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(54) Title: DENTAL COMPOSITIONS CONTAINING NANOZIRCONIA FILLERS

(57) Abstract: The present invention features ionomer compositions containing nanozirconia fillers. The compositions can be used in a variety of dental and orthodontic applications, for example, as adhesives, cements, restoratives, coatings and sealants.

## DENTAL COMPOSITIONS CONTAINING NANOZIRCONIA FILLERS

### Field of the Invention

5 The present invention relates to hardenable dental and orthodontic compositions filled with zirconia nanoparticles. More specifically, the invention relates to ionomer and resin modified ionomer compositions containing nanozirconia fillers. The compositions can be used in a variety of applications, for example, as adhesives, cements, restoratives, coatings, and sealants.

### Background

10 The restoration of decayed dental structures including caries, decayed dentin or decayed enamel, is often accomplished by the sequential application of a dental adhesive and then a dental material (e.g., a restorative material) to the relevant dental structures. Similar compositions are used in the bonding of orthodontic appliances (generally utilizing an orthodontic adhesive) to a dental structure. Often  
15 various pretreatment processes are used to promote the bonding of adhesives to dentin or enamel. Typically, such pretreatment steps include etching with, for example, inorganic or organic acids, followed by priming to improve the bonding between the tooth structure and the overlying adhesive.

20 A variety of dental and orthodontic adhesives, cements, and restoratives are currently available. Compositions including fluoroaluminosilicate glass fillers (also known as glass ionomer or "GI" compositions) are among the most widely used types of dental materials. These compositions have a broad range of applications such as filling and restoration of carious lesions; cementing of, for example, a  
25 crown, an inlay, a bridge, or an orthodontic band; lining of cavity; core construction; and pit and fissure sealing.

There are currently two major classes of glass ionomers. The first class, known as conventional glass ionomers, generally contains as main ingredients a homopolymer or copolymer of an  $\alpha,\beta$ -unsaturated carboxylic acid, a

fluoroaluminosilicate ("FAS") glass, water, and optionally a chelating agent such as tartaric acid. These conventional glass ionomers typically are supplied in powder/liquid formulations that are mixed just before use. The mixture undergoes self-hardening in the dark due to an ionic acid-base reaction between the acidic repeating units of the polycarboxylic acid and cations leached from the basic glass.

The second major class of glass ionomers is known as hybrid glass ionomer or resin-modified glass ionomers ("RMGI"). Like a conventional glass ionomer, an RMGI employs an FAS glass. An RMGI also contains a homopolymer or copolymer of an  $\alpha,\beta$ -unsaturated carboxylic acid, an FAS glass, and water; however, the organic portion of an RMGI is different. In one type of RMGI, the polyacid is modified to replace or end-cap some of the acidic repeating units with pendant curable groups and a photoinitiator is added to provide a second cure mechanism. Acrylate or methacrylate groups are typically employed as the pendant curable group. In another type of RMGI, the composition includes a polycarboxylic acid, an acrylate or methacrylate-functional monomer or polymer, and a photoinitiator. The polyacid may optionally be modified to replace or end-cap some of the acidic repeating units with pendant curable groups. A redox or other chemical cure system may be used instead of or in addition to a photoinitiator system. RMGI compositions are usually formulated as powder/liquid or paste/paste systems, and contain water as mixed and applied. They may partially or fully harden in the dark due to the ionic reaction between the acidic repeating units of the polycarboxylic acid and cations leached from the glass, and commercial RMGI products typically also cure on exposure of the cement to light from a dental curing lamp.

There are many important benefits provided by glass ionomer compositions. For example, fluoride release from glass ionomers tends to be higher than from other classes of dental compositions such as metal oxide cements, compomer cements, or fluoridated composites, and thus glass ionomers are believed to provide enhanced cariostatic protection. Another advantage of glass ionomer materials is

the very good clinical adhesion of such cements to tooth structure, thus providing highly retentive restorations. Since conventional glass ionomers do not need an external curing initiation mode, they can generally be placed in bulk as a filling material in deep restorations, without requiring layering.

5           One of the drawbacks of conventional glass ionomers is that these compositions are somewhat technique sensitive when mixed by hand. They are typically prepared from a powder component and a liquid component, thus requiring weighing and mixing operations prior to application. The accuracy of such operations depends in part on operator skill and competency. When mixed by  
10 hand, the powder component and the liquid component are usually mixed on paper with a spatula. The mixing operation must be carried out within a short period of time, and a skilled technique is needed in order for the material to fully exhibit the desired characteristics (i.e., the performance of the cement can depend on the mixture ratio and the manner and thoroughness of mixing). Alternatively some of  
15 these inconveniences and technique sensitivities have been improved by utilization of powder liquid capsule dispensing systems that contain the proper proportion of the powder and liquid components. While capsules provide proper proportions of the powder and liquid components, they still require a capsule activation step to combine the two components followed by mechanical mixing in a dental triturator

20           Conventional glass ionomers may also be quite brittle as evidenced by their relatively low flexural strength. Thus restorations made from conventional glass ionomers tend to be more prone to fracture in load bearing indications. In addition, glass ionomers are often characterized by high visual opacity (i.e., cloudiness), especially when they come into contact with water at the initial stage of hardening,  
25 resulting in relatively poor aesthetics.

Cured RMGIs typically have increased strength properties (e.g., flexural strength), are less prone to mechanical fracture than conventional glass ionomers, and typically require a primer or conditioner for adequate tooth adhesion.

### Summary

The present invention features stable ionomer compositions containing nanozirconia fillers that provide the compositions with improved properties over previous ionomer compositions. In particular, the inclusion of one or more nanozirconia fillers provides ionomer systems that are optically translucent and radiopaque. The nanozirconia is surface modified with silanes to aid in the incorporation of the nanzirconia into ionomer compositions, which generally contain a polyacid that might otherwise interact with the nanozirconia causing coagulation or aggregation resulting in undesired visual opacity.

Accordingly, in one aspect, the present invention features a hardenable dental composition comprising a polyacid; an acid-reactive filler; a nanozirconia filler having a plurality of silane-containing molecules attached onto the outer surface of the zirconia particles; and water. In one embodiment, the composition further comprises a polymerizable component. Generally, the polymerizable component is an ethylenically unsaturated compound, optionally with acid functionality.

The polyacid component of the composition typically comprises a polymer having a plurality of acidic repeating groups. The polymer may be substantially free of polymerizable groups, or alternatively it may comprise a plurality of polymerizable groups.

The acid-reactive filler is generally selected from metal oxides, glasses, metal salts, and combinations thereof. Typically, the acid-reactive filler comprises an FAS glass. Traditionally, ionomer compositions have used reactive glass to impart radiopacity. Incorporation of nanozirconia into the composition may allow for the formulation of radiopaque, optically translucent ionomer compositions while using less acid-reactive filler than previous GI and RMGI compositions. Accordingly, in one embodiment, the composition of the invention comprises less than 50 percent by weight acid-reactive filler, typically an FAS glass.

In another embodiment of the invention, the acid-reactive filler comprises an oxyfluoride material, which is typically nanostructured, e.g., provided in the form of nanoparticles. Generally, the acid-reactive oxyfluoride material is non-fused and includes at least one trivalent metal (e.g., aluminum, lanthanum, etc.), oxygen, a  
5 fluorine, and at least one alkaline earth metal (e.g. strontium, calcium, barium, etc.). The oxyfluoride material may be in the form of a coating on particles or nanoparticles, such as metal oxide particles (e.g., silica).

The compositions of the invention may also include one or more optional additives, such as, for example, other fillers, pyrogenic fillers, fluoride sources,  
10 whitening agents, anticaries agents (e.g., xylitol), remineralizing agents (e.g., calcium phosphate compounds), enzymes, breath fresheners, anesthetics, clotting agents, acid neutralizers, chemotherapeutic agents, immune response modifiers, medicaments, indicators, dyes, pigments, wetting agents, tartaric acid, chelating agents, surfactants, buffering agents, viscosity modifiers, thixotropes, polyols,  
15 antimicrobial agents, anti-inflammatory agents, antifungal agents, stabilizers, agents for treating xerostomia, desensitizers, and combinations thereof.

The compositions of the invention may further include a photoinitiator system and/or a redox cure system.

Additionally, the compositions may be provided in the form of a multi-part  
20 system in which the various components are divided into two or more separate parts. Typically, the composition is a two-part system, such as a paste-paste composition, a paste-liquid composition, a paste-powder composition, or a powder-liquid composition.

As discussed above, one of the features of the present invention is that it  
25 provides a radiopaque, optically translucent ionomer composition while using less acid-reactive filler than conventional glass ionomers. This facilitates the preparation of a two-part, paste-paste composition, which is generally desirable because of the ease of dispensing and mixing of such a system compared to, for example, a powder-liquid system.

Compositions according to the invention are useful in a variety of dental and orthodontic applications, including in dental restoratives, dental adhesives, dental cements, cavity liners, orthodontic adhesives, dental sealants, and dental coatings. The compositions may be used to prepare a dental article by hardening to form, for example, dental mill blanks, dental crowns, dental fillings, dental prostheses, and orthodontic devices.

