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REMINERALISIERUNG VON VERKALKTEM GEWEBE

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Description

Field of the invention

[0001] The invention concerns cosmetic and therapeutic treatment of tissue, such as tooth, to effect, for instance, whitening and tissue re-building through mineralisation.

Background of the invention

[0002] Iontophoresis is a non-invasive method of propelling high concentrations of a charged substance, normally a medication or a bioactive agent, using a small electric charge applied to an iontophoretic chamber.

[0003] It is known to use iontophoresis in transdermal drug delivery. Also, iontophoresis is known to be used in conjunction with fluoride containing compounds to treat dentine hypersensitivity.

[0004] Simone, J. L., et al, Iontophoresis: An Alternative in the Treatment of Incipient Caries? Braz. Dent. J, 1995, 6(2), 123-129 describes, *inter alia*, treating dental lesions iontophoretically with sodium fluoride and claimed to find good remineralisation due to the formation of calcium fluoride, though this was not validated.

[0005] CPP-ACP is a casein derived peptide, with added calcium and phosphate, specifically, casein phosphopeptide - amorphous calcium phosphate. CPP-ACP acts as a calcium and phosphate reservoir.

[0006] Conventionally, CPP-ACP is delivered to a tooth surface in several vehicles, such as chewing gum, mouth wash, toothpaste and other restorative materials.

[0007] Thus, for example, International Patent Application No. WO 02/094204 describes a composition for dental restoration including a dental restorative material and an effective amount of a casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) complex or casein phosphopeptide-amorphous calcium fluoride phosphate (CPP-ACFP) complex.

[0008] When used herein, the term remineralisation is used to mean mineralisation of an area to which further material is being added, whether or not there was insufficient material at the area before the treatment.

[0009] WO 2006/130913 A1 discloses a method for mineralizing a dental surface. GB 1 219 632 discloses an improved toothbrush.

Summary of the Invention

[0010] The invention is directed to a remineralising agent for use in iontophoretic remineralising treatment of tissue with the features of the independent claim 1. Preferred embodiments thereto are given in the dependent claims.

[0011] According to a first aspect of the invention, there is provided a method of remineralising tissue which comprises pre-conditioning the tissue to remove protein and/lipids, and then applying to the tissue a remineralising agent whilst separately, sequentially or simultaneously applying iontophoresis.

[0012] Preferably, the remineralising agent is a source of phosphate, calcium and water. Preferably, the method comprises the remineralisation of hypo-mineralised or demineralised tooth.

[0013] In one aspect, the method is a cosmetic treatment which is directed to lightening or whitening tooth.

[0014] The method may be directed to the prevention or treatment of tooth erosion.

[0015] Preferably, the remineralising agent comprises casein phosphopeptide-amorphous calcium phosphate (CPP-ACP).

[0016] The remineralising agent preferably contains fluoride. An example of such a remineralising agent is casein phosphopeptide-amorphous calcium fluoride phosphate (CPP-ACFP). Preferably, the remineralising agent includes one or more remineralisation enhancers. Typically the remineralising enhancers are sources of calcium and phosphate ions.

[0017] Examples of remineralisation enhancers may include, but are not limited to; Dicalcium phosphate dehydrate (DCPD), mineral brushite; Dicalcium phosphate anhydrous (DCPA), mineral monetite; Octacalcium phosphate (OCP); alpha-tricalcium phosphate (alpha-TCP); beta-tricalcium phosphate (beta-TCP); Amorphous calcium phosphate (ACP); Calcium-deficient hydroxyapatite (CDHA); Hydroxyapatite (HA or OHAp); Fluorapatite (FA or FAp); Tetrcalcium phosphate (TTCP or TetCP), mineral hilgenstockite). More preferably, the remineralisation enhancer is strontium.

[0018] The remineralising agent may include at least two remineralisation enhancers wherein one of the enhancers is a source of calcium ions and the other is a source of phosphate ions. For example the remineralising agent may include a source of calcium e.g. calcium hydroxide and a source of phosphate e.g. orthophosphoric acid. The ratio of calcium:phosphate in the remineralising agent may be between 1:1 and 22:10. Preferably the ratio of calcium:phosphate is about 10:6 (i.e. 1.67), which represents the ratio of calcium to phosphate ions in calcium hydroxyapatite. Alternatively the ratio of calcium:phosphate in the remineralising agent may be between 9:6 and 22:10. Alternatively still the ration of calcium:phosphate in the remineralising agent may greater than 1:1 but less than 3:2 (i.e. 1.0 up to 1.49).

[0019] The remineralising agents may thus be selected from the following:

i) Ca:P ratio = 1.67: e.g. Hydroxyapatite: Fluorapatite.

ii) Ca: P ratio = 1.5 - 2.2 (but not 1.67): e.g. Alpha-Tricalcium phosphate; Beta-Tricalcium phosphate; Amorphous calcium phosphate; Calcium deficient Hydroxyapatite; Tetracalcium phosphate, mineral hilgenstockite.

iii) Ca:P ratio = 1-1.49: e.g. Dicalcium phosphate dehydrate, mineral brushite; Dicalcium phosphate an-

hydrous, mineral monetite.

[0020] The remineralising agent may be prepared from its component parts by 'driving' in calcium ions iontophoretically (in aqueous solution) and subsequently changing the polarity of the set-up and 'drive' in phosphate ions (in aqueous solution) with a second sequence of iontophoresis - the calcium and phosphate ions would thus 'meet' within the lesion during the second sequence of iontophoresis and precipitate out as a calcium phosphate mineral (or minerals). The hydroxyl ion of the generated apatite would come from the aqueous solution. The water-soluble calcium-containing agent might be, for example, calcium hydroxide, calcium chloride, or calcium nitrate; the water-soluble phosphate-containing agent might be, for example, orthophosphoric acid (H_3PO_4), sodium (or potassium) hydrogen phosphate, sodium (or potassium) dihydrogen phosphate or magnesium phosphate. The calcium agent containing solution may be separate from the phosphate agent containing solution, or combined into one solution.

