# Radiopaque Polymers Based on Acrylated Phosphonate Esters Derived from Polyols

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## Synopsis

A number of miscible metal salt–polymer systems of acrylated phosphonates derived from various polyols such as glycerol, D-mannitol, D-sorbitol, pentaerythritol, and dipentaerythritol are described. The salt–monomer systems could be polymerized radically to form homogeneous transparent glassy polymers. Incorporation of heavy metal salts in polymers imparts radiopacity on otherwise radiolucent materials rendering them useful for X-ray imaging. The polymer–salt systems have been characterized with the aid of infrared spectroscopy and thermal and radiographic analyses. In these salt–polymer systems, salts are bonded to the polymers predominantly through the phosphoryl's oxygen. The results indicate that about 11 wt % of uranyl nitrate hexahydrate and 12.5 wt % of bismuth bromide impart a radiopacity equivalent to that of aluminum. The glass transition temperatures ($T_g$) of the salt-containing polymers are substantially higher than the salt-free polymers. The $T_g$ values seem to depend on the chemical nature of the polymers, concentration of metal salts, and the extent of crosslinking induced through chelation. The analysis indicated complete solubility in the polymer matrices. No melting point endotherms of free salt crystals were detected. Some preliminary adhesion measurements revealed that acrylated phosphonates are excellent adhesion promoters for hard tissues.

## INTRODUCTION

In view of the ever-increasing use of synthetic polymers in biomedical applications, stringent specifications are imposed on their fabrication to optimize efficiency and safety to eliminate risks involved in the event of their failure.[1,2] Therefore, it is recognized and often recommended that all synthetic polymers used in medical implants and restorative and prosthetic dentistry should be radiopaque, and readily available for X-ray detection.[3–6] The synthetic polymers used hitherto are largely radiolucent acrylics, polyurethanes, and others, which cannot be detected by conventional radiographic methods. There are several documented cases of medical emergency caused by impaction, swallowing, or ingestion of implant materials.[6] Such situations prompted the use of radiopaque polymers in dental materials, for example, to determine the location of aspirated dentures and fragments.[5–8] Few studies on radiopaque restorative composites are available.[9–14] Radiopaque materials have been reported to help differentiate secondary caries or decalcified dentin and allow the detection and location of the pulp, gingival overhangs, and voids or other defects present in the restoration.[9] A higher percentage of secondary carious lesions and marginal defects

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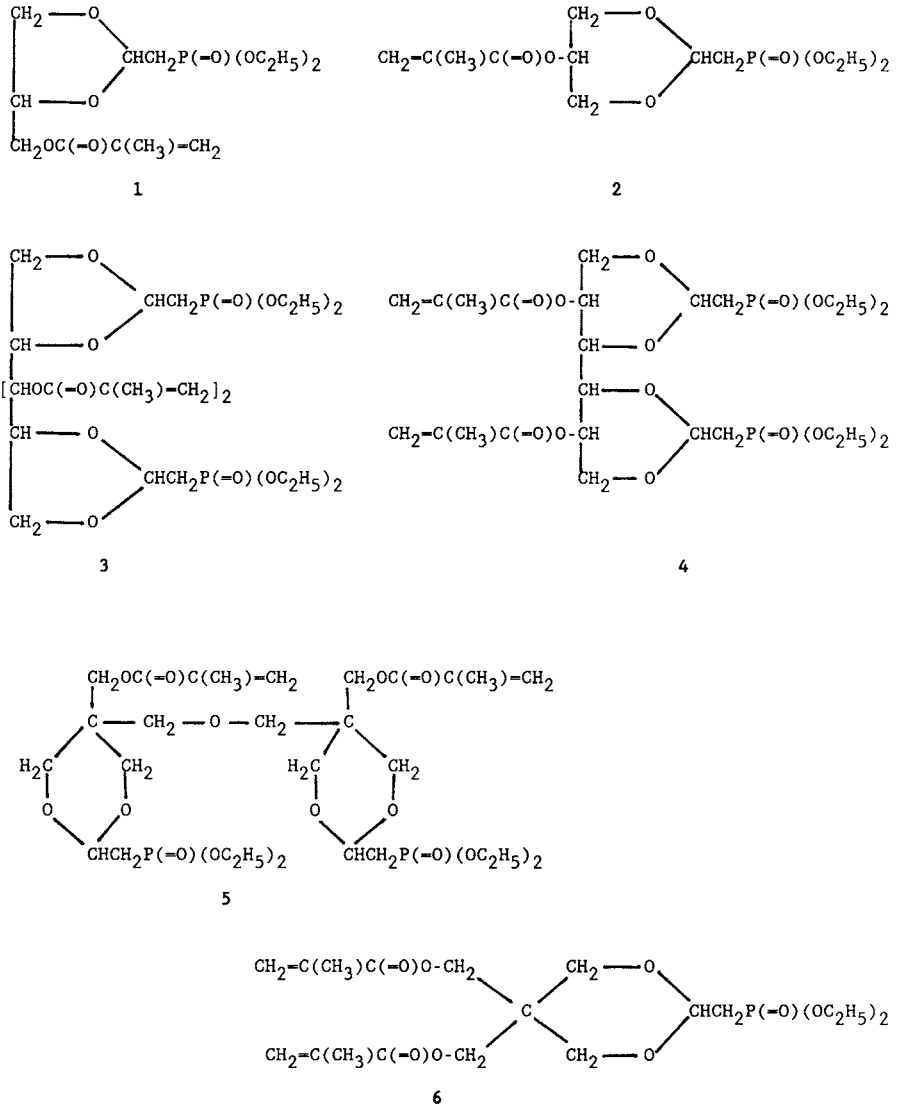



Fig. 1. Schematic depiction of the structures of acrylated polyphosphonates derived from glycerol (**1** and **2**), D-mannitol (**3**), D-sorbitol (**4**), dipentaerythritol (**5**), and pentaerythritol (**6**).

could be detected near the radiopaque composites rather than near the amalgam fillings.[10] With widespread acceptance and use of composite materials, a number of radiopaque composites possessing varied degree of radiopacity are now commercially available.[9,14] Radiopacities of several commercial composites, including those of posterior composites, have been compared and some of these composites exhibit higher radiopacity than enamel and dentin. Composite resins for posterior teeth are expected to be at least as radiopaque as enamel.[9,14]

Most of the radiopaque materials currently used are composed of glasses containing high atomic number components such as barium fluoride, barium oxide, or lanthanide oxide.[7,11,14,15] Halogenated polymers containing bromine[16]

and mixtures of PMMA and organoiodine compounds have also been reported to exhibit high radiopacity.[17,18] However, most of these lack stability on prolonged contact with body fluids and light.[16] Imparting radiopacity to polymers can be accomplished via physical mixing with heavy metal salts of barium or bismuth; however, the heterogeneous nature of this mixture results in deleterious effects on their physical and mechanical properties and, thus, their effectiveness is limited.[19,20]

The use of polymers and monomers that solubilize heavy metal salts such as barium bromide, bismuth halides, uranyl nitrate, and lanthanides, capable of imparting radiopacity to radiolucent plastics, has been reported from this laboratory.[21-24] Most of these systems are chelates of partially hydrated barium bromide with methoxypoly(ethyleneglycol)mono-methacrylates containing a $CH_3O(CH_2CH_2O)_n$ as an interacting moiety. Such compounds are commercially available[21] and others are based on bismuth halides or hydrated uranyl nitrate dissolved in monomers containing carbonyl functional groups such as methyl methacrylate.[22-24] These homogeneous salt–monomer mixtures have been conventionally polymerized to yield transparent plastics with radiopacities exceeding that of aluminum. These systems exhibit improved mechanical properties compared with those mentioned earlier.[17-20] Their drawbacks are lack of adhesion promoting components required in restorative resins used for hard tissues, such as enamel and dentin, and the inability to cure them at ambient temperature with the commonly used amine accelerators. These systems still show a slight tendency for discoloration as a result of salt leaching from their surfaces on prolonged exposure to aqueous solutions.

