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(54) Title: ENZYME CONTAINING DENTURE CLEANSER

(57) Abstract

Enzyme containing denture cleanser composition effective in plaque, calculus and stain removal utilizing proteolytic enzymes, and EDTA.

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ENZYME CONTAINING DENTURE CLEANSER

This invention relates to denture cleanser compositions and more particularly to an improved water-soluble denture cleanser composition containing enzymatic and chelating cleansing agents.

Dentures may be cleansed either by immersion in a cleansing solution or by brushing with a cleansing agent in the manner of natural teeth. The former method is generally preferred, partly for convenience but primarily since brushing tends to mar the smooth surfaces of plastic dentures.

Cleansing solutions may be made from preformed liquid solutions but for storage convenience are usually in solid form in which case the cleansing solution is prepared at the time of use by dissolving the solid form in tap water. The solid form cleanser may be in the form of loose powder or granules or may be in the form of tablets. In addition, denture cleanser tablets usually also contain one or more active oxygen compounds such as sodium perborate monohydrate, potassium peroxydisulfate, potassium monopersulfate, sodium carbonate peroxide, potassium peroxydiphosphate, diperisophthalic acid, monoperphthalic acid and the like, which cause the tablets to evolve micro-bubbles of active or nascent oxygen as they are dissolved in water and provide an oxidizing cleansing action including a bleaching effect on the denture stains. Generally, they also contain a surfactant to lower the surface tension and to enhance the cleansing action.

Further, denture cleanser tablets usually also contain various other relatively inactive ingredients such as fillers, extenders, binders, indicators or dyes, flavors and the like. Lubricant systems, such as magnesium stearate or talc, to facilitate smooth and even flow of the dry granular materials of the formulations during tableting operations may also be added.

Improvement in denture cleansers has been primarily carried out by manipulating the oxidizing system, e.g.,

perborate and persulfate, and pH in order to achieve improved food stain removal. Hypochlorite generating formulations are well known to achieve a high level of plaque removal and moderate level of food stain removal, but it is known that they are harmful to denture metals and generate an odor unacceptable to the consumer.

Food stain does not adhere directly to denture materials but to biological accretions, such as denture plaque and calculus. Denture plaque is a complex glycoprotein which is believed responsible, in part, for denture odor. It is this substance which forms on the surface of the dentures initially. Upon its disintegration, there remains a residue composed of hydroxyapetite and other components which contain calcium. It is this residue which hardens to form calculus which continues to obtain new layers of plaque if not removed. This layering sequence also aids in stain retention by preferential stain adsorption.

It is well known that enzymes improve the removal of plaque by its disruption of the proteinaceous material by catalyzing the hydrolysis of peptide bonds and by increasing the water solubility of the proteinaceous material allowing it to be removed during treatment and subsequent rinses. In addition it is known that chelating agents are also able to remove to some extent calcium deposits and the calculus deposits on dentures and thus may also disrupt the deposits. Formerly, chelating agents were added to denture cleansers in small amounts to help reduce (a) the turbidity of the resultant solution due to hard water content and were essentially spent in the process or (b) to sequester the heavy metals which tend to spend the available titratable oxygen in such systems and thus extend the shelf life of the product. Such products however even when used at relatively high levels of either chelating agents or enzymes fail to remove significant amounts of both plaque and calculus deposits from the denture surface thus leaving a significant amount of stain on the dentures.

The incorporation and use of enzymes in denture cleansers is taught by U.S. Patents 4,155,868 and 3,962,107.

Although it has been thought to be desirable to incorporate enzymes in denture cleanser tablets, difficulties have arisen because of the inactivating effect of the enzyme resulting from the active oxygen when compressed with the enzyme. U.S. Patent No. 3,962,107 purports to obviate this problem by the separation of the enzyme and active oxygen cleansing components in separate layers of a denture tablet. It is stated that the faster dissolving enzyme layer permits enzymatic cleansing activity to proceed before dissolution of the active oxygen layer reaches a level which would inactivate the enzyme. On the other hand, U.S. Patent No. 4,155,868 discloses a single layer tablet in which an enzyme, active oxygen compounds and an effervescence producing composition are allegedly incorporated in such a manner that they are retained in a stable form until the tablet is ready for use. The patentee states that by careful control of the particle sizes and the surface treatments of selective components, the enzyme is not detrimentally inactivated during storage. The patentee further states that they provide added stability while in the dry tablet, the enzyme may be granulated or coated.

Both of the aforementioned U.S. Patents fail to recognize the significant enzyme deactivation partially attributable to the presence of chloride ions in their formulations when potassium persulfate is used as the source of active oxygen. The presence of both components, even when chlorides are present as minor impurities in the formulation components, results in the formation of compositions believed to be hypochlorites which deactivates the enzymes causing the system to become ineffective.