The ionomer compositions of the invention exhibit good aesthetics, low visual opacity (generally no more than about 0.50 upon hardening, as determined by the Visual Opacity (MacBeth Values) Test Method described herein), radiopacity, durability, excellent polish, polish retention, and wear properties, and good physical properties including mechanical strengths, e.g., flexural strength, and adhesive strength to tooth structures. Furthermore, the compositions may also provide adhesion to both dentin and enamel without the need for primers, etchants, or preconditioners. In addition, the invention provides for easy mixing and convenient dispensing options made possible by formulation of a paste-paste composition.

Other features and advantages of the present invention will be apparent from the following detailed description thereof, and from the claims.

### **Definitions**

By "hardenable" is meant that the composition can be cured or solidified, e.g. by heating, chemical cross-linking, radiation-induced polymerization or crosslinking, or the like.

By "filler" is meant a particulate material suitable for use in the oral environment. Dental fillers generally have an average particle size of at most 100 micrometers.

By "nanozirconia filler" is meant a filler comprising zirconia nanoparticles. Typically these nanozirconia fillers comprise non-pyrogenic nanoparticles.

By "paste" is meant a soft, viscous mass of solids dispersed in a liquid.

By “acid-reactive filler” is meant a filler that chemically reacts in the presence of an acidic component.

By “oxyfluoride” is meant a material in which atoms of oxygen and fluorine are bonded to the same atom (e.g., aluminum in an aluminum oxyfluoride).

5 Generally, at least 50% of the fluorine atoms are bonded to an atom bearing an oxygen atom in an oxyfluoride material.

By “nanostructured” is meant a material in a form having at least one dimension that is, on average, at most 200 nanometers (e.g., nanosized particles).

Thus, nanostructured materials refer to materials including, for example,  
10 nanoparticles as defined herein below; aggregates of nanoparticles; materials coated on particles, wherein the coatings have an average thickness of at most 200 nanometers; materials coated on aggregates of particles, wherein the coatings have an average thickness of at most 200 nanometers; materials infiltrated in porous structures having an average pore size of at most 200 nanometers; and combinations  
15 thereof. Porous structures include, for example, porous particles, porous aggregates of particles, porous coatings, and combinations thereof.

As used herein “nanoparticles” is used synonymously with “nanosized particles,” and refers to particles having an average size of at most 200 nanometers.

As used herein for a spherical particle, “size” refers to the diameter of the particle.

20 As used herein for a non-spherical particle, “size” refers to the longest dimension of the particle.

By “nanocluster” is meant an association of nanoparticles drawn together by relatively weak intermolecular forces that cause them to clump together, i.e. to aggregate. Typically, nanoclusters have an average size of at most 10 micrometers.

25 The term “ethylenically unsaturated compounds with acid functionality” is meant to include monomers, oligomers, and polymers having ethylenic unsaturation and acid and/or acid-precursor functionality. Acid-precursor functionalities include, for example, anhydrides, acid halides, and pyrophosphates.

By "dental compositions and dental articles" is meant to include orthodontic compositions (e.g., orthodontic adhesives) and orthodontic devices (e.g., orthodontic appliances such as retainers, night guards, brackets, buccal tubes, bands, cleats, buttons, lingual retainers, bite openers, positioners, and the like).

5

### Detailed Description

The present invention is directed to dental (including orthodontic) compositions, specifically ionomer compositions, e.g., glass ionomer compositions, containing one or more nanozirconia fillers. These hardenable compositions further comprise a polyacid, an acid-reactive filler, an optional polymerizable component, and water. The incorporation of one or more nanozirconia fillers into the composition provides for improved properties, including enhanced aesthetics (e.g., low visual opacity), polish retention, and radiopacity as compared to previously known glass ionomer compositions.

10

#### POLYMERIZABLE COMPONENT

As mentioned above, the hardenable dental compositions of the present invention optionally include a polymerizable component. The polymerizable component can optionally be an ethylenically unsaturated compound with or without acid functionality.

15

The polymerizable component of the present invention can be part of a hardenable resin. These resins are generally thermosetting materials capable of being hardened to form a polymer network including, for example, acrylate-functional materials, methacrylate-functional materials, epoxy-functional materials, vinyl-functional materials, and mixtures thereof. Typically, the hardenable resin is made from one or more matrix-forming oligomer, monomer, polymer, or blend thereof.

20

In certain embodiments where the dental composition disclosed in the present application is a dental composite, polymerizable materials suitable for use

include hardenable organic materials having sufficient strength, hydrolytic stability, and non-toxicity to render them suitable for use in the oral environment. Examples of such materials include acrylates, methacrylates, urethanes, carbamoylisocyanurates, epoxies, and mixtures and derivatives thereof.

5 One class of preferred hardenable materials includes materials having polymerizable components with free radically active functional groups. Examples of such materials include monomers having one or more ethylenically unsaturated group, oligomers having one or more ethylenically unsaturated group, polymers having one or more ethylenically unsaturated group, and combinations thereof.

10 In the class of hardenable resins having free radically active functional groups, suitable polymerizable components for use in the invention contain at least one ethylenically unsaturated bond, and are capable of undergoing addition polymerization. Such free radically ethylenically unsaturated compounds include, for example, mono-, di- or poly-(meth)acrylates (i.e., acrylates and methacrylates) such as, methyl (meth)acrylate, ethyl acrylate, isopropyl methacrylate, n-hexyl acrylate, stearyl acrylate, allyl acrylate, glycerol triacrylate, ethyleneglycol diacrylate, diethyleneglycol diacrylate, triethyleneglycol dimethacrylate, 1,3-propanediol di(meth)acrylate, trimethylolpropane triacrylate, 1,2,4-butanetriol trimethacrylate, 1,4-cyclohexanediol diacrylate, pentaerythritol tetra(meth)acrylate, sorbitol hexacrylate, tetrahydrofurfuryl (meth)acrylate, bis[1-(2-acryloxy)]-p-ethoxyphenyldimethylmethane, bis[1-(3-acryloxy-2-hydroxy)]-p-propoxyphenyldimethylmethane, ethoxylated bisphenol A di(meth)acrylate, and trishydroxyethyl-isocyanurate trimethacrylate; (meth)acrylamides (i.e., acrylamides and methacrylamides) such as (meth)acrylamide, methylene bis-(meth)acrylamide, and diacetone (meth)acrylamide; urethane (meth)acrylates; the bis-(meth)acrylates of polyethylene glycols (preferably of molecular weight 200-500); copolymerizable mixtures of acrylated monomers such as those in U.S. Pat. No. 4,652, 274 (Boettcher et al.); acrylated oligomers such as those of U.S. Pat. No. 4,642,126 (Zador et al.); and vinyl compounds such as styrene, diallyl phthalate, divinyl

succinate, divinyl adipate and divinyl phthalate. Other suitable free radically polymerizable compounds include siloxane-functional (meth)acrylates as disclosed, for example, in WO-00/38619 (Guggenberger et al.), WO-01/92271 (Weinmann et al.), WO-01/07444 (Guggenberger et al.), WO-00/42092 (Guggenberger et al.) and  
5 fluoropolymer-functional (meth)acrylates as disclosed, for example, in U.S. Pat. No. 5,076,844 (Fock et al.), U.S. Pat. No. 4,356,296 (Griffith et al.), EP-0 373 384 (Wagenknecht et al.), EP-0 201 031 (Reiners et al.), and EP-0 201 778 (Reiners et al.). Mixtures of two or more free radically polymerizable compounds can be used if desired.

10 The polymerizable component may also contain hydroxyl groups and free radically active functional groups in a single molecule. Examples of such materials include hydroxyalkyl (meth)acrylates, such as 2-hydroxyethyl (meth)acrylate and 2-hydroxypropyl (meth)acrylate; glycerol mono- or di-(meth)acrylate; trimethylolpropane mono- or di-(meth)acrylate; pentaerythritol mono-, di-, and tri-  
15 (meth)acrylate; sorbitol mono-, di-, tri-, tetra-, or penta-(meth)acrylate; and 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (bisGMA). Suitable ethylenically unsaturated compounds are also available from a wide variety of commercial sources, such as Sigma-Aldrich, St. Louis, MO. Mixtures of ethylenically unsaturated compounds can be used if desired.

#### 20 POLYMERIZABLE COMPONENT WITH ACID FUNCTIONALITY

When present, the polymerizable component optionally comprises an ethylenically unsaturated compound with acid functionality. Preferably, the acid functionality includes an oxyacid (i.e., an oxygen-containing acid) of carbon, sulfur,  
25 phosphorous, or boron.