[0021] Thus a preferred method of the invention comprises the steps of: i) pre-conditioning the tissue to remove protein and/lipids, and ii) applying to the tissue a calcium-containing aqueous solution and/or phosphate-containing aqueous solution whilst separately, sequentially or simultaneously applying iontophoresis. Optionally after sufficient time for the ingress of a predetermined amount of calcium ions, determined (indirectly) by measurement of the amount of current discharged into the tooth, this first phase of remineralisation would be stopped and the polarity of the iontophoresis electrode at that surface would be changed to negative; the remineralising agent would be changed to an aqueous solution of orthophosphoric acid and the iontophoresis method re-applied in order to cause the ingress of phosphate ions into the tooth. The reversal of the previous iontophoresis polarity will cause the previously migrated calcium ions within the tooth to migrate towards the surface as the phosphate ions are migrating into the tooth - this combination of calcium and phosphate ions, in aqueous solution, within the tooth will result in the deposition of orthophosphates within the tooth - i.e. remineralisation. This second phase of iontophoresis will be stopped when a pre-determined level of current has been discharged into the tooth.

[0022] Thus a further preferred method of the invention comprises the steps of i) pre-conditioning the tissue to remove protein and/lipids ii) applying to the tissue a calcium-containing aqueous solution or phosphate-containing aqueous solution whilst separately, sequentially or simultaneously applying iontophoresis, and iii) either (a) applying a phosphate-containing aqueous solution where in (ii) a calcium-containing aqueous solution was applied or (b) applying a calcium-containing aqueous solution where in (ii) a phosphate-containing aqueous solution was applied whilst separately, sequentially or simultaneously applying iontophoresis.

[0023] Preferably, the pre-conditioning step is performed, with or without the application of iontophoresis, prior to application of the remineralising agent/iontophoresis. Preferably, the pre-conditioning step comprises treatment with an acid, more preferably, phosphoric acid.

[0024] Preferably, the pre-conditioning step comprises treatment with a hypochlorite.

[0025] A preferred method of the invention involves the treatment or alleviation of dental caries and/or dental fluorosis in a mammal.

[0026] A further preferred method of the present invention comprises the remineralising of hypo-mineralised or de-mineralised (carious) dentine.

[0027] The present invention also provides a remineralising agent for use in iontophoretic remineralising treatment of tissue which has been subject to pre-conditioning to remove protein and/or lipids, the remineralising agent being a source of both phosphate and calcium.

[0028] Preferably, the remineralising agent comprises casein phosphopeptide-amorphous calcium phosphate (CPP-ACP).

[0029] The present invention further provides a kit for use in iontophoretic remineralising treatment of tissue comprising a pre-conditioning agent and a remineralising agent.

[0030] Preferably, the pre-conditioning agent and the remineralising agent are present in the kit in a suitable form for application, for instance, a liquid or a gel form.

[0031] The kit may also provide an applicator for applying the or each agent to the site of treatment.

More detailed description of the invention

[0032] As indicated above, the present invention provides a method of remineralising hypo-mineralised or demineralised tooth.

[0033] A variety of remineralising agents may be used, including a mixture of remineralising agents. The remineralising agent may depend upon the tissue to be treated. However, preferably, the remineralising agent is a phosphate or calcium source, preferably a source of phosphate and calcium. An especially preferred remineralising agent is casein phosphopeptide-amorphous calcium phosphate (CPP-ACP). For use in the remineralisation of tooth, the remineralising agent may be a fluoride containing agent as hereinbefore described, such as casein phosphopeptide-amorphous calcium fluoride phosphate (CPP-ACFP). Other remineralising agents may comprise calcium phosphate compounds, such as fluoroapatite, monetite, brushite, amorphous calcium phosphate, hydroxyapatite, etc. Furthermore, it may be possible to incorporate additional elements in the remineralising agent of the invention which may enhance the remineralisation effect, such as strontium.

[0034] It will be understood by the person skilled in the art that the terms hypo-mineralised tissue and demineralised tissue are intended to include any tissue that is

deficient in its level of mineralization and includes tissue, such as tooth, that is substantially or completely demineralised, e.g. as a result of the dental caries process, thus including dental caries lesions, or a result of acid erosion, thus including 'surface-softened' enamel or dentine.

[0035] The iontophoresis may comprise the application of a voltage, e.g. a fixed voltage, or a current, e.g. a fixed current. Alternatively, the iontophoresis may comprise the application of a mixture of voltage and current, for example, the combination of voltage and current may be applied in specific sequences so as to optimise remineralisation.

[0036] In addition, in the method of the invention a preconditioning step is also included prior to application of the remineralising agent/iontophoresis. The pre-conditioning step may vary but may, for example, comprise the removal of proteins and/or lipids prior to application of the remineralising agent/iontophoresis. Although a variety of pre-conditioning steps may be used, preferably, the preconditioning step comprises a variety of processes or a mixture of processes. Any suitable protein removing agent can be used in the preconditioning step of the present invention. The agent is required to reduce the proteinaceous barrier formed over the surface to be treated, such as the pellicle over teeth or the exogenous protein within a caries lesion. The preconditioning step may optionally include the use of iontophoresis and the various preconditioning agents, e.g. protein removing agents, may be used in a variety of combinations and/or sequences. Furthermore, any of the pre-conditioning agents may be propelled into a hypo-mineralised or demineralised region, e.g. caries lesion, by iontophoresis to optimise the disruption of the protein layer and then the polarity of the iontophoresis reversed in order to aid the removal the proteinacious material from the hypo-mineralised or demineralised tissue. Examples of suitable agents include bleach, detergent, chaotropic agents such as urea, high phosphate concentrations, cocktails of proteases (e.g. endopeptidases, proteinases and exopeptidases) and any other protein solubilising, disrupting or hydrolysing agent. Examples of suitable bleaches include sodium hypochlorite, and peroxide bleaches. In a preferred embodiment, the bleach is an alkaline bleach. In a further preferred embodiment the alkaline bleach is sodium hypochlorite. The protein disrupting agent acts to solubilise and partially or wholly remove proteins from the surface of the tooth mineral, e.g. proteins of the pellicle on the tooth surface. However, preferably the preconditioning step comprises treatment with an acid, such as an organic acid, e.g. acetic acid, an inorganic acid, e.g. phosphoric acid, or a bleaching agent, e.g. hypochlorite, for example, sodium hypochlorite.