Thus, while the art has proposed storage stable denture cleanser compositions which incorporate enzymes with active oxygen bleaching components, the art has not

heretofor addressed the problem of deactivation of enzyme in the cleaning solution formed when the cleanser composition is added to water. Additionally, the art has not provided compositions designed to remove calculus deposits from dentures thereby removing embedded stains. The compositions of this invention overcome the prior art deficiencies by utilizing an effective amount of chelating agent along with an effective amount of enzyme to synergistically remove calculus/plaque deposits within a short period of time.

Preferred compositions of the present invention provide for the addition of a bleaching component, which does not react with halides to produce an enzyme deactivating composition such as a hypohalide, to an effective amount of a chelating agent along with an effective amount of enzyme to synergistically remove calculus/plaque deposits within a short period of time.

It has also been discovered that a water soluble denture cleanser composition may be prepared which comprises:

(a) an effective amount of a proteolytic enzyme to disrupt the proteinaceous material in plaque, and

(b) an effective amount of a sequestering agent to remove calcium deposits and calulus deposits, wherein the concomitant disruption of proteinaceous material and removal of calcium deposits and calculus deposits results in the removal of calculus and plaque.

It has further been discovered that a water soluble denture cleanser composition may be prepared which comprises:

(a) an effective amount of a proteolytic enzyme to disrupt the proteinaceous material in plaque, and

(b) an effective amount of a sequestering agent to remove calcium deposits and calulus deposits, and

(c) an effervescence producing composition,

wherein the concomitant disruption of proteinaceous material and removal of calcium deposits and calculus deposits results in the removal of calculus and plaque.

It has been discovered that a water soluble denture cleanser composition may be prepared which comprises:

(a) an effective amount of a proteolytic enzyme to disrupt the proteinaceous material in plaque, and

(b) an effective amount of a sequestering agent to remove calcium deposits and calulus deposits, and

(c) an effective amount of a bleaching component which does not react with halide to produce an enzyme deactivating composition,

wherein the concomitant disruption of proteinaceous material and removal of calcium deposits and calculus deposits results in the removal of calculus and plaque.

A preferred embodiment of the present invention is a water soluble effervescent denture cleanser composition which comprises:

(a) an effective amount of a proteolytic enzyme to disrupt the proteinaceous material in plaque, and

(b) an effective amount of a bleaching component which does not react with a halide to produce an enzyme deactivating composition, and

(c) an effective amount of a sequestering agent to remove calcium deposits and calculus deposits,

(d) an effervescense producing composition

wherein the concomitant disruption of proteinaceous material and removal of calcium deposits and calculus deposits results in the removal of calculus and plaque.

The invention also contemplates a method for cleansing dentures which method comprises placing the water-soluble denture cleanser composition and denture to be cleaned in an amount of water sufficient to dissolve

the composition and to completely cover the denture for a sufficient time to effect the desired cleaning. Cleaning times of up to about 15 minutes and even up to about 5 minutes have been found suitable to clean dentures with the formulations of this invention even though such times are not considered essential to the invention.

In accordance with the present invention there is provided a water-soluble denture composition comprising two essential components, a proteolytic enzyme and a sequestering agent. This formulation functions in cleansing the denture by removal of surface plaque by the enzyme and concurrent degradation of proteinaceous material along with the chelating effect to remove calcium and calculus deposits achieved by the sequestrant. The effervescence-producing and bleaching materials of the preferred composition aid in removing stains and debris from the object being cleaned as it is being reacted upon by the other components. The composition once prepared may be used as a powdered formulation or compressed into tablet form or other suitable format which is effective upon dissolution in water to remove denture plaque, calculus and food stains. In a preferred embodiment, the enzyme is incorporated in the compositions of the present invention in a granular encapsulated form. The denture cleanser compositions of the present invention may be in single layered or multi-layered tablet form.

In accordance with the present invention, the enzyme component of the denture composition herein is a proteolytic enzyme and most preferably a neutral or alkaline proteolytic enzyme which is capable of acting on food, food degradation products, mucin and plaque. In furtherance of the present invention, the proteolytic enzyme is preferably employed in a granulated, encapsulated form. The enzymes may be of plant, animal or microbial origin and even synthetically produced. Many are available commercially under various tradenames which are useable in this invention. The enzyme particle size is not critical for the compositions of this

invention but are preferably able to pass through a 10 to 20 mesh sieve (U.S. standard screen) when the composition is to be tabletted. The enzymes should be active within a pH range of about 7.0 to 12.0 and preferably 7 to 10.5.

The proteolytic enzyme, used in the present invention, can be of vegetable, animal or microorganism origin. Preferably it is of the latter origin, which includes yeasts, fungi, molds and bacteria. Particularly preferred are bacterial subtilisin type proteases, obtained from e.g. particular strains of B. subtilis and B. licheniformis. Examples of suitable commercially available proteases are Alcalase, Savinase, Esperase, all of NOVO Industri A/S; Maxatase and Maxacal of Gist-Brocades; Kuzusase of Showa Denko; BPN and BPN' proteases and so on. The activity of the proteolytic enzyme included in the composition, typically ranges from about 0.1-150 AU/g or its equivalent. Naturally, mixtures of different proteolytic enzymes may be used.