Such compounds include, for example,  $\alpha,\beta$ -unsaturated acidic compounds such as glycerol phosphate monomethacrylates, glycerol phosphate dimethacrylates, hydroxyethyl methacrylate phosphates, citric acid di- or tri-methacrylates, poly(meth)acrylated oligomaleic acid, poly(meth)acrylated polymaleic acid,

poly(meth)acrylated poly(meth)acrylic acid, poly(meth)acrylated polycarboxyl-  
polyphosphonic acid, poly(meth)acrylated polychlorophosphoric acid,  
poly(meth)acrylated polysulfonic acid, poly(meth)acrylated polyboric acid, and the  
like, may be used as components in the hardenable resin system.

5           Certain of these compounds are obtained, for example, as reaction products  
between isocyanatoalkyl (meth)acrylates and carboxylic acids. Additional  
compounds of this type having both acid-functional and ethylenically unsaturated  
components are described in U.S. Pat. Nos. 4,872,936 (Engelbrecht) and 5,130,347  
(Mitra). A wide variety of such compounds containing both the ethylenically  
10           unsaturated and acid moieties can be used. Mixtures of such compounds can be  
used if desired.

          Additional ethylenically unsaturated compounds with acid functionality  
include, for example, polymerizable bisphosphonic acids as disclosed for example,  
in U.S.S.N. 10/729,497; AA:ITA:IEM (copolymer of acrylic acid:itaconic acid with  
15           pendent methacrylate made by reacting AA:ITA copolymer with sufficient 2-  
isocyanatoethyl methacrylate to convert a portion of the acid groups of the  
copolymer to pendent methacrylate groups as described, for example, in Example  
11 of U.S. Pat. No. 5,130,347 (Mitra)); and those recited in U.S. Pat. Nos.  
4,259,075 (Yamauchi et al.), 4,499,251 (Omura et al.), 4,537,940 (Omura et al.),  
20           4,539,382 (Omura et al.), 5,530,038 (Yamamoto et al.), 6,458,868 (Okada et al.),  
and European Pat. Application Publication Nos. EP 712,622 (Tokuyama Corp.) and  
EP 1,051,961 (Kuraray Co., Ltd.).

          When ethylenically unsaturated compounds with acid functionality are  
present, the compositions of the present invention typically include at least 1% by  
25           weight, more typically at least 3% by weight, and most typically at least 5% by  
weight ethylenically unsaturated compounds with acid functionality, based on the  
total weight of the unfilled composition. Typically, compositions of the present  
invention include at most 50% by weight, more typically at most 40% by weight,

and most typically at most 30% by weight ethylenically unsaturated compounds with acid functionality, based on the total weight of the unfilled composition.

Partial or complete hardening of the composition may occur through an acid-reactive filler/polyacid reaction (i.e. an acid/base reaction). In certain  
5 embodiments, the composition also contains a photoinitiator system that upon irradiation with actinic radiation initiates the polymerization (or hardening) of the composition. Such photopolymerizable compositions can be free radically polymerizable.

## 10 FREE RADICAL INITIATION SYSTEMS

For free radical polymerization (e.g., hardening), an initiation system can be selected from systems that initiate polymerization via radiation, heat, or redox/auto-cure chemical reaction. A class of initiators capable of initiating polymerization of free radically active functional groups includes free radical-generating  
15 photoinitiators, optionally combined with a photosensitizer or accelerator. Such initiators typically can be capable of generating free radicals for addition polymerization upon exposure to light energy having a wavelength between 200 and 800 nm.

Suitable photoinitiators (i.e., photoinitiator systems that include one or more  
20 compounds) for polymerizing free radically photopolymerizable compositions include binary and ternary systems. Typical ternary photoinitiators include an iodonium salt, a photosensitizer, and an electron donor compound as described in U.S. Pat. No. 5,545,676 (Palazzotto et al.). Preferred iodonium salts are the diaryl iodonium salts, e.g., diphenyliodonium chloride, diphenyliodonium  
25 hexafluorophosphate, diphenyliodonium tetrafluoroborate, and tolylcumyliodonium tetrakis(pentafluorophenyl) borate. Preferred photosensitizers are monoketones and diketones that absorb some light within a range of about 400 nm to 520 nm (preferably, 450 nm to 500 nm). More preferred compounds are alpha diketones that have some light absorption within a range of 400 nm to 520 nm (even more

preferably, 450 to 500 nm). Preferred compounds are camphorquinone, benzil, furil, 3,3,6,6-tetramethylcyclohexanedione, phenanthraquinone, 1-phenyl-1,2-propanedione and other 1-aryl-2-alkyl-1,2-ethanediones, and cyclic alpha diketones. Most preferred is camphorquinone. Preferred electron donor compounds include substituted amines, e.g., ethyl dimethylaminobenzoate. Other suitable ternary photoinitiator systems useful for photopolymerizing cationically polymerizable resins are described, for example, in U.S. Pat. Publication No. 2003/0166737 (Dede et al.).

Other suitable photoinitiators for polymerizing free radically photopolymerizable compositions include the class of phosphine oxides that typically have a functional wavelength range of 380 nm to 1200 nm. Preferred phosphine oxide free radical initiators with a functional wavelength range of 380 nm to 450 nm are acyl and bisacyl phosphine oxides such as those described in U.S. Pat. Nos. 4,298,738 (Lechtken et al.), 4,324,744 (Lechtken et al.), 4,385,109 (Lechtken et al.), 4,710,523 (Lechtken et al.), and 4,737,593 (Ellrich et al.), 6,251,963 (Kohler et al.); and EP Application No. 0 173 567 A2 (Ying).

Commercially available phosphine oxide photoinitiators capable of free-radical initiation when irradiated at wavelength ranges of greater than 380 nm to 450 nm include, for example, bis(2,4,6-trimethylbenzoyl)phenyl phosphine oxide available under the trade designation IRGACURE 819 from Ciba Specialty Chemicals, Tarrytown, NY; bis(2,6-dimethoxybenzoyl)-(2,4,4-trimethylpentyl) phosphine oxide available under the trade designation CGI 403 from Ciba Specialty Chemicals; a 25:75 mixture, by weight, of bis(2,6-dimethoxybenzoyl)-2,4,4-trimethylpentyl phosphine oxide and 2-hydroxy-2-methyl-1-phenylpropan-1-one available under the trade designation IRGACURE 1700 from Ciba Specialty Chemicals; a 1:1 mixture, by weight, of bis(2,4,6-trimethylbenzoyl)phenyl phosphine oxide and 2-hydroxy-2-methyl-1-phenylpropane-1-one available under the trade designation DAROCUR 4265 from Ciba Specialty Chemicals; and ethyl

2,4,6-trimethylbenzylphenyl phosphinate available under the trade designation LUCIRIN LR8893X from BASF Corp., Charlotte, NC.

Typically, the phosphine oxide initiator is present in the photopolymerizable composition in catalytically effective amounts, such as from 0.1% by weight to 5%  
5 by weight, based on the total weight of the composition.

Tertiary amine reducing agents may be used in combination with an acylphosphine oxide. Illustrative tertiary amines useful in the invention include ethyl 4-(N,N-dimethylamino)benzoate and N,N-dimethylaminoethyl methacrylate. When present, the amine reducing agent is present in the photopolymerizable  
10 composition in an amount from 0.1% by weight to 5% by weight, based on the total weight of the composition. Useful amounts of other initiators are well known to those of skill in the art.

Another free-radical initiator system that can alternatively be used in the dental materials of the invention includes the class of ionic dye-counterion complex  
15 initiators including a borate anion and a complementary cationic dye. Borate salt photoinitiators are described, for example, in U. S. Pat. Nos. 4,772,530 (Gottschalk et al.), 4,954,414 (Adair et al.), 4,874,450 (Gottschalk), 5,055,372 (Shanklin et al.), and 5,057,393 (Shanklin et al.).

The hardenable resins of the present invention can include redox cure  
20 systems that include a polymerizable component (e.g., an ethylenically unsaturated polymerizable component) and redox agents that include an oxidizing agent and a reducing agent. Suitable polymerizable components and redox agents that are useful in the present invention are described in U.S. Pat. Publication No. 2003/0166740 (Mitra et al.) and U.S. Pat. Publication No. 2003/0195273 (Mitra et al.).

25 The reducing and oxidizing agents should react with or otherwise cooperate with one another to produce free-radicals capable of initiating polymerization of the resin system (e.g., the ethylenically unsaturated component). This type of cure is a dark reaction, that is, it is not dependent on the presence of light and can proceed in the absence of light. The reducing and oxidizing agents are preferably sufficiently

shelf-stable and free of undesirable colorization to permit their storage and use under typical dental conditions. They should be sufficiently miscible with the resin system (and preferably water-soluble) to permit ready dissolution in (and discourage separation from) the other components of the polymerizable composition.

