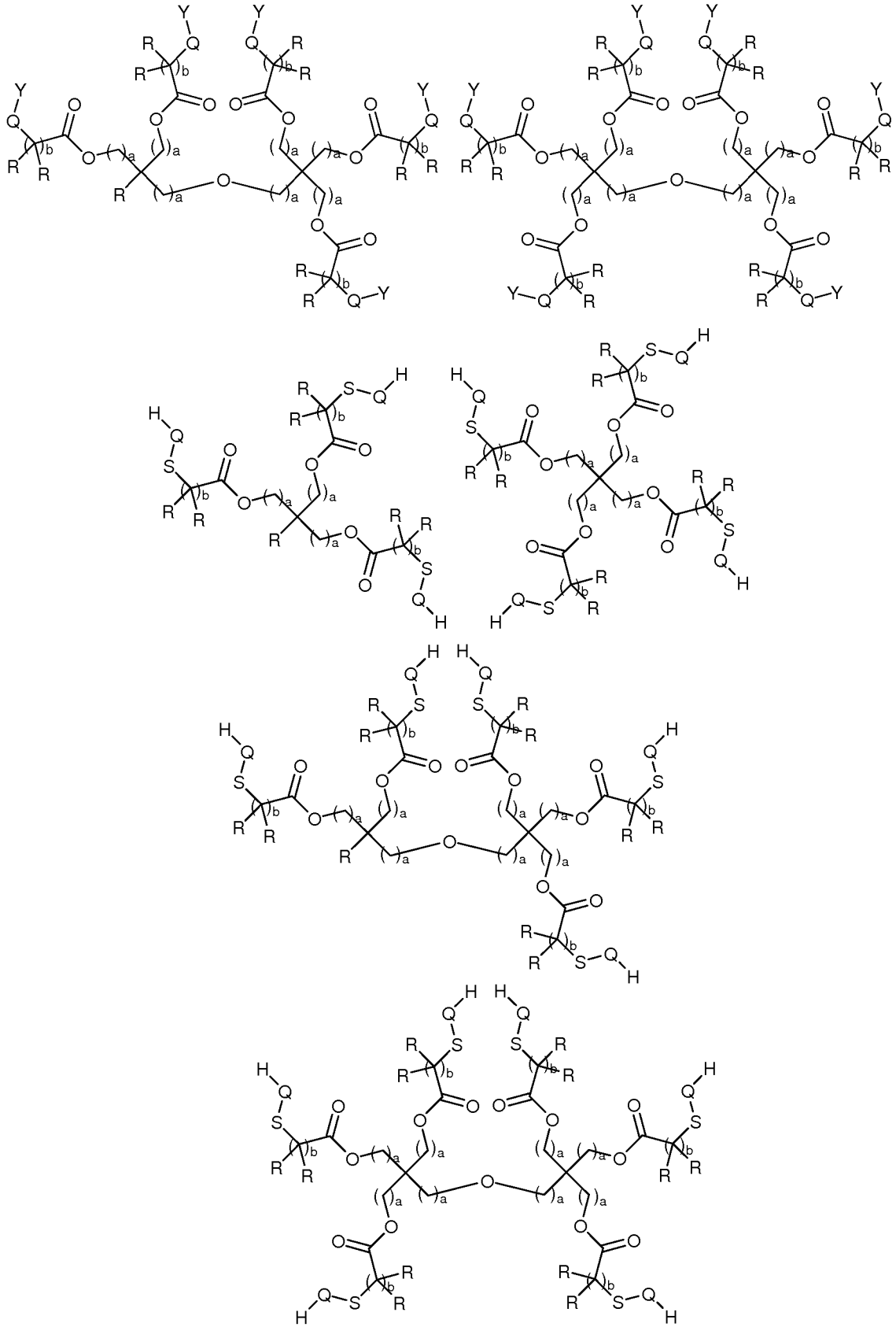
29. The process of claim 28 wherein the acrylic acid monomers are selected from the group consisting of acrylic acid, methacrylic acid, itaconic acid, and combinations thereof.

30. The process of claim 28 or claim 29 further comprising the step of (c) preparing the ester derivative of the product of step (b) with glycidyl methacrylate, where about 10% to about 80% of the acid groups are esterified.

31. A bioactive cement system comprising a crosslinkable polyfunctional prepolymer and a bioactive glass, where the crosslinkable polyfunctional prepolymer comprises a polymer core initiator covalently bonded to a plurality of polycarboxylic acids, and wherein at least a portion of said plurality of polycarboxylic acids are esters or amides, or combinations thereof, of one or more acryloyloxyalkanols, acryloyloxyalkylamines, acryloylaminoalkanols, or acryloylaminoalkylamines.

32. The system of claim 31 wherein the crosslinkable polyfunctional prepolymer is a compound selected from the group of formulae consisting of





and combinations thereof;

wherein in each instance R is hydrogen or an independently selected alkyl group; a is an independently selected integer from 1 to about 4; b is an independently selected integer from 1 to about 4; Y in each instance is an independently selected radical chain reaction

terminating group; and Q is in each instance an independently selected polymer comprising one or more acrylic acids, where at least a portion of said acrylic acids are esters or amides, or combinations thereof, of one or more acryloyloxyalkanols, acryloyloxyalkylamines, acryloylaminoalkanols, or acryloylaminoalkylamines,.

33. The system of claim 31 wherein Y is bromide.

34. The system of claim 31 wherein a is 1; and b is 1 or 2.

35. The system of claim 31 wherein R is in each instance hydrogen or methyl.

36. The system of claim 31 wherein R is in each instance methyl.

37. The system of claim 31 further comprising a filler.

38. The system of claim 37 wherein the filler is a FUJI II LC filler.

39. The system of claim 31 wherein the bioactive glass is BAG S53P4.

40. The system of claim 31 further comprising water.

41. The system of any one of claims 31 to 40 wherein Q is a polymer consisting of acrylic acid.

42. The system of any one of claims 31 to 40 wherein Q is a polymer consisting of acrylic acid and methacrylic acid.

43. The system of any one of claims 31 to 40 wherein Q is a polymer comprising acrylic acid and itaconic acid.

44. The system of any one of claims 31 to 40 wherein Q is a polymer consisting of acrylic acid and itaconic acid.

45. The system of any one of claims 31 to 40 wherein at least a portion of said acrylic acids are esters of an acryloyloxyalkanol.

46. The system of claim 45 wherein the acryloyloxyalkanol is an acryloylglycerol.

47. The system of any one of claims 31 to 40 wherein at least a portion of said acrylic acids are amides of an acryloyloxyalkylamine.

48. The system of claim 45 wherein the acryloyloxyalkylamine is an acryloylethylamine.

49. The system of any one of claims 31 to 40 exhibiting a compressive strength of about 100 MPa or greater.

50. The system of any one of claims 31 to 40 exhibiting a compressive strength of about 150 MPa or greater.

51. The system of any one of claims 31 to 40 exhibiting a compressive strength of about 100 MPa or greater after being conditioned in simulated body fluid (SBF) at 37 °C prior to testing.

52. The system of any one of claims 31 to 40 exhibiting a compressive strength of about 150 MPa or greater after being conditioned in simulated body fluid (SBF) at 37 °C prior to testing.

53. The system of any one of claims 31 to 40 exhibiting a diametral tensile strength of about 10 MPa or greater .

54. The system of any one of claims 31 to 40 exhibiting a diametral tensile strength of about 15 MPa or greater .

55. The system of any one of claims 31 to 40 exhibiting a hardness of about 15 KNP or greater .

56. The system of any one of claims 31 to 40 exhibiting a hardness of about 20 KNP or greater .

57. A method for treating a bone or dental defect, the method comprising the step of introducing the system of any one of claims 31 to 40 into a site in need of treatment.

58. The method of claim 57 wherein the defect is a dental defect.

59. The method of claim 57 wherein the defect is a root surface filling.

60. The method of claim 57 wherein the defect is a high stress bearing site.

61. The method of claim 60 wherein the high stress bearing site is a class 1 or class II cavity.

62. The method of claim 57 wherein the treatment results in at least a portion of the dentin being mineralized.

63. A kit comprising the system of any one of claims 31 to 40; a container adapted for mixing the components of the system to prepare a light curable bioactive glass-ionomer cement; and instructions.