[0037] The remineralising agent may be applied in a variety of forms, for example, in the form of a gel or mousse. For use in the treatment of tooth other oral applications known *per se* may be used.

[0038] Pre-conditioning is preferably carried out not more than one minute before the application of the remineralising agent. More preferably, the remineralising agent is applied almost contemporaneously, i.e. within seconds, of the preconditioning.

[0039] A preferred treatment sequence involves repeated conditioning followed by remineralising, particularly in a case where the remineralising agent includes material, such as protein, which is removed in a subsequent conditioning step.

[0040] The present invention further provides a method of cosmetic treatment of tissue by application to the tissue of a remineralising agent whilst separately, sequentially or simultaneously applying iontophoresis.

[0041] The present invention provides improved remineralisation of tissue. However, conventional methods of remineralisation of tooth generally comprise remineralisation of the surface tissue, i.e. remineralisation of enamel. It is a particular advantage of the present invention that the method and/or use provide for remineralisation of dentine. Dentine is the term for a hard substance which is related to bone and forms the core of the tooth in mammals and man. Dentine consists to the extent of approximately 30% of a cell-free organic base substance, in particular glycoproteins in which collagen fibres are incorporated. The inorganic constituents are predominantly hydroxyapatite, fluoroapatite and small amounts of carbonates, magnesium and trace elements.

[0042] The present invention further provides a kit for use in iontophoretic remineralising treatment of tissue comprising a pre-conditioning agent and a remineralising agent. The remineralising agent may comprise a source of calcium and phosphate ions such as defined herein.

[0043] Preferably, the pre-conditioning agent and the remineralising agent are present in the kit in a suitable form for application, for instance, a liquid or a gel form.

[0044] The kit may also provide an applicator for applying the, or each, agent to the site of treatment.

[0045] The EAER pre-treatment and iontophoresis remineralisation treatment procedure is implemented with the aid of a kit comprising several or all of the following: (1) the EAER remineralisation smart applicator pen; (2) battery pack and/or optional mains supply/recharger; (3) a set of disposable pre-treatment electrode pads which attach to the electrode of the EAER pen; (4) bottle of hypochlorite pre-treatment hydrogel, paste or liquid; (5) a bottle of peroxide pre-treatment hydrogel, paste or liquid; (6) a set of disposable EAER remineralisation electrode pads which attach to the electrode of the EAER pen; (7) one or more bottles of hydrogel, paste or liquid containing the remineralisation agents specified above including: CPP-ACP, CPP-ACPF, etc; (8) all necessary wiring to complete the iontophoresis circuit, including a wrist-attached or mouth-attached counter electrode; (9) full instructions. The gels complete the electrical path between the electrode pad and the tooth. Further optional add-on kits would supply dental trays, strips or holders or extension applicators.

[0046] The pre-treatment electrode pads (3) and rem-

ineralisation electrode pads (6) provide a disposable barrier between the EAER pen electrode and the gel for cross-infection control purposes, and also provide a support for the hydrogel. Alternatively, the pads could be washable and sterilisable. They would preferably be composed of electrically conductive material such as carbon-filled polymer or graphite felt, or high surface area silver/silver chloride electrodes. Alternatively, they may be thin, non-conductive, open, porous sponge-like materials such as silicone or dried hydrogel which allow the applied hydrogel, paste or liquid to permeate throughout the material, providing an ionically conductive path to the underlying EAER pen electrode. In another embodiment the hydrogels may be applied directly to the EAER pen electrode without the use of an intervening electrode pad (3) or (6).

[0047] To increase shelf-life, the pre-treatment gels or pastes (4) and (5) would preferably use an inorganic-based hydrogel or paste, such as inorganic gel formers tricalcium silicate, dicalcium silicate, and sodium silicate, or a non-reactive organic hydrogel such as polyvinyl acetate, polyvinyl butyral, polyvinyl alcohols, hydroxymethyl cellulose, konjac, p-HEMA (polyhydroxyethylmethacrylate) and polyoxypropylene-polyoxyethylene. Alternatively, the pre-treatment gel would be prepared immediately before application by mixing the dried or partially-dried hydrogel with the water-based pre-treatment agent. The remineralisation gels or pastes (7) may be based on organic hydrogels or pastes. The hydrogel should be non-toxic, non-irritant and easily mouldable to the tooth contour. Examples of such hydrogels are the non-reactive hydrogels mentioned above. These viscous gels would have viscosities on the order of 100,000 to 1,000,000 cp. Solutions or preparations with lower viscosities, such as aqueous solutions and glycerin-based compositions can also be used. Generally, neutral pH gels are advantageous; however, the pH is preferably optimized to allow the ionized form of the pre-treatment or remineralization agent to exist at a sufficient concentration.

[0048] The Tooth-whitening (TW) and pre-treatment procedure is implemented with a similar kit, comprising of the above parts with the addition of: various tooth whitening agents in the form of a gel, paste or liquid substituted for, or used in addition to, the remineralisation agent (7). In addition, the EAER pen supplied would be modified with the TW (Tooth Whitening) voltage modulation programme memory card and/or processor. The gels or pastes would be organic-based as outlined above.

