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Amino acid containing glass -ionomer cement for orthopedic applications.

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AMINO ACID CONTAINING GLASS-IONOMER CEMENT FOR ORTHOPEDIC APPLICATIONS

by

WEI WU

A DISSERTATION

Submitted to the graduate faculty of The University of Alabama in Huntsville, The
University of Alabama, and The University of Alabama at Birmingham,
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

BIRMINGHAM, ALABAMA

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ABSTRACT OF DISSERTATION
GRADUATE SCHOOL, UNIVERSITY OF ALABAMA AT BIRMINGHAM

Degree Ph. D. Program Materials Science

Name of Candidate Wei Wu

Conmmittee Chair Jimmy W. Mays

Title Amino Acid Containing Glass-Ionomer Cement for Orthopedic Applications

Amino acid containing glass-ionomer cements were synthesized, formulated, and evaluated for orthopedic application. The formulation of different amino acid containing glass-ionomer bone cements was optimized, and conventional and resin-modified glass-ionomer bone cements were compared. Properties of interest included handling characteristics, physical and chemical properties, and mechanical strength of the bone cement. The study was based on the synthesis of different vinyl containing amino acids, different polyelectrolytes containing these amino acid residues, and different resin-modified polyelectrolytes, as well as formulation and evaluation of conventional and resin-modified glass-ionomer bone cements using these polyelectrolytes. Systematic preparation of polyelectrolytes and formulation of glass-ionomer bone cements were essential features of this work, since we anticipated that the mechanical properties of the glass-ionomer bone cements could be strongly affected by the nature of the polyelectrolytes and formulation. Mechanical properties were evaluated in a screw driven mechanical testing machine, and structure-property relationships were determined by scanning electron microscopic (SEM) observation of the fracture surface of the specimens. How the structure of polyelectrolytes, such as different amino acid residues, molecular weight, different modifying resin, and formulation of glass-ionomer bone cement, affected the mechanical properties was also studied.

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Thanks are extended to all members of Dr. Mays' group, students, and faculty in the Chemistry Department. Many thanks to the Department of Chemistry, the Materials Science Program, and the UAB Graduate School for their continuous support with equipment and finances.

I am grateful to my parents, who are with me while I am preparing the final defense of my dissertation.

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SYNTHESIS OF POLY(CARBOXYL ACID)S WITH NEW PENDENT VINYL FUNCTIONALITIES AND THEIR APPLICATION IN RESIN-MODIFIED GLASS-IONOMER CEMENTS

LIST OF ABBREVIATIONS

η_{sp}	Specific viscosity
AA	Acrylic acid
ABA	Acryloyl β-alanine
AC	Acryloyl chloride
AGA	Acryloyl glutamic acid
AIBN	2,2'-Azobisisobutyronitrile
ANOVA	ANalysis Of VAriance
ASTM	American Society for Testing and Materials
Au-Pd	Golden-palladium
BA	β-alanine
BHT	Butylated hydroxytoluene
CAB	Cellulose acetate butyrate
CGIC	Conventional glass-ionomer cement
CQ	dl-Camphoroquinone
CS	Compressive strength
DBTL	Dibutyltin dilaurate
DC	Diphenyliodonium chloride
DCC	N,N'-Dicyclohexylcarbodiimide
DMA	N,N-Dimethylaniline
DMAP	4-Dimethylamino pyridine

LIST OF ABBREVIATIONS (Continued)

DMF	N,N-dimethylformamide
DTS	Diametral tensile strength
FS	Flexural strength
G	Glycine
GA	L-glutamic acid
GICs	Glass-ionomer cements
GM	Glycidyl methacrylate
GPC	Gel permeation chromatography
HCl	Hydrochloric acid
HEMA	2-Hydroxyethyl methacrylate
IA	Itaconic acid
IEM	2-isocyanatoethyl methacrylate
$K_2S_2O_8$	Potassium perfulfate
KOH	Potassium hydroxide
LC	Light-cure
MC	Methacryloyl chloride
MeOH	Methanol
$MgSO_4$	Magnesium sulfate
Mn	Number average molecular weight
Mw	Weight average molecular weight
NaCl	Sodium chloride
NMR	Nuclear magnetic resonance

LIST OF ABBREVIATIONS (Continued)

PMMA	Poly(methyl methacrylate)
P/L	Powder/liquid ratio
RMGIC	Resin modified glass ionomer cement
SD	Standard deviation
SEM	Scanning electron microscopy
THF	Tetrahydrofuran
TPS	Triphenylstibine
Vc	Ascorbic acid

INTRODUCTION

1. Background

The first glass-ionomer (GIC) cement developed by Wilson and Kent [1] amd McLean and Wilson [2] was the product of an acid-base reaction between basic fluoroaluminosilicate glass powder and polyacrylic acid in the presence of water. The set cement comprised an organic-inorganic complex with high molecular weight (MW). Therefore, GIC can be viewed as a water-based material that hardens following an acid-base reaction between fluoroaluminosilicate glass powder and an aqueous solution of polyacid [3].

GICs have been successfully applied as dental restoratives for over 20 years since their invention. GIC is well-known for its unique properties such as direct adhesion to tooth structure and base metals [4,5], anticariogenic properties due to release of fluoride [6], thermal compatibility with tooth enamel and dentin because of low coefficients of thermal expansion similar to that of tooth structure [7], minimized microleakage at the tooth-enamel interface due to low shrinkage [8], biological compatibility, and low cytotoxicity [9,10].

GICs have a variety of applications [11]. Because of salt bridge formation between the cements and tooth structures, these cements have mainly been used as dental adhesives and anterior tooth restoratives [12]. They were originally intended as substitutes for dental silicate cements as restorative materials for Class III and Class V cavities [2] and first applied for restoring erosion lesions and as a fissure sealant [11,13,14], due to their adhesive properties. Glass-ionomer cements were developed as a luting agent by Wilson and co-workers [15] and have been used for the restoration of deciduous teeth, lining, and core buildup [11]. More recently they have been used in minimal cavity preparation, including tunnel preparations [16-19], and as a dentin substitute in so-called laminate restorations [11,20-22].

As mentioned above, GICs are composed of a calcium fluoride-alumino-silicate glass powder (a base) and a polyelectrolyte (an acid). They are special materials with unique properties. They are neither purely organic nor purely inorganic but a hybrid of both and neither a polymer nor a hydraulic cement but a material that sets by chemical gelation as a result of acid-base reaction [23,24]. The material is a type of composite resin but one where the filler takes part in the setting reaction. The acid-base interaction plays a major role in conventional glass-ionomer cements (CGIC) or self-cured cements [12,25].

The powder of a GIC is calcium fluoroaluminosilicate glass with the formula of

$$SiO_2\text{-}Al_2O_3\text{-}CaF_2\text{-}Na_3AlF_6\text{-}AlPO_4$$

The nominal composition of the glass is listed in Table 1. The maximum grain size of the powder is between 13 and 19 μm. The powder is an ion-leachable glass that is susceptible to acid attack when the Si/Al atomic ratio is less than 2:1. Barium glass or zinc oxide may be added to some powders to provide radiopacity.

Table 1
Nominal composition of calcium fluoroaluminosilicate glass used in powder of glass-ionomer cement [26]

Chemical	Percent by weight
SiO_2	29.0
Al_2O_3	16.6
CaF_2	34.3
Na_3AlF_6	5.0
AlF_6	5.3
$AlPO_4$	9.9

The polyelectrolytes used in GICs are poly(alkenoic acid)s. These polyacids include the homopolymers or copolymers of unsaturated mono-, di-, and tri-carboxylic acids, particularly those of acrylic acid [27]. The most important carboxylic acids in the ionomer system include acrylic acid, maleic acid, and itaconic acid [27,28]. The number of homopolymers and copolymers that can be built from these three structural units of different configurations and molecular weights is considerable. Examples are depicted in Fig. 1. There are differences in functionality and acid strength between these polyacids. Poly(maleic acid) contains twice as many carboxyl groups as poly(acrylic acid) and is a stronger acid. It would be expected to be more reactive and require less reactive glasses than those used in combination with poly(acrylic acid).

The possible reasons for the mildness of poly(acrylic acid) were given by McLean and Wilson [13] as long ago as 1974:

1. Poly(acrylic acid) is a weak acid.
2. The dissociated H^+ ions are constrained to the nearby area of the polyanion chain due to electrostatic attraction.

3. When partly neutralized, the tendency of poly(acrylic acid) to dissociate into hydrogen and polyacrylate ions is reduced because of the increase in the negative charge on the chain. As a result, it becomes a weaker acid.
4. Diffusion of the polyacid in the dentinal tubules is restricted because of its high molecular weight and chain entanglement.
5. Poly(acrylic acid) will be readily precipitated by calcium ions in the tubules. Thus, the thinnest layer of dentin will be sufficient to bind poly(acrylic acid) as insoluble salts.

The setting reaction of CGICs starts when the fluoroaluminosilicate glass powder and the aqueous solution of polyacrylic acid are combined, producing an acid-base reaction with powdered fluoroaluminosilicate glass as the base (Fig. 2)

A similar interaction occurs when the cements contact enamel or dentin, which mainly contains hydroxyapatite (Ca^{2+} and PO_4^{3-}), and Type I collagen. Salt bridge formation results in adhesion. Like enamel or dentin, bone also contains hydroxyapatite and Type I collagen [8,29]. Based on their compositions, bone is very similar to dentin [8]. This is the basis for GIC use in orthopedics for bone restorative applications. Its positive effects on promoting bone growth when used as bone cement even show that these materials are not only biocompatible but also bioactive.

Conventional bone cements are poly(methylmethacrylate) cements, which mainly function with the help of formation of so called "mechanical interlock" between the acrylate resins and porous bone structures [30]. Unlike these conventional bone cements, GICs adhere to the bone by means of formation of ionic bonding or salt-bridges. If hybrid systems are introduced, *in situ* addition polymerization occurs and dual-curing cements will form. As a result, not only salt bridges but also mechanical interlocks play an important role in strengthening the interfacial bonding [8,29,31]. The resulting resin-modified GICs exhibit many advantages of both resin cements and GICs.

GICs used as bone cements have been reported elsewhere [32-34]. So far, two commercialized conventional GIC type bone cements have been manufactured in Germany, one called IONOS and the other called Ionocem. They both are two-component systems, which are composed of a copolymer of acrylic and maleic acid in aqueous solution and a calcium-aluminium-fluoro-silicate glass [32,33]. This formulation is similar to that of the dental GICs manufactured by ESPE Dental Co. (Germany) [35]. One preliminary study on otological surgery showed that these cements are very promising in both adhesion and biocompatibility [32]. Another study showed such materials to be of great value in translabyrinthine acoustic neuroma surgery and concluded that the cements were easy to use and no side effects were observed [33]. Negative results related to lower bonding strengths have been reported elsewhere [34]. There is little literature which has reported the improvement or formulation of GICs for use in orthopedics.

As we know from dental GICs, current conventional dental glass-ionomer cement systems such as poly(acrylic acid) or poly(acrylic acid-co-itaconic acid) are not ideal systems. Brittleness and low tensile and flexural strengths have limited the current CGICs for use only at certain low stress-bearing sites such as Class III and Class V cavities. Two major problems regarding the polymer matrix may exist. One problem resides in the direct or very close attachment of all the carboxylic acid (-

COOH) groups to the polymer backbone. Not all the carboxyl groups of polyacids are converted to carboxylate groups during the course of the reaction and utilized in salt-bridge formations [36,37]. Some free –COOH groups remain unreacted because they are inaccessible for steric reasons, and also because, when the polyacrylate chain is largely ionized, the remaining protons become firmly bound by electrostatic forces; as a result, the metal ions are increasingly hindered in their movements to react at carboxyl sites. It is postulated that the strength and fracture resistance of the material are therefore compromised due to this steric hindrance, which brings about significantly reduced $-\mathrm{COO}^{-+++}\mathrm{Al}$ interactions (cluster or salt bridge formation) in the cement.

The other problem involves optimizing molecular weight. It is well known that mechanical strengths are very much molecular weight dependent [38]. An increase of molecular weight will enhance the mechanical performance of the materials [39]. Highly ordered poly(acrylic acid) or similar copolymers severely limit the increment of molecular weight of these polyelectrolytes since their aqueous solutions are highly viscous, easily form gel, and show limited shelf life. Introduction of monomers with various spacer lengths connecting the carboxylic acid groups to the polymer backbone could be another way to allow the use of higher molecular weight polymers.

As mentioned earlier, compared to a composite resin, CGICs also have some inferior mechanical properties such as bending strength, tensile strength, and fracture toughness. These properties can be improved by incorporating water-soluble monomers into an aqueous solution of polyacrylic acid. Hence, resin-modified glass-ionomer cement (RMGIC) is defined as a material that undergoes both an addition polymerization reaction and acid-base reaction [3]. The basic composition of the cement liquid is polycarboxylic acid, water, and 2-hydroxyethylmethacrylate (HEMA). It may also contain a small amount of cross-linking material. Some products such as 3M Vitremer are said to contain a polycarboxylic acid modified with pendant methacrylate groups. The composition and structure of the fluoroaluminosilicate glass for RMGICs are similar to those of CGICs.

The essential acid-base reaction between the fluoroaluminosilicate glass and the polycarboxylic acid is initiated by mixing the powder and liquid. At the same time, the polymerization of HEMA and cross-liking material is started by an oxidation-reduction reaction or a photopolymerization catalyst. This forms a hardened mixture in which HEMA polymer and polycarboxylic acid are linked by hydrogen bonding (Fig. 3).

When polyacids are modified with pendant methacrylate groups, these glass-ionomer hybrid materials not only undergo an acid-base reaction but also contain methacrylate side chains grafted onto the polyacid molecules which can participate in polymerization [31]. These vinyl containing GICs have gained popularity in the restorative dental community, since they have more attractive properties, as compared to CGICs. In addition to maintaining the clinical advantages of CGICs, these RMGICs reduce the problems of moisture sensitivity and low early mechanical strength associated with CGICs [40,41], are easier to handle clinically [41], exhibit extended working time, and have significantly improved mechanical strengths such as higher flexural strength (FS) and diametral tensile strength (DTS) [31,42]. The strengths of these RMGICs are increased as much as two to three times compared to their conventional counterparts [31]. So far, three major types of RMGICs have been investigated. One is made of a fluoroaluminoslicate glass powder and an aqueous solution of a copolymer of acrylic and maleic acid, HEMA, water, an initiator, and an activator [43]. Another is composed of sodium lanthanum calcium aluminum fluorosilicate glass combined with a copolymer of acrylic acid and maleic acid in dry form and a solution of glass-ionomer-compatible monomers and oligomers, HEMA, water, an initiator, and an activator [35]. The third is composed of a calcium fluoroaluminosilicate glass powder and an aqueous solution of a copolymer of acrylic and itaconic acid with pendant methacrylate groups, HEMA, water, initiators, and activators [43]. Different commercial RMGICs may vary around these three types. New efforts have been made to further improve the mechanical properties [44].

2. Hypotheses

Polymers containing a flexible spacer linking the main chain to the pendent functionality will allow greater mobility of both the main chain and/or spacer linked functionality to assume desired configurations. While the reactivity of the functionality at the end of the spacer chain has not changed, it has become more liberated to undergo assembly and reactions. Such functional groups have a greater degree of freedom from constraint by the backbone and are not as sterically hindered by the backbone. Spacer group-linked -COOH groups will show a much greater degree of freedom to react with Ca^{2+} and Al^{3+} cations to form ionic clusters (salt bridges) and allow more efficient use of all the -COOH groups in setting reactions, thus resulting in improved mechanical performance in the cement. The idea that amino acid functionalized GICs would result in improved strengths has been found valid in dentistry [45,46]. These modified GIC systems have preliminarily shown good potential in dentistry [45-47]. The two problems discussed above may be solved by using this concept.

Amino acids as components of proteins are likely biocompatible with human tissue. In addition, acrylic functional amino acids and their derivatives have been found to be good pressure sensitive adhesives [48]. The results showed that, due to introduction of the acrylamide (-CONH-) residue, the tack, adhesion, and cohesion were greatly increased. This is another reason for incorporation of amino acids into the bone cement system.

2.1 Hypothesis 1

It is hypothesized that varying the spacer length between the carboxylic acid groups and the polymer backbone, will provide a route to improve glass-ionomer compositions. Polymers of this type would be expected to have greater flexibility, offering improved fracture resistance and toughness, along with increasing the extent of ion crosslinking. Variation of both the pK_a and different types of carboxyl groups resulting from the amino acid moiety would be expected to increase the interaction between polyacids and glasses and improve the strength of the cements. In addition, use of these natural or synthetic amino acids might provide stronger adhesion to tooth structures and better biocompatibility to tooth or tissue compared to those organic acids in present commercial products.

HEMA is one of the major components in RMGIC composites. It acts as both cosolvent and comonomer in the system. Because of their relatively low water solubility, methacrylated polyacids need some amphiphilic difunctional monomers like HEMA to help them dissolve in water. However, this amphiphilic molecule was reported to have certain cytotoxity, especially when used as a bone cement [49-51]. Oliva et al. [49] found that HEMA exhibited great cytotoxicity toward the osteoblasts and pure HEMA led to complete cell death. Goodwin et al. [50] found that HEMA caused enhanced cytotoxicity and inhibited the release of the bioactive hormone. A hydroxyl group on HEMA molecule seemed to enhance cytotoxicity [51]. Therefore, we have to find an alternative to replace HEMA in order to make the cement more biocompatible to the bone, even though HEMA is a very good cosolvent for the RMGICs. Hydrophilic vinyl-containing amino acids have both polymerizable and hydrophilic functionalities and may be used as a good alternative to replace HEMA. These monomers are expected to be biocompatible and if so will benefit both soft and hard tissues.

2.2 Hypothesis 2

Based on the above simple discussion, it is hypothesized that developing and formulating vinyl containing amino acid modified hybrid glass-ionomer bone cements will promote biocompatibility and enhance mechanical properties, providing a route to generate biocompatible bone cements with higher mechanical strengths for orthopedic surgery.

It is known that heat, light, and redox initiators can initiate free radical addition polymerization [52]. Dentists apply the light initiator systems quite successfully in restorative dentistry [53]. However, large exotherms and limited light penetrating depth make such initiators useless in orthopedic application. Therefore, a redox system is the logical choice to initiate the polymerization of glass-ionomer bone cements. A common redox system (benzoyl peroxide-N, N-dimethyl-para-toluidine), which has been used in conventional poly(methyl methacrylate) (PMMA) bone cement, cannot be used in the glass-ionomer system, since it does not dissolve in aqueous solution. As an alternative, $K_2S_2O_8$-ascorbic acid redox system has been used in the 3M Vitremer tricure dental glass-ionomer system for so-called "dark cure" [35]. To extend the working time, which is necessary in clinics, we can microencapsulate the ascorbic acid using certain polymers, such as cellulose acetate butyrate (CAB).

2.3 Hypothesis 3

It is hypothesized that water soluble redox initiator systems can be used in RMGICs to yield products with comparable mechanical strength to light cure systems.

2.4 Hypothesis 4

Compared to CGICs, vinyl-containing glass ionomer cements (VCGICs) have FS and DTS and relatively long working time prior to light initiation. However, the grafting agent being used so far, 2-isocyanatoethyl methacrylate (IEM), is too expensive and toxic. In order to find an alternative, in this study we proposed to synthesize polyacid with pendent methacrylate by using two new grafting agents.

3. Outline of dissertation

In the first paper, the use of amino acid residue containing polyacids to formulate self-cured GICs is described. Effects of polymer structure and cement formulations will be evaluated based on mechanical strengths. In the second paper, the use of vinyl containing polyacids to synthesize and formulate improved light-cured GICs is described. In the third paper, the use of redox initiation systems in RMGICs for orthopedic usage is described. The use of two new grafting agents to modify polyacids and replace the expensive and toxic IEM is described in the last paper.

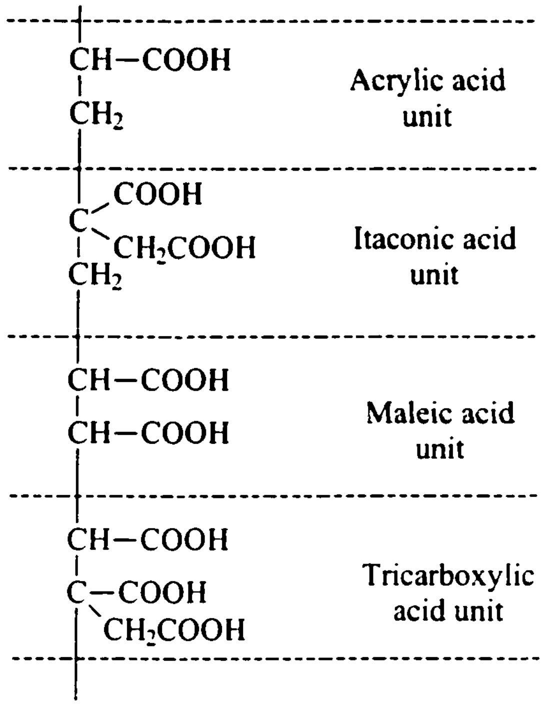

Fig. 1. Structure of poly(alkenoic acid)s. The drawing shows various types of carboxylic acid units used in ionomer polyacids.

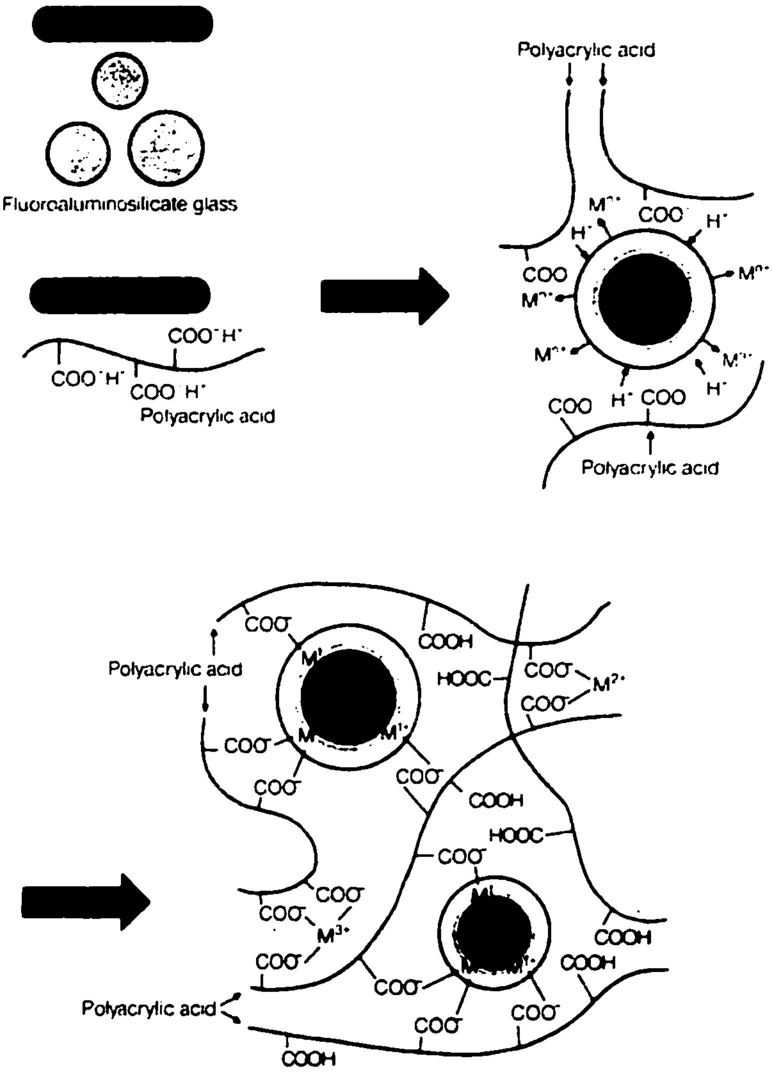

Fig. 2. Setting reaction of glass-ionomer cement. Glass powder and polyacrylic acid are mixed, and the H^+ ion released from the polyacrylic acid attacks the glass surface. Metal ions are released from the glass following the H^+ ion attack. The metal reacts with the polyacrylic acid, and the surface of the glass particle is transformed into a silica gel layer.[3]

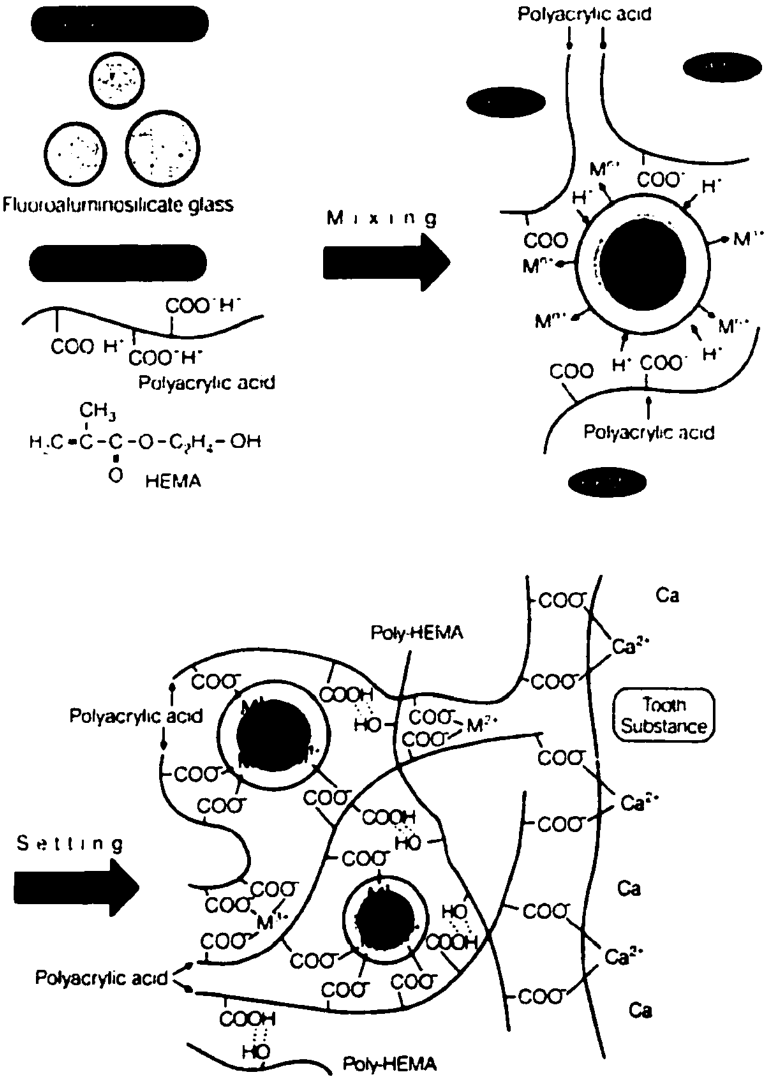

Fig. 3. Setting reaction of resin-modified glass-ionomer cement. The glass powder and cement liquid are mixed, and the H^+ ion in the liquid attacks the glass surface. The metal ion released from the glass particle reacts with polyacrylic acid while HEMA cures concurrently. The surface layer of the glass particle is transformed into a silica gel layer.

