THE EFFECTS OF A SANTIMARINE MOUTH RINSE AFTER
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The Effects of a Sanquinarine Mouthrinse after Periodontal Surgery

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Abstract of Thesis

The Effects of a Sanguinarine Mouthrinse after Periodontal Surgery

The purpose of this thesis is to evaluate the effects of a sanguinarine containing oral rinse on plaque formation and inflammation following periodontal surgery.

A double blind parallel methodology was utilized for the mouthrinse following periodontal surgery. The Gingival Index, Plaque Index, Gingival Crevicular Fluid were determined for thirty patients prior to surgical intervention. Their routine oral hygiene regimen was continued after periodontal surgery. The patients were instructed to use a sanguinarine or placebo mouthrinse. Patients were further divided into groups by either a single or twice daily rinsing regimen. Data was collected at 1, 2, 3, and 4 weeks post surgically.

Results indicate that the Gingival Index, Plaque Index, and Gingival Crevicular Fluid increased at the first week evaluation period in all groups. There was no statistical differences between the sanguinarine and placebo mouthrinse, except for the gingival crevicular fluid at the molar surgical site. There appears to be no clinical significance between the sanguinarine and the zinc containing placebo mouthrinse.

Paul W. Kroger, D.M.D.

Date
THE EFFECTS OF A SANGUINARINE MOUTHRINSE AFTER PERIODONTAL SURGERY

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THE EFFECTS OF A SANGUINARINE 
MOUTH RINSE AFTER PERIODONTAL SURGERY

THESIS

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Dentistry at The University of Kentucky

By

Paul W. Kroger, D.M.D.
Lexington, Kentucky

Director: Dr. Herbert Abrams, Associate Professor of Periodontics
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1987
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INTRODUCTION

Previously published longitudinal studies suggest that mechanical plaque control may be used to effectively prevent and treat periodontal disease (Suomi, et al. 1971; Lightner, et al. 1971; Axelsson and Lindhe, 1978). Because adequate plaque control is not always practiced by patients, a search for alternate plaque control measures has led to the use of various chemotherapeutic agents which may alter or inhibit plaque accumulation (Lobene, 1979). The best results appear to be associated with the use of chlorhexidine, antibiotics and sanguinarine (Lobene, 1979; Southard, et al., 1984).


Several problems are associated with the use of chlorhexidine; toxicity, unpleasant taste, discoloration and altered taste sensation have been identified (Goldschmidt, et al. 1977; Kenney, et al. 1972; Flotra, et al. 1971; Gjermo and Rolla, 1971). Also,
animal studies suggest that exposure to drinking water containing 0.2% chlorhexidine for 14 days may result in hyperkeratosis and dysplasia of the tongue (Sonis, et al. 1978). Since the Food and Drug Administration has only recently approved the use of chlorhexidine in the United States, other plaque control agents are being used. Furthermore, the American Academy of Periodontology feels that chlorhexidine should only be used as an adjunct to standard oral hygiene practices.

Sanguinarine has minimal side effects when compared to chlorhexidine (Flotra, et al. 1971) and has less toxic systemic effects when compared to antibiotics (Barry, 1976). The anti-plaque effect is the result of both retention in the oral cavity and the chemotherapeutic effect (Yankell, 1984). Sanguinarine inhibits the acid producing ability of organisms and its retention in saliva compares favorably with both achlorhexidine and cetylpyridinium chloride (Southard, et al. 1984).