There are standard measures of enzyme activity such as the Anson Unit (AU) and the Novo Protease Unit (NPU) and the Glycine Unit (GU). These measurers of activity are well known and defined as follows:

Unit Definition - Anson Unit (AU)

1 Anson Unit = the amount of enzyme* which digests hemoglobin

at an initial rate such that there is liberated per minute an amount of TCA-soluble product which gives the same color with phenol reagent as one milliequivalent of tyrosine

* under reaction conditions given in NIAS method AF4/5-GB Modified Anson-Hemoglobin Method for the Determination of Proteolytic Activity

Unit Definition - Kilo Novo Protease Unit (KNPU)

1 Novo Protease Unit (NPU) = the amount of enzyme* which hydrolyzes casein at such a rate that the initial rate of formation of peptides/minute corresponds to 1 micromole of glycine/minute

* standard conditions given in NIAS method AF 162/3-6B Manual DMC Method for the Determination of Proteolytic Activity formation of peptides from casein is measured by color changes resulting from reaction of primary amino groups with trinitrobenzene-sulfonic acid to form a colored compound.

1000 NPU = 1 KNPU

A GU is a glycine unit, which is the amount of proteolytic enzyme which under standard incubation conditions produces an amount of terminal NH_2-groups equivalent to 1 microgramme/ml of glycine.

When utilized in the denture cleanser composition of this invention the enzymes should be used in amounts of about 0.5% to about 15% by weight of the total formulation and preferably 1% to about 7% by weight. Amounts below these amounts are not effective in removing sufficient plaque to be economical whereas higher amounts do not achieve any added benefit other than speed of cleaning. Typically, the enzymes useful in the present invention will have an activity of about about 2AU or its equivalent when expressed in other units.

The chelating or sequestering agents useful in the present invention are to be used in amounts of about 8% up to about 99.9% by weight of the total composition. Sequestering agents useful in the present invention are carboxylic acid derivatives and phosphonic acid and its derivatives.

Those carboxylic acid derivatives useful as chelating or sequestering agents include the hydroxycarboxylic acids and salts thereof, as well as

amino carboxylates. For example, the hydroxycarboxylic acid compounds include gluconic acid and citric acid, among others known in the art. The amino carboxylates include nitriloacetic acid, ethylenediaminetetraacetic acid (EDTA) and isoserine diacetate and their salts. Among those specific phosphonic acid derivatives are the salts of ethane-1- hydroxy-1, 1-diphosphonic acid. For example, aminotriomethylene phosphonic acid), 1-hydroxyethylidene- 1,1-diphosphonic acid, ethylenediamine tetra(methylene phosphonic acid), ethylenediaminetetra(methylene phosphonic acid), hexamethylenediaminetetra(methylene-phosphonic acid), diethylene triamine penta(methylene-phosphonic acid), among others. The alkali metal salts and analoges of the above phosphonates are also useful. Mixtures of any or all of the chelating or sequestering agents is also contemplated.

The preferred chelating or sequestering agent used in this invention is EDTA, most preferred is the tetra sodium salt of ethylenediamine tetraacetic acid, dihydrate. Another preferred sequestering agent is isoserine diacetate trisodium salt. This component is essential for use in the denture cleanser compositions of this invention and is employed in an amount of about 8% up to about 99.5% by weight of the total composition. A preferred amount is about 15% to about 80% and a most preferred amount is 15 to 50% by weight of the total composition.

The sequestering agent is believed to function in the inventive compositions by reacting with the calcium present in the calculus rendering the underlying proteinous material susceptible to attack by the proteolytic enzyme. The enzyme in turn attacks plaque thereby exposing more calculus to attack by the sequestering agent. This combination reaction results in the synergistic removal of the plaque and calculus along with adsorbed stain beyond that which can be achieved by using these materials separately.

Bleaching or active oxygen components useful in the present invention are those which do not inactivate proteolytic enzymes directly and which do not interact with halides to produce an enzyme deactivating composition. Examples of suitable bleaching components include alkali metal and alkaline earth metal perborates and percarbonates. Perborates are the preferred bleaching component and sodium perborate monohydrate is the most preferred.

The bleaching component when utilized in the denture cleanser composition is present in amounts up to about 55% preferably from about 12% to about 55% and most preferably from about 25% to about 55% by weight of the total denture cleanser composition. When used throughout the specification the term "bleaching component" shall include those compounds known in the art as "active oxygen" compounds. These compounds reduce stain and remove calculus and plaque.

The effervescence-producing composition may be selected from a wide range of materials which aid in cleaning the denture surfaces by causing the active components to be rapidly dissolved.

