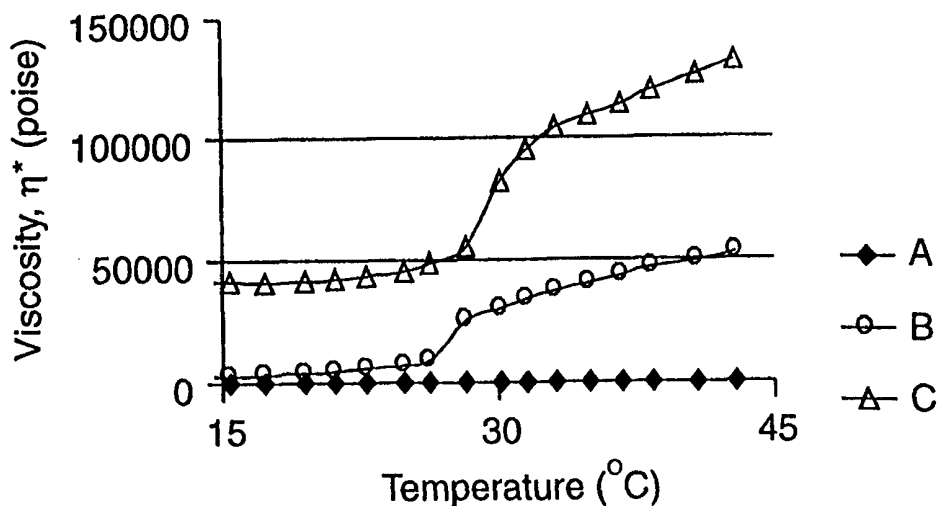




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 7/20, 7/16	A1	(11) International Publication Number: WO 00/28955 (43) International Publication Date: 25 May 2000 (25.05.00)
(21) International Application Number: PCT/US99/06146 (22) International Filing Date: 16 March 1999 (16.03.99) (30) Priority Data: 09/190,541 12 November 1998 (12.11.98) US (71) Applicant: MINNESOTA MINING AND MANUFACTURING COMPANY [US/US]; 3M Centre, P.O. Box 33427, Saint Paul, MN 55133-3427 (US). (72) Inventors: OXMAN, Joel, D.; P.O. Box 33427, Saint Paul, MN 55133-3427 (US). TROM, Matt, C.; P.O. Box 33427, Saint Paul, MN 55133-3427 (US). (74) Agents: BJORKMAN, Dale, A. et al.; Office of Intellectual Property Counsel, P.O. Box 33427, Saint Paul, MN 55133-3427 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>

(54) Title: DENTAL WHITENING COMPOSITION



(57) Abstract

Dental whitening compositions are provided that have the capability of undergoing an increase in viscosity in response to an increase in temperature. In a preferred embodiment, the composition also have the ability to reverse their viscosity in response to a decrease in temperature.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

Dental Whitening Composition

Field of the Invention

5 This invention relates to dental whitening or brightening compositions having viscosities capable of responding to a change in temperature. The invention also relates to methods of whitening or brightening teeth surfaces using the composition, particularly methods of whitening or brightening teeth by dispensing the composition into a dental tray or directly onto tooth surfaces and keeping it in the mouth for some period of time.

10 **Background**

Home teeth whitening systems have been available since the late 1980's, acquired either through a dental professional or over-the-counter. Prior to these systems, persons desiring whiter or brighter teeth were subjected to various heat or light activated systems provided by their dental practitioner in the dental chair. Typically, these practices
15 involved the dental practitioner applying a hydrogen peroxide solution on the teeth, protecting the sensitive soft tissues with a ligated rubber dam, and applying heat to the applied solution to effectuate oxidation. Such oxidation removed discoloration from the tooth surfaces.

With the greater consumer demand for cosmetically enhancing products, aesthetic
20 dentistry has correspondingly grown. The demand for these products also created interest in products which could be administered at a more convenient time and place, and/or with less equipment. Thus, numerous products have since been developed which provide a person with the means to treat and whiten his or her teeth in the privacy and convenience of the home.

25 Generally, to begin the whitening process, a user is provided with a dental tray, either by a dental practitioner or as part of a purchased dental whitening kit. The tray is intended to retain the whitening composition at the desired location(s) and maintain contact between the tooth surface and the whitening composition. When the treatment involves a dental practitioner, the dental tray is typically custom fitted to the user's
30 personal dentition. Some dental practitioners may choose to have selectively enlarged tooth-treating compartments or reservoirs fabricated within the dental tray which are

adapted to receive a sufficient amount of tooth whitening composition. The purpose for having such reservoirs is to provide more whitening composition and to ensure, if desired, long-lasting exposure of the teeth to the whitening agent. The dental tray loaded with whitening composition is typically worn by the patient for some extended period of time (e.g. 30 minutes to 8 hours), depending on the degree of discoloration the user desires to remove. This treatment is repeated over a sufficient period of time to effect the tooth whitening and bleaching process.