Sanguinarine is found commercially in a toothpaste and oral rinse. The toothpaste is effective in reducing plaque scores when compared to a placebo over a four week period (Klewansky & Vernier, 1984). Moreover, inhibition of plaque formation may occur when a sanguinarine containing oral rinse is used in lieu of mechanical tooth cleaning (Lindhe, 1984). If sanguinarine mouthrinses are able to inhibit bacterial plaque formation (Klewansky & Vernier, 1984; Lindhe, 1984), reduced inflammation with enhanced postsurgical healing of periodontal tissues may result. Therefore, the objective of this research project is to
investigate the effects of a sanguinarine containing oral rinse on plaque formation and inflammation following periodontal surgery.
REVIEW OF LITERATURE

Dental plaque which is the bacterial aggregation on teeth has been implicated as the primary etiological factor in periodontal disease (Loe, et al., 1965). Longitudinal studies, fortunately, have shown that the progression of periodontal disease can be retarded in patients demonstrating a high level of oral hygiene (Suomi, et al., 1971; Axelsson & Lindhe, 1978; Axelsson & Lindhe, 1981). Moreover, previous research has demonstrated that repetitive oral hygiene instructions and frequent prophylaxis, are crucial in maintaining health (Shick, 1981). The difficulty lies in motivating the patient to make a commitment to practice daily plaque control (Woodall, 1984).

Wound Healing

It has been documented that plaque infected areas influence wound healing. Yumet and Polson, (1985) evaluated histologically the healing of incisional wounds in the presence and absence of plaque in the supracrestal gingival region of squirrel monkeys. Epithelial continuity over the wound was re-established earlier in plaque infected area. Unfortunately, epithelial proliferation into the wound may predispose to an accelerated loss of connective tissue attachment (Yumet and Polson, 1985; Levy, et al. 1969) which Yumet and Polson (1985) claim is due to a combination of bacterial, cellular, and tissue factors which affect the degradation of fibrin and collagen.

The effect of frequent recall visits on healing following periodontal surgery with and without bone resection was evaluated
in a unique study by Rosling, et al., (1976). Their patients received a dental prophylaxis and plaque control instructions once every two weeks for two years following periodontal surgery. Their results indicate that if plaque control is adequate following surgery, periodontal disease can be stopped or reversed irrespective of the surgical technique utilized for pocket elimination.

Antibiotics

The bacterial etiology of periodontal disease and the antibiotic susceptibility of these organisms support the use of antibiotics in patients who have periodontal disease (Genco, 1981).

The use of topical antibiotics as antiplaque agents may result in undesirable effects (Ciancio and Genco, 1983). Long term use of systemic antibiotics for this purpose may lead to the development of a resistant microflora (Genco, 1981; Ciancio and Genco, 1983). The resistant bacteria exist because they have the genetic capability to resist the inhibiting effects of the antibiotic and then proliferate. They may also pass genetic material in the form of plasmid resistant factors to other organisms with little regard to species boundaries (Sack, 1979).

Systemic tetracycline and minocycline both have been shown to achieve and cause higher antibiotic concentrations in the gingival crevicular fluid than in serum (Gordon, et al., 1981a; Ciancio and Genco, 1983 and Gordon, et al., 1981b). A crevicular
fluid concentration of 4 to 8 ug/ml which is associated with inhibited bacterial growth in the crevicular fluid (Walker, et al., 1985; Walker, et al., 1981), follows a dosage of one gram per day (Gordon, et al., 1981b).

Tetracycline is relatively safe but some side effects do exist: photosensitivity (Blank, et al., 1968), diarrhea and vomiting (Ciancio & Genco, 1983), staining of teeth (Demers, et al., 1968), and superinfections (Solomon, 1964) do occur. Additionally, tetracycline may interfere in the effectiveness of oral contraceptives.

Unfortunately, antibiotic resistance to tetracycline is easily acquired. Both gram positive and gram negative organisms may be affected (Pallasch, 1984). Subgingival plaque collected from periodontal patients receiving two different tetracycline regimens was tested for bacterial resistance after periodontal therapy (Williams, et al., 1979). Patients who received 1000 mg/day for one week followed by 250 mg/day for extended time periods have more anaerobic gram negative rods and a microflora more varied in terms of number of species represented in each plaque sample than the group taking 1000 mg/day for two weeks. Tetracycline resistance was also greater for gram negative rods in the lower dosage group.

Scopp, et al., (1977) found no significant differences in patient discomfort or inflammation when tetracycline was given following periodontal surgery. Consequently they do not
recommend prophylactic use of this medication following periodontal surgery.