The effervescence-producing composition may be comprised of an acid selected from the group consisting of citric acid, tartaric acid, gluconic acid and malic acid and an alkali metal carbonate selected from the group consisting of sodium bicarbonate, potassium bicarbonate, sodium carbonate and potassium carbonate. These formulations are preferably employed when a neutral proteolytic enzyme is employed since they impart pH values around 7 to 8.5 when employed in the formulations of this invention.

In addition the effervescence-producing composition may be anhydrous sodium perborate. This particular component is the preferred effervescence-producing composition when the enzyme employed has a higher pH activity range, namely an alkaline proteolytic enzyme. This material exhibits a pH value around 9.5 to 10.5 when employed in the compositions of this invention.

The effervescence-producing composition should be employed in amounts up to about 75% by weight of the total composition and preferably in amounts of about 15% to about 25% by weight. Amounts above 75% do not enable sufficient active components to be present to remove adequate levels of plaque and calculus whereas levels below about 15% do not adequately disperse the components in solution.

In a preferred embodiment, the bleaching agent is sodium perborate monohydrate and the effervescence-producing agent is anhydrous sodium perborate. The weight ratio of sodium perborate monohydrate and anhydrous sodium perborate in a preferred embodiment is from about 5:3 to about 3:5.

In addition to the ingredients set forth above, the present compositions may contain a variety of additional ingredients selected on the basis of desired end use. Thus, for example, the compositions may include detergent compounds, such as organic and inorganic detergents, including non-ionic detergents such as the various polyoxyethylene esters of aromatic and alaphatic alcohols, as well as the polyoxyethylene esters of hydrophobic propylene oxide polymers. These compounds assist in maintaining a foaming action, in the instance where the cleansing compositions are placed in aqueous solution.

Also, the compositions may contain other adjuvant materials, that may be inorganic or organic in structure. Thus, inorganic water-soluble alkaline builders such as alkali and alkaline earth metal carbonates, hydroxides, and mixtures may be added.

The present compositions may optionally contain additional sequestrants for the purpose of maintaining solution clarity, in the instance where the compositions are placed in solution. The additional sequestrants may also assist in the inhibition of corrosion and tarnish of articles soaked in solution containing the present compositions. Useful sequestrants include polyfunctional

organic acids, such as citric acid, maleic acid and their corresponding salts.

Other additives such as flavorings, colorants, perfumes and the like may be added in various amounts, as mentioned earlier. For example, the flavorings may include varieties of mint, oil of clove, artificial vanilla flavoring and others. These materials may be included and blended in various combinations within the scope of the present invention. The choice of the required amounts is likewise within the skill of the art.

In the instance where the present cleansing compositions are formulated for use as denture cleansers, the colorants useful herein are those known as F.D.& C. & D.& C. dyes and lakes. These materials are certified by the Federal Food and Drug Administration as acceptable for use in food, drug and cosmetic applications, and drug and cosmetic colorings. The materials acceptable for the foregoing spectrum of use are preferably water-soluble, and include indigoid dye, known as F.D.& C. Blue No. 2, or its Lake which is the disodium salt of 5,5-indigo-tindisulfonic acid. Similarly, the dye known as F.D.& C. Green No. 1, comprises a triphenylmethane dye or F.D. & C. Green #3 and is the monosodium salt of 4-[4-N-ethyl-p-sulfobenzylamino)diphenylmethylene]-[1-(N-ethyl-N-p-sulfoniumbenzyl)2,5-cyclohexadienimine] or F.D. & C. Green #3. A full recitation of all F.D. & C. and D. & C. colorants and their corresponding chemical structures may be found in the Kirk-Othmer Encyclopedia of Chemical Technology, 3rd edition, at Volume 6, pages 561-595, which text is accordingly incorporated herein by reference. Dyes and colorants will fade at different rates and may be chosen to provide specific end points.

The foregoing colorants may be blended with each other in a variety of combinations. It is particularly desirable that the colorants be chosen so that the composition when initially dissolved will present a deep hue. This is important in the instance where the composition serves as a denture cleanser, as the fading

phenonmenon embodied in denture cleansers can be more easily observed by the end user.

The use of F.D. & C. Blue #1 Lake is particularly important in that the tablet color is blue without adversely affecting the color of the solution.

In addition, the inventive denture cleanser compositions of the present invention include a peroxygen or active oxygen component. These materials are compounds which form hydrogen peroxide or active oxygen when placed in solution. Typical active oxygen compounds include sodium perborate monohydrate and tetrahydrate, potassium monopersulfate, sodium carbonate peroxide, diperisophthalic acid, monoperphthalic acid, potassium peroxydiphosphate, sodium aluminum amino- hydroperoxide and the like. The peroxygen or active oxygen component is preferably employed in a granular form and in an amount of from about 10 to about 40% weight, preferably from about 15 to about 25% based on the total composition.

