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(54) **Title**: COMPOSITION AND METHOD FOR IRRIGATION OF A PREPARED DENTAL ROOT CANAL

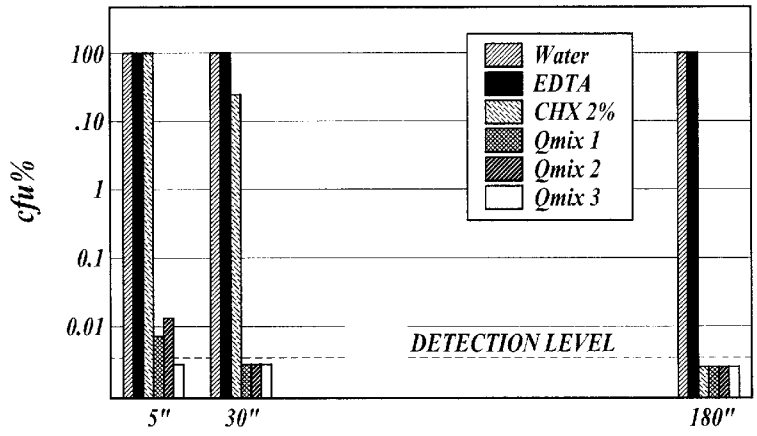

Fig. 5.

(57) **Abstract**: Composition and method for irrigating a prepared dental root canal. The composition is an aqueous composition of ethylenediamine tetraacetic acid, chlorhexidine or orally acceptable addition salt, and N-cetyl-N,N,N-trimethylammonium bromide, and is effective for simultaneous smear layer removal and disinfection.

COMPOSITION AND METHOD FOR IRRIGATION OF A PREPARED DENTAL ROOT CANAL

FIELD OF THE INVENTION

The present invention provides a composition and method for irrigating prepared tooth surfaces. The composition and method remove buildup of undesirable debris formed during the preparation of tooth surfaces during dental procedures and further disinfect the tooth surface. The irrigation composition is an aqueous composition that includes ethylenediamine tetraacetic acid (EDTA), chlorhexidine, and cetrimide.

BACKGROUND OF THE INVENTION

While various chemical and physical irritants can cause irritation and even necrosis of the pulp, the most common causes for pulpal inflammation (pulpitis) are bacteria and/or their products entering the pulp through a deep caries lesion or a leaking filling; an inflammatory reaction in the pulp starts long before bacteria invade the pulp tissue. The inflammatory reaction is first initiated by bacterial antigens interacting with the local immune system. As long as the carious lesion has not entered the pulp, the pulpal inflammation is likely to be reversible. However, when the carious lesion does reach the pulp and the hard tissue barrier is breached, bacteria can invade the pulp. Even after this point, the infection may remain relatively superficial and most of the pulp tissue is vital and bacteria free. For this reason, endodontic treatment of pulpitis should be considered to be treatment of an inflammation and prevention of an infection.

In apical periodontitis, bacteria invade further and colonize the entire root canal system. Apical periodontitis is an inflammatory process in the periradicular tissues caused by microorganisms in the necrotic root canal. Accordingly, to promote healing of apical periodontitis, microorganisms within the root canal system must be eliminated.

Apical periodontitis (AP) is caused by microbes, usually bacteria, residing in the necrotic root canal system of the affected tooth. Although healing of the periapical lesion in some rare cases might be prevented by nonmicrobial factors, microbes are always the etiologic factor in apical periodontitis. The microbes present in the necrotic root canal originate from the oral cavity. However, ecology in the root canal environment is the main factor in the selection of the composition of the infective microflora. As a result of the ecologic pressure, primary apical periodontitis (no previous endodontic treatment) is dominated by anaerobic bacteria, with only a few or no facultative or aerobic species per

canal. Endodontic treatment, even when unsuccessful, dramatically changes the ecology in the root canal; availability of oxygen and nutrients is different, and in many cases substances with antimicrobial activity are introduced into the root canal, which might further contribute toward a more resistant, facultative microflora. Post-treatment endodontic infections are therefore dominated by ecologically tolerant bacteria and sometimes also by yeasts, which are characterized by higher resistance to treatment procedures and disinfecting agents than the anaerobic microflora in cases of primary apical periodontitis.

On the basis of our knowledge of the etiology of apical periodontitis, there is a strong consensus that elimination of the microbes in the root canal system is the main immediate goal of the treatment to obtain complete healing of the lesion. There is mounting evidence, however, that obtaining sterility of the infected root canal by presently available treatment methods might be more difficult than once thought.

Locally used endodontic disinfectants, either irrigating solutions or interappointment medicaments, are effective against a wide spectrum of microorganisms. They affect a range of vital functions of the microbial cell, resulting rapidly in cell death. Hypochloric acid interferes with oxidative phosphorylation and other membrane-associated functions of the cell as well as DNA synthesis inside the cell. Hypochlorite is effective against bacteria and yeast; even bacterial spores are killed with high concentration (5%) sodium hypochlorite.

Chlorhexidine (CHX) penetrates the outer cell wall layers of the microbes and attacks the inner membrane, cytoplasmic membrane in bacteria and plasma membrane in yeast cells. In high concentrations CHX has the ability to coagulate intracellular constituents of the microbial cells. The antiviral effect of CHX has also been reported.

The exact mechanism of action of iodine compounds is not fully understood, but these compounds also penetrate into the microorganisms and interact with key molecules of the cells (proteins, fatty acids, and nucleotides). Iodine compounds kill their target cells rapidly, and they are active against bacteria (including spores), fungi, and viruses.