In vitro susceptibilities of more than 369 bacterial isolates to eight antibiotics was tested by Walker, et al., (1985) to determine which antimicrobial agents were inhibitory for the plaque bacteria associated with destructive periodontal disease. They found that clindamycin and metronidazole are effective against gram negative rods but not as effective against capnophilic and facultative organisms; minocycline has better antibacterial activities than tetracyclines for actinobacillus actinomycetemcomitans; most bacteria are susceptible to penicillins; and erythromycin is less effective than the other antibiotics against the majority of plaque bacteria.

Because periodontal disease is not a life threatening disease, the risk of using broad spectrum antibiotics may be contraindicated due to the easily acquired bacterial resistance (Pallasch, 1984).

**Antiplaque Rinses**

Chlorhexidine is a symmetrical molecule consisting of two 4 chlorophenol rings and two biguanide groups connected by a central hexamethylene chain with cationic properties (Gjermo, 1974). It is used as a disinfectant because of its broad antibacterial spectrum against gram positive and gram negative organisms (Hennessey, 1973). Total inhibition of plaque formation and prevention of gingivitis may occur following a 0.2% chlorhexidine mouthrinse used twice daily (Loe & Schiott, 1970; Flotra, et
al., 1972 and Hellden, 1981). Once the chlorhexidine is discontinued plaque formation occurs at a normal rate. Lang and Ramseirier-Grossman (1981), reported that a daily irrigation with 0.2% chlorhexidine is the weakest dose that can result in the inhibition of plaque. At this dilution chlorhexidine reduces plaque accumulation which lowers gingival and plaque indices, plaque net weight and bacterial colony forming units when compared to a 0.1% stannous fluoride solution (Hellden, 1981).

The claimed antibacterial effects of Betadine (polyvinylpyrrolidone-iodine with 1% active iodine) and Blend-a-Med (an antiinflammatory dialkylcyclopentacycloheptene and a bacteriostatic polyhalogendiaryalkane) mouthrinses were compared to a 0.2% chlorhexidine by Saxen, et al. (1976). Chlorhexidine reduced plaque formation while Betadine and Blend a Med failed to prevent plaque growth. As a result, Betadine and Blend a Med are not recommended for treating gingivitis.

Foulkes (1973), reports that after 20 years of experience with chlorhexidine it does not seem to have any serious systemic side effects. However, local side effects do exist such as a brownish discoloration of teeth, fillings and tongue (Loe & Schiott, 1970; Gjermo, et al., 1970; Soldheim, et al., 1980; Flotra, et al., 1971) as well as an altered taste sensation (Flotra, et al., 1971; Loe & Schiott, 1970). Three cases of severe desquamative reactions of the oral mucosa have also been reported (Skolund & Holst, 1982). Helgeland, et al., (1971) found that chlorhexidine had cytotoxic qualities when it
contacted epithelial cells in vitro. In fact, Goldschmidt, et al., (1977) found that human cells exposed to chlorhexidine in concentrations greater than or equal to 0.004% resulted in impaired cellular function or cell death. In contrast, in vivo tests on rats resulted in hyperkeratosis and epithelial dysplasia (Sonis, et al., 1978).

Soh and his coworkers (1982), investigated the effect of irrigation of periodontal pockets with chlorhexidine. Even though their patients practiced no oral hygiene for 28 days, chlorhexidine caused a significant reduction in inflammation and subgingival plaque. However, Flotra, et al., (1971) found that subgingival plaque in periodontal pockets greater than 3mm deep is not affected by the chlorhexidine mouthrinse. Because of the incompatible results of these studies, further research in this area is indicated.