A further feature of the invention comprises the preparation of a compacted granulated mixture containing the anhydrous perborate salt in combination with a monohydrate perborate salt and optional addition of a polymeric fluorocarbon. Such mixtures are recited in Reissue Patent 32,771 and 4,405,486 which is incorporated herein by reference. In general such formulations comprise a combination of anhydrous perborate and monohydrate perborate in the amount of about 50% to about 70% by weight of the total cleansing compositions, wherein the combination includes at least 20% by weight of the total cleansing composition of anhydrous perborate, said combination having a portion present in a compacted, granulated mixture with up to about 0.70% by weight of said combination of a polymeric fluorocarbon.

The instant compositions and tablets described herein are superior in efficacy to the prior art in removal of stains, plaque and calculus. The efficacy of these compositions is of course a function of time, temperature and water volume used and as such comparisons

must be based on an amount of cleansing per a specific set of values for these factors.

The effervescent, denture cleanser compositions prepared as described are employed to clean dentures by placing them in water with the denture to be cleaned for a time sufficient to effect the desired cleaning. When the cleanser is in tablet form, the tablets may be from about 2 to about 3.2 grams in total weight, and are usually employed with warm water, preferably about 120ml initially about 40 to about 50°C in an amount sufficient to completely cover the denture. Tablet weight is not critical. When so employed, effective and desired cleaning may be achieved in about 5 to about 15 minutes but in more highly stained dentures, longer periods may be desirable. The tablets when thus employed are found to effectively remove mucin, plaque, calculus, and stains which are not as readily removed by tablets not containing enzymes and sequesterants utilized herein. Moreover, this is accomplished without brushing and usually without the overnight soaking necessary with the generally available tablets.

The compositions of the invention are prepared by mixing the components together until a homogenous mixture is obtained. The composition may then be stored or compressed into tablets. Prior to packaging or compression, the optional ingredients may be added and blended to obtain a uniform mixture. To limit enzyme inactivation during storage the components may be dried prior to blending so that they are substantially moisture free. Drying procedures are well known in the art and do not constitute a novel aspect of this invention.

The present invention is further illustrated by the following examples. All percentages in the examples and throughout the specification and claims are by total weight of the final denture cleanser composition unless otherwise indicated.

Examples

With Reference to Table I

Example A represents a preferred composition of the instant invention. Example I represents the prior art composition whereby the amount of EDTA is low (3.83%), it contains no enzymes and the solution pH is 8.4. Example II represents a typical composition of the prior art using enzymes in a potassium monopersulfate formula. Example III represents the prior art whereby the amount of EDTA is high (39.2%), it contains no enzymes and the solution pH is 10.3. Example IV represents the use of only one enzyme (Milezyme APUG-330) in solution. Example A which represents the composition of the instant invention contains a large amount of the chelating agent, ethylene diamine tetraacetic acid tetra sodium salt dihydrate (EDTA), and an effective amount of Enzyme (Milezyme APUG-330) at a pH of 10.3 and contains an equivalent amount of titratable oxygen initially to the prior art levels in I, II, and III.

The preferred composition of the instant invention Example A was prepared according to the Reissue Patent #32,771 as follows. Initially, a quantity of anhydrous sodium perborate, in the form of a fluffy powder, tetra sodium EDTA dihydrate and sodium perborate monohydrate was combined in a container with a quantity of polytetrafluorothylene powder identified as Grade F5A by Allied Chemical Corp. The polytetrafluoroethylene was added in the amounts based upon the weight of the perborate, as indicated with respect to each of the examples. Blending was performed for about 3 minutes, after which the mixture was predried for 1 hour at 90°C. The dried materials which represent almost 94% of the formula were added to the other excipients and the enzyme. The granulation was compressed into a cohesive tablet having a hardness of 13 to 14 SCU. and the tablets were not heat cured. The tablets showed excellent stability results including the absence of any ballooning of the final package at elevated storage conditions (45°C) for 4 months. For comparison purposes, Example

III, the prior art composition was also not heat cured. Reissue Patent #32,771 is incorporated herein by reference.

Cleaning Process

The denture (food stained plaque/calculus matrix) tiles were immersed in 125 ml. of water at 45°C, and one of the compositions indicated in Table I were added. At the end of 15 minutes, the tiles were dunked in a 200ml volume of tap water 20 times the water replaced with a fresh 200ml volume and the dunking process repeated another 20 times and allowed to air dry at (20°C) room temperature. The tiles were visually inspected. The extent of the calculus and plaque removal was further determined both by a reflectance method and the SEM method.

Tables II and III represent the analysis of the tiles to determine the percent plaque/tartar removal using the (SEM) Scaning Electron Microscope method and the
Reflectance Method respectively. Table II represents the percent Ca, P, O, N, and Ti remaining on the surface of the plaque/tartar coated tiles after treatment with the test compositions I, II, III, A and IV. Both the virgin tiles and the untreated tartar/plaque coated tiles were also examined to determine the baseline. As evidenced, as the Ca, P and O increases the higher the calculus coating on the surface of the tile. In Table II, the results of using composition A as the plaque/tartar tiles gives the lowest Ca, P and O values indicating that (A is the most efficient in removing the surface coating of tartar/plaque.

