Abstract:

A bleaching composition (10) includes a matrix material (12) and plurality of solid microparticles (14) dispersed therein. Each microparticle includes a bleaching agent (14) encapsulated in a shell (20) which modifies the release of bleaching agent from the microparticle. The composition can be used for whitening teeth.
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SYSTEM AND METHOD FOR WHITENING TEETH

The following relates to the dental care arts, and related arts and more specifically concerns a method for whitening teeth and a composition which includes a matrix material and an encapsulated whitening agent.

Tooth whitening products that are based on hydrogen peroxide and other bleaching agents, such as sodium percarbonate, include toothpastes, peroxide gel strips, whitening solutions, and mouthwashes. The aim is usually to deliver the whitening agent to the teeth in a sufficient amount to effect a color change in the surface of the teeth in an acceptable period of time without causing harm to the user. Some methods rely on using a high concentration for a short time (e.g., 25% hydrogen peroxide for 30 minutes). Others use a much lower concentration for a longer time (e.g., 1-6% hydrogen peroxide for 10-40 hours, either in a single treatment or over several treatments). Care has to be taken when using high concentrations of hydrogen peroxide to avoid damage to soft tissue, such as the gums, and thus such methods are often regulated and are best employed by dental professionals. Peroxide gel strips use lower concentrations of hydrogen peroxide, but entail wearing a plastic strip on the teeth to be treated for an extended period, or inserting fresh strips repeatedly over a long period.

Another problem with hydrogen peroxide is that it rapidly decomposes and becomes ineffective as a bleaching agent. Recently, methods have been proposed for encapsulating carbamide peroxide in shellac to form microspheres. See, Jing Xue and Zhibing Zhang, "Preparation and characterization of calcium-shellac spheres as a carrier of carbamide peroxide," Journal of Microencapsulation 25(8), p. 523 (2008); and Jing Xue and Zhibing Zhang, "Physical, Structural and Mechanical Characterisation of Calcium-Shellac Microspheres as a Carrier of Carbamide Peroxide," Journal of Applied Polymer Science Vol. 113, p. 1619 (2009). The resulting microspheres are suggested as being suitable for combining with a vehicle, such as a toothpaste or gum. However, the shellac-coated microspheres tend to release the hydrogen peroxide fairly slowly, if at all, unless ruptured by application of a significant pressure.
A composition and method are disclosed which can overcome some of the problems with existing systems.

An advantage of the exemplary composition is that a release rate of a bleaching agent can be tailored to suit a particular application.

In accordance with one aspect of the invention, a bleaching composition includes a matrix material and a plurality of solid microparticles dispersed in the matrix material, each microparticle comprising a bleaching agent encapsulated in a shell formed of a carrier material.

In accordance with another aspect of the invention, a method of whitening teeth includes applying the bleaching composition to the teeth.

The invention may take form in various components and arrangements of components, and in various process operations and arrangements of process operations. The drawings are only for the purpose of illustrating preferred embodiments and are not to be construed as limiting the invention.

FIGURE 1 diagrammatically shows a composition including encapsulated particles in a film forming polymer in accordance with one embodiment disclosed herein.

FIGURE 2 illustrates an applicator for applying the exemplary composition in accordance with another embodiment disclosed herein.

FIGURE 3 is a flow chart illustrating methods for using the exemplary composition, in accordance with embodiments disclosed herein.

FIGURE 4 is a flow chart illustrating methods for forming the exemplary composition, in accordance with embodiments disclosed herein.

FIGURE 5 diagrammatically illustrates a device forming the composition in accordance with another embodiment disclosed herein.

FIGURE 6 graphically shows results of release of hydrogen peroxide from different types of encapsulated particles over time.

FIGURES 7-14 graphically illustrate results of treatment of teeth with varnishes loaded with carbamide peroxide.

With reference to FIGURE 1, a whitening composition in the form of a varnish is shown. The whitening composition includes a matrix material and particles.
containing a tooth bleaching agent dispersed in the matrix material 12. The matrix material 12 includes a resin component, the resin component can include at least one of a polymerizable monomer and a film-forming polymer. The composition is applied as a layer 16 to teeth 18. The layer 16 may be bounded, on the side away from the teeth 18, by a barrier layer 20 formed from a moisture-resistant material, such as a polymer material which hardens more completely than the underlying matrix material 12.

The matrix material 12 (and the composition 10 containing it) can be adhesive (to the teeth) and/or capable of film forming on the teeth.

The particles 14 illustrated in FIGURE 1 each include a core 22, formed of the bleaching agent, which is encapsulated in a shell 24 formed of a carrier material. The carrier material can be formed of any suitable material, which is different, at least in some respects, from that of the core, to space the bleaching agent from the matrix material 12 and/or to modify the rate of release of bleaching agent from the composition, and can be a solid at ambient temperature.

The bleaching agent may be present, expressed as the equivalent weight of hydrogen peroxide in the composition 10, at from 0.1 wt. % to 50 wt. %. In one embodiment, the bleaching agent may be present, expressed by weight of hydrogen peroxide, at from 2 wt. % to 25 wt. % of the composition 10, or when formulated for home use, the composition may be from 2 wt. % to 8 wt. % equivalent of hydrogen peroxide. The particles may be homogeneously dispersed in the matrix material.

The exemplary carrier material forming the shell 24 may include a hydrophobic material 26 and optionally a release rate modifier 28 in contact with, e.g., dispersed in, the hydrophobic material 26. In other embodiments the hydrophobic material 26 and release rate modifier 28 may form two distinct layers, with the hydrophobic material forming the outermost layer. The microencapsulation may serve to control release of the bleaching agent from the core and/or to separate the bleaching agent from other chemicals in the varnish with which it might react. In some embodiments, the matrix material can provide for slow release of the bleaching agents and the microencapsulation simply the separation, in which case, the shell 4 may provide a quick release from the microparticles. In other embodiments, the shell provides for slow release of the bleaching agents.
In addition to the particles 14, which are referred to herein as microparticles, the matrix 12 of the composition may further include other particles 30 which serve as viscosity modifiers, such as silica particles, which are dispersed in the resin component of the matrix material 12. Other optional additives which may be present in the composition 10 and/or the barrier layer 20 include other viscosity modifiers, tartar control (anticalculus) agents, abrasives, fluoride ion sources, remineralization agents tooth desensitizers, anticaries agents, antimicrobial agents, antioxidants, anti-plaque agents, anti-inflammatory agents, coloring agents, such as titanium dioxide, flavoring agents, and the like. These additives may each be present in one or more of the matrix material 12, the barrier layer 20, the shell 24, and the core 22 of the particles, as appropriate.

To evaluate candidate compositions for durability and removal, samples of the composition can be applied to teeth, such as bovine teeth, tested to see if they cure sufficiently to retain their integrity for a few hours, for example, and can be removed by brushing.

As will be appreciated, FIGURE 1 is intended to be illustrative only and is not intended to be to scale.

FIGURE 2 illustrates an exemplary applicator 34 which can be used to apply the composition 10. The applicator includes a suitably shaped dental tray 36 and a source 38 of light of a curing wavelength. In another embodiment, the composition 10 is applied using a pen type device. Parts of the composition may be stored in separate chambers of the pen to be mixed when the two parts are applied to the teeth. For example, a photoinitiator may be in one compartment and a monomer in the other. In other embodiments, all components of the composition are kept in a single chamber of the pen. Separate pens may be used for multilayer compositions.

The composition, when applied on the teeth, may be allowed to cure or in some embodiments at least one of heat, an air jet, and light may be applied to speed up the process. Lip retraction may be used to keep the lips from coming into contact with the composition as it cures. Curing is used herein to describe any process by which the composition forms an intact layer on the teeth which is capable of remaining on the teeth throughout the whitening process. Vibration may be used during curing to improve the smoothness of the layer. Soft tissue in the mouth, such as the gums, may be protected, prior
to applying the composition 10, with a layer of a suitable material which is free of the microparticles.

**Method of using the composition**

The composition 10 and optional barrier layer 20 may be applied to the teeth 18 of a person, to whiten the teeth.

With reference to FIGURE 3, a method for treating teeth with the exemplary composition is shown. The method begins at S100. At S102, the composition 10 is provided. Details on forming the exemplary composition are described with reference to FIGURE 4.

At S104 the composition is applied to the teeth of a person or animal to be treated. The composition may be applied by a dental professional, such as a dentist, or by the wearer. For example, the composition 10 may be applied to the teeth using an applicator, such as a pen, brush, piece of foam, or cloth applicator to form a layer. In other embodiments, the composition 10 may be inserted into an applicator, such as into the dental tray 36 of the applicator 34 shown in FIGURE 2, which is positioned adjacent the teeth and then removed, for example, after partial curing of the composition.

The composition 10 may be applied to the teeth at a thickness t of for example, from 50-500µm, such as from 50-300µm, e.g., about 200µm. In the exemplary embodiment, the film is greater in thickness than the average diameter of the particles 14, for example, at least twice or at least three times the average diameter of the particles. This allows the varnish to be smooth to the touch, when cured.