SYNTHESIS OF AMINO ACID-CONTAINING POLYACIDS AND THEIR APPLICATION IN SELF-CURED GLASS-IONOMER CEMENTS

by

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Abstract

Six methacrylate or acrylate derivatives of natural amino acids were synthesized and characterized. Six terpolymers [poly(acrylic acid-co-itaconic acid-co-amino acid] modified with these amino acids were also prepared and characterized. These polymers were used to formulate glass-ionomer cements (GICs) with the Fuji II glass filler. The effects of the molecular weight (MW) and powder/liquid (P/L) ratio were evaluated. Scanning electron microscopy (SEM) was used to examine the fracture surfaces of selected cement specimens. Results show that all the amino acid modified GICs demonstrated higher compressive strengths (CS, 193-236 MPa) and much higher flexural strengths (FS, 55-71 MPa) as compared to commercial Fuji II GIC (191 in CS and 16 in FS). Both molecular weight and P/L ratio affected the strength of the formed cement. It was important to find the optimal MW and P/L ratio in order to obtain the highest FS. In this study, optimized MW (number average) of the polyacids and P/L ratio were around 50,000 and 2.7/1, respectively. The microstructures of the fracture surfaces helped explain the strength differences among the materials tested in the study. SEM analysis suggests that more integrated microstructures and fewer defects can lead to higher FS.

1. Introduction

Glass-ionomer cements (GICs) have been successfully applied as dental restoratives for over 20 years since their invention by Wilson and Kent [1] and McLean and Wilson [2]. GIC is well-known for its unique properties such as direct adhesion to tooth structure and base metals [3,4], anticariogenic properties due to release of fluoride [5], thermal compatibility with tooth enamel and dentin because of low coefficients of thermal expansion similar to that of tooth structure [6], minimized microleakage at the tooth-enamel interface due to low shrinkage [7], biological compatibility, and low cytotoxicity [8,9].

As we know from the study of dental GICs, current conventional (or self-cured) dental GIC systems using poly(acrylic acid) or poly(acrylic acid-co-itaconic acid) as a polymer matrix are not ideal systems. Brittleness and low tensile and flexural strengths have limited the current conventional (or self-cured) GICs for use only at certain low stress-bearing sites such as Class III and Class V cavities. Two major problems regarding the polymer matrix may exist. One problem resides in the direct or very close attachment of all the carboxylic acid (-COOH) groups to the polymer backbone. Not all the carboxyl groups of such polyacids are converted to carboxylate groups during the course of the curing reaction and utilized in salt-bridge formations [10,11]. Some free –COOH groups remain unreacted because they are inaccessible for steric reasons and also because, when the polyacrylate chain is largely ionized, the remaining hydrogens become firmly bound by electrostatic forces; as a result, the metal ions are increasingly hindered in their movements to react at carboxyl sites [12,13]. It is postulated that the strength and fracture resistance of the material are therefore compromised due to this steric hindrance, which brings about significantly reduced $-COO^{-+++}Al$ interactions (cluster or salt bridge formation) in the cement.

The other problem is related to molecular weight of the polyacid. In general, increase of MW will enhance the mechanical performance of the materials [14].

Highly ordered poly(acrylic acid) or similar copolymers severely limit the increment of MW of these polyelectrolytes since their aqueous solutions easily form gels and show limited shelf life [15]. Introduction of monomers with various spacer lengths of the carboxylic acid group to the polymer backbone could be another way to increase the MW of these polymers [12].

The idea that use of amino acid functionalized GICs would result in improved strengths has been found valid in dentistry [12,13]. These modified GIC systems have preliminarily shown good potential in dentistry [12,13,16]. Using this concept may solve the two problems discussed above. Amino acids as a basic component of proteins are no doubt biocompatible with human tissue [17]. In addition, acrylic functional amino acids and their derivatives have been found to be good pressure sensitive adhesives [18].

The objectives of this study were to synthesize and characterize methacrylate or acrylate derivatives of several natural amino acids, to synthesize and characterize the terpolymers comprising these synthesized derivatives, to formulate the GICs using these synthesized terpolymers, and to evaluate the mechanical strengths of the formed GICs using compressive and flexural strengths. Effects of MW and P/L ratio on strengths and surface microstructure were evaluated.

2. Experimental part

2.1. Materials

Methacryloyl chloride (MC), acryloyl chloride (AC), methanol (MeOH), anhydrous magnesium sulfate ($MgSO_4$) and ethyl acetate were used as received from

Acros Chemical Co. Sodium hydroxide (NaOH), sodium chloride (NaCl), and hydrochloric acid (HCl) (37%) were used as received from Fisher Scientific Co. Glycine (G), L-glutamic acid (GA), β-Alanine (BA), acrylic acid (AA), itaconic acid (IA), N,N-dimethylformamide (DMF) (anhydrous), potassium persulfate ($K_2S_2O_8$), and L-tartaric acid were used as received from Aldrich Chemical Co. GC Fuji II glass powders were supplied by GC American Dental Co.

2.2. Synthesis and characterization of amino acid derivitives and their terpolymers with acrylic acid and itconic acid

2.2.1. Synthesis of methacrylate or acrylate derivatives of amino acids

The methacryloyl and acryloyl derivatives of the amino acids including glycine, L-glytamic acid, and β-alanine, were prepared using the Schotten-Baumann reaction, as described by Varaprasad et al. [19]. Briefly, to a three-neck flask, equipped with a thermometer and a mechanical stirrer, containing amino acid and NaOH (moles changing with the number of carboxylic acid) aqueous solution, methacryloyl chloride or acryloyl chloride equivalent to the amino group on the amino acid was added dropwise with vigorous stirring at a temperature below 5 °C. After addition was completed, an additional 1 h was allowed to complete the reaction. The solution was acidified to pH = 2 with a solution of concentrated HCl (37%) and extracted four times with ethyl acetate. The extract was separated, dried with anhydrous $MgSO_4$, filtered, and concentrated using a rotary evaporator to obtain white crystals. The crystals were recrystallized from ethyl acetate. The schematic diagram for monomer synthesis is shown in Fig. 1.

2.2.2. Preparation of terpolymer

The terpolymers composed of AA, IA, and methacryloyl or acryloyl amino acid were synthesized using free-radical polymerization. To a three-neck flask, equipped with a thermometer, a nitrogen inlet and a mechanical stirrer, containing an aqueous solution of deionized water and $K_2S_2O_8$, a mixture of AA, IA and methacryloyl or acryloyl amino acid in water was added. The reaction was run under N_2 purging at 93 °C for 18 h. The molar feed ratios for the terpolymers were 8:2:1 (AA:IA:M- or A-amino acid). Polymers with different molecular weight were prepared by changing the amount of initiator and reaction temperature. The final products were freeze-dried and ground. The scheme for terpolymer synthesis is shown in Fig. 2.

2.2.3. Characterization of synthesized monomers and polymers

The methacrylate or acrylate derivatives of amino acids were characterized by melting point identification and nuclear magnetic resonance (NMR) spectroscopy. The terpolymers were characterized by gel permeation chromatography (GPC) and viscosity measurement. The melting points were measured using a digital melting point apparatus (Electrothermal IA9000 Series, Electrothermal Engineering Ltd., Essex, United Kingdom). ^1H NMR spectra were obtained on an ARX-300 NMR Spectrometer using deuterated methyl sulfoxide as a solvent. For determination of molecular weight, the terpolymers 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 [20], having solubility in tetrahydrofuran (THF) for molecular weight estimation. Molecular weights were estimated on the Waters GPC unit (Model 410 differential refractometer), using standard GPC techniques, with polystyrene standards as calibrants. Specific viscosity was measured using an Ubbelohde viscometer, with both DMF and deionized water as solvent.

2.3. Formulation and evaluation of self-cured GICs

2.3.1. Preparation of specimens of self-cured GICs

All terpolymers were dissolved in distilled water to make polyacid solutions, with the proportion of copolymer:water = 46:54 (wt/wt). The glass powder from Fuji II (GC International, Tokyo, Japan) was used as a reactive filler, and the P/L ratio (2.7/1) was used as recommended by the manufacturer. Specimens were mixed and fabricated at room temperature. The cylindrical specimens were prepared in glass tubing, with dimensions of 4 mm diameter by 8 mm length for compressive strength (CS) tests. The specimens for the FS test were prepared using a rectangular Teflon mold with dimensions of 3 mm width by 3 mm depth by 25 mm length. The specimens were removed from molds after 10 to 20 minutes and conditioned in distilled water at 37 °C for 1 day, 1 week, or 1 month, prior to testing.

2.3.2. Strength determinations

Testing of specimens was performed on a screw-driven mechanical testing machine (Model 858 Mini Bionix, MTS Systems Corp., Eden Prairie, MN, USA), with a crosshead speed of 1 mm/min for the CS and FS measurements. The FS test was performed in three-point bending, with a span of 20 mm between supports. The sample size was n = 7 for the each test.

The compressive strength was determined from the relationship $CS = 4P/\pi d^2$, where P = the load at fracture, and d = the diameter of the cylinder. The flexural strength in three-point bending 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.

2.3.3. Estimates of working time of the cement

A metal rod was used to evaluate the working time. The rod was inserted into the center of the mixture of the cement, which was mixed and packed into a small vial with a hole at the bottom. Working time began once the mixing process was started. The time from the start of mixing to the moment at which the metal rod could not be moved was defined as the working time for this self-cured system.

2.3.4. Statistical analysis

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

2.3.5. Scanning electron microscopic (SEM) analysis

The fracture surface of one representative specimen from selected materials was observed over a range of magnifications with an SEM (Model 515, Philips

Electronics N.V., Eindhoven, The Netherlands) in order to investigate the effects of microstructure on the mechanical properties. The specimens were vacuum sputter-coated with gold-palladium (Au-Pd), and a high vacuum (5.5×10^{-5} Torr) was used for dehydration of the coated specimens before SEM analysis.

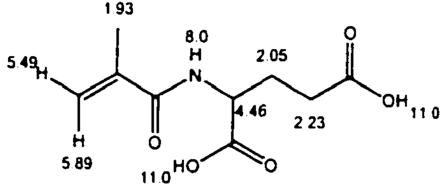
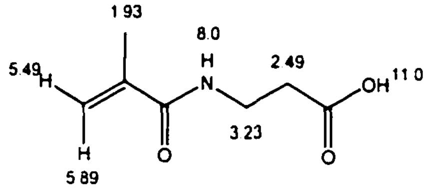
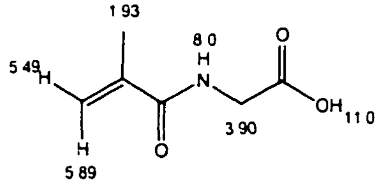
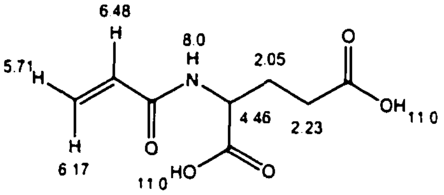
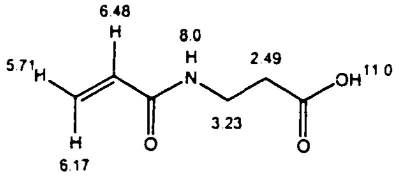
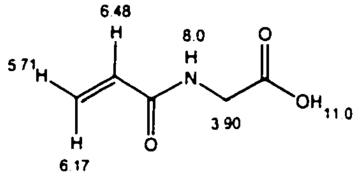
3. Results and discussion

3.1. Characterization of amino acid derivitives and their terpolymers with acrylic acid and itconic acid

3.1.1. Yield, melting point, and NMR spectra of synthesized monomers

The structures of six amino acid derivatives are illustrated in Table 1. Codes, names, and schematic structure descriptions of these derivatives are also listed in the table. The chemical shift numbers of the protons in ^{1}H NMR calculated by *ChemDraw* are also listed in Table 1. Yields and melting points of these monomers are shown in Table 2.

Table 1.
Monomers and their structures

Code	Monomer	Schematic structures and ^1H NMR assignment*
MGA	Methacryloyl glutamic acid	
MBA	Methacryloyl β-analine	
MG	Methacryloyl glycine	
AGA	Acryloyl glutamic acid	
ABA	Acryloyl β-analine	
AG	Acryloyl glycine	

*Numbers on the protons are the chemical shifts in ^1H NMR calculated by *ChemDraw*.

Table 2.
Yield and Melting Point of Synthesized Monomers

Code	Yield (%)	Melting Point (°C)
MGA	85~93	120.8~121.5
MBA	73~80	69.7~69.9
MG	72~81	103.0~104.0
AGA	52~59	118.5~119.5
ABA	63~70	95.0~96.0
AG	41~48	132.5~132.7

The measured ^{1}H NMR spectra of six synthesized monomers are shown in Fig. 1, with their schematic structures on the side. The peaks in the ^{1}H NMR spectra almost perfectly fit the values calculated by standard software *ChemDraw*. From Fig. 3, we can see that the synthesized monomers exhibited high purity.

From Table 2, it may be seen that the yields for acrylate derivatives of the amino acids (from 41 to 70%) were lower than those for their methacrylate counterparts (from 72 to 93%). The reason may be attributed to the methyl group on the methacryloyl amino acids, since this group makes these amino acids more hydrophobic. The acryloyl amino acids are, in other words, thought to be more hydrophilic, compared to their methacryloyl counterparts. This is very evident because the monomer synthesis was carried out in aqueous solution, but the recovery of the synthesized monomer was completed with ethyl acetate. The difference of hydrophilicity between the two types of monomers led to the yield differences.

Most acrylate derivatives of the amino acid in this study showed higher melting points than their methacrylate counterparts, except for glutamic acid. Acryloyl and methacryloyl glutamic acids exhibited similar melting points. Among the three methacrylate derivatives of the amino acids, methacryloyl glutamic acid showed the highest melting point since it has two carboxyl groups per molecule which may form stronger intermolecular hydrogen bonding. Methacryloyl β-alanine showed the lowest melting point since it may form intramolecular hydrogen bonds.

3.1.2. Characterization of synthesized terpolymers

All the amino acid containing polyacids were synthesized using a molar ratio of AA:IA:Amino-acid = 8:2:1, as indicated by Xie et al. [17], because this ratio was the optimal for the poly(acrylic acid-co-itaconic acid-co-amino acid) terpolymer systems. The terpolymers synthesized based on the six monomers are described in Table 3, including their codes, names, and schematic structures. Their relative viscosities and MWs (number average) are shown in Table 4.

As results indicated, even with the same initiator concentration (1.0% of total weight of monomers) and reaction temperature (93 °C), acrylate derivatives of amino acid-containing termpolymers showed higher MW than their methacrylate counterparts, which may also be due to the reason that the more hindered methyl group on methacrylate interfered with the polymerization. To increase the MW, C12 was synthesized with the initiator concentration of 1.0% and at 80 °C, while C13 was synthesized at the same temperature but with a lower initiator concentration (0.5%). As a result, C13 had the highest MW and relative viscosity, as shown in Table 4. From Table 4, we can also see that the relative viscosity values of these polyacids in both DMF and water showed the same trend, which were generally consistent with the MW data estimated by GPC. This means that the viscosity can be used for estimating the relative MW for these polyacids in case GPC data are not available.

Table 3.
Structures of terpolymers

Code	Terpolymer	R_1	R_2
C1	Poly (AA-IA-MGA)	$-CH_3$	$-CH(COOH)(CH_2)_2COOH$
C2	Poly (AA-IA-MBA)	$-CH_3$	$-(CH_2)_2COOH$
C3	Poly (AA-IA-MG)	$-CH_3$	$-CH_2COOH$
C4	Poly (AA-IA-AGA)	-H	$-CH(COOH)(CH_2)_2COOH$
C5	Poly (AA-IA-ABA)	-H	$-(CH_2)_2COOH$
C6	Poly (AA-IA-AG)	-H	$-CH_2COOH$

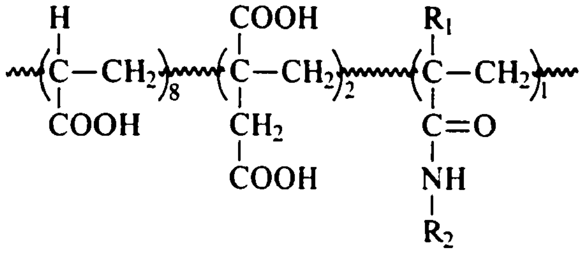


Table 4.
Inherent viscosity and molecular weight (number average) of polyacids

Code	Polymer	Mn × 10^{-3}	η_r (DMF)	η_r (H_2O)
C1	P(AA-IA-MGA)	31.4	0.261	0.164
C2	P(AA-IA-MBA)	38.0	0.402	0.228
C3	P(AA-IA-MG)	33.1	0.342	0.188
C4	P(AA-IA-AGA)	46.1	0.321	0.216
C5	P(AA-IA-ABA)	45.6	0.503	0.350
C6	P(AA-IA-AG)	47.6	0.429	0.278
C12	P(AA-IA-MGA)	56.2	0.419	0.278
C13	P(AA-IA-MGA)	97.3	0.565	0.394
C0	Fuji II	7.6	0.083	0.044

3.2 Evaluation of the formed GIC specimens

The mean values and standard deviations (SD) in CS and FS of all tested specimens are shown in Tables 5 and 6 and Figs. 4, 5, and 6. For each test the values marked with the same superscript letters were not significantly different ($p > 0.05$).

It is known that the FS test is a strength test of a beam supported at each end under a static load, which is a combination of tensile, compressive, and shear strengths. It can be assumed that the principal stresses on the upper surface (or the load bearing side) are compressive, those on the lower surface (or away from the loading bearing site) are tensile, and those at the surface parallel to the load are shear [7,21]. Prosser et al. [22] have commented that the most appropriate measure of the strength of the GICs is obtained with a flexural test. In general, many brittle materials such as cements and ceramics have a strength under tension that is markedly lower than the corresponding strength under compression, since these materials often have many microcracks, defects, and voids inside or on the surface. Direct tensile testing is not recommended for these materials, because tremendous variations and erroneous values will be easily obtained. Therefore, it is suggested that the measurement of FS offers the best practical and reliable estimate of tensile strength [23].

3.2.1. Effect of molecular weight

Table 5 shows the effect of MW on strengths. The estimated working time ranged from 2.5-5.5 min. It is apparent that the higher the MW, the shorter the working time, which was consistent with previous reports [13,14]. The mean values in strength were compared using one-way ANOVA followed by the post hoc Tukey-Kramer multiple range test. The mean values with the same superscript letter were not significantly different ($p > 0.05$), as shown in Table 5. From Table 5 and Fig. 4, we can see that mechanical strength increased with the MW to a certain point and then decreased, which was caused by poor handling during the mixing process. We found that it was very hard to fabricate the specimens with too high MW of polyacids, especially cylindrical specimens for CS test, due to very short working time.

Strength is usually increased by increasing the MW of the polyacids [12,24], because intermolecular forces are significantly increased with increase of MW and polymer chain length. Increase in polymer chain length also increases the bonding between filler particles and the polymer matrix. However, handling characteristics become poor as the MW increases. In this study, it was found that the optimal MW (number average) of the polyacid was around 50,000, which gave us good mechanical strength and satisfactory handling properties.

Table 5.
Effect of Molecular Weight on Mechanical Strengths

Code	Polymers	Mn × 10^{-3}	WT (min)	CS (MPa)*	FS (MPa)*
C1	P(AA-IA-MGA)	31.4	5.5	206.0(21.7)[a]	55.14(6.47)[a]
C12	P(AA-IA-MGA)	56.2	3.5	220.5(11.5)[a]	66.64(4.06)[a]
C13	P(AA-IA-MGA)	97.3	2.5	–	62.26(4.53)[a]

*Entries are mean values with standard deviations in parentheses. [a]The mean values were not significantly different ($p > 0.05$).

3.2.2. Effect of P/L ratios

From Fig. 5, we can see that FS increased with the P/L ratio to a certain point and then decreased after that. This is also due to handling difficulties, which were very similar to those observed when varying MW, even though the mechanism might be different. High MW polymer can lead to more plastic deformation during the FS test, whereas more glass powder in the system may result in higher compression resistance since the FS test is actually a combination of tensile, compressive and shear strengths. The P/L ratio of 2.7/1 is believed to be optimal because it demonstrated a good mechanical strength, and acceptable handling characteristics for this system.

3.2.3. Significance of amino acid-modified GICs

Table 6 and Fig. 6 show the CS and FS of different amino acid-modified GICs, accompanied by the estimated working time. Estimated working time was in the range of 4 to 5.5 min. The mean values of strength were compared using statistics, and the mean values with the same superscript letter were not significantly different ($p > 0.05$). Basically, acrylate amino acid residue-containing polyacids have relatively higher mechanical strengths than their methacrylate counterparts, even though there were almost no significant differences in statistics among some of the cements. The relatively high strengths for acrylate derivative-containing cements may be due to the fact that the former had higher MWs. It is evident that all the amino acid-modified GICs exhibited comparable CS and almost four times higher FS than the commercial product Fuji II.

Table 6.
Mechanical Strength of Amino Acid Modified GICs and Fuji II

Code	Polymer	WT (min)	CS (MPa)*	FS (MPa)*
C1	P(AA-IA-MGA)	5.5	206.0(21.7)^a	55.14(6.47)^a
C2	P(AA-IA-MBA)	4.0	221.5(27.3)^a	62.96(2.92)^a
C3	P(AA-IA-MG)	4.0	228.2(13.3)^a	60.80(6.51)^a
C4	P(AA-IA-AGA)	5.5	235.0(11.1)^a	70.83(1.54)^a
C5	P(AA-IA-ABA)	4.5	236.1(16.4)^a	68.46(7.50)^a
C6	P(AA-IA-AG)	4.5	193.2(14.9)^a	64.10(6.07)^a
C0	Fuji II	5.0	191.1(19.1)^a	15.79(0.67)

*Entries are mean values with standard deviations in parentheses. ^{a}The mean values were not significantly different ($p > 0.05$).

Microstructures of the fracture surfaces also supported the results in strength differences between the amino acid-modified cements and Fuji II control. Figs. 7-10 illustrate representative regions of the fracture surfaces for several GICs obtained via

SEM. Many of the cracks in the microstructures were found in all microphotographs due to dehydration during preparation for SEM analysis and the paths of crack propagation typically linked microstructural porosity or voids [23]. Compared with Fuji II (Fig. 7), amino acid-modified GICs (Figs 8-10) showed either fewer or smaller pores on the fracture surfaces. In addition, the modified GICs showed a more integrated and highly fused surface texture, whereas Fuji II exhibited more isolated glass particles and larger pores or voids. The more integrated microstructures account for higher FS of the modified cements. The SEM images of the fracture surfaces of the modified cements containing different amino acid residues were fairly similar to each other regarding the main surface texture. However, upon a closer look, differences can be found between Fig. 8 and Figs. 9-10. The cement of Fig. 8 exhibited more voids or pores and isolated filler particles than did the cements in Figs. 9 and 10, which is consistent with results for both CS and FS. C1 (corresponding to Fig. 8) had 206 MPa in CS and 55 MPa in FS, compared to 235 MPa in CS and 70 MPa in FS for C4 (Fig. 9) and 236 MPa in CS and 68 MPa in FS for C5 (Fig. 10), respectively. Fewer defects and more integrated microstructures in C4 (Acryloyl glutamic acid -modified cement) and in C5 (Acryloyl β-alanine) led to a higher CS and FS, which can be attributed to their higher MWs (see Table 6).

4. Conclusions

All the amino acid-modified GICs demonstrated higher CS (193-236 MPa) and much higher FS (55-71 MPa) as compared to commercial Fuji II cement (191 in CS and 16 in FS). Both molecular weight and P/L ratio affected the strength of the formed cement. It was important to find the optimal MW and P/L ratio in order to obtain the highest FS. In this study, optimized MW (number average) of the polyacids and P/L ratio were around 50,000 and 2.7/1, respectively. The microstructures of the fracture surfaces helped explain the strength differences among the materials tested in the study. SEM analysis suggests that more integrated microstructures and fewer defects can lead to higher FS.

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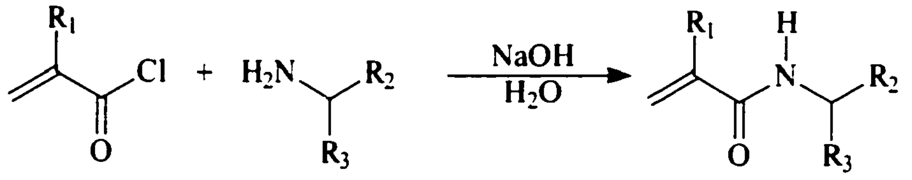

Where R_1 = -H or $-CH_3$,

when R_2 = -H, R_3 = -COOH, or $-CH_2COOH$

R_2 = -COOH, R_3 = $-(CH_2)_2COOH$

Fig. 1. Scheme for monomer synthesis.

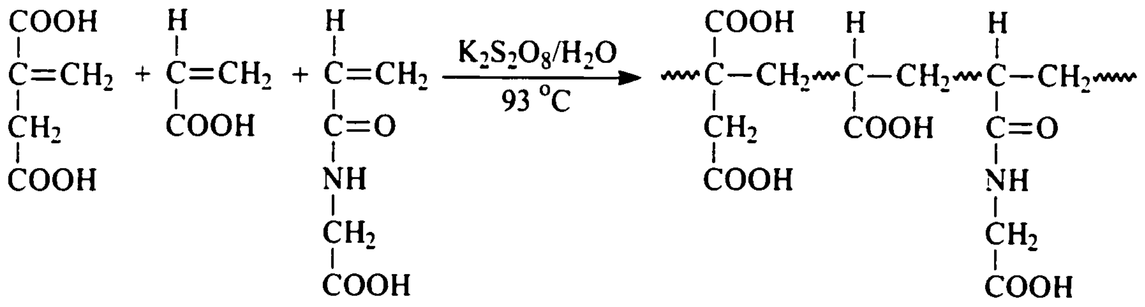

Fig. 2. Scheme for terpolymer synthesis.