The Reflectance Method (Table III) determines the plaque/tartar remaining on the surface after treatment with the test compositions I, II, III, A and IV. Again the use of composition A gives the highest % plaque/tartar removal.

TABLE I

Ingredients	I	II	III	A	IV
Sodium Bicarbonate	10.9	10.60			
Citric Acid	3.8	3.60			
Sodium Carbonate	9.11	8.84			
Colorant	0.16	0.145	0.1	0.095	
Oxone	39.0	37.80			
Ethylenediamine Tetraacetic Acid Tetra Sodium DiHydrate	3.83	3.71	39.2	36.6	
Flavor & Fragrance	0.96	0.93	0.7	0.67	
Magnesium Stearate	0.03	0.03	0.025	0.024	
Sodium Perborate Monohydrate	12.39	12.0	36.3	34.6	
Anhydrous Sodium Perborate	2.66	2.58	22.3	21.2	
Sodium Benzoate	1.44	1.40			
Polytetrafluoro-ethylene	0.095	0.092	0.6	0.57	
Filler	4.80	4.65			
Milezyne APUG-330	--	3.10	--	4.70	100%*
Sodium Tripoly-phosphate	10.16	9.85			
Detergent**	0.64	0.62	0.7	0.67	
% Tartar/Plaque Removal	13.25	15.29	28.75	55.97	16.11

* The amount used for the cleaning test all had the equivalent of 100 mg of Enzyme (alcalase)/Treatment.

** The detergent is athanol LAL Powder which contains 30% NaCl

TABLE II

SEM analysis of the said invention composition versus prior art products.

Before treatment	Ca	P	O	N	Ti
Virgin tile	0.02	0.0	5.75	1.18	3.27
Tartar/plaque	10.88	4.35	15.71	6.41	0.47
After treatment					
Example					
I	12.69	4.61	15.01	4.36	0.68
II	7.59	3.01	11.56	5.74	0.42
III	6.16	1.55	10.67	6.59	2.01
A	2.42	0.80	6.14	9.75	1.49
IV	5.10	1.63	8.45	3.04	0.43

TABLE III

Percent Plaque/Tartar Removal as determined by the Reflectance Method

Example	% Removed
I	13.25
II	15.59
III	28.75
A	59.97
IV	16.10

TABLE IV

Example #	Storage Period	Storage Temp.	Soaking Time	% Plaque Removal
A	4 months	RT	15 min.	36.5%
III	4 months	RT	15 min.	23.8%
A	4 months	45°C	15 min.	36.3%
A	0	RT	15 min.	36.3%
A	7 days	RT	30 min.	61.9%
A	7 days	RT	16 hours	74.3%
III	1 month	RT	30 min.	25.5%
III	1 month	RT	16 hours	24.1%

In Table IV, Examples A represents the preferred composition of the instant invention which contains both the EDTA (a chelating agent) and the said enzyme (Milezyme APUG-330) and III represents a composition without an enzyme. The objective is to demonstrate that the Example A synergistically removes plaque from tiles which have very little calculus accumulations as evidenced by an SCM analysis. See Table V where the calcium level is only 0.03.

TABLE V

Plaque coated	Ca	P	O	N	Ti
Tile	0.03	0.18	7.72	13.50	0.31

Based on the results of Table IV, the stability of the preferred composition A is further evidenced when tablets are subjected to aging at room temperature and accelerated aging by maintaining the temperature at 45°C for 4 months. At the end of this period, the tablets were tested for % plaque removal to determine the stability of the enzymes. The 4 month aged tablets were compared to freshly prepared tablets and the results on Table IV indicate an equal amount of plaque removal. In addition thereto, Table IV results indicate that when the tablets are dissolved, the preferred composition (Example A) continues to remove plaque, that is, 61.9% after 30 minutes of soaking and 74.3% plaque removal after 16 hours of soaking. The comparative formulation (Example III) does not remove more plaque with increased soaking time and stops cleaning after removing around 25% plaque in about 15 minutes.

This invention being thus described, it will be obvious that the same may be varied in many ways. Such variations are not to be regarded as a departure from the spirit and scope of the invention and all such modifications are intended to be included within the scope of the following claims.

CLAIMS

1. A denture cleanser composition which comprises:

(a) an effective amount of a proteolytic enzyme to disrupt the proteinaceous material in plaque, and

(b) an effective amount of a sequestering agent to remove calcium deposits and calculus deposits.

Wherein the concomitant disruption of proteinaceous material and removal of calcium deposits and calculus deposits results in the removal of calculus, plaque and stains.

2. The composition of Claim 1 further comprising a bleaching component which does not react with halides to form an enzyme deactivating composition.

3. The composition of Claim 1 further comprising an effervescense producing composition.

4. The composition of Claim 2 wherein the bleaching component is a perborate.

5. The composition of Claim 4 wherien said perborate is selected from the group consisting of alkali metal and alkaline earth metal perborate and mixtures thereof.

