Review Article

Current trends in root conditioning agents

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Abstract

The ultimate goal of periodontal therapy has been to achieve predictable regeneration of the periodontium at the diseased site. A critical step in periodontal regenerative therapy is to alter the periodontitis affected root surface and to make it a hospitable substrate, to support and encourage migration, attachment, proliferation and proper phenotypic expression of periodontal connective tissue progenitor cells. Root biomodification procedures, have been introduced to detoxify, decontaminate, and demineralize root surfaces, thereby, aiding in new attachment.

The local application of various chemical substances like Citric acid, Tetracycline hydrochloride, EDTA, Fibronectin etc, have been tried with encouraging postoperative results in periodontal therapy. It is claimed that the chemicals eliminate cytotoxic material from the affected root surface and decalcify the planed root surface, exposing dentin or cementum matrix collagen and facilitate connective tissue attachment to the root surface. However, still the controversy exist amongst the researchers regarding its beneficaility on periodontal regeneration.

Thus the present article describes a thorough literature on available chemical root biomodifiers and presents the current status of root biomodification in periodontal regenerative therapy.
Key-words: Root Biomodifiers, Periodontal regeneration, laser, root canal irrigants, literature review

INTRODUCTION

One of the important goals in periodontal therapy is to facilitate formation of new connective tissue attachment on the denuded root surface. This type of regeneration is described by the term 'New attachment'. It can be described as embedment of new periodontal ligament fibers on to new cementum previously denuded by the periodontal disease. Research regarding periodontal therapy has made it clear that Standard treatment techniques do not result in periodontal regeneration. It has also become apparent that, if the goal of periodontal regeneration is to be realized, the problem of regeneration needs to be approached from a basic biological perspective. The periodontium consists of a cell and tissue complex organized into basic components of cementum, periodontal ligament and alveolar bone. The challenge of regeneration is to reconstitute this complex onto the root surface.

HISTORICAL BACKGROUND:

The concept of acid demineralization in periodontal therapy was first introduced in the 1800s as a substitute for scaling and calculus removal. The use of acids as an adjunct to scaling and calculus removal was reported in the New York Dental Records in 1846. As early as 1833, Marshall presented a case of pocket eradication with “presumable clinical reattachment” after the use of Aromatic sulfuric acid. In the 1890s, Younger and Stewart described the use of acids in conjunction with the mechanical removal of calculus and cementum. Their rationale for its use as an aid to reattachment was the microscopic evidence of hypermineralization of diseased roots with obliteration of lacunae of cellular cementum by calcific deposits.

The potential of acid demineralization of root surfaces as an adjunct to new attachment procedures gained popularity following studies by Urist that suggested that dentin following acid demineralization possessed inductive properties.

Urist demonstrated in a series of experiments that allogenic dentin matrix, following partial or total demineralization with 0.6N HCL possessed the ability to induce the formation of new bone or cementum on the implant surface. It was suggested that the dentin matrix contained a protein or a series of proteins (referred to as bone morphogenic protein) that possessed the ability to induce differentiation of cells. The inductive property, however, was only available following acid demineralization, suggesting that the inorganic component of dentin may obscure potential inductive proteins associated with the organic component. The results of the studies by Urist encouraged Register et al to perform the first controlled study on the use of acid on root surfaces. They investigated whether new attachment, cementogenesis and osteogenesis could be induced adjacent to tooth roots demineralized in vivo.

Register & Burdick evaluated various acids for their potential to promote new connective tissue attachment. The acids tested were hydrochloric, lactic, citric, phosphoric, trichloroacetic and formic. Optimal cementogenesis and new connective tissue attachment occurred when roots were demineralized with citric acid pH 1.0 for 2-3 min. These findings have provided the basis for later
studies using root surface demineralization in periodontal regeneration attempts in both in vitro and in vivo model systems.

**CITRIC ACID:** It was suggested for smear layer removal by Register in 1973 and has been studied extensively. It is essential to human metabolism and is found in many foods. It has been used in the form of citrates as anticoagulants. Endogenous citric acid from the metabolic acid cycle has been associated with solubility of bone mineral during bone resorption. Within vitro systems, citric acid has consistently enhanced features thought to be relevant in the regeneration of periodontal tissues: exposing collagen, inducing mesenchymal cell differentiation, extracting endotoxins and other toxic products, accelerating cementogenesis and widening dentinal tubules. It has been shown that citric acid demineralization enhances new attachment or reattachment and regeneration by one or more of the following mechanism. (Table 1)