In order to overcome some of the drawbacks mentioned above, new acrylated phosphonate esters containing 1,3-dioxane and 1,3-dioxolane moieties derived from polyols such as glycerol, D-mannitol, D-sorbitol, pentaerythritol, and dipentaerythritol have been developed in this laboratory.[25] The structures of various acrylated phosphonates are depicted in Figure 1. The phosphoryl group (P=O) provides a stronger coordinating site than the ether or carbonyl group and also imparts adhesive properties toward hard tissues.[26] These monomers can be cured at ambient temperature by self-initiation of 1,3-dioxolane ring in the presence of a metal salt,[27] yielding a stable crosslinked matrix which is suggested to have improved biocompatibility due to the presence of phosphonate ester groups.[26a] In this paper the spectroscopic, thermal, and radiographic properties of miscible systems of bismuth bromide and uranyl nitrate hexahydrate with several acrylated phosphonate polymers are described.

## EXPERIMENTAL

### Materials and Methods

Anhydrous bismuth bromide (III) (Alfa Products, Morton Thiokol, Inc., Danvers, MA) and uranyl nitrate hexahydrate (Spi-Chem, West Chester, PA) were used as supplied. All solvents such as tetrahydrofuran and chloroform were dried prior to use and benzoyl peroxide and 2,2-azobisisobutyronitrile (AIBN) were purified by recrystallization.

Elemental analysis (C, H, P) was performed by Microanalysis Inc., Wilmington, DE. Proton NMR spectra were recorded on Varian A-60 and Varian

XL-100 MHz spectrometers using $CDCl_3$ as a solvent and TMS as an internal reference. Decoupled $^{13}C$-NMR spectra were recorded on a Varian XL-100 MHz spectrometer employing 10–15% $CDCl_3$ solution at 25.2 MHz and $^{31}P$-NMR spectra were run on a Mohawk NMC-250 spectrometer using 20–25% solutions in $CDCl_3$, employing 85% phosphoric acid as an external reference. Infrared spectra were recorded on a Perkin-Elmer 1820 and Nicolet DX-20 FT-IR spectrometer.

Radiographic analysis was carried out with a Picker condenser discharge mobile X-ray diagnostic unit, Model 1010, operating at 90 kV and 6 mA. A Hitachi tungsten anode, cathode ray tube no. UG 4605, was used in the unit. The polymer samples were made into pellets 1 mm thick, in an infrared pellet press at 20,000 psi for ca. 60 s. In an alternative method, transparent cylindrical polymer samples were prepared by polymerization in a glass tube and then carefully cut into pellets of the proper thickness, and the surfaces were subsequently polished. The specimen's radiopacity was measured against an aluminum stepwedge bar (1 mm steps), and both were placed about 55 cm below the tungsten anode. The images were recorded on Kodak Ultraspeed double sided dental X-ray film no. DF 49. The exposed film was scanned with a Joyce microdensitometer and the radiopacities of the samples measured relative to that of the aluminum stepwedge bar. Aluminum was chosen as reference material because its linear coefficient ($\mu$) is of the same order as dental enamel and due to the similar variation of $\mu/\rho$ with the wavelength for aluminum and hydroxyapatite.[10]

Differential scanning calorimetry measurements were conducted with a Perkin-Elmer differential scanning calorimeter, DSC-4, equipped with a microprocessor. Scans conducted in the range −80–100°C were performed at a scanning rate of 20°C/min under a helium atmosphere and in the range 40–300°C under a steady flow of nitrogen. Indium and cyclohexane were used to calibrate the DSC for high and low temperature range, respectively. The glass transition temperature $T_g$, was taken at the midpoint of the heat capacity change, $\Delta C_p$, at $T_g$. The change in $\Delta C_p$ at $T_g$ was calculated from the vertical distance between the two extrapolated baselines at $T_g$ (see Fig. 2).

**Synthesis of Acrylated Phosphonate Esters.**[25] The esters containing 1,3-dioxane moieties were prepared via a transacetalation reaction between a polyol such as glycerol and a phosphonylating agent, 2,2-diethoxy ethylphosphonate under acidic conditions, and the resulting phosphonylated alcohol was subsequently converted into a methacrylate derivative through its coupling with methacryloyl chloride as depicted in Scheme 1. In a typical preparation, glycerol (4.63 g) was mixed with diethyl 2,2-diethoxyethylphosphonate (11.74 g) and concentrated hydrochloric acid (6 mL), the mixture was stirred at 60–65°C for 24 h, and a fraction of (I) distilled at 151°C/0.04 mm Hg was collected in 58% yield. The 2-(2,2-diethoxyphosphonomethyl)-5-hydroxy-1,3-dioxane (I) obtained was then reacted with excess (20%) of methacryloyl chloride in the presence of proton acceptor, such as triethylamine, in dry ether at 0–5°C. A methacrylate derivative of (II) was obtained in ca. 65% yield.

ANAL. Calcd for $C_{13}H_{23}O_7P$: C, 48.44%; H, 7.19%; P, 9.60%. Found C, 47.59%; H, 7.28%; P, 8.92%.

Phosphonylated alcohols containing 1,3-dioxolane moieties were synthesized via the Arbuzov reaction with brominated cyclic acetals (obtained through a transacetalation reaction of polyols with bromoacetaldehyde diethyl acetal under

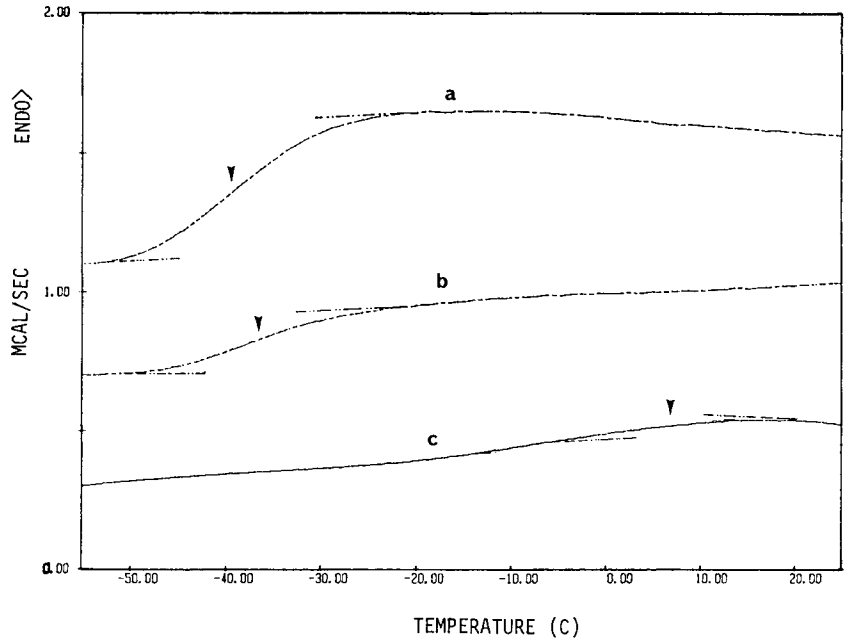


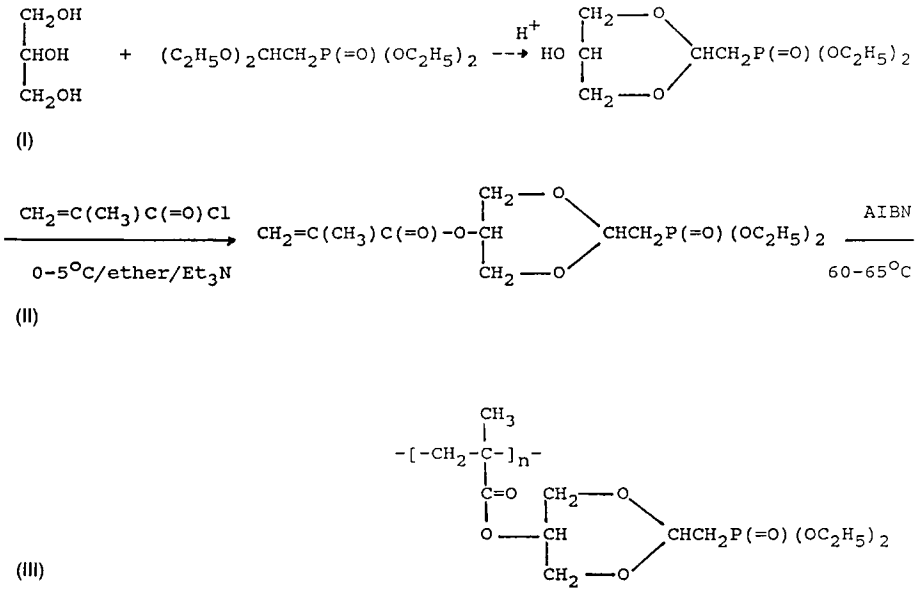

Fig. 2. Differential scanning calorimetry thermograms of acrylated polyphosphonates derivatives of (a) glycerol with 1,3-dioxane moieties, (b) glycerol with 1,3-dioxolane moieties, and (c) D-mannitol.