[0049] Throughout the description and claims of this specification, the singular encompasses the plural unless the context otherwise requires. In particular, where the indefinite article is used, the specification is to be understood as contemplating plurality as well as singularity, unless the context requires otherwise.

[0050] Features, integers, characteristics, compounds, chemical moieties or groups described in conjunction with a particular aspect, embodiment or example of the invention are to be understood to be applicable to any other aspect, embodiment or example described herein unless incompatible therewith.

[0051] Throughout the description and claims of this specification, the words "comprise" and "contain" and variations of the words, for example "comprising" and "comprises", mean "including but not limited to", and are not intended to (and do not) exclude other moieties, additives, components, integers or steps.

[0052] The invention will now be described by way of examples only and with reference to the accompanying figures:

Figure 1 is a graph showing the effect of pre-conditioning on iontophoretic treatment of a tooth. This figure shows current-time responses of a tooth obtained using a saline pad to complete the circuit between the working and reference of the counter-electrodes;

Figure 2 shows a comparison of two lesions in one tooth before and after treatment using CPP-AVP as the remineralising agent;

Figure 3 shows (a) an incisor tooth before any treatment, (b) after pre-conditioning and (c) after the iontophoresis-remineralising method has been applied.

Examples

Example 1

[0053] In this experiment the current-time responses of an extracted tooth after the application of -1 V at the working electrode were recorded. One electrode (the shorted reference/counter electrode) was a 0.5 mm stainless steel wire inserted into the tooth root. The other electrode (the working electrode) was a Pt sheet electrode of area *ca* 0.25 cm^2 held in contact with a saline-soaked tissue pad, which in turn was held in contact with the tooth surface close to the enamel lesion.

[0054] Figure 1 shows the saline response (upper dotted line) measured after the tooth was previously held in contact with a hypochlorite-soaked pad for 3 mins. The initial current after this topical hypochlorite pre-treatment was 18 μA, over 20% higher than that of the tooth before pre-treatment, and the extended-time current was similar. The lower, solid trace shows the saline tooth response for the same tooth measured after being held in contact with a hypochlorite pad under electrically-assisted (EA) pre-treatment for 3 mins at -1 V applied at the working electrode. The initial current is similar, but the extended-time current is over five times larger (i.e. the current is more negative, being lower down the negative current scale) after EA hypochlorite pre-treatment.

Example 2

[0055] Figure 2 shows a comparison of two lesions in one tooth before and after treatment using CPP-ACP (Tooth Mousse) as the remineralising agent. Analysis of the mean mineral density of the lesions resulted in Demineralisation Parameters of 0.76 (left side) and 0.83 (right side) prior to treatment and 0.92 (left) and 0.83 (right) after treatment. This Demineralisation Parameter was derived by a comparison of average grey-scale levels within the Micro-CT image of: a) the lesion and b) the healthy tissue.

[0056] This in vitro demonstration indicates that, applying a current at a level safe and not perceived by patients at a fixed voltage to a pre-conditioned natural caries lesion, in combination with CPP-ACP in the form of Tooth Mousse resulted in significant (approximately 67%) remineralisation of the lesion (as measured by Image Analysis of Micro-CT images of the tooth before and after treatment) after 3 hours electrophoresis/iontophoresis application. The passive application of the agent Tooth Mousse-Plus (also known as MI paste) to the other natural caries lesion on the same tooth for 3 hours resulted in minimal remineralisation (measured on Micro-CT images).

[0057] The comparison in Figure 2 is of two lesions in one tooth before and after treatment. The images represent an approximately 10 micron thickness horizontal Micro-CT (XCT slice) through the same path of the tooth with separate mesial and distal lesions. The XCT image on the left shows the lesions prior to any treatment. The image on the right shows the lesions after the lesions were pre-treated to remove protein and lipids. The lesion on the left was treated with CPP-ACP and iontophoresis for three hours, whilst the lesion on the right was treated only with CPP-ACP plus Fluoride (MI paste) for three hours.

Example 3

[0058] Figure 3 shows an incisor tooth before any treatment, after pre-conditioning and after the iontophoresis-remineralising method has been applied.

[0059] The uppermost image shows an extracted incisor tooth which exhibits both a large carious cavity (caused by tooth decay), which is significantly discoloured, and areas of dark discolouration on the labial (flat) facing surface of the crown of the tooth, adjacent to the carious cavity in the direction of the incisal (lower) edge of the tooth. This image was taken prior to any treatment being carried out.

[0060] The middle image shows the same tooth after 2 minutes of pre-conditioning with sodium hypochlorite solution. There is very little difference between the uppermost and middle images in terms of tooth discolouration.

[0061] The lowermost image shows the tooth after the iontophoresis-remineralisation has been carried out using Tooth Mousse (CPP-ACP) as the re-mineralising agent for 1 hour. It is clear that the cavity has now lost its dark discolouration completely. The dark discolourations in the enamel of the crown of the tooth adjacent to the cavity have also disappeared. There is some increased whitening of the edges of the carious cavity at both the upper and lower margins of the cavity.

[0062] These images demonstrate the tooth-whitening effect of the iontophoresis-remineralising method.

Claims

1. A remineralising agent for use in a method for the treatment of dental caries and/or dental fluorosis in a mammal, wherein the remineralising agent is applied by iontophoretic remineralising treatment of tissue which has been subject to pre-conditioning to remove protein and lipids, the remineralising agent being a source of phosphate and/or calcium wherein the pre-conditioning step comprises treatment with preconditioning agents to remove proteins and lipids wherein one of the preconditioning agents is an acid.

2. A remineralising agent for use in preventional treatment of tooth erosion, wherein the remineralising agent is applied by iontophoretic remineralising treatment of tissue which has been subject to pre-conditioning to remove protein and lipids, the remineralising agent being a source of phosphate and/or calcium wherein the pre-conditioning step comprises treatment with preconditioning agents to remove proteins and lipids wherein one of the preconditioning agents is an acid.