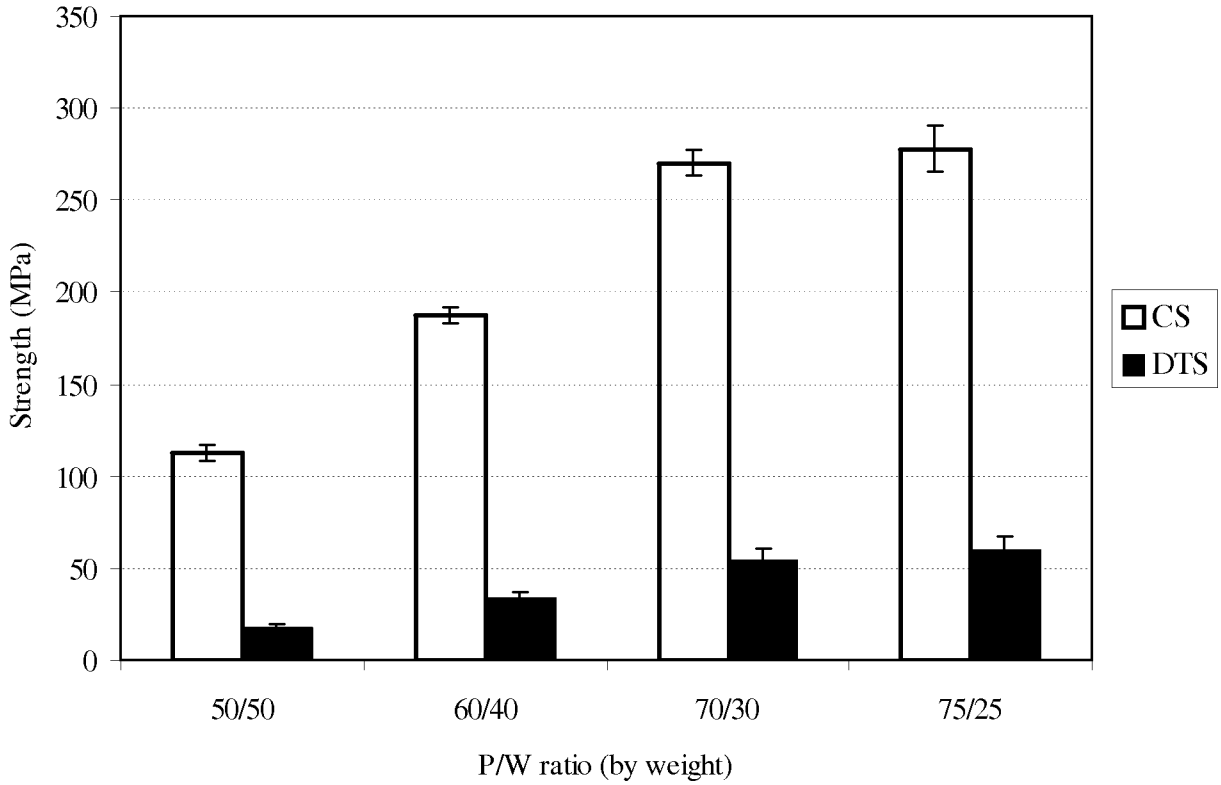

350
300
250
200
150
100
50
0
Strength (MPa)
50/50
60/40
70/30
75/25
P/W ratio (by weight)
CS
DTS

Fig. 1

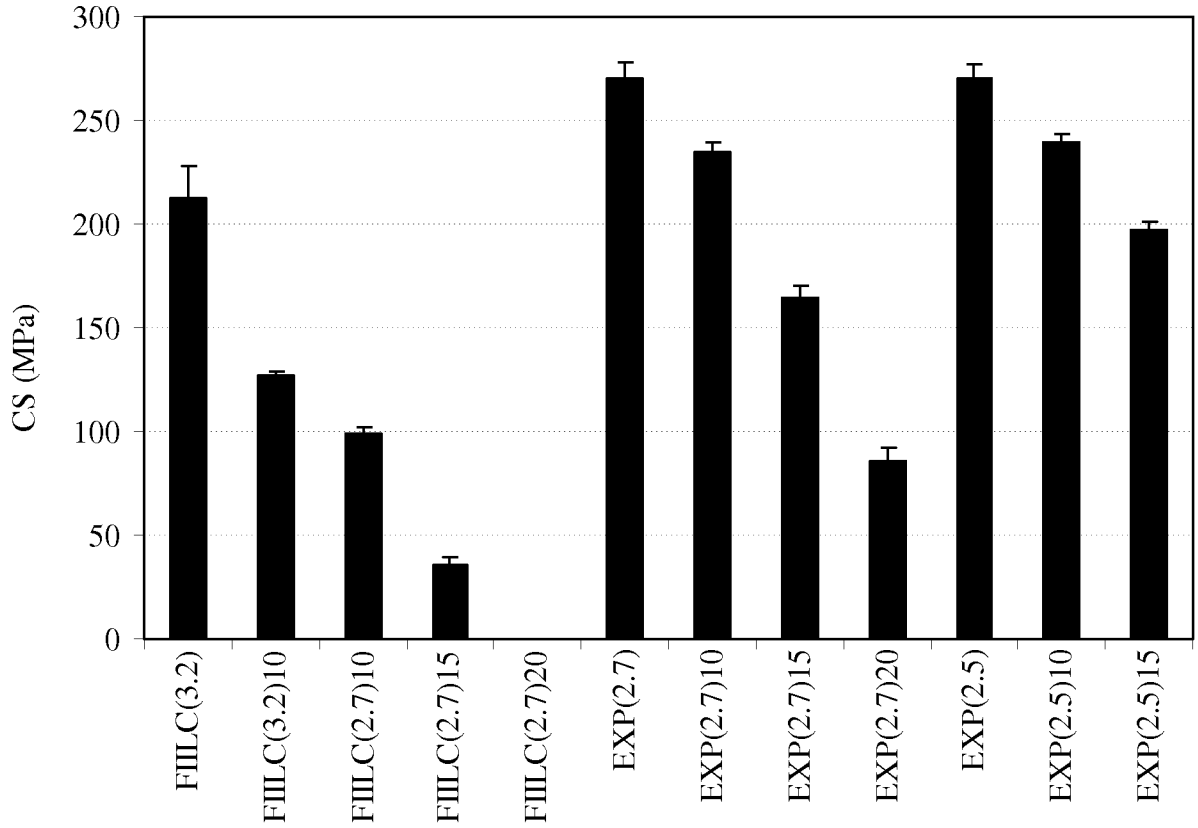

CS (MPa)
300
250
200
150
100
50
0
FIILC(3.2)
FIILC(3.2)10
FIILC(2.7)10
FIILC(2.7)15
FIILC(2.7)20
EXP(2.7)
EXP(2.7)10
EXP(2.7)15
EXP(2.7)20
EXP(2.5)
EXP(2.5)10
EXP(2.5)15

Fig. 2

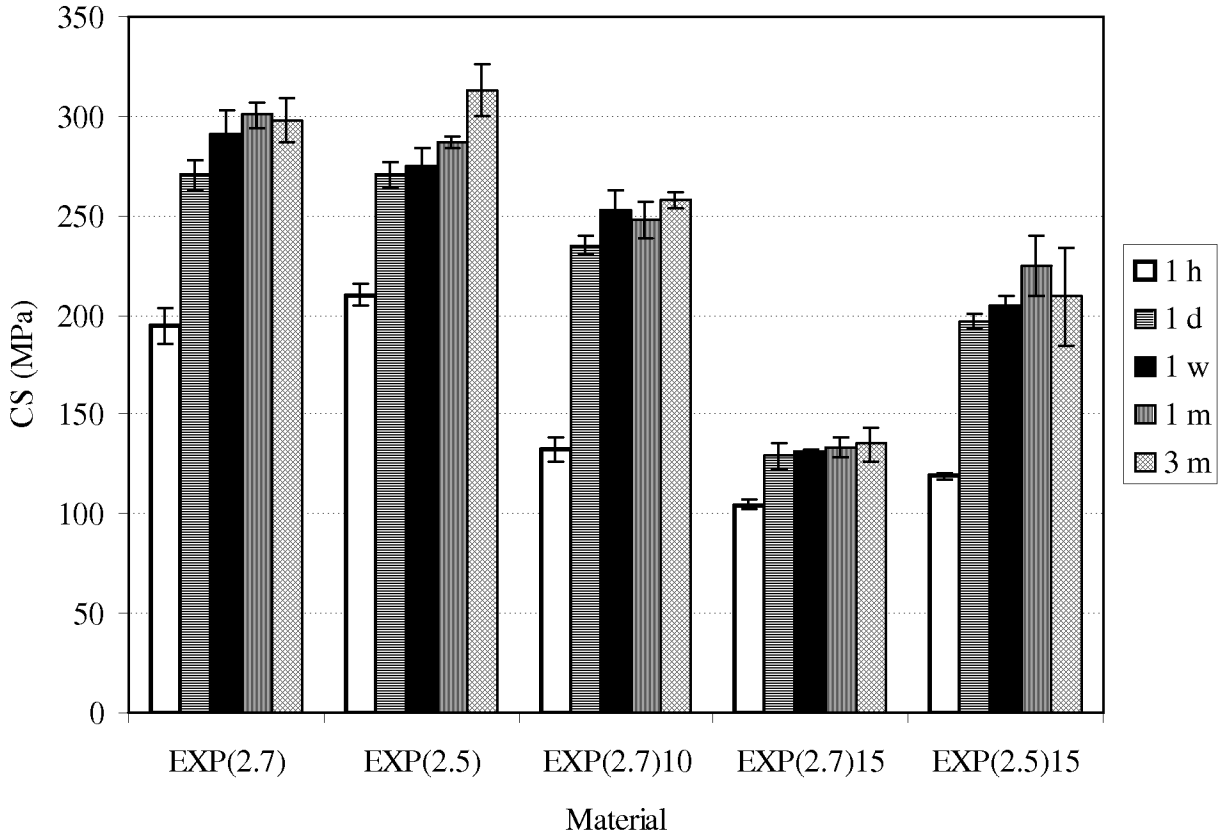

350
300
250
200
150
100
50
0
CS (MPa)
EXP(2.7)
EXP(2.5)
EXP(2.7)10
EXP(2.7)15
EXP(2.5)15
Material
1 h
1 d
1 w
1 m
3 m