Optionally, at S106, a barrier layer 24 is applied over the layer 16 of composition 10.

At S108, the composition may be cured or otherwise hardened to form a film containing the microparticles on the teeth. The curing/hardening may be performed with light, moisture, solvent evaporation, or a combination of these. In one embodiment, the matrix material 12 includes a resin component which is moisture-cured, for example, by saliva naturally present on the teeth. In another embodiment, the matrix material includes a solvent which evaporates. In yet another embodiment, the resin component of the matrix material includes a curing agent and is cured by light, such as blue light, form a suitably
positioned light source 38. Different compositions for these types of matrix material are discussed below. In one embodiment, the exemplary composition cures rapidly, for example in 10 minutes or less, such as in under three minutes, for example, from a few seconds to a minute. For compositions which take minutes or longer to cure, soft tissue in the mouth, such as the lips and/or gums, may be protected with a coating or held away from the teeth, e.g., with a lip retractor.

In one embodiment, the source 38 of light in wavelengths suitable for curing the composition, such as blue light, is positioned adjacent the layer 18 and optional layer 24, if present. The light of the specified wavelength range may be applied by a light source 38 integral with the applicator 34, if used, or by a separate light source. Barrier layer 20 may be cured contemporaneously with the composition 10 or applied subsequently and cured or allowed to cure.

At step 10, after sufficient time to effect at least a partial whitening of the teeth, e.g., a change in color of at least 1 \( \Delta E \), the layer of varnish (and optional barrier layer) is removed. For example, at the end of the treatment period, the composition 10 is removed from the teeth by peeling it away from the teeth and/or by brushing the teeth. The process may be repeated, for example, once a day, week, or month or less frequently, until a desired color change is effected or to maintain whiteness of the teeth.

\( \Delta E \) is computed according to the CIE76 definition, using the \( L^*, a^*, b^* \) values of the teeth (which may be averaged values), before whitening (denoted by the subscript 1) and after whitening (denoted by the subscript 2), according to the formula:

\[
\Delta E = \sqrt{(L_2^* - L_1^*)^2 + (a_2^* - a_1^*)^2 + (b_2^* - b_1^*)^2}
\]

The method ends at SI 12.

The matrix material 12 is formulated to form a film on the teeth which retains the particles in close proximity to the surface of the teeth. Over a period of from about 30 minutes to several days, such as from 2-10 hours, the bleaching agent in the particles 14 is activated by moisture and whitens the teeth by removing stains and optionally whitening the tooth enamel. In particular, moisture penetrates the matrix material 12 and contacts the shell 24 of the particles, which serves as a slow release layer. Over time, the shell 24 becomes more permeable to water, allowing the bleaching agent within the core 22 to
escape. For example, pores 40 may form in the shell 24 which extend from an outer surface 42 of the particle to the core 22 (FIG. 1). The shell 24 can be tailored, e.g., by changing its composition or thickness, to allow for a slower or a faster release of the bleaching agent.

In the exemplary embodiment, the varnish 10 whitens the tooth using just the moisture within the tooth itself, and can then be easily removed from the teeth. Due to the slow release properties of the shell 24 (and optional barrier layer 20), the concentration of bleach in the oral cavity remains fairly low and does not pose a significant risk of damage or irritation to the soft tissue in the mouth. The prolonged contact of the composition 10 with the teeth, however, allows the bleaching agent to be released progressively from the core 22 and to whiten the teeth.

**Microparticles**

The exemplary microparticles 14 are generally spherical in shape. They can be dry, solid particles of up to 200 micrometers (μm) in diameter, on average, or up to 100 μm in diameter. By "solid" it is meant that the particles are solid at ambient temperatures, e.g., solid at a temperature of up to 30°C, at least. By "diameter," it is meant the average dimension, to the extent that the particles are non-spherical. For example, the microparticles 14 can be at least 1 or at least 10 μm in diameter, on average, and in one embodiment, at least 20 μm in diameter on average. In some embodiments, the microparticles are up to 50 μm in diameter, on average. The core 22 may occupy from 1 to 99% of the volume of the microparticle, such as from 10-90%, on average. The shell 24 may be at least 20 nm in thickness, on average, such as at least 0.1 μm, or at least 1 μm in thickness, and in some embodiments, up to 40 μm in thickness, on average. The core 22 may be at least 0.1 μm in diameter, on average, such as at least 1 μm in diameter, and in some embodiments, at least 10 μm, or at least 20 μm, and can be up to about 100 μm, in average diameter. In some embodiments, the core may be up to 10 μm, or up to 20 μm, or up to 50 μm in average diameter. In one embodiment, the particles have a core which is up to 15 μm in average diameter and the microparticles are between 20 and 100 μm in average diameter. A ratio of a weight of the shell 24 to a weight of the core 22 can be for example, from 0.1:99.9 to 99.9:0.1, or 1:99 to 99:1, or 10:90 to 90:10, or 50:50 to 70:30, such as 60:40.
The core 22 may be partly or entirely formed from the dental bleaching agent. For example, at least 10%, or at least 20%, or at least 50%, or at least 80%, by weight of the core and up to 100% by weight is bleaching agent. Exemplary bleaching agents are solid at ambient conditions and include carbamide peroxide, which is an adduct of urea and hydrogen peroxide (CH₄N₂O-H₂O₂). This material releases hydrogen peroxide on contact with water. Other example bleaching agents include alkali metal percarbonates, sodium perborate, potassium persulfate, calcium peroxide, zinc peroxide, magnesium peroxide, strontium peroxide, other hydrogen peroxide complexes, sodium chlorite, combinations thereof, and the like. The term "bleaching agent," herein refers to compounds which are themselves bleaches and to compounds which are bleach precursors, such as carbamide peroxide, which react or decompose to form a bleach, such as hydrogen peroxide.

The microparticles 14 can include the bleaching agent, e.g., carbamide peroxide, at a concentration of at least 5 wt. % or at least 10 wt. %, such as up to about 95 wt. %, or up to about 60 wt. %, 20 wt. % carbamide peroxide, as an example, corresponds to a hydrogen peroxide concentration per particle of about 6 wt. %. This relatively low level may be suited to home use, particularly when the microparticles at relatively high concentrations in the composition (such as at least 20 wt. % or at least 50 wt. % of the composition). However, higher concentrations of the bleaching agent in the particles may be employed to achieve an overall concentration in the composition 10 of at least 2 wt. % or more, as noted above.

In some embodiments, the shell 24 provides a moisture-resistant barrier which releases the bleaching agent slowly, on contact of the microparticle 14 with water, such as with saliva on the teeth or moisture within the teeth. This provides a controlled release of the bleaching agent. In some embodiments, controlled release of the bleaching agent is provided solely or partly by the matrix material 12 and the shell 24 serves to separate the bleaching agent from components in the matrix material 12 with which it may react, such as water and or organic solvents, e.g., alcohols.

In some embodiments, the hydrophobic material 26 of the shell 24 is a water-insoluble and/or hydrophobic material, such as a waxy solid, i.e., is solid at ambient temperature (25°C) and may be a solid at relatively higher temperatures. Exemplary waxes suitable to use as the hydrophobic material include hydrocarbon waxes, such as paraffin.
wax and the like, which are substantially or entirely free of unsaturation. Exemplary paraffin waxes are higher alkanes and mixtures of higher alkanes of the general formula CₙH₂n+2, where typically, 20 ≤ n ≤ 50, and thus have no unsaturation. They are solid at ambient temperatures and melt-processable. The melting point of the waxy solid may be within the range of from 30°C to 100°C. To avoid decomposition of the bleaching agent in the core, the waxy solid may have a melting point of below 80°C, and in one embodiment, below 65°C. Paraffin waxes with a melting point of 40°C-60°C may be used, by way of example. Paraffin wax with a melting point of 53-57°C can be obtained from Sigma-Aldrich. Other paraffin waxes are available with melting points of 45°C, 50-52°C, 53-57°C, and 60°C. The melting point of waxes is determined according to ASTM D87 - 09, "Standard Test Method for Melting Point of Petroleum Wax (Cooling Curve)."

The hydrophobicity of the hydrophobic material 26 can be expressed in terms of its contact angle to water. In one embodiment, the water contact angle is at least 75°, such as at least 85°, and in some embodiments, at least 100°, such as up to 120°. The water contact angle can be determined using a contact angle goniometer, for example. The contact angle can be measured on a flat sheet of wax prepared by spraying the molten wax onto a smooth surface, such as a plastic Petri dish to form a wax layer with thickness of approximately 5 mm. After solidification, the rigid, flat wax layer can be removed from the Petri dish and cut into sheets suitable for contact angle analysis. The contact angle of water in air on the surface of such a sheet can be measured using a goniometer, such as an EasyDrop™ (Kruss, Germany). 4μL of double distilled water in a micro-syringe is dropped on the surface of the sheet placed on a moveable sample stage. The drop is illuminated from one side and the camera on the opposite side records and images the drop. This image is then analyzed by DSA software to calculate the contact angle.