Whitening compositions are generally formulated with thickening rheological modifiers such as carboxypolymethylene, cellulosic polymers, or fumed silicas in order for the compositions to be provided as a thickened composition. For example, Pellico, U.S. Patent No. 5,361,000 is directed to dental whitening compositions thickened with glycerin and carboxypolymethylene. Pellico, U.S. Patent No. 5,718,886 discloses a stabilized anhydrous dental whitening composition utilizing Xanthum gum as a thickening agent.

During the intraoral application of a tray and whitening composition, a system can increase from ambient temperature of about 22-25°C, to about 37°C. As a result of this temperature rise, the whitening composition may have a tendency to decrease in viscosity and become more flowable. In addition, the composition may also become diluted from saliva moving in and out of the tray, resulting in dilution of the composition. This thinning and viscosity decrease creates a tendency for the composition and thus the whitening agent, to flow out of the tray, resulting in a reduced amount of whitening composition available for treatment at the target location for the desired length of time.

To overcome the effect of temperature and salivation, a series of patents by Fischer, namely U.S. Patent Nos. 5,098,303; 5,234,342; 5,376,006; 5,409,631; 5,770,105; 5,725,843; and 5,746,598 disclose teeth whitening compositions characterized with high viscosity and stickiness to minimize dilution from saliva and prolong the period of time the whitening agent is in contact with the teeth surfaces. These patents describe the use of high concentrations of carboxypolymethylene to provide the high viscosity characteristic of the whitening composition as it is stored in its container.

Summary of the Invention

The invention provides a dental whitening composition whose viscosity is responsive to temperature changes, wherein the viscosity increases with an increase in

temperature. These compositions also preferably have the ability to reverse their viscosity upon the lowering of temperature. The compositions of the invention comprise a whitening agent and a thermally responsive modifier.

5 Compositions of the invention work very well in the oral environment where temperature is generally higher than ambient or the pre-treatment temperature of a composition. This differential in temperature thickens the composition and thus provides a thickened, semi-solid or gel-like composition in the oral environment.

10 A preferred method of use of the invention comprises dispensing the composition into a dental tray that is subsequently placed into a user's mouth. Upon exposure of the composition to the oral temperature, the composition thickens to a semi-solid or gel-like state. Alternatively, the composition can be dispensed into a pre-warmed tray such that the composition thickens upon its contact with the tray.

Brief Description of the Drawing

15 Fig. 1 is a graphic illustration of the viscosity versus temperature data as described in Example 3.

Description of the Invention

This invention overcomes the shortcomings of previous dental whitening compositions that experience a decrease in viscosity due to the increase in temperature from the intraoral environment. This is accomplished by providing dental whitening
20 compositions that exhibit an increase in viscosity in response to an increase in temperature. As a separate advantage, compositions and methods of the present invention provide easy delivery of tooth whitening compositions, especially with those compositions that are initially a low viscosity liquid at its pre-treatment temperature. These
25 compositions can be dispensed from delivery devices that have small orifices, require less force to dispense and become thicker or more viscous only upon being exposed to the temperature of the oral environment.

Compositions of this invention are particularly suitable for use in the intraoral environment where a composition having a pre-treatment temperature at or lower than
30 ambient (room temperature) is applied to a user's tooth surfaces that is near or at oral temperature of about 30°C – 39°C. For certain dental applications, it is preferred that the

composition be thermally reversible. In that application, the composition not only has the ability to increase its viscosity at an elevated intra-oral temperature, but also reverses or decreases its viscosity upon a decrease in temperature.

5 The capacity of the dental composition to thicken at human body temperatures is a critical feature of the invention, for it is in this property that many of the disadvantages of previous approaches are overcome. The dissipative characteristic of liquid solutions is avoided since the compositions herein experience thickening at the site of treatment. Moreover, the problems of formulation, handling, delivery and application of viscous compositions are overcome since the present compositions may be free-flowing liquids
10 prior to treatment.

A "semi-solid," as used herein, is a material whose physical state is between a liquid and solid state, pure or mixed solvent or solution entrained within a network, and can be alternatively be considered as a gel. By "pure or mixed solvent and/or solution," as stated herein, it is recognized that a mixture of solvents may be absorbed by the network.
15 Additionally, the solvent may include salts or other additives so as to form a solution, which may also be absorbed or entrained within the network.

"Thickening" as used herein, is where a composition undergoes a substantial increase in the viscosity of the composition. The degree of thickening is dependent on the initial viscosity of the composition.

20 In a preferred embodiment of the invention, the initial viscosity of the composition may be low enough such that the composition is in a liquid state. Subsequently, upon exposure to a temperature of about near or at body temperature, the viscosity increases to result in a thickened composition. A viscosity increase in the range of about 10- to about 100-fold can be experienced when the initial viscosity is low enough such that the
25 composition is a liquid. Thus, for example, a composition in a liquid state may have a viscosity of about 0 to about 7000 poise. In response to an increase in temperature, the viscosity of the composition can increase to at least about 10,000 poise. Upon the lowering of the temperature, the composition preferably has the ability to reverse its viscosity and return to flow properties of a liquid.