Fig. 3

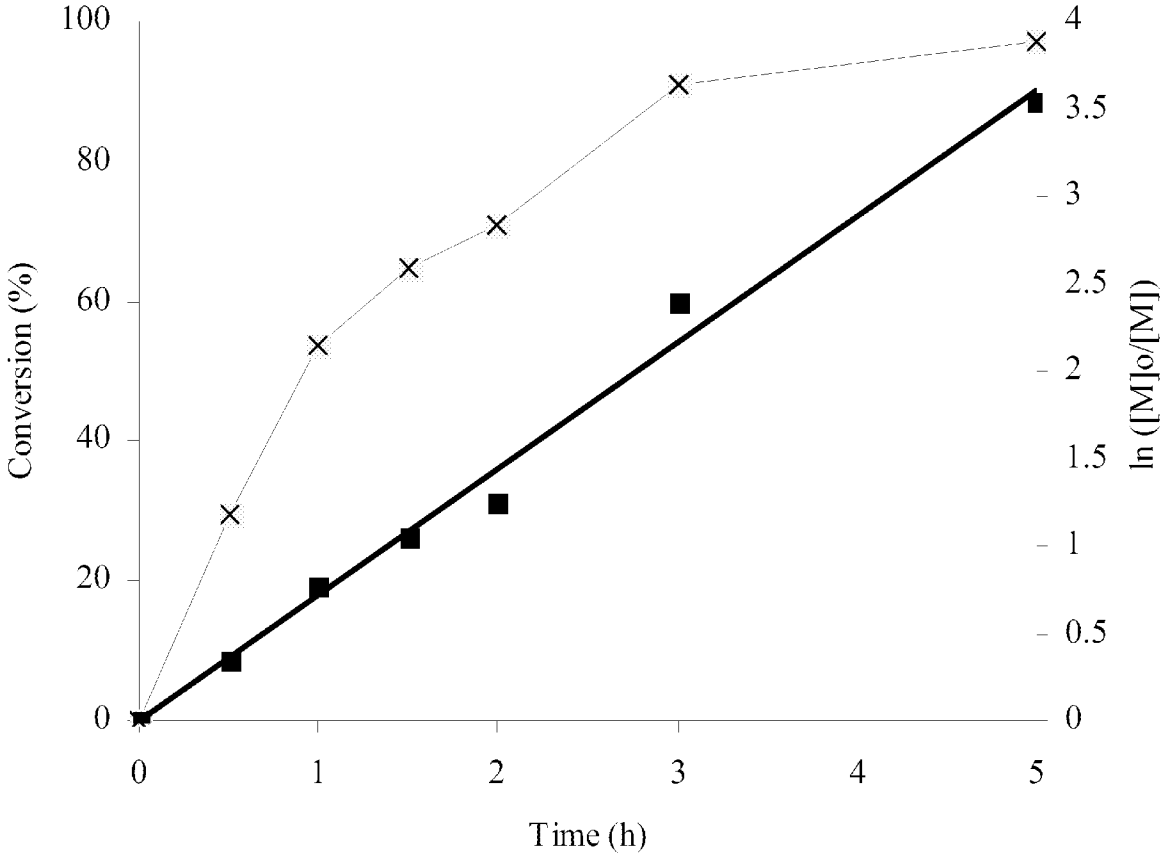

100
80
60
40
20
0
Conversion (%)
4
3.5
3
2.5
2
1.5
1
0.5
0
ln ([M]o/[M])
0
1
2
3
4
5
Time (h)

Figure 4

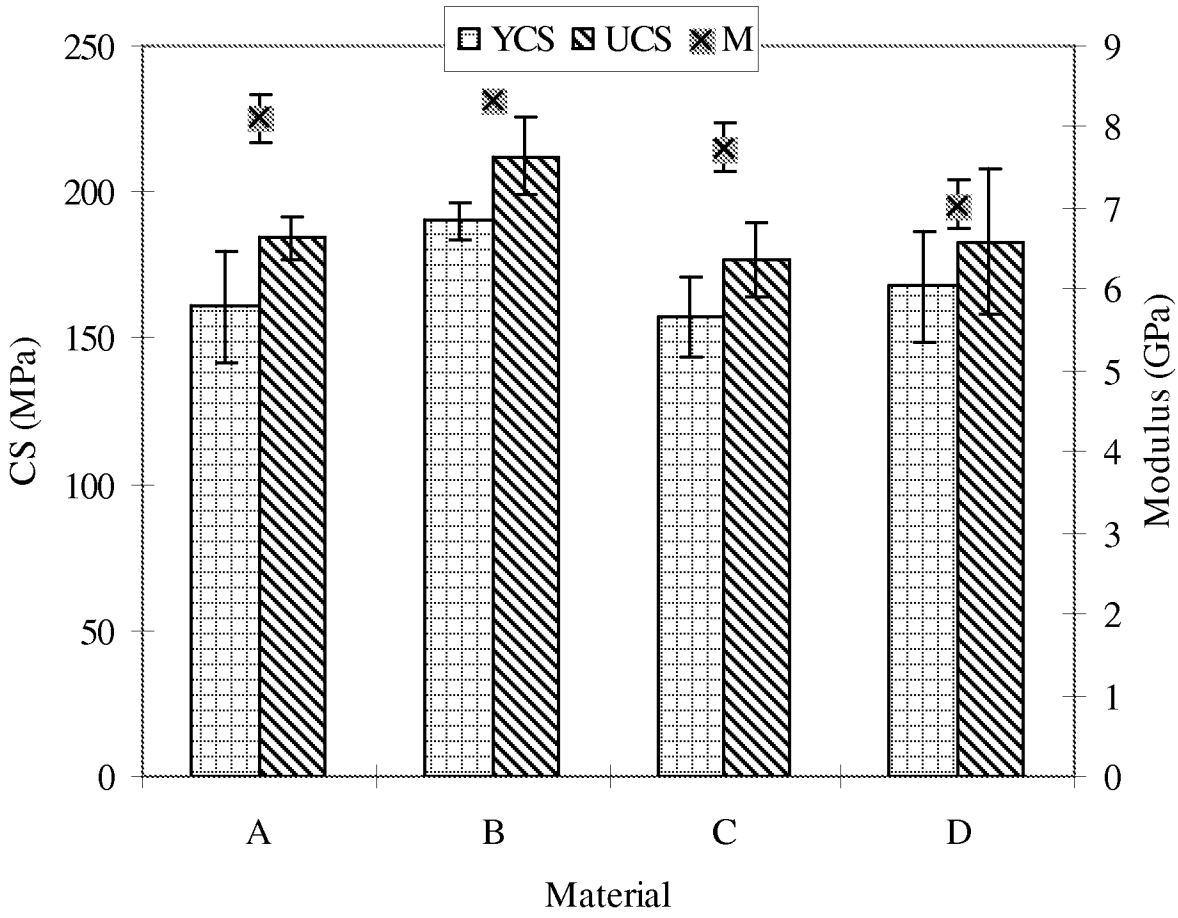

YCS
UCS
M
250
200
150
100
50
0
CS (MPa)
9
8
7
6
5
4
3
2
1
0
Modulus (GPa)
A
B
C
D
Material