By way of example, two different molecular weights of paraffin wax with melting point of 50-52°C and 53-57°C (Sigma Aldrich, UK) were tested and the measured contact angle was 110.3° ±0.5 and 111.0° ±1, respectively.

The release rate modifier 28 controls the rate of release of the bleaching agent from the core of the microparticles 14. Exemplary release rate modifiers 28 include hydrophilic organic polymers which are capable of hydrogen bonding and that are solid at ambient temperatures (25°C), hydrophilic and/or water soluble powders, and combinations thereof.
The release rate modifier 28 is more hydrophilic than the hydrophobic material 26. The release rate modifier may be dispersed in the hydrophobic material. In the case of organic polymers, the release rate modifier 28 may be a material which is insoluble or substantially insoluble in the hydrophobic material 26 such that it forms discrete regions where it is of high concentration in the hydrophobic material (or forms a separate layer). The regions may be spaced from each other by the hydrophobic material 26. In the case of hydrophilic and/or water soluble powders as the release rate modifier, the powder may be dispersed throughout the hydrophobic material, or in one embodiment, more highly concentrated near an outer surface thereof. The release rate modifier(s) may be present in the particles 12 at a total concentration of from 0.001 wt. % to 40 wt. %.

In the case of hydrophilic and/or water soluble powders as release agents, these may be present in the microparticles 12 in a total concentration of from 0.001 wt. % to 30 wt. %, such as 0.1-20 wt. %, or 1.0 to 10 wt. %. Examples of hydrophilic powders include anhydrous inorganic particles, such as silicon dioxide, e.g., hydrophilic silica and silica nanopowders. Exemplary water-soluble powders include water-soluble acids and salts thereof, such as anhydrous phosphate salts, e.g., sodium polyphosphate, sodium tripolyphosphate, sodium pyrophosphate; anhydrous citric acid and salts thereof, such as alkali metals salts, e.g., sodium citrate; anhydrous sodium sulfate, anhydrous magnesium salts, such as magnesium sulfate and magnesium chloride. Combinations of such release agents may be employed. The hydrophilic and/or water soluble powders remain solid during formation of the shell. The hydrophilic and/or water soluble powders, such as silica, may have an average particle size of, for example, 1-100 nanometers (nm), e.g., 5-20 nm, and a surface area of, for example 50-400 m²/g. Hydrophilic fumed silica, for example, may be obtained under the tradename AEROSIL™ from Evonik Industries with a specific surface area (measured by the BET method) in the range of 90-300 m²/g. As an example, AEROSIL™ 200 has a specific surface area of 200 m²/g.

When hydrophilic organic polymers are used as release rate modifiers 28, these may be present in the microparticles 14 at a total concentration of from 0.5 wt. % to 40 wt. %, e.g., 1-35 wt. %, or 10-30 wt. %. The hydrophilic organic polymers may be liquefied during formation of the shell. In one embodiment, the hydrophilic polymer has a melting point of at least 30°C or at least 40°C, such as up to 80°C. The hydrophilic polymer can
have a weight average molecular weight of at least 300. Examples of suitable hydrophilic organic polymers include polyalkylene glycols, such as polyethylene glycol and polypropylene glycol, and esters thereof, polyamide compounds (e.g., polyvinylpyrrolidone), poly(vinyl acetate), poly(vinyl alcohol), poly(acrylic acid), polyacrylamide, polyoxylglycerides, such as lauroyl, oleoyl, and stearoyl polyoxylglycerides, which are mixtures of monoesters, diesters, and triesters of glycerol and monoesters and diesters of polyethylene glycols (e.g., lauroyl macrogolglycerides, such as GELUCIRE™ 44/14, available from Gattefosse, which has a melting point of 44°C and an HLB of 14), and ethylene oxide derivatives thereof, poloxamers, which are triblock copolymers having a central hydrophobic block of poly(propylene oxide) and two side blocks of poly(ethylene oxide) (e.g., poloxamer 188, which has a melting point 52°C), and derivatives thereof, and mixtures thereof.

Exemplary polyethylene glycols (PEG) suitable for the release rate modifier may have a weight average molecular weight of from 300 daltons to 50,000 daltons, such as about 600-35000, or 1000 to 5,000 daltons. Such materials are commercially available as PEG 1000 (melting point 37-40°C), PEG 1500 (melting point 44-48°C), PEG 2000 (melting point 49-52°C), and the like. A combination of polyethylene glycols having different molecular weights may be employed to tailor the release rate. For example a mixture may be formed by combining, e.g., in a ratio of from 1:10 to 10:1, a polyethylene glycol having a molecular weight of about 500-1200 (on average), such as PEG 1000, with a polyethylene glycol having a molecular weight of at least 1500 or at least 1800 (on average), such as PEG 1500 or PEG 2000. In one embodiment, a combination of PEGs with average molecular weight ranging from 300 daltons to 50,000 daltons may be mixed on appropriate amounts to provide a mixture which is liquid at a temperature of 35-70°C, such as 45-60°C. For example, PEG with an average molecular weight of 20,000 and PEG 1500 have melting points of 60-65°C and 44-48°C, respectively, and a mixture of PEG 1500 and PEG 20,000 may be liquid at about 55°C, depending on the ratio.

In the case of hydrophilic organic polymers, such as PEG, the discrete regions in which the polymer is localized may have an average size of, for example, at least 0.1 or at least 0.5 nm, and can be up to 100 nm, or up to 20 nm, e.g., 0.5-5 nm. For example, the
hydrodynamic radius of glycerol is 0.3 nm and that of PEG 1000, PEG 2000 and PEG 4000 is approximately 0.9, 1.4 and 1.9 nm, respectively.

A ratio of hydrophobic material 26 to the release rate modifier 28 in the microparticles 14 may be from 1:99 to 99:1, expressed by weight, such as from 2:98 to 98:2, or from 10:90 to 90:10, or from 15:85 to 85:15. The ratio can be at least 30:70, or at least 40:60, or at least 60:40. For example, in the case of polymers, such as PEG, the ratio of hydrophobic material to release rate modifier may be about 60:40 or about 50:50. For hydrophilic and/or water soluble powders, the ratio of hydrophobic material to the release rate modifier may be higher, such as at least 85:15, or at least 90:10.

The microparticles generally have a low water content, such as less than 5 wt. %, or less than 1 wt. %, or less than 0.2 wt. % of the microparticles is made up of water (free and bound).

In some embodiments, the release rate modifier 28 increases the rate of release of the bleaching agent, as compared with the hydrophobic material 26 alone. For example, the amount of bleaching agent released from the microparticles with the exemplary release rate modifier 28 (e.g., expressed as weight of hydrogen peroxide), may be at least 10% greater or at least 50% greater, over an initial period of two hours, than for the equivalent microparticles formed without the release rate modifier 28, when exposed to the same aqueous conditions (e.g., a buffered release medium, at a temperature of 30-40°C, e.g., as discussed in the Example below). By "equivalent microparticles," it is meant the microparticles are identically formed except that no release rate modifier is employed.

In some embodiments, the release rate modifier 28 may provide the exemplary microparticles 14 with a more uniform rate of release of hydrogen peroxide than equivalent microparticles formed without the release rate modifier 28, when exposed to the same aqueous conditions (e.g., buffered release medium at a temperature of 30-40°C). For example, the initial release rate (expressed as wt. of hydrogen peroxide/hr), over about two hours, may be, on average, less than that of equivalent microparticles without the release rate modifier and may be on average, higher than that of equivalent microparticles in the subsequent two hour period.

In some embodiments, the exemplary microparticles 14 formed with the release rate modifier 28 release at least 10%, or at least 20%, or at least 30% by weight of the total
amount of bleaching agent (expressed in terms of hydrogen peroxide) that they contain over a period of 12 hours after contact of the composition 10 with the teeth or aqueous medium at 30°-40°C. In some embodiments, the exemplary microparticles formed with the release rate modifier 28 release less than 40%, or at less than 30%, or less than 25% by weight of the bleaching agent (expressed in terms of hydrogen peroxide), over a period of 4 hours after contact with the teeth or with an aqueous medium at 30°-40°C.

As will be appreciated from the foregoing, the amount and type of release rate modifier can be selected to tailor the release rate according to the desired application. For example, if the composition 10 containing the microparticles is to remain in contact with the teeth for a period of several hours, a slower release rate may be more desirable than when the composition is to be removed more quickly.