3. An agent for use according to any of the preceding claims, wherein the remineralising agent is a source of phosphate, calcium and water.

4. An agent for use according to any of the preceding claims, comprising casein phosphopeptide - amorphous calcium phosphate (CPP-ACP).

5. An agent for use according to any of the preceding claims, containing or comprising fluoride, preferably wherein the remineralising agent is casein phosphopeptide - amorphous calcium fluoride phosphate (CPP-ACFP).

6. An agent for use according to any of the preceding claims, including one or more remineralisation enhancers, preferably wherein the remineralising agent includes at least two remineralisation enhancers wherein one of the enhancers is a source of calcium ions and the other is a source of phosphate ions.

7. An agent for use according to claim 6, having an

associated ratio of calcium:phosphate between 1 :1 and 22:10; preferably between about 3:2 and 22:10; more preferably about 10:6.

8. An agent for use according to Claim 6, wherein the remineralisation enhancer is strontium.

9. An agent for use according to any of the preceding claims, wherein the preconditioning step is performed, with or without the application of iontophoresis, prior to application of the remineralising agent/iontophoresis.

10. An agent for use according to any of the preceding claims, wherein the preconditioning step comprises treatment with phosphoric acid.

11. An agent for use according to any of Claims 1 to 9, wherein the protein removing agent comprises a hypochlorite.

12. A kit for use in iontophoretic remineralising treatment of dental tissue comprising a preconditioning agent including an acid, a protein removing agent and a lipid removing agent and a remineralising agent being a source of phosphate and/or calcium.

Patentansprüche

1. Remineralisierungsagens zur Anwendung in einem Verfahren für die Behandlung von Zahnkaries und/oder Zahnfluorose in einem Säugetier, wobei das Remineralisierungsagens mittels iontophoretische Remineralisierungsbehandlung von Gewebe angewendet wird, welches einer Vorbehandlung unterlegen ist, um Proteine und Lipide zu entfernen, das Remineralisierungsagens ist eine Quelle von Phosphat und/oder Calcium, wobei der Vorbehandlungsschritt eine Behandlung mit Vorbehandlungsagenzien aufweist, um Proteine und Lipide zu entfernen, wobei eines der Vorbehandlungsagenzien eine Säure ist.

2. Remineralisierungsagens zur Anwendung in Präventivbehandlung von Zahnerosion, wobei das Remineralisierungsagens mittels iontophoretische Remineralisierungsbehandlung von Gewebe angewendet wird, welches einer Vorbehandlung unterlegen ist, um Proteine und Lipide zu entfernen, das Remineralisierungsagens ist eine Quelle von Phosphat und/oder Calcium, wobei der Vorbehandlungsschritt eine Behandlung mit Vorbehandlungsagenzien aufweist, um Proteine und Lipide zu entfernen, wobei eines der Vorbehandlungsagenzien eine Säure ist.

3. Agens zur Anwendung gemäß einem der vorangehenden Ansprüche, wobei das Remineralisierungsagens eine Quelle von Phosphat, Calcium und Wasser ist.

4. Agens zur Anwendung gemäß einem der vorangehenden Ansprüche, aufweisend Caseinphosphopeptid - amorphes Calciumphosphat (CPP-ACP).

5. Agens zur Anwendung gemäß einem der vorangehenden Ansprüche, beinhaltend oder aufweisend Fluorid, wobei das Remineralisierungsagens bevorzugt Caseinphosphopeptid - amorphes Calciumfluoridphosphat (CPP-ACFP) ist.

6. Agens zur Anwendung gemäß einem der vorangehenden Ansprüche, enthaltend einen oder mehrere Remineralisierungsverstärker, bevorzugt wobei das Remineralisierungsagens zumindest zwei Remineralisierungsverstärker enthält, wobei einer der Verstärker eine Quelle von Calciumionen ist und der andere eine Quelle von Phosphationen ist.

7. Agens zur Anwendung gemäß Anspruch 6, das ein dazugehöriges Verhältnis von Calcium:Phosphat zwischen 1:1 und 22:10; vorzugsweise zwischen ungefähr 3:2 und 22:10; mehr bevorzugt ungefähr 10:6 hat.

8. Agens zur Anwendung gemäß Anspruch 6, wobei der Remineralisierungsverstärker Strontium ist.

9. Agens zur Anwendung gemäß einem der vorangehenden Ansprüche, wobei der Vorbehandlungsschritt durchgeführt wird, mit oder ohne der Anwendung von Iontophorese, vor Anwendung des Remineralisierungsagens / der Iontophorese.

10. Agens zur Anwendung gemäß einem der vorangehenden Ansprüche, wobei der Vorbehandlungsschritt Behandlung mit phosphoriger Säure aufweist.

11. Agens zur Anwendung gemäß einem der Ansprüche 1 bis 9, wobei das Proteinentfernungsagens ein Hypochlorid aufweist.

12. Kit zur Anwendung in einer iontophoretischen Remineralisierungsbehandlung von Zahngewebe, aufweisend ein Vorbehandlungsagens enthaltend eine Säure, ein Proteinentfernungsagens und ein Lipidentfernungsagens und ein Remineralisierungsagens, das eine Quelle von Phosphat und/oder Calcium ist.

Revendications

1. Un agent de reminéralisation destiné à être utilisé dans un procédé de traitement de caries dentaires

et / ou de fluorose dentaire chez un mammifère, l'agent de reminéralisation étant appliqué par un traitement de reminéralisation iontophorétique d'un tissu qui a été soumis à un conditionnement préalable pour éliminer les protéines et les lipides, l'agent de reminéralisation étant une source de phosphate et / ou de calcium, l'étape de conditionnement préalable comprenant un traitement avec des agents de conditionnement préalable pour éliminer les protéines et les lipides, l'un des agents de conditionnement préalable étant un acide.