Calcium hydroxide has a high pH, which is the main reason for its antibacterial activity. It has been suggested that the hydroxyl ions denature proteins of the cytoplasmic membrane of bacteria, thus killing the cell. It has been shown with *Enterococcus hirae* that the tolerance to alkaline pH was dependent on a proton antiport system; mutant cells lacking the proton transport system showed highly increased sensitivity to alkali. This

was later also confirmed with a strain of *E. faecalis*. The susceptibility to high pH of enterococci and oral yeasts has been compared and found that yeasts were equally or more resistant to high pH by calcium hydroxide than *E. faecalis*. It is likely that tolerance of high pH by oral yeasts is also dependent on a proton pump in the plasma membrane of the yeast cells. Nevertheless, in a saturated calcium hydroxide solution ($pH \geq 12.5$) in vitro enterococci were killed within 20 minutes and yeasts within 6 hours.

A mixture of tetracycline isomer (doxycycline), acid, and detergent (MTAD) is a new member in the group of antibacterial root canal irrigants. MTAD contains bacteriostatic antibiotic (doxycycline) in high concentration, which might alter its antibacterial effect to bactericidal, although this has not been directly shown. Other components of MTAD include citric acid and TWEEN 80, which together with doxycycline might have a synergistic effect on the bacterial cell wall and the cytoplasmic membrane.

Despite the advances in the development of root canal irrigation compositions noted above, there exists a need for effective and easy to use compositions for root canal irrigation. The present invention fulfills this need and provides further related advantages.

SUMMARY OF THE INVENTION

The present invention provides a composition and method for irrigating a prepared dental root canal. The composition is a stable aqueous solution of ethylenediamine tetraacetic acid, chlorhexidine or orally acceptable addition salt, and N-cetyl-N,N,N-trimethylammonium bromide, and is effective for simultaneous smear layer removal and disinfection.

In one aspect of the invention, an irrigation composition is provided. In one embodiment, the composition includes ethylenediamine tetraacetic acid, chlorhexidine or orally acceptable addition salt, N-cetyl-N,N,N-trimethylammonium bromide, and water.

In one embodiment, ethylenediamine tetraacetic acid is present in an amount from about 0.5 to about 20 percent by weight of the composition.

In one embodiment, chlorhexidine or orally acceptable addition salt is present in an amount from about 0.01 to about 5.0 percent by weight of the composition.

In one embodiment, N-cetyl-N,N,N-trimethylammonium bromide is present in an amount from about 0.001 to about 3.0 percent by weight of the composition.

In one embodiment, the composition includes ethylenediamine tetraacetic acid in an amount from about 1 to about 17 percent by weight of the composition, chlorhexidine

or orally acceptable addition salt in an amount from about 0.1 to about 0.5 percent by weight of the composition, and N-cetyl-N,N,N-trimethylammonium bromide in an amount from about 0.1 to about 0.5 percent by weight of the composition.

In another aspect, the invention provides a method for making a chlorhexidine-containing composition. In one embodiment, the method includes combining chlorhexidine or orally acceptable addition salt and N-cetyl-N,N,N-trimethylammonium bromide in water to provide chlorhexidine-containing aqueous solution; and adding ethylenediamine tetraacetic acid to the chlorhexidine-containing aqueous solution to provide a chlorhexidine-containing composition.

In a further aspect, the invention provides a method for removing smear layer and disinfecting in a root canal. In one embodiment, the method includes irrigating the root canal with a composition that includes ethylenediamine tetraacetic acid, chlorhexidine or orally acceptable addition salt, N-cetyl-N,N,N-trimethylammonium bromide; and water.

DESCRIPTION OF THE DRAWINGS

The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same become better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

FIGURE 1 is a scanning electron microscope image of a tooth surface (control) in which a smear layer was removed by treatment with 5 percent aqueous sodium hypochlorite (5% NaOCl) for 5 minutes followed by treatment with 17 percent aqueous ethylenediamine tetraacetic acid (17% EDTA, disodium, pH 7) for 4 minutes, open dentinal canals are clearly observable;

FIGURE 2 is a scanning electron microscope image of a tooth surface treated with a representative composition of the invention (Qmix 1); smear layer was removed by treatment with 5% NaOCl for 5 minutes followed by treatment with a representative composition of the invention (13.6 percent by weight EDTA, 0.1 percent by weight chlorhexidine, and 0.1 percent by weight cetrimide in distilled water) for 1 minute, open dentinal canals are clearly observable;

FIGURE 3 is a scanning electron microscope image of a tooth surface treated with a representative composition of the invention (Qmix 2); smear layer was removed by treatment with 5% NaOCl for 5 minutes followed by treatment with a representative composition of the invention (5.6 percent by weight EDTA, 0.1 percent by weight

chlorhexidine, and 0.1 percent by weight cetrimide in distilled water) for 2 minutes, open dentinal canals are clearly observable;

FIGURE 4 is a scanning electron microscope image of a tooth surface treated with a representative composition of the invention (Qmix 3); smear layer was removed by treatment with 5% NaOCl for 5 minutes followed by treatment with a representative composition of the invention (1.0 percent by weight EDTA, 0.1 percent by weight chlorhexidine, and 0.1 percent by weight cetrimide in distilled water) for 5 minutes, open dentinal canals are clearly observable; and

FIGURE 5 is a graph comparing the survival of *Enterococcus faecalis* A197A (colony forming units percent, cfu%) after exposure to water, 17% EDTA, chlorhexidine (2 percent by weight in water, CHX 2%, and three representative compositions of the invention (Qmix 1, Qmix 2, and Qmix 3); exposure times were 5 seconds, 30 seconds, and 3 minutes; detection level is at 99.995% killing; survival in water and EDTA was 100% for all exposure times.