30 Yet another preferred embodiment of the invention is when the initial viscosity of the composition is at a level at which the composition is in a semi-solid or gelatinous state at pre-treatment temperature, and upon exposure to a higher treatment temperature, the

composition transforms into an "ultra-thick" or "ultra-gel" composition or one with a substantially higher viscosity and very low flow characteristics. These compositions typically have an initial viscosity of no less than about 7000 poise, which then thicken about 2- to about 5-fold.

- 5 The pre-treatment temperature is the temperature at which the composition is subjected to prior to application or treatment. The range for the pre-treatment temperature can be about 5°C to about 29°C, although there may be certain instances where the temperature may be outside this range. Having a pre-treatment temperature at about 20°C to 25°C allows the composition to be easily stored at ambient or room temperature.
- 10 Alternatively, the compositions of the invention can also be advantageously stored at lower, refrigeration pre-treatment temperatures of about 5°C to about 10°C to provide improved stability and shelf life.

- The treatment temperature is the temperature at which the composition is exposed to during intraoral application. This can be at or near body temperature, or about 30°C to
- 15 about 39°C.

- In accordance with the invention, the dental composition consists of a water-miscible, physiologically compatible medium which is a liquid or gel at ambient temperature below about 30°C and experiences thickening at oral temperatures above about 30°C. It has been found that a composition having a thickening transition
- 20 temperature in the range of from about 25°C to about 40°C is useful in the practice of the present invention. Preferably, the thickening occurs in a temperature range of from about 25°C to about 39°C, and more preferably from about 30° to about 35°C.

- Compositions of this invention are comprised of a solvent, a whitening agent and a thermally responsive viscosity modifier that provides the desired viscosity increase at the
- 25 desired elevated temperature range. Optionally, other adjuvants may be added to the composition. Preferably, the composition of this invention should be physiologically compatible so that no adverse reaction occurs if the tooth whitening composition comes in contact with human tissue or fluids. The solvent, whitening agent, and thermally responsive viscosity modifier may be contained in one mixture or contained separately in
- 30 a multiple-part system. In a multiple-part system, the whitening agent may be kept physically separate from the viscosity modifier, to be admixed just prior to treatment.

As used herein, a "thermally responsive viscosity modifier" is one or more polymeric substances that provides the composition or polymeric system the capability of substantially increasing its viscosity in response to an increase in temperature. Suitable polymeric substances useful as thermally responsive viscosity modifiers include
5 polyoxyalkylene polymers, particularly the polymeric surfactants available under the tradename PLURONIC. This class of polymers is available commercially from BASF Wyandotte Corporation. Other polyoxyalkylene polymers may also be useful as a thermally-responsive composition material.

A preferred dental composition in accordance with this invention comprises an
10 aqueous solution of a selected polyoxyethylene-polyoxypropylene block copolymer. A composition comprising polyoxyethylene-polyoxypropylene block copolymers in which the number of polyoxyethylene units is at least about 50% of the number of units in the total molecule, and the block copolymer having an average molecular weight of from about 1100 to about 15,500 has been found to be particularly useful. It is more preferable
15 that a composition comprises about 70% polyoxyethylene units of the total number of monomeric units in the copolymer and the copolymer has an average molecular weight of about 11,500. PLURONIC F-127 is a material that meets these criteria.

The PLURONIC polymers are closely related block copolymers that may be generically classified as polyoxypropylene-polyoxyethylene condensates that terminate
20 in primary hydroxyl groups. These polymers are formed by the condensation of propylene oxide into a propylene glycol nucleus followed by the condensation of ethylene oxide onto both ends of the polyoxypropylene base. The polyoxyethylene hydrophilic groups on the ends of the base pre-polymer are controlled in length to constitute from about 10% to about 80% by weight of the final polymer.

25 The PLURONIC polymer series of products may be represented empirically by the formula: $HO(C_2H_4O)_a(C_3H_6O)_b(C_2H_4O)_cH$ where **a** and **c** are statistically equal.

The concentration of the block copolymers is an important parameter and can be formulated in such a manner corresponding to the other components' concentrations. By adjusting the concentration of the copolymer to accommodate other solutes present in the
30 composition, any desired liquid to semi-solid transition temperature in the critical range of above ambient temperature and below body temperature can be achieved. Thus, the principal consideration is the selection of a concentration which, in conjunction with all of

the constituents of the composition, will provide a liquid to semi-solid transition or alternatively, a gel to "ultra-gel" transition temperature in the required range.

It has been found that a useful block copolymer concentration is from about 5% to about 40% by weight (wt. %) of the composition, preferably from about 15 wt. % to about 26 wt. % of the composition. Excellent results have been obtained using aqueous solutions having from about 17 wt. % to about 26 wt. % of PLURONIC F-127.