Useful reducing agents include, for example, ascorbic acid, ascorbic acid derivatives, and metal complexed ascorbic acid compounds as described in U.S. Pat. No. 5,501,727 (Wang et al.); amines, especially tertiary amines, such as 4-tert-butyl dimethylaniline; aromatic sulfinic salts, such as p-toluenesulfinic salts and benzenesulfinic salts; thioureas, such as 1-ethyl-2-thiourea, tetraethyl thiourea, tetramethyl thiourea, 1,1-dibutyl thiourea, and 1,3-dibutyl thiourea; and mixtures thereof. Other secondary reducing agents may include cobalt (II) chloride, ferrous chloride, ferrous sulfate, hydrazine, hydroxylamine (depending on the choice of oxidizing agent), salts of a dithionite or sulfite anion, and combinations thereof. Preferably, the reducing agent is an amine.

Suitable oxidizing agents will also be familiar to those skilled in the art, and include, for example, persulfuric acid and salts thereof, such as sodium, potassium, ammonium, cesium, and alkyl ammonium salts. Additional oxidizing agents include, for example, peroxides such as benzoyl peroxides, hydroperoxides such as cumyl hydroperoxide, t-butyl hydroperoxide, and amyl hydroperoxide, as well as salts of transition metals such as cobalt (III) chloride and ferric chloride, cerium (IV) sulfate, perboric acid and salts thereof, permanganic acid and salts thereof, perphosphoric acid and salts thereof, and combinations thereof.

It may be desirable to use more than one oxidizing agent or more than one reducing agent. Small quantities of transition metal compounds may also be added to accelerate the rate of redox cure. In some embodiments it may be preferred to include a secondary ionic salt to enhance the stability of the hardenable composition as described, for example, in U.S. Pat. Publication No. 2003/0195273 (Mitra et al.).

The reducing and oxidizing agents are present in amounts sufficient to permit an adequate free-radical reaction rate. This can be evaluated by combining all of the ingredients of the hardenable composition except for the filler, and observing whether or not a hardened mass is obtained.

5 Preferably, the reducing agent is present in an amount of at least 0.01% by weight, and more preferably at least 0.10% by weight, based on the total weight (including water) of the components of the hardenable composition. Preferably, the reducing agent is present in an amount of no greater than 10% by weight, and more preferably no greater than 5% by weight, based on the total weight (including  
10 water) of the components of the polymerizable composition.

Preferably, the oxidizing agent is present in an amount of at least 0.01% by weight, and more preferably at least 0.10% by weight, based on the total weight (including water) of the components of the polymerizable composition. Preferably, the oxidizing agent is present in an amount of no greater than 10% by weight, and  
15 more preferably no greater than 5% by weight, based on the total weight (including water) of the components of the hardenable composition.

The reducing or oxidizing agents can be microencapsulated as described, for example, in U.S. Pat. No. 5,154,762 (Mitra et al.). This will generally enhance shelf stability of the polymerizable composition, and if necessary permit packaging the  
20 reducing and oxidizing agents together. For example, through appropriate selection of an encapsulant, the oxidizing and reducing agents can be combined with an acid-functional component and optional filler and kept in a storage-stable state. Likewise, through appropriate selection of a water-insoluble encapsulant, the reducing and oxidizing agents can be combined with an FAS glass and water and  
25 maintained in a storage-stable state.

In a further alternative, heat may be used to initiate the hardening, or polymerization, of free radically active groups. Examples of heat sources suitable for the dental materials of the invention include inductive, convective, and radiant. Thermal sources should be capable of generating temperatures of at least 40°C and

at most 150°C under normal conditions or at elevated pressure. This procedure is preferred for initiating polymerization of materials occurring outside of the oral environment.

Yet another alternative class of initiators capable of initiating polymerization of free radically active functional groups in the hardenable resin are those that include free radical-generating thermal initiators. Examples include peroxides (e.g., benzoyl peroxide and lauryl peroxide) and azo compounds (e.g., 2,2-azobis-isobutyronitrile (AIBN)).

Photoinitiator compounds are preferably provided in dental compositions disclosed in the present application in an amount effective to initiate or enhance the rate of cure or hardening of the resin system. Useful photopolymerizable compositions are prepared by simply admixing, under safe light conditions, the components as described above. Suitable inert solvents may be used, if desired, when preparing this mixture. Any solvent that does not react appreciably with the components of the inventive compositions may be used. Examples of suitable solvents include, for example, acetone, dichloromethane, and acetonitrile.

## POLYACID

Compositions of the present invention include at least one polyacid, which may be a non-curable or non-polymerizable polyacid, or a curable or polymerizable polyacid (e.g., a resin-modified polyacid). Typically, the polyacid is a polymer having a plurality of acidic repeating units and a plurality of polymerizable groups. In alternative embodiments, the polyacid may be substantially free of polymerizable groups. The polyacid need not be entirely water soluble, but it should be at least sufficiently water-miscible so that it does not undergo substantial sedimentation when combined with other aqueous components. Suitable polyacids are listed in U.S. Pat. No. 4,209,434 (Wilson et al.), column 2, line 62, to column 3, line 6. The polyacid should have a molecular weight sufficient to provide good storage, handling, and mixing properties. A typical weight average molecular weight is

5,000 to 100,000, evaluated against a polystyrene standard using gel permeation chromatography.

In one embodiment, the polyacid is a curable or polymerizable resin. That is, it contains at least one ethylenically unsaturated group. Suitable ethylenically unsaturated polyacids are described in U.S. Pat. No. 4,872,936 (Engelbrecht), e.g., at columns 3 and 4, and EP 323 120 B1 (Mitra), e.g., at page 3, line 55 to page 5, line 8. Typically, the numbers of acidic groups and ethylenically unsaturated groups are adjusted to provide an appropriate balance of properties in the dental composition. Polyacids in which 10% to 70% of the acidic groups have been replaced with ethylenically unsaturated groups are preferred.

In other embodiments, the polyacid is hardenable in the presence of, for example, an acid-reactive filler and water, but does not contain ethylenically unsaturated groups. That is, it is an oligomer or polymer of an unsaturated acid. Typically, the unsaturated acid is an oxyacid (i.e., an oxygen containing acid) of carbon, sulfur, phosphorous, or boron. More typically, it is an oxyacid of carbon. Such polyacids include, for example, polyalkenoic acids such as homopolymers and copolymers of unsaturated mono-, di-, or tricarboxylic acids. Polyalkenoic acids can be prepared by the homopolymerization and copolymerization of unsaturated aliphatic carboxylic acids, e.g., acrylic acid, 2-chloroacrylic acid, 3-chloroacrylic acid, 2-bromoacrylic acid, 3-bromoacrylic acid, methacrylic acid, itaconic acid, maleic acid, glutaconic acid, aconitic acid, citraconic acid, mesaconic acid, fumaric acid, and tiglic acid. Suitable monomers that can be copolymerized with the unsaturated aliphatic carboxylic acids include, for example, unsaturated aliphatic compounds such as acrylamide, acrylonitrile, vinyl chloride, allyl chloride, vinyl acetate, and 2-hydroxyethyl methacrylate. Ter- and higher polymers may be used if desired. Particularly preferred are the homopolymers and copolymers of acrylic acid. The polyalkenoic acid should be substantially free of unpolymerized monomers.

The amount of polyacid should be sufficient to react with the acid-reactive filler and to provide an ionomer composition with desirable hardening properties. Typically, the polyacid represents at least 1 wt-%, more typically at least 3 wt-%, and most typically at least 5 wt-%, based on the total weight of the unfilled composition. Typically, the polyacid represents at most 90 wt-%, more typically at most 60 wt-%, and most typically at most 30 wt-%, based on the total weight of the unfilled composition.

#### ACID-REACTIVE FILLERS

Suitable acid-reactive fillers include metal oxides, glasses, and metal salts. Typical metal oxides include barium oxide, calcium oxide, magnesium oxide, and zinc oxide. Typical glasses include borate glasses, phosphate glasses, and fluoroaluminosilicate ("FAS") glasses. FAS glasses are particularly preferred. The FAS glass typically contains sufficient elutable cations so that a hardened dental composition will form when the glass is mixed with the components of the hardenable composition. The glass also typically contains sufficient elutable fluoride ions so that the hardened composition will have cariostatic properties. The glass can be made from a melt containing fluoride, alumina, and other glass-forming ingredients using techniques familiar to those skilled in the FAS glassmaking art. The FAS glass typically is in the form of particles that are sufficiently finely divided so that they can conveniently be mixed with the other cement components and will perform well when the resulting mixture is used in the mouth.

Generally, the average particle size (typically, diameter) for the FAS glass is no greater than about 12 micrometers, typically no greater than 10 micrometers, and more typically no greater than about 5 micrometers as measured using, for example, a sedimentation analyzer. Suitable FAS glasses will be familiar to those skilled in the art, and are available from a wide variety of commercial sources, and many are found in currently available glass ionomer cements such as those commercially

available under the trade designations VITREMER, VITREBOND, RELY X LUTING CEMENT, RELY X LUTING PLUS CEMENT, PHOTAC-FIL QUICK, KETAC MOLAR and KETAC-FIL PLUS(3M ESPE Dental Products, St. Paul, MN), FUJI II LC and FUJI IX (G-C Dental Industrial Corp., Tokyo, Japan) and  
5 CHEMFIL Superior (Dentsply International, York, PA). Mixtures of fillers can be used if desired.