Figure 5

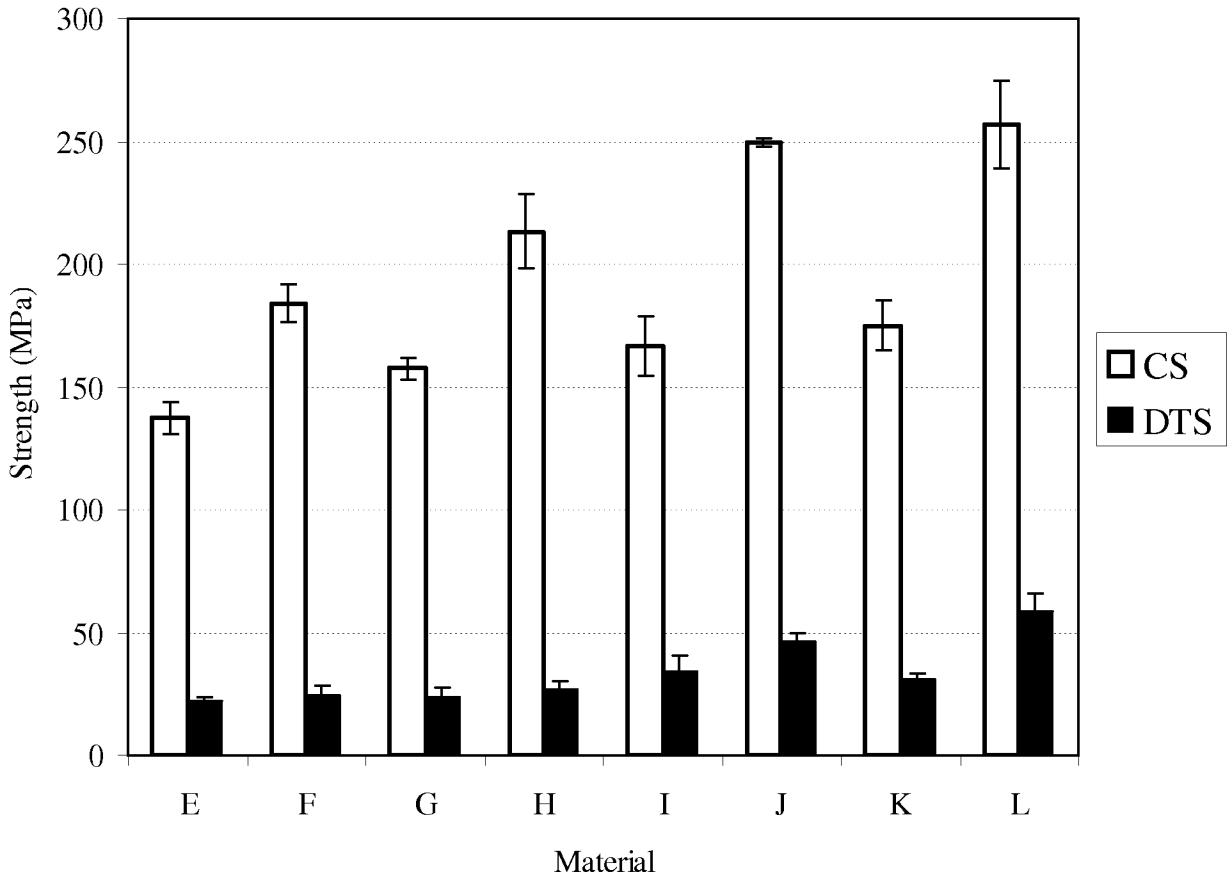

300
250
200
150
100
50
0
Strength (MPa)
E
F
G
H
I
J
K
L
Material
CS
DTS

Figure 6

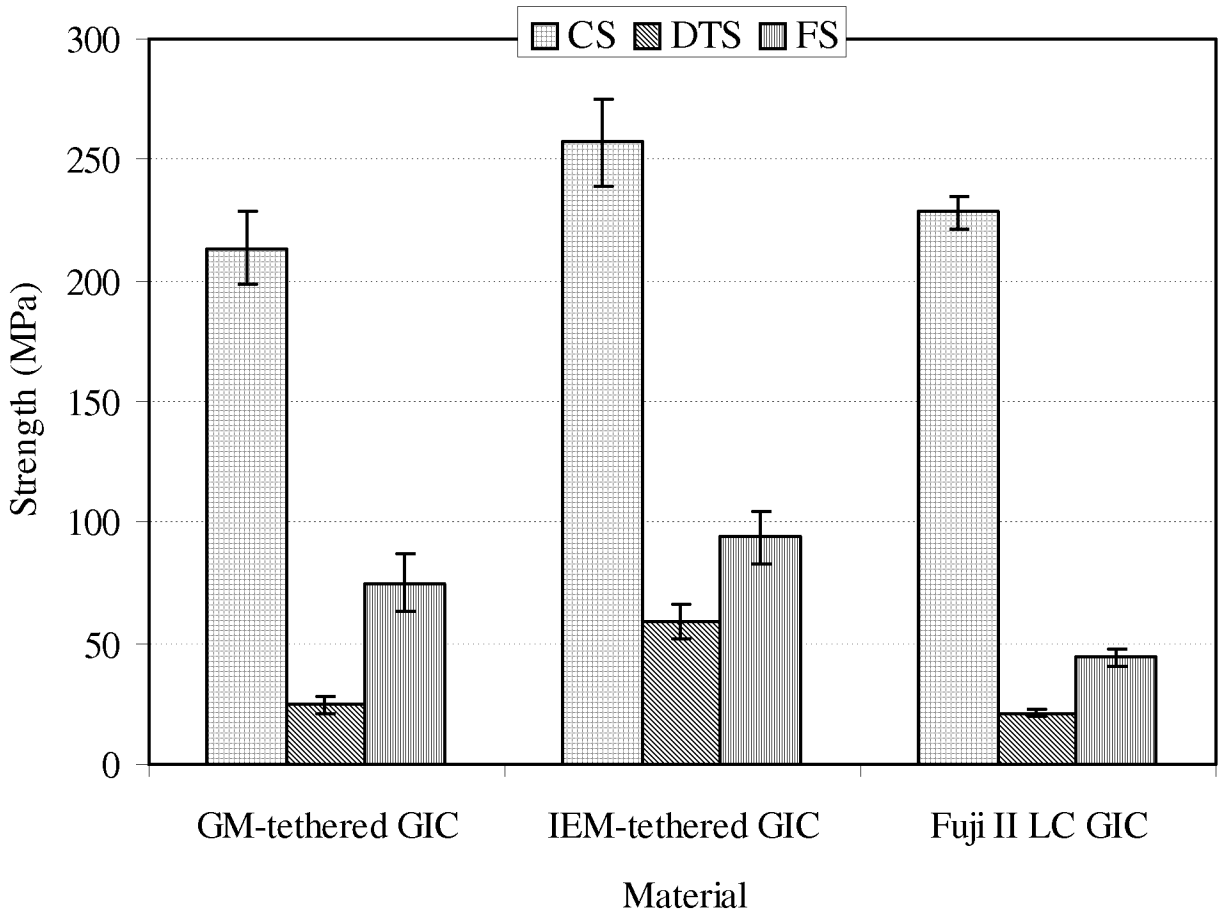

CS
DTS
FS
300
250
200
150
100
50
0
Strength (MPa)
GM-tethered GIC
IEM-tethered GIC
Fuji II LC GIC
Material

Figure 7(a)

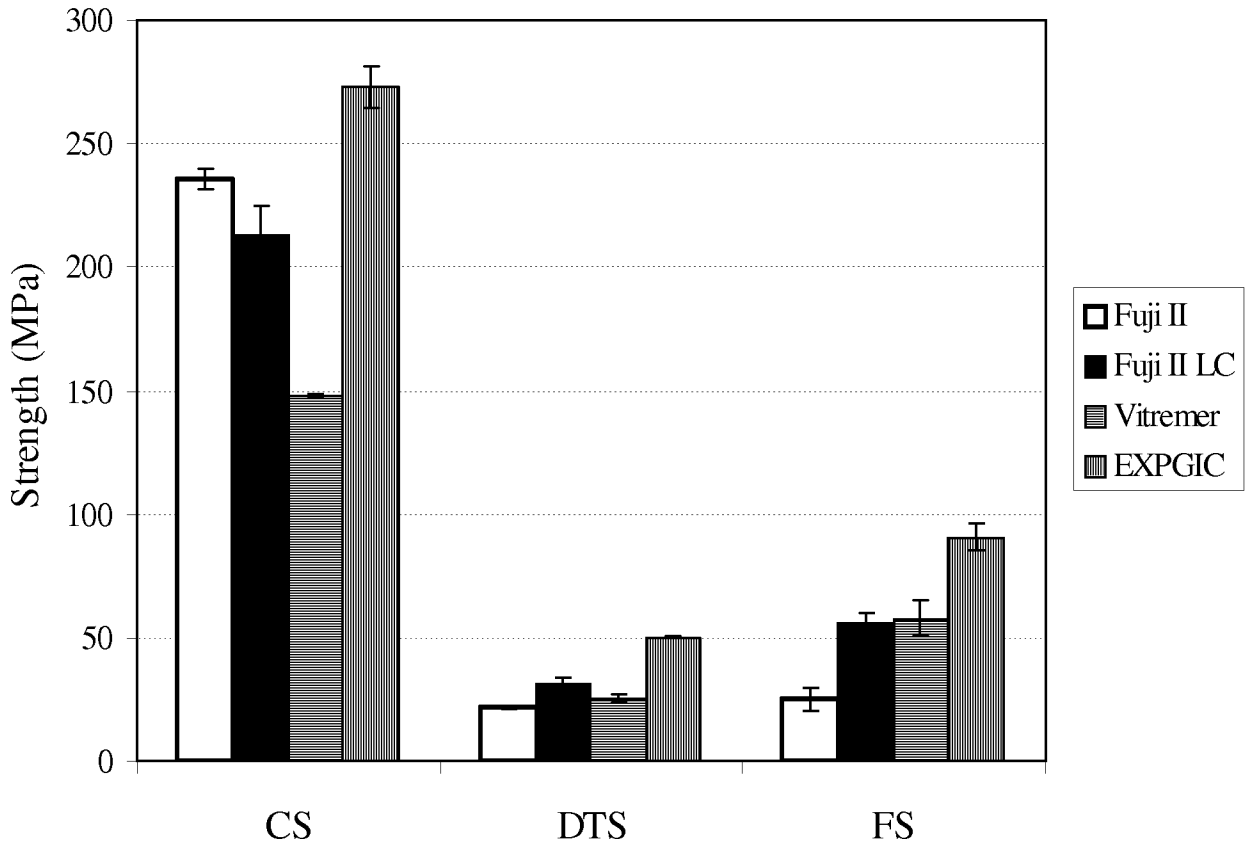

300
250
200
150
100
50
0
Strength (MPa)
CS
DTS
FS
Fuji II
Fuji II LC
Vitremer
EXPGIC