controlled conditions), as depicted in Scheme 2. For example, 2-(1'-bromomethyl)-4-hydroxymethyl-1,3-dioxolane (IV), a precursor of phosphonated alcohol (V), was prepared through transacetalation of glycerol with bromoacetaldehyde diethyl acetal, in the presence of catalytic amounts of sulfosalicylic acid dihydrate. [(2-Diethylphosphonomethyl)-4-hydroxymethyl-1,3-dioxolane] (V) was prepared by refluxing a mixture of (IV) with triethyl phosphite (8.20 g) under a gentle stream of nitrogen, at 160–165°C for 18 h. A fraction of (V) distilled at 152/0.05 mm Hg was collected in 80% yield (10.1 g). The phosphonylated-1,3-dioxolane derivative glycerol (V) was treated with methacryloyl chloride to obtain its methacrylate (VI) in the same way, as described earlier. The methacrylate of (V) on polymerization in the presence of AIBN yielded a polymer of the structure depicted in VII.

The details of synthesis of other acrylated phosphonate esters containing 1,3-dioxane and 1,3-dioxolane moieties derived from D-mannitol, D-sorbitol, pentaerythritol, and dipentaerythritol have been published elsewhere.[25]

## Preparation of Polymer–Salt Complexes

Polymer salt complexes were obtained by mixing a solution of a metal salt in tetrahydrofuran (THF) with a solution of an appropriate monomer in THF. In general, the polymer salt complexes can be prepared by mixing a metal salt with a monomer and subsequently polymerizing the mixture under standard conditions. In this case, a solvent had to be employed because of the highly viscous nature of the monomers. The solvent was first removed under a gentle

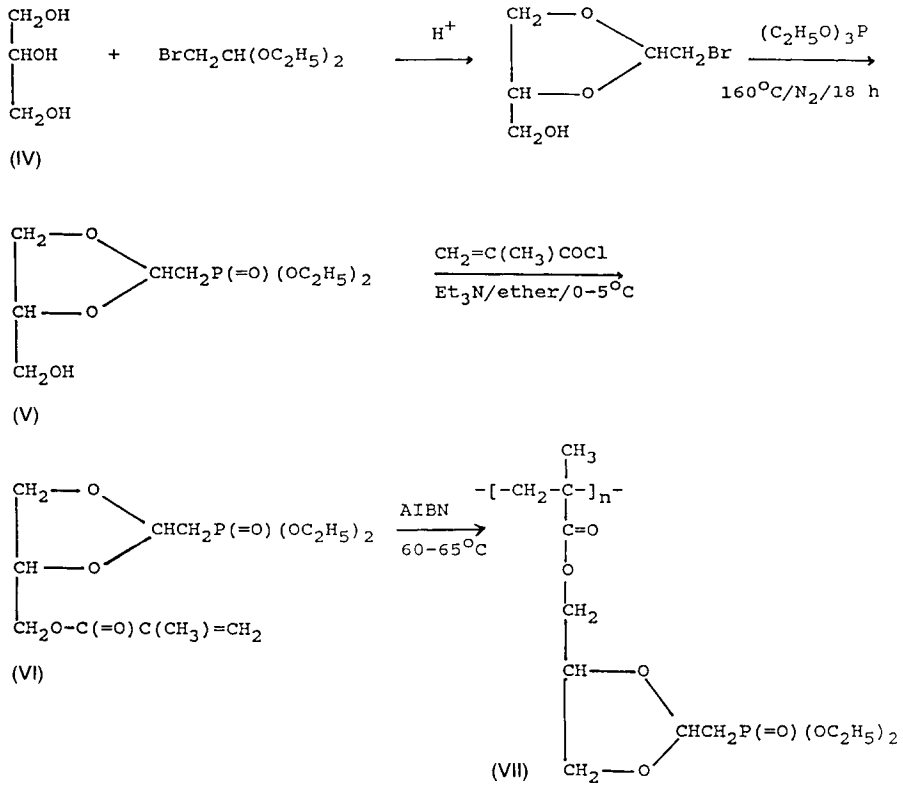


Scheme 1. Reaction sequence depicting the synthesis of 2-(2,2-diethoxyphosphonomethyl)-5-hydroxy-1,3-dioxane (I), its methacrylic derivative (II), and polymerization (III).

stream of nitrogen, later its traces were removed under vacuum. To this solvent free mixture, an initiator, preferably 2,2-azobisisobutyronitrile (AIBN) (0.5 wt %), was added and the mixture was subsequently polymerized at 65–70°C for 48 h.

In a typical preparation, the acrylated phosphonate derivative of glycerol (0.975 g) was dissolved in THF (10 mL) with vigorous stirring and to it was added a solution of uranyl nitrate hexahydrate (0.025 g), also dissolved in THF (5 mL). A yellow solution developed which was stirred for ca. 2 h, and later THF was slowly evaporated under a stream of nitrogen. The last traces of THF were removed under vacuum. A small amount of initiator (0.5 wt % AIBN) was mixed thoroughly with this viscous solution, which was flushed with nitrogen. The salt-containing solution of the acrylated monomer was polymerized at 65–70°C for ca. 48 h. A bright yellow resin, obtained by cutting the polymerization tube, was powdered and dried under vacuum at room temperature.

A serious drawback encountered with the bismuth halide is the inability to conduct polymerization at ambient temperature using curing agents, such as benzoyl peroxide–dimethyl-*p*-toluidine system and others, commonly employed for curing dental acrylic resins. This is due to complexation of bismuth bromide with the amine component of the system which hinders the polymerization reaction. This problem seems to be circumvented when the acrylated phosphonate esters are used; the phosphoryl moiety of the latter is a Lewis base and can probably compete with amines for complexing metal salts present in radiopaque composites. A slight discoloration of the composite containing bismuth bromide was observed in such a formulation. The acrylated phosphonate esters incorporating 1,3-dioxolane moieties can be effectively polymerized by photoirradiation.[27] It is well known that polymerization of the systems con-



Scheme 2. Reaction sequence depicting the synthesis of [2-(1'-bromomethyl)-4-hydroxymethyl]-1,3-dioxolane (IV), its phosphonylation through Arbuzov reaction to yield [(2-diethylphosphonomethyl)]-4-hydroxy-1,3-dioxolane (V), its methacrylation (VI), and polymerization (VII).

taining 1,3-dioxolane moieties can be initiated by employing 1,3-dioxolan-2-ylium salts formed by the abstraction of an active hydrogen atom present between two alkoxy groups in such cyclic acetals.[27b] The radicals generated from the cyclic acetals by means of photoirradiation are known to initiate the polymerization of vinyl compounds.

## RESULTS AND DISCUSSION

Anhydrous bismuth bromide and hydrated uranyl nitrate have been found to be soluble in a number of acrylated phosphonate esters containing 1,3-dioxane and 1,3-dioxolane moieties derived from glycerol, D-mannitol, D-sorbitol, pentaerythritol, and dipentaerythritol. The largest amounts of bismuth bromide (ca. 18 wt %) and uranyl nitrate hexahydrate (ca. 24 wt %) could be solubilized in the phosphonate esters derived from glycerol. These mixtures of metal salts and phosphonated monomers were polymerized (using AIBN) into homogeneous transparent glassy polymers, which can either be cut into different shapes or powdered. The bismuth derivatives were completely colorless; the uranyl mixtures were slightly yellow.