In one embodiment, the shell 24 may further include an emulsifier, dispersed in the hydrophobic material. Exemplary nonionic surfactants suitable as emulsifiers include fatty acids, polyol fatty acid esters, such as polyglycerol esters, fatty alcohol polyglycol ethers, alkylphenol polyglycol ethers, fatty acid polyglycol esters, fatty acid amide polyglycol ethers, fatty amine polyglycol ethers, alkoxylated triglycerides, mixed ethers and mixed formals, optionally partly oxidized alk(en)yl oligoglycosides or glucuronic acid derivatives, fatty acid-N-alkyl glucamides, protein hydrolyzates (particularly wheat-based vegetable products), sugar esters, sorbitan esters, polysorbates, amine oxides and combinations thereof. As examples of suitable emulsifiers, nonionic surfactants with a low hydrophile-lipophile balance (HLB) may be used. The HLB may be from 2-5. Surfactants that are able to form micelles are able to improve the stability of hydrogen peroxide. Examples of these emulsifiers include C12-C24 fatty acids, such as lauric acid (C12), myristic acid (C14), palmitic acid (C16), stearic acid (C18), oleic acid (C18), linoleic acid (C18), and mixtures thereof. Such fatty acid emulsifiers can be obtained from Sigma-Aldrich under the tradename SPAN™, such as SPAN™ 60, which has an HLB of 4.7, SPAN™ 65, with an HLB of 2.1, SPAN™ 80, with an HLB of 4.3. Exemplary polyglycerol esters include polyglycerol polyricinoleate (PGPR), which has an HLB of 3, and is available from Evronik Industries, Essen Germany, or Danisco. A blend of surfactants having a high HLB and low HLB value may be used.
The emulsifier may be present in the microparticles at a concentration of at least 0.001 wt. %, such as at least 0.1 wt. %, or at least 1 wt. %, and can be present at up to 5 wt. % or up to 10 wt. %, e.g., about 2 wt. %.

Release rate modifiers and emulsifiers may be suitably selected such that they do not adversely affect the stability of the bleaching agent, e.g., of hydrogen peroxide.

Mechanisms by which the release rate is controlled by the release rate modifier are proposed by way of example. In one embodiment, the release rate modifier 28 dissolves in water, leaving pores 40 in the shell 24 where the release rate modifier was previously located. In other embodiments, the release rate modifier attracts and/or absorbs water, increasing in volume and causing a localized disruption in the integrity of the shell.

For example, in the case of a wax/PEG mixture as the encapsulation medium, the wax is hydrophobic, repelling water, while the solid PEG is hydrophilic, attracting water. The release rate can be engineered by varying the ratio of these components. When water is present, it is attracted to hydrophilic regions on the surface of the microsphere (FIG. 1) that are defined by the regions of PEG release rate modifier, or through small cracks in the hydrophobic layer to an underlying hydrophilic layer. The PEG region/layer becomes the site of a pore as water swells the PEG. When a pore penetrates to the carbamide peroxide core 22, the core releases hydrogen peroxide when it gets wet.

The emulsifier present may also affect the release rate.

In some embodiments, the core 22 and/or shell 24 may include additives, such as colorants, preservatives, abrasive materials, emulsifiers, and the like.

A method for optimizing a release rate of the bleaching agent from the particles may include formulating sets of microparticles, each set having a different ratio of hydrophobic material to release rate modifier and testing the sets of microparticles to determine the release rates or amount of bleaching agent released in a selected time period. The method can further include selecting an optimal ratio of hydrophobic material to release rate modifier, based on the results of the tests, for example, to provide a desired release rate of the bleaching agent. Similar tests may be performed with combinations of release rate modifiers and/or emulsifiers, such as different combinations of PEG molecular weight, and selecting a combination of release rate modifiers to identify an optimal
combination of release rate modifiers for optimizing a release rate of the bleaching agent. Various combinations of these tests are also contemplated.

**Exemplary Varnish Compositions**

Suitable varnish compositions 10 include self-cured and light-cured compositions. Example compositions 10 may include (the components totaling 100%):

A. 2-95 wt. % (or 5-90 wt. %, or 20-80 wt. %) of microparticles 14; and

B. 98-2 wt. % (or 10-95 wt. %, or 80-20 wt. %) of the matrix material 12, the matrix material consisting of (the matrix material components totaling 100%):

- Bl. 1-70 wt. % (or 5-50 wt. %, or 10-20 wt. %) of a resin component, which may comprise at least one of a polymerizable monomer and the reaction product of a polymerizable monomer and a curing agent,

- B2. 0-30 wt. % (or 2-20 wt. %, or 5-10 wt. %) of an organic solvent,

- B3. 0-40 wt. % viscosity modifier, and

- B4. 0-50 wt. % (or 1-20 wt. %) other additives (i.e., other than the components A, Bl, B2, and B3), such as one or more of particles, colorants, anti-tartar agents, anti-caries agents, surfactants, antimicrobial agents, antioxidants, anti-plaque agents, and the like.

The matrix material (12) can be substantially free of water (includes less than 5 wt. % water, or less than 1 wt. % water). In some embodiments, no water is used in forming the composition. Additionally, the components used in forming the composition may be dry, and may be anhydrous, where possible.

A ratio, expressed by weight, of microparticles to the matrix material in the composition 10 can range from 1:50 to 50:1, such as at least 1:10 (or at least 1:2, or at least 1:1, or at least 5:1, or at least 10:1, or at least 15:1).

The resin component B1 can include one or more polymerizable monomers and a curing agent. In some embodiments, the resin component B1 can include a film forming polymer and/or resin. A "monomer," as used herein includes polymerizable monomers, dimers, and oligomers, except as noted.
The solvent B2 can be any compatible pharmaceutically-acceptable organic solvent, such as an alcohol, unsaturated hydrocarbon, ketone, or the like, which is liquid and/or volatile at ambient temperatures (20-30°C).

The viscosity modifier may include one or more of particles, waxes, gums, and other thickeners, and.

Example matrix compositions are now described.

1. **Self-cure compositions:** these include moisture cured varnishes and solvent based varnishes.

   a. **Moisture Cured Varnishes:**

      Examples of these include varnishes based on natural resins, such as colophonium resin which cures when in contact with saliva. Varnishes of this type are disclosed for example, in WO2009/12431. Shellac may also be used in such compositions, alone or in combination with another resin. An example moisture-cured matrix material B suited to use in such varnishes may include (totalling 100%):

      B1. 1-70 wt. % (or 5-50 wt. %, or 10-20 wt. %) of a resin (moisture-cured and/or air-cured),

      B2. 1-30 wt. % (or 2-20 wt. %, or 5-10 wt. %) of a solvent,

      B3. 0-40 wt. % viscosity modifiers (or 1-20 wt. %, or 5-10 wt. %),

      such as one or more of:

      B3a. particles (e.g., at 1-20 wt. %, or 5-10 wt. %),

      B3b. waxes (e.g., 1-20 wt. %, or 5-10 wt. %), and

      B3b. gums (e.g., 1-20 wt. %, or 5-10 wt.), and

      B4. 0-20% (or 1-20%) of other additives.

      The composition containing such a matrix material is applied on damp teeth and the mouth closed to allow saliva to cure the resin.

      As an example, a matrix composition 12 can be formed from colophonium resin and/or shellac, a solvent, and optionally one or more waxes and/or gums. Example solvents include C1-C20 alcohols and ketones, e.g., ethanol, propanol, cetyl alcohol, stearyl alcohol, and C6-C20 hydrocarbons, such as hexane. Example hydrocarbon waxes include esters of fatty acids and long chain alcohols that are solid or viscous liquids at room temperature.
These include naturally occurring waxes such as beeswax, and C40-C100 alkanes and fatty acid esters. Gums, such as mastic (a resin obtained from *Pistacia lentiscus Var. Chia*) may be included in the matrix material.

One example moisture-curable composition 10 includes a matrix material 12 comprising colophonium resin and an organic solvent (e.g., one or more of ethanol, methanol, n-hexane, and cetostearyl alcohol), and the exemplary microparticles 14.

Another example moisture-curable composition 10 includes a matrix material 12 comprising shellac, colophonium resin, a solvent (such as ethanol), beeswax, and mastic, and the exemplary microparticles 14.

b. Solvent-based varnishes: these are based on solvent evaporation. An exemplary matrix material of this type can include a conventional polyacrylic acid based polymer in combination with a solvent, such as C1-C10 mono-alcohol or polyol, e.g., one or more of methanol, ethanol, n-hexane, and glycerol, and optionally a buffer agent. The polyacrylic acid-based polymer may include functional groups which increase the permeability of the polymer matrix to water, such as ammonium groups, e.g., as their salts.

As an example, the matrix material can be formed from acrylic acid polymers such as Carbomer, optionally a surfactant such as a polysorbate or sorbitan ester (e.g., sobitan monooleate), glycerol, and EDTA as buffering agent. Other components may be present, such as arginine and potassium nitrate.

A composition 10 containing such a resin can be applied on dry teeth and the mouth kept open to allow the resin to cure in 30 seconds to 2 minutes.