DETAILED DESCRIPTION OF THE INVENTION

In one aspect, the invention provides a composition useful for irrigating prepared tooth surfaces. The action of the composition is two-fold. The composition effectively removes buildup of undesirable debris (smear layer) formed during the preparation of tooth surfaces during dental procedures. The composition further disinfects the tooth surface.

The term "smear layer" is known to those of skill in the art of dentistry and refers to the complex accumulation of organic and inorganic debris resulting from the mechanical preparation of a tooth surface. The smear layer includes cutting debris, tooth particles, microorganisms, necrotic material, and other substances resulting form preparation, and can include a superficial layer on the surface of a prepared tooth along with a layer or layers that are packed into the adjacent dentinal tubules at varying depths.

The composition of the invention useful for irrigating prepared tooth surfaces is an aqueous composition that includes ethylenediamine tetraacetic acid (EDTA), chlorhexidine or orally acceptable addition salt, and N-cetyl-N,N,N-trimethylammonium bromide (cetrimide).

Smear layer removal is achieved by the composition, at least in part, by the presence of EDTA. As used herein the term "ethylenediamine tetraacetic acid" or "EDTA" refers to orally acceptable ethylenediamine tetraacetic acid salts including, for

example, ethylenediamine tetraacetic acid disodium. Ethylenediamine tetraacetic acid is present in an amount from about 0.5 to about 20 percent by weight of the composition. In one embodiment, ethylenediamine tetraacetic acid is present in an amount from about 1 to about 17 percent by weight of the composition.

As noted above, in addition effectively removing smear layer, the composition further disinfects the tooth surface. Disinfection is due at least in part to the presence of chlorhexidine or orally acceptable addition salt in the composition. As used herein, the term "chlorhexidine" refers to 1,1'-hexamethylenebis[5-(p-chlorophenyl)biguanide], a substance having a strongly basic action with only low water solubility. By reacting chlorhexidine base with acids, water-soluble salts can be obtained. As used herein, the term "chlorhexidine" refers to chlorhexidine in free base form and the term "orally acceptable addition salt" refers to chlorhexidine salts that are acceptable for use as oral irrigating compositions. Suitable orally acceptable chlorhexidine addition salts include chlorhexidine digluconate, chlorhexidine diformate, chlorhexidine diacetate, chlorhexidine dipropionate, chlorhexidine dilactate, chlorhexidine dinitrate, chlorhexidine sulfate, and chlorhexidine tartarate. Chlorhexidine or orally acceptable addition salt is present in an amount from about 0.01 to about 5 percent by weight of the composition. In one embodiment, chlorhexidine or orally acceptable addition salt is present in an amount less than 1.0 percent by weight of the composition. In one embodiment, chlorhexidine or orally acceptable addition salt is present in an amount from about 0.1 to about 0.5 percent by weight of the composition.

The irrigating composition further includes N-cetyl-N,N,N-trimethylammonium bromide (cetrimide), a microbially active quaternary ammonium bromide. N-cetyl-N,N,N-trimethylammonium bromide is present in an amount from about 0.001 to about 3 percent by weight of the composition. In one embodiment, N-cetyl-N,N,N-trimethylammonium bromide is present in an amount from about 0.1 to about 0.5 percent by weight of the composition.

In one embodiment of the composition, ethylenediamine tetraacetic acid is present in an amount from about 1 to about 17 percent by weight of the composition, chlorhexidine or orally acceptable addition salt is present in an amount from about 0.1 to about 0.5 percent by weight of the composition, and N-cetyl-N,N,N-trimethylammonium bromide is present in an amount from about 0.1 to about 0.5 percent by weight of the composition.

The present invention solves the problem associated combining a smear layer remover with a disinfectant. The present composition overcomes the problem of maintaining effective amounts of EDTA and disinfectant (chlorhexidine or orally acceptable addition salt) in solution. Previously, EDTA and chlorhexidine or orally acceptable addition salt could not be prepared having an EDTA concentration sufficient for effective smear layer removal. The present invention solves this problem and provides a ready-to-use irrigation composition that simultaneously effectively removes smear layer and disinfects. The composition of the invention has an EDTA concentration of at least 0.5 percent by weight, up to about 20 percent by weight, and a chlorhexidine or orally acceptable addition salt concentration of at least about 0.1 percent by weight, up to about 5.0 percent by weight. The present invention provides a stable chlorhexidine solution containing up to about 20 percent by weight EDTA.

The composition of the invention offers advantages over a commercially available product, BIOPURE MTAD Cleanser (Dentsply International, York, PA), an antibacterial root canal cleanser (smear layer removal and root canal disinfectant). The disinfectant in MTAD is an antibiotic, doxycycline, and does not kill *Enterococcus faecalis* nearly as rapidly as the composition of the present invention. Furthermore, unlike the ready-to-use composition of the invention, MTAD must be prepared chair side by mixing two components either during or immediately before treatment.

In another aspect, a method for making the irrigation composition is provided. In the method, the chlorhexidine-containing composition of the invention is made by combining chlorhexidine or orally acceptable addition salt and N-cetyl-N,N,N-trimethylammonium bromide in water to provide chlorhexidine-containing aqueous solution; and then adding ethylenediamine tetraacetic acid to the chlorhexidine-containing aqueous solution to provide a chlorhexidine-containing composition.