The ability of phosphonate derivatives to dissolve these inorganic salts is well documented.[28] Phosphonic acids and phosphonate esters are versatile complexing agents and are known to interact with a large number of transition and nontransition metal salts to form a variety of monomeric and polymeric complexes.[28] In most of these complexes, a coordination bond is formed between the phosphoryl oxygen and the metal component of a metal salt [$-C-P=O \rightarrow M$].

The relatively large fraction of the heavy metal salts that is miscible with the phosphonate esters reflects the strong interactions between the two species. Some of these complexes with monomers and their corresponding polymers relevant to this study have been qualitatively characterized with the aid of infrared spectroscopy and thermal analysis.

## Infrared Spectra and Thermal Analysis of Miscible Salt–Polymer Systems

The various acrylated phosphonate esters and their corresponding polymers exhibit strong bands at ca. 950, 1030, and 1250 $cm^{-1}$ which can be assigned to $\nu(P-O-CH_2)$, $\nu(P-O-Et)$, and $\nu(P=O)$ vibrations,[29] respectively. A strong band occurs at ca. 1720 $cm^{-1}$ due to $\nu(C=O)$ vibration of the ester group. In the infrared spectra of salt–polymer composites, the band assigned to $\nu(P=O)$ either shifts towards lower frequencies (ca. 30–40 $cm^{-1}$) or splits into two components appearing between 1180 and 1250 $cm^{-1}$. These shifts in $\nu(P=O)$ vibrations are consistent with the existence of strong interactions with metal salts as previously reported.[28] The carbonyl band $\nu(C=O)$ has also been found

TABLE I
Glass Transition Temperatures of Miscible Salt–Polyphosphonate Systems Containing Uranyl Nitrate and Bismuth Bromide[a]

| Designation | Metal salt (wt %) | Glass transition temp. $T_g$ (°C) |
|---|---|---|
| Polyglyphosphonate[b] | 0 | −38 |
| Polyglycidylphosph[c] | 0 | −36 |
| Polymanniphosph[d] | 0 | 3 |
| Polydienphosphonate[e] | 0 | 58 |
| Poly[$UO_2(NO_3)_2$–glycidylphosphonate] | 2.5 | 95 |
| Poly[$UO_2(NO_3)_2$–glyphosphonate] | 4.0 | 108 |
| Poly[$UO_2(NO_3)_2$–glyphosphonate] | 10.0 | 114 |
| Poly[$UO_2(NO_3)_2$–glyphosphonate] | 19.0 | 156 |
| Poly[$UO_2(NO_3)_2$–mannitolphosph] | 9.0 | 128 |
| Poly($BiBr_3$–glycidylphosph) | 4.5 | 95 |
| Poly($BiBr_3$–glycidylphosph) | 8.3 | 108 |
| Poly($BiBr_3$–glyphosphonate) | 9.0 | 114 |
| Poly($BiBr_3$–glyphosphonate | 11.0 | 115 |
| Poly($BiBr_3$–glyphosphonate) | 19.0 | 118 |
| Poly($BiBr_3$–mannitolphosph) | 15.0 | 108 |

[a] In this study uranyl nitrate hexahydrate and anhydrous bismuth bromide were used.

[b,c,d,e] Polymers derived from the monomers depicted in Figure 1 as (**1**), (**2**), (**3**), and (**5**), respectively.

to either split or broaden with the introduction of a salt in the polymer, similar to the observation made for the miscible uranyl nitrate–poly(methyl methacrylate) systems.[24] These results suggest that the metal salts are linked with poly(acrylated phosphonate ester)s through both phosphoryl and carbonyl groups. It is known that the oxygen atom of these groups is an electron donor forming, for example, a 1 : 2 (metal : ligand) adduct with uranyl nitrate.[28] The hydrated uranyl nitrate–polyphosphonate systems show additional bands at ca. 920 and 860 $cm^{-1}$ due to $\nu_{asym}(UO_2)$ and $\nu_{sym}(UO_2)$ vibrations of the uranyl moiety.[30] The bidentate coordination mode of the nitrate groups of uranyl nitrate hexahydrate also seems to be retained in its miscible systems with acrylated phosphonate polymers, as indicated by the appearance of two bands at ca. 1510 and 820 $cm^{-1}$, typical of the coordinated nitrate groups.[30]

Differential scanning calorimetry has been employed to determine the impact of salt on the glass transition temperature for the detection of the presence of free (crystalline) salt in the polymer matrix. Metal ions are known to have a profound effect on the thermal properties of polymers.[31] The incorporation of metal salts into the polymer matrix often results in elevation of the glass transition temperature. The $T_g$ values of the acrylated phosphonate ester polymers and their complexes with metal salts are listed in Table I. Although very low $T_g$ values are observed for some polymers, e.g., the $T_g$ of acrylated phosphonate derivative of glycerol is ca. −36°C (Fig. 2), the values recorded for the relevant polymer–salt systems are relatively very high, in the 95–158°C range (Figs. 3 and 4). A plot of glass transition temperatures of salt-containing polymers vs.

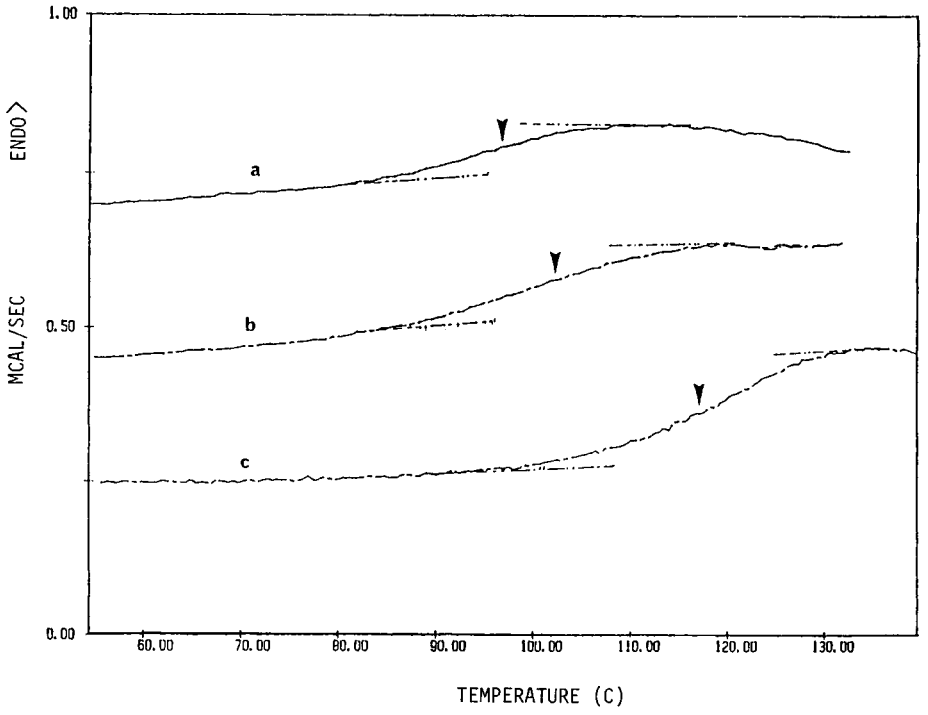



Fig. 3. Differential scanning calorimetry thermograms of acrylated polyphosphonate, derivatives of glycerol 1,3-dioxane moieties compounded with $BiBr_3$: (a) 4.5 wt %; (b) 8.3 wt %; (c) 19 wt %.