2. Un agent de reminéralisation destiné à être utilisé dans le traitement préventif de l'érosion dentaire, l'agent de reminéralisation étant appliqué par un traitement de reminéralisation iontophorétique d'un tissu qui a été soumis à un conditionnement préalable pour éliminer les protéines et les lipides, l'agent de reminéralisation étant une source de phosphate et / ou du calcium, l'étape de conditionnement préalable comprenant un traitement avec des agents de conditionnement préalable pour éliminer les protéines et les lipides, l'un des agents de conditionnement préalable étant un acide.

3. Un agent pour une utilisation selon l'une quelconque des revendications précédentes, dans lequel l'agent de reminéralisation est une source de phosphate, de calcium et d'eau.

4. Un agent pour une utilisation selon l'une quelconque des revendications précédentes, comprenant du phosphopeptide de caséine - phosphate de calcium amorphe (CPP-ACP).

5. Un agent pour une utilisation selon l'une quelconque des revendications précédentes, contenant ou comprenant du fluorure, l'agent de reminéralisation étant de préférence du phosphopeptide de caséine - phosphate de fluorure de calcium amorphe (CPP-ACFP).

6. Un agent pour une utilisation selon l'une quelconque des revendications précédentes, comprenant un ou plusieurs activateurs de reminéralisation, l'agent de reminéralisation comprenant de préférence au moins deux activateurs de reminéralisation, l'un des activateurs étant une source d'ions calcium et l'autre étant une source d'ions phosphate.

7. Un agent pour une utilisation selon la revendication 6, ayant un rapport associé de calcium:phosphate compris entre 1:1 et 22:10; de préférence compris entre environ 3:2 et 22:10; de façon encore préférée d'environ 10:6.

8. Un agent pour une utilisation selon la revendication 6, dans lequel l'agent de reminéralisation est du strontium.

9. Un agent pour une utilisation selon l'une quelconque des revendications précédentes, dans lequel l'étape de conditionnement préalable est mise en oeuvre, avec ou sans application d'iontophorèse, avant l'application de l'agent de reminéralisation / de l'iontophorèse.

10. Un agent pour une utilisation selon l'une quelconque des revendications précédentes, dans lequel l'étape de conditionnement préalable comprend un traitement avec de l'acide phosphorique.

11. Un agent pour une utilisation selon l'une quelconque des revendications 1 à 9, dans lequel l'agent d'élimination des protéines comprend un hypochlorite.

12. Un kit pour une utilisation dans le traitement de reminéralisation iontophorétique d'un tissu dentaire comprenant un agent de conditionnement préalable incluant un acide, un agent d'élimination des protéines et un agent d'élimination des lipides et un agent de reminéralisation qui est une source de phosphate et / ou de calcium.

Figure 1

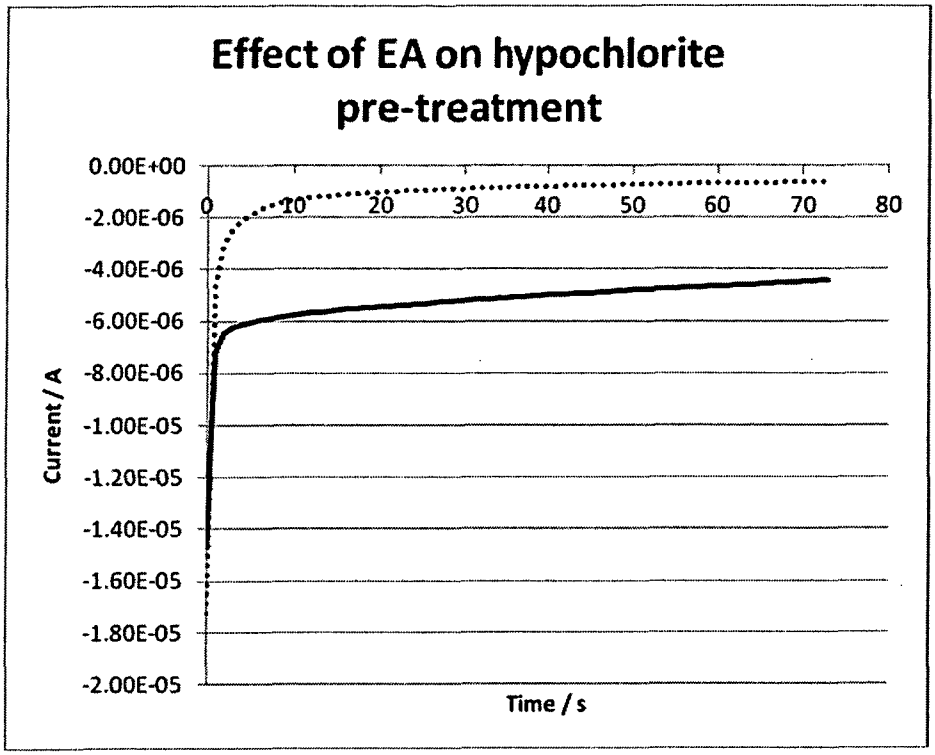

Effect of EA on hypochlorite pre-treatment
0.00E+00
-2.00E-06
-4.00E-06
-6.00E-06
-8.00E-06
-1.00E-05
-1.20E-05
-1.40E-05
-1.60E-05
-1.80E-05
-2.00E-05
Current / A
0
10
20
30
40
50
60
70
80
Time / s