Another known system which is liquid at room temperature, but forms a semi-solid when warmed to about body temperature is formed from tetrafunctional block polymers of polyoxyethylene and polyoxypropylene condensed with ethylenediamine, commercially available under the tradename TETRONIC polymer (BASF Wyandotte Corp.). These compositions are formed from approximately 10% to 50% by weight of the polymer in an aqueous medium. See, for example, U.S. Patent No. 5,252,318 which is incorporated by reference herein.

Particularly preferred polymers for compositions of the invention are the PLURONIC F-127 and F-108 and the class of TETRONIC polymers. These viscosity modifiers are block copolymers of ethylene oxide and propylene oxide. Thickening tendencies of block copolymers increase as ethylene oxide content and total molecular weight increase. Thermally responsive block copolymers have been disclosed in U.S. Patent Nos. 4,474,751; 4,474,752; 5,441,732; and 5,252,318, as well as the Product Catalog, "BASF Performance Chemicals," all the teachings of which are incorporated by reference herein. These block copolymers offer extremely low toxicity and a high degree of mildness for applications involving human contact.

A preferred solvent for the composition of this invention is water. The concentration of water in the composition can be in the range of from about 30 wt.% to about 90 wt. % of the composition, and is preferably from about 50 wt. % to about 80 wt. %. More preferably, water can exist in the range of about 50 wt. % to about 75 wt. % of the composition. The water used in forming the aqueous solution is preferably purified, as by distillation, filtration, ion-exchange or the like.

Other solvents may be used, including anhydrous solutions comprising a polyol component such as propylene glycol or polyethylene glycol. Propylene glycol may be present in the composition in an amount from about 10 wt. % to about 55 wt. % of the composition. Polyethylene glycol may be used in the practice of this invention, having a

molecular weight from about 400 to about 1500 and may be in an amount from about 10 wt. % to about 50 wt. % of the composition. Glycerin may also be used as a constituent of the composition.

5 The whitening agent used in the present invention may be any material that has the effect of whitening teeth. Whitening agents are preferably selected from hydrogen peroxide and its urea complex: carbamide peroxide ($\text{CO}(\text{NH}_2)_2\text{H}_2\text{O}_2$). These whitening agents are also known by alternative names, including urea hydrogen peroxide, hydrogen peroxide carbamide, or perhydrol-urea. Alternatively, sodium hypochlorite may be suitable for use as the whitening agent. The concentration of a whitening agent in the composition can vary depending upon its reactivity. With carbamide peroxide, for
10 example, the currently preferred concentration range is from about 3% to about 40%, with a range from about 4% to about 21% being most preferred. In the case of hydrogen peroxide, which is more reactive than carbamide peroxide, the currently preferred concentration range is from about 2% to about 10%.

15 Other adjuvants can be added to the composition for certain purposes. For example, a preferred embodiment of the invention can contain fluoride, a desirable additive in oral compositions. Additives may also be included in the composition to promote the stability of the formulation. Anti-microbial agents, antifungal agents, and preservatives may be added to the composition to improve its shelf-life. Adhesive
20 modifiers, which reduce or increase the stickiness of the composition may also be included in the formulation. The compositions may further include other adjuvants such as fillers, dyes, cariostatic agents, flavorings, sweeteners, medicaments and sodium bicarbonate.

Various methods can be employed in using the composition of this invention. One method of use of these whitening compositions entails application of the composition to
25 the tooth structure directly from the composition's container or dispenser such as a bottle, syringe, or tube. Alternatively, the whitening composition can be applied by using a brush to paint it onto the tooth surface. The composition is kept on the user's tooth surface(s) for a desired time period to effectuate whitening. The length of time the composition is in contact with the tooth surface(s) would depend on the amount of discoloration the user
30 prefers to remove.

In a preferred method, the whitening composition is loaded into a dental tray. Such dental trays can be custom fitted to a user's dentition and be made with or without

reservoirs. A preferred reservoir is described in U.S. Patent Application 53911USA1A, filed on August 13, 1998, entitled Medication Delivery Tray, assigned to the assignee of the present invention, the disclosure of which is incorporated herein by reference. Dental trays can be made from varying thicknesses and softness of pliable thermo-formable plastic materials. Typically, these materials are 0.02 – 0.08 inches thick. After dispensing or loading the whitening composition into the dental tray, the user then places the loaded tray into the mouth and initiates thickening of the composition. The thickening occurs when the composition is exposed to the elevated treatment temperature of the oral environment. The tray is retained in the mouth to effectuate whitening of the tooth surface(s) for a sufficient period of time to remove discoloration.

An alternative method of use incorporates a pre-warmed dental tray into which the composition is loaded. Upon contact of the composition having a pre-treatment temperature, with the tray having a higher temperature, the composition experiences thickening. This method provides easy handling of a loaded tray into a user's mouth, with minimal fear of the composition moving to an undesired section of the tray or having the composition flow out of the tray.