<table>
<thead>
<tr>
<th>Antibacterial Effect (Daly et al, 1982)</th>
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<tr>
<td>Exposure of root collagen and opening of dentinal tubules (Polson et al, 1984)</td>
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<tr>
<td>Root Detoxification (Aleo et al, 1974)</td>
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<td>Removal of smear layer (Polson et al, 1984)</td>
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<td>Initial clot stabilization (Wikesjo et al, 1991)</td>
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<tr>
<td>Demineralization prior to cementogenesis (Register, 1975)</td>
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<tr>
<td>Enhanced fibroblast growth and stability (Boyko et al, 1980)</td>
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<tr>
<td>Prevention of epithelial migration along the denuded roots (Polson et al 1983)</td>
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**TETRACYCLINE:** They are broad-spectrum antibiotics which are effective in controlling periodontal pathogens. They are the derivatives of the polycyclic naphthalene carboxamide. Tetracycline hydrochloride, Doxycycline hydrochloride and Minocycline's have been used as root conditioning agents to demineralize the root surface as it binds strongly to the root surface and can be released in an active form over extended periods of time. Sub lethal concentrations of tetracycline reduces adherence and co-aggregation properties of a number of disease associated bacteria including, Porphyromonas gingivalis and Prevotella intermedia. It has a low pH in concentrated solution and this can act as a calcium chelator resulting in demineralization. Tetracyclines possess several unique antibacterial characteristics that may contribute to their efficacy in periodontal therapy. (Table 2)
Rationale for use of Tetracycline hydrochloride (VP Terranova et al., 1986)

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Rationale</th>
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<tr>
<td>Increases fibronectin binding which stimulates fibroblast attachment and growth</td>
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<tr>
<td>Smear layer removal, exposure of dentin tubules</td>
<td></td>
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<tr>
<td>Endothelial cell growth factor binding to dentin, stimulating periodontal ligament cell proliferation / migration</td>
<td></td>
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<tr>
<td>Adsorbs to enamel and dentin. acts as antimicrobial local delivery system</td>
<td></td>
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<tr>
<td>Collagenolytic enzyme inhibition preventing bone resorption</td>
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It inhibits tissue collagenase production and bone resorption. In addition it is known that tetracycline is adsorbed to and subsequently desorbed from dentin. It also exposes the collagen matrix, and uncovers and widens the orifice of dentinal tubules. A matrix is thereby provided supporting migration and proliferation of cells related to periodontal wound healing. It has also been found to be effective for removing smear layer. Another beneficial effect of tetracycline conditioning was that the drug was released in a biologically active concentration for 48 hours and up to 14 days after application. Various types of tetracyclines have been suggested, but tetracycline hydrochloride used for at least 30 seconds, has proven most effective in removing smear layer and opening dentinal tubules. They are generally used as a 0.5% solution at a PH of 3.2 and is applied for 5 minutes. The solution is prepared by adding 1 standard ml of sterile water to the contents of each capsule, then thoroughly mixing the two. The material is applied with lateral pressure using passive burnishing technique using a sterile cotton pellet.

**FIBRONECTIN:** It is a high molecular weight glycoprotein that is found in the extracellular tissue and is the main component that holds the clot together. It promotes cell adhesion to both collagen and scaled root surfaces and has a chemotactic effect on fibroblasts and mesenchymal cells. It also performs several functions (Table 3) that fosters the reattachment of periodontal tissues to the root surface in the surgical treatment of periodontal disease.
Rationale for use of Fibronectin.

<table>
<thead>
<tr>
<th>Rationale</th>
<th>Details</th>
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<tbody>
<tr>
<td>It facilitates fibrin formation and its linkage to the root surface which is an initial stage after demineralization and prior to new attachment.</td>
<td>(Poison &amp; Proye 1983)</td>
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<tr>
<td>Promotes mesenchymal cell adhesion, Chemotaxis and growth</td>
<td>(Okochi et al ,2008)</td>
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<td>It stimulates the coronal growth of cells from the periodontal ligament which are responsible for new attachment</td>
<td></td>
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<tr>
<td>Favors the growth and attachment of fibroblasts over epithelial cells to the root surface</td>
<td>(Terranova et al 1982)</td>
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<tr>
<td>Speeds the linkage process by being chemoattractive for fibroblasts and stabilizing the clot between the exposed root surface collagen and new fibers within the tissue.</td>
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Table 3

EDTA (Ethylene diamine Tetracetic acid): A chelating agent such as EDTA working at a neutral pH appears preferable with respect to preserving the integrity of exposed collagen fibers, early cell colonization and periodontal wound healing. It is suggested that neutrally buffered EDTA will reduce the probability that the soft tissues of the periodontium will be damaged. It has been shown that pH that is not close to neutral, inhibit periodontal ligament fibroblasts. Thus, it is suggested that neutrally buffered EDTA will reduce the probability that the soft tissues of the periodontium will be damaged. Various concentrations of EDTA has been used in studies ranging from 12%-24%, neutral pH for 30 s to 3 min aiming at removing smear layer and widening dentin tubules without damaging biological structures. However, fibrin clot adhesion is limited with its use.