The FAS glass can optionally be subjected to a surface treatment. Suitable surface treatments include, but are not limited to, acid washing (e.g., treatment with a phosphoric acid), treatment with a phosphate, treatment with a chelating agent  
10 such as tartaric acid, and treatment with a silane or an acidic or basic silanol solution. Desirably the pH of the treating solution or the treated glass is adjusted to neutral or near-neutral, as this can increase storage stability of the hardenable composition.

In another embodiment, the acid-reactive filler comprises a non-fused  
15 oxyfluoride material. The oxyfluoride material may include a trivalent metal, oxygen, fluorine, and an alkaline earth metal. Preferably the trivalent metal is aluminum, lanthanum, or combinations thereof. More preferably the trivalent metal is aluminum. Preferably the alkaline earth metal is strontium, calcium, barium, or combinations thereof. In some embodiments of the present invention, the  
20 oxyfluoride material may further include silicon and/or heavy metal (e.g., zirconium, lanthanum, niobium, yttrium, or tantalum), or more specifically, oxides, fluorides and/or oxyfluorides thereof.

In some embodiments of the present invention, at least a portion of the  
oxyfluoride material is nanostructured. Such nanostructured materials include the  
25 oxyfluoride material in the form of, for example, nanoparticles, coatings on particles, coatings on aggregates of particles, infiltrate in a porous structure, and combinations thereof. Preferably at least 90% by weight, more preferably at least 95% by weight, and most preferably at least 98% by weight of the oxyfluoride material is nanostructured.

A description of suitable oxyfluoride materials and their use in dental compositions is provided in U.S. Patent Application entitled, "Acid Reactive Dental Fillers, Compositions, and Methods," (Attorney Docket No. 58618US002) filed on May 17, 2004.

5           The amount of acid-reactive filler should be sufficient to provide an ionomer composition having desirable mixing and handling properties before hardening and good physical and optical properties after hardening. Generally, the reactive filler represents less than about 85% of the total weight of the composition. Typically, the acid-reactive filler represents at least 10 wt-%, and more typically at least 20 wt-  
10   %, based on the total weight of the composition. Typically, the acid-reactive filler represents at most 75 wt-%, and more typically at most 50 wt-%, based on the total weight of the composition.

#### NANOZIRCONIA FILLERS

15           The ionomer compositions of the invention are formulated with nanozirconia fillers. These fillers impart the compositions with radiopacity, allowing for preparation of ionomer compositions that are both radiopaque and optically translucent while using less FAS glass than was previously required. This, in turn, allows for ionomer compositions to be prepared as, for example, as two-part paste-  
20   paste systems.

Zirconia is a highly radiopaque metal oxide possessing X-ray scattering ability and filler reinforcement properties. Nanozirconia is nanosized crystalline  $ZrO_2$  particles. Such nanozirconia fillers typically have an average particle size of at most 100 nanometers, more typically at most 75 nanometers, even more typically  
25   at most 50 nanometers, and most typically at most 20 nanometers. Such nanozirconia fillers typically have an average particle size of at least 2 nanometers and more typically at least 5 nanometers. The primary particles of the nanozirconia fillers can be aggregated or nonaggregated. In certain embodiments, the zirconia nanoparticles have an aggregated size of typically not more than 150 nm, and more

typically not more than 100 nm. The very small overall particle size in combination with good dispersion decreases light scattering and gives optically translucent materials.

In addition, the zirconia nanoparticles are surface modified so they can preferably be dispersed in the dental composition in a nonagglomerated state. Acidic functionalities, such as carboxylic acids and phosphonic acids, readily adsorb to the surface of  $ZrO_2$  particles. Adsorption of these types of molecules is, in many instances, a very good means of surface modification. One can use combinations of carboxylic acids for instance to give good dispersion and reactivity into composite formulations. However, for use in ionomer composition, a surface modification is needed which will allow the particles to be dispersed but also passivate the surface towards the adsorption of the polyacid. A surface modification using silanes or a combination of silanes and phosphonic acids can passivate the surface and allow the incorporation of nanozirconia into ionomer formulations. As illustrated by the Examples included herein, ionomer compositions containing surface-modified nanozirconia fillers have been formulated into paste/paste systems with good radiopacity, visual opacity, and good physical properties.

The amount of nanozirconia filler should be sufficient to provide an ionomer composition having desirable mixing and handling properties before hardening and good physical and optical properties after hardening. Typically, the nanozirconia filler represents at least 0.1 wt-%, more typically at least 10 wt-%, and most typically at least 20 wt-% based on the total weight of the composition. Typically, the nanozirconia filler represents at most 80 wt-%, more typically at most 70 wt-%, and most typically at most 60 wt-%, based on the total weight of the composition.

#### OTHER FILLERS

In addition to the acid-reactive filler and the nanozirconia filler components, the compositions of the present invention can also optionally include one or more

other fillers. Such fillers may be selected from one or more of a wide variety of materials suitable for the use in dental and/or orthodontic compositions.

The other filler can be an inorganic material. It can also be a crosslinked organic material that is insoluble in the resin component of the composition, and is optionally filled with inorganic filler. The filler should in any event be nontoxic and suitable for use in the mouth. The filler can be radiopaque or radiolucent. The filler typically is substantially insoluble in water.

Examples of suitable inorganic fillers are naturally occurring or synthetic materials including, but not limited to: quartz; nitrides (e.g., silicon nitride); glasses derived from, for example, Zr, Sr, Ce, Sb, Sn, Ba, Zn, and Al; feldspar; borosilicate glass; kaolin; talc; titania; low Mohs hardness fillers such as those described in U.S. Pat. No. 4,695,251 (Randklev); and silica particles (e.g., submicron pyrogenic silicas such as those available under the trade designations AEROSIL, including "OX 50," "130," "150" and "200" silicas from Degussa AG, Hanau, Germany and CAB-O-SIL M5 silica from Cabot Corp., Tuscola, IL). Examples of suitable organic filler particles include filled or unfilled pulverized polycarbonates, polyepoxides, and the like. Other fillers, including other nanofillers, that may be used in the compositions of the invention are described in a U.S. Patent Application entitled, "Dental Compositions Containing Nanofillers and Related Methods," (Attorney Docket No. 59610US002) and a U.S. Patent Application entitled, "Use of Nanoparticles to Adjust Refractive Index of Dental Compositions," (Attorney Docket No. 59611US002) both of which were filed on May 17, 2004.

Suitable non-acid-reactive filler particles are quartz, submicron silica, and non-vitreous microparticles of the type described in U.S. Pat. No. 4,503,169 (Randklev). Mixtures of these non-acid-reactive fillers are also contemplated, as well as combination fillers made from organic and inorganic materials.

The surface of the filler particles can also be treated with a coupling agent in order to enhance the dispersion of the filler in the resin and the bond between the filler and the resin. The use of suitable coupling agents include gamma-

methacryloxypropyltrimethoxysilane, gamma-mercaptopropyltriethoxysilane, gamma-aminopropyltrimethoxysilane, and the like. Examples of useful silane coupling agents are those available from Crompton Corporation, Naugatuck, CT, as SILQUEST A-174 and SILQUEST A-1230.

5 For some embodiments of the present invention that include other fillers (e.g., dental restorative compositions), the compositions may include at least 1% by weight, more preferably at least 2% by weight, and most preferably at least 5% by weight other filler, based on the total weight of the composition. For such  
embodiments, compositions of the present invention preferably include at most 40%  
10 by weight, more preferably at most 20% by weight, and most preferably at most 15% by weight other filler, based on the total weight of the composition.

#### WATER

The compositions of the invention contain water. The water can be distilled,  
15 deionized, or plain tap water. Typically, deionized water is used.

The amount of water should be sufficient to provide adequate handling and mixing properties and to permit the transport of ions, particularly in the filler-acid reaction. Preferably, water represents at least 2 wt-%, and more preferably at least 5 wt-%, of the total weight of ingredients used to form the composition. Preferably,  
20 water represents no greater than 90 wt-%, and more preferably no greater than 80 wt-%, of the total weight of ingredients used to form the composition.

#### OPTIONAL ADDITIVES

Optionally, the hardenable compositions may contain other solvents,  
25 cosolvents (e.g., alcohols) or diluents. If desired, the hardenable composition of the invention can contain additives such as indicators, dyes, pigments, inhibitors, accelerators, viscosity modifiers, wetting agents, tartaric acid, chelating agents, surfactants, buffering agents, stabilizers, and other similar ingredients that will be apparent to those skilled in the art. Additionally, medicaments or other therapeutic

substances can be optionally added to the dental compositions. Examples include, but are not limited to, fluoride sources, whitening agents, anticaries agents (e.g., xylitol), remineralizing agents (e.g., calcium phosphate compounds), enzymes, breath fresheners, anesthetics, clotting agents, acid neutralizers, chemotherapeutic agents, immune response modifiers, thixotropes, polyols, anti-inflammatory agents, antimicrobial agents, antifungal agents, agents for treating xerostomia, desensitizers, and the like, of the type often used in dental compositions.