Where the compositions are thermally reversible, the composition can be readily removed from the dentition or tray by cooling the material below the liquid to semi-solid transition temperature, thus reversing the thickening effect. This can be accomplished with cool water or other physiologically compatible liquid. Alternatively, the concentrations of the components in the whitening composition may be adjusted and diluted by adding water or other liquid solution in the oral cavity. By adjusting the concentrations of the components, the transition temperature is correspondingly adjusted, and thus provides the user the ability to remove the composition even with warm solutions. Water or other liquid solutions may be administered through a rinsing cup, squirt bottle, a liquid dispensing dental tool, or any other liquid dispensing device that can provide solution to the oral environment. Preferably, administering of cool or cold water onto the composition can provide a significant decrease in viscosity. Alternatively, the composition may be brushed, wiped, or blown off.

These and other aspects of the invention are illustrated by the following examples which should not be viewed as limiting in scope. Unless otherwise indicated, all

molecular weights are number average molecular weights and all ratios, parts and percentages are by weight.

EXAMPLES

5 *Preparation of Stock Solution 1*

An aqueous stock solution containing approximately 15% hydrogen peroxide(H_2O_2) was prepared by transferring 5 grams of a 30% H_2O_2 (J.T. Baker) and 5 grams of distilled water to a glass vial. The stock solution was mixed thoroughly.

10 *Preparation of Stock Solution 2*

An aqueous stock solution containing approximately 20% urea hydrogen peroxide (carbamide peroxide) was prepared by transferring 4 grams of 97% urea hydrogen peroxide (Sigma) and 16 grams of distilled water to a glass vial. The stock solution was mixed thoroughly. (The hydrogen peroxide content of the urea hydrogen
15 peroxide was about 35%). Stock solution contained about 7% H_2O_2 .

Example 1

A thermally-reversible hydrogen peroxide composition was prepared by transferring the ingredients below to a glass vial and mixing thoroughly until a colorless
20 and transparent liquid solution was obtained.

Stock Solution 1	1.60 grams
PLURONIC F127 (BASF)	<u>0.40 grams</u>
	2.00 grams

The above solution contained approximately 12% hydrogen peroxide, 68% water and 20%
25 PLURONIC F127. The glass vial containing the liquid peroxide solution was warmed to body temperature by holding the vial in a human hand. Following about one to two minutes, the liquid was transformed into a colorless, transparent composition that did not flow upon inverting the vial. The vial was allowed to cool to room temperature wherein the composition was transformed back to the low viscosity state. This cycle was repeated
30 several times with the same outcome.

The liquid and semi-solid (gel) states were both semi-quantitatively evaluated for hydrogen peroxide utilizing hydrogen peroxide analysis strips. The analysis utilized "EM

Quant Peroxide Test Strips" (EM Science Gibbstown, New Jersey, Catalog No. 10011-1). The compositions were evaluated according to the manufacturer's directions.

Results of the tests indicated that both the liquid and semi-solid states contained significant amounts of available peroxide.

5 The same sample was re-evaluated 2 months later and found to still exhibit thermally-reversible characteristics and comparable hydrogen peroxide levels based on the semi-quantitative analysis.

Example 2

10 A thermally reversible composition containing urea hydrogen peroxide was prepared by transferring the ingredients below to a glass vial and mixing thoroughly until a colorless and transparent liquid solution was obtained.

Stock Solution 2 4.00 grams

PLURONIC F127 (BASF) 1.00 grams

15 5.00 grams

The above solution contained approximately 16% urea hydrogen peroxide (or about 5.6% hydrogen peroxide), 64% water and 20% PLURONIC F127. The glass vial containing the liquid peroxide solution was warmed to body temperature by holding the vial in a human hand. After about 1 minute, the liquid transformed to a colorless, transparent composition
20 that did not flow upon inverting the vial. The vial was allowed to cool to room temperature wherein the semi-solid composition was transformed back to the low viscosity state. This cycle was repeated several time with the same outcome.

The liquid and semi-solid states were both semi-quantitatively evaluated for hydrogen peroxide utilizing hydrogen peroxide analysis strips, EM Quant Peroxide Test
25 Strips (EM Science; Gibbstown, New Jersey, Catalog No. 10011-1), according to the manufacturer's directions. Both the liquid and semi-solid states indicated the presence of significant amounts of available peroxide.

The same sample was re-evaluated 9 days later and found to still exhibit thermally-reversible characteristics and comparable hydrogen peroxide levels based on the semi-
30 quantitative analysis.

Table 1 summarizes the results of the two previous examples. The "+" indicates an increase in the viscosity. The "-" indicates a decrease in the viscosity. The presence of

hydrogen peroxide as indicated in the table are the results obtained from the semi-quantitative test using the EM Quant Peroxide Test Strips and test method.