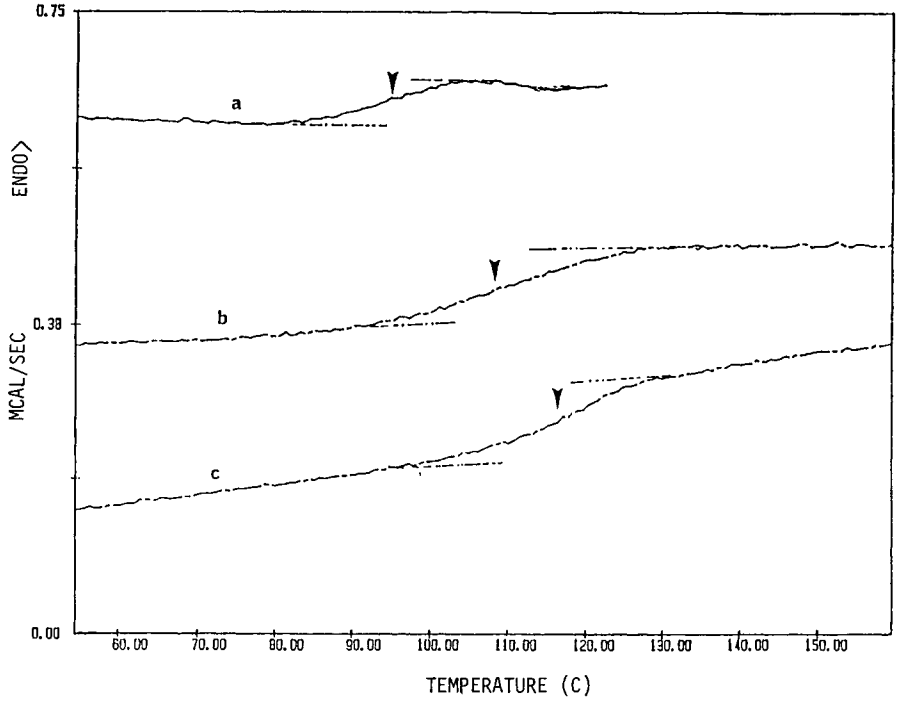



Fig. 4. Differential scanning calorimetry thermograms of acrylated polyphosphonate-uranyl nitrate hexahydrate complexes: (a) $UO_2(NO_3)_2$ 1.4 wt %; (b) 2.5 wt %; (c) 10.0 wt %.

concentration of uranyl nitrate and bismuth bromide in the acrylated phosphonate derivative of glycerol (**1**) is depicted in Figure 5. A similar trend has also been reported for miscible uranyl nitrate hexahydrate- and other metal salts in poly(methyl methacrylate)[24] and other salt-polymer systems.[32] The large increase in $T_g$ of salt-polymer systems suggests strong interactions between a salt and the polymer, leading to reduction in the free volume and segmental mobility of the systems; this is also indicated by the progressive increase in the $T_g$ with increase in salt content. Quantitative evaluation of this aspect of miscible salt-polymer systems is a subject for further investigation. It appears that the presence of hydrated uranyl nitrate indeed causes transient crosslinking through its interactions with two acrylated phosphonate ester's moieties simultaneously.[28,33] Inspection of some of the DSC traces of the miscible salt-polymer systems revealed that no melt endotherm for bismuth bromide or uranyl nitrate hexahydrate exists (melting at ca. 218 and 60.2°C, respectively), implying that neither prevail as free crystal in the polymer-salt systems.

## Radiographic Evaluation

The absorption of X-rays is directly related to the atomic number of atoms present in a material. The absorption coefficient $\mu$ of the material can be expressed as[34]

$$\mu = k\lambda^3 Z^4 + 0.2$$

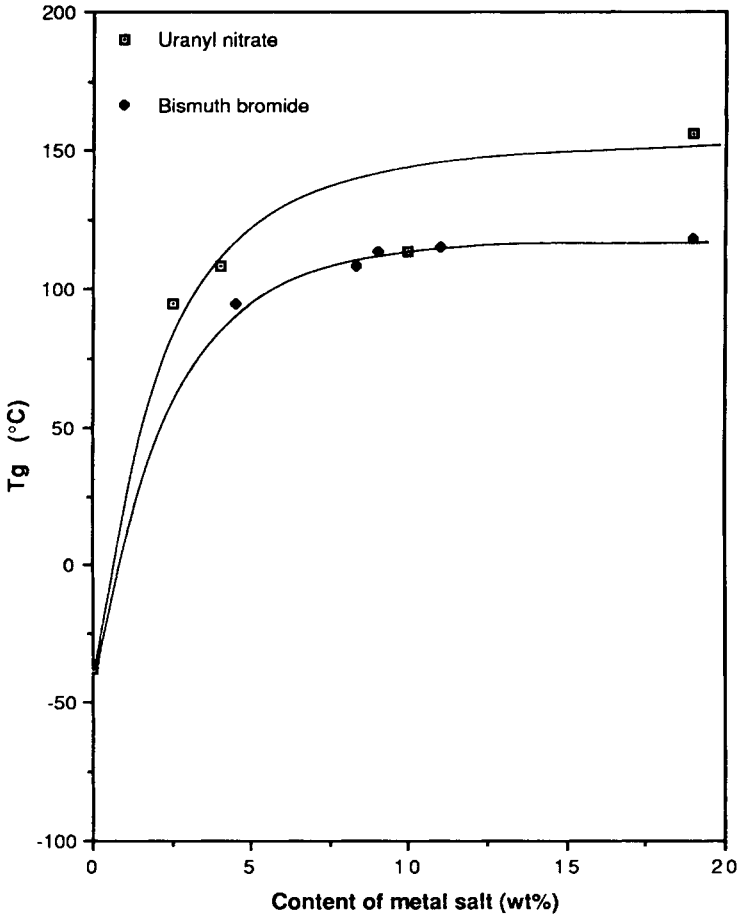



Fig. 5. Plots of glass transition temperature vs. concentration of metal salts in polyacrylated phosphonate derivative of glycerol.

where $k$ is a constant, $\lambda$ is the wavelength, $Z$ the atomic number, and 0.2 is the average coefficient of scattering. Therefore, X-ray absorption of the phosphonylated polymers should increase significantly with the atomic number and concentration of the heavy metal salts they are bound with. Bismuth and uranium, and to a much lesser extent bromine, are considered good absorbers of X-rays especially in the dose range administrated in medical diagnosis.[5] Positive radiographs of transparent 1-mm-thick pellets, prepared with the phosphonylated polymers containing varied amounts of salts described above, are shown in Figures 6–9. Specimens with as low as 3.5 wt % of uranyl nitrate could be easily detected, as shown in Figure 9. These results can be compared to the data recently obtained from this laboratory for the hydrated uranyl nitrate–PMMA miscible systems containing up to 30 wt % of the metal salt,[22,24] and those obtained for bismuth bromide–PMMA and barium bromide dihydrate–MG22 systems [where MG22 is a glyme methacrylate of the general formula $CH_2 = C(CH_3)COO(CH_2CH_2O)_nCH_3$, where $n = 22$].[21,23] It has been established during these studies that the radiopacifying capacity of these salts indeed

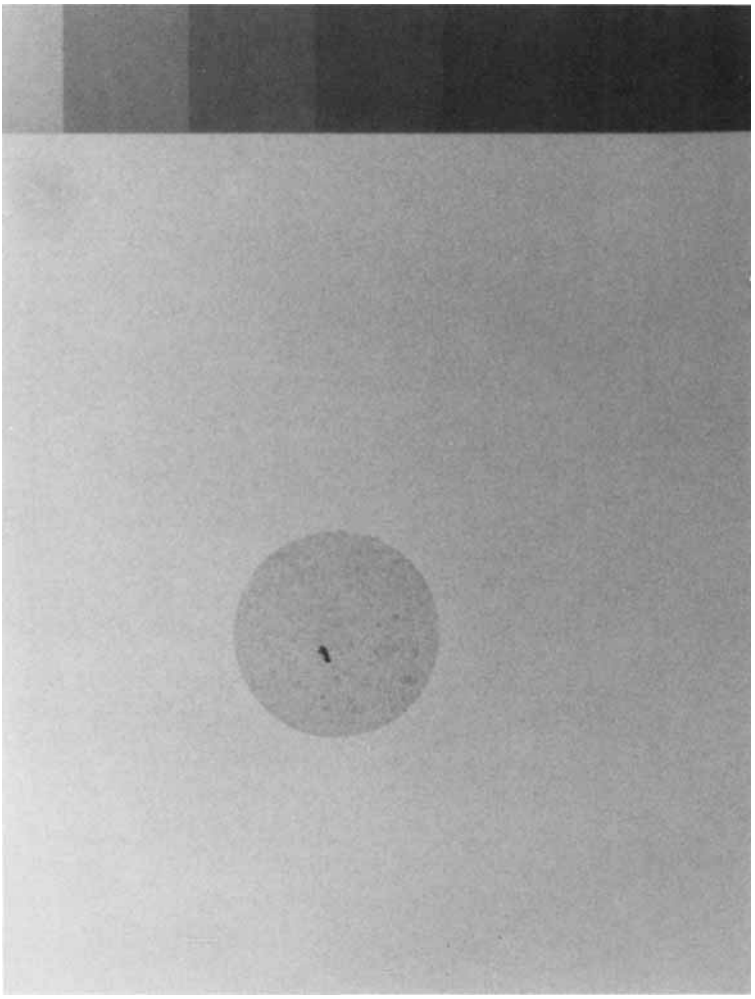


Fig. 6. Positive radiograph of a bulk-polymerized $BiBr_3$-polyglycerphosphonate complex containing ca. 12 wt % salt, along with that of an aluminum stepwedge bar (steps 1–7 mm).

follows the order of their increasing atomic number. In the present systems, phosphonylated-salt, uranyl nitrate hexahydrate (11 wt %), bismuth bromide (14 wt %), and barium bromide dihydrate (19 wt %), each needed to impart radiopacity to phosphonylated-salt systems equivalent to that of 1-mm-thick aluminum.