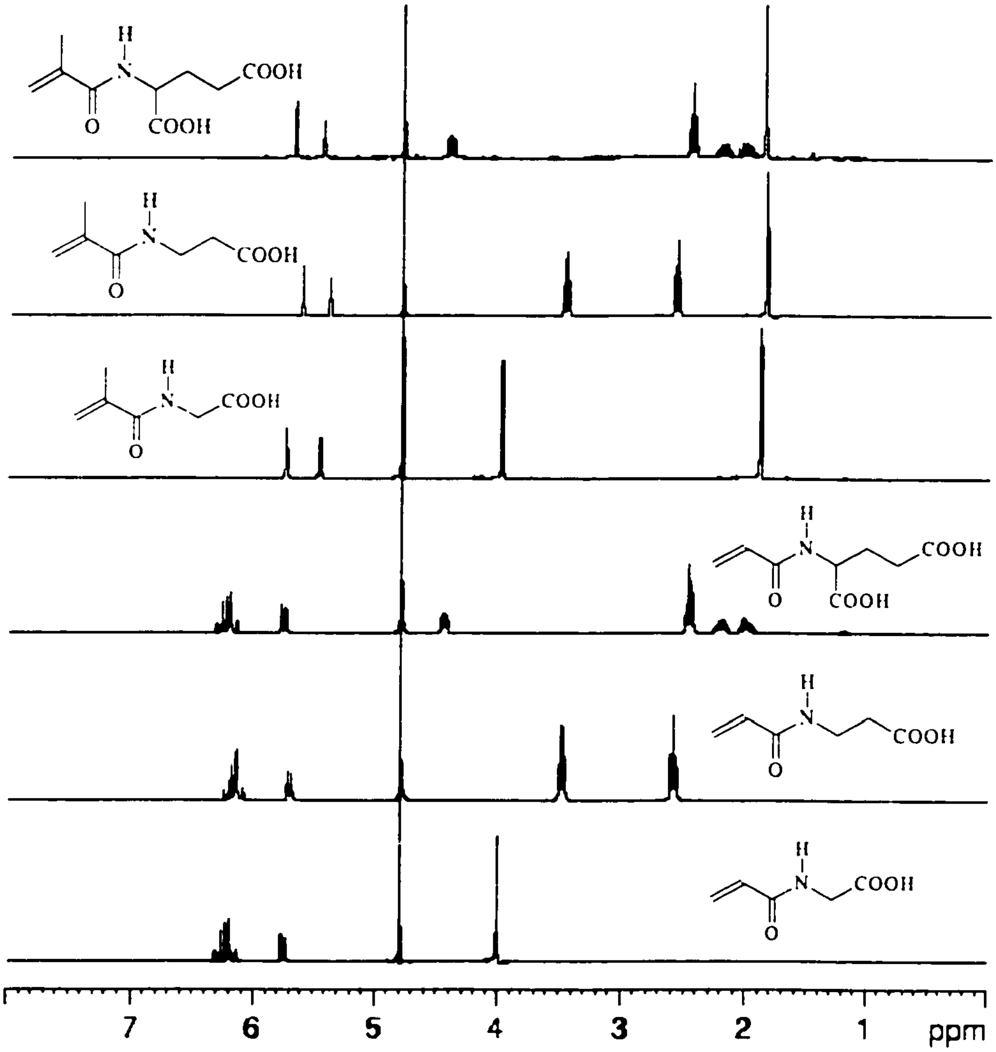

Fig. 3. ^{1}H NMR spectra of synthesized monomers.

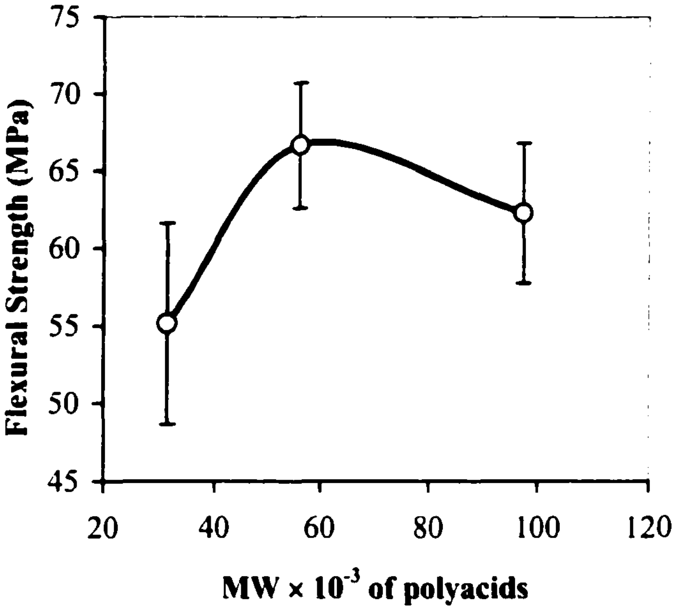

Fig. 4. Effect of molecular weight on FS.

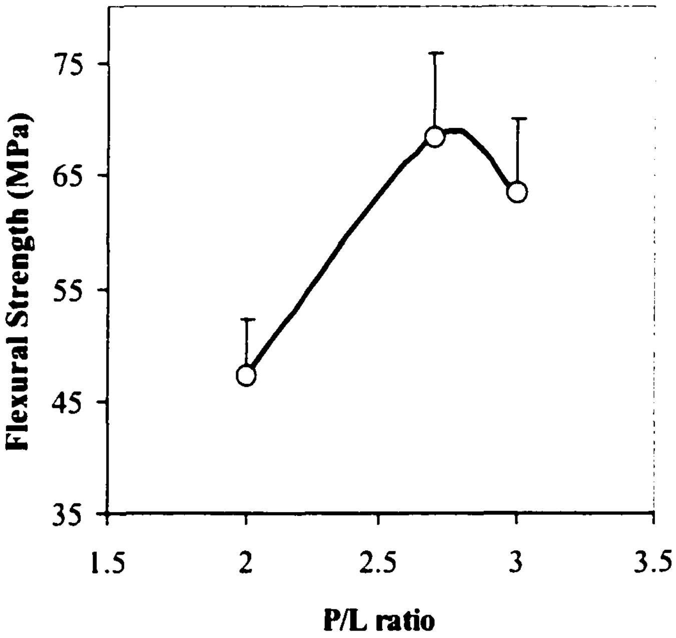

Fig. 5. Effect of P/L ratio on FS.

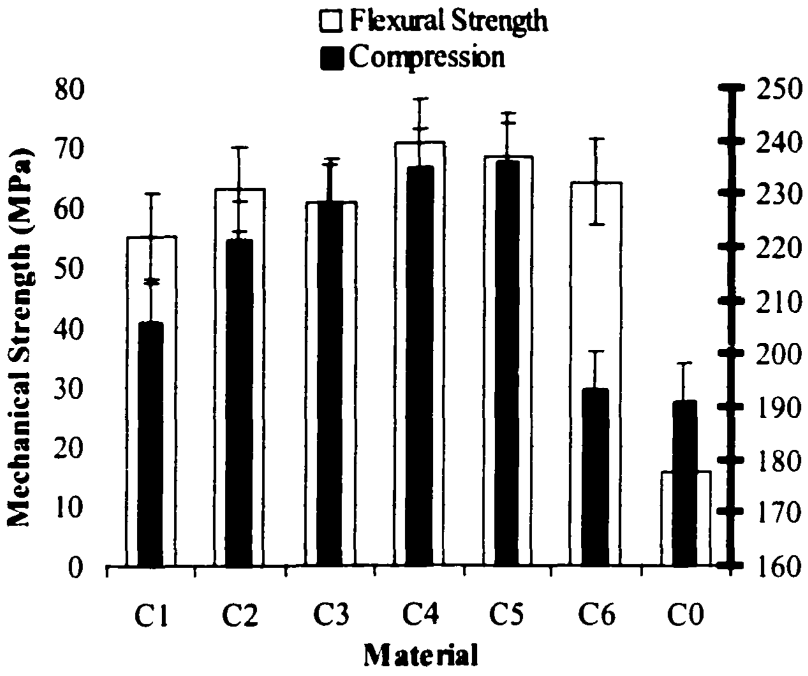

Fig. 6. CS and FS of the amino acid-modified GICs and Fuji II.

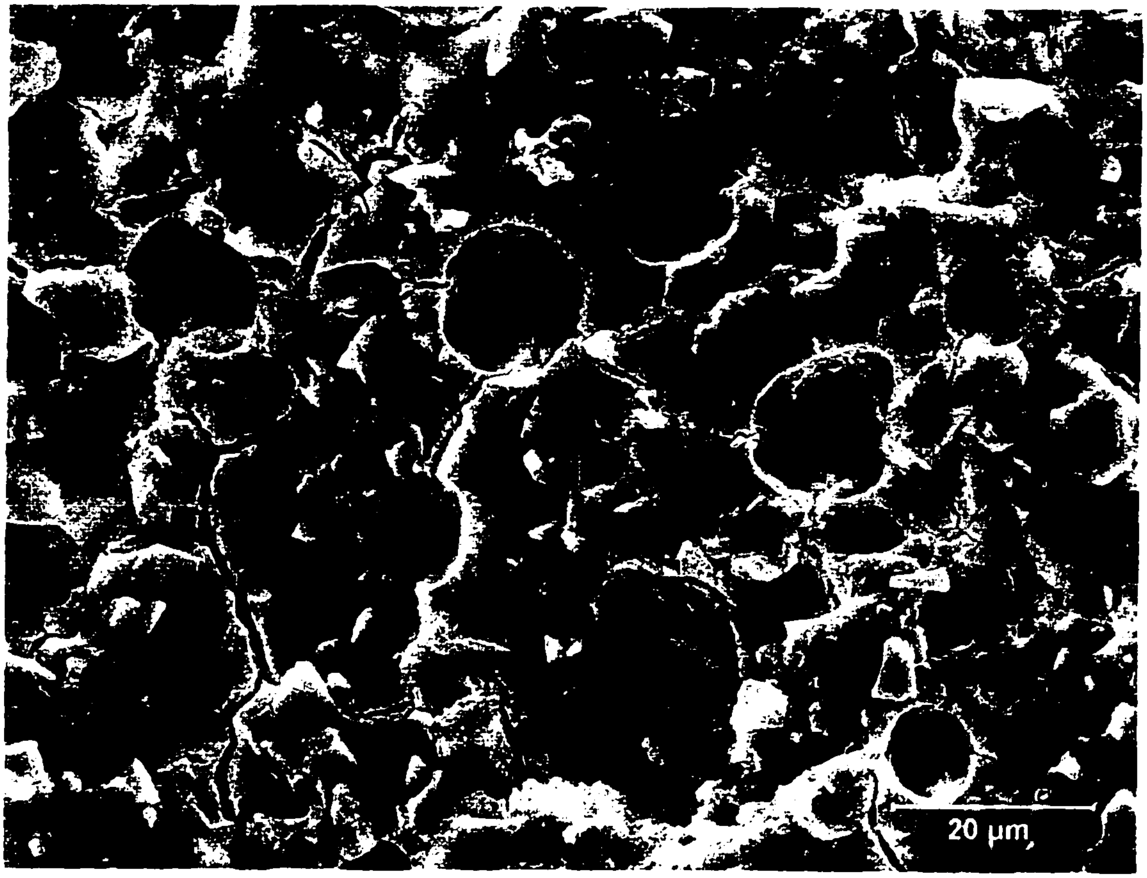

Fig. 7. SEM photomicrograph of Fuji II GICs with original magnification of 1500x.

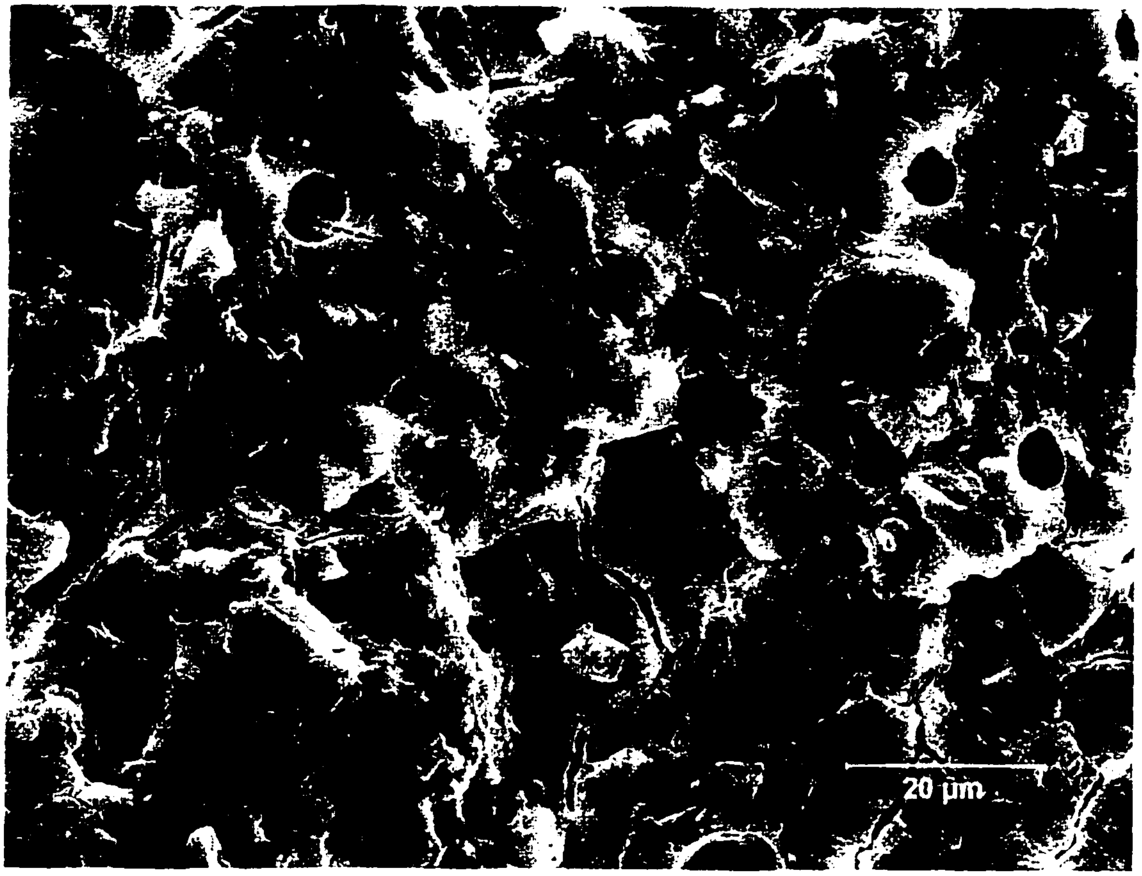

Fig. 8. SEM photomicrograph of MGA modified GICs with original magnification of 1500x.

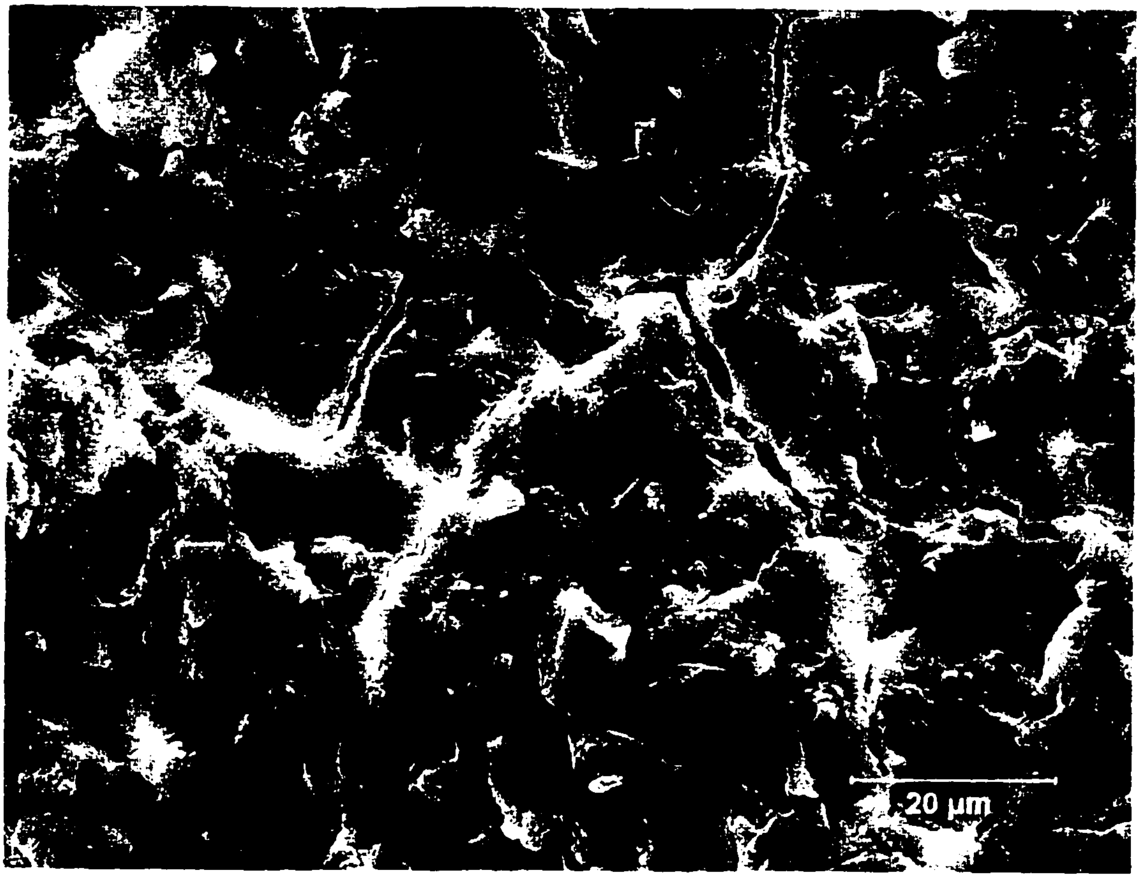

Fig. 9. SEM photomicrograph of AGA-modified GICs with original magnification of 1500x.

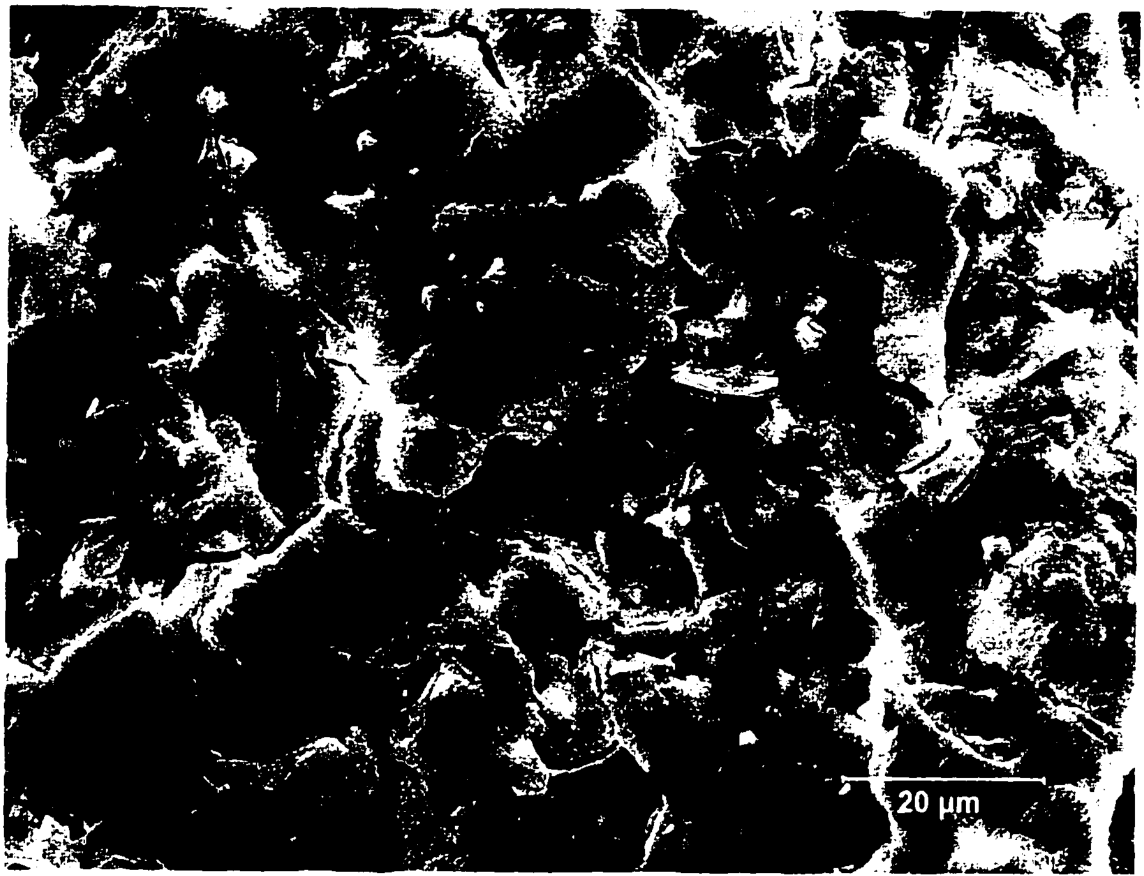

Fig. 10. SEM photomicrograph of ABA modified GICs with original magnification of 1500x.

SYNTHESIS AND FORMULATION OF VINYL-CONTAINING POLYACIDS FOR IMPROVED LIGHT-CURED GLASS-IONOMER CEMENTS

by

WEI WU, DONG XIE, AND JIMMY W. MAYS

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Format adapted for dissertation

Abstract

Vinyl-containing poly(acrylic acid-co-itaconic acid) copolymers were synthesized and used to formulate light-curable cements with reactive glass fillers (Fuji II LC). The conditions for light exposure were studied. Effects of MW, grafting ratio, comonomer, liquid composition, powder/liquid (P/L) ratio, glass powder, and aging were evaluated. Results show that the vinyl-containing glass-ionomer cements (GICs) prepared in this study demonstrated higher compressive strength (CS, 225.6 MPa), diametral tensile strength (DTS, 28.4 MPa), and much higher flexural strength (FS, 116.4 MPa), compared to commercial Fuji II LC GIC (186.6 in CS, 19.1 in DTS, and 57.1 in FS). The optimal light-exposure time was found around 10 min, and concentrations of CQ and DC were 0.5% (by weight) and 1.0%, respectively. Effects of MW, grafting ratio, P/L ratio, and contents of polymer in the liquid formulation were significant. The highest strengths were found at the optimal formulations where the MW was 15,000 (weight average), grafting ratio 25 mole%, P/L ratio 2.7, and liquid composition 50:20:30. During aging, the cements showed an increase of strength in the first week and then no change in strength for a month. Scanning electron microscopic (SEM) analysis suggests that more integrated microstructures and smaller glass particles can lead to higher FS, and higher polymer content in GICs results in a tough fracture surface and plastic deformation.

1. Introduction

Glass-ionomer cement (GIC) is a water-based material that hardens following an acid-base reaction between calcium fluoroaluminosilicate glass powder and an aqueous solution of polyacid [1]. Because of its many clinically attractive properties [2-8], GIC has been widely used as a restorative and adhesive material [9].

When polyacids are modified with pendant methacrylate groups, the GICs not only undergo an acid-base reaction but also participate in in situ free-radical polymerization [10]. These cements are called resin-modified glass-ionomer cements (RMGICs). RMGICs have gained popularity in the restorative dental community, since they demonstrate superior properties relative to conventional glass-ionomer cements (CGICs). In addition to maintaining the clinical advantages of CGICs, RMGICs reduce the problems of moisture sensitivity and low early mechanical strength associated with CGICs [11,12], are easier to handle clinically [12], exhibit extended working time, and have significantly improved mechanical strengths such as higher flexural strength (FS) and diametral tensile strength (DTS) [10,13]. The strengths of these RMGICs are increased as much as two to three times as compared to their conventional counterparts [10]. So far, three major types of RMGICs have been investigated, as described elsewhere [14]. Although RMGICs have exhibited relatively higher mechanical strengths than CGICs, the strengths, especially FS, are still not as high as most resin composites, which are mainly applied in Class I and II dental restorations (stress-bearing sites) where a major routine occlusion work can be executed. In order to improve the mechanical strengths, we propose to modify the formulation by changing different factors such as MW, (P/L) ratio, and grafting ratio

The objectives of this study were to synthesize and characterize polyacids with pendant double bonds, to formulate the GICs using different parameters, such as MW of the polyacids, grafting ratios of pendent methacrylate, P/L ratios and liquid compositions of the cements, and to evaluate the mechanical strengths of the formed cements. The effects of amount of initiators, length of light exposure time and aging of the cement were also studied.

2. Experimental

2.1. Materials

Diethyl ether (anhydrous or laboratory grade), dl-camphoroquinone (CQ), diphenyliodonium chloride (DC), and butylated hydroxy toluene (BHT) were used as received from Acros Chemical Co. Acrylic acid (AA), itaconic acid (IA), N,N-dimethylformamide (DMF) (anhydrous), dibutyltin dilaurate (DBTL), triphenylstibine (TPS), 2,2'-azobisisobutyronitrile (AIBN), 2-hdroxyethyl methacrylate (HEMA), and 2-isocyanatoethyl methacrylate (IEM) were used as received from Aldrich Chemical Co. AIBN was recrystallized from methanol (MeOH) before use. GC Fuji II LC and Vitremer glass powders were supplied by GC American Dental Corp. and 3M Dental Corp., respectively.

2.2. Synthesis and characterization of vinyl-containing polymers

A two-step reaction was used for synthesis of the vinyl-containing polymers. In the first step, the polymers consisting of AA and itaconic acid IA were synthesized using a free-radical polymerization. Then IEM was grafted onto the polymers.

To summarize, to a three-neck flask, equipped with a thermometer, a nitrogen inlet, and a mechanical stirrer, containing a solution of distilled tetrahydrofuran (THF), a mixture of AA, IA, and recrystallized AIBN was added. The reaction was run under N_2 purging at 60 °C for 18 h. The molar feed ratio for the polymers was 4:1 (AA:IA). Polymers with different MWs were prepared by changing the amount of initiator and the reaction temperature. After the polymerization was completed and terminated by cooling 40 °C, a solution of IEM, DBTL, TPS, BHT and distilled THF were added dropwise at the temperature of 37 °C. After the addition was completed, an additional 1 h was used to complete the reaction. The polymers were then precipitated in hexanes and purified by dissolving them in methanol and precipitating them in ethyl ether. The final products were dried in a vacuum oven at room temperature. The schematic diagram for the vinyl-containing polymer synthesis is shown in Fig. 1.