Table 1

5

	% Peroxide	35°C viscosity	35°C viscosity @ 9 days	25°C viscosity	25°C viscosity @ 9 days	H ₂ O ₂ Present	H ₂ O ₂ Present @ 9 days
Example 1	12	+	+	-	-	Yes	Yes
Example 2	16	+	+	-	-	Yes	Yes

Example 3

Several compositions that have been evaluated for viscosity as a function of temperature. The compositions are described below:

10

Table 2. Comparative Sample A

Component	parts by weight (g)	% by weight	Physical Appearance at 23°C	Physical Appearance at body temp
Urea hydrogen peroxide	20	20	Low viscosity, colorless liquid	Low viscosity, Colorless liquid
Water	80	80		

Table 3. Sample B

Component	Parts by weight (g)	% by weight	Physical Appearance at 23°C	Physical Appearance at Body temp
Urea hydrogen peroxide	20	16	Low viscosity, Colorless liquid	non-flowing, colorless gel
Water	80	64		
PLURONIC F-127	25	20		

5

Table 4. Sample C

Component	Parts by weight (g)	% by weight	Physical Appearance at 23°C	Physical Appearance at body temp
Urea hydrogen peroxide	1.6	14.7	Non-flowing, colorless gel	Non-flowing, colorless gel
Water	6.4	58.7		
PLURONIC F-127	2.0	18.3		
CAB-O-SIL M-5* (fumed silica)	0.9	8.3		

* available from Cabot Corp. (Boston, MA)

- 10 Samples were further evaluated for viscosity as a function of temperature between 15°C and 45°C utilizing a Rheometrics RDA II Rheometer. Complex viscosity, η^* (units of measure is in Poise), versus temperature data were obtained using a controlled strain rheometer ("RDA2", Rheometrics Scientific, Piscataway, New Jersey). A parallel plate geometry was used with a plate diameter of 25 mm and a gap of approximately 1 mm.
- 15 Samples were subjected to an oscillatory strain of 10% applied at a frequency of 1 rad/sec while the temperature was ramped from 15°C and 45°C (3°C/ min).

Set out below is the RDA viscosity data. Figure 1 illustrates that aqueous compositions containing PLURONIC F127 polymer exhibit a relatively sharp increase in viscosity upon warming from room temperature to about 45°C. Sample C which

exhibited semi-solid-like characteristics at room temperature (due to the incorporation of a fumed silica) also increased substantially upon an increase in temperature.

Table 5

5

A		B		C	
Temp	η^*	Temp	η^*	Temp	η^*
°C	P	°C	P	°C	P
14.02	9.75424	17.88	2308.56	18.5	52951.5
14.28	3.35258	17.88	2379.72	18.3	42757.9
15.36	7.33292	18.54	2587.46	18.79	41559.9
17.28	3.46242	19.42	3111.41	19.64	41144.7
19.46	5.85152	20.91	3711.59	20.76	41347.4
21.12	5.79953	22.36	4580.71	22.09	42047
22.89	7.09599	23.72	5661.42	23.51	43615.7
24.91	4.19887	25.46	7221.65	24.04	45494.3
26.31	0.87001	26.85	8940.38	26.03	48768.7
28.23	3.13629	28.73	25375.6	27.94	55250.6
30.12	4.57411	30.7	29698.2	29.57	82062.6
31.6	4.7215	32.07	33651.8	31.31	94988.5
33.2	9.01765	33.57	37181.2	32.83	1.04E+05
35.02	8.0025	35.22	40557.8	34.36	1.09E+05
36.75	2.94618	36.89	43766.3	36.09	1.13E+05
38.44	4.24626	38.43	46677.4	37.49	1.20E+05
40.85	1.08273	40.01	49322.7	38.95	1.26E+05
42.92	5.04081	41.84	52296.6	40.7	1.32E+05
		43.52	54490.4	42.2	1.36E+05
				43.9	1.39E+05

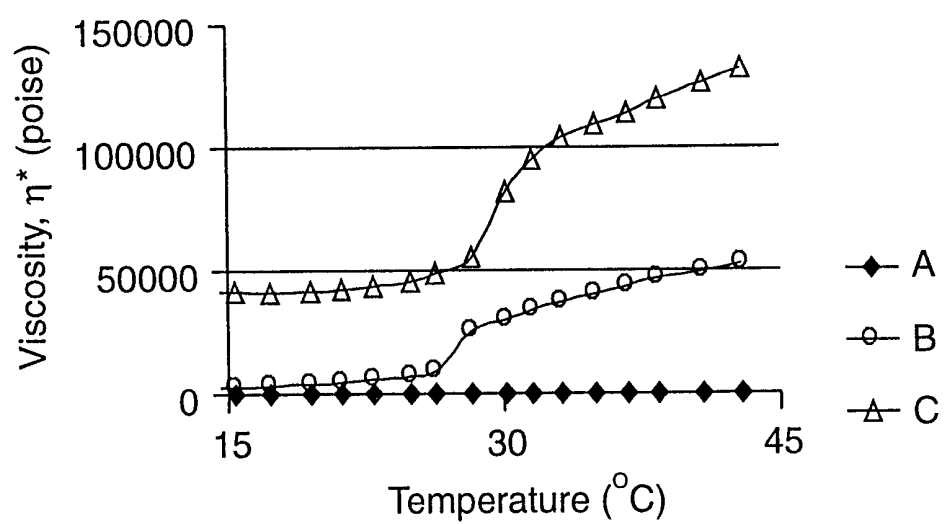
We claim:

1. A tooth whitening composition suitable for the oral environment comprising a tooth whitening agent and a thermally responsive viscosity modifier wherein the composition is capable of undergoing an increase in viscosity in response to a temperature increase from a pre-treatment temperature to a treatment temperature.
2. The composition of claim 1 wherein the composition is capable of reversible thermal response by undergoing a decrease in viscosity in response to a decrease in temperature.
3. The composition of claim 1 wherein the pre-treatment temperature is no more than about 29°C.
4. The composition of claim 1 wherein the pre-treatment temperature is about 5°C to about 10°C.
5. The composition of claim 1 wherein the pre-treatment temperature is about 20°C to about 25°C.
6. The composition of claim 1 wherein the treatment temperature is no less than about 30°C.
7. The composition of claim 1 wherein the viscosity modifier is a polyoxyalkylene polymer.
8. The composition of claim 1 wherein the composition has an initial viscosity of about 0 to about 7000 poise and increases to about 10,000 poise in response to the increase in temperature.
9. The composition of claim 1 wherein the composition has an initial viscosity of more than about 7000 poise and increases at least about 2-fold in response to the increase in temperature.
10. The composition of claim 1 wherein the tooth whitening agent and the thermally responsive modifier are physically separated until mixing just prior to treatment.
11. The composition of claim 1 further comprising a solvent.
12. The composition of claim 11 wherein the solvent comprises water.
13. The composition of claim 1 wherein the tooth whitening agent is no less than about 3 wt % and no more than about 40 wt % of the composition, the viscosity modifier is no less than about 5 wt % and no more than about 40 wt % of the composition.

14. The composition of claim 11 wherein the water is no less than 30 wt % and no more than about 90 wt % of the composition.
15. A method of whitening teeth using a tooth whitening composition suitable for the oral environment comprising a tooth whitening agent and a thermally responsive viscosity modifier wherein the composition is capable of undergoing an increase in viscosity in response to a temperature increase from a pre-treatment temperature to a treatment temperature, the method comprising the steps of:
- (a) dispensing the composition into a dental tray
 - (b) placing the dental tray into a user's mouth
 - (c) creating contact between the composition and at least one tooth surface, thereby initiating an increase in viscosity of the composition
 - (d) keeping the tray in the mouth for a period of time sufficient to whiten or brighten at least one tooth surface and
 - (e) removing the dental tray from the mouth
16. The method of claim 15 further comprising a step f) removing the composition in the mouth by initiating a decrease in viscosity of the composition or a decrease in weight percentage of the thermally responsive viscosity modifier by rinsing the mouth's interior with a solution.
17. The method of claim 15 wherein the dental tray has reservoirs.
18. The method of claim 15 wherein the dental tray has a temperature higher than the pre-treatment temperature of the composition.
19. A method of whitening teeth using a tooth whitening composition suitable for the oral environment comprising a tooth whitening agent and a thermally responsive viscosity modifier wherein the composition is capable of undergoing an increase in viscosity in response to a temperature increase from a pre-treatment temperature to a treatment temperature, the method comprising the steps of:
- (a) storing the composition at a pre-treatment temperature,
 - (b) applying the composition onto at least one tooth surface of a user's mouth thereby initiating an increase in viscosity of the composition, and
 - (c) keeping the composition in contact with the tooth surface or surfaces for a period of time sufficient to whiten or brighten at least one tooth surface

20. A method of claim 19 further comprising a step d) removing the composition by initiating a decrease in viscosity of the composition or a decrease in weight percentage of the thermally responsive viscosity modifier by rinsing the mouth with a solution.
21. A multiple-part dental whitening system for whitening at least one tooth surface comprising:
- 5 (a) dental tray material and
- (b) a tooth whitening composition suitable for use in the oral environment comprising a tooth whitening agent and a thermally responsive viscosity modifier, wherein the composition is capable of undergoing a change in viscosity in response to a change
- 10 in temperature, such that the viscosity of the composition is lower at a pre-treatment temperature than the viscosity at a treatment temperature.
22. The system according to claim 21, wherein the dental tray material is custom-fitted to a user's dentition.
23. The system according to claim 21, wherein the tooth whitening composition comprises
- 15 physically separate components of a whitening agent and a thermally responsive viscosity modifier, to be admixed just prior to treatment.
24. A multiple-part dental whitening system for whitening at least one tooth surface comprising:
- (a) a tooth whitening composition suitable for use in the oral environment comprising
- 20 a tooth whitening agent and a thermally responsive viscosity modifier, wherein the composition is capable of undergoing an increase in viscosity in response to a temperature increase from a pre-treatment temperature to a treatment temperature and
- (b) a dental composition applicator for applying said whitening composition onto a
- 25 user's tooth surface or surfaces.
25. The system according to claim 23, wherein the tooth whitening composition comprises physically separate components of a whitening agent and a thermally responsive viscosity modifier, to be admixed just prior to treatment.