An example solvent-based matrix material B may include (totalling 100 %):

Bl. 1-70 wt. % (or 5-50 wt. %, or 10-20 wt. %) of resin,

B2. 1-30 wt. % (or 2-20 wt. %, or 5-10 wt. %) of a solvent,

B3. 0-40 wt. % viscosity modifiers, such as particles 30, waxes, and/or gums, and

B4. 0-20% other additives, such as 0.001-5 wt. % of a surfactant and 0.001-5 wt. % of a buffering agent.

In one embodiment, the solvent based varnish may include, in the above amounts:

Bl. Copolymer derived from esters of acrylic and methacrylic acid, e.g., available under the tradename Eudragit® from Evonik (e.g., Eudragit® RL PO, a
poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethyl methacrylate chloride), which is a copolymer of ethyl acrylate, methyl methacrylate and a low content of methacrylic acid ester (ratio of 1:2:0.2) with quaternary ammonium groups, which are present as their salts. The polymer has the general formula:

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_2 & \quad \text{CH}_2 \\
\text{H}_3 & \quad \text{H}_3 \\
\text{N}^+ & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

B2. Solvent such as n-hexane, ethanol, cetostearyl alcohol

B4. Other additives (optional) to increase efficiency, product delivery, product shelf life and wearer suitability, such as:

- Stabilizer such as polyphosphates, benzoic acid, salicylic acid, EDTA, sodium perborate
- Saliva inhibitor such as sodium fluoride
- Flavoring, such as mint or peppermint oil
- Emulsifier, such as Tween 20, Span 80
- Humectant, such as glycerin, sorbitol, xylitol, PEG
- pH control agent, such as sodium bicarbonate, sodium hydroxide, citric acid

This matrix material is combined with an encapsulated whitening agent, such as carbamide peroxide, calcium peroxide, sodium perborate, hydrogen peroxide

2. **Light-cure varnishes:** In the case of light-cured compositions, the resin component B1 may comprise one or more polymerizable monomers Bla, Bib and optionally one or more
curing agents Blc, Bid. Example polymerizable monomers may include one or more
functional monomers Bla and optionally a crosslinking monomer Bib. The curing agent
may include at least one of a photoinitiator Blc and a co-initiator Bid.

An example light-curable matrix material B may include (totalling 100 %):

- **Bl.** 1-70 wt. % (or 5-50 wt. %, or 10-20 wt. %) of resin,
- **B2.** 1-30 wt. % (or 2-20 wt. %, or 5-10 wt. %) of an organic solvent,
- **B3.** 0-40 wt. % viscosity modifying particles 30 and/or waxes, and
- **B4.** 0-20% other additives.

An example light-curable resin component B1 may include (totalling 100 %):

- **B1a.** Functional monomer (e.g., HEMA): 10-50 wt. %
- **B1b.** Crosslinking monomer (e.g., Bis-GMA): 50-90 wt. %
- **B1c.** Initiator (e.g., Camphorquinone): 0.1-2 wt. %
- **B1d.** Co-initiator (e.g., DMAEMA) 0-3 wt. %, e.g., at least 1 wt. %.
- **B1e.** Inhibitor (to reduce self-polymerization in storage) 0-3 wt. %, e.g., at least
0.01 wt. %, such as about 0.1%.

Suitable functional monomers Bla include mono-functional and multifunctional
acrylates and methacrylates (referred to jointly herein as (meth)acrylates). Suitable
(meth)acrylates include those having a viscosity of about 0.1 to about 100 cps at 25°C. Use
of multifunctional (meth)acrylates can increase cure speed of the resin composition.
Examples of these monomers include hydroxyalkyl methacrylates, such as 2-hydroxyethyl
methacrylate (HEMA) and 2-hydroxypropyl methacrylate; ethylene glycol methacrylates,
including ethylene glycol methacrylate, diethylene glycol methacrylate, tri(ethylene glycol)
dimethacrylate and tetra(ethylene glycol) dimethacrylate; and diol dimethacrylates such as
butanediorthymethacrylate, dodecanediothymethacrylate, and 1,6-hexanedioldimethacrylate
(HDDMA), and mixtures of these.

Suitable crosslinking monomers Bib include bisphenol glycerolate dimethacrylate
(Bis-GMA), which is the condensation product of bisphenol A and glycidyl methacrylate;
triethylene glycol dimethacrylate (TEDGMA); aliphatic and aromatic polyurethane
dimethacrylate (PUDMA); and urethane dimethacrylate (UDMA), and mixtures of these.
Other viscous resins having a viscosity of greater than about 1000 centipoise (cps) at 60°C
can also be used. The amount of crosslinking monomer can have an influence on mechanical property and viscosity of the resin.

Other examples of suitable (meth)acrylates include higher viscosity (meth)acrylates, such as aliphatic and aromatic diurethane dimethacrylates (DUDMA), polycarbonate dimethacrylate (PCDMA), a condensation products of two parts of a hydroxyalkylmethacrylate and 1 part of a bis(chloroformate), as disclosed in U.S. Pat. Nos. 5,276,068 and 5,444,104; and ethoxylated bisphenol A dimethacrylate (EBPDMA), as disclosed in U.S. Pat. No. 6,013,694.

Most methacrylates are moderately hydrophobic. Some form films which are very strong and do not release easily from the teeth. In some embodiments, a first (meth)acrylate Bla, which forms strong bonds with teeth is combined with a second (meth)acrylate Bib, e.g., a dimer, as a crosslinker which forms less strong bonds. As an example, HEMA (hydroxyethyl methacrylate), which is semi-soluble in water, is combined with a less-strong dimer, such as polyethylene glycol (PEG) dimethacrylate (a polymer of ethylene oxide which is terminated at each end by a methacrylate unit). The molecular weight of the PEG can be controlled/chosen to achieve the desired bonding and release properties. This gives cross linking with a weaker backbone and moderate hydrophilicity. As an example, the PEG dimethacrylate can have a number average molecular weight of 100-2000, such as at least 500. Additionally or alternatively, by modifying the stoichiometry, e.g., by overloading the blend with HEMA, the crosslink density can be controlled.

Example photoinitiators Blc include camphoroquinone (CQ), phenylpropanedione (PPD), benzoin esters, benzophenone, acylphosphine oxides, and lucirin. A co-initiator Blc may be used in combination with the photoinitiator, such as a tertiary aliphatic amine, e.g., dimethylaminoethylmethacrylate (DMAEMA).

Suitable co-initiators Bid. include DMAEMA, and aliphatic and aromatic amines (e.g., in the case of CQ as an initiator).

Suitable inhibitors Ble. include butylated hydroxytoluene, butylhydroxytoluene (BHT), monomethyl ether hydroquinone (MEHQ).

Exemplary solvents B2 for such resins include C2-C20 alcohols e.g., ethanol, propanol, cetyl alcohol, stearyl alcohol, C3-C20 ketones, such as acetone, and C6-C20 hydrocarbons, such as hexane.
Such formulations may be cured with blue light, or other wavelengths in the visible range. Suitable light absorption/curing is from 400-490nm, such as from 475-480 nm (depending on the actual formulation). As an example, CQ is a photo initiator which absorbs with a peak in the blue wavelength range and produces radicals when excited in the 460-490nm range. Co-initiators, such as DMAEMA, accelerate the light-cure process. When formulated as a composition 10 and applied to dry teeth, the composition may cure in 10 seconds to 1 minute under blue light illumination. PPD uses a shorter wavelength (420-430nm).

As one example, a mixture of acrylic acid, Bis-GMA, CQ, HEMA and optionally DMAEMA is combined with a solvent, such as acetone and/or ethanol, the exemplary microparticles 14 and optionally silica particles. The composition can cure in 30 seconds under blue light. Such a composition stays intact in excess saliva, and can be completely removed by peeling and brushing.

As another example, a mixture of acrylic acid, itaconic acid, and HEMA is combined with calcium glycerophosphate, Bis-GMA, camphoroquinone, silica beads, and the exemplary microparticles and applied to the teeth. The composition can cure in 10 to 20 seconds under blue light.

**Viscosity Modifiers (B3)**

The exemplary composition 10 may include at least 1 wt. % (or at least 2 wt. %, or at least 5 wt. %, or at least 10 wt. %, or at least 15 wt. %) of component B3, such as up to 50 wt. %, or up to 20 wt. %.

Component B3 of the composition 10 disclosed herein may include from 0-100 wt. %, e.g., at least 5 wt. % (or at least 20 wt. %, or at least 40 wt. %) of particles 30. The particles may have a Mohs hardness of at least 2 (or at least 3, or at least 5).

Particles 30 may serve as viscosity modifiers and/or abrasives. An abrasive may be useful, for example, as a polishing agent. Suitable particles include silica, for example in the form of silica gel, hydrated silica or precipitated silica, alumina, insoluble phosphates, orthophosphates, polymetaphosphates, and beta calcium pyrophosphate, calcium carbonate, resinous abrasives such as urea-formaldehyde condensation products and mixtures thereof.
Suitable waxes and gums useful as viscosity modifiers include those mentioned elsewhere herein.