The copolymers were characterized by gel permeation chromatography (GPC) and viscosity measurements. For determination of MW, the copolymers 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 [15], having solubility in THF for MW estimation. MWs were estimated on a Waters GPC unit (Model 410 differential refractometer), using standard GPC techniques, with polystyrene standards as calibrants.

2.3. Formulation and evaluation of light-curable GICs

2.3.1. Preparation of specimens of light-curable GICs

The formulations for light-curable polymer solutions were made by mixing the vinyl-containing polymers with 0.5% (wt/wt) of CQ (photoinitiator), 1% (wt/wt) of DC (activator), HEMA or acrylic acid, and distilled water [14]. Fuji II LC glass powder was used to formulate the cement with a P/L ratio of 2.7/1. Specimens were fabricated at room temperature, which was similar to the procedures described for CGICs [15-17], except that the curing process was completed by using an EXAKT 520 Blue Light Polymerization Unit (9W/71, GmbH, Germany). The cylindrical specimens were prepared in glass tubing, with dimensions of 4 mm diameter by 8 mm length for a compressive strength (CS) test and dimensions of 4 mm diameter by 2 mm length for a DTS. A split Teflon mold with a glass window for light exposure was used to make the specimens with 3 mm in width × 3 mm in thickness × 25 mm in length for FS. Specimens were exposed to blue light for about 10 min, then removed from the split mold after 15 min in 100% humidity, and stored in deionized water at 37 ^{o}C for 1 week, prior to testing.

2.3.2. Strength determinations

Testing of specimens was performed on a screw-driven mechanical testing machine (Model 858 Mini Bionix, MTS Systems Corp., Eden Prairie, MN, USA), with a crosshead speed of 1 mm/min for all CS, DTS, and FS measurements. The FS test was performed in three-point bending, with a span of 20 mm between supports. The sample sizes were n = 7 for CS, DTS, and FS tests.

The CS values were determined from the relationship $CS = 4P/\pi d^2$, where P = the load at fracture, and d = the diameter of the cylinder. The DTS values were 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. The FS values in three-point bending were 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.

2.3.3. Statistical analysis

One-way analysis of variance (ANOVA) with the post hoc Tukey-Kramer multiple range test was used to determine significant differences among the materials in each test. A level of a = 0.05 was used for statistical significance.

2.3.4. Scanning electron microscopic (SEM) analysis

The fracture surface of one representative specimen from selected materials was observed over a range of magnifications with an SEM (Model 515, Philips Electronics N.V., Eindhoven, The Netherlands) in order to investigate the effects of microstructure on the mechanical properties. The specimens were vacuum sputter-coated with gold-palladium (Au-Pd), and a high vacuum (5.5×10^{-5} Torr) was used for dehydration of the coated specimens before SEM analysis.

3. Results and discussion

3.1. Characterization

The copolymer and vinyl-containing copolymer were characterized using proton NMR, as shown in Fig. 2. For poly(AA-IA) copolymer, the typical proton NMR chemical shift for the carboxyl group was found at 12.20 ppm. For the copolymer grafted with IEM, the typical chemical shifts at 12.20, 8.05, and 6.10 as well as 5.70 ppm were observed for carboxyl, amide, and carbon-carbon double bond, respectively, which corresponded to the chemical shifts in the spectra for poly(AA-IA) and for IEM (6.10 and 5.70 ppm for double bond), except for the new peak for amide generated from the reaction between carboxyl and isocyanate functionalities.

3.2. Formulations and property determinations

All the IEM-grafted polyacids used in this paper had a grafting ratio of 25% and a MW of 15,800 (weight average, Mw) or 5,700 (number average, Mn). Specimens were prepared under the same conditions unless specified: P/L ratio = 2.7/1, Glass powder = Fuji LC glass, liquid composition = 50:20:30 (Polymer:HEMA:H_2O), [CQ] = 0.5%, [DC] = 1.0%, light exposure time = 10 min, and aging condition = in deionized water at 37 °C for 7 days. For each test the values with the same superscript letters were not significantly different ($p > 0.05$).

In our previous work [15], we have discussed why the measurement of flexural strength offers the best practical and reliable estimate of tensile strength for cements exhibiting plastic deformation. The cements in this study were RMGICs that contained more plastic components compared to CGICs. Therefore, we mainly used FS as a screening tool even though CS and DTS were also determined for some of the materials.

3.2.1. Determination of optimal light-initiation system

The initiation conditions were optimized before any further formulation. Time for starting initiation, light exposure time, and initiator concentrations were studied.

From Table 1, we can see that an immediate initiation by light exposure was favorable to obtain high FS. Delay led to low strength. The reason can be explained as that an acid-base reaction is an automatic (self-cured) reaction and it would occur within a certain time (working time). Even though the acid-base reaction will be slowed down because some of the carboxyl groups in the polymer are substituted by vinyl groups, the reaction will still occur. Immediate initiation of polymerization avoids the interference due to salt-bridge formation because salt-bridges (ionic-crosslinking) formed from the acid-base reaction may relatively freeze or limit movement of the pendent double bond, leading to reduced conversion and thus lower FS, as can seen from L1 and L2 in Table 1.

Table 1.
Selection of light exposure conditions

Code	Parameter	Time (min)	FS (MPa)*
L1	Time delay of light exposure after the sample molded	0	116.4 (9.5)
L2		10	85.2 (6.6)
L3	Time for light exposure	1	75.2 (1.9)
L4		5	97.1 (7.3)^a
L5		10	110.2 (9.5)^a
L1		15	116.4 (9.5)^a

*Entries are mean values with standard deviations in parentheses. ^{a}The mean values were not significantly different ($p > 0.05$).

Light exposure time is also very crucial to the FS because it affects the degree of conversion. From Table 1 and Fig. 3, the FS of the specimens increased with the light exposure time, especially in the first 5 minutes. There were significant differences in FS between 1 and 5 and between 1 and 10 min exposure time. There was no significant change in FS between 5 and 10 and between 10 and 15 min. Therefore, 5 to 10 min will be the optimal length for light exposure time.

Table 2 shows the effect of initiators on FS. CQ and DC is a pair of initiators, one is a photo-initiator and the other is a co-initiator. The ratio of CQ/DC is generally 1:2 [6], because the actual initiator is DC instead of CQ. By looking at L6, L1, and L7, L1 (CQ = 0.5% and DC = 1.0%) was the best with a FS of 116.4 MPa, which was significantly higher than both L6 and L7. Either higher or lower concentrations of CQ led to a decreased FS. This can be explained as the reason that polymerization was not completed when the concentrations of the initiators were too low. On the other hand, higher concentrations of the initiators can lead to sudden gel (highly cross-linked network) formation in a very short time, thus hindering movements of both carboxyl groups and metal ions released from glass particles to reach each other to form ionic cross-links. Therefore the concentrations of initiators in L1 were selected as the concentration that we used throughout the study.

Table 2.
Effect of photo-initiator concentration

Code	[CQ] (wt%)	[DC] (wt%)	FS (MPa)*
L6	0.2	0.4	87.5 (13.2)
L1	0.5	1.0	116.4 (9.5)
L7	1.5	3.0	84.2 (13.0)

*Entries are mean values with standard deviations in parentheses.

3.2.2. Effect of molecular weight

Table 3 and Fig. 4a illustrate the effect of MW of the polymers on mechanical strengths of the cements. It is apparent that neither the lowest nor highest MW polymers gave the highest mechanical strengths. The one with intermediate MW exhibited the highest strengths. In the study, we were not able to make specimens containing MW of 28,300 (Mw) well for CS and DTS because it was very difficult to handle this high MW polymer in our cement formulations. Therefore, there are no data in CS and DTS available for L8. Generally, the higher the MW, the higher the mechanical strengths [9]. However, manipulation difficulties led to lower strength for L8.

Table 3. Effects of Molecular Weight and Grafting Ratio

Effect of Molecular Weight

Code	$Mw \times 10^{-3}/Mn \times 10^{-3}$	CS (MPa)*	DTS (MPa)	FS (MPa)
L8	28.3/9.9	-	-	104.3 (14.5)[a]
L1	15.8/5.7	225.6 (6.9)	28.4 (2.3)	116.4 (9.5)[a]
L9	8.3/2.9	190.9 (3.6)	19.8 (3.9)	72.2 (13.9)

Effect of Grafting Ratio

Code	Grafting Ratio	CS (MPa)	DTS (MPa)	FS (MPa)
L10	10	220.6 (5.8)[a]	26.1 (3.9)[a]	72.2 (6.7)
L1	25	225.6 (6.9)[a]	28.4 (2.3)[a]	116.4 (9.5)
L11	50	200.9 (10.3)	24.3 (0.8)[a]	59.9 (8.0)

*Entries are mean values with standard deviations in parentheses. [a]The mean values were not significantly different ($p > 0.05$).

3.2.3. Effect of grafting ratio

Effect of grafting ratio was determined, as shown in Table 3 and Fig. 4b. Polymer grafted with 25% of IEM showed the highest values in CS, DTS, and FS, which means that the optimal grafting ratio is also important to a mechanical strength increase. Both higher and lower grafting ratios led to lower strengths, especially in FS. The role of grafting is to add more resin component into the brittle GIC system, which often enhances plastic deformation of the polymer. FS is a test that measures a combination of three individual strengths (compressive, tensile, and shear) [6,18], among which shear strength takes a leading role in plastic deformation. Excessive grafting may lead to lower strengths due to decreased capacity for acid-base reactions in GICs, causing glass particles to only play a role as filler instead of as reactive species. On the contrary, an insufficient grafting also caused a lower strength because there were not enough double bonds to result in high strength due to covalent crosslinking. In this situation, the GIC still behaved like a CGIC. That is why a grafting ratio of 25% was superior to grafting at 10% and 50%.

3.2.4. Effect of comonomer

We have compared two comonomers in this study, including HEMA and (AA). HEMA is one of the major components in RMGICs. It acts as both cosolvent and comonomer in the system. Vinyl-containing polyacids require some amphiphilic difunctional monomers like HEMA to help them dissolve in water because of their relatively low water solubility. However, HEMA has been reported to have certain cytotoxity to soft tissue such as pulp. Unreacted HEMA can cause inflammatory reaction to dental pulp if the dentin barrier is not thick enough [19-21]. Therefore, we compared AA with HEMA and thought that AA might replace the HEMA as a comonomer. It was found that there was no significant difference in FS between cements formulated using these two comonomers (L12 and L1), as shown in Table 4.

Table 4.
Effect of Formulations of the Cements on FS

Code	Comonomer	Polymer: comonomer: water	P/L	Glass Powder	FS (MPa)*
L12	AA	50:20:30	2.7/1	Fuji II LC	105.9 (14.5)^a
L1	HEMA				116.4 (9.4)^a
L13		60:20:20			105.5 (14.7)^a
L14		40:30:30			56.46 (8.9)
L15		50:20:30	3.2/1		103.7 (11.4)^a
L16			2.2/1		79.7 (14.5)
L17			2.7/1	Vitremer	80.7 (8.5)

*Entries are mean values with standard deviations in parentheses. ^{a}The mean values were not significantly different ($p > 0.05$).

3.2.5. Determination of liquid composition

In formulating the liquid in our GICs, three components need to be considered. They are the amounts of grafted copolymer, comonomer, and water. A suitable balance among them is very important. Usually, higher content of polymer leads to higher strengths [14]. In this study, we compared three formulations, i.e., 60:20:20, 50:20:30, and 40:30:30 (polymer:HEMA:water). From the results (Table 4), the formulation with 60:20:20 showed almost the same FS (105.5 ± 14.7 MPa) as the one with 50:20:30 (116.4 ± 9.4 MPa) (no difference in statistics between the two). Too much polymer in the formulation seemed to not significantly increase the strength, which was attributed to difficult handling when it was mixed. We found that the liquid with 60:20:20 was very viscous and hard to mix with the powder. The formulation with 40:30:30 showed the lowest FS (56 MPa), which can be attributed to low content of polymer. Microstructures of the fracture surfaces also correlated with the results in strength differences among the cements with different liquid compositions. Using

SEM, the representative regions of the fracture surfaces for two GICs using liquid compositions of 60:20:20 and 40:30:30 were examined and compared, as shown in Figs. 5a and 5b, respectively. It is apparent that the SEM photograph for the 60:20:20 composition (Fig. 5a) showed a toughened fracture surface having large fractured polymer resin fragment and more plastic deformation, as compared to the resin from a 40:30:30 mixture (Fig 5b). The fracture surface for 40:30:30 looked very homogeneous, and no significant large resin fragments were observed in the matrix. It seems that the formulation with the 50:20:30 composition was the best among the three cements, with comparable FS and better handling property.

3.2.6. Effect of P/L ratio

By definition, composites are composed of combinations of two or more than two components that have their own properties when they are not combined. In making a composite it is hoped that synergetic properties will be generated and exhibited after they are combined. Therefore, the proportion or ratio of these components in the mix is very important. From Table 4 and Fig. 6, we can see that the FS increased with the P/L ratio to a certain point and then decreased after that. The result was very similar to that for MW. As we know, more glass powder in the system can result in higher compression resistance [22]. As mentioned earlier, the FS test actually reflects a combination of tensile, compressive, and shear strengths, so significant contribution to CS by glass powder affects the value of FS, thus resulting in a higher FS. However, too much glass will lead to lower strength because of difficult handling. In fact, we experienced a relatively difficult time mixing the cement when high P/L ratios (3.2/1) were used. Based on the result, the P/L ratio of 2.7/1 is believed to be optimal because it demonstrated a combination of good mechanical strength and acceptable handling characteristics.

3.2.7. Use of different glass powder

In order to test compatibility of our polymers with different glasses, we incorporated another commercial glass powder, Vitremer, into our polymer solution to form cements under similar conditions. It was found that the FS (80.7 MPa) of the cement with Vitremer glass was lower than that (116.4 MPa) with Fuji II LC glass (see Table 4). The value (80.7 MPa) with Vitremer glass was almost the same as the one (82.1 MPa) for commercial Vitremer reported by Xie et al. [23] This indicates that our polymer liquid is also suitable for use in a system where Vitremer glass powder is used as the reactive filler.

Microstructures of the fracture surfaces also supported the observed strength differences between the cements using Vitremer and Fuji II LC glass powder. As shown in Figs. 7a and 7b, the cement with Fuji II LC glass showed a more integrated and highly fused surface texture, whereas the cement with Vitremer glass exhibited more and larger isolated glass particles. The more integrated microstructures account for the higher FS of the cements with Fuji II LC glass.

3.2.8. Effect of aging

It is known that GICs usually exhibit increased strengths with time [24]. Thus we conditioned our cements for 1 day, 1 week, and 1 month and tested their CS, DTS, and FS. As shown in Table 5, all the CS, DTS, and FS significantly increased after 1 week of aging but remained almost unchanged after that (1-month data). The reason is attributed to gradual salt-bridge formations after initial covalent crosslinks are formed by photopolymerization. Post salt-bridges usually take a while to form due to slow water penetration and polyacid network reorganizations [10]. After 1 week, basic ionic bond formations between metal ions and polyacids reached to a balance and thus no more strength changes were observed.

Table 5. Effect of Aging

Code	Length of Aging	CS (MPa)*	DTS (MPa)	FS (MPa)
L18	1 day	201.9 (5.8)	26.0 (1.8)^{b}	99.8 (10.1)^{d}
L1	1 week	225.6 (6.9)^{a}	28.4 (2.3)^{b}	116.4 (9.5)^{c}
L19	1 month	229.8 (5.5)^{a}	26.8 (3.1)^{b}	109.9 (11.3)^{c,d}

*Entries are mean values with standard deviations in parentheses. $^{a, b, c, d}$The mean values were not significantly different ($p > 0.05$).

4. Conclusions

The vinyl-containing GICs synthesized and formulated in this study demonstrated higher CS (225.6 MPa) and DTS (28.4 MPa) and much higher FS (116.4 MPa), as compared to commercial Fuji II LC GIC (186.6 in CS, 19.1 in DTS, and 57.1 in FS). The optimal light-exposure time was found to be around 10 min, and optimal concentrations of CQ and DC were 0.5% (by weight) and 1.0%, respectively. Effects of MW, grafting ratio, P/L ratio, and contents of polymer in the liquid formulation were significant. The highest strengths were found for the optimal formulations where the MW was 15,000 in Mw, 25% in mole grafting ratio, 2.7 P/L ratio, and 50:20:30 liquid composition. During aging, the cement showed an increase in strength over the first week and then no change for a month. SEM analysis suggests that more integrated microstructures and smaller glass particles can lead to higher FS, and higher polymer content in GICs results in a tough fracture surface and plastic deformation.

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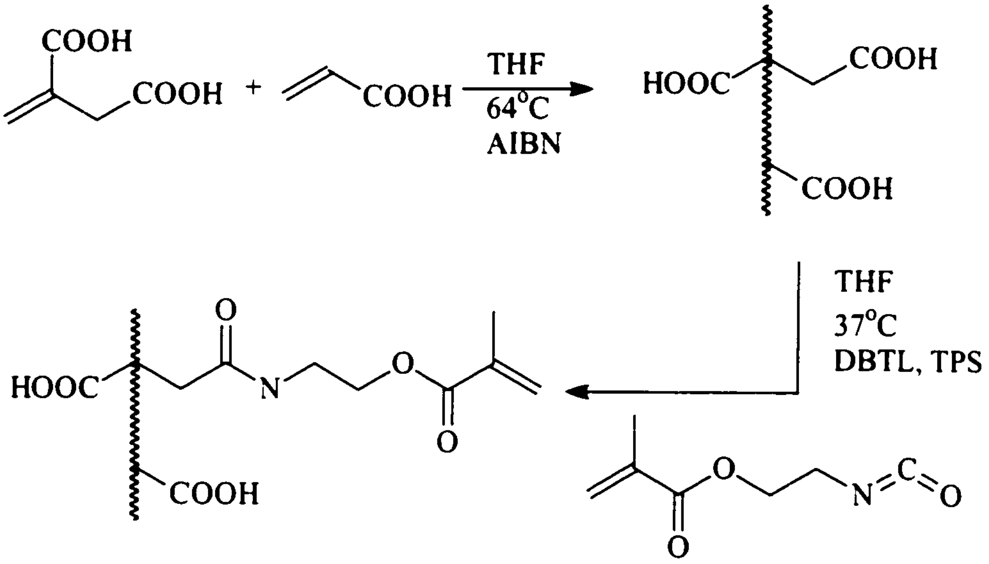

Fig. 1. Scheme for vinyl-containing polymer synthesis.

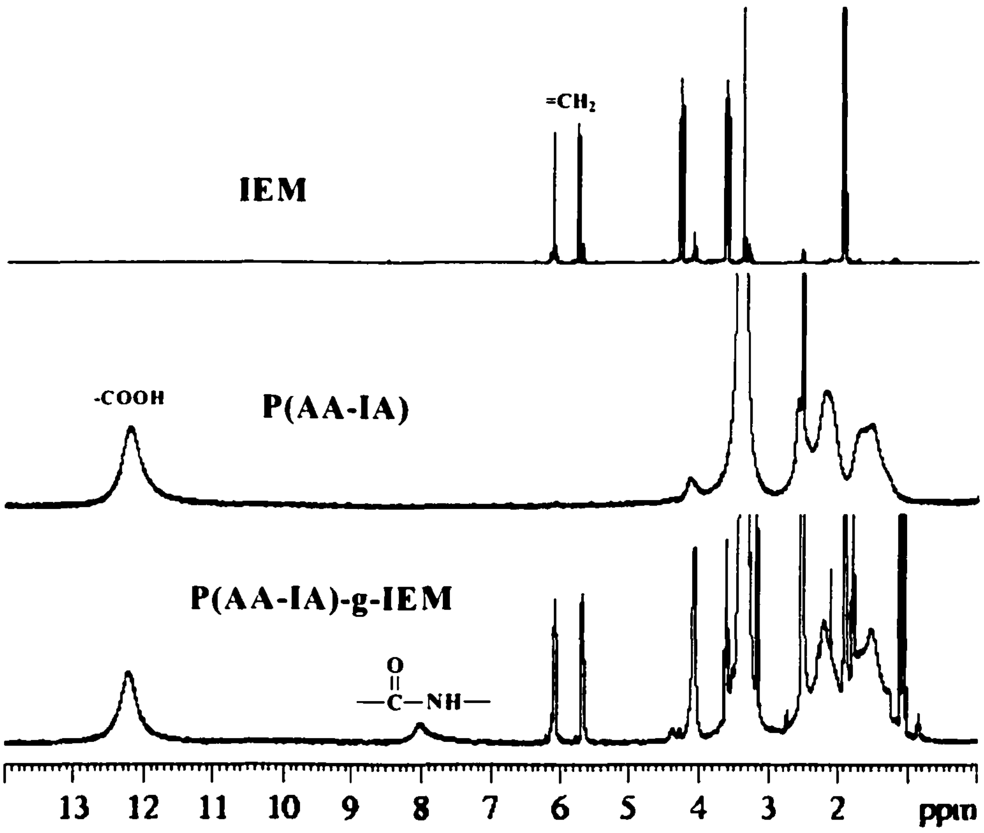

Fig. 2. ^{1}H NMR spectra for IEM, copolymer, and vinyl-containing copolymer.

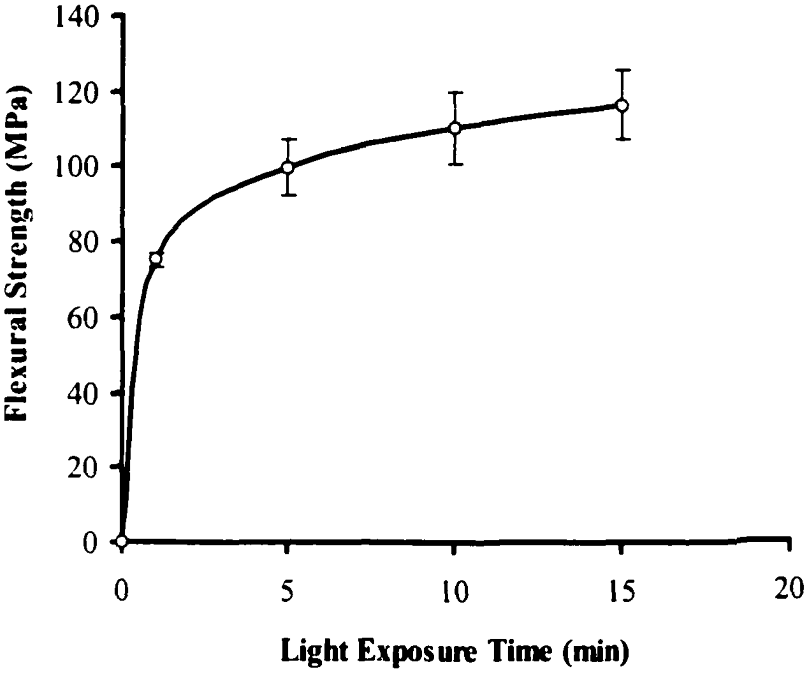

Fig. 3. Effect of light exposure time on FS.