The samples shown in Figures 6–9 display a different level of radiopacity, but one aspect that is common to all preparations is the uniformity of absorption. One of the goals set up and fulfilled during the present study was for all the samples to display uniform shade as a result of an even distribution of the salt in the polymer. Conversely, the heterogeneous mixtures of the polymer with radiopacifying agents such as $BaSO_4$ do not display a uniform micrograph at low loading levels (10–15 wt %), and at higher loading the mixtures are not only optically opaque, but also display substantial deterioration of mechanical properties.[21-23]

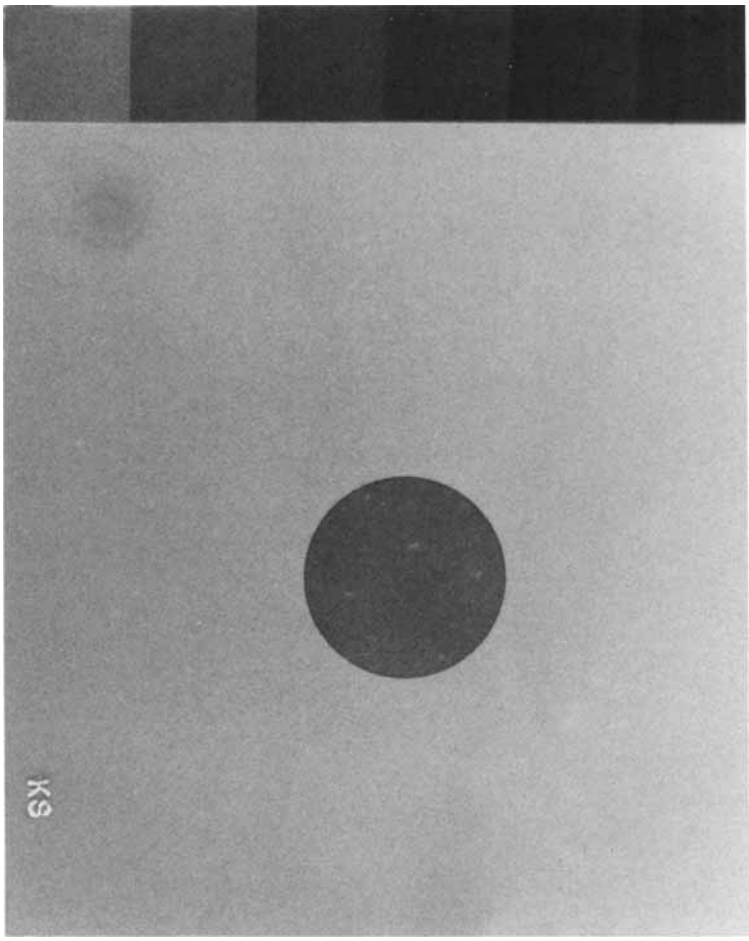



Fig. 7. Positive radiograph of a bulk-polymerized polyglycerphosphonate–uranyl hexahydrate miscible system (ca. 19 wt % salt), along with that of an aluminum stepwedge bar (1–7 mm).

The salt–polymer systems containing bismuth bromide display a tendency to discolor upon long exposure to aqueous solution and become opaque (presumably due to the formation of BiOBr)[19]; however, any loss in radiopacity of these composites has not been detected.[23] Such discoloration has not been found to occur in uranyl nitrate hydrate–polymer systems which remain transparent on prolonged contact with water.

## Preliminary Evaluation of Adhesion Promoting Properties of Acrylated Phosphonates

The acrylated phosphonate esters, employed in the preparation of the radiopaque composites reported herein, have also been evaluated for their role as adhesion promoters, especially for hard dental tissues such as dentin. Most of currently available composites, sealants, and bonding agents containing bis-GMA and other dimethacrylates inherently lack adhesion to enamel or den-

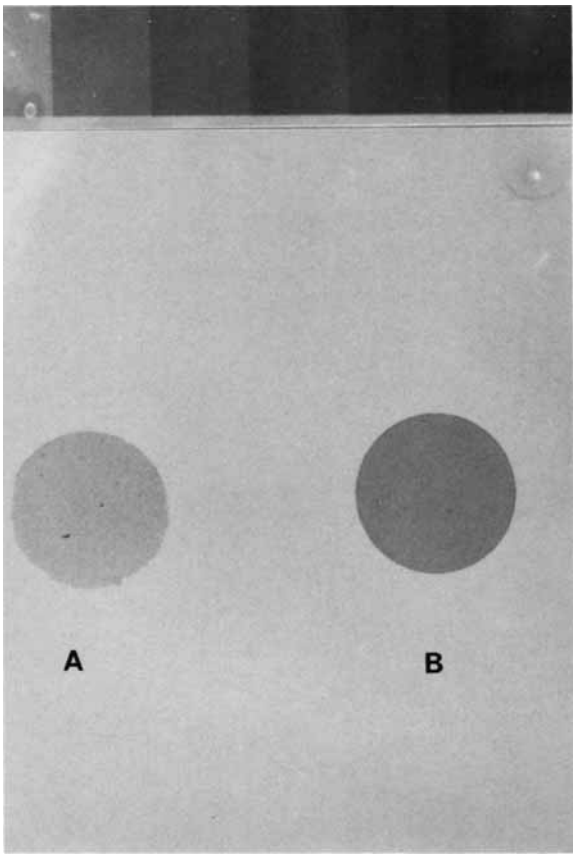



Fig. 8. Positive radiographs of uranyl nitrate–polymannitolphosphonate (ca. 10 wt % salt) (A) and bismuth bromide–polyglycerphosphonate (ca. 15 wt % salt) (B) systems, relative to an aluminum stepwedge bar.

tin.[33,35,36] These resins can be effectively bonded to acid-etched enamel surfaces.[37] However, the use of the acid-etch technique is not recommended on vital dentin as it results in poor adhesion.[38,39] The present studies have been directed toward dentin, because of a need for an effective adhesion promoter-containing composite that would eliminate the undesirable practice of mechanical cutting of dentinal tissues, often employed for retention of restorations, and which would improve treatment of cervical erosions, root caries, and other similar disorders.[37] Some of these acrylated phosphonate monomers have been found to be effective adhesion-promoting agents when compounded with poly(methyl methacrylate) or its copolymers with bis-GMA and organic filler along with a polymerization initiator for vinylic adhesion promoters.[35,36] Adhesion tests were conducted by Caulk/Dentsply, Inc., using the adhesion promoter derivatives (shown in Fig. 1) mixed with standard dental composite resins (such as bis-GMA derivatives) on dentin surface. The composites were applied to well-cleaned, sanded, and preteeth treated with the monomers shown in Figure 1. The monomers were deposited on the clean dentin surface of the teeth (layer of ca. 1 $\mu$m) and cured through photoirradiation techniques using a visible light source (visible light