Suitable thickeners useful as viscosity modifiers may include starches, anionic polymers, and the like.

Other additives (B4)

The composition 10 may include at least 1 wt. % (or at least 2 wt. %, or at least 5 wt. %, or at least 10 wt. %, or at least 15 wt. %) of component B4, such as up to 50 wt. %, or up to 20 wt. %.

As examples of other additives, the composition 10 may include one or more of the following:

Colorants: The colorant may be selected to provide the film with a white appearance or a tint.

Tartar control (anticalculus) agents: these may include phosphates and polyphosphates (for example pyrophosphates), polyaminopropanesulfonic acid (AMPS), polyolefin sulfonates, polyolefin phosphates, diphosphonates such as azacycloalkane-2,2-diphosphonates (e.g., azacycloheptane-2,2-diphosphonic acid), N-methyl azacyclopentane-2,3-diphosphonic acid, ethane-1-hydroxy-1,1-diphosphonic acid (EHDP) and ethane-1-amino-1,1-diphosphonate, phosphonoalkane carboxylic acids and salts of any of these agents, for example their alkali metal and ammonium salts, and mixtures thereof.

Fluoride ion sources: These may be useful, for example, as an anti-caries agent. Orally acceptable fluoride ion source which can be used include potassium, sodium and ammonium fluorides and monofluorophosphates, stannous fluoride, indium fluoride and mixtures thereof.

Tooth and soft tissue desensitizers: these may include stannous ions, such as halides and carboxylate salts, arginine, potassium citrate, potassium chloride, potassium tartrate, potassium bicarbonate, potassium oxalate, potassium nitrate, strontium salts, and mixtures thereof.

Antimicrobial (e.g., antibacterial) agents: these may include orally acceptable antimicrobial agents, such as Triclosan (5-chloro-2-(2,4-dichlorophenoxy)phenol); 8-hydroxyquinoline and salts thereof, zinc and stannous ion sources such as zinc citrate; copper (II) compounds such as copper (II) chloride, fluoride, sulfate and hydroxide;
phthalic acid and salts thereof such as magnesium monopotassium phthalate; sanguinarine; quaternary ammonium compounds, such as alkylpyridinium chlorides (e.g., cetylpyridinium chloride (CPC), combinations of CPC with zinc and/or enzymes, tetradecylpyridinium chloride, and N-tetradecyl-4-ethylpyridinium chloride); bisguanides, such as chlorhexidine digluconate.; halogenated bisphenolic compounds, such as 2,2'-methylenebis-(4-chloro-6-bromophenol); benzalkonium chloride; salicylanilide, domiphen bromide; iodine; sulfonamides; bisbiguanides; phenolics; piperidino derivatives such as delmopinol and octapinol; magnolia extract; grapeseed extract; thymol; eugenol; menthol; geraniol; carvacrol; citral; eucalyptol; catechol; 4-allylcatechol; hexyl resorcinol; methyl salicylate; antibiotics such as augmentin, amoxicillin, tetracycline, doxycycline, minocycline, metronidazole, neomycin, kanamycin and clindamycin; and mixtures thereof. Other useful antimicrobials are disclosed in U.S. Pat. No. 5,776,435.

Antioxidants: orally acceptable antioxidants which can be used include butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), vitamin A, carotenoids, vitamin E, flavonoids, polyphenols, ascorbic acid, herbal antioxidants, chlorophyll, melatonin, and mixtures thereof.

Antiplaque (e.g., plaque disrupting) agent: orally acceptable antiplaque agents can include stannous, copper, magnesium and strontium salts, dimethicone copolyols such as cetyl dimethicone copolyol, papain, glucoamylase, glucose oxidase, urea, calcium lactate, calcium glycerophosphate, strontium polyacrylates, and mixtures thereof.

Anti-caries agents: examples of these include calcium glycercylphosphate and sodium trimetaphosphate.

Anti-inflammatory agents: orally acceptable anti-inflammatory agents can include steroidal agents, such as flucinolone and hydrocortisone, and nonsteroidal agents (NSAIDs) such as ketorolac, flurbiprofen, ibuprofen, naproxen, indomethacin, diclofenac, etodolac, indomethacin, sulindac, tolmetin, ketoprofen, fenoprofen, piroxicam, nabumetone, aspirin, diflunisal, meclofenamate, mefenamic acid, oxyphenbutazone, phenylbutazone, and mixtures thereof.

H₂ antagonists: antagonists useful herein include cimetidine, etintidine, ranitidine, ICIA-5165, tiotidine, ORF-17578, lupitertidine, donetidine, famotidine, roxatidine, pifatidine, lamtidine, BL-6548, BMY-25271, zaltidine, nizatidine, mifentidine, BMY-

Nutrients: Suitable nutrients include vitamins, minerals, amino acids, proteins, and mixtures thereof.

Anti-staining agents: such as silicone polymers.

Flavoring agents: any of the flavoring agents commonly used in toothpastes may be used, by way of example.

Forming the Composition

Exemplary methods of forming the composition are illustrated in FIGURE 4. The method begins at S120. At S122, the hydrophobic material is melted. At S124, separately or with S122, the release agent may be melted (e.g., in the case of PEG). At S126 the hydrophobic material and release agent may be combined, if not already combined in S122. A molten mixture of the hydrophobic material and release rate modifier may be formed, for example, by heating the hydrophobic material, and optionally the release rate modifier and emulsifier, to a sufficient temperature to melt at least the hydrophobic material. The components may be stirred to disperse the release rate modifier throughout the hydrophobic material to form a shell material. At S128, the bleaching agent may be coated with the shell material. The bleaching agent is incorporated into the molten mixture, for example, by combining solid particles of bleaching agent with the molten mixture. The molten mixture is separated into solid microparticles (SI30), for example, by spraying the mixture into a coolant, such as carbon dioxide, or dissolving the mixture in liquefied carbon dioxide and quickly releasing the pressure, or spraying the mixture onto a cooled surface. At S132, the solid microparticles are combined with matrix material 12. The method ends at S134.

In another embodiment, suited to forming the composition, the method proceeds from S124 to S136, where the bleaching agent, e.g., in particulate form, is coated with a layer of the molten release agent, and, thereafter, at S138, by a layer of the hydrophobic material. The method then proceeds to S130. As will be appreciated, steps S136 and S138 may be reversed and/or repeated one or more times.
The microparticles can be formed by a variety of methods including spray cooling, precipitation, and the like. Spray cooling/chilling methods can be used where the molten hydrophobic material containing the core material is sprayed into a cold chamber or onto a cooled surface and allowed to solidify. For example, small particles of carbamide peroxide, or other bleaching agent, are combined with a molten mixture of wax and release rate modifier, e.g., PEG. The mixture is sprayed through a nozzle into a fluid at a sufficiently low temperature to solidify the mixture as microparticles. For example, carbon dioxide at low temperature may be used as the cooling fluid.

FIGURE 5 schematically illustrates an exemplary apparatus 50 for forming the microparticles 14. A first reservoir 52 holds the bleaching agent, e.g., a solution of the bleaching agent in a suitable solvent, such as carbamide peroxide dissolved in glycerol, or carbamide peroxide powder dispersed in a liquid. The contents of the first reservoir 52 may be agitated with an agitator 54, such as a vibrator, stirrer, rotation device, or the like. A second reservoir 56 holds the carrier material, e.g., a mixture of molten wax and PEG. A nozzle assembly 58 includes an inner nozzle tube 60, connected with the first reservoir 52, and a concentric outer tube 62, connected with the second reservoir 56. A jet of bleach agent (e.g., pressurized by a pump or the like), exits the first nozzle tube 60 into a concentric annular jet of molten carrier material from the second nozzle tube. The nozzle assembly 58 terminates in a chilled vessel 64, which is optionally fed with a coolant, such as carbon dioxide at low temperature and optionally under pressure, through a feed tube 66. The molten carrier solidifies upon exiting the annular jet. The release rate modifier may be present in the inner and/or the outer jet. In another embodiment, the particles 14 may be formed on contact with a chilled surface.

In other embodiments, C02 at low temperature and optionally under pressure is used to encapsulate the bleaching agent in PEG or other polymer as first coat, and then a thin layer of wax is applied to avoid rapid dissolution.

Other methods for forming encapsulated particles 14, which may be used herein are disclosed, for example, in U.S. Patent No. 4,919,841, to Kamel, et al. (deposition and annealing of wax coated particles), U.S. Pat. Nos. 4,078,099, 4,136,052 and 4,327,151, all to Mazzola (spray methods), EP 0 132 184 to Scotte (spraying encapsulant onto bleach in a mixer), U.S. Pat. Nos. 3,015,128, 3,310,612 and 3,389,194 to Somerville, et al. (concentric
tube with rotary head), U.S. Pat. No. 3,943,063 to Morishita, et al. (core dispersed in film
forming polymer solution), U.S. Pat. No. 3,856,699 to Miyano, et al. (crushed, wax-
covered core particles are heated in an aqueous medium), U.S. Pat. No. 3,847,830 to
Williams, et al. (peroxygen compounds are held in a fluidized bed and enveloping agent is
molten hot prior to spraying onto the peroxygen particles), and EP 0 337 523 (spray drying
methods). Other encapsulation techniques are disclosed in MICROENCAPSULATION:
Methods and Industrial Applications, Edited by Benita and Simon (Marcel Dekker, Inc.,
1996).