6. The composition of Claim 3 wherein said effervescense producing composition is anhydrous sodium perborate.

7. The composition of Claim 4 wherein said perborate is sodium perborate monohydrate.

8. The composition of Claim 1 further comprising a bleaching agent and an effervescence producing composition.

9. The composition of Claim 8 wherein the bleaching agent is sodium perborate monohydrate and the effervescense producing composition is anhydrous sodium perborate.

10. The composition of Claim 9 wherein the weight ratio of sodium perborate monohydrate to sodium perborate anhydrous is from about 5:3 to about 3:5.

11. The composition of Claim 4 wherein the perborate is present in an amount of about 12% to about 55% by weight of the composition.

12. The composition of Claim 4 wherein the perborate is present in an amount of about 25% to about 55% by weight of the composition.

13. The composition of Claim 1 wherein the sequestering agent is selected from the group consisting of phosphonic acid derivatives, carboxylic acid derivatives and mixtures thereof.

14. The composition of Claim 13 wherein the carboxylic acid derivative is selected from the group consisting of amino carboxylate, hydroxycarboxylate and mixtures thereof.

15. The composition of Claim 1 wherein the sequestering agent is ethylenediaminetetraacetic acid.

16. The composition of Claim 1 wherein the sequestering agent is isoserine diacetate.

17. The composition of Claim 1 wherein the sequestering agent is present in an amount of about 8% to about 99.5% by weight.

18. The composition of Claim 1 wherein the sequestering agent is present in an amount of about 15% to about 80% by weight.

19. The composition of Claim 1 wherein the proteolytic enzyme is selected from the group consisting of Alcalase, Savinase, Esperase, Maxatase, Maxacal, Kuzusase, BPN, BPN', Mylezyme and mixtures thereof.

20. The composition of Claim 1 wherein the proteolytic enzyme is esperase.

21. The composition of Claim 1 wherein the enzyme is milezyme.

22. The composition of Claim 1 wherein the enzyme is present in an amount of about 0.5% to about 15% by weight.

23. The composition of Claim 1 wherein the enzyme is present in an amount of about 1% to about 7% by weight.

24. The composition of Claim 1 wherein the proteolytic enzyme is active over a pH range of about 7 to about 11.

25. The composition of Claim 1 wherein the proteolytic enzyme is a neutral or alkaline proteolytic enzyme.

26. The composition of Claim 3 wherein said effervescence-producing composition is comprised of an acid selected from the group consisting of citric acid, tartaric acid, gluconic acid and malic acid and an alkali metal carbonate selected from the group consisting of sodium bicarbonate, potassium bicarbonate, sodium carbonate and potassium carbonate.

27. The composition of Claim 3 wherein said effervescence-producing composition is sodium perborate anhydrous.

28. The composition of Claim 3 wherein the effervescence-producing composition is present in an amount from about 15 to about 60% by weight of the total composition.

29. The composition of Claim 3 wherein the effervescence-producing composition is present in an amount of about 15% to about 30% by weight of the total composition.

30. The composition of Claim 1 wherein the proteolytic enzyme is present in a granular encapsulated form.

31. A method for cleansing dentures, said method comprising placing a water-soluble denture cleanser composition and denture to be cleaned in an amount of water sufficient to completely cover said denture for a sufficient time to dissolve the composition and to effect the desired cleaning, wherein said composition removes plaque and calculus deposits on said dentures which composition comprises:

(a) an effective amount of a proteolytic enzyme to disrupt the proteinaceous material in plaque, and

(b) and effective amount of a sequestering agent to rmeove calcium deposits and calculus deposits.

Wherein the concomitant disruption of proteinaceous material and removal of calcium deposits and calculus deposits results in the removal of calculus and plaque.

32. The method of Claim 31 further comprising a bleaching component which does not react with halides to form an enzyme deactivating composition.

33. The method of Claim 31 further comprising an effervescense producing composition.

34. The method of Claim 32 wherein the bleaching component is a perborate.

35. The method of Claim 34 wherien said perborate is selected from the group consisting of alkali metal and alkaline earth metal perborate and mixtures thereof.

36. The method of Claim 31 wherein said effervescense producing composition is anhydrous sodium perborate.

37. The method of Claim 34 wherein said perborate is sodium perborate monohydrate.

38. The method of Claim 31 further comprising a bleaching agent and an effervescense producing composition.

39. The method of Claim 38 wherein the bleaching agent is sodium perborate monohydrate and the effervescense producing composition is anhydrous sodium perborate.

40. The method of Claim 39 wherein the weight ratio of sodium perborate monohydrate to anhydrous sodium perborate is from about 5:3 to about 3:5.

41. The method of Claim 39 wherein the perborate is present in an amount of about 12% to about 55% by weight of the composition.

42. The method of Claim 39 wherein the perborate is present in an amount of about 25% to about 55% by weight of the composition.