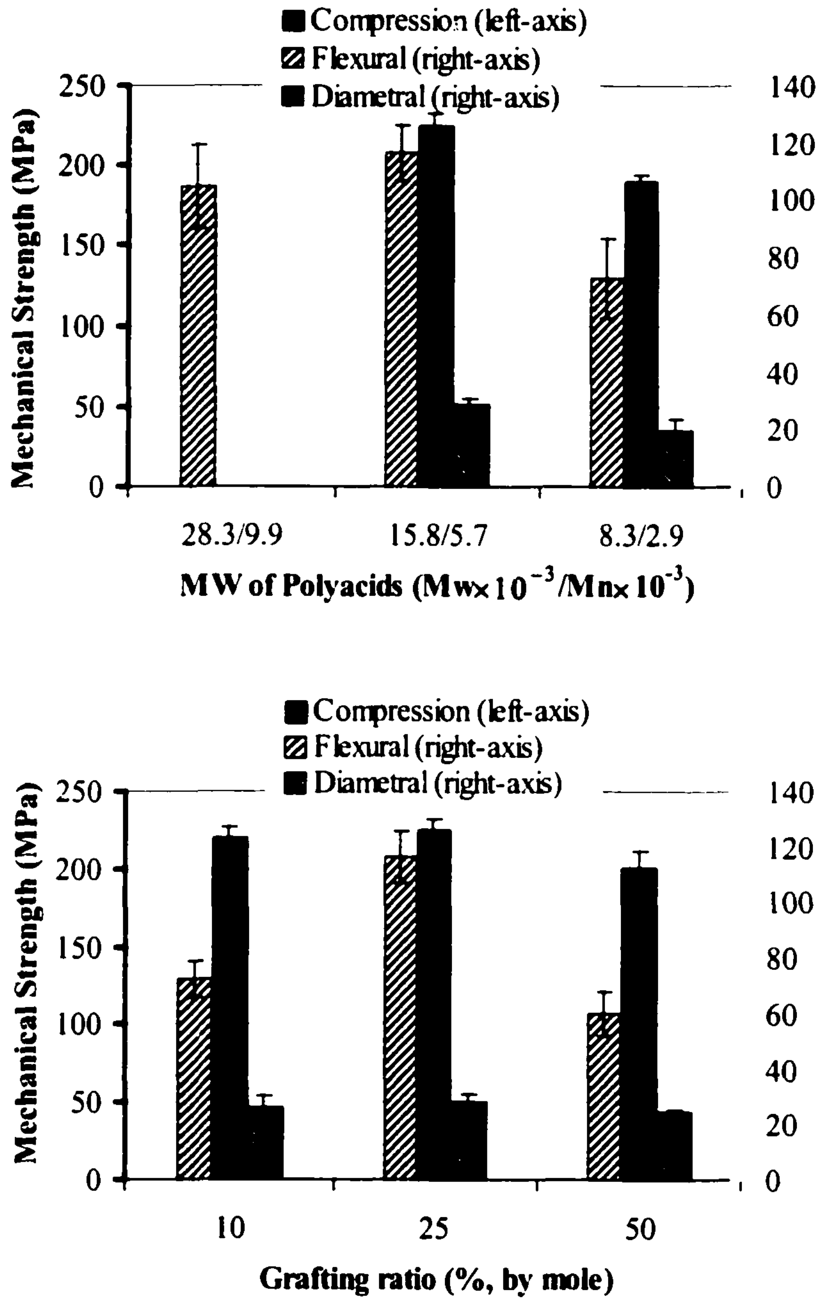

Fig. 4. MW and grafting ration effects on mechanical strength (a) MW effect (b) Grafting ratio

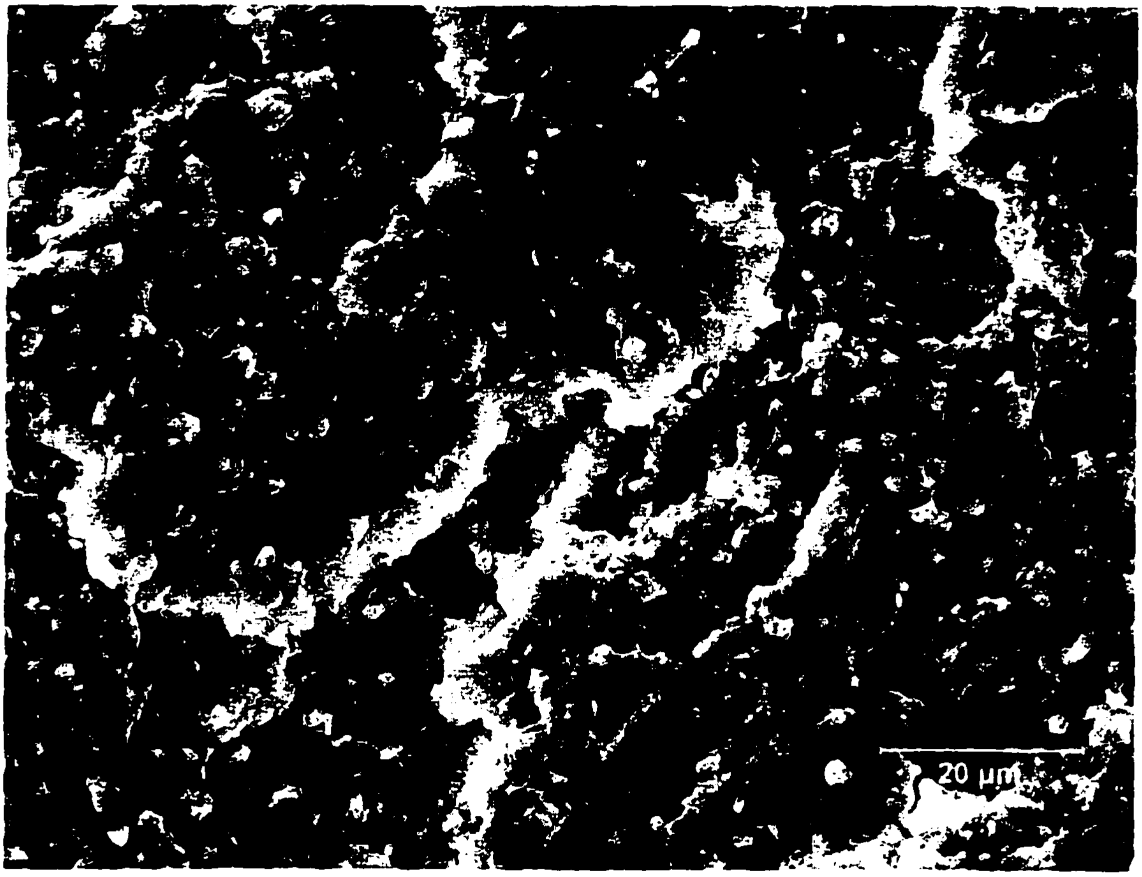

Fig. 5. SEM photomicrograph of the cements having different liquid composition (a) SEM photomicrograph of the cement having a liquid composition of 60:20:20 with original magnification of 1500x

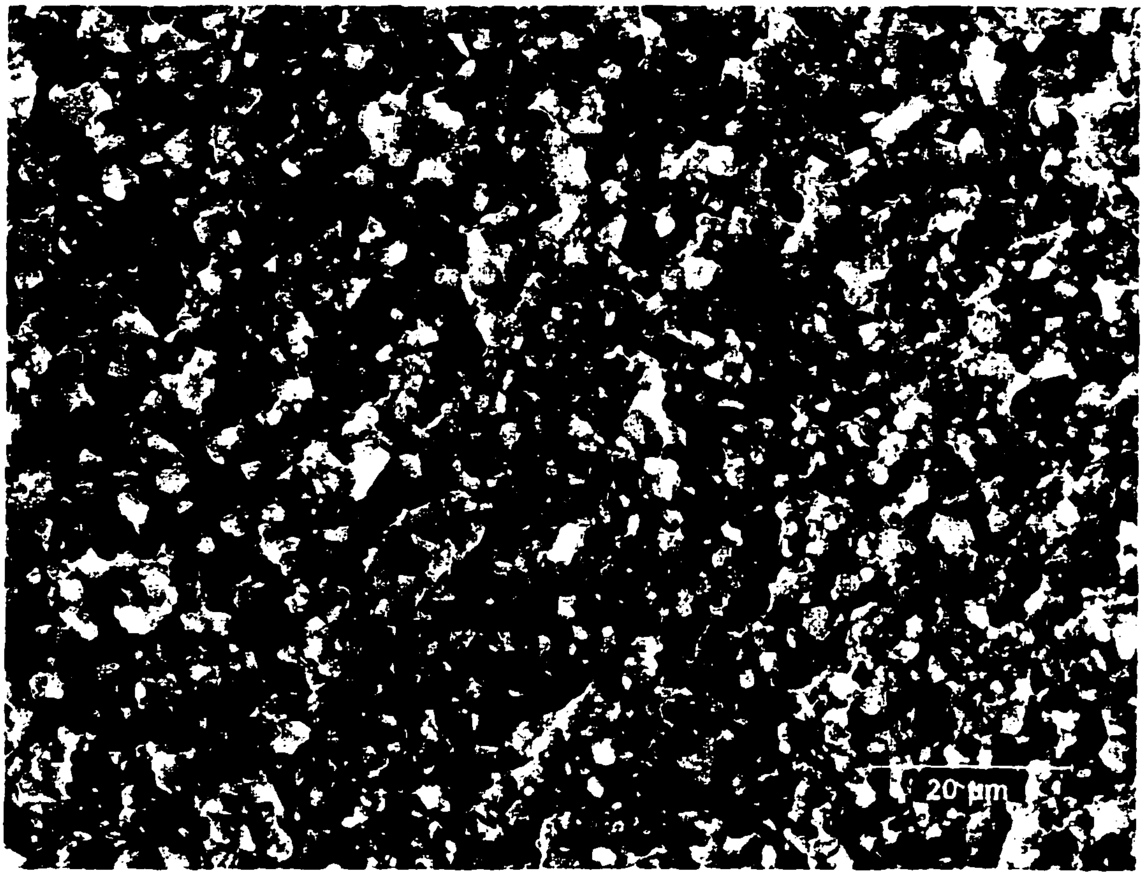

Fig. 5. SEM photomicrograph of the cements having different liquid composition (b)SEM photomicrograph of the cement having a liquid composition of 40:30:30 with original magnification of 1500x

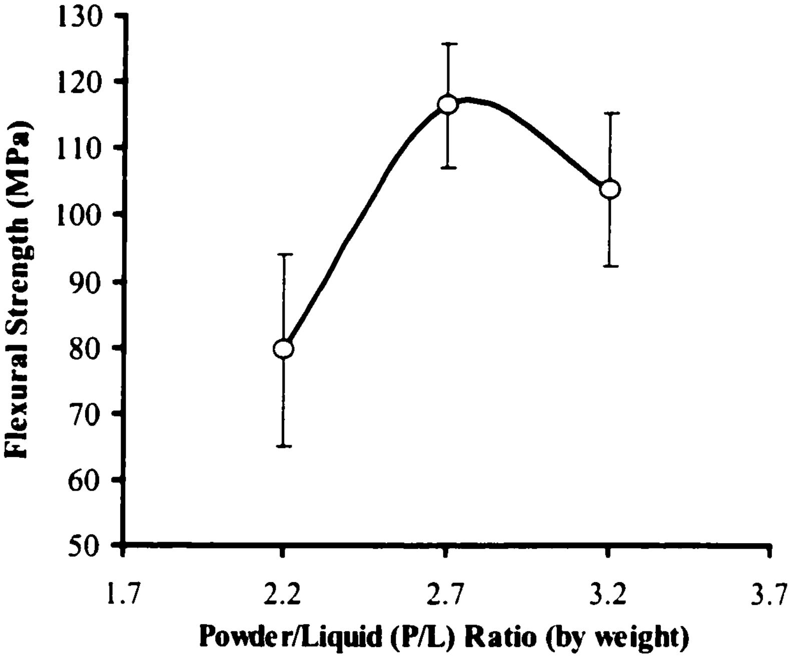

Fig. 6. Effect of P/L on FS

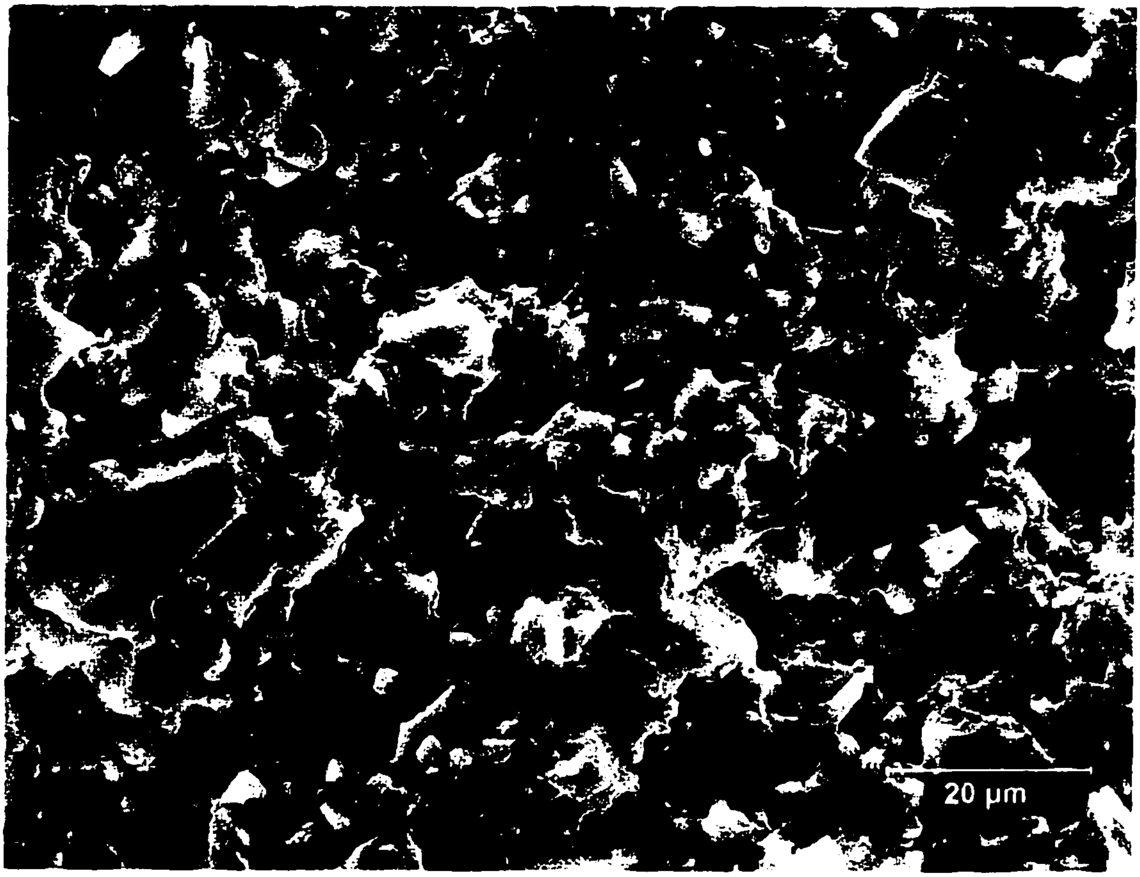

Fig. 7. SEM photomicrograph of the cements formulated with different class powder (a) SEM photomicrograph of the cement formulated with commercial Vitremer glass powder with original magnification of 1500x

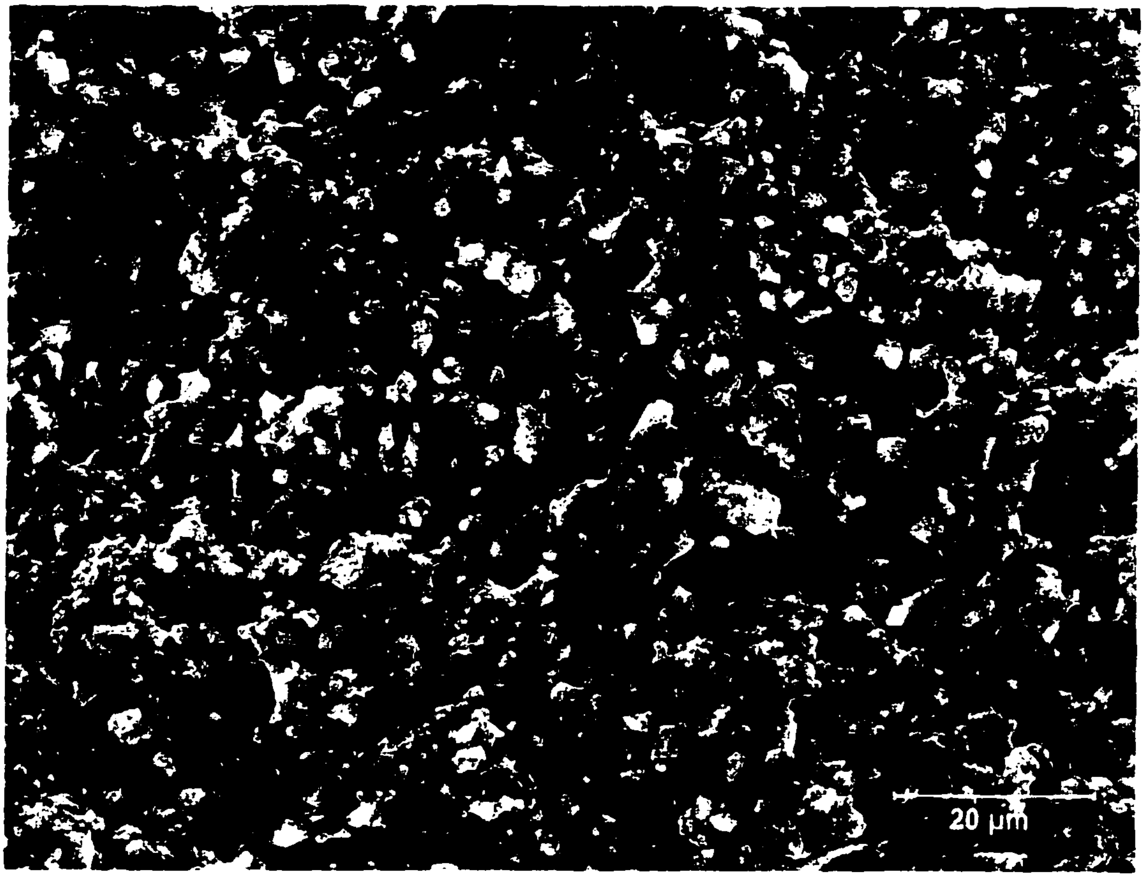

Fig. 7. SEM photomicrograph of the cements formulated with different class powder (b) SEM photomicrograph of the cement formulated with commercial Fuji II LC glass powder with original magnification of 1500x

VINYL-CONTAINING GLASS-IONOMER CEMENT FOR ORTHOPEDIC APPLICATIONS

by

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Abstract

Partially methacrylated poly(acrylic acid-co-itaconic acid) copolymers were synthesized and used to formulate redox-initiated cements with reactive glass fillers (Fuji II LC). The conditions for redox initiation were studied. Effects of MW, grafting ratio, comonomer, liquid composition, powder/liquid (P/L) ratio, glass powder, and aging were evaluated. Results show that the new resin-modified glass-ionomer cements (RMGICs) prepared in this study demonstrated higher flexural strength (FS, 96.3 MPa), as compared to commercial Fuji II LC GIC (57.1 in FS). The optimal redox initiator concentration was 0.15% (by weight) of potassium persulfate, and 0.6% of microcapsule, respectively. Effects of MW, grafting ratio, P/L ratio and contents of polymer in the liquid formulation were significant. The highest strengths were found at the optimal formulations where the molecular weight was 15,000 (weight average, Mw), grafting ratio was 25 mole%, P/L ratio was 2.7 and liquid composition was 50:20:30. During aging, the cement showed no significant change of strengths over a 1-month period. Setting exotherm measurements showed that during the hardening the cement generated a moderate level of heat which could be tolerated by soft tissue.

1. Introduction

Glass-ionomer cements (GICs) have been widely applied as dental restoratives for many years [1] because of their many unique properties [2]. Based on the similarity between the compositions of bone and dentin [3], GIC can also be used in orthopedics for bone restorative applications. Its positive effects on promoting bone growth when used as bone cement even show that these materials are not only biocompatible but also bioactive [4].

Conventional bone cements are poly(methylmethacrylate) cements, which mainly function through the formation of a so called "mechanical interlock" between the acrylate resins and porous bone structures [5]. Unlike these conventional bone cements, GICs adhere to the bone by means of formation of ionic bonding of salt bridges. If hybrid systems are introduced, in situ addition polymerization occurs in addition to ionic crosslinking, and dual-curing cements will form. As a result, not only salt bridges but also mechanical interlocks play an important role in strengthening interfacial bonding [3,6,7]. The resulting resin-modified glass-ionomer cements (RMGICs) exhibit many advantages of both resin cements and conventional glass-ionomer cements (CGICs).

GICs used as bone cements have been reported elsewhere [8-10]. However, there is little literature which has reported the improvement or formulation of GICs for use in orthopedics.

It is known that heat, light and redox initiators can initiate free radical addition polymerization [11]. Dentists apply light initiating systems quite successfully in restorative dentistry [12]. However, large exotherms and limited light penetrating depth make such initiators useless in orthopedic application. Therefore, a redox system is considered the logical choice to initiate the polymerization of glass-ionomer bone cements. A common redox system (benzoyl peroxide-N,N-dimethyl-para-toluidine), which has been used in conventional poly(methyl methacrylate) bone cement, cannot be used in the glass-ionomer system, since it does not dissolve in aqueous solution. As an alternative, the potassium perfulfate - ascorbic acid redox system has been used in this study. To extend the working time, which is necessary in clinics, we can microencapsulate the ascorbic acid using certain polymers such as cellulose acetate butyrate (CAB).

In our previous work [13], we used amino acid modified polymer to formulate CGICs with Fuji II glass and obtained promising data for the mechanical strength. In this paper, we used resin-modified amino acid containing polymers to formulate RMGICs and compared their mechanical strengths with non-amino-acid RMGICs, CGICs, and their commercial counterparts.

The objectives of this study were to synthesize and characterize vinyl containing polyacids; to formulate the GICs using different parameters, such as molecular weight of the polyacids, grafting ratios of pendent resin, powder/liquid (P/L) ratios, and liquid compositions of the cements; and to evaluate the mechanical strengths of the formed cements. The effects of varying the amount of initiators and aging of the cement were studied. Exotherm of the setting reaction was measured, and the setting time was also measured.

2. Experimental

2.1. Materials

Methanol (MeOH), diethyl ether (anhydrous or laboratory grade), ethyl acetate, hexanes, sodium hydroxide (NaOH), sodium chloride (NaCl), hydrochloric acid (HCl) (37%) anhydrous magnesium sulfate ($MgSO_4$), acryloyl chloride (AC), butylated hydroxy toluene (BHT), and CAB were used as received from Acros

Chemical Co. N,N-dimethylformamide (DMF) (anhydrous), β-alanine (BA), acrylic acid (AA), itaconic acid (IA), $K_2S_2O_8$, dibutyltin dilaurate (DBTL), triphenylstibine (TPS), ascorbic acid (Vc), 2-hydroxyethyl methacrylate (HEMA), and 2-isocyanatoethyl methacrylate (IEM) were used as received from Aldrich Chemical Co. 2,2'-azobisisobutyronitrile (AIBN) from Aldrich Chemical Co. was recrystallized from MeOH before use. GC Fuji II LC and Vitremer glass powders were supplied by GC American Dental Corp. and 3M Dental Corp., respectively.

2.2. Synthesis and characterization of acryloyl β-alanine (ABA) and vinyl-containing polymers with or without amino acid derivitives

2.2.1. Synthesis of ABA

The ABA was prepared using the Schotten-Baumann reaction; details were described in our previous work [13]. The schematic diagram for ABA synthesis is shown in Fig. 1.

2.2.2. Synthesis of vinyl-containing polymers

A two-step reaction was used for synthesis of the vinyl-containing polymers. In the first step, the polymers consisting of AA and IA or ABA were synthesized using free-radical polymerization. Then IEM was grafted onto the polymers. Details were described previously [14]. The schematic diagram for the vinyl-containing polymer synthesis is shown in Fig. 2.

2.2.3. Characterization of synthesized monomers and polymers

The ABA was characterized by melting point identification and nuclear magnetic resonance (NMR). The vinyl containing polymers were characterized by gel permeation chromatography (GPC) and viscosity measurements. The melting points were measured using a digital melting point apparatus (Electrothermal IA9000 Series, Electrothermal Engineering Ltd., Essex, United Kingdom). ^{1}H NMR spectra were obtained on an ARX-300 NMR Spectrometer using deuterated methyl sulfoxide as a solvent. For determination of MW, 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 [13] having solubility in tetrahydrofuran (THF) for MW estimation. MWs were estimated on the Waters GPC unit (Model 410 differential refractometer), using standard GPC techniques, and calibrated using polystyrene standards. Specific viscosity was measured using an Ubbelohde viscometer, with DMF as solvent.

2.3. Microencapsulation of Vc in CAB

14.3 g of CAB (MW = 200,000, Butyrate content = 17%) was stirred and heated with 360 ml of ethyl acetate for 2 h to form a homogeneous solution. Then the solution was filtered and charged into a round bottom flask. The water bath was placed under the flask for cooling later. Then 4.83 g of freshly-sieved Vc (with particle size smaller than 45 μm) was added and suspended in the solution for about 15 to 30 min, with a vigorous stirring. 200 ml of hexanes was added dropwise at a rate of about 60 drops per min. After completion of addition of hexanes, ice water was added into the bath to help harden the formed microcapsules (MC). After 5 to 10 minutes, cold hexanes were added to wash the microcapsules. The microcapsules were recovered by decantation, washed with cold hexanes, and air-dried or vacuum-dried.

2.4. Formulation and evaluation of vinyl-containing hybrid GICs using redox initiator

2.4.1. Formulation of vinyl-containing hybrid GICs using redox initiator

The formulations for polymer solutions were made by mixing the vinyl-containing polymers with 0.15% (wt/wt) of $K_2S_2O_8$ (oxidizing agent), HEMA or acrylic acid, and distilled water. Fuji II LC glass powder, mixed with 0.6% (wt/wt) of CAB encapsulated Vc, was used to formulate the cement with a P/L ratio of 2.7/1. Specimens were fabricated at room temperature, which was similar to the procedures described for CGICs [13]. A split Teflon mold (3 mm in width × 3 mm in thickness × 25 mm in length) was used to make the specimens for FS. Specimens were removed from the split mold after 15 min in 100% humidity and stored in deionized water at 37 °C for 1 week prior to testing.

2.4.2. Strength determinations

Testing of specimens was performed on a screw-driven mechanical testing machine (Model 858 Mini Bionix, MTS Systems Corp., Eden Prairie, MN, USA), with a crosshead speed of 1 mm/min for FS measurements. The FS test was performed in three-point bending, with a span of 20 mm between supports. The sample sizes were n = 7 for all the tests.

The FS values in three-point bending were 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.

2.4.3. Statistical analysis

One-way analysis of variance (ANOVA) with the post hoc Tukey-Kramer multiple range test was used to determine significant differences among the materials in each test. A level of a = 0.05 was used for statistical significance.

2.4.4. Estimates of working time of the redox system

A metal rod was used to evaluate the working time. The rod was inserted into the center of mixture of the cement, which was mixed and packed into a small vial with a hole at the bottom. Working time was the time from the start of the mixing process until the moment at which the metal rod could not be moved.

2.4.5 Setting exotherm and setting time measurement

The temperature and time evolution during the setting reaction were investigated by using a cylindrical Teflon mold, with inner diameter of 30 mm and depth of 5 mm, and continuous temperature measurements were made via a thermocouple in the center of the mass. The most representative curing parameters were obtained: peak temperature and setting time. The peak temperature was taken as the maximum temperature reached during the setting reaction. The setting time was taken as the time when the temperature rise was at a point halfway between the maximum temperature attained and room temperature. It can be determined according to the American Society for Testing and Materials (ASTM) Standard F451-99a (section 7.7) as follows: T_{room} + (T_{max} - T_{room})/2, where T_{max} is the maximum temperature in degrees Celsius, and T_{room} is the room temperature.

3. Results and discussion

3.1. Characterization

The schematic structure of ABA is shown in Fig. 3. The numbers appeared on the protons are chemical shifts in ^{1}H NMR calculated using *ChemDraw*.

Since peaks on the ^{1}H NMR spectra almost perfectly fit to the chemical shifts calculated using *ChemDraw*, we can see that the synthesized monomers exhibited a high purity [14], with a melting point range of 95.0 - 96.0 °C and yield of 63 - 70%.

The polyacids and vinyl-containing polymers were characterized using ^{1}H NMR, as shown in Fig. 4. For poly(AA-IA) copolymer, the typical ^{1}H NMR chemical shift for the carboxyl group was found at 12.20 ppm. For the copolymer grafted with IEM, the typical chemical shifts at 12.20, 8.05, and 6.10 as well as 5.70 ppm were observed for carboxyl, amide, and carbon-carbon double bond, respectively, which corresponded to the chemical shifts in the spectra for poly(AA-IA) and for IEM (6.10 and 5.70 ppm for double bond), except for the new peak for amide generated from the reaction between carboxyl and isocyanate functionalities.

Besides the peak at 12.20 ppm for the carboxyl group, poly(AA-IA-ABA) also showed a peak at 7.60 ppm (1) for amide from ABA, while another peak at 8.05 ppm

(2) appeared in the poly(AA-IA-ABA)-g-IEM spectrum reflecting the newly formed amide bonds from the reaction between carboxyl and isocyanate functionalities.

3.2. Formulations and property determinations

All the IEM grafted polyacids used in this paper had a grafting ratio of 25% and an average MW of 15,800 (weight average, Mw) or 5,700 (number average, Mn). Specimens were prepared under the same conditions unless specified: P/L ratio = 2.7/1, glass powder = Fuji LC glass, liquid composition = 50:20:30 (Polymer:HEMA:H_2O), [$K_2S_2O_8$] = 0.15% (wt of the liquid), [MC] = 0.6% (wt of the glass powder), and aging condition = in deionized water at 37 °C for 7 days. For each test the values with the same superscript letters were not significantly different ($p > 0.05$).