Combination of any of the above additives may also be employed. The selection and amount of any one such additive can be selected by one of skill in the art to accomplish the desired result without undue experimentation.

#### PREPARATION AND USE OF THE COMPOSITIONS

The hardenable dental compositions of the present invention can be prepared by combining all the various components using conventional mixing techniques.

As discussed above, the compositions may be partially or fully hardened by an ionic reaction between an acid-reactive filler and a polyacid. Optionally, the compositions may contain a polymerizable component and a photoinitiator and be hardened by photoinitiation, or may be partially or fully hardened by chemical polymerization such as a redox cure system in which the composition contains a free-radical initiator system, e.g., including an oxidizing agent and a reducing agent.

Alternatively, the hardenable composition may contain different initiator systems, such that the composition can be both a photopolymerizable and a chemically polymerizable composition, as well as an ionically hardenable composition.

The hardenable compositions of the invention can be supplied in a variety of forms including one-part systems and multi-part systems, e.g., two-part powder/liquid, paste/liquid, paste/powder and paste/paste systems. Other forms employing multi-part combinations (i.e., combinations of two or more parts), each of which is in the form of a powder, liquid, gel, or paste are also possible. The various components of the composition may be divided up into separate parts in

whatever manner is desired; however, the polyacid, acid-reactive filler and water generally would not all be present in the same part, although any two of these may be grouped together in the same part along with any combination of other components. Furthermore, in a redox multi-part system, one part typically contains the oxidizing agent and another part typically contains the reducing agent.

However, the reducing agent and oxidizing agent could be combined in the same part of the system if the components are kept separated, for example, through use of microencapsulation.

Proper surface treatment of a nanozirconia filler is required to achieve good dispersion in a resin composition, to impart the desired rheological, aesthetic, and strength characteristics to the composition, and to obtain a stable composition, especially in the presence of an acidic component. Silane treatment of zirconia nanoparticles is typically accomplished by the reaction of a silane coupling agent or a combination of silane coupling agents with the zirconia in the form of an aqueous sol. The zirconia sol is typically acidic with a pH of 2-5 and an optional cosolvent can be used. The resulting mixture is typically heated for 3 to 16 hours at 80°C - 90°C, however other times and temperatures can also be used. Upon completion of the heating cycle, the silane-treated zirconia can be incorporated into a resin system either by solvent removal in the presence of the resin (solvent exchange) or solvent removal followed by dispersion of the isolated solid filler in the resin. Optionally, addition of a base such as aqueous ammonia, may be used to raise the pH of sol. Typically, this addition of base is made after the heating cycle under acidic conditions. Optionally, the addition of base may be made prior to the heating cycle.

In a preferred embodiment, the zirconia sol is heated with at least two silane coupling agents under acidic conditions (e.g., in the presence of 2-[2-(2-methoxyethoxy)ethoxy]acetic acid (MEEAA)). After cooling, the mixture is added to a dilute aqueous ammonia solution. Other base materials may be used as alternatives to the ammonia solution. The addition to base will generally lead to precipitation of the zirconia solids. The base is believed to facilitate removal of the

attached (e.g., adsorbed) acids from the surface of the silane-treated zirconia.

Subsequent filtration and washing of the solids allow for further removal of acids.

This removal of acids can be especially beneficial in cases where the zirconia is surface treated with high molecular weight nonvolatile acids such as MEEAA. If

5 high molecular weight acids are not removed after silane treatment, a substantial amount of residual acid may be incorporated into the final composition, which can lead to undesirable composition properties and decreased composition stability. Following filtration, the silane-treated nanozirconia filler can be redispersed in a solvent and subsequently incorporated into a resin via solvent exchange or typically

10 the solids can be dried to a powder and redispersed into a resin.

The nanozirconia fillers can be surface treated with a combination of silane coupling agents to impart desired rheological and physical properties (e.g., visual opacity) to a composition. In particular, the use of typical reactive silanes, such as SILQUIST A-174, in combination with hydrophilic silanes, such as SILQUIST A-

15 1230, may be beneficial for surface-treating nanozirconia fillers for use in ionomer compositions of the present invention that in some embodiments include relatively polar resin systems.

In some embodiments, two-part dental compositions of the present invention can be provided in a dual barrel syringe having a first barrel and a second barrel,

20 wherein the part A resides in the first barrel and the part B resides in the second barrel. In other embodiments, two-part dental compositions of the present invention can be provided in a unit-dose capsule. In some embodiments, each part of a multi-part dental system can be mixed together using a static mixer. The components of the hardenable composition can be included in a kit, where the

25 contents of the composition are packaged to allow for storage of the components until they are needed.

When used as a dental composition, the components of the hardenable compositions can be mixed and clinically applied using conventional techniques. A curing light is generally required for the initiation of photopolymerizable

compositions. The compositions can be in the form of composites or restoratives that adhere very well to dentin and/or enamel. Optionally, a surface conditioner or a primer layer can be used on the tooth tissue on which the hardenable composition is used. The compositions, e.g., containing a FAS glass or other fluoride-releasing material, can also provide very good long-term fluoride release. Some  
5 embodiments of the invention may provide glass ionomer cements or adhesives that can be cured in bulk without the application of light or other external curing energy, do not require a pre-treatment, have improved physical properties including improved flexural strength, and have high fluoride release for cariostatic effect.

10 The hardenable dental compositions of the invention are particularly well adapted for use in the form of a wide variety of dental materials. They can be used in prosthodontic cements, which are typically filled compositions (preferably containing greater than about 25 wt-% filler and up to about 60 wt-% filler). They can also be used in restoratives, which include composites which are typically filled  
15 compositions (preferably containing greater than about 10 wt-% filler and up to about 85 wt-% filler) that are polymerized after being disposed adjacent to a tooth, such as filling materials. They can also be used in prostheses that are shaped and hardened for final use (e.g., as a crown, bridge, veneer, inlay, onlay, or the like), before being disposed adjacent to a tooth. Such preformed articles can be ground or  
20 otherwise formed into a custom-fitted shape by the dentist or other user. Although the hardenable dental composition can be any of a wide variety of materials preferably, the composition is not a surface pre-treatment material (e.g., etchant, primer, bonding agent). Rather, preferably, the hardenable dental composition is a restorative (e.g., composite, filling material or prosthesis), cement, sealant, coating,  
25 or orthodontic adhesive.

Features and advantages of this invention are further illustrated by the following examples, which are in no way intended to be limiting thereof. The particular materials and amounts thereof recited in these examples, as well as other conditions and details, should not be construed to unduly limit this invention.

Unless otherwise indicated, all parts and percentages are on a weight basis, all water is deionized water, and all molecular weights are weight average molecular weight.

5

## **EXAMPLES**

### Test Methods

#### Compressive Strength (CS) Test Method

Compressive strength was evaluated by first injecting a mixed paste-paste test sample into a glass tube having a 4-mm inner diameter. The ends of the glass tube were plugged with silicone plugs. The filled tubes were subjected to 0.275 megapascal (MPa) pressure for 5 minutes, irradiated with a XL 1500 curing light (3M Company) for 60 seconds, and placed in a KULZER UniXS (Kulzer, Inc., Germany) light box for 90 seconds. Five such cured samples were cut to a length of 8 mm and placed in 37°C water for 1 day. Compressive strength was determined according to ISO Standard 7489 using an INSTRON universal tester (Instron Corp., Canton, MA) operated at a crosshead speed of 1 millimeter per minute (mm/min). Results were reported as the average of 5 replicates.

20

#### Diametral Tensile Strength (DTS) Test Method

Diametral tensile strength was measured using the above-described CS procedure, but using samples were cut to a length of 2 mm. Results were reported as the average of 7 replicates.

25

#### Visual Opacity (MacBeth Values) Test Method

Disc-shaped (1-mm thick x 15-mm diameter) paste samples were cured by exposing them to illumination from a VISILUX 2 curing light (3M Co , St. Paul, MN) for 60 seconds on each side of the disk at a distance of 6 mm. Hardened

samples were measured for direct light transmission by measuring transmission of light through the thickness of the disk using a MacBeth transmission densitometer Model TD-903 equipped with a visible light filter, available from MacBeth (MacBeth, Newburgh, NY). Lower MacBeth Values indicate lower visual opacity and greater translucency of a material. The reported values are the average of 3 measurements.

#### Radiopacity Test Method

Disc-shaped (1-mm thick x 15-mm diameter) paste test samples were cured by exposing them to illumination from an VISILUX 2 (3M Company) curing light for 60 seconds on each side of the disk at a distance of 6 mm. The cured samples were then evaluated for radiopacity as follows.