LAMININ: It is a glycoprotein of high molecular weight and capable of adhering to various substrates. Fibronectin and laminin have been implicated in the directed movement of different cell types. Studies have demonstrated that Laminin promotes gingival epithelial Chemotaxis and in addition, movement of gingival fibroblasts from confluent cultures to dentin has been observed.

CHLORHEXIDINE: Bogle G et al studied the effect of post operative use of chlorhexidine on regeneration of bifurcation defects in dogs. Chlorhexidine applied to the root surface during surgical treatment of bifurcation defects in dogs resulted in an increase in bone height but not in the level of connective tissue attachment.

CHONDROITIN SULFATE: Moss M, Kruger and Reynolds DC observed that the use of chondroitin sulfate in extraction sites accelerated the repair but did not affect the ultimate quantity or quality of bone produced.

POLYACRYLIC ACID: Wiland et al in a
comparative study on the healing of the periodontium using Polyacrylic acid for 20 seconds and citric acid for 3 minutes to condition root surface during periodontal therapy, observed that Polyacrylic acid treated teeth have shown more apical migration. They also observed a greater connective tissue adhesion to root surfaces compared to citric acid treated root surfaces.

SODIUM HYPOCHLORITE: Sodium hypochlorite acts as a bactericidal and cleaning agent. It degrades endotoxins by hydrolysis. Lasho DJ et al in a study comparing citric acid, EDTA and sodium hypochlorite observed that surfaces treated with sodium hypochlorite were uneven with debris. When compared to the control group, however, the surface, showed a better appearance by exposing dentinal tubules and less debris. Sodium hypochlorite solution was prepared from chlorinated lime (22gms), Anhydrous Sodium Carbonate (8.5g) and water up to 100ml

SODIUM DEOXY CHOLATE AND HUMAN PLASMA FRACTION COHN IV: These agents can dissociate endotoxin into subunits and might thereby detoxify the diseased root surface. The human plasma fraction possibly contains fibronectin. WirthlinMR and Hancock EB in a tissue culture study applied 2% NAD and 5% Cohn's fraction IV to periodontally diseased root surfaces from which plaque and calculus had been removed. This resulted in significantly more fibroblast attachment to the surfaces than treatment with phosphate buffered physiologic saline.

FORMALIN: Morris and Singh reported clinical responses in 44 cases treated by interproximal denudation and root surface conditioning with a formalin solution. Radiographic evaluations indicated bone growth in 45 of 65 defects and clinical attachment gain of 2.7mm. Since there were no controls, they did not determine how much of the response was due to the surgical approach and how much resulted from the formalin application.

ENZYMES: Willey and Steinberg evaluated the effect of topical applications of Hyaluronidase, Elastase and collagenase to citric acid - demineralized root surface. All of the enzyme treatments appeared to expose more collagen than demineralization one. Collagenase application appeared to clear all ground substance from the collagen fibrils. The other enzymes appeared to clear partially the intercollagenous ground substance.

STANNOUS FLUORIDE: Selvig et al studied the use of stannous fluoride and tetracycline on repair after delayed replantation of root planed teeth in dogs. Root surface treatment with SnF followed by tetracycline, resulted in complete absence of inflammatory resorption and ankylosis as compared to the control group. UM Wikesjo et al undertook a study in beagles to assess the effect of stannous fluoride as an adjunct to regenerative surgery. Those surfaces treated with stannous fluoride showed almost complete epithelialization of the defect and sometimes even epithelialization of the supporting alveolar bone. The mechanism, whereby stannous fluoride has this untoward effect on the connective tissue dentine wound interface is not yet clear.

GROWTH FACTORS: Growth factors are polypeptide molecules released by cells in the inﬂamed area that regulate events in wound healing.
Rubins RP et al\textsuperscript{21} in a prospective consecutive case series, used recombinant human platelet-derived growth factor BB (rhPDGF-BB) with CTGs for the treatment of Miller Class I or II gingival recession defects and observed improved outcomes in terms of keratinized tissue gains and percent root coverage at 6 months postsurgery when compared to historic norms and concluded that the addition of rhPDGF-BB appeared to improve early wound healing as well.

**Root Canal Irrigants**

The use of intracanal irrigant on periodontally affected root surface was first suggested by B. Houshmand et al\textsuperscript{22} using MTAD (root canal irrigant) as a root conditioner. He suggested that a statistically significant difference were seen in smear layer removal from periodontally affected root surface when compared with saline. C. Tandon et al\textsuperscript{23} concluded that MTAD as a root biomodifier have a significant role in periodontal wound healing and future new attachment both in vitro and in vivo. Shewale and D. Gattani\textsuperscript{24} in an Invitro study studied the potential of Q mix\textsuperscript{8}, a root canal irrigant containing Chlorhexidine and EDTA as a root biomodifier and concluded that Q mix was efficient in removing smear layer from periodontally affected root surface.