Smear layer removal from instrumented root canal surfaces is essential for effective cleaning and disinfection. Traditionally, EDTA has been used for smear layer removal. However, as noted above, chlorhexidine cannot be combined with high concentration EDTA without precipitation formation and the consequence that the mixture cannot remove the smear layer.

In the method for making the composition of the invention, chlorhexidine is first mixed with cetrimide before EDTA is added. In the method, no precipitate is formed.

Without being bound to any theory, chlorhexidine and cetrimide in water appear to form a micelle formulation that protects the combination from precipitation.

In one embodiment of the method, the ratio of N-cetyl-N,N,N-trimethylammonium bromide to chlorhexidine or orally acceptable addition salt is from about 5 to about 1. In one embodiment, the ratio of N-cetyl-N,N,N-trimethylammonium bromide to chlorhexidine or orally acceptable addition salt is from about 3 to about 1. In another embodiment, the ratio of N-cetyl-N,N,N-trimethylammonium bromide to chlorhexidine or orally acceptable addition salt is from about 1 to about 1.

In one embodiment, the chlorhexidine-containing aqueous solution has a chlorhexidine concentration of from about 1 to about 20% by weight.

In one embodiment, the ethylenediamine tetraacetic acid is added as a solid. In another embodiment, the ethylenediamine tetraacetic acid is added as a solution. In this embodiment, the ethylenediamine tetraacetic acid is added as a solution having an ethylenediamine tetraacetic acid concentration of from about 5 to about 50% by weight.

The chlorhexidine-containing composition prepared by the method is an aqueous solution that includes ethylenediamine tetraacetic acid in an amount from about 1 to about 20 percent by weight, chlorhexidine or orally acceptable addition salt in an amount from about 0.01 to about 5.0 percent by weight, and N-cetyl-N,N,N-trimethylammonium bromide in an amount from about 0.001 to about 3.0 percent by weight.

The preparation of representative compositions of the invention containing chlorhexidine, cetrimide, and EDTA (13.6, 5.6, and 1.0 percent by weight), are described in Examples 1-3. The efficacy of these compositions in smear layer removal are illustrated in FIGURES 2-4 (17% EDTA control illustrated in FIGURE 1). The antibacterial activity of the representative compositions is illustrated in FIGURE 5.

The present invention provides a method for removing a smear layer from and sterilizing endodontic excavations and other prepared tooth surfaces by irrigating with a chlorhexidine-containing composition of the invention. Thus, in a further aspect of the invention, a method for irrigating a prepared tooth surface is provided. In the method, a prepared tooth surface is irrigated with a sterile composition comprising ethylenediamine tetraacetic acid, chlorhexidine or orally acceptable addition salt, N-cetyl-N,N,N-trimethylammonium bromide, and water. In one embodiment, the prepared surface is irrigated with sodium hypochlorite prior to irrigating with the composition comprising

ethylenediamine tetraacetic acid, chlorhexidine or orally acceptable addition salt, N-cetyl-N,N,N-trimethylammonium bromide, and water.

In one embodiment, the prepared surface is irrigated with a composition that includes ethylenediamine tetraacetic acid in an amount from about 1 to about 17 percent by weight, chlorhexidine or orally acceptable addition salt in an amount from about 0.1 to about 0.5 percent by weight, and N-cetyl-N,N,N-trimethylammonium bromide in an amount from about 0.1 to about 0.5 percent by weight.

The method for irrigating is effective for a variety of prepared tooth surfaces. The surface can be a surface that is an endodontic situs, a surface that is an instrumented root canal, a surface prepared for a periodontic procedure, a surface that is prepared site for tooth restoration, or a surface prepared for tooth reconstruction.

In the method, the surface is irrigated from about 1 minute to about 1 hour. In one embodiment, the surface is irrigated from about 1 minute to about 10 minutes.

The following examples are provided for illustrating, not limiting the invention.

EXAMPLES

Example 1

The Preparation and Effectiveness of a Representative Irrigation Composition: 13.6% EDTA

In this example, the preparation and effectiveness of a representative irrigation composition of the invention is described. The composition includes 13.6 percent by weight EDTA, 0.1 percent by weight chlorhexidine, and 0.1 percent by weight cetrimide in distilled water.

A three (3) percent cetrimide solution (by weight) is prepared by mixing cetrimide powder with distilled water. Heating helps dissolution of the powder. Chlorhexidine (CHX) is purchased as a 20% aqueous stock solution. CHX is diluted in distilled water to a 1% solution. A 17% EDTA solution is prepared, the pH is adjusted to 7 by adding sodium hydroxide (thus EDTA becomes disodium EDTA). To make 100 ml of the irrigation solution, the ingredients are mixed as follows: 10 ml of 1% CHX solution is added to 10 ml of 3% cetrimide solution. After gentle mixing, 80 ml of 17% EDTA solution is added, and the solution is gently mixed. This solution contains EDTA (13.6%), cetrimide (0.3%) and chlorhexidine (0.1%).

The effectiveness of the composition in removing smear layer was evaluated by treating a smear layer in a root canal with 5% NaOCl for 5 minutes followed by treatment

with the representative composition prepared as described above for 1 minute. The effectiveness of the composition in removing the smear layer is illustrated in FIGURE 2 where open dentinal canals are clearly observable.

The antibacterial activity of the composition was evaluated by exposing a planktonic culture (in suspension) of *Enterococcus faecalis* A197A, a resistant bacterial species often isolated from treatment resistant endodontic infections (root canal infections). In the evaluation, cultures were exposed for 5 seconds, 30 seconds, and 3 minutes. Detection level was at 99.995% killing.