Figure 2

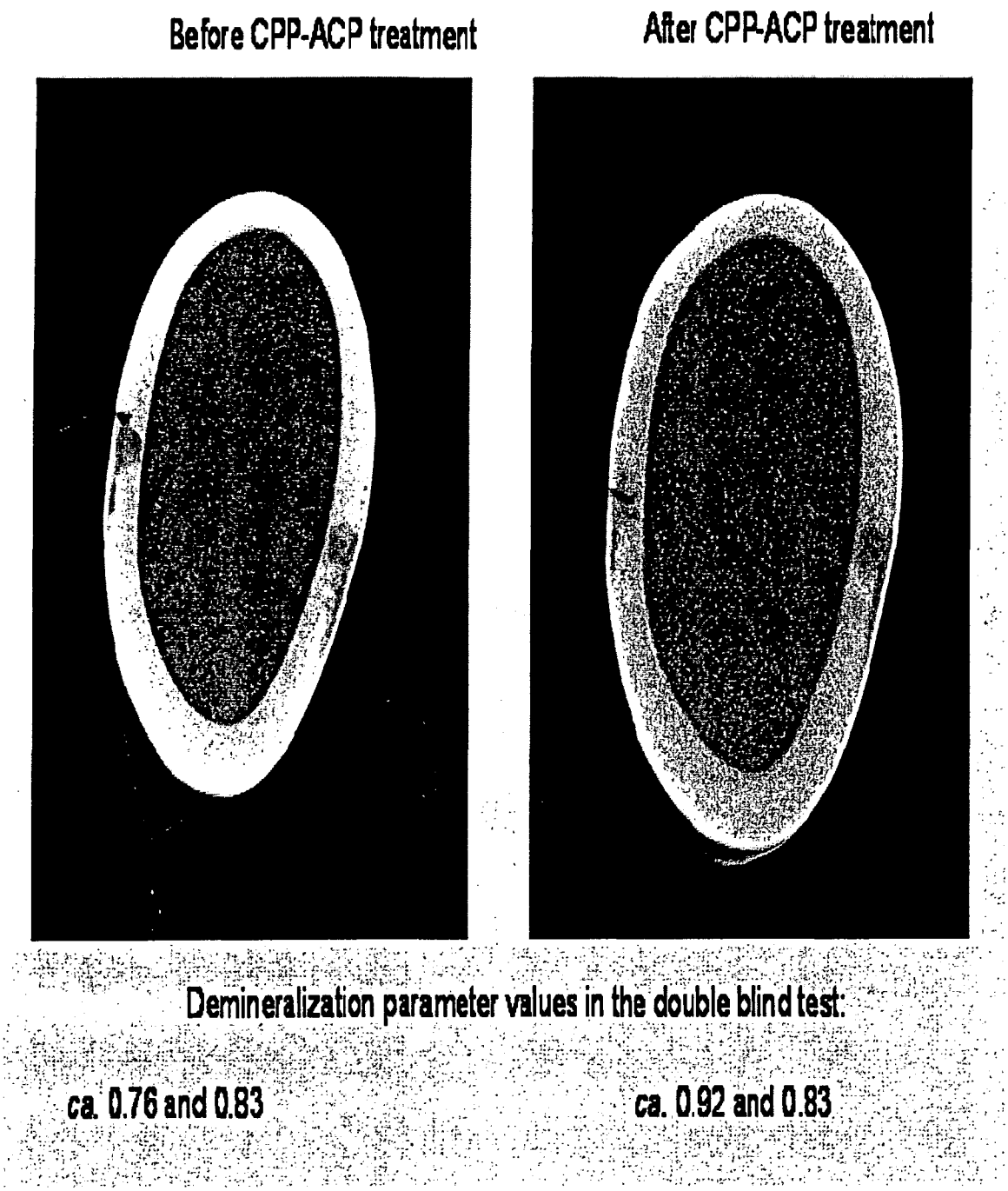
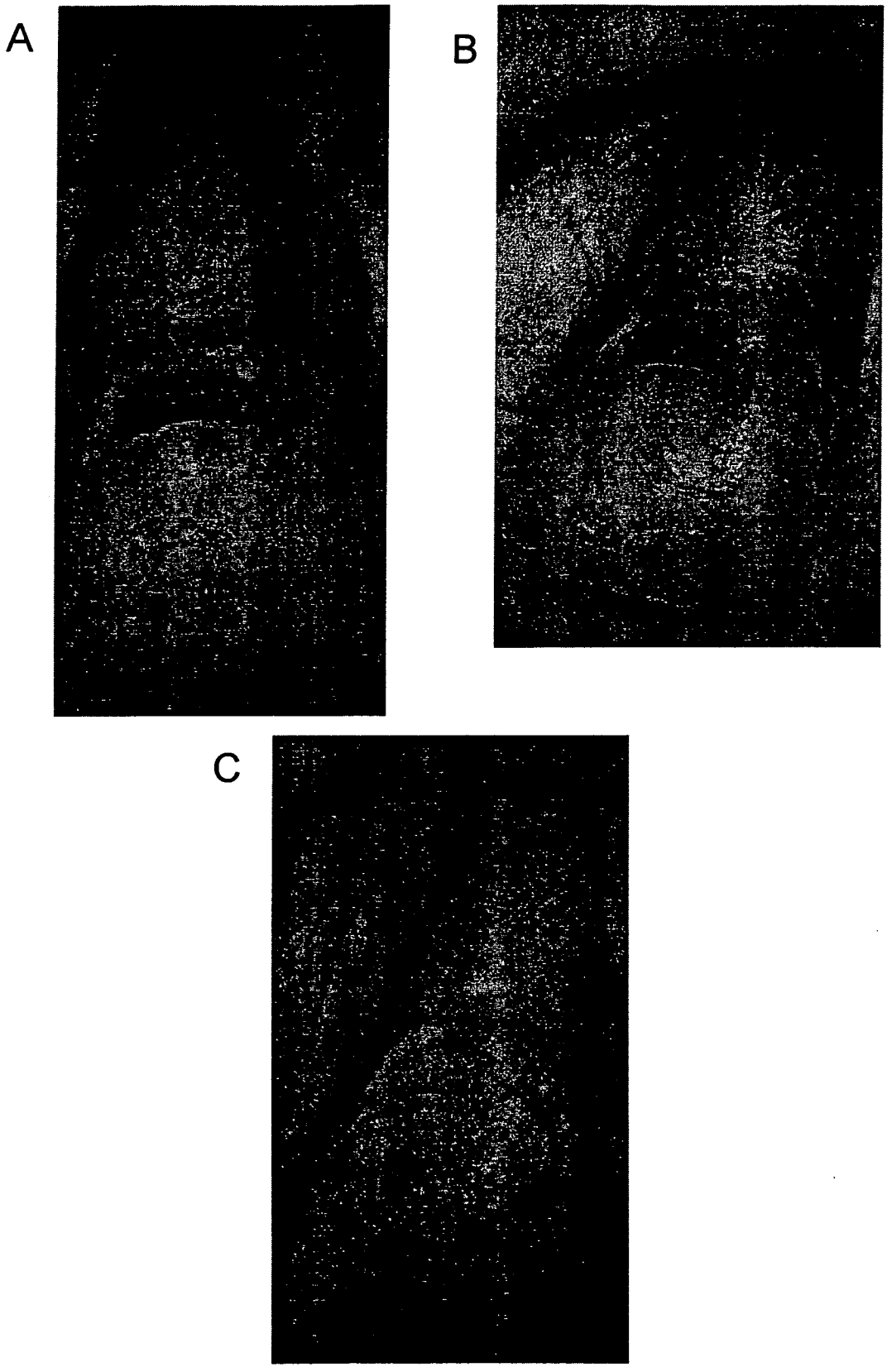