In our previous work [13] we have discussed why the measurement of flexural strength offers the best practical and reliable estimate of tensile strength for cements exhibiting plastic deformation. The cements in this study were RMGICs that contained more plastic components as compared to conventional GICs. Therefore, we mainly used FS as a screening tool for the materials.

3.2.1. Determination of optimal vinyl-containing polymer

In orthopedic application, FS has more importance than that in dental materials, so here we focused on improving the FS. In our previous work [13] we found that GICs incorporating amino acid modified polyacids demonstrated higher compressive strength and almost four times higher FS as compared to commercial Fuji

II cement. We chose one of the best amino acid containing polyacids [13], which is ABA, to be modified with pendant vinyl groups and compare it with grafted copolymer poly(AA-IA)-g-IEM.

From Table 1, we can see that both RMGICs using poly(AA-IA)-g-IEM or poly(AA-IA-ABA)-g-IEM showed significantly higher FS (96.3 and 95.8 MPa, respectively) than CGICs using poly(AA-IA-ABA) (68.5 MPa), while there was no significant difference between the FS values of two resin modified polyacids. This might be due to the reason that, after grafting with methacrylate groups, the structure difference was reduced and also the MWs of resin modified polyacids were kept relatively lower than non-modified polyacids in order to obtain enough working time for RMGICs.

Table 1 also shows that the working time for RMGICs was shorter than CGICs. The working time could be adjusted by choosing different concentrations of redox initiator pairs, and this will be discussed next.

Table 1
Working time and FS comparison of different polyacids with or without resin modification

Code	Polymer	WT (min)	FS (MPa)*
C0	F II control	5.0	15.8(0.7)
C5	Poly(AA-IA-ABA)	4.5	68.5(7.5)
R1	Poly(AA-IA)-g-IEM	3.0	96.3(8.8)[a]
R2	Poly(AA-IA-ABA)-g-IEM	3.0	95.8(4.9)[a]

*Entries are mean values with standard deviations in parentheses. [a]The mean values were not significantly different ($p > 0.05$).

3.2.2. Determination of optimal redox initiation system

Table 2 and Fig. 5. show the effect of concentration of redox initiator pair on FS. Since we need at least 3 min for the working time, when we set the concentration of oxidizing agent, we can only adjust the reducing agent to lower concentration than the one that showed 3-min-working-time. When one agent of the redox pair was used in very low concentration, such as R5 and R8 (0.25-0.1 and 0.05-2.0 for [$K_2S_2O_8$]-[MC], respectively), even with high concentrations of the other, cements showed low FS (74.0 and 66.9 MPa, respectively). This reflects the fact that low concentrations of either oxidizing or reducing agent can not initiate the polymerization very well. From the curves in Fig. 5, we can see the pair 0.15-0.6 showed the highest FS. Therefore, the concentrations of initiators in R1 were selected as the concentration that we used throughout this study.

Table 2
Effect of concentration of redox initiator pair on FS

Code	Polymer	$K_2S_2O_8$/liquid (%)	Microcapsule/glass (%)	WT (min)	FS (MPa)*
R3	P(AA-IA)-IEM	0.25	0.4	3.0	88.8(8.6)
R4			0.2	3.5	76.3(7.3)
R5			0.1	4.0	74.0(7.2)
R1		0.15	0.6	3.0	96.3(8.8)
R6			0.3	3.5	83.8(15.7)
R7			0.2	4.0	81.0(9.0)
R8		0.05	2.0	3.0	66.9(5.6)
R9			1.0	3.5	82.9(9.5)
R10			0.6	4.0	85.8(10.7)

*Entries are mean values with standard deviations in parentheses.

3.2.3. Effect of MW

Table 3 and Fig. 6 illustrate the effect of MW of the polymers on FS of the cements. It is apparent that neither the lowest nor highest MWs of polymers gave the highest mechanical strengths. Instead, the ones with medium MW exhibited the highest strengths. In our previous work [13] we found that 50,000 was the optimal molecular weight for CGICs. Since there is less water used in the formulation of liquid in RMGICs, 30 wt% here compared to 50 wt% in CGICs, high MW is not acceptable since the liquid will be very viscous and not mixable. On the other hand, the higher the MW, the higher the mechanical strengths [10]. However, manipulation difficulties led to lower strength for R11.

Table 3
MW effect on FS

Code	Polymers	$Mw \times 10^{-3}/Mn \times 10^{-3}$	FS (MPa)*
R11		28.3/9.9	63.0(9.7)[a]
R1	P(AA-IA)-IEM	15.8/5.7	96.3(8.8)
R12		8.3/2.9	60.7(7.5)[a]

*Entries are mean values with standard deviations in parentheses. [a]The mean values were not significantly different ($p > 0.05$).

3.2.4. Effect of grafting ratio

From Table 4 and Fig. 7, we can see that polymer grafted with 25% of IEM showed the highest values in FS, which means that using the optimal grafting ratio is also important for a mechanical strength increase. Both higher and lower grafting ratios led to lower strengths. Grafting not only adds more resin component into the brittle GIC system, which often enhances plastic deformation of the polymer, but also strenthens the polymer matrix by increasing the MW through the polymerization of the vinyl groups. FS is a test that measures a combination of three individual strengths (compressive, tensile, and shear) [6,12], among which shear strength plays a leading role in plastic deformation. The fact that excessive grafting led to lower strengths may be due to a decreased capacity for acid-base reactions in GICs, whereby glass particles only play a role as filler instead of reactive species. On the contrary, insufficient grafting also caused lower strength because there were not enough double bonds to increase the final MW in the polymer matrix. In this situation, the GIC still behaved like a CGIC. That is why the properties of cements with the grafting ratio of 25% was better than those of cements grafted at 10% and 50% levels.

Table 4
Grafting ratio effect on FS

Code	Polymers	Grafting ratio	FS (MPa)*
R13	P(AA-IA)-IEM	10	81.6(8.8)^a
R1		25	96.3(8.8)^a
R14		50	73.5(4.7)^a

*Entries are mean values with standard deviations in parentheses. ^{a}The mean values were not significantly different ($p > 0.05$).

3.2.5. *Effect of comonomer*

HEMA is one of the major components in RMGICs. It acts as both cosolvent and comonomer in the system. Because of their relatively low water solubility, methacrylated polyacids require the addition of some amphiphilic difunctional monomers like HEMA to help them dissolve in water. However, the amphiphilic molecule HEMA was reported to exhibit cytotoxity, especially when used as a bone cement [15-17]. Therefore, we need to find an alternative to replace HEMA in order to make the GIC bone cement more biocompatible to the bone, even though HEMA is a very good cosolvent for the RMGICs. Hydrophilic vinyl-containing amino acids have both polymerizable and hydrophilic functionalities and may be used as a good alternative to replace HEMA. These monomers are expected to be biocompatible and if so will benefit both soft and hard tissues. Therefore, ABA was selected as comonomer. AA was also chosen as a comonomer to be compared with HEMA and ABA.

It was found there was no significant difference in FS between R1 and R16 using HEMA and ABA respectively, while R15 with AA showed much higher FS than the other two, as shown in Table 5. This might attribute to the fact that AA showed the advantage of liquid-like HEMA, which made the cement mixing easier, and of the acidic nature of ABA, which suppress the ionization and expansion of the polyacid mainchain and leads to a longer working time.

Table 5.
Effect of Formulations of the Cements on FS

Code	Comonomer	P:Como:H_2O	P/L	Glass powder	FS (MPa)*
R15	AA	50:20:30	2.7/1	FIILC	123.2(15.6)
R16	ABA				89.6(9.8)[a]
R1	HEMA				96.3(8.8)[a]
R17		60:20:20			65.0(9.9)[a]
R18		40:40:20			62.5(6.0)[a]
R19			3.2/1		111.1(13.5)[a]
R20		50:20:30	2.2/1		79.1(11.3)[a]
R21			2.7/1	Vitromer	75.9(9.4)

*Entries are mean values with standard deviations in parentheses. [a]The mean values were not significantly different ($p > 0.05$).

3.2.6. *Determination of liquid composition*

In pursuit of the proper balance of the three components in formulating the liquid in our GICs, we changed the liquid compostion of grafted copolymer, comonomer, and water. Usually, higher content of polymer leads to higher strengths [18]. In this study, we compared three formulations, i.e., 60:20:20, 50:20:30 and 40:30:30 (polymer:HEMA:water). From the results (Table 5), both the formulation with 60:20:20 composition and the one with 40:30:30 composition showed lower FS values than the one with 50:20:30. Too much polymer in the formulation did not improve the strength, which may be attributed to difficult handling when it was mixed. We found that the liquid with 60:20:20 composition was very viscous and hard to mix with the powder. The formulation with 40:30:30 composition showed the lowest FS (62.5 MPa) among them, which can be attributed to low content of polymer. It seems that the formulation with 50:20:30 composition was the best among three cements, with high FS and good handling properties.

3.2.7. Effect of P/L ratio

The proportion or ratio of the components in the composite is very important. From Table 5 and Fig. 8, we can see that the FS increased with the P/L ratio almost linearly in the range of 2.2/1 to 3.2/1. The result was different from that observed for CGICs [12] and RMGICs using light-cured initiator [13]. As we know, more glass powder in the system can result in higher compression resistance [19]. As mentioned earlier, the FS test is actually a combination of tensile, compressive, and shear strengths, so a significant contribution to CS by glass powder will affect the value of FS, resulting in a higher FS. However, too much glass will lead to difficult handling. In fact, we experienced difficulty in mixing the cement when a high P/L ratio (3.2/1) was used. Based on the result, the P/L ratio of 2.7/1 is believed to be optimal because it resulted in both good mechanical strength and acceptable handling characteristics.

3.2.8. Use of different glass powder

In order to test the usefulness of the redox initiation system applied here with different glasses, we have incorporated another commercial glass powder, Vitremer, into our polymer solutions in order to form cements under the same conditions. It was found that the FS (75.9 MPa) of the cement with Vitremer glass was lower than that (96.3 MPa) with Fuji II LC glass (see Table 5). The value (75.9 MPa) with Vitremer glass was almost the same as the one (82.1 MPa) for commercial Vitremer reported by Xie et al. [2]. This indicates that our polymer liquid and redox initiation system are also suitable for use in a system where Vitremer glass powder is used as a reactive filler.

3.2.9. Effect of aging

GICs usually increase their strengths with time [20] because of gradual salt-bridge formation due to slow water penetration and polyacid network reorganization [7]. Thus, we conditioned our cements for 1 day, 1 week, and 1 month and then tested their FS. As shown in Table 6, there was no significant difference in properties when the cements were conditioned in deionized water for different times. This tells us that the redox initiation system causes a fast set of GICs.

Table 6
Effect of aging

Code	Polymers	Aging time	FS (MPa)*
R22	P(AA-IA)-IEM	1 day	86.3(4.8)[a]
R1		1 week	96.3(8.8)[a]
R23		1 month	87.0(17.9)[a]

*Entries are mean values with standard deviations in parentheses. [a]The mean values were not significantly different ($p > 0.05$).

3.3. Setting exotherm and setting time measurement

Research has shown that the temperature rise from the acid-base reaction of the cement may cause damage to the tooth pulp [21]. According to ASTM Standards, PMMA, which is currently overwhelmingly used in hip-replacement operations [22], may show a rise in temperature of up to 90 °C [23] and lead to thermal necrosis of the soft tissue.

In order to investigate the exothermic behavior of our redox initiated RMGICs system, we measured the setting exotherm and calculated the setting time. Based on the results shown in Table 7, we can see the reaction temperature was below 40 °C when using resin grafting ratios from 10 to 50% and P/L ratios from 2.2/1 to 3.2/1.

The temperature and time evolution during the setting for three different grafting ratios (10, 25, and 50%) are shown in Fig. 9 and Table 7. Cement using 50% methacrylated polyacid showed the highest reaction temperature and shortest setting time since more heat was generated from the polymerization of vinyl groups. In contrast, the one with 10% grafting exhibited the lowest exotherm and longest setting time.

Table 7
Effect of P/L and grafting ratio on setting exotherm

Code	Grafting ratio	T_{peak} (°C)	Setting time (min)
R13	10	33.4	3.3
R1	25	35.2	3.2
R14	50	39.7	2.9
	P/L ratio		
R20	2.2/1	37.2	3.2
R1	2.7/1	35.2	3.2
R19	3.2/1	33.9	3.2

Fig. 10 shows the temperature variation with time during the setting for different P/L ratios. It is easy to understand that the cement with P/L of 2.2/1 exhibited the highest setting temperature because of its higher polymer content. We obtained the very interesting result that the measured setting times for these different P/L ratios were exactly the same. It is believed that the acid-base reaction in the cement with P/L of 2.2/1 should be slower than for the one with 3.2/1, since the former had lower reaction surface area, but the high extherm generated from higher content of vinyl-containing polymer actually accerated the acid-base reaction and balanced the low glass content factor.

4. Conclusions

The redox initiated vinyl-containing GICs synthesized and formulated in this study demonstrated higher FS (96.3 MPa), as compared to commercial Fuji II LC GIC (57.1 in FS). The optimal redox initiator concentration was 0.15% (by weight) of $K_2S_2O_8$ and 0.6% of microcapsule. Effects of MW, grafting ratio, P/L ratio, and contents of polymer in the liquid formulation were significant. The highest strengths were found for the optimal formulations where the MW was 15,000 in Mw, grafting ratio was 25% in mole, P/L ratio was 2.7, and liquid composition was 50:20:30. During aging, the cement showed no significant change of strengths over a 1-month period. Setting exotherm measurements showed that the cement hardening generated moderate heat which could be tolerated by soft tissue.

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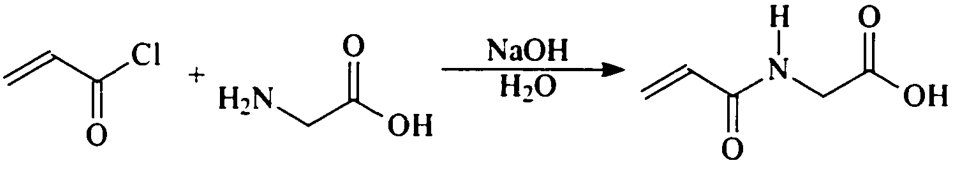

Fig.1. Scheme for ABA synthesis.

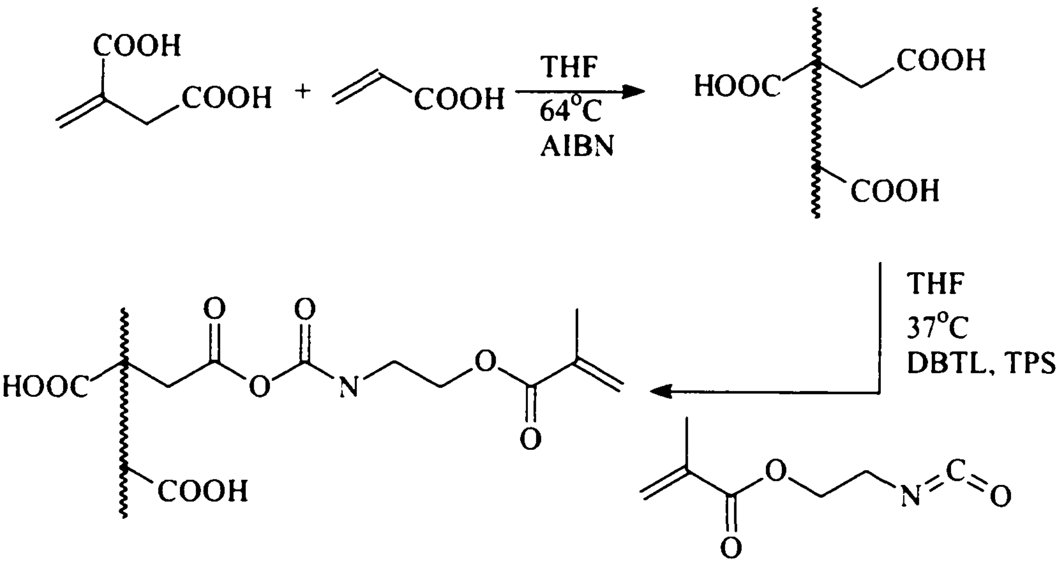

Fig.2. Scheme for vinyl-containing copolymer synthesis.

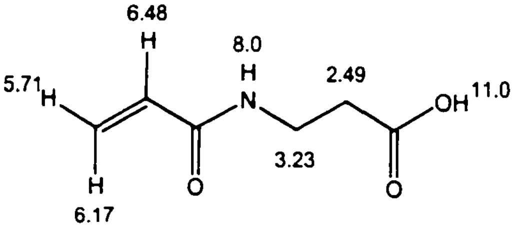

Fig. 3. The schematic structure of ABA

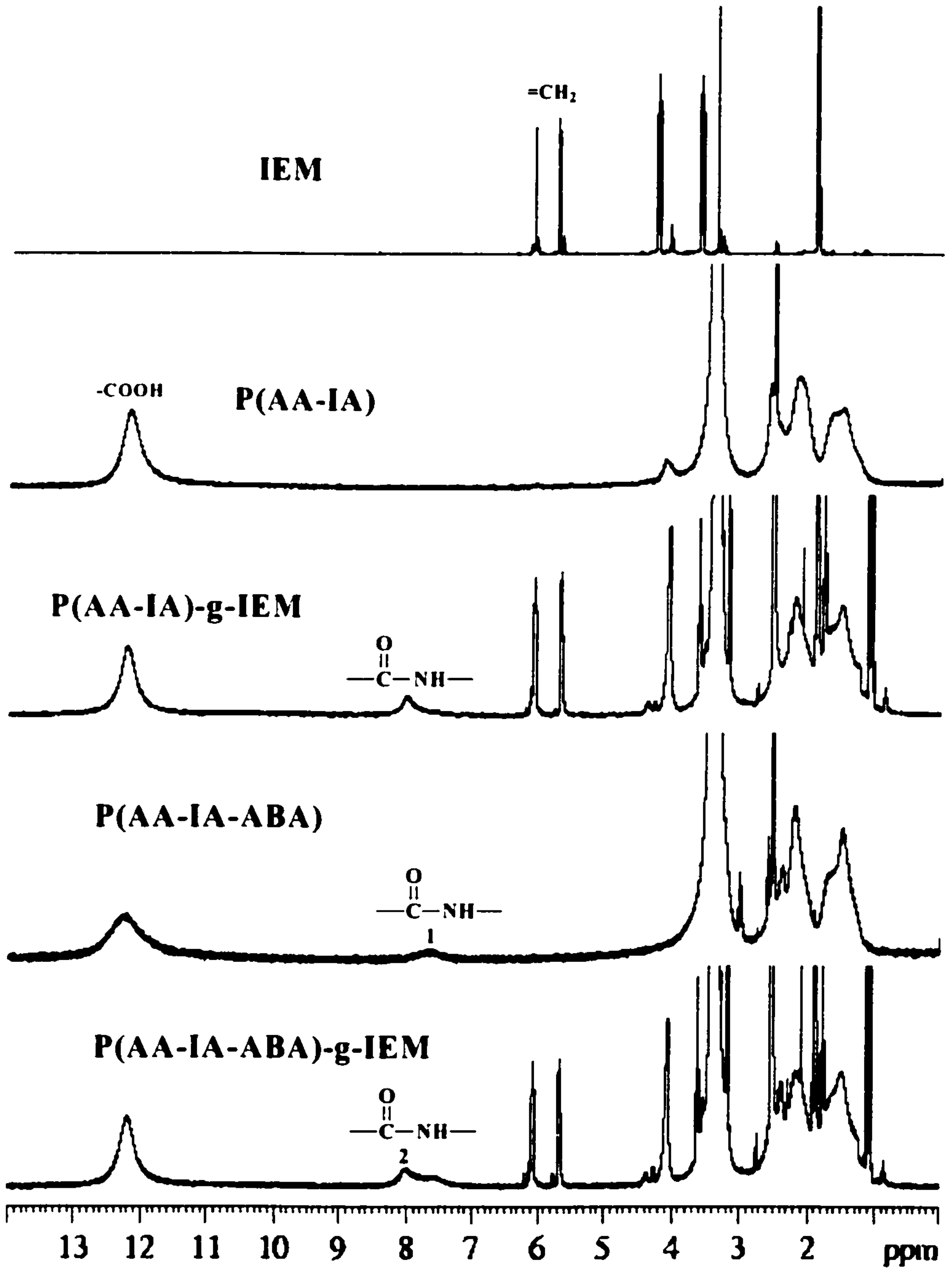

Fig. 4. ^{1}H NMR spectra for IEM, copolymers, and vinyl-containing copolymers.

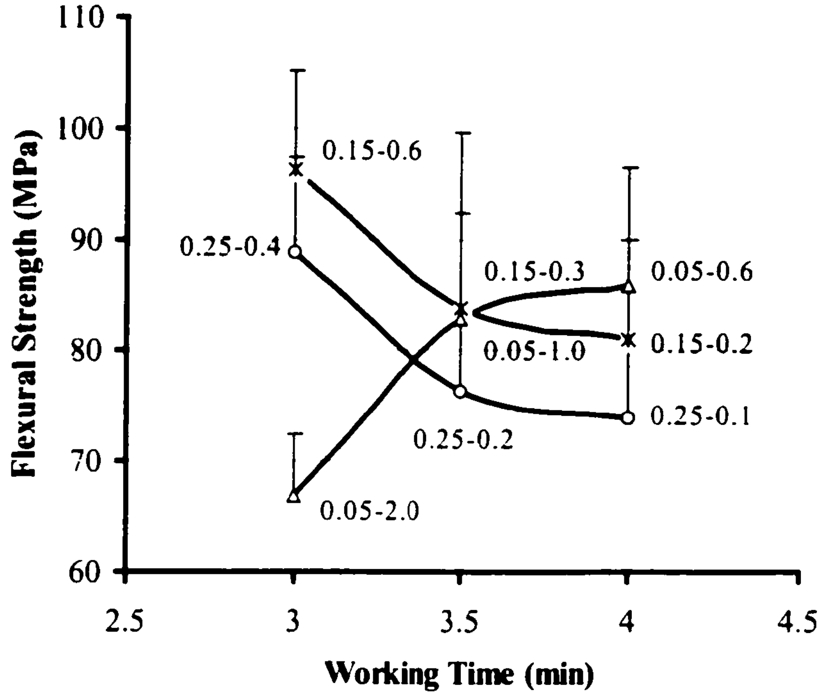

Fig. 5. Effect of concentration of redox initiator pair on FS.

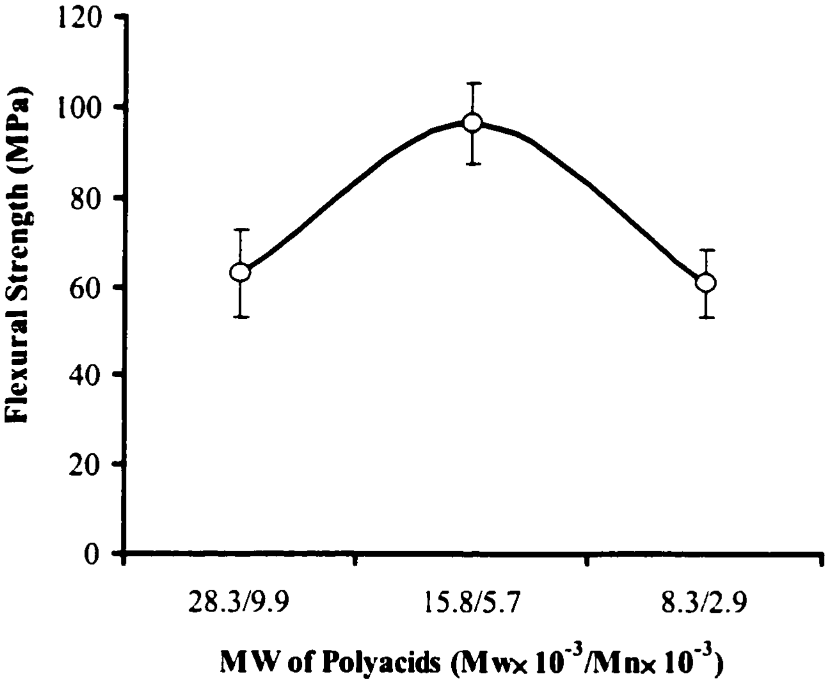

Fig. 6. MW effect on FS.

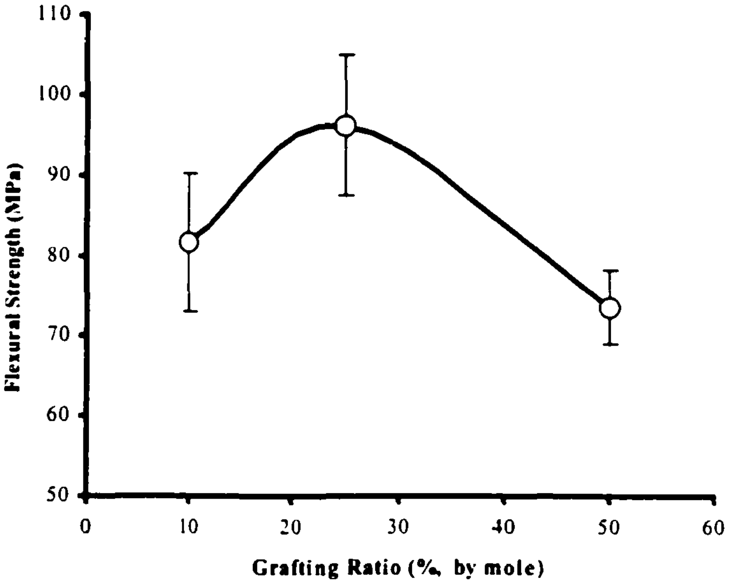

Fig. 7. Grafting ratio effect on FS.