For radiopacity evaluation, the procedure used followed the ISO-test procedure 4049 (1988). Specifically, cured composite samples were exposed to radiation using a Gendex GX-770 dental X-ray (Milwaukee, WI) unit for 0.73 seconds at 7 milliamps and 70 kV peak voltage at a distance of about 400 millimeters. An aluminum step wedge was positioned during exposure next to the cured disk on the X-ray film. The X-ray negative was developed using an Air Techniques Peri-Pro automatic film processor (Hicksville, NY). A Macbeth densitometer was used to determine the optical density of the sample disk by comparison with the optical densities of the aluminum step wedge. The reported values of optical density (i.e., radiopacity) are the average of 3 measurements.

#### **Abbreviations, Descriptions, and Sources of Materials**

Abbreviation	Description and Source of Material
HEMA	2-Hydroxyethyl methacrylate (Sigma-Aldrich, St. Louis, MO)
BisGMA	2,2-Bis[4-(2-hydroxy-3-methacryloyloxy-propoxy)phenyl]propane; CAS No. 1565-94-2
PEGDMA-400	Polyethyleneglycol dimethacrylate (Sartomer 603; MW about 570; Sartomer, Exton, PA)

Resin A	Mixture of PEGDMA-400 (62 wt. %) and HEMA (38 wt.%)
AA:ITA	Copolymer made from a 4:1 mole ratio of acrylic acid:itaconic acid, prepared according to Example 3 of U.S. Pat. No. 5,130,347 (Mitra), MW (average) = 106,000; polydispersity $\rho = 4.64$ .
IEM	2-Isocyanatoethyl methacrylate (Sigma-Aldrich)
VBCP	Polymer made by reacting AA:ITA copolymer with sufficient IEM to convert 16 mole percent of the acid groups of the copolymer to pendent methacrylate groups, according to the dry polymer preparation of Example 11 of U.S. Pat. No. 5,130,347.
GDMA	Glycerol dimethacrylate (Rohm Tech, Inc., Malden, MA)
Kayamer PM-2	Bis(methacryloxyethyl) phosphate (Nippon Kayaku, Japan)
Ebecryl 1830	Polyester hexaacrylate resin (UCB-Radcare Specialties, Brussels, Belgium)
BHT	Butylated hydroxytoluene (Sigma-Aldrich)
DPIPF6	Diphenyliodonium hexafluorophosphate (Johnson Matthey, Alpha Aesar Division, Ward Hill, NJ)
CPQ	Camphorquinone (Sigma-Aldrich)
MEEAA	2-[2-(2-methoxyethoxy)ethoxy]acetic acid (Sigma-Aldrich)
Zirconia Sol	Aqueous zirconia sol containing 23% solids prepared as described in U.S. Pat. No. 5,037,579 (Matchette). Average primary particle size was determined to be 5 nm based on the Crystallite Particle Size and Crystal Form Content Test Method described in U.S. Pat. No. 6,387,981 (Zhang et al.), and average aggregated particle size was determined to be 50-60 nm based on the Photon Correlation Spectroscopy Test Method described in U.S. Pat. No. 6,387,981 (Zhang et al.)
SILQUEST A-174	$\gamma$ -Methacryloxypropyltrimethoxysilane used for silane treatment of fillers (Crompton Corporation, Naugatuck, CT)
SILQUEST A-1230	PEG Silane used for silane treatment of fillers (Crompton Corporation)
AEROSIL R812S	Fumed silica filler (Degussa, Germany)
Filler A (FAS Glass)	Schott Glass (Product No. G 018-117; average particle size 1.0 micrometers; Schott Electronic Packaging, GmbH, Landshut, Germany). The filler was silane-treated as

	described for Filler FAS VI in U.S. Pat. Publication No. 2003/0166740 (Mitra et al.).
Filler E (Nanofiller)	Silane-treated, non-aggregated, nano-sized silica particles in the form of a dry powder were prepared according to the procedure for Filler A in U.S. Pat. No. 2003/0181541 (Wu et al.). The nominal particle size of Filler E was assumed to be the same as in the starting Nalco 2329 silica sol, i.e., about 75 nanometers.
Filler F (Nanofiller)	Silane-treated, non-aggregated, nano-sized silica particles in the form of a dry powder were prepared according to the procedure for Filler A in U.S. Pat. No. 2003/0181541 (Wu et al.), except that Nalco 2327 was used in place of Nalco 2329. The nominal particle size of Filler F was assumed to be the same as in the starting Nalco 2327 silica sol, i.e., about 20 nanometers.
Filler I (Example 1) (Nanozirconia)	Silane-treated nanozirconia filler prepared according to Example 1 described herein.
Filler I/Resin A (Nanozirconia)	Translucent paste containing 80% by weight Filler I in Resin A. (See Example 1.)
Filler K (Comp. Ex. 1) (Nanozirconia)	Acid-treated nanozirconia filler prepared according to Comparative Example 1 described herein.
Filler K/Resin A (Nanozirconia)	Translucent, somewhat viscous material containing 80% by weight Filler K in Resin A. (See Comparative Example 1.)

### Example 1:

#### Silane-Treated Nanozirconia (Filler I)

5           Zirconia Sol (800.0 g; 184 g zirconia) and MEEAA (72.08 g) were charged to a 1-liter round-bottom flask. The water and acid were removed via rotary evaporation to afford a powder (291.36 g) that was further dried in a forced-air oven (90°C) to provide a dried powder (282.49 g). Deionized (DI) water (501.0 g) was added and the powder redispersed. The resulting dispersion was charged to a 2-

10       liter beaker followed by the addition with stirring of 1-methoxy-2-propanol (783 g; Sigma-Aldrich), SILQUEST A-174 (83.7 g) and SILQUEST A-1230 (56.3 g). The resulting mixture was stirred 30 minutes at room temperature and then separated

into two quart jars and sealed. The jars were heated to 90°C for 4.0 hours, and the contents concentrated via rotary evaporation to afford a liquid concentrate (621 g).

DI water (2400 g) and concentrated ammonia/water (80.0 g; 29% NH<sub>3</sub>) were charged to a 4-liter beaker followed by the addition over about 5 minutes of the liquid concentrate to afford a white precipitate. The precipitate was recovered by vacuum filtration and washed with DI water. The resulting wet cake was dispersed in 1-methoxy-2-propanol (661 g) to afford a dispersion that contained 15.33 weight % silane-treated nanozirconia. The silane-treated nanozirconia filler was designated Filler I (Example 1).

The above dispersion (1183 g) was combined with Resin A [HEMA (24.06 g) and PEGDMA-400 (39.59 g)] and the water and alcohol removed via rotary evaporation to afford a translucent paste that contained 80 weight % silane-treated nanozirconia filler (Filler I). The primary and aggregated particle sizes of Filler I were assumed to be the same as in the starting Zirconia Sol, i.e., about 5 nanometers and 50-60 nanometers, respectively.

### **Comparative Example 1:**

#### **Acid-Treated Nanozirconia (Filler K)**

Zirconia Sol (30.0 g; 9.39 g zirconia) and MEEAA (3.67 g) were charged to a 100-ml round-bottom flask. The water was removed via rotary evaporation to afford a dried powder (8 g) that was designated Filler K (Comparative Example 1).

The dry powder (8 g) was combined with Resin A [HEMA (0.756 g) and PEGDMA-400 (1.244 g)] and speed mixed to afford a translucent, somewhat viscous material that contained approximately 80 weight % acid-treated nanozirconia filler (Filler K). The primary and aggregated particle sizes of Filler K were assumed to be the same as in the starting Zirconia Sol, i.e., about 5 nanometers and 50-60 nanometers, respectively.

**Examples 2-3 and Comparative Examples 2-4:  
Paste A – Paste B Compositions**

Five first paste compositions (designated with the letter A as A1 through A5) were prepared by combining the ingredients (indicated as parts by weight) as listed in Table 1. Filler I and Filler K were added to the compositions as mixtures (about 80% by weight) in Resin A and reported in the Tables on a dry filler parts by weight basis; the Resin A components were reported as part of the HEMA and PEGDMA-400 components.

Components (Parts by Weight)	Paste A1	Paste A2	Paste A3	Paste A4	Paste A5
HEMA	3.0	3.0	6.86	6.86	5.3
PEGDMA-400	2.3	2.3	5.26	5.26	6.1
CPQ	0.10	0.10	0.10	0.10	0.10
Filler A (FAS)	40.0	40.0	0	0	60.0
Filler F (Nano)	16.4	16.4	0	0	20.0
Filler I (Silane-Treated Nanozirconia)	29.4	0	67.3	0	0
Filler K (Acid-Treated Nanozirconia)	0	29.4	0	67.3	0
DI Water	8.9	8.9	20.3	20.3	9.1
Total	100	100	100	100	100

Two second paste compositions (designated with the letter B as B1 through B2) were prepared by combining the ingredients (indicated as parts by weight) as listed in Table 2.

Components (Parts by Weight)	Paste B1	Paste B2
HEMA	20.15	45.5
VBCP	10.85	24.5
GDMA	4.6	10.38
BisGMA	2.7	6.09
Kayamer PM-2	5.2	11.74
Ebecryl 1830	0.6	1.35
BHT	0.01	0.01
DPIPF6	0.20	0.45
Filler E (Nano)	53.5	0
AEROSIL R812S	1.8	0
Total	100	100

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Hardenable compositions (Examples 2-3 and Comparative Examples 2-4) were prepared by spatulating a first paste with a second paste for 25 seconds. The relative parts by weight of pastes utilized and the parts by weight components in the compositions are provided in Table 3.