Figure 7(b)

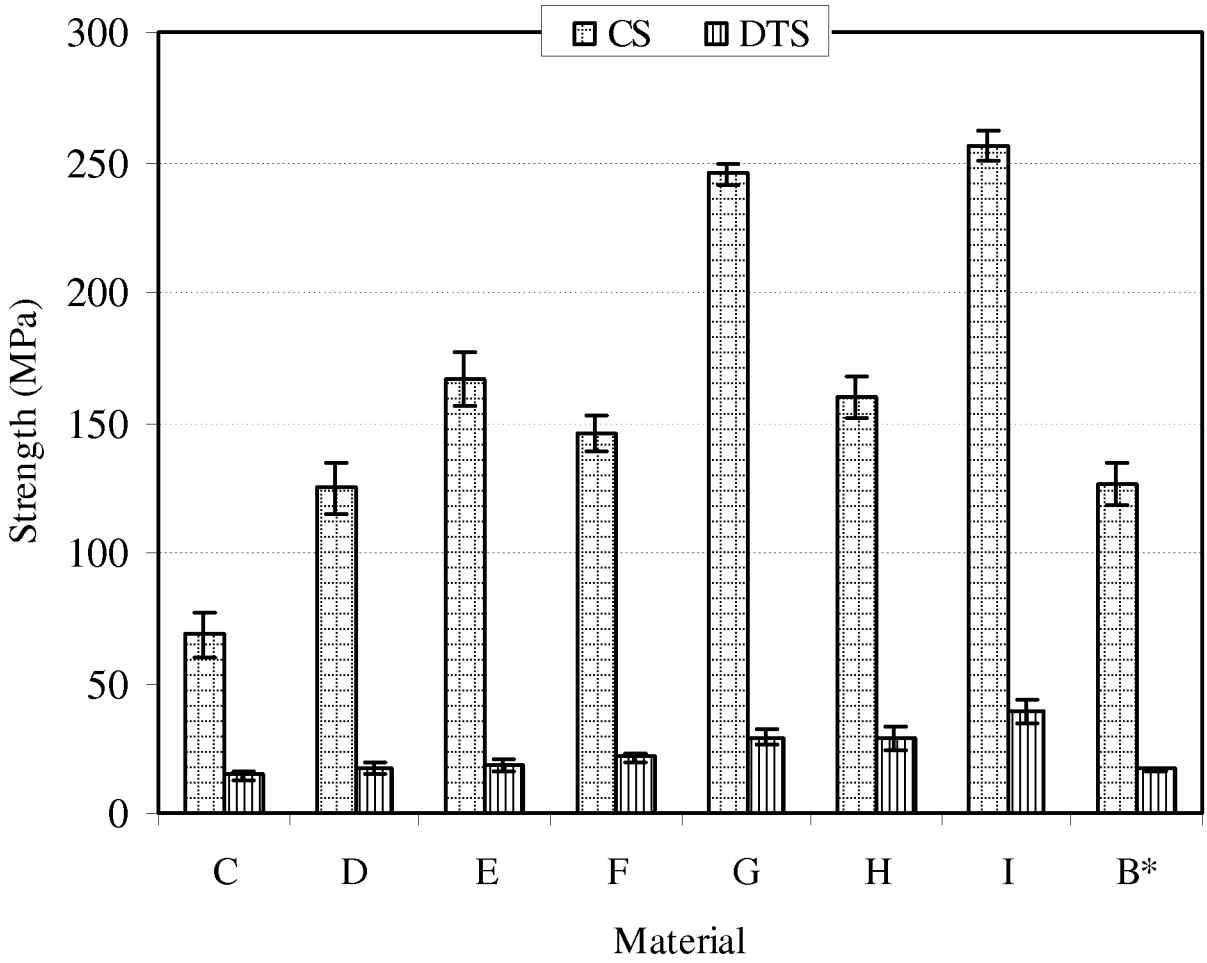

CS
DTS
300
250
200
150
100
50
0
Strength (MPa)
C
D
E
F
G
H
I
B*
Material

Figure 8

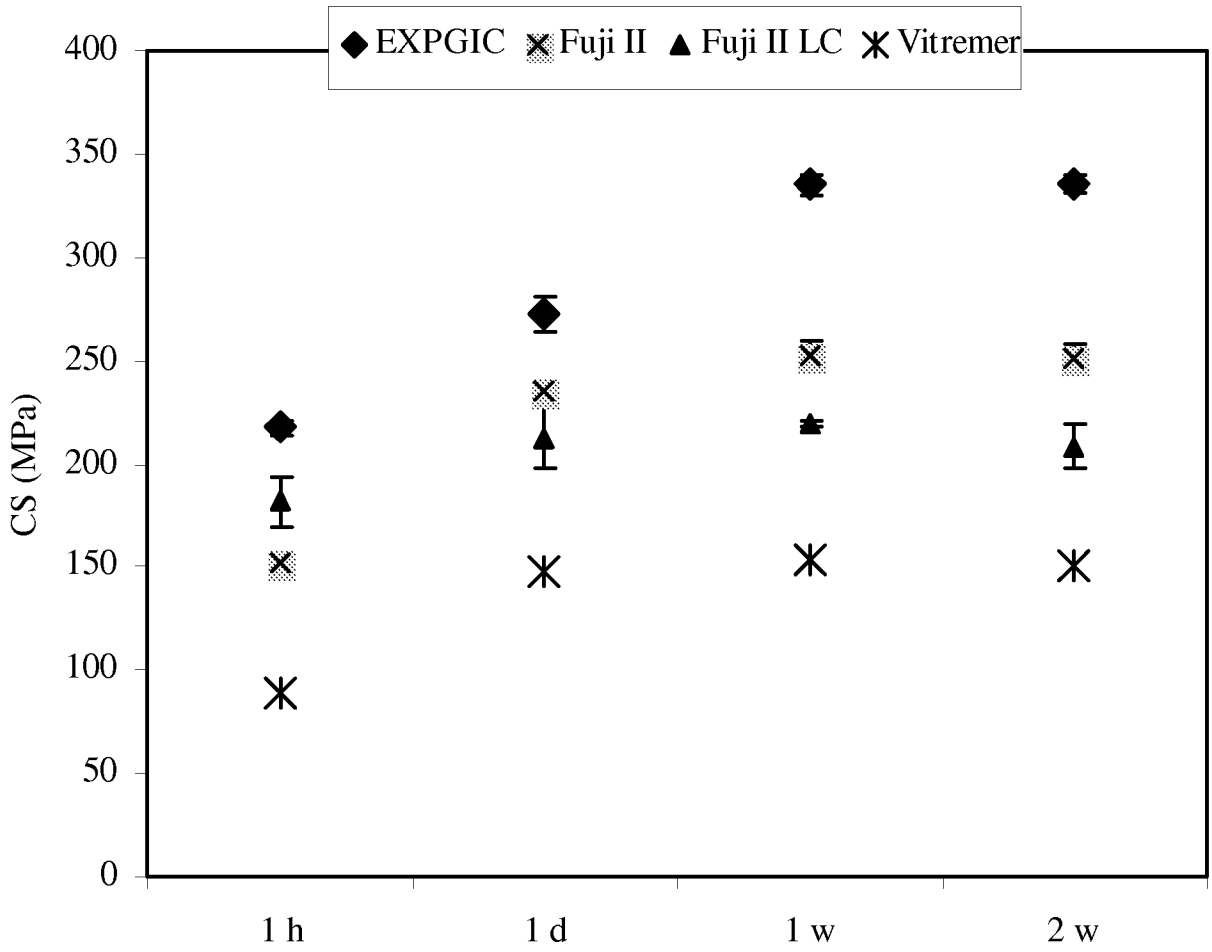

EXPGIC
Fuji II
Fuji II LC
Vitremer
CS (MPa)
400
350
300
250
200
150
100
50
0
1 h
1 d
1 w
2 w