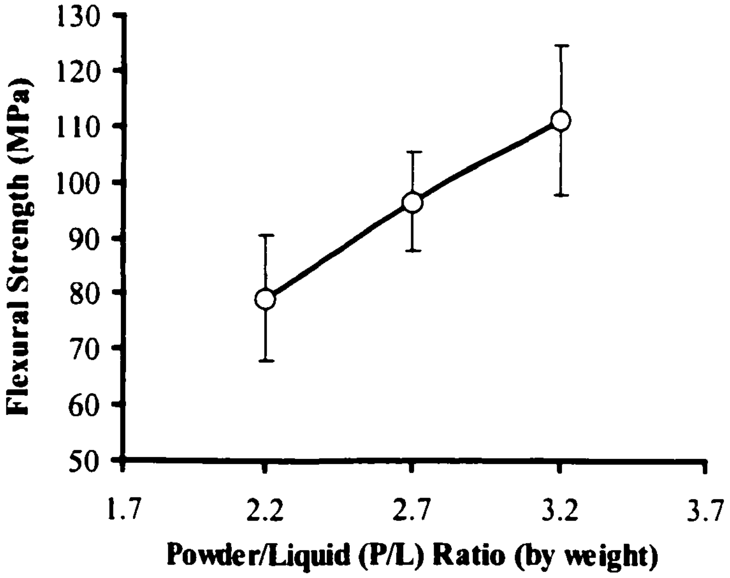

Fig. 8. Effect of P/L on FS.

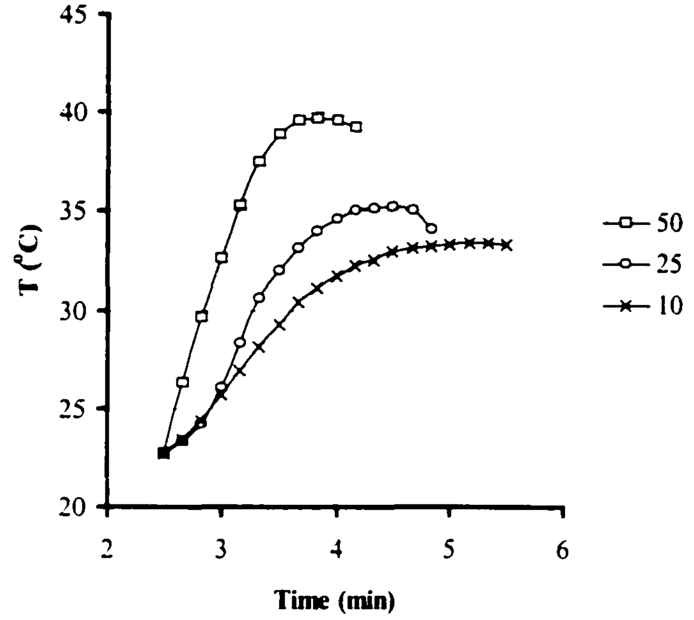

Fig. 9. Grafting ratio effect on setting exotherm.

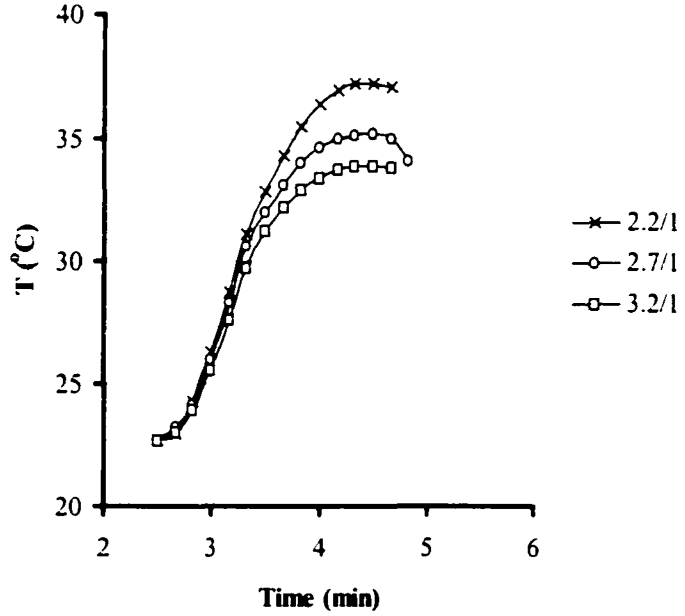

Fig. 10. Effect of P/L on setting exotherm.

SYNTHESIS OF POLY(CARBOXYL ACID)S WITH NEW PENDENT VINYL FUNCTIONALITIES AND THEIR APPLICATION IN RESIN-MODIFIED GLASS-IONOMER CEMENTS

by

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Format adapted for dissertation

Abstract

Two new pendent methacrylate grafted polyacids (poly[acrylic-co-itaconic acid]-g-glycidyl methacrylate and poly[acrylic-co-itaconic acid]-g-2-hydroxyethyl methacrylate) were synthesized and characterized. Resin-modified glass-ionomer cement (RMGICs) were formulated using these polymers and compared with the one using 2-isocyanatoethyl methacrylate (IEM) grafted polymers. Redox initiation system was also applied as well as the light-cured system. New polymers exhibited comparable mechanical strength to the IEM grafted polymer when light-cured system was applied while lower flextural strengths when redox initiation system was used, which need to be further improved in the future.

1. Introduction

Since glass-ionomer cements (GIC) were introduced by Wilson and Kent [1] and McLean and Wilson [2], they have been widely used in the dentistry[3]. Recently, those materials have been considered for use as bone cements in orthopedic surgery [4,5]. There exist two major types of glass-ionomer systems in the market: one is conventional glass-ionomer cement (CGICs) and the other is vinyl-containing cements. CGICs undergo an acid-base reaction between glass and polyacid aqueous solution, while vinyl containing GICs are glass-ionomer hybrid materials, which not only undergo an acid-base reaction but also undergo polymerization of some methacrylate side chains grafted onto the main polyacid backbone. Because of their higher flexural strength (FS) and diametral tensile strengths (DTS) and relatively long working times prior to light-initiation, as compared to CGICs, these vinyl-containing

GICs are attractive to the orthopedic surgery community. However, the grafting agent used so far is too expensive and toxic. In order to find an alternative, in this study we synthesized polyacids with pendent methacrylate functionality using two new grafting agents.

The objectives of this study were to synthesize and characterize the polyacids grafted with new pendent methacrylate functionality, formulate these polymers with calcium alumofluorosilicate glass to form composites, and evaluate mechanical properties of the formed composites. Nuclear magnetic resonance (NMR) was used to characterize the polymers. 2-Hydroxyethyl methacrylate (HEMA) was used as comonomer to improve the solubility of the synthesized polyacid in water. Both light-cured and redox initiator systems were used to initiate in situ polymerization. The compressive strength (CS), DTS, and FS of the composites were measured after the specimens were conditioned in distilled water for 7 days and 1 month, respectively. Conventional Fuji II GIC was used as the control.

2. Experimental

2.1. Materials

N,N'-dicyclohexylcarbodiimide (DCC), 4-dimethylamino pyridine (DMAP), N,N-dimethylaniline (DMA), methanol (MeOH), diethyl ether (anhydrous or laboratory grade), dl-camphoroquinone (CQ), diphenyliodonium chloride (DC), cellulose acetate butyrate (CAB), and butylated hydroxy toluene (BHT) were used as received from Acros Chemical Co. Acrylic acid (AA), itaconic acid (IA), N,N-dimethylformamide (DMF) (anhydrous), dibutyltin dilaurate (DBTL), triphenylstibine

(TPS), 2,2'-azobisisobutyronitrile (AIBN), potassium persulfate ($K_2S_2O_8$), ascorbic acid (Vc), HEMA, glycidyl methacrylate (GM), and 2-isocyanatoethyl methacrylate (IEM) were used as received from Aldrich Chemical Co. AIBN was recrystallized from MeOH before use. GC Fuji II LC glass powders were supplied by GC American Dental Corp.

2.2. Synthesis and characterization of vinyl-containing polymers

2.2.1. Synthesis of poly(AA-IA)-g-IEM

A two-step reaction was used for synthesis of the vinyl-containing polymers. In the first step, the polymers consisting of AA and IA were synthesized using a free-radical polymerization. Then IEM was grafted onto the polymers. Details were given in the previous chapters.

2.2.2. Synthesis of poly(AA-IA)-g-GM

To summarize, to a three-neck flask, equipped with a thermometer, a nitrogen inlet, and a mechanical stirrer, containing a solution of distilled tetrahydrofuran (THF), a mixture of AA, IA, and recrystallized 2,2'azobisisobutyronitrile (AIBN) was added. The reaction was run under N_2 purging at 64 °C for 40 h. The molar feed ratio for the polymers was 4:1 (AA:IA). Polymers with different molecular weights (MWs) were prepared by changing the amount of initiator and the reaction temperature. After the polymerization was completed and terminated using a small amount of BHT, a solution of GM, DMA, and distilled THF were added dropwise at the temperature of 60 °C. The reaction was kept at 60 °C for 24 h. The product was precipitated in ethyl ether and dried in a vacuum oven at room temperature. The schematic diagram for the GM grafted polymer synthesis is shown in Fig. 1a.

2.2.3. Synthesis of poly(AA-IA)-g-HEMA

The first half of the two-step reaction was the same as described above. Briefly, to a three-neck flask, equipped with a thermometer, a nitrogen inlet and a mechanical stirrer, containing a solution of distilled THF, a mixture of AA, IA, and recrystallized AIBN was added. The reaction was run under N_2 purging at 60 °C for 18 h. The molar feed ratio for the polymers was 4:1 (AA:IA). Polymers with different MWs were prepared by changing the amount of initiator and the reaction temperature. After the polymerization was completed and terminated by cooling to room temperature, a solution of HEMA, DMAP, BHT, and distilled THF were added dropwise at room temperature. After the solution became clear, a mixture of 1,3-dicyclohexylcarbodiimide (DCC) and THF was added. The reaction was kept at room temperature for 24 h. The solution was filtered to remove insoluble by-products. The product was precipitated in ethyl ether and dried in a vacuum oven at room temperature. The schematic diagram for the HEMA grafted polymer synthesis is described in Fig. 1b.

2.2.4. Characterization of partially methacrylated polyacids

The polymers were characterized using NMR, gel permeation chromatography (GPC), and viscosity measurements. ^1H NMR spectra were obtained on an ARX-300 NMR Spectrometer using deuterated oxide or deuterated methyl sulfoxide as solvent. For determination of MW, 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 [6], having solubility in THF for MW estimation. MWs were estimated on the Waters GPC unit (Model 410 differential refractometer), with standard GPC techniques, using a polystyrene standard. Specific viscosity was measured using an Ubbelohde viscometer, with DMF as solvent.

2.3. Microencapsulation of Vc in CAB

CAB was stirred and heated with ethyl acetate for 2 h to form a homogeneous solution. Then the solution was filtered and charged into a round bottom flask. Freshly-sieved Vc (the size appears to be smaller than 45 μm) was added and suspended in the solution for about 15 to 30 min, with a vigorous stirring. Hexanes were added dropwise at a rate of about 60 drops per minute. After complete addition of hexanes, an ice/water bath was applied to help harden the formed microcapsules. After 5 to 10 min, cold hexanes were added to wash the microcapsules. The microcapsules were recovered by decantation, washed with cold hexanes, and air-dried or vacuum-dried.

2.4. Formulation and evaluation of vinyl-containing hybrid GICs

2.4.1. Preparation of specimens of light-curable GICs

The formulations of light-curable polymer solutions were made by mixing the vinyl-containing polymers with 0.5% (wt/wt) of CQ (photoinitiator), 1% (wt/wt) of DC (activator), HEMA, and distilled water. Fuji II LC glass powder was used to formulate the cement with a P/L ratio of 2.7/1. Specimens were fabricated at room temperature. Cylindrical specimens were prepared in glass tubing, with dimensions of 4 mm diameter by 8 mm length for the CS test and dimensions of 4 mm diameter by 2 mm length for the DTS. A split Teflon mold with a glass window for light exposure was used to make specimens of 3 mm in width × 3 mm in thickness × 25 mm in length for FS measurements. Specimens were exposed to blue light for about 10 min, then removed from the split mold after 15 min in 100% humidity, and stored in deionized water at 37 °C for 1 week prior to testing.

2.4.2. Formulation of vinyl-containing hybrid GICs using redox initiator

The formulations for polymer solutions were made by mixing the vinyl-containing polymers with 0.15% (wt/wt) of $K_2S_2O_8$ (oxidizing agent), HEMA, and distilled water. Fuji II LC glass powder, mixed with 0.6% (wt/wt) of CAB encapsulated Vc, was used to formulate the cement with a P/L ratio of 2.7/1. Specimens were fabricated at room temperature, which was similar to the procedures described in the previous chapter. A split Teflon mold was used to make specimens of 3 mm in width × 3 mm in thickness × 25 mm in length for FS evaluations. Specimens were removed from the split mold after 15 min in 100% humidity and stored in deionized water at 37 °C for 1 week prior to testing.

2.4.3. Strength determinations

Testing of specimens was performed on a screw-driven mechanical testing machine (Model 858 Mini Bionix, MTS Systems Corp., Eden Prairie, MN, USA), at a crosshead speed of 1 mm/min for all of the CS, DTS, and FS measurements. The FS test was performed in three-point bending, with a span of 20 mm between supports. The sample sizes were n = 7 for the CS, DTS, and FS tests.

The CS was determined from the relationship $CS = 4P/\pi d^2$, where P = the load at fracture, and d = the diameter of the cylinder. The 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. The FS in three-point bending 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.

2.4.4. Estimates of working time of the redox system

A metal rod was used to evaluate the working time. The rod was inserted into the center of mixture of the cement, which was mixed and packed into a small vial with a hole at the bottom. Working time was the time from the start of the mixing process to the moment at which the metal rod could not be moved by hand.

2.3.5. Scanning electron microscopic (SEM) analysis

The fracture surface of representative specimens from selected materials was observed over a range of magnifications with an SEM (Model 515, Philips Electronics N.V., Eindhoven, The Netherlands) to investigate the effects of microstructure on the mechanical properties. The specimens were vacuum sputter-coated with gold-palladium (Au-Pd), and a high vacuum (5.5×10^{-5} Torr) was used for dehydration of the coated specimens before SEM analysis.

3. Results and discussion

3.1. Synthesis and characterization of vinyl-containing polymers

3.1.1. Synthesis and characterization of poly(AA-IA)-g-IEM

Poly(AA-IA)-g-IEM was characterized using NMR, GPC and viscosity measurements. Details were described in previous chapters.

3.1.2. Synthesis and characterization of poly(AA-IA)-g-GM

The grafting agent we used in the work described in previous chapters, IEM, is expensive and toxic. In order to find an alternative, here we used GM for grafting onto the polyacid. Gao et al. studied the kinetics of tertiary amine catalyzed esterification of acrylic acid and epoxy resin [7] and found that the conversion of the reaction increased with the temperature and time, and the reaction underwent a cyclization mechanism [8]. The schematic diagram for the catalized esterification is shown in Fig. 2.

GM modified polyacids were characterized using ^{1}H NMR, as shown in Fig. 3. The spectrum is similar to that obtained using IEM. Besides the peak at 12.20 ppm for the carboxyl group appear in the spectrum for poly(AA-IA) copolymer, 6.10 and 5.70 ppm for double bond of GM, poly(AA-IA)-g-GM also showed two peaks (7.90 and 7.60 ppm) which might be caused by the residual catalyst DMA. It is difficult to completely eliminate the residual DMA due to the formation of complexes between the basic DMA and carboxyl groups of the polymer. So far, the toxicity of residual DMA to tissue is not known.

3.1.3. Synthesis and characterization of poly(AA-IA)-g-HEMA

Moore et al. [9] reported that the esterification of carboxylic acids and phenols in the carbodiimide-based reaction could proceed under mild conditions, and the side reaction leading to N-acylurea was suppressed by the catalysis with the 1:1 molecular complex formed by DMAP and p-toluenesulfonic acid. The reaction pathways in carbodiimide condensation are shown in Fig. 4. We can see that the use of DMAP and an acidic environment led to a high conversion in the esterification reaction. Here we grafted HEMA onto polyacid using carbodiimide-based reaction in the presence of DMAP.

The ^{1}H NMR spectra of HEMA, poly(AA-IA), and poly(AA-IA)-g-HEMA are shown in Fig. 5. Poly(AA-IA)-g-HEMA showed not only a peak at 12.20 ppm corresponding to the carboxyl group but also the doublet at 6.10 and 5.70 ppm for the double bond. However, the peak for the hydroxyl group at 4.85 ppm in HEMA did not appear in the spectrum of poly(AA-IA)-g-HEMA after the esterification reaction between hydroxyl groups and carboxyl groups.

3.2. Formulations and property determinations

All the resin grafted polyacids used here had a grafting ratio of 25% and an average MW of 15,500 (Mw) or 5,700 (Mn) for IEM grafted polymers and 22,000 (Mw) or 8,000 (Mn) for GM and HEMA grafted polymers unless noted. Specimens were prepared under the same conditions unless specified: P/L ratio = 2.7/1, glass powder = Fuji LC glass, liquid composition = 50:20:30 (Polymer:HEMA:H_2O), and aging condition = in deionized water at 37 °C for 7 days. For light-cured system, 2[CQ] = [DC] = 1.0% of weight of polymer solution. For the redox initiation system, [$K_2S_2O_8$] = 0.15% (wt of the liquid), [MC] = 0.6% (wt of the glass powder). For each test the values with the same superscript letters were not significantly different ($p > 0.05$).

In our previous work [6], we have discussed why the measurement of FS offered the best practical and reliable estimate of tensile strength for cements with plastic deformations. The cements in this study were RMGICs that contained more plastic components compared to CGICs. Therefore, we mainly used FS as a screening tool even though CS and DTS were also determined for some of the materials.

3.2.1. Effect of MW

Table 1 illustrates the effect of MW of the polymers on mechanical strengths of the light-cured cements. Obviously, both GM and HEMA grafted polyacids with high MW exhibited higher mechanical strength than for the lower MW ones. This is the same as that occurred with IEM grafted polymers. Use of an even higher MW is not acceptable since the liquid will be very viscous and have no practical usage.

Table 1

Effect of MW on the mechanical strength of the cement

Code	Polymers	$Mw \times 10^{-3}/Mn \times 10^{-3}$	CS(MPa)*	DTS(MPa)	FS(MPa)
G1	P(AA-IA)-IEM	8.3/2.9	190.9(3.6)	19.8(3.9)	72.2(13.9)
G2	P(AA-IA)-IEM	15.5/5.7	225.6(6.9)	28.4(2.3)	116.4(9.5)
G3	P(AA-IA)-GM	9.4/3.3	199.4(5.3)	20.4(2.8)	85.7(4.9)
G4	P(AA-IA)-GM	22.0/8.0	215.7(9.9)	26.6(2.1)	110.2(7.4)
G5	P(AA-IA)-HEMA	9.4/3.3	183.6(7.5)	20.5(3.5)	78.1(9.2)
G6	P(AA-IA)-HEMA	22.0/8.0	184.1(3.6)	23.4(2.7)	89.0(4.7)

*Entries are mean values with standard deviations in parentheses.

3.2.2. Effect of grafting ratio

From Table 2, we can see that, just like the IEM grafted polyacids, either GM or HEMA grafted polyacids with 25% grafting ratio showed higher mechnical strength than the 10% ones. The reason is similar to the explaination for IEM grafted polymer given in the previous chapters, reflecting the fact that the GIC made using 10% grafting ratio behaved like a CGIC.

Table 2

Effect of grafting ratio on the mechanical strength of the cement

Code	Polymers	Grafting ratio	CS(MPa)*	DTS(MPa)	FS(MPa)
G7	P(AA-IA)-IEM	10	220.6(5.8)	26.1(3.9)	72.2(6.7)
G2	P(AA-IA)-IEM	25	225.6(6.9)	28.4(2.3)	116.4(9.5)
G8	P(AA-IA)-GM	10	181.3(4.4)	19.3(3.2)	61.3(4.9)
G4	P(AA-IA)-GM	25	215.7(9.9)	26.6(2.1)	110.2(7.4)
G9	P(AA-IA)-HEMA	10	179.1(12.9)	19.3(0.8)	65.2(5.1)
G6	P(AA-IA)-HEMA	25	184.1(3.6)	23.4(2.7)	89.0(4.7)

*Entries are mean values with standard deviations in parentheses.

3.2.3. Effect of initiation system

Table 3 lists the mechanical strengths of the cements made using two different initiation systems – redox and light-cured initiation system. Unlike the IEM grafted polymers, whose FS values statistically showed no significant difference between using redox and light-cured initiation systems, both GM and HEMA grafted polymers showed lower FS values using redox initiators than the light-cured counterpart. Comparison of FS of the cements made using different initiation systems is shown in Fig. 6.

Table 3
Effect of different initiation system on FS

Code	Polymer	FS(MPa)*	
		Redox	LC
G2	P(AA-IA)-IEM	96.3(8.8)	116.4(9.5)
G4	P(AA-IA)-GM	57.3(9.3)	110.2(7.4)
G6	P(AA-IA)-HEMA	68.7(11.4)	89.0(4.7)
C0	Fuji II	15.8(0.7)	

*Entries are mean values with standard deviations in parentheses.

Figs. 7 – 9 illustrate representative regions of the fracture surfaces of GICs made using different resin-modified polyacids and a light-cured initiator system. The fracture surface of the commercial product Fuji II is shown in Fig. 10. All the RMGICs showed more integrated and highly fused surface textures as compared to the commercial product Fuji II, which exhibited more isolated glass particles and larger pores or voids. This correlates with the result that the mechanical strengths of GICs with different resin-modified polymers were higher than the commercial product, especially the FS, which showed four to seven times higher values than the latter ones. There was not much difference among the fracture surfaces of cements made using different resin grafted polyacids because of the similar polymer structures and fabrication methods of the cements.

4. Conclusion

Light-cured RMGICs made using new pendent methacrylate grafted polyacids demonstrated good mechanical strength, similar to that observed when using IEM grafted polymer, and much higher FS than the commercial product Fuji II. A redox initiation system was also used to cure the new polymers, and the resulting materials exhibited lower FS than their light-cured counterparts. The reason for this difference needs to be further studied in the future.

Acknowledgement

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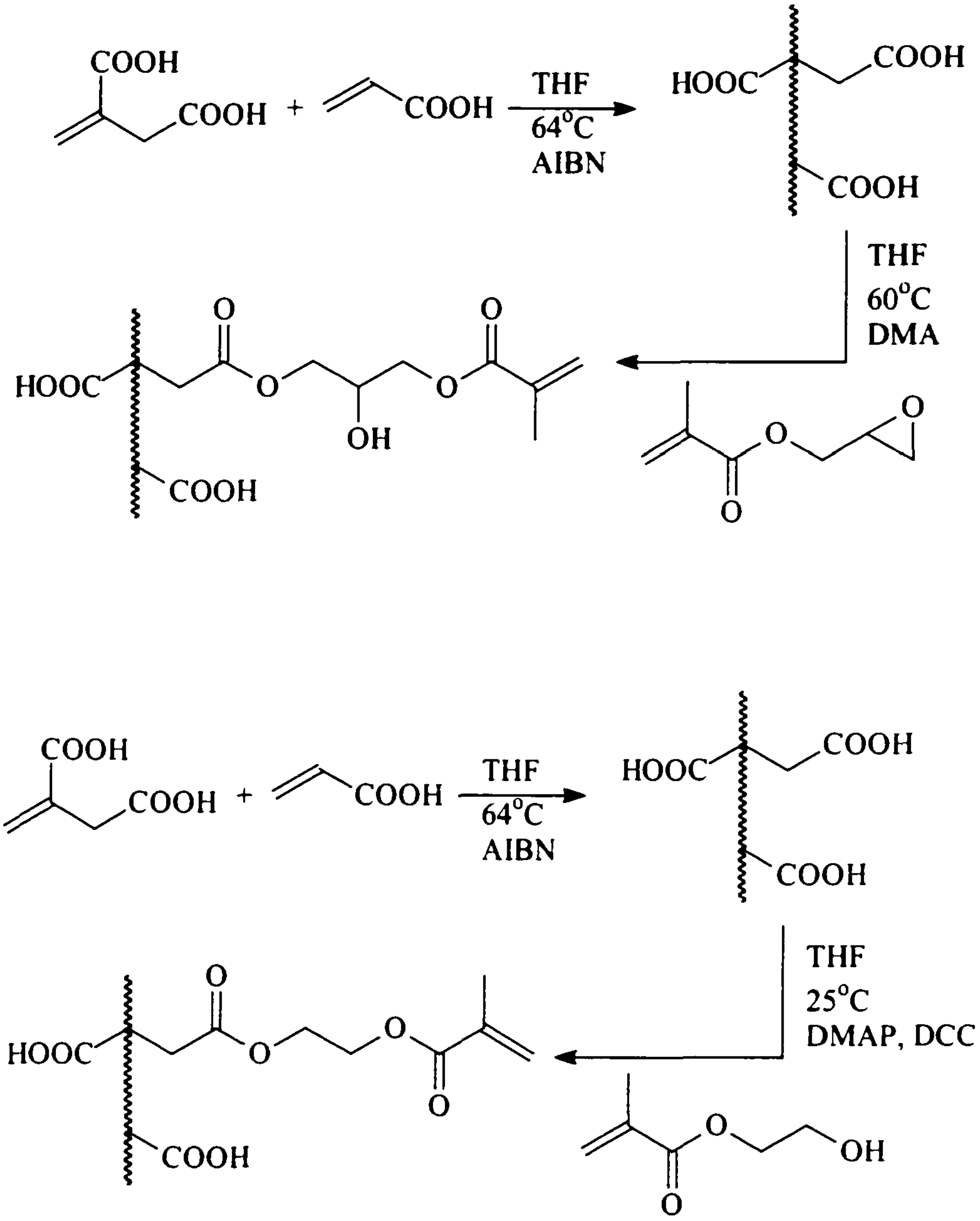

Fig. 1. Scheme for vinyl-containing polymer synthesis. a. GM grafted polymer. b. HEMA grafted polymer.