**LASERS:**

Recently, lasers have been recommended as an alternative or adjunctive therapy in the control and treatment of periodontally diseased root surface. Lasers are capable of sterilizing the diseased root surface and thus ultimately promoting cell reattachment. (Hess and Myers 1990)\textsuperscript{25} said that the removal of root surface contaminants with these techniques allows for the elimination of inflammation and possible attachment to adjacent hard tissue.

**Commercially available laser systems:**

The number of commercially available laser systems is limited to some infrared laser namely, ER:YAG (Erbium: Yttrium, aluminum and garnet) lasers, ND:YAG (Neodymium: Yttrium; aluminum and garnet) and Carbon dioxide.

**ER: YAG LASER:**

Hibst et al (1988)\textsuperscript{26} gave a first description of effects of Er: YAG laser on dental hard tissues. It is a very promising laser system because the emission wavelength of 2.9μm coincides with the absorption peak of water resulting in good absorption in all biological tissues including enamel and dentin. Er: YAG laser is also absorbed by hydroxyapatite. Therefore, the Er: YAG laser would ablate hard tissues containing some water more effectively and causes less thermal damage to the adjacent tissues. Yamaguchi et al (1997)\textsuperscript{27} have demonstrated the ability of Er: YAG laser to remove lipopolysaccharides from root surfaces, facilitate removal of smear layer after root planing, remove calculus and cementum and leave a surface similar to an acid etched appearance.

**ND: YAG LASER:**

ND: YAG LASER was developed by Geusicin 1964 and it has been proposed as an instrument with great potential for effective root preparation. Use of Nd: YG lasers as an adjunct to hand instruments and ultrasonics may have a role in both surgical and nonsurgical periodontal therapy.\textsuperscript{28} However, there are certain limitations with use of ND: YAG for the treatment of dental hard tissues. They cause thermal side effects such as cracking or
charring at the target site and also pulpal damage unlike Er: YAG laser.

**Application of the Nd: YAG laser to root surfaces results in**

- Alterations in root surface protein to mineral ratio,
- Affects the ability of fibroblasts to attach,
- Alters the nature of the smear layer following conventional scaling and root planing.

**CARBON-DI-OXIDE LASER:**

**Patel et al (1964)** were the first to develop CO₂ laser. CO₂ lasers are capable of ablating calcified tissues effectively. However, they have the same limitations of thermal side effects such as cracking or charring at target site and pulpal damage like the Nd: YAG laser. Based on the various characteristics of lasers such as ablation, vaporization and sterilization, researchers have suggested their use for scaling, root planing and root conditioning.

**Misra V et al (1999)*** In an in vitro study evaluates the effect of CO₂ laser on the periodontally involved root surface observed that Laser irradiation of 1 second at 3W completely removed the smear layer with minimal change in the diameter of the dentinal tubules.

**Pant V et al (2004)*** In an in vitro study observed the attachment behavior of human periodontal ligament fibroblasts on periodontally involved root surface after conditioning with CO₂ laser and compare its efficacy with chemical conditioning agents, namely tetracycline hydrochloride, citric acid, hydrogen peroxide (H₂O₂) and EDTA, using scanning electron microscopy and found that CO₂ laser irradiation for 1.0 s promote comparatively better attachment of periodontal ligament fibroblast on dentinal root surfaces than the conventional chemical conditioning agents used in the study.

**R Crespi et al** in a randomized clinical trial comparing modified widman flap surgery with that of coronally advanced flap surgery with Co₂ laser root conditioning for a follow up period of 15 years found that CAF + Co₂ resulted in statistically significant result in terms pocket reduction at sites ≥7mm and clinical attachment level at 5 to 6 mm.

**CONCLUSION:**

It is well established that the periodontally diseased root surface does not favour regeneration of the periodontium due to its surface characteristics. Demineralization, alters the diseased root surface, creating a more acceptable surface that can influence events in wound healing. Studies, indicate a greater potential for cell and fiber attachment to demineralized root surfaces.

. An understanding of the early events in wound healing, appears critical to the selection of appropriate agents and their potential to promote regeneration. Root canal irrigants are newly emerging agents tested for its therapeutic efficacy on root surface and still more studies are required. However, the present status of root biomodification as suggested by systematic reviews suggested that root surface modifiers does not have any added advantage in periodontal regeneration and large Size randomized clinical trials are necessary to give a definite conclusion.

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