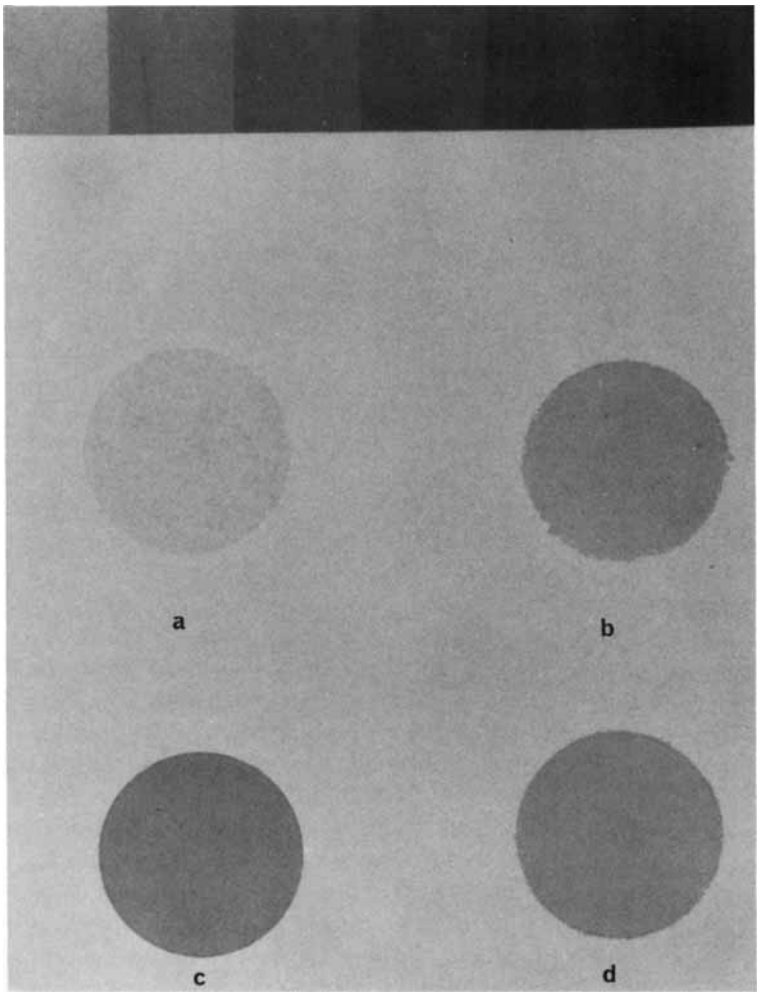



Fig. 9. Positive radiographs of 1 mm thick pellets of bulk-polymerized uranyl nitrate and bismuth bromide–polymer systems: (a) uranyl nitrate–polyglycerphosphonate (3.5 wt % salt), (b) uranyl nitrate–PMMA (16 wt % salt), (c) uranyl nitrate–PMMA (24 wt % salt), and (d) bismuth bromide–PMMA (30 wt % salt), along with that of an aluminum stepwedge bar (steps from 1 to 7 mm).

polymerization unit, Prisma-Lite, Model 1123 of Caulk/Dentsply). The cured specimens were placed in distilled water at 30°C for 24 h and some were thermocycled in water, between 4 and 54°C for 540 cycles (1 min in each temperature) to determine the effect of thermal stress and hydrolytic stability prior to debonding. An Instron universal testing machine was employed to apply a comparative shear force to remove the bonded composite from the teeth. The shear strength values of a bond, formed between the dentin part of teeth for various composites containing different monomers, have been found to be in the range of 1.10–7.48 MPa (Table II). The comparative data shown in the table suggest that the bond strength increases with increasing number of vinylic groups in these acrylated phosphonates. This supports the claim that mono-

TABLE II
Comparative Bond Strength between Various Resin Composites Containing Acrylated Phosphonates and Dentin

| Sample designation | Monomer formula (cf. Fig. 1) | Average bond strength[a] (MPa) |
|---|---|---|
| MP-12 | **2** | 2.1 (0.42) |
| MP-14 | **1** | 1.8 (0.17) |
| MP-24 | **6** | 2.2 (0.45) |
| MP-25 | **5** | 7.5 (0.53) |
| MP-41 | **3** | 1.2 (0.64) |
| MP-43 | **4** | 1.8 (0.77) |

[a] Bond strengths were measured through shear strength method. In each case, five samples were evaluated. The values in parentheses designate standard deviation.

phosphates containing more than one terminal vinylic group act as effective adhesion promoting agents for hard tissues.[39] Among the various derivatives reported herein, the highest bond strength value was obtained for composites with the acrylated dipentaerythritol derivative, which contains two terminal vinylic groups along with two phosphonate ester groups (Fig. 1). The samples prepared with derivatives of D-sorbitol and D-mannitol which contain less accessible terminal vinylic groups exhibited lower bond strength values. Several other composites containing phosphoric, phosphonic, or phosphinic acid and their corresponding ester derivatives were reported to form strong bonds with hard tissues.[26,35,39,40] Among these compounds, the acids have been shown to mediate stronger bonds than esters which may be attributed to their dual bonding capacity (i.e., bonding to surface via coordinative and ionic bonds). The exact bonding mechanism, however, is still the subject of lively debate.[35,36] As adhesion promoters to acrylic polymer in medical applications, it is believed that the phosphoryl groups, of acrylated phosphonate monomers and polymers, form coordination bonds with calcium ions present in hydroxyapatite fraction of dentin and enamel, and their acrylic moiety copolymerizes with comonomers present in the polymer matrix.[36] Thus, the phosphonate moieties which bind metal salts also promote adhesion of the material to hard tissue such as dentin and enamel. It may be emphasized here that the phosphonates have a distinct advantage over phosphate derivatives because they contain a hydrolytically stable carbon–phosphorus (C—P) bond. Further discussion on the adhesive property of these compounds will be published elsewhere.[41]

Earlier studies on $BiBr_3$–PMMA composites indicate that this composite is nonmutagenic, while their toxicity index has been found to be lower than other formulations commonly used in dentistry.[22] Biocompatibility evaluations of bismuth bromide and uranyl nitrate–poly(acrylated phosphonate)s are underway.

## CONCLUSIONS

This study was designed to explore the possibility of producing monomeric derivatives of acrylated phosphonate esters which can interact with heavy metal

salts to produce radiopaque polymers. Radiopaque polymer systems have been obtained by combining chelating acrylated phosphonate ester monomers derived from various polyols such as glycerol, D-mannitol, D-sorbitol, pentaerythritol, and dipentaerythritol with heavy metal salts such as bismuth bromide and uranyl nitrate hexahydrate. These salt–monomer systems yield radiopaque materials which display uniform image in radiographic analysis. The materials seem to possess inherent potential capacity to effectively adhere to hard tissues and lend themselves to ambient curing temperature. These properties might be useful in various biomedical applications and others, especially when nondestructive methods for detection of plastics and their integrity are required.

Although thermal analysis indicates solidification and stiffening of the acrylated phosphonate with loading of the salts, mechanical properties as a function of salt concentration have yet to be determined. This and other relevant studies concerning these materials are underway.

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## References

1. A. S. Hoffman, in *Polymeric Biomaterials,* E. Piskin and A. S. Hoffman, Eds., Nijhoff, Boston, 1986, p. 1.

2. (a) C. Migliaresi and L. Nicolais, in *Polymeric Biomaterials,* E. Piskin and A. S. Hoffman, Eds., Nijhoff, Boston, 1986, p. 79; (b) D. J. Lyman, in *Polymers in Medicine and Surgery,* R. L. Kronental, Z. Osci and E. Martin, Eds., Plenum, New York, 1975.

3. J. A. von Fraunhofer (Ed.), *Scientific Aspects of Dental Materials,* Butterworths, Boston, 1975.

4. G. M. Brauer and J. M. Antonucci, in *Encyclopedia of Polymer Science and Engineering,* 2nd ed., J. I. Kroschwitz, Ed., Wiley, New York, 1986, p. 698.

5. P. G. Stecher (Ed.), *New Dental Materials,* Noyes Data Corp., Park Ridge, NJ, 1980.

6. (a) ISO: DP4049(1985) Dental Resin-based Restorative Materials, International Standards Organization (Draft Proposal), Clause 6.10; (b) G. M. Brauer, *J. Am. Dent. Assoc.,* **102,** 347 (1981); (c) H. C. Alderman, *J. Forensic Sci.,* **33,** 389 (1988); (d) B. M. Sherman and J. S. Karliner, *New Engl. J. Med.,* **279,** 1275 (1968).