1/1

*Fig. 1*

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/06146

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K7/20 A61K7/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GB 1 571 832 A (FLOW PHARMA INC) 23 July 1980 see the whole document ---	1,2, 7-15, 19-25
Y	WO 91 14650 A (ULTRADENT PRODUCTS INC) 3 October 1991 see page 8, line 25 - line 35 see page 14, line 3 - line 6 see examples see claims ---	1,2, 7-15, 19-25
Y	GB 2 170 406 A (COLGATE PALMOLIVE CO) 6 August 1986 see page 3, line 8 - line 11 see examples 7-13 --- -/--	1-15, 19-25

☒ Further documents are listed in the continuation of box C.

☒ 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

28 June 1999

Date of mailing of the international search report

05/07/1999

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

Pelli Wablat, B

INTERNATIONAL SEARCH REPORT

Int: International Application No

PCT/US 99/06146

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 718 886 A (PELLICO MICHAEL A) 17 February 1998 cited in the application see column 2, line 42 - line 67 see column 3, line 1 - line 9 see claims ---	1-15, 19-25
A	WO 86 00813 A (SCHERING AG) 13 February 1986 see the whole document ---	1-14
A	WO 97 11675 A (COLGATE PALMOLIVE CO) 3 April 1997 see abstract see page 4, last paragraph see page 6, line 20 - line 26 see examples ---	1,7, 11-13
A	US 4 980 152 A (FRAZIER WILLIAM F ET AL) 25 December 1990 see the whole document -----	1-14

INTERNATIONAL SEARCH REPORT

information on patent family members

Intr onal Application No

PCT/US 99/06146

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 1571832 A	23-07-1980	US 4100271 A	11-07-1978
		AU 515420 B	02-04-1981
		AU 2794977 A	22-02-1979
		CA 1090252 A	25-11-1980
		CH 629385 A	30-04-1982
		DE 2708152 A	08-09-1977
		FR 2400903 A	23-03-1979
		JP 1157132 C	15-07-1983
		JP 52125619 A	21-10-1977
		JP 57048049 B	14-10-1982
		NL 7709273 A	27-02-1979
		US 4188373 A	12-02-1980
WO 9114650 A	03-10-1991	US 5098303 A	24-03-1992
		AT 129485 T	15-11-1995
		AU 654955 B	01-12-1994
		AU 7753291 A	21-10-1991
		CA 2078776 A,C	23-09-1991
		DE 69114128 D	30-11-1995
		DE 69114128 T	13-06-1996
		DE 522087 T	03-02-1994
		DK 522087 T	04-03-1996
		EP 0522087 A	13-01-1993
		ES 2079659 T	16-01-1996
		GR 3018468 T	31-03-1996
		JP 9224962 A	02-09-1997
		JP 9224963 A	02-09-1997
		JP 8113520 A	07-05-1996
		JP 2670497 B	29-10-1997
		US 5770182 A	23-06-1992
		US 5846058 A	08-12-1998
		US 5234342 A	10-08-1993
		US 5759037 A	02-06-1998
		US 5759038 A	02-06-1998
		US 5770105 A	23-06-1998
		US 5725843 A	10-03-1998
		US 5746598 A	05-05-1998
		US 5409631 A	25-04-1995
		US 5851512 A	22-12-1998
		US 5855870 A	05-01-1999
		US 5376006 A	27-12-1994
GB 2170406 A	06-08-1986	AU 5076390 A	21-06-1990
		AU 5266586 A	07-08-1986
		DE 3602951 A	07-08-1986
		DK 51386 A	05-08-1986
		FR 2576790 A	08-08-1986
		PH 23523 A	25-08-1989
		US 4684517 A	04-08-1987
US 5718886 A	17-02-1998	US 5631000 A	20-05-1997
WO 8600813 A	13-02-1986	DE 3428264 A	06-03-1986
		AU 4672385 A	25-02-1986
		DK 111686 A	11-03-1986
		EP 0227656 A	08-07-1987
		JP 61502817 T	04-12-1986

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 99/06146

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9711675 A	03-04-1997	AU 701758 B AU 7243896 A CA 2233006 A CN 1200665 A	04-02-1999 17-04-1997 03-04-1997 02-12-1998
US 4980152 A	25-12-1990	NONE	