The exemplary microparticles 14 loaded, for example, with a carbamide peroxide
core 22 are able to provide slow and sustained release of hydrogen peroxide for teeth
whitening.

The exemplary microparticles may be formulated as a composition 10 for home use
or for use by a dental professional. They may be employed in professional treatments
where high concentrations of bleaching agent are released in a short period of time, by
tailoring the concentration of the release rate agent appropriately. Since the hydrogen
peroxide release is local to the teeth, the composition containing the exemplary
microparticles may be used without soft tissue isolation. Alternatively, the microparticles
may be used for home treatments. For example, the whitening composition may be applied,
and the hydrogen peroxide released slowly and locally over an extended period.

Additives, such as any of those listed above as components of the matrix material,
may alternatively or additionally be incorporated in the microparticles.

While the exemplary compositions are particularly suited to tooth whitening, it is to
be appreciated that they may find use in other bleaching applications.

The following examples, which are not intended to limit the scope of the invention,
demonstrate how the release rate can be tailored using different release rate modifiers and
provide illustrative matrix compositions.

EXAMPLES

EXAMPLE 1: Production of hydrogen peroxide-loaded microparticles

Reagents

The following reagents were obtained:
As a whitening agent, carbamide peroxide was obtained from Sigma (15-17% active oxygen basis, 04078, Fluka). The particle size distribution of the carbamide peroxide in this material is relatively broad with particle size ranging from 200 to 2000 µm and the majority of crystals being around 800 µm. Smaller particles would be expected to be more effective for this application.

As a carrier material, paraffin wax (melting point 53-57°C) was supplied by Sigma, UK.

The following release rate modifiers were obtained:

Polyethylene glycols with different molecular weight (PEG1500 and PEG2000) were obtained from Sigma, UK.

Colloidal silicone dioxide AEROSIL™ 200, a fumed silica having an average particle size of about 12 nm and a moisture content (measured according to DIN 55921) of less than 1%, was supplied by Evronik Industries, Essen Germany.

Anhydrous sodium tripolyphosphate (STPP) was supplied by Sigma and particles less than 40 µm were used after sieving through screens of 40 µm.

As a processing aid (emulsifier), polyglycerol polyricinoleate (PGPR) was supplied by Palsgaard, Sweden.

Formation of Microparticles

Microparticles loaded with carbamide peroxide (CP) were prepared by spray cooling/congealing according to Table 1. Release rate modifiers were used in the following amounts:

Formula A: Control- no release rate modifier.
Formula B: PEG1500 at 29.4 wt. % of the microparticles.
Formula C: PEG2000 at 29.4 wt. % of the microparticles.
Formula D: AEROSIL™ 200 at 2 wt. % of the microparticles
Formula E: Sodium tripolyphosphate (STPP)- anhydrous powder, at 2 wt. % of the microparticles.

A ratio of carrier material (everything but CP) to carbamide peroxide, by weight, was 3:2 for all formulations.
The carrier material was heated in a jacketed beaker at a temperature of 5°-10°C above its melting point and the release rate agent added. For example, 58.8 g of paraffin wax was allowed to melt at 65°C and 2 g of PGPR, AEROSIL™ or STPP was added to the molten wax while stirring at 700 rpm for 3 min. 39.2 g of CP were then added to the mixture whilst stirring for another 3 min and the obtained suspension was loaded into a preheated 1 mL syringe to avoid solidification of the suspension in the syringe orifice. The molten suspension in the syringe, used to simulate a nozzle, was allowed to drop on a cold glass plate placed above an ice tray. The solid pastille-like capsules were then scraped from the plate with a spatula and stored in tightly closed plastic containers at 4°C.

The particles were all solid at room temperature and also at 37°C in PBS buffer.

When a mixture of paraffin wax and PEG was used as a carrier, they were melted separately. The emulsifier (PGPR) was added to the paraffin wax after the melting step. CP was added to the molten paraffin containing the PGPR, followed by PEG while stirring, under the same conditions as above.

The encapsulation efficiency (% EE) can be calculated as follows:

\[
\% \text{EE} = \frac{\text{Mass of hydrogen peroxide recovered from the capsules}}{\text{Mass of hydrogen peroxide input}} \times 100
\]

The mass of hydrogen peroxide recovered is determined after its extraction from the capsule using HPLC grade isopropanol as a solvent. The extract is filtered with a hydrophilic polyethersulfone filter unit (Millex-GP, 0.22 μm) and the quantity of hydrogen peroxide determined spectrophotometrically at 351 nm. PEG was found to improve encapsulation efficiency.
Table 1: Composition of different formulations of hydrogen peroxide-loaded microparticles with a theoretical H$_2$O$_2$ content of 12 % (w/w)

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Composition (% w/w)</th>
<th>%EE (%w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Paraffin wax</td>
<td>PEG 1500</td>
</tr>
<tr>
<td>A</td>
<td>58.8</td>
<td>-</td>
</tr>
<tr>
<td>B</td>
<td>29.4</td>
<td>29.4</td>
</tr>
<tr>
<td>C</td>
<td>29.4</td>
<td>-</td>
</tr>
<tr>
<td>D</td>
<td>58.8</td>
<td>-</td>
</tr>
<tr>
<td>E</td>
<td>58.8</td>
<td>-</td>
</tr>
</tbody>
</table>

CP= carbamide peroxide; STPP= anhydrous sodium tripolyphosphate; PGPR= polyglycerol polyricinoleate

**Hydrogen peroxide (FL$_2$O$_3$) release study**

An H$_2$O$_2$ release study was performed with 0.5 g of each of the CP-loaded microparticles of Formulations A-E in a release medium (Phosphate Buffered Saline (PBS), pH 7.4 at 37°C) designed to mimic the release of hydrogen peroxide from the particles when contacting the teeth of a user. The microparticles were dispersed in 20 mL of the release medium, placed in an orbital shaker at 150 rpm. 1mL of aliquots were withdrawn at predetermined times, suitably diluted with the release medium, and the amount of H$_2$O$_2$ quantified spectrophotometrically at 351 nm. The withdrawn volume was immediately replaced with an equivalent volume of the fresh medium maintained at the same temperature.

FIGURE 6 shows the hydrogen peroxide release profiles from the different microparticles. As can be seen, the release rate can be tailored by using different release agents.

**EXAMPLE 2: Light-Curable compositions**

Example compositions 10 were prepared without microparticles 14 by combining components in the amounts, by weight shown in Table 2.
The resin component B1 included:
Bla. Functional monomer: HEMA (to ensure good wetting and thus adhesion)
Bib. Crosslinking monomer: Bis-GMA
Blc. Initiator: Camphorquinone
Bid. Co-initiator: DMAEMA (optional)
Ble inhibitor-not used in these examples

As an organic solvent B2: ethanol
As particles B4, silica was optionally used.

The hydrophilic monomer and solvent can improve the wetting behaviour of the composition.

Camphorquinone is a photo initiator which absorbs with a peak at blue wavelength. Together with co-initiator produces radicals when excited. Co-initiators such as DMAEMA accelerate the light-cure process

Inhibitor: a small amount is added to the resin to prevent it from self-polymerization. Silica particles can be added to promote adhesion as well as modifying the viscosity of the resin.

The matrix compositions were tested according to the following procedure:
1. Spread an even layer of light-cure gel on a bovine tooth, which may have been stained, for example with tea.
2. Light-cure for around 10s per 1cm² area.
3. The cured film can be pulled off.

Table 2: Matrix compositions

<table>
<thead>
<tr>
<th></th>
<th>Example 1</th>
<th>Example 2</th>
<th>Example 3</th>
<th>Example 4</th>
<th>Example 5</th>
<th>Example 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bis-GMA</td>
<td>78.4</td>
<td>53</td>
<td>85</td>
<td>78.2</td>
<td>58.6</td>
<td>67.2</td>
</tr>
<tr>
<td>HEMA</td>
<td>20.6</td>
<td>46</td>
<td>14</td>
<td>19.5</td>
<td>39.1</td>
<td>28.8</td>
</tr>
<tr>
<td>Camphorquinone</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>DMAEMA</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Observation</td>
<td>Cures in around 3 minutes.</td>
<td>does not cure in under 5 mins tested</td>
<td>cures in around 1 minute</td>
<td>hardens in less than 10 secs forming a hard layer</td>
<td>hardens in less than 10 seconds.</td>
<td>hardens in less than 10 seconds</td>
</tr>
</tbody>
</table>
The examples above illustrate that a ratio of CQ:DMAEMA of 0.6:1.7 was useful. With the co-initiator, the curing time is significantly reduced. The polymer hardens in less than 10 seconds. Example 5 shows good properties for both hardening time and ease of release after treatment.