Survival of *E. faecalis* in water and EDTA was 100% for all exposure times. The representative composition killed *E. faecalis* in seconds, and was superior to 2% chlorhexidine alone. The effectiveness of the composition in killing *Enterococcus faecalis* A197A is illustrated in FIGURE 5.

Example 2

The Preparation and Effectiveness of a Representative Irrigation Composition: 5.6% EDTA

In this example, the preparation and effectiveness of a representative irrigation composition of the invention is described. The composition includes 5.6 percent by weight EDTA, 0.1 percent by weight chlorhexidine, and 0.1 percent by weight cetrimide in distilled water.

This representative composition was prepared as described above, except that the EDTA solution was a 5.6 percent by weight EDTA solution.

The effectiveness of the composition in removing smear layer was evaluated by treating a smear layer in a root canal with 5% NaOCl for 5 minutes followed by treatment with this representative composition for 2 minutes. The effectiveness of the composition in removing the smear layer is illustrated in FIGURE 3 where open dentinal canals are clearly observable.

The antibacterial activity of the composition was evaluated as described above in Example 1. The representative composition killed *E. faecalis* in seconds, and was superior to 2% chlorhexidine alone. The effectiveness of the composition in killing *Enterococcus faecalis* A197A is illustrated in FIGURE 5.

Example 3

The Preparation and Effectiveness of a Representative Irrigation Composition: 1.0% EDTA

In this example, the preparation and effectiveness of a representative irrigation composition of the invention is described. The composition includes 1.0 percent by weight EDTA, 0.1 percent by weight chlorhexidine, and 0.1 percent by weight cetrimide in distilled water.

This representative composition was prepared as described above, except that the EDTA solution was a 1.0 percent by weight EDTA solution.

The effectiveness of the composition in removing smear layer was evaluated by treating a smear layer in a root canal with 5% NaOCl for 5 minutes followed by treatment with this representative composition for 5 minutes. The effectiveness of the composition in removing the smear layer is illustrated in FIGURE 4 where open dentinal canals are clearly observable.

The antibacterial activity of the composition was evaluated as described above in Example 1. The representative composition killed *E. faecalis* in seconds, and was superior to 2% chlorhexidine alone. The effectiveness of the composition in killing *Enterococcus faecalis* A197A is illustrated in FIGURE 5.

While the preferred embodiment of the invention has been illustrated and described, it will be appreciated that various changes can be made therein without departing from the spirit and scope of the invention.

CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A composition, comprising:
   (a) ethylenediamine tetraacetic acid;
   (b) chlorhexidine or orally acceptable addition salt;
   (c) N-cetyl-N,N,N-trimethylammonium bromide; and
   (d) water.

2. The composition of Claim 1, wherein ethylenediamine tetraacetic acid is present in an amount from about 0.5 to about 20 percent by weight of the composition.

3. The composition of Claim 1, wherein the orally acceptable addition salt is chlorhexidine digluconate.

4. The composition of Claim 1, wherein chlorhexidine or orally acceptable addition salt is present in an amount from about 0.01 to about 5.0 percent by weight of the composition.

5. The composition of Claim 1, wherein N-cetyl-N,N,N-trimethylammonium bromide is present in an amount from about 0.001 to about 3.0 percent by weight of the composition.

6. The composition of Claim 1, wherein ethylenediamine tetraacetic acid is present in an amount from about 1 to about 17 percent by weight of the composition, chlorhexidine or orally acceptable addition salt is present in an amount from about 0.1 to about 0.5 percent by weight of the composition, and N-cetyl-N,N,N-trimethylammonium bromide is present in an amount from about 0.1 to about 0.5 percent by weight of the composition.

7. A method for making a chlorhexidine-containing composition, comprising:
   (a) combining chlorhexidine or orally acceptable addition salt and N-cetyl-N,N,N-trimethylammonium bromide in water to provide chlorhexidine-containing aqueous solution; and

(b) adding ethylenediamine tetraacetic acid to the chlorhexidine-containing aqueous solution to provide a chlorhexidine-containing composition.

8. The method of Claim 7, wherein the ratio of N-cetyl-N,N,N-trimethylammonium bromide to chlorhexidine or orally acceptable addition salt to is from about 5:1 to about 1:1.

9. The method of Claim 7, wherein the chlorhexidine-containing aqueous solution has a chlorhexidine concentration of from about 1 to about 20% by weight.

10. The method of Claim 7, wherein the ethylenediamine tetraacetic acid is added as a solution.

11. The method of Claim 7, wherein the ethylenediamine tetraacetic acid is added as a solution having an ethylenediamine tetraacetic acid concentration of from about 1 to about 50% by weight.

12. The method of Claim 7, wherein the chlorhexidine-containing composition, comprises ethylenediamine tetraacetic acid in an amount from about 1 to about 17 percent by weight, chlorhexidine or orally acceptable addition salt in an amount from about 0.1 to about 0.5 percent by weight, and N-cetyl-N,N,N-trimethylammonium bromide in an amount from about 0.1 to about 0.5 percent by weight.

13. The method of Claim 7, wherein the chlorhexidine-containing composition is a solution.

14. A method for removing smear layer and disinfecting in a root canal, comprising irrigating the root canal with a composition comprising:

(a) ethylenediamine tetraacetic acid;

(b) chlorhexidine or orally acceptable addition salt;

(c) N-cetyl-N,N,N-trimethylammonium bromide; and

(d) water.