After the removal of periodontal dressings the application of chlorhexidine mouthrinses hastens the healing process and causes a reduction in gingival inflammation (Langbaek & Bay, 1976). When used for gingivectomy wounds, it decreases pocket formation (Addy & Dolby, 1976). Also, chlorhexidine, when mixed with periodontal dressings, results in decreased gingival crevicular fluid, less gingival inflammation and increased healing (Asboe-Jorgenson, et al., 1974; Addy and Douglas, 1975). Bakaeen and Strahan, (1980) reported similar results but wound healing appeared unaffected.
Neuman & Addy, (1978), report that post-operatively 0.2% chlorhexidine rinses result in less plaque accumulation and bleeding than coepack periodontal dressings. Consequently, they claim that chlorhexidine is an important adjunct in plaque control during the early post-surgical phase. In a later study, Westfeld, et al. (1983), confirms these findings and concludes that a 0.2% chlorhexidine rinse is a good alternative to mechanical plaque control during the healing phase. In contrast, Bassetti & Kallenberger (1980), report poor healing following chlorhexidine rinses in rats. They also claim that greater concentrations of chlorhexidine result in longer delayed wound healing than lower concentrations.

The FDA recently approved the use of a 0.12% chlorhexidine solution in the United States. Although some research has been done at this concentration (Sturzenberger, et al., 1986) much more will need to be done to determine if this concentration will be as effective as the 0.2% concentration.

Rokita, et al. (1975), studied the effect of a macrolide antibiotic (cc10232) mouthrinse used for one week on five known calculus formers. This antibiotic is bacteriostatic and bacteriocidal against gram positive but not gram negative organisms. Their results suggest that the antibiotic mouthrinse decreases plaque and calculus in four out of five patients. Spirochetes are not found in patients using this antibiotic mouthrinse.

Shaver and Schiff, (1981), studied the effect of an enzyme mouthrinse containing a mixture of neutral protease, alkaline
protease and amylase. They demonstrated a 34% plaque reduction following daily use of the rinse. In earlier studies, Robinson, et al., (1975), and Formicola, et al., (1972), did not find a significant difference when using this enzyme mouthrinse. The reasons for this disagreement are not known.

Historically, many other rinses have been tried. Octenidine, a bispyridine antimicrobial compound, completely inhibits plaque formation and decreases gingival crevicular fluid. However, toothstaining is a problem (Patters, et al., 1983). Because of poor oral retention, a 1% Providone Iodine oral rinse disappointed Addy, et al. (1977). Waerhaug and his coworkers (1984), found that a copper sulfate mouthrinse reduced plaque accumulation and gingivitis; but not as much as the chlorhexidine rinse. Dextranase mouthrinses have also been tested but are ineffective in young adults and children (Caldwell, et al., 1971; Lobene, 1971)

Alexidine (Spolsky, et al., 1975; Spolsky and Forsythe, 1977) reduces plaque scores.

Cetylpridinium chloride causes decreased plaque formation in patients not performing routine oral hygiene (Ciancio, et al., 1978; Llwelyn, 1980; Lobene, et al., 1979). However, mixed results occur when using cetylpyridinium chloride to control gingivitis in patients not performing routine oral hygiene (Ciancio, et al., 1978; Lobene, et al., 1979). In patients practicing routine oral hygiene, cetylpridinium chloride decreases plaque formation but does not reduce or eliminate gingi-

Listerine* reduces plaque accumulation when routine oral hygiene is used (Menaker, et al., 1979; Gordon, et al., 1985; Gomer, et al., 1972). However, Listerine may not produce any significant effects on gingivitis until the ninth month of daily use (Gordon, et al., 1985). In contrast, Fornell, et al., (1975), and Lusk, et al. (1974), claim that Listerine significantly reduces plaque scores and gingivitis when oral hygiene is discontinued for two weeks.

Advocates of stannous fluoride mouthrinses claim that it inhibits plaque formation (Tinanoff, et al., 1980; Svantun, et al., 1977; Yankell, et al., 1978; Hoffman, et al., 1974; Lewell, et al., 1978). A stannous fluoride dentifrice is also effective in plaque control (Wieder, et al., 1983) while a 1.64% stannous fluoride solution used for subgingival irrigation can dramatically decrease subgingival motile bacteria and spirochetes and reduce bleeding (Mazza, et al., 1981). Daily irrigation with 0.02% stannous fluoride results in significant improvement in the periodontal health in teeth with bleeding from pockets over 4mm deep (Boyd, et al., 1985).