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The hardenable compositions were evaluated for Compressive Strength (DS), Diametral Tensile Strength (DTS), Visual Opacity, and Radiopacity, according to the Test Methods described herein and the results are reported in Table 4.

<b>Table 3</b>					
<b>Paste A + Paste B Compositions</b>					
	Example 2	Example 3	Comp. Ex. 2	Comp. Ex. 3	Comp. Ex. 4
Components (Parts by Weight)	Paste A1 + Paste B1 (1.27:1 wt. ratio)	Paste A3 + Paste B2 (1.27:1 wt. ratio)	Paste A2 + Paste B1 (1.27:1 wt. ratio)	Paste A4 + Paste B2 (1.27:1 wt. ratio)	Paste A5 + Paste B1 (1.27:1 wt. ratio)
HEMA	11.82	26.77	11.82	26.77	11.82
PEGDMA- 400	3.33	7.62	3.33	7.62	3.41
VBCP	4.78	10.80	4.78	10.80	4.77
GDMA	2.04	4.58	2.04	4.58	2.02
BisGMA	1.19	2.69	1.19	2.69	1.19
Kayamer PM-2	2.29	5.18	2.29	5.18	2.29
CPQ	0.056	0.056	0.056	0.056	0.056
Ebecryl 1830	0.264	0.595	0.264	0.595	0.264
BHT	0.0044	0.0044	0.0044	0.0044	0.0044
DPIPF6	0.088	0.194	0.088	0.194	0.088
Filler A (FAS)	22.40	0	22.40	0	33.51
Filler E (Nano)	23.60	0	23.60	0	23.529
Filler F (Nano)	9.19	0	9.19	0	11.17
Filler I (Silane- Treated)	13.174	30.149	0	0	0

Filler K (Acid-Treated)	0	0	13.174	30.149	0
AEROSIL R812S	0.794	0	0.794	0	0.792
DI Water	4.985	11.37	4.985	11.37	5.082
Total	100	100	100	100	100

<b>Table 4</b>					
<b>Paste A + Paste B Compositions – Evaluation Results</b>					
	Ex. 2	Ex. 3	Comp. Ex. 2	Comp. Ex. 3	Comp. Ex. 4
Test	Paste A1 + Paste B1 (1.27:1 wt. ratio)	Paste A3 + Paste B2 (1.27:1 wt. ratio)	Paste A2 + Paste B1 (1.27:1 wt. ratio)	Paste A4 + Paste B2 (1.27:1 wt. ratio)	Paste A5 + Paste B1 (1.27:1 wt. ratio)
Compressive Strength (MPa)	276	NT*	NT	NT	NT
Diametral Tensile Strength (MPa)	48	NT	NT	NT	NT
Visual Opacity	0.25	0.13	0.65	0.54	0.47
Radiopacity	1.73	1.49	1.74	1.40	1.18

\*NT = Not Tested

- 5 It can be concluded from the data in Table 4 that Examples 2 and 3 (both representing compositions containing silane-treated nanozirconia filler) had good radiopacity and excellent Visual Opacity (e.g., MacBeth values less than 0.30),

whereas Comparative Examples 2 and 3 (both containing acid-treated nanozirconia filler) had good radiopacity, but much poorer Visual Opacity (e.g., MacBeth values greater than 0.30). Comparative Example 4 lacked a zirconia filler and had a poorer radiopacity value.

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What is claimed is:

1. A hardenable dental composition comprising:
  - (a) a polyacid;
  - (b) an acid-reactive filler;
  - 5 (c) water; and
  - (d) a nanozirconia filler comprising:
    - (i) zirconia particles having an outer surface, and
    - (ii) a plurality of silane-containing molecules attached onto the  
outer surface of the zirconia particles.
- 10 2. The composition of claim 1, further comprising a polymerizable component.
3. The composition of claim 1, wherein the nanozirconia filler has an average  
particle size of no more than about 100 nanometers.
- 15 4. The composition of claim 2, wherein the polymerizable component  
comprises an ethylenically unsaturated compound.
5. The composition of claim 2, wherein the polymerizable component  
20 comprises an ethylenically unsaturated compound with acid functionality.
6. The composition of claim 1, wherein the polyacid comprises a polymer  
having a plurality of acidic repeating groups but is substantially free of  
polymerizable groups.
- 25 7. The composition of claim 6, further comprising a polymerizable component.

8. The composition of claim 1, wherein the polyacid comprises a polymer having a plurality of acidic repeating groups and a plurality of polymerizable groups.
- 5 9. The composition of claim 8, further comprising a polymerizable component
10. The composition of claim 1, wherein the acid-reactive filler is selected from the group consisting of metal oxides, glasses, metal salts, and combinations thereof.
- 10 11. The composition of claim 10, wherein the acid-reactive filler comprises a fluoroaluminosilicate (FAS) glass.
12. The composition of claim 11, wherein the composition comprises less than 50 weight percent FAS glass.
- 15 13. The composition of claim 11, wherein the composition comprises less than 30 weight percent FAS glass.
14. The composition of claim 11, wherein the composition comprises less than 20 weight percent FAS glass.
- 20 15. The composition of claim 10, wherein the acid-reactive filler comprises an oxyfluoride material.
- 25 16. The composition of claim 15, wherein at least 90% by weight of the oxyfluoride material is nanostructured.
17. The composition of claim 5, wherein the acid functionality includes an oxygen-containing acid of carbon, sulfur, phosphorous, or boron.

18. The composition of claim 5, wherein the polyacid and the ethylenically unsaturated compound with acid functionality are the same.
- 5 19. The composition of claim 1, wherein the polymerizable component and the polyacid are the same compound.
20. The composition of claim 1, wherein the nanozirconia filler is substantially free of fumed silica and pyrogenic fillers.
- 10 21. The composition of claim 2, further comprising a redox cure system.
22. The composition of claim 2, further comprising a photoinitiator system.
- 15 23. The composition of claim 1, further comprising at least one additive selected from the group consisting of other fillers, pyrogenic fillers, fluoride sources, whitening agents, anticaries agents, remineralizing agents, enzymes, breath fresheners, anesthetics, clotting agents, acid neutralizers, chemotherapeutic agents, immune response modifiers, medicaments, indicators, dyes, pigments, tartaric acid, wetting agents, chelating agents, surfactants, buffering agents, viscosity modifiers, thixotropes, polyols, antimicrobial agents, anti-inflammatory agents, antifungal agents, stabilizers, agents for treating xerostomia, desensitizers, and combinations thereof.
- 20 24. The composition of claim 1, wherein the composition is selected from the group consisting of dental restoratives, dental adhesives, dental cements, cavity liners, orthodontic adhesives, dental sealants, and dental coatings.
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25. The composition of claim 1, wherein the composition comprises a multi-part composition comprising a first part and a second part, wherein each part can independently be selected from the group consisting of a liquid, paste, gel, or powder.

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26. A method of preparing a dental article said method comprising the steps of:

- (a) providing a dental composition of claim 1; and
- (b) hardening the dental composition to form the dental article.

10 27. The method of claim 26, wherein the dental article is selected from the group consisting of dental mill blanks, dental crowns, dental fillings, dental prostheses, and orthodontic devices.

28. A multi-part hardenable dental composition comprising:

- 15 (a) a first part comprising a polyacid;
- (b) a second part comprising an acid-reactive filler;
- (a) water present in either or both parts;
- (b) an optional polymerizable component present in either or both parts;
- and
- 20 (c) a nanozirconia filler present in either or both parts, the zirconia filler comprising:
- (i) zirconia particles having an outer surface, and
  - (ii) a plurality of silane-containing molecules attached onto the
- outer surface of the zirconia particles.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2005/010410

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 A61K6/083		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61K C01G C08K B01J		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)  EPO-Internal, WPI Data, PAJ		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 03/086328 A (3M INNOVATIVE PROPERTIES COMPANY) 23 October 2003 (2003-10-23) examples 1,2 tables 1,2 claims	1-28
A	WO 01/30307 A (3M INNOVATIVE PROPERTIES COMPANY) 3 May 2001 (2001-05-03) page 39, line 5 - line 12 page 49, line 19 - page 50, line 7 examples claims	1-28
<input type="checkbox"/> Further documents are listed in the continuation of box C.		
<input checked="" type="checkbox"/> Patent family members are listed in annex.		
° Special categories of cited documents :		
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family	
Date of the actual completion of the international search  <p style="text-align: center; font-weight: bold;">9 August 2005</p>	Date of mailing of the international search report  <p style="text-align: center; font-weight: bold;">19/08/2005</p>	
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  <p style="text-align: center; font-weight: bold;">Thornton, S</p>	

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Information on patent family members

International Application No

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