7. (a) H. H. Chandler, R. L. Bowen, and G. C. Paffenbarger, *J. Biomed. Mater. Res.,* **5,** 245 (1971); (b) G. C. Paffenbarger and N. W. Rupp, *Int. Dent. J.,* **24,** 1 (1974).

8. J. E. Primack, *J. Prosth. Dent.,* **28,** 363 (1972).

9. Z. M. Abou-Tabl, D. C. Tidy, and E. C. Combe, *Br. Dent. J.,* **147,** 187 (1979).

10. W. D. Cook, *Aust. Dent. J.,* **26,** 105 (1981).

11. (a) R. L. Bowen and G. W. Cleek, *J. Dent. Res.,* **48,** 79 (1969); (b) H. H. Chandler, R. L. Bowen, G. C. Paffenbarger, and A. L. Mullineaux, *J. Am. Dent. Assoc.,* **80,** 935 (1970); (c) J. A. Barton, Jr., C. C. Burns, H. H. Chandler, and R. L. Bowen, *J. Dent. Res.,* **52,** 731 (1973); (d) H. H. Chandler, R. L. Bowen, G. C. Paffenbarger, and A. L. Mullineaux, *J. Dent. Res.,* **52,** 1128 (1973).

12. O. E. Omer, N. H. F. Wilson, and D. C. Watts, *J. Dent.,* **14,** 178 (1986).

13. A. B. Tveit and I. Espelid, *Dent. Mater.,* **2,** 159 (1986).

14. (a) S. Rogers, U.S. Pat. 3,808,170 (1974); (b) D. C. Watts, *J. Dent.,* **15,** 38 (1987); (c) F. Lutz, R. W. Phillips, J. F. Roulet, and J. C. Setcos, *J. Dent. Res.,* **63,** 914 (1984); (d) E. D. Dietz, U.S. Pat. 3,975,203 (1976); (e) A. Jurecic, U.S. Pat. 3,971,754 (1976).

15. (a) H. H. Chandler, R. L. Bowen, and G. C. Paffenbarger, *J. Biomed. Mater. Res.,* **5,** 254, 335, 359 (1971); (b) C. P. Mabie and D. L. Memis, *J. Biomed. Mat. Res.,* **12,** 435 (1978).

16. (a) K. W. M. Davy and B. E. Causton, *J. Dent.,* **10,** 254 (1982); (b) E. J. Molnar, U.S. Pat. 3,715,331 (1973).

17. E. C. Combe, *Br. Dent. J.*, **127,** 355 (1969).

18. D. Horak, M. Metalova, F. Svec, J. Drobnik, J. Kalal, M. Borovicka, A. A. Adamyan, O. S. Voronkava, and K. Z. Gumargalieva, *Biomaterials,* **8,** 142 (1987).

19. E. C. Combe, *J. Dent.*, **1,** 93 (1972).

20. E. C. Combe, *Dent. Practnr. Dent. Rec.*, **22,** 51 (1971).

21. D. W. Xia, R. Silberman, I. Cabasso, and J. Smid, *Am. Chem. Soc. Div. Polym. Sci. Polym. Prepr.*, **26**(1), 72 (1985).

22. J. Smid, I. Cabasso, H. R. Rawls, A. Obligin, Y. Delaviz, S. K. Sahni, and Z-X. Zhang, *Makromol. Chem. Rapid. Commun.*, **8,** 543 (1987).

23. (a) I. Cabasso, A. S. Obligin, J. Smid, H. R. Rawls, and B. F. Zimmerman, *J. Dent. Res. Suppl.*, **66,** 169 (1987), Abst. 176; (b) J. Smid, I. Cabasso, A. Obligin, S. K. Sahni, H. R. Rawls, and B. F. Zimmerman, *Am. Chem. Soc. Div. Polym. Sci. Polym. Prepr.*, **28**(1), 133 (1987).

24. I. Cabasso, J. Smid, and S. K. Sahni, *J. Appl. Polym. Sci.*, **38,** 1653 (1989).

25. (a) I. Cabasso, D. Vofsi, and S. K. Sahni, *J. Polym. Sci. Polym. Chem. Ed.*, **26,** 2997 (1988); (b) S. K. Sahni and I. Cabasso, *J. Polym. Sci. Polym. Chem. Ed.*, **26,** 3251 (1988).

26. (a) J. Yamauchi, E. Mashuhara, N. Nakabayashi, K. Shibatani, and T. Wada, U.S. Pat. 4,368,043 (1983); (b) E. P. Farley, R. L. Jones, and M. Anbar, *J. Dent. Res.*, **56,** 943 (1977).

27. (a) T. Ouchi, S. Nakamura, M. Hamada, and M. Oiwa, *J. Polym. Sci. Polym. Chem. Ed.*, **13,** 455 (1975); (b) M. Gibas, *Makromol. Chem.*, **188,** 675 (1987).

28. (a) N. M. Karayannis, C. M. Mikulski, and L. L. Pytlewski, *Inorg. Chim. Acta Rev.*, **5,** 69 (1971); (b) M. W. G. de Bolster, *Topics Phosphorus Chem.*, **11,** 69 (1983).

29. D. E. C. Corbridge, *Topics Phosphorus Chem.*, **5,** 235 (1969).

30. (a) J. I. Bullock, *J. Inorg. Nucl. Chem.*, **29,** 2257 (1967); (b) C. C. Addison and N. Logan, *Adv. Inorg. Radiochem.*, **6,** 72 (1964).

31. (a) A. Eisenberg, *Macromolecules,* **4,** 125 (1971); (b) A. Eisenberg (Ed.), *Ions in Polymers,* American Chemical Society, Washington, DC, 1980.

32. (a) K. F. Wissbrun and M. J. Hannon, *J. Polym. Sci. Polym. Phys. Ed.*, **13,** 113, 223 (1975); (b) M. S. Jacovic, I. Perovic, W. J. Macknight, and R. W. Lenz, *J. Appl. Polym. Sci.*, **35,** 903 (1988).

33. S. K. Sahni and I. Cabasso, *J. Biomed. Mat. Res.*, to appear.

34. J. O. Hoppe, in *Medicinal Chemistry,* E. C. Camaigne and W. H. Hartung, Eds., Wiley, New York, 1963, Vol. 6, p. 290.

35. (a) N. Nakabayashi, *Int. Dent. J.*, **35,** 145 (1985); (b) N. Nakabayashi, *CRC Crit. Rev. Biocompat.*, **1,** 25 (1984) and references therein; (c) R. L. Bowen, *Int. Dent. J.*, **35,** 155 (1985); (d) R. L. Bowen, E. N. Cobb, and J. E. Rapson, *J. Dent. Res.*, **61,** 1070 (1982).

36. (a) G. Vanherle and D. C. Smith (Eds.), *Posterior Composite Resins Dental Restorative Materials,* Peter Szulc Publishing, The Netherlands (1985) and references therein; (b) E. C. Munksgaard and E. Asmussen, in *Dentin and Dentin Reactions in the Oral Cavity,* A. Thylstrup, S. A. Leach, and V. Qvist, Eds., IRL Press, Oxford, 1988, p. 209.

37. R. L. Bowen, E. N. Cobb, and L. E. Setz, *Dentistry,* **2,** 11 (1982) and references therein.

38. (a) M. G. Buonocore, *J. Dent. Res.*, **34,** 849 (1955); (b) H. R. Laswell, D. A. Welk, and J. W. Regenos, *J. Am. Dent. Assoc.*, **82,** 558 (1971).

39. R. W. Billington, G. R. Blackwell, and J. E. Prodger, U.S. Pat. 4,514,342 (1985).

40. (a) K. Shibatani, I. Omura, and J. Yamauchi, U.S. Pat. 4,222,780 (1980); (b) M. Higo, Y. Kikuchi, S. Kitoh, H. Shinya, S. Suzuki, and H. Toda, Ger. Pat. DE 3150285 A1 (1981).

41. S. K. Sahni and I. Cabasso, *J. Biomed. Mat. Res.*, **24,** 705 (1990).

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