15. The method of Claim 14, wherein the composition comprises ethylenediamine tetraacetic acid in an amount from about 1 to about 17 percent by weight, chlorhexidine or orally acceptable addition salt in an amount from about 0.1 to about

0.5 percent by weight, and N-cetyl-N,N,N-trimethylammonium bromide in an amount from about 0.1 to about 0.5 percent by weight.

16. The method of Claim 14, wherein the root canal is an endodontic situs.

17. The method of Claim 14, wherein the root canal is an instrumented root canal.

18. The method of Claim 14, wherein the root canal is prepared for a periodontic procedure.

19. The method of Claim 14, wherein the root canal is a prepared site for tooth restoration.

20. The method of Claim 14, wherein the root canal is prepared for tooth reconstruction.

21. The method of Claim 14, wherein the root canal is irrigated from about 1 minute to about 1 hour.

22. The method of Claim 14 further comprising irrigating the root canal with sodium hypochlorite prior to irrigating with the composition comprising ethylenediamine tetraacetic acid, chlorhexidine or orally acceptable addition salt, N-cetyl-N,N,N-trimethylammonium bromide, and water.

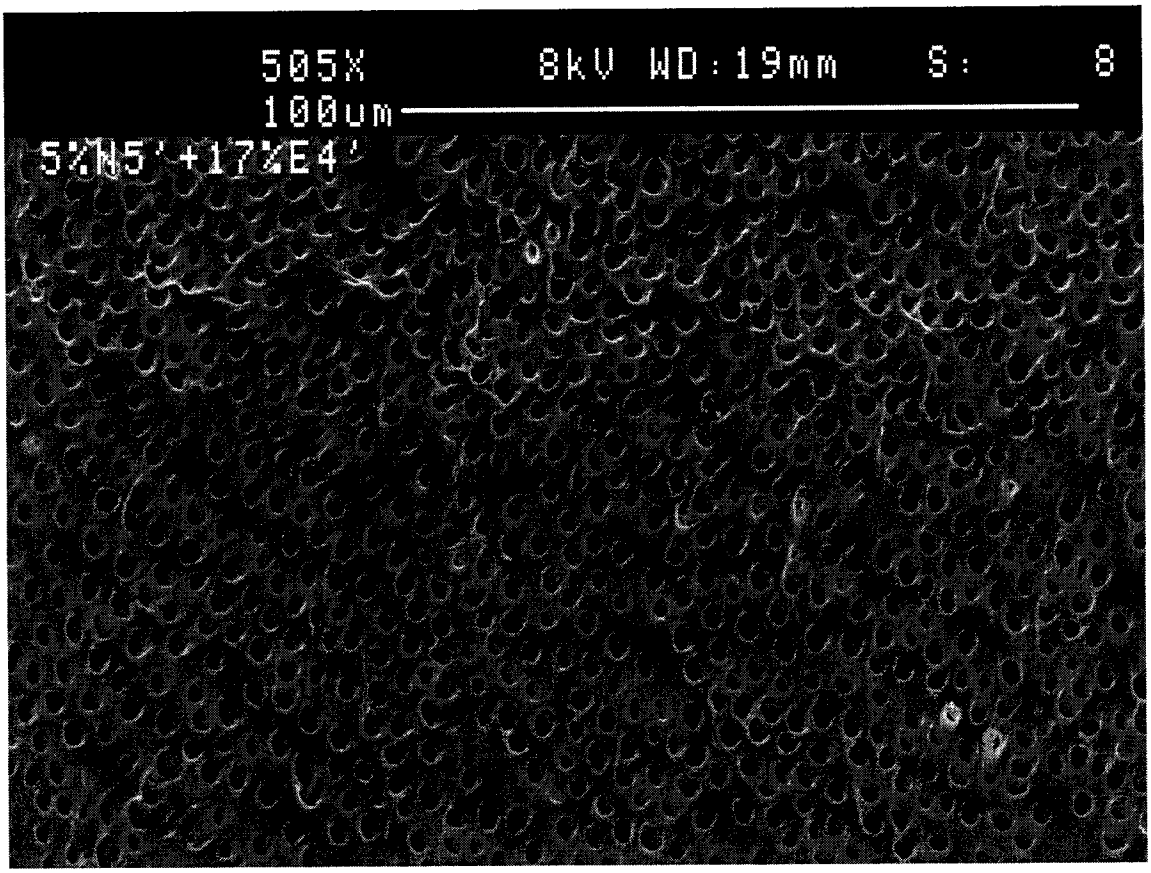

Fig.1.

Fig.2.