Figure 9

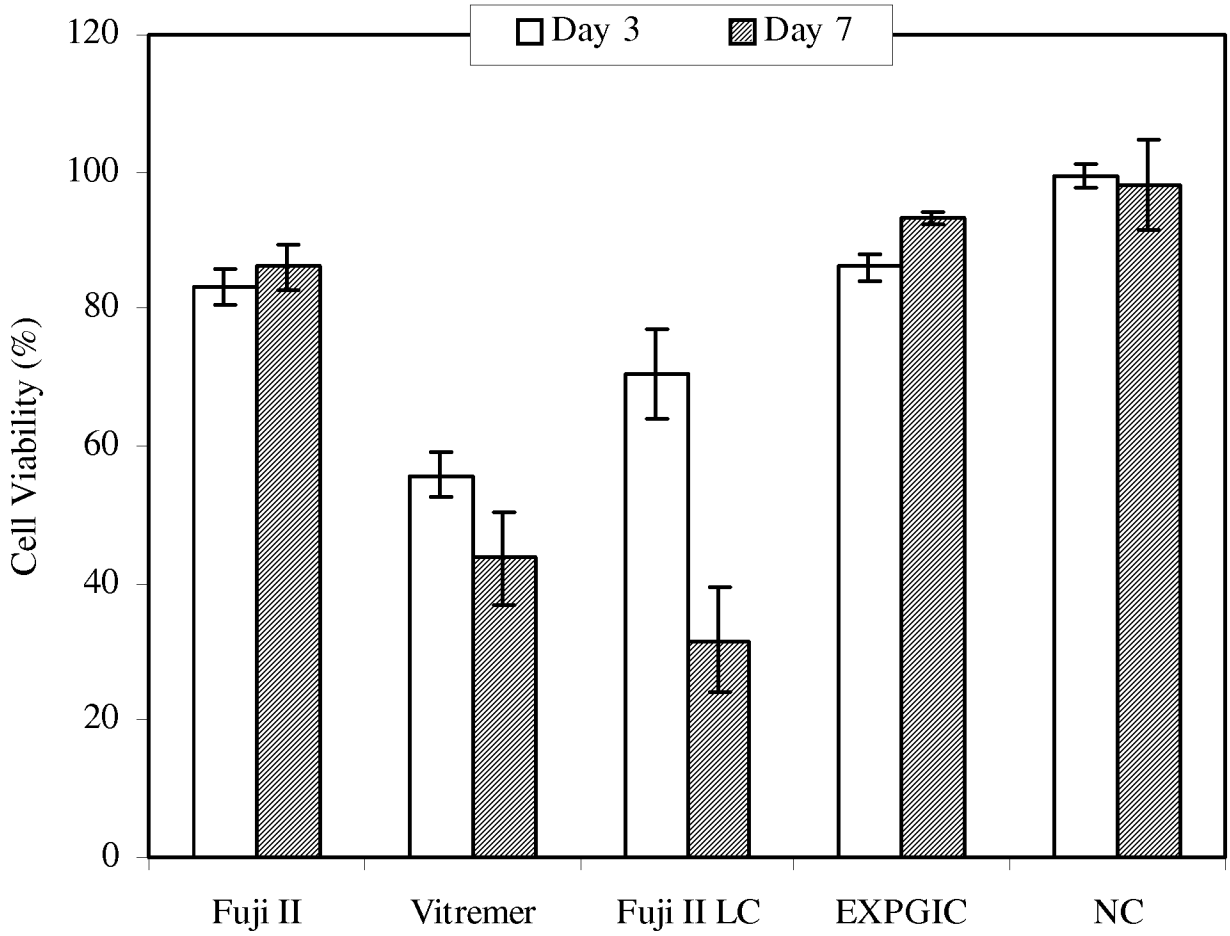

Day 3
Day 7
Cell Viability (%)
120
100
80
60
40
20
0
Fuji II
Vitremer
Fuji II LC
EXPGIC
NC

Figure 10

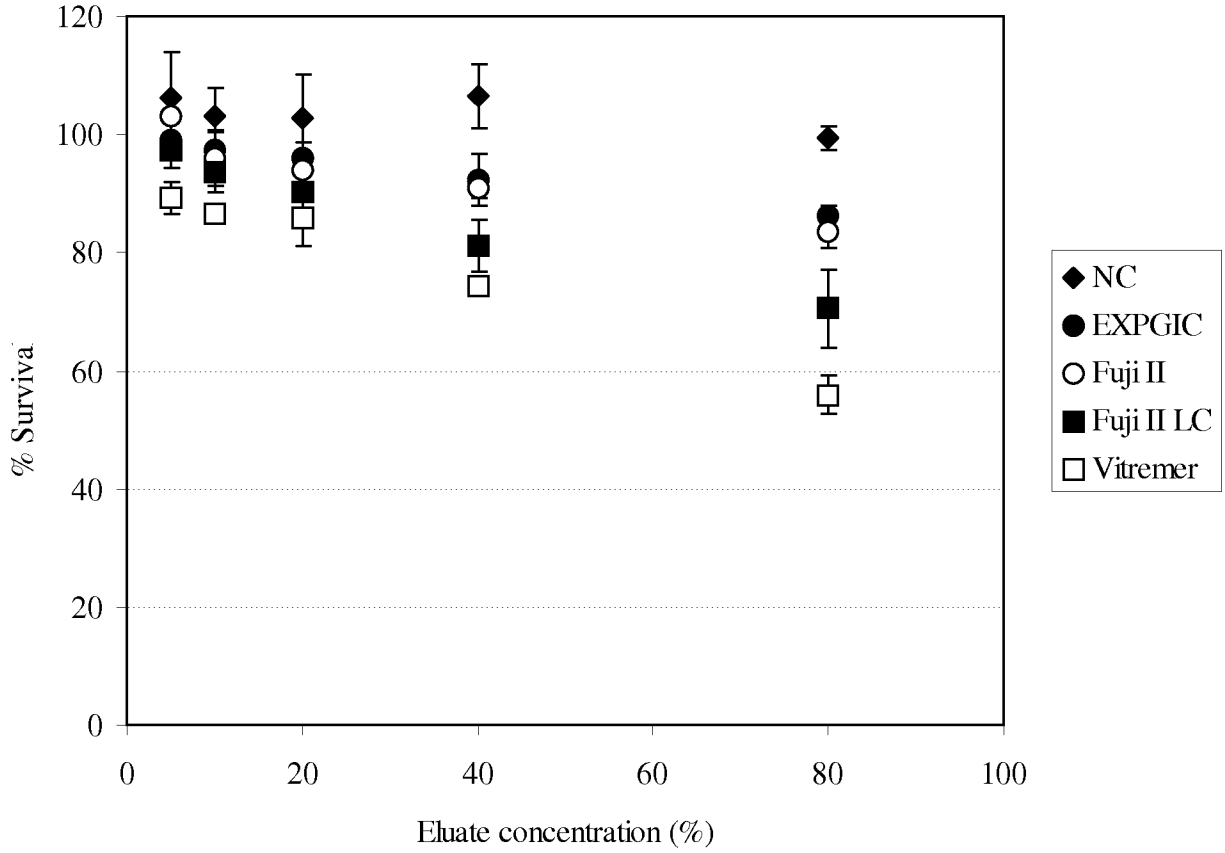

120
100
80
60
40
20
0
% Surviva
0
20
40
60
80
100
Eluate concentration (%)
NC
EXPGIC
Fuji II
Fuji II LC
Vitremer

Figure 11(a)