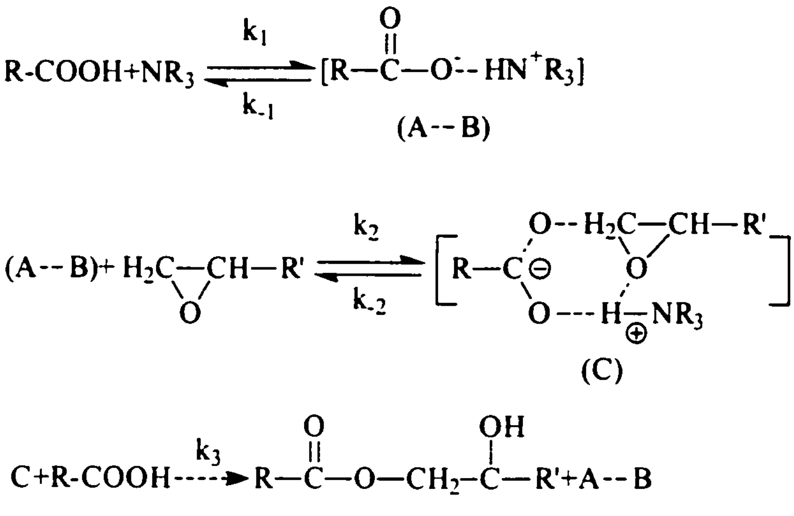

Fig. 2. Scheme for the mechanism of catalized esterification between GM and polyacids

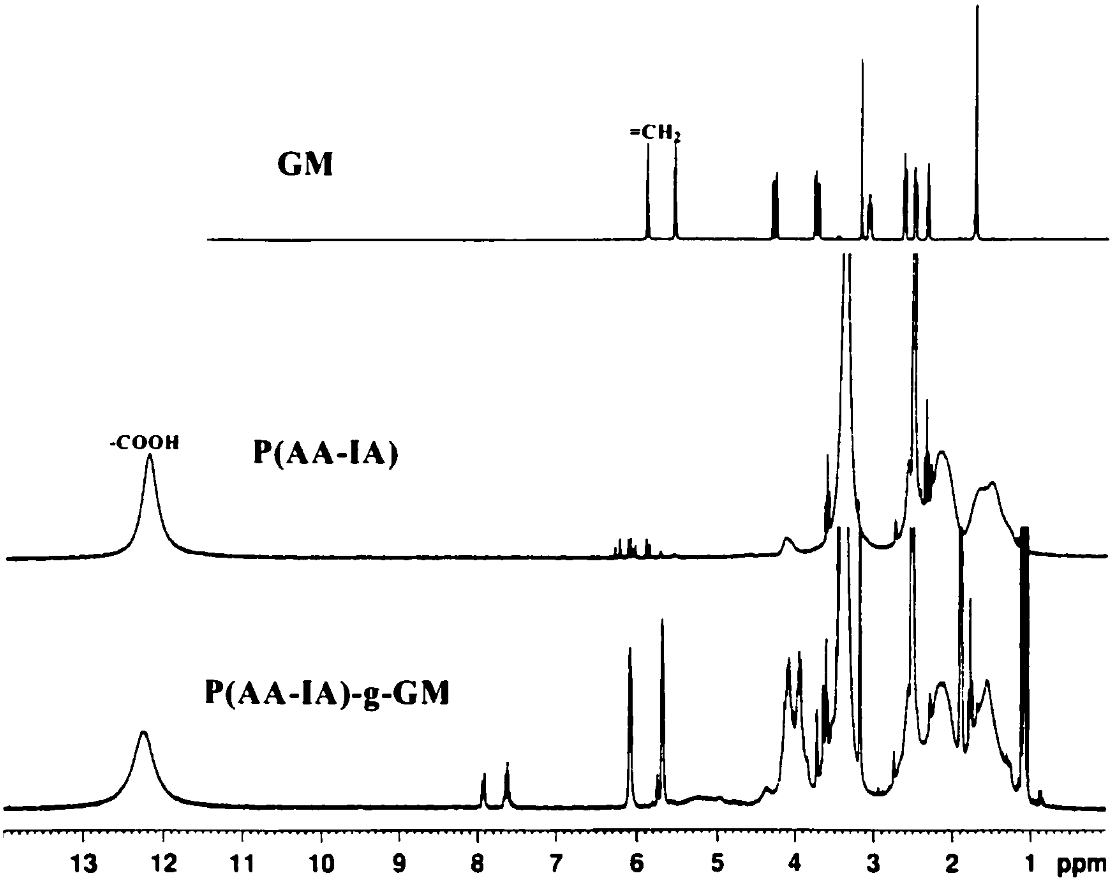

Fig. 3. ^{1}H NMR spectra for GM, copolymer, and vinyl-containing copolymer

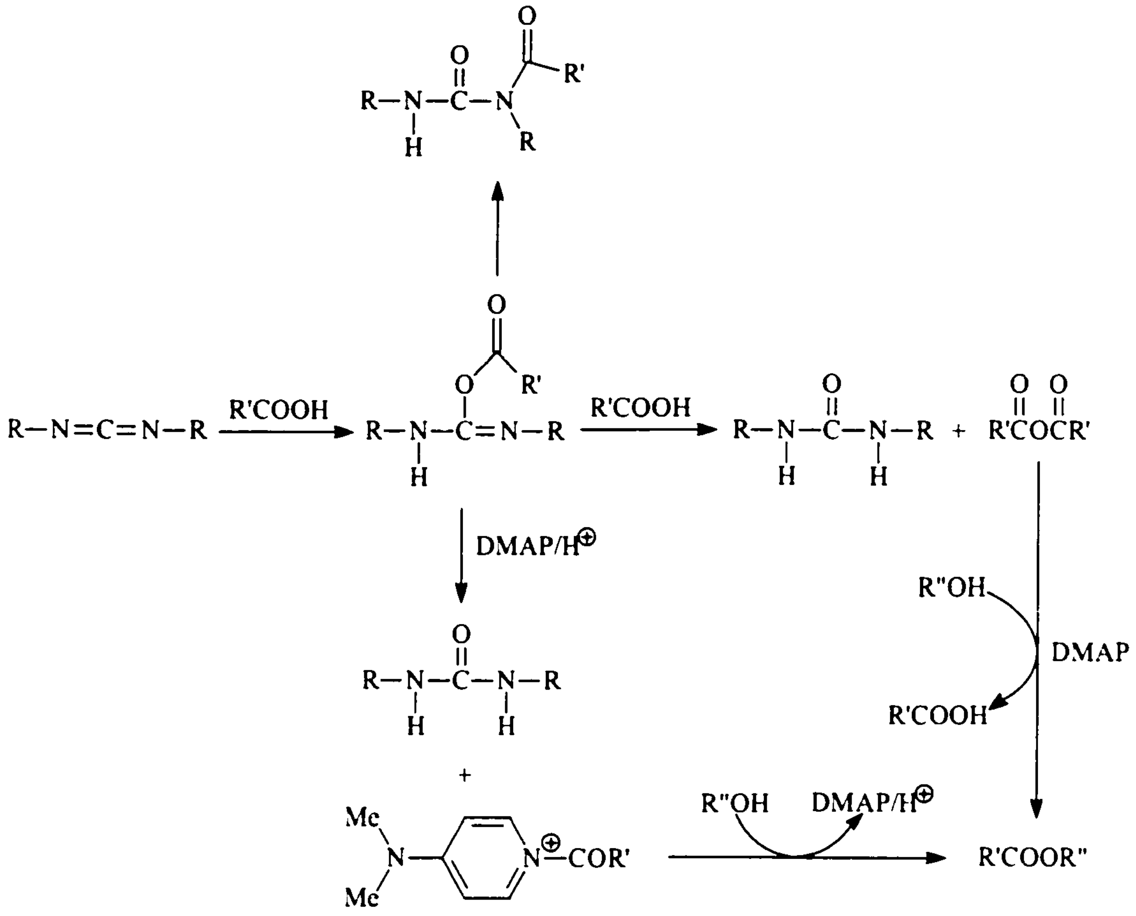

Fig. 4. Scheme for the mechanism of catalized esterification between HEMA and polyacids [9].

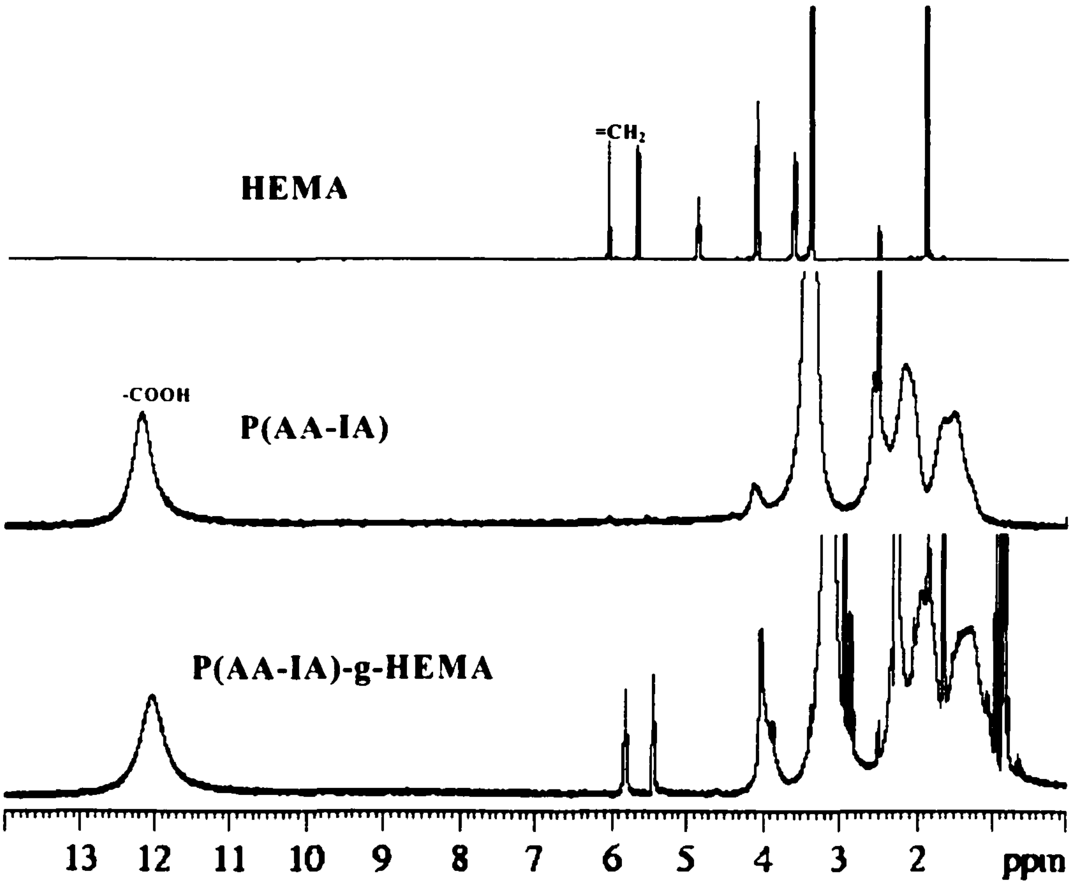

Fig. 5. ^{1}H NMR spectra for HEMA, copolymer, and vinyl-containing copolymer.

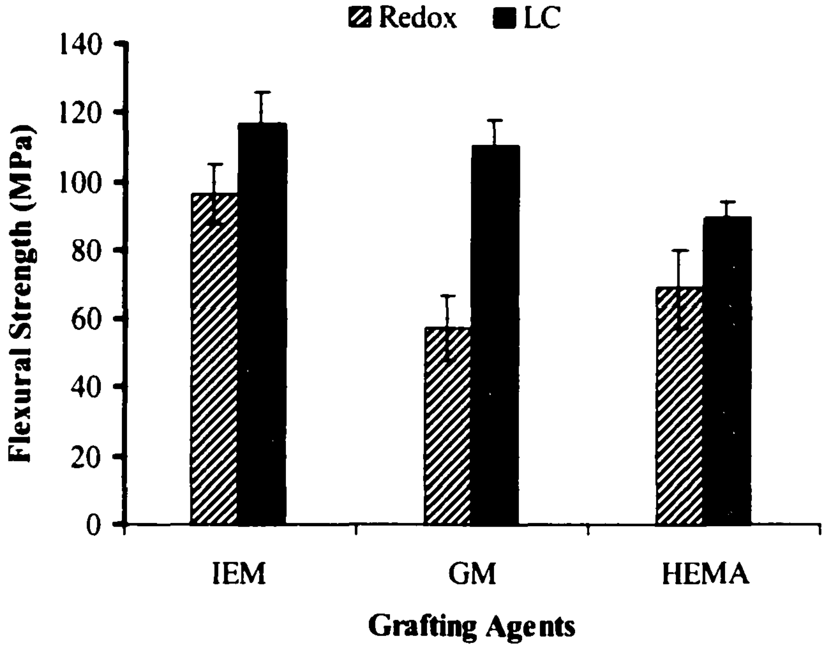

Fig. 6. Effect of initiation system on FS.

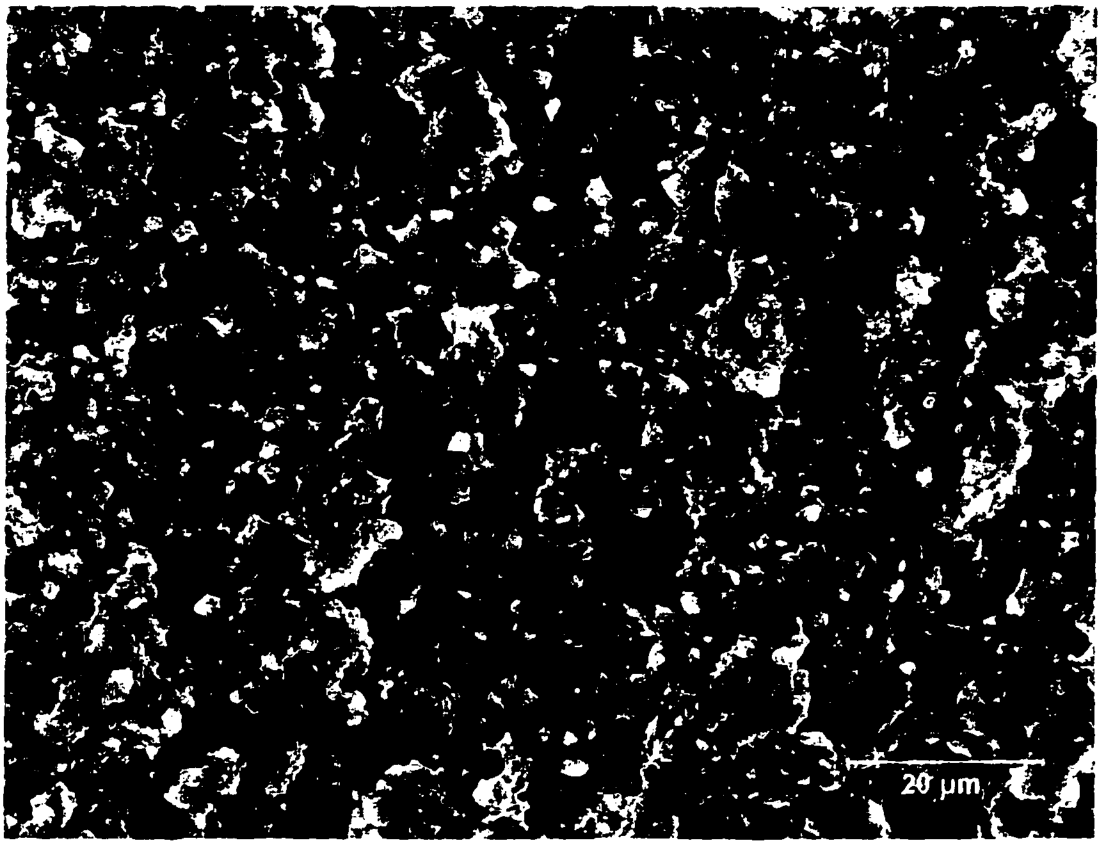

Fig. 7. SEM photomicrograph of the cement using IEM grafted polyacids with original magnification of 1500x.

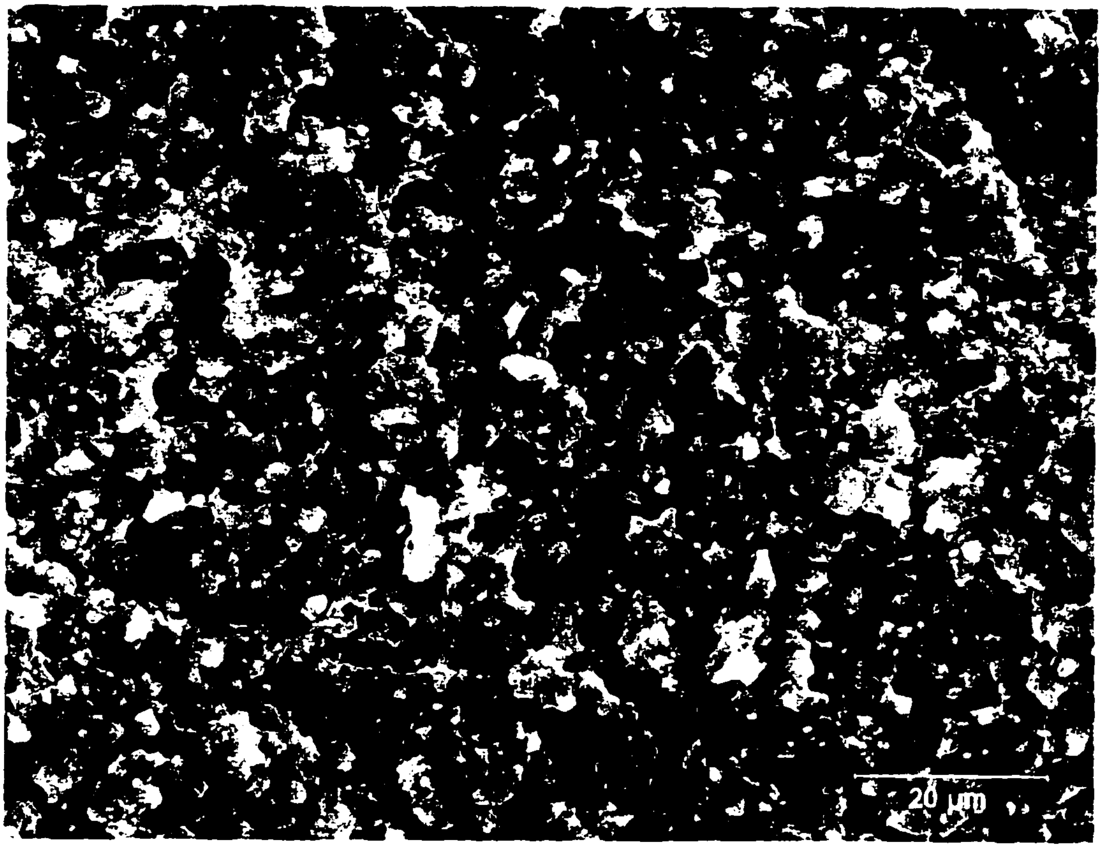

Fig. 8. SEM photomicrograph of the cement using GM grafted polyacids with original magnification of 1500x

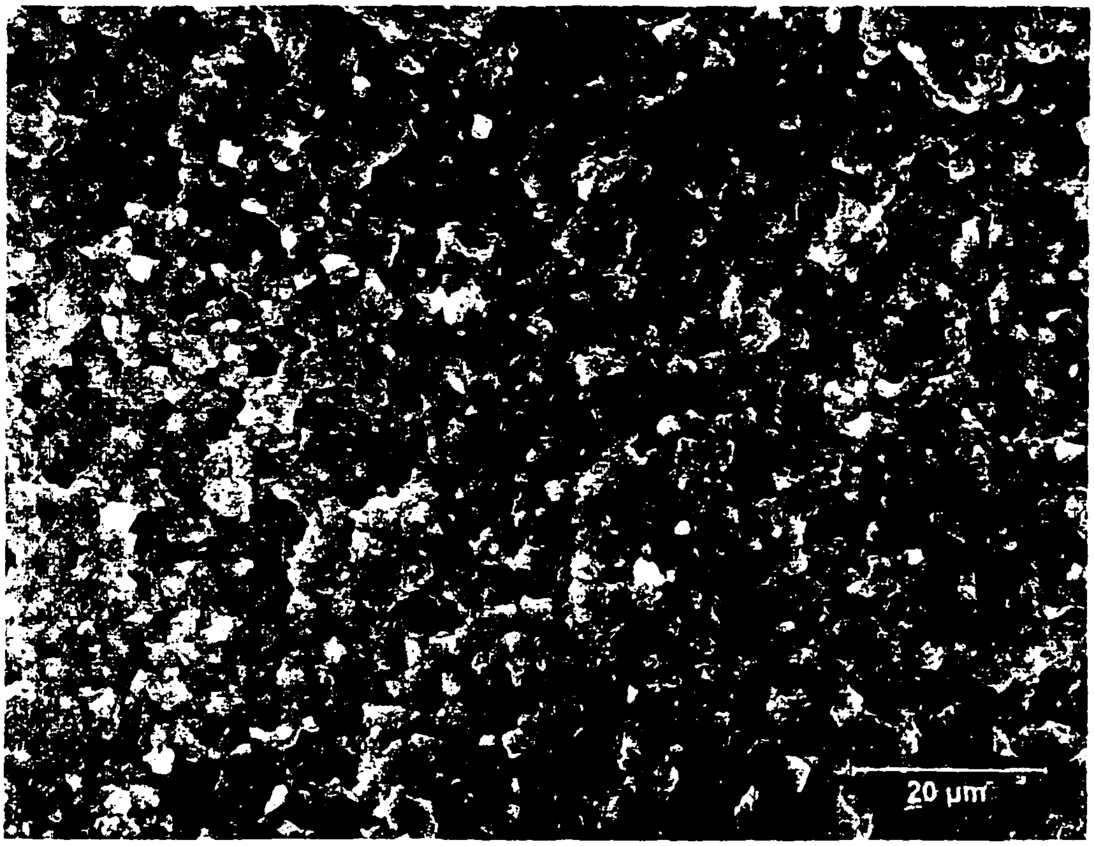

Fig. 9. SEM photomicrograph of the cement using HEMA grafted polyacids with original magnification of 1500x.

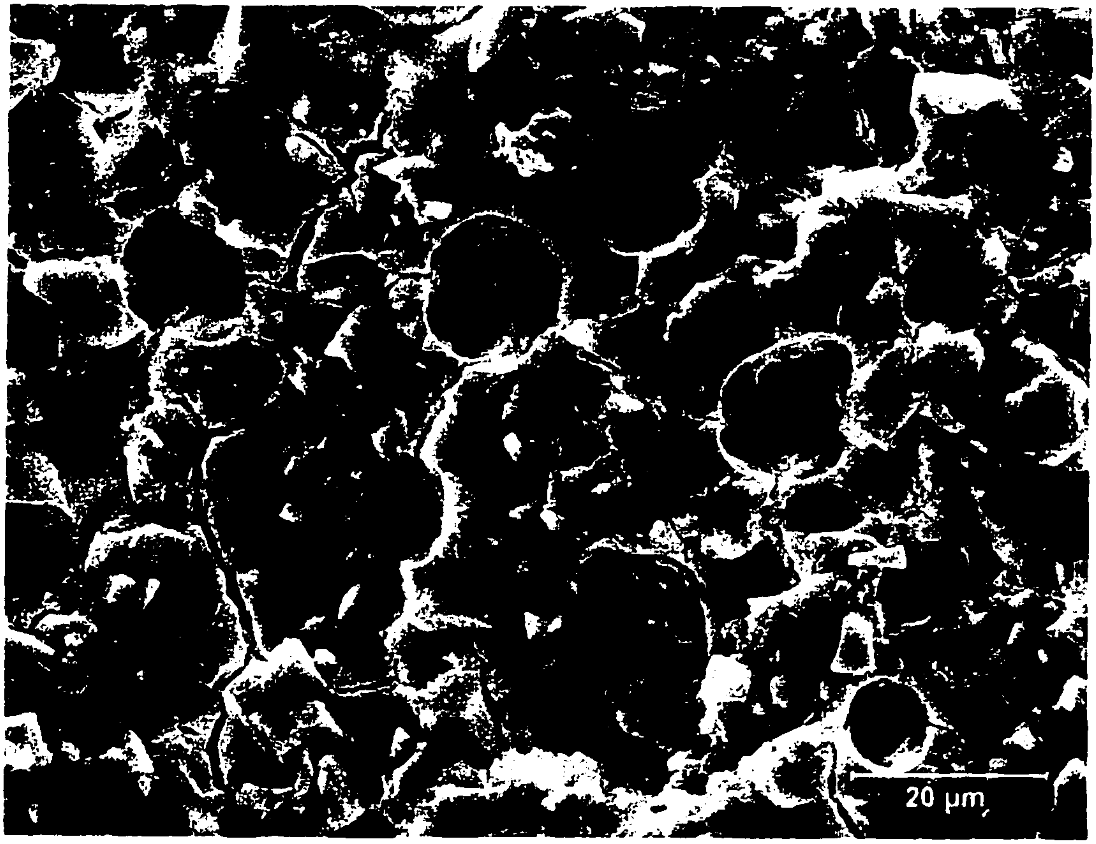

Fig. 10. SEM photomicrograph of the commercial product Fuji II with original magnification of 1500x.

CONCLUSIONS AND SUGGESTED FUTURE WORK

Since GICs were first introduced, their properties have been improved, and there are now many versions for various applications. After they began to be used in orthopedics, some encouraging results from preliminary clinical studies have already been obtained in patients for whom the use of conventional poly(methyl methacylate) cements are contra-indicated.

We have found that mechanical strengths of self-cured GICs could be improved without sacrificing handling characteristics by introducing amino acid residues into the polyacid backbone. This was proved in the first paper (Hypothesis 1), although fracture resistance and toughness of the cement need to be tested in the future. Besides the six amino acids used in this research, it needs to be determined whether other natural amino acids can also be used and even improve the cement properties because of the variation of both the pK_a and different types of carboxyl groups. Biocompatibility needs to be tested for this self-cured GIC system even though it is believed that glass-ionomer material is not only biocompatible but also bioactive [59].

When vinyl containing polyacids were applied, mechanical strengths could be even improved when either light-cured or redox initiation systems were used. This was proven in papers 2 and 3 (Hypotheses 2 and 3). The toxic HEMA, which is normally used as a comononer in resin-modified GICs, can be replaced by methacryloyl β–alanine or acrylic acid. The latter two materials were expected to be nontoxic, although the biocompatibility of the c 127 eds to be validated. We also showed that water soluble redox initiator systems can be applied in resin-modified glass ionomer bone cements. The next step is to test the mechanical properties of the cements using larger sample sizes.

Paper 4 showed how two new grafting agents (GM and HEMA) could be used to modify polyacids, replacing the expensive and toxic IEM (Hypothesis 4). The mechanical properties of the cements made using polyacids grafted with the new grafting agents need to be further improved, especially when redox initiator systems are applied.

Future developments in use of GICs in orthopedic surgery are promising, and more effort needs to be put into the improvement of handling characteristics and mechanical strength of the formed cements. Biocompatibility also needs to be addressed, which is not included in this research. Other important aspects, such as packaging, long-term storage, sterilization, delivery in operating room, and cost issue, which are crucial to actual implementation of GICs, need to be addressed in the future work.

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I certify that I have read this document and examined the student regarding its content. In my opinion, this dissertation conforms to acceptable standards of scholarly presentation and is adequate in scope and quality, and the attainments of this student are such that he may be recommended for the degree of Doctor of Philosophy.

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