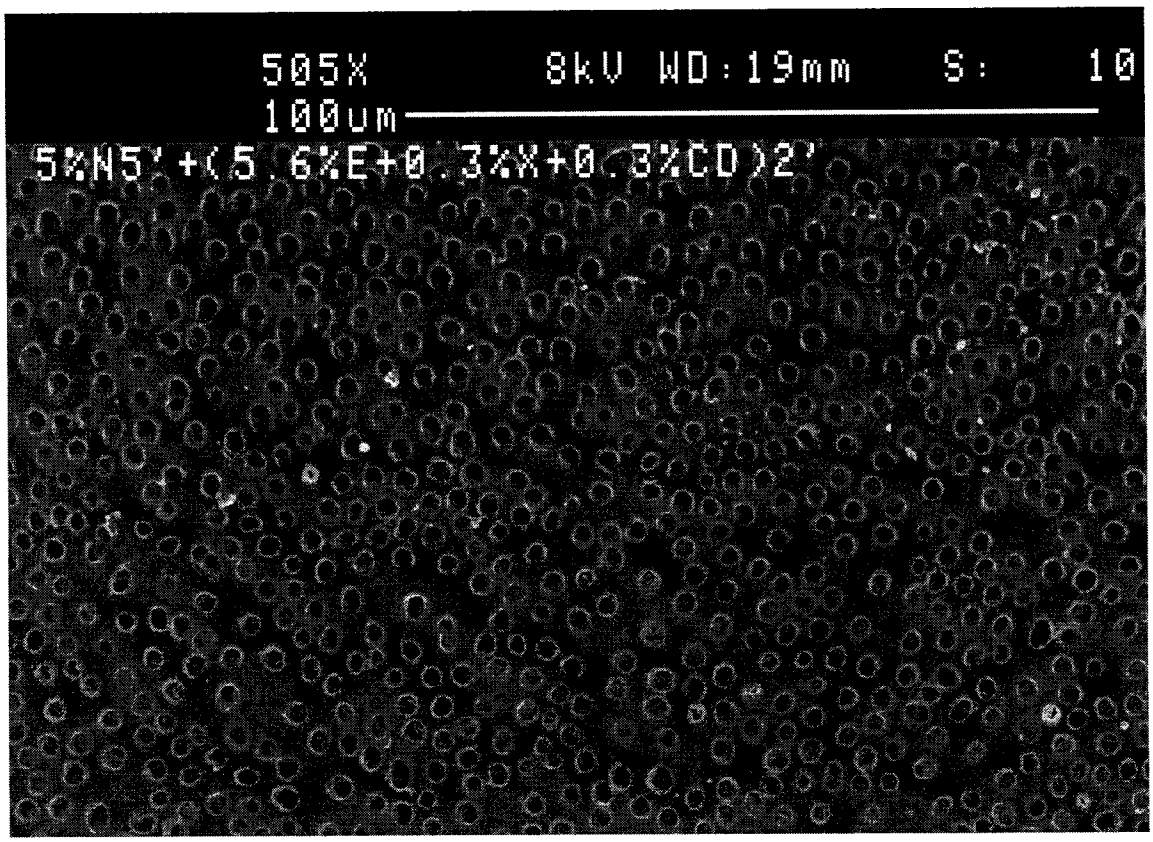

Fig.3.

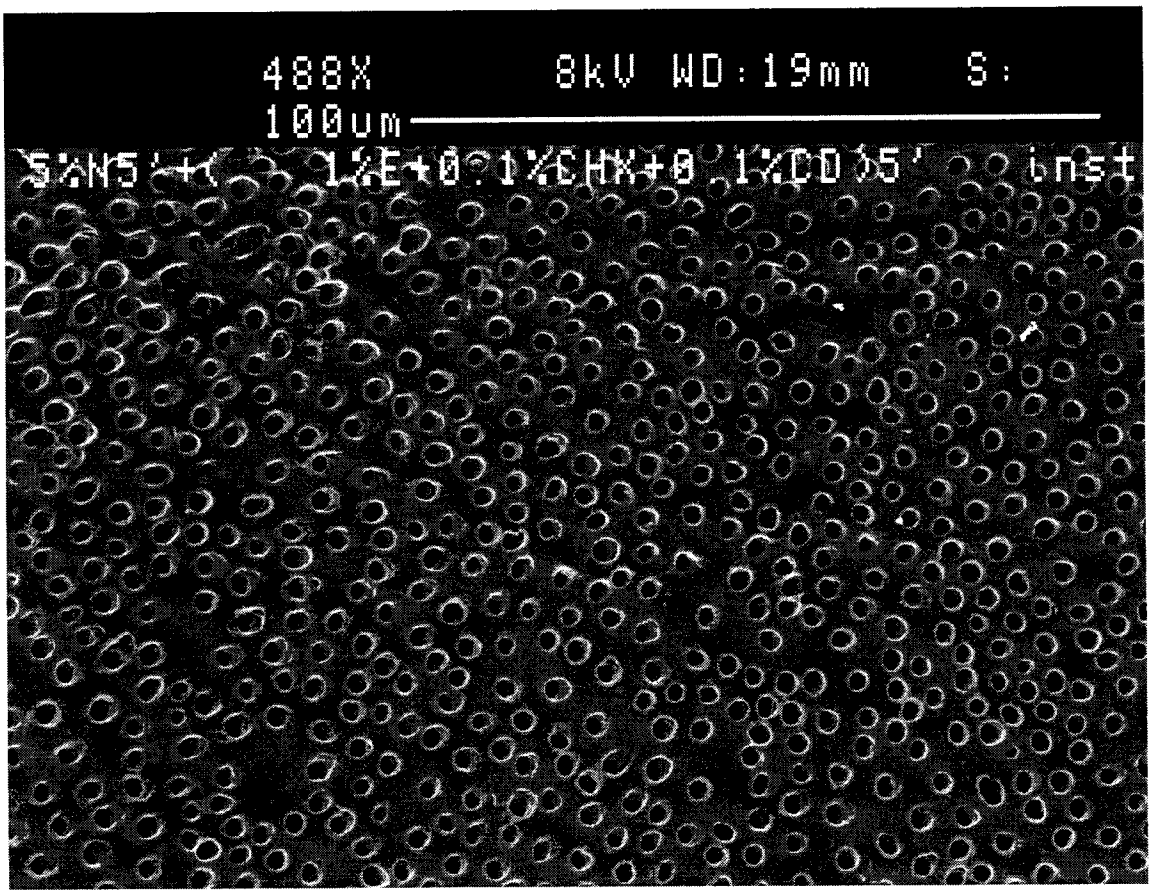

Fig.4.