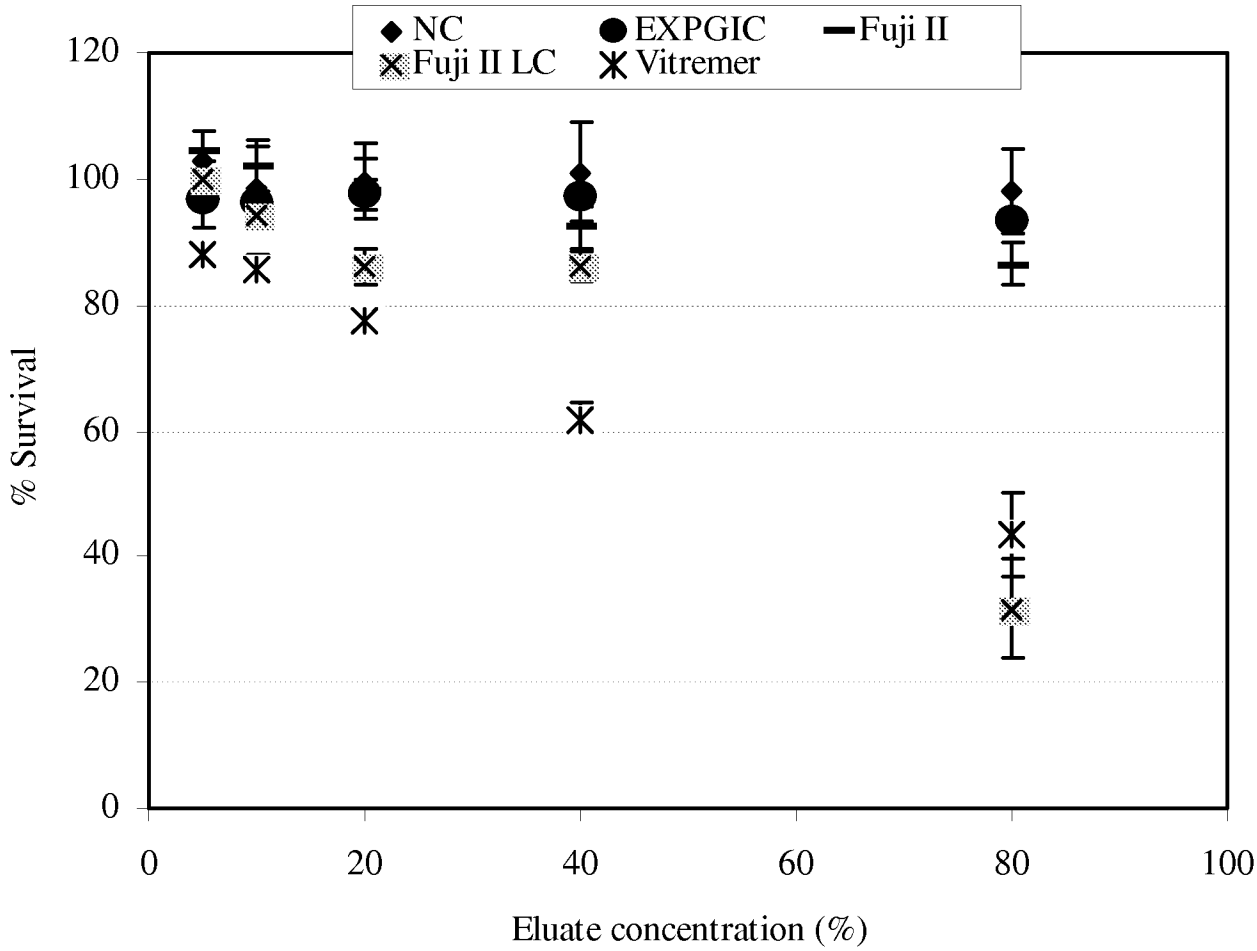

NC
EXPGIC
Fuji II
Fuji II LC
Vitremer
120
100
80
60
40
20
0
% Survival
0
20
40
60
80
100
Eluate concentration (%)

Figure 11(b)

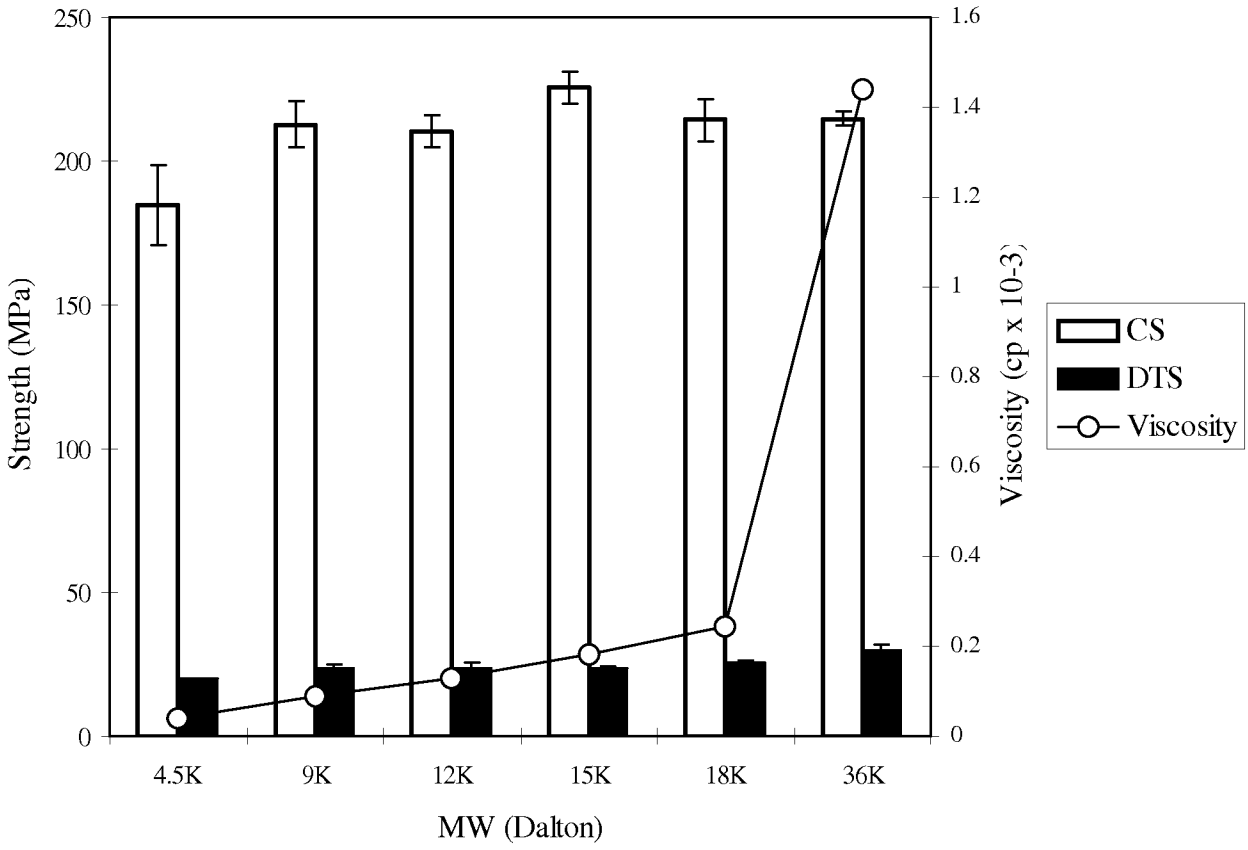

250
200
150
100
50
0
Strength (MPa)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Viscosity (cp x 10-3)
4.5K
9K
12K
15K
18K
36K
MW (Dalton)
CS
DTS
Viscosity

Figure 12

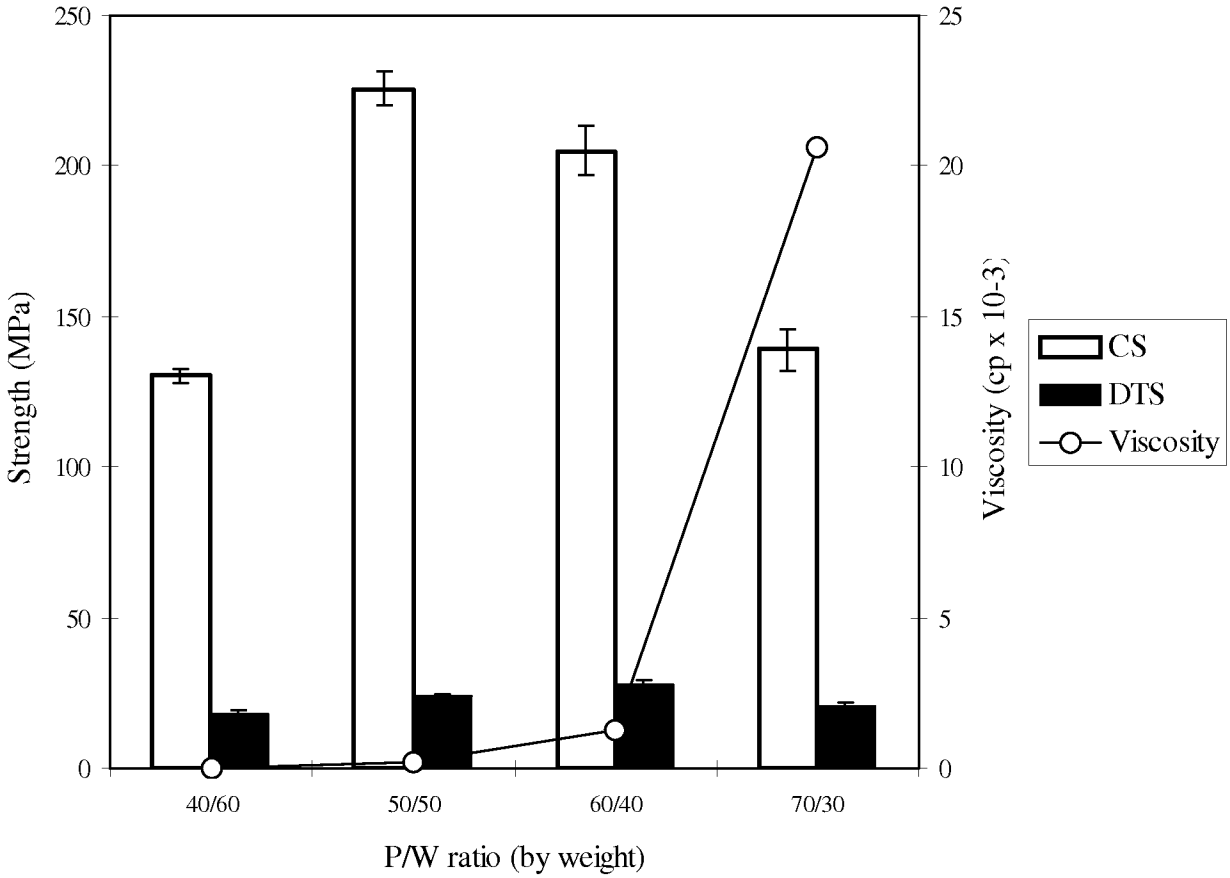

250
200
150
100
50
0
Strength (MPa)
25
20
15
10
5
0
Viscosity (cp x 10-3)
40/60
50/50
60/40
70/30
P/W ratio (by weight)
CS
DTS
Viscosity