43. The method of Claim 31 wherein the sequestering agent is selected from the group consisting of phosphonic acid derivatives, carboxylic acid derivatives and mixtures thereof.

44. The method of Claim 43 wherein the carboxylic acid is selected from the group consisting of amino carboxylate, hydroxycarboxylate and mixtures thereof.

45. The method of Claim 31 wherein the sequestering agent is ethylenediaminetetraacetic acid.

46. The method of Claim 31 wherein the sequestering agent is isoserine diacetic Tri Sodium Salt. (ISDA Na_3)

47. The method of Claim 31 wherein the sequestering agent is present in an amount of about 8% to about 99.5% by weight.

48. The method of Claim 31 wherein the sequestering agent is present in an amount of about 15% to about 80% by weight.

49. The method of Claim 31 wherein the proteolytic enzyme is selected from the group consisting of Alcalase, Savinase, Esperase, Maxatase, Maxacal, Kuzusase, BPN, BPN^1, Mylezyme and mixtures thereof.

50. The method of Claim 31 wherein the proteolytic enzyme is esperase.

51. The method of Claim 31 wherein the proteolytic enzyme is milezyme.

52. The method of Claim 31 wherein the enzyme is present in an amount of about 0.5% to about 15% by weight.

53. The method of Claim 31 wherein the enzyme is present in an amount of about 1% to about 7% by weight.

54. The method of Claim 31 wherein the proteolytic enzyme is active over a pH range of about 7 to about 12.

55. The method of Claim 31 wherein the proteolytic enzyme is a neutral or alkaline proteolytic enzyme.

56. The method of Claim 33 wherein said effervescence-producing composition is comprised of an acid selected from the group consisting of citric acid, tartaric acid, gluconic acid and malic acid and an alkali metal carbonate selected from the group consisting of sodium bicarbonate, potassium bicarbonate, sodium carbonate and potassium carbonate.

57. The method of Claim 33 wherein said effervescence-producing composition is sodium perborate anhydrous.

58. The method of Claim 33 wherein the effervescence-producing composition is present in an amount from about 15 to about 60% by weight of the total composition.

59. The method of Claim 33 wherein the effervescence-producing composition is present in an amount of about 15% to about 25% by weight.

60. The method of Claim 31 wherein the proteolytic enzyme is present in a granular encapsulated form.

INTERNATIONAL SEARCH REPORT

International Application No PCT/US 91/08107

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl.5 A 61 K 7/30

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl.5	A 61 K

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category °	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No.[13]
X	DE,A,1943441 (LEO-WERKE) 4 March 1971, see examples 1-3; claims	1,2,4-7,11,13-14,19-20,22-25,31-32, 34-37, 43-44, 49-50, 52-55
X	FR,A,2520614 (ROHTO PHARMACEUTICAL) 5 August 1983, see example 16; claims	1,3,14-15,17, 19,22-23,25-26,28-29,

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° Special categories of cited documents : [10]

"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

"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

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
12-02-1992	20. 03. 92
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	Natalie Weinberg

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
		31,33, 44-45, 47-49, 52-53, 55-56, 58-59
X	EP,A,0258186 (WARNER-LAMBERT COMPANY) 2 March 1988, see the whole document	1-12,17 -19,21- 42,47- 49,51- 60
Y		1-60
Y	EP,A,0123525 (WARNER-LAMBERT COMPANY) 31 October 1984, see the whole document	1-60
Y	EP,A,0225658 (AKZO N.V.) 16 June 1987, see the whole document	1-60
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X	DE,A,3236966 (STECKMANN) 12 April 1984, see the whole document	1,13-14 ,22-23, 25,31, 43-44, 47-48, 52,53, 55
X	LU,A, 59503 (BEECHAM INC.) 26 February 1970, see example VI; claims	1,3,13- 14,22- 23,25- 26,28- 29,31, 33,

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III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
		43-45, 52-53, 55-56, 58-59
X,P	EP,A,0446982 (UNILEVER) 18 September 1991, see page 8, lines 16-32; claims 1-3,9,11,13	1-2,4-5,13-15, 17-23, 25,31-32,34-35, 43-45, 47-53, 55
X	GB,A,1391318 (MILES LABORATORIES) 23 April 1975, see the whole document	1-5,13-15,19, 21-23, 25-26, 31-35, 43-45, 49,51-53,55-56
Y	WO,A,8802600 (POULSEN) 21 April 1988, see the whole document	1-5,13-15,19, 21-23, 25-26, 31-35, 43-45, 49,51-53,55-56

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. US 9108107 SA 54347

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 12/03/92
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
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		JP-A-	58134014	10-08-83
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		US-A-	4486330	04-12-84
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EP-A- 0225658	16-06-87	None		
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		JP-A-	2073008	13-03-90
		WO-A-	9002544	22-03-90
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LU-A- 59503	26-02-70	None		
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ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. US 9108107 SA 54347

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The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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