Before CPP-ACP treatment
After CPP-ACP treatment
Demineralization parameter values in the double blind test:
ca. 0.76 and 0.83
ca. 0.92 and 0.83

Figure 3



REFERENCES CITED IN THE DESCRIPTION

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- GB 1219632 A **[0009]**

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EP 2 273 964

Meszes szövet remineralizációja

Szabadalmi igénypontok

1. Remineralizáló hatóanyag fogszuvasodás és/vagy fogfluorózis kezelésére irányuló eljárásban történő alkalmazásra említésben, ahol a remineralizáló hatóanyagot iontoforézises reminarlizáló kezeléssel visszük fel a szövetre, amely előzetesen a protein és lipidek eltávolítása céljából előkondicionálásnak lett alávetve, amely remineralizáló hatóanyag egy foszfát- és/vagy kalciumforrás, ahol az előkondicionálási lépés a proteinek és lipidek eltávolítása érdekében előkondicionáló hatóanyagokkal végzett kezelést foglal magában, ahol az előkondicionáló hatóanyagok egyike egy sav.

2. Remineralizáló hatóanyag fogerózió megelőzési célú kezelésére történő alkalmazásra, ahol a remineralizáló hatóanyagot iontoforézises remineralizáló kezeléssel visszük fel a szövetre, amely előzetesen a protein és lipidek eltávolítása céljából előkondicionálásnak lett alávetve, amely remineralizáló hatóanyag egy foszfát- és/vagy kalciumforrás, ahol az előkondicionálási lépés a proteinek és lipidek eltávolítása érdekében előkondicionáló hatóanyagokkal végzett kezelést foglal magában, ahol az előkondicionáló hatóanyagok egyike egy sav.

3. Az előző igénypontok bármelyike szerinti hatóanyag az igényelt alkalmazásra, ahol a remineralizáló hatóanyag egy foszfát-, kalcium- és vízforrás.

4. Az előző igénypontok bármelyike szerinti hatóanyag az igényelt alkalmazásra, amely kazein-foszfopeptid – amorf kalcium-foszfátot (CPP-ACP) tartalmaz.

5. Az előző igénypontok bármelyike szerinti hatóanyag az igényelt alkalmazásra, amely fluoridot tartalmaz vagy foglal magában, előnyösen ahol a remineralizáló hatóanyag kazein-foszfopeptid – amorf kalcium-fluorid-foszfátot (CPP-ACFP).

6. Az előző igénypontok bármelyike szerinti hatóanyag az igényelt alkalmazásra, amely magában foglal egy vagy több remineralizációt serkentő anyagot, előnyösen ahol a remineralizáló hatóanyag magában foglal legalább két remineralizációt serkentő anyagot, ahol a serkentő anyagok egyike kalciumion-forrás, és a másik foszfátion-forrás.

7. A 6. igénypont szerinti hatóanyag az igényelt alkalmazásra, amelynek asszociált kalcium:foszfát aránya 1:1 és 22:10 közötti, előnyösen körülbelül 3:2 és 22:10 közötti, még előnyösebben körülbelül 10:6.

8. A 6. igénypont szerinti hatóanyag az igényelt alkalmazásra, ahol a remineralizációt serkentő anyag stroncium.

9. Az előző igénypontok bármelyike szerinti hatóanyag az igényelt alkalmazásra, ahol az előkondicionáló lépést, iontoforézis alkalmazásával vagy anélkül, a remineralizáló hatóanyag/iontoforézis alkalmazását megelőzően hajtjuk végre.

10. Az előző igénypontok bármelyike szerinti hatóanyag az igényelt alkalmazásra, ahol az előkondicionáló lépés foszforsavval végzett kezelést foglal magában.

11. Az 1-9. igénypontok bármelyike szerinti hatóanyag az igényelt alkalmazásra, ahol a protein-eltávolító anyag hipokloritot tartalmaz.

12. Készlet fogszövet iontoforézises remineralizáló kezelésére történő alkalmazáshoz, amely készlet tartalmaz egy előkondicionáló anyagot, beleértve egy savat, egy protein-eltávolító anyagot és egy lipid-eltávolító anyagot, valamint egy remineralizáló hatóanyagot, amely egy foszfát- és/vagy kalcium-forrás.