Figure 13

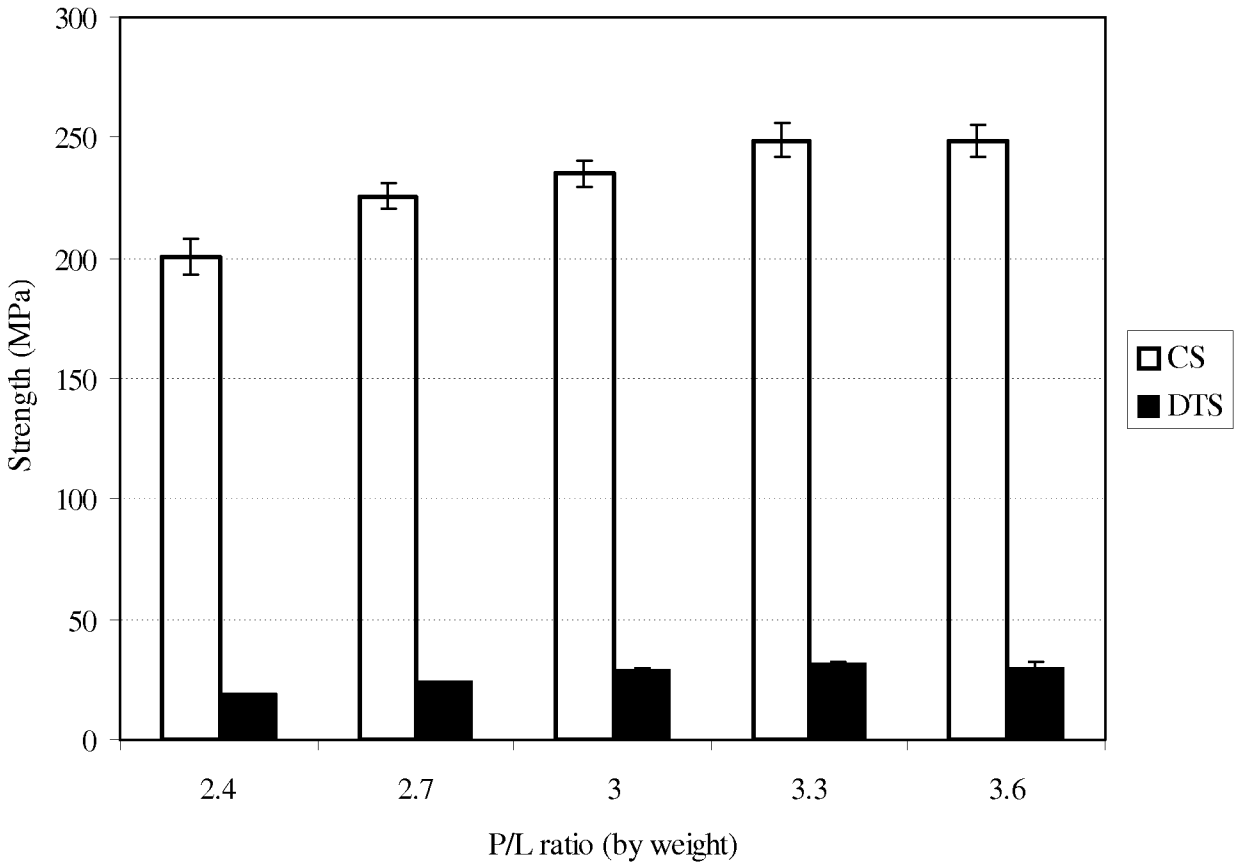

300
250
200
150
100
50
0
Strength (MPa)
2.4
2.7
3
3.3
3.6
P/L ratio (by weight)
CS
DTS

Figure 14

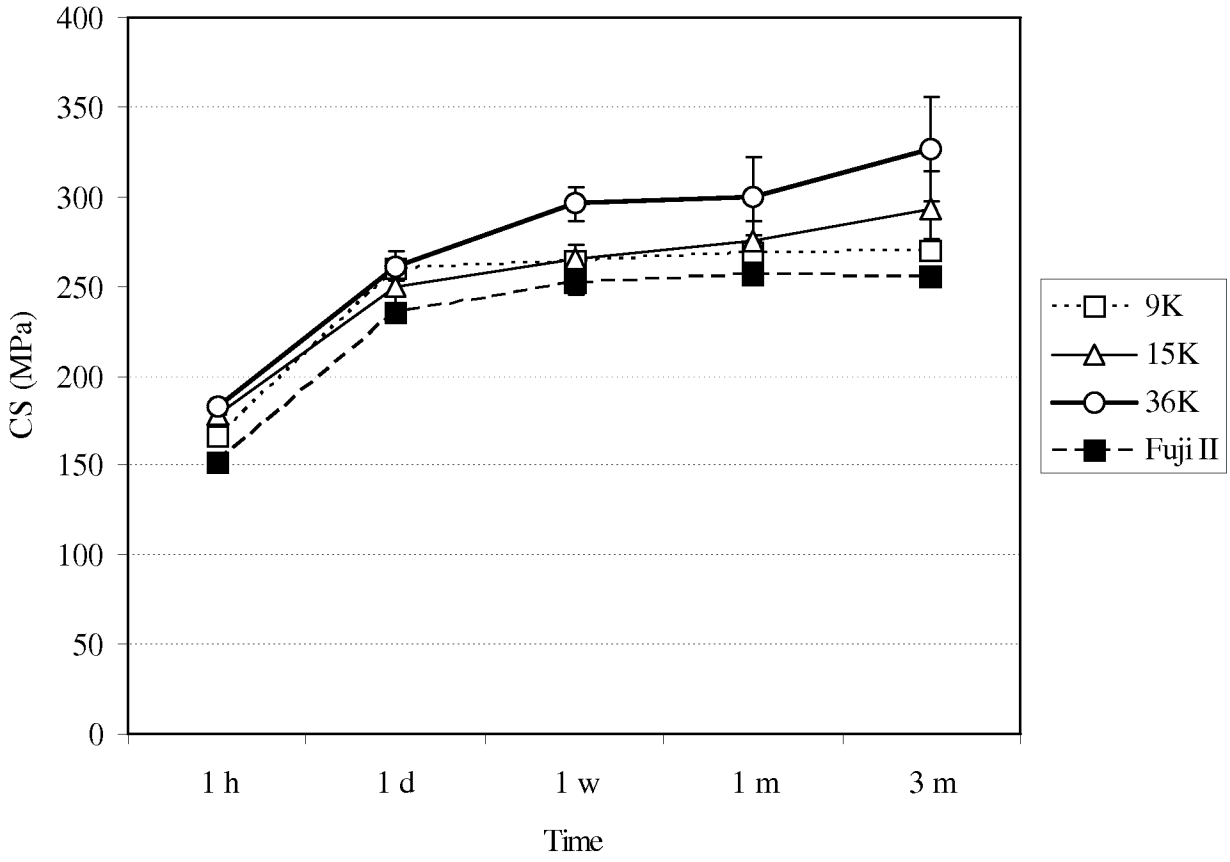

400
350
300
250
200
150
100
50
0
CS (MPa)
1 h
1 d
1 w
1 m
3 m
Time
9K
15K
36K
Fuji II

Figure 15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 09/40482

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61F 2/00 (2009.01)
USPC - 523/115
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC - 523/115

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 560/129; 560/171 (see search terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWest (PGPB,USPT,USOC,EPAB,JPAB); Google
Search Terms Used:
glass ionomer compounds, dental cement, bioactive glass, crosslinkable polyfunctional prepolymer, itaconic acid, hardness knp

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	WO 2007/103665 A2 (XIE) 13 September 2007 (13.09.2007) pg 3-14	1-27 ---- 29-63
X --- Y	US 2007/0185230 A1 (BOWMAN et al.) 09 August 2007 (09.08.2007) abstract	28 --- 29-30
Y	US 2007/0122356 A1 (KESSLER et al.) 31 May 2007 (31.05.2007) para [0023], [0045], [0072]	31-63
Y	US 6,281,271 B1 (RUMPHORST et al.) 28 August 2001 (28.08.2001) col 5, ln 36-37	30
Y	US 2004/0115240 A1 (NARHI et al.) 17 June 2004 (17.06.2004) para [0091]	39
Y	US 6,196,843 B1 (KAWAGUCHI et al.) 06 March 2001 (06.03.2001) Table 1	55-56
Y	US 4,524,824 A (SHIMOKOBE et al.) 25 June 1985 (25.06.1985) col 1, ln 19-23	59-61
Y	US 6,206,192 A (WINSTEAD et al.) 27 March 2001 (27.03.2001) col 2, ln 4-46	63

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 July 2009 (16.07.2009)	24 JUL 2009
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)