Testing on wet and dry stained bovine teeth

It is known that CP reacts with water to break down and release hydrogen peroxide. Humans naturally produce saliva, although very little during sleep. The following example was designed to evaluate whether the composition could be used on dry teeth, without addition of water. Two sets of teeth were prepared for testing:

1. Bovine teeth (stained) kept in a damp-tissue in a closed tube
2. Bovine teeth (stained) kept in a silica-gel in a closed tube

The staining procedure for the teeth was as follows: A staining solution was prepared from 3 g of fine ground leaf tea, 3 g of fine ground coffee, and 300 ml of boiling ddH₂O. This was allowed to infuse for 10 min with stirring. The solution was filtered and cooled to 37°C. Open sides of the tooth samples are sealed with clear nail varnish. The teeth are then etched using sequential immersion in 0.2M HCl, saturated Na₂CO₃, 1% phytic acid (30 sec each) and finally rinsed with dd H₂O.

Substrates: 10 mm x 10 mm bovine incisor (enamel) fragments were mounted in clear resin, 600 grit finished surface, unsealed. Substrates were stored at 100% relative humidity at 4°C in dd H₂O or in PBS solution prior to staining and were not allowed to fully dry out. Bovine tooth samples to be stained were kept in 200 ml of the staining solution for 4 days then rinsed with Millipore water and stored in PBS solution.

Matrix compositions, as described above were combined with CP at 20 wt. % of the composition (a hydrogen peroxide equivalence of ~6%). 2 g of the mixture was used per treatment. The CP used for these Examples was not encapsulated. Around 2 g of varnish is applied to each tooth. The composition cured in under 1 minute. The procedure was as follows:

3. Illuminate blue light for 30 seconds to 1 minute
4. The tooth is placed in close contact with a damp tissue paper
5. Some bubbles are visible on the tooth surface
6. The polymer layer can be wiped off or peeled off after treatment before the measurements are made on the tooth.

7. The L*, a*, b* values are measured.

FIGURES 7-10 show the effect of the composition on previously-stained damp and dry bovine teeth using sieved CP particles with a particle size of <45 µη. L, a, and b values are shown separately. The dashed lines show the respective L, a, and b values prior to staining the teeth.

As can be seen from these FIGURES, the composition is able to effectively whiten teeth (increasing L*, and reducing b*) even on dry teeth. On dry teeth, the whitening takes longer, but within a timeframe which would be acceptable for whitening human teeth, especially if more than one treatment were to be used.

Example compositions were prepared to investigate cure time, as follows:
Bis-GMA 59.5 wt.%, HEMA 39.5 wt.%, CQ 1 wt%, cures in over five minutes.
Bis-GMA 75 wt.%, HEMA 24 wt.%, CQ 1 wt%, cures in about two minutes.
Bis-GMA 85 wt.%, HEMA 13 wt.%, CQ 2 wt%, cures in 45 seconds to 1 minute.

EXAMPLE 3: Self-cured varnish

A self-curing varnish was prepared with as follows:
10.9g Shellac,
13.5g Ethanol,
16.15g colophonium resin,
0.25g beeswax,
5.95g mastic, and
sufficient sieved carbamide peroxide (<45 µη) to make a 20% solution.

Experiments were performed on new teeth (not previously whitened), which had been stained.

FIGURES 11-14 show average results on the stained bovine teeth for silica dried, tissue dried, and wet teeth. The results show the ΔE values (FIG. 11) and change in L*, a*, and b* values (FIGS. 12-14). As can be seen, both wet and dry teeth (tissue-dried or silica-dried) exhibit a whitening effect. Varnishes prepared without carbamide peroxide as a control exhibit lesser change.
EXAMPLE 4: Evaluation of slow-release properties

Carbamide peroxide light curable varnishes similar to those described in EXAMPLE 3 were applied to bovine teeth and after a few hours, the varnish was replenished. The teeth exhibited a continued whitening effect up to about 500 hours, when a plateau was reached.

5 Each of the documents referred to above is incorporated herein by reference.

Except in the Examples, or where otherwise explicitly indicated, all numerical quantities in this description specifying amounts of materials, reaction conditions, molecular weights, number of carbon atoms, and the like, are to be understood as modified by the word "about." Unless otherwise indicated, each chemical or composition referred to herein should be interpreted as being a commercial grade material which may contain the isomers, by-products, derivatives, and other such materials which are normally understood to be present in the commercial grade. It is to be understood that the upper and lower amount, range, and ratio limits set forth herein may be independently combined. Similarly, the ranges and amounts for each element of the invention may be used together with ranges or amounts for any of the other elements. As used herein any member of a genus (or list) may be excluded from the claims.

The invention has been described with reference to the preferred embodiments. Obviously, modifications and alterations will occur to others upon reading and understanding the preceding detailed description. It is intended that the invention be construed as including all such modifications and alterations insofar as they come within the scope of the appended claims or the equivalents thereof.
CLAIMS:

1. A bleaching composition (10) comprising:
   a matrix material (12); and
   a plurality of solid microparticles (14) dispersed in the matrix material, each microparticle comprising a bleaching agent encapsulated in a shell (24) formed of a carrier material.

2. The composition of claim 1, wherein a ratio, expressed by weight, of the microparticles to the matrix material is from 1:50 to 50:1.

3. The composition of either of claims 1-2, wherein the ratio of the microparticles to the matrix material is at least 1:10.

4. The composition of any one of claims 1-3, wherein the matrix material (12) includes less than 5 wt. % water.

5. The composition of any one of claims 1-4, wherein the composition consists of:
   2-95 wt. % of microparticles; and
   98-2 wt. % of the matrix material, the matrix material consisting of:
   1-70 wt. % of a resin component,
   0-30 wt. % of an organic solvent,
   0-40 wt. % viscosity modifiers, and
   0-50 wt. % other additives.

6. The composition of any one of claims 1-5, wherein the matrix material (12) is at least one of light and moisture curable.

7. The composition of claim 6, wherein the matrix material (12) is light curable and comprises:
10-50 wt. % of a functional monomer;
50-90 wt. % of a crosslinking monomer;
0.1-2 wt. % of an initiator;
0-3 wt. % of a co-initiator; and
0-3 wt. % of an inhibitor.

8. The composition of claim 8, wherein the functional monomer comprises at least one of an acrylate and a methacrylate.

9. The composition of claim 8 or 9, wherein the functional monomer comprises 2-hydroxyethyl methacrylate (HEMA).

10. The composition of claim 6, wherein the matrix material (12) is moisture curable and comprises at least one of colophonium resin and shellac.

11. The composition of any one of claims 1-5, wherein the matrix material is cured by solvent evaporation.

12. The composition of claim 11, wherein the matrix material comprises a polymer derived from acrylic acid and an organic solvent.

13. The composition of any one of claims 1-11, wherein the microparticles in the composition have an average diameter of less than 100 µm.

14. The composition of any one of claims 1-13, wherein the bleaching agent is a solid bleaching agent.

15. The composition of any one of claims 1-14, wherein the bleaching agent is selected from the group consisting of carbamide peroxide, alkali metal percarbonates, sodium perborate, potassium persulfate, calcium peroxide, zinc peroxide, magnesium peroxide, strontium peroxide, and combinations thereof.
16. The composition of any one of claims 1-15, wherein the bleaching agent is present in the composition in an amount equivalent to at least 2 wt. % hydrogen peroxide.

17. The composition of claim 1, wherein the shell (24) carrier material comprises: a hydrophobic material (26), and optionally, a release rate modifier (28), which modifies the release of bleaching agent from the microparticle.

18. The composition of claim 17, wherein the hydrophobic material comprises a waxy solid.

19. The composition of claim 17 or 18, wherein the release rate modifier is present and comprises a hydrophilic or water-soluble material.

20. The composition of any one of claims 17-19, wherein the release rate modifier is selected from the group consisting of polyethylene glycol, silica, water-soluble alkali metal salts, and combinations thereof.

21. A method for whitening teeth comprising applying the composition (10) of any one of claims 1-20 to a person's teeth (18).

22. The method of claim 21, further comprising providing a barrier layer (20) over the composition.

23. The method of either one of claims 20 and 21, further comprising illuminating the composition with light from an electrically powered light source (38) to cure the matrix material to provide a cured film on the teeth.
FIG. 2

S100 Start

S102 Provide composition

S104 Apply composition to teeth

S106 Apply barrier layer

S108 Cure composition (and barrier layer)

S110 Remove varnish from teeth

S112 End

FIG. 3
$\Delta A$  Bovine teeth treatment: wet and dry teeth

$\Delta B$  Bovine teeth treatment: wet and dry teeth

FIG. 9

FIG. 10