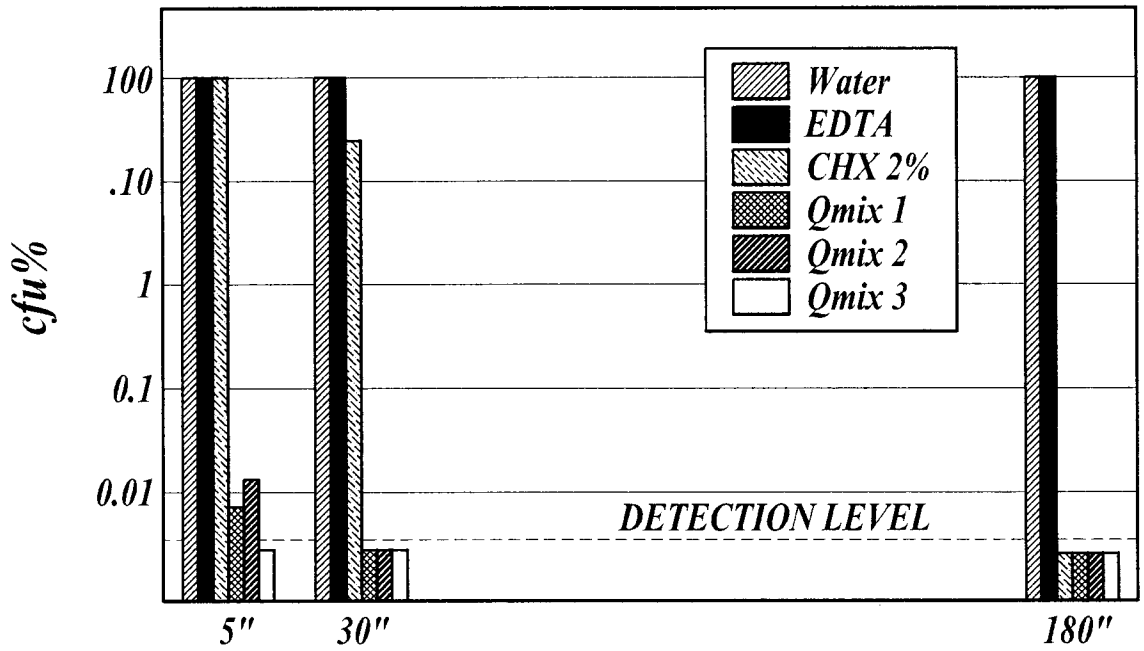
100
.10
1
0.1
0.01
cfu%
Water
EDTA
CHX 2%
Qmix 1
Qmix 2
Qmix 3
DETECTION LEVEL
5"
30"
180"
TIME IN SECONDS

Fig.5.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2009/000218

A. CLASSIFICATION OF SUBJECT MATTER
IPC: ***A61K 31/155*** (2006.01) , ***A61P 31/04*** (2006.01) , ***A61K 47/18*** (2006.01)
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: ***A61K 31/155*** (2006.01) , ***A61P 31/04*** (2006.01) , ***A61K 47/18*** (2006.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
Delphion, Scopus, Questel Orbit, and Canadian Patent Database
Keywords: EDTA, chlorhexidine, cetrimide, cetrixidin, savrolin, EDTAC, root canal, irrigant and other related search terms

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DE VASCONCELOS, B.C., et al., "Cleaning Ability of Chlorhexidine Gel and Sodium Hypochlorite Associated or Not with EDTA as Root Canal Irrigant: A Scanning Electron Microscopy Study", Journal of Applied Oral Science, 2007, Vol. 15, No. 5, pages 387-391. (See abstract; page 390, column 1, lines 23-26 and conclusion)	1-22
Y	DE MENEZES, A.C.S.C., et al., "Smear Layer Removal Capacity of Disinfectant Solutions Used with and without EDTA for the Irrigation of Canals: a SEM Study", Brazilian Oral Research, 2003, Vol. 17, No. 4, pages 349-355. (See abstract, page 350, column 1, lines 18-25 and page 354)	1-22
Y	ÖNÇAĞ, Ö., et al., "Comparison of Antibacterial and Toxic Effects of Various Root Canal Irrigants", International Endodontic Journal, 2003, Vol. 36, pages 423-432. (See abstract and Tables 1-5)	1-22
Y	PORTENIER, I., et al., "Killing of *Enterococus faecalis* by MTAD and Chlorhexidine Digluconate with or without Cetrimide in the Presence or Absence of Dentine Powder or BSA", Journal of Endodontics, February 2006, Vol. 32, No. 2, pages 138-141. (See abstract and Tables 2A and 2B)	1-22

[ ] Further documents are listed in the continuation of Box C.

[ ] See patent family 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 application or patent 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	Date of mailing of the international search report
5 May 2009 (05-05-2009)	12 June 2009 (12-06-2009)
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Authorized officer Olivia Koentjoro 819- 994-1546

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2009/000218

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. [X] Claim Nos. : 14-22

because they relate to subject matter not required to be searched by this Authority, namely :

Claims 14-22 are directed to a method for treatment of the human or animal body by surgery or therapy, which the International Search Authority is not required to search (Rule 39.1(iv), PCT). However, this Authority has carried out a search based on the alleged effect or purpose/use of the product defined in claims 14-22.

2. [ ] Claim Nos. :

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

3. [ ] Claim Nos. :

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. :

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.