Although mouthrinses containing stannous fluoride can reduce the bacterial count in plaque and saliva (Svanberg & Westergren, 1983) gingivitis is not affected by stannous fluoride (Yankell,

et al., 1978; Yankell, et al., 1982; Tinanoff, et al., 1980). Following this train of thought, Burgoyne (1982) questioned the clinical significance of stannous fluoride. Even though he found a significant reduction in plaque and gingivitis, he felt that the effect clinically had little meaning.

Fluoride in excess of 250ppm is needed to inhibit bacterial growth (Bibby & Kesteren, 1940). This antibacterial effect is associated with a large uptake of tin into the bacterial cells. Even though stannous fluoride interferes with bactericidal activity, sodium fluoride has negligible bactericidal properties. These properties of the stannous fluoride mouthrinse are attributed to the tin rather than the fluoride ion (Tinanoff and Camosi, 1980).

Tinanoff, et al., (1980), showed that 250ppm of stannous fluoride reduces plaque net weight, number of bacteria per milligram of plaque, and the total number of bacteria per sample colony forming units by inhibiting acid production in bacteria (Edgar, et al., 1970; Bibby & Kesteren, 1940); inhibiting glucose transport into cells preventing its subsequent phosphorylation; or, if fluoride enters the cell membrane, it may inhibit one or more enzymes needed for acid production and storage of carbohydrates (Sandham & Kleinberg, 1969).

Patients report a strong metallic taste, dryness of the mouth and slight yellowish brown discoloration of the teeth and tongue after rinsing with stannous fluoride. The staining problem differs from chlorhexidine which is very tenacious
Oddly enough patients using stannous fluoride (0.02%) in home irrigation devices show no signs of tooth discoloration (Boyd, et al., 1985).

A very important trace element in the human body is zinc. It is required for the proper function of over 70-100 metalloenzymes (Prasad, 1979; Kay, 1981). These metalloenzymes allow the production of carbon dioxide, alcohol metabolism, protein digestion, hydrolysis of phosphate esters and thymidine triphosphate (Underwood, 1981).

Higher concentrations of zinc are found in healing tissue in contrast to healthy tissue (Savlov, et al., 1962; Williamson, et al., 1984). When zinc is added to the diet it results in a higher concentration in both normal tissue and healing tissue (Williamson, et al., 1984). Consequently, many investigators believe that wound healing is accelerated with zinc supplementation (Mesiobian and Shklar, 1968; Porries, et al., 1967; Wallace, et al., 1978; Williamson, et al., 1984). This has led to using zinc as a post-operative oral supplement and as a topical agent in impregnated surgical tape (Hallmans, et al., 1979). It has even been postulated that the harmful effects of endotoxin can be reversed by zinc supplementation (Aleo, 1976) which is retained in plaque 13-19 fold one hour after rinsing and 3 fold six hours later (Harrap, et al., 1984).

Plaque formation is inhibited by zinc salts (Harrap, et al., 1984; Alseth, 1983) because zinc depresses bacterial growth and initial plaque formation (Bates and Navia, 1979).
Addy, et al., (1980), believe that zinc citrate has a significant but small antiplaque effect which is of questionable clinical significance. On the other hand, zinc chloride is totally ineffective as an antiplaque agent (Compton and Beagrie, 1975). Even when zinc chloride is added to benzethonium chloride, a proven antiplaque agent, it results in a lesser antiplaque effect (Compton & Beagrie, 1975).

Although zinc is an anticalculus agent (Schmid, et al., 1974). Ritchey, et al., (1982), believe that the antiplaque ability of zinc is questionable. The weak antiplaque effect of zinc in vivo may be due to factors such as saliva dilution, differences in retention time in the mouth, zinc binders in plaque, saliva and food, and inaccessibility of tooth sites such as pits and fissures (Bates and Navia, 1979). Harrap, et al., 1983, believe that the poor results of zinc salts in reducing plaque growth may be due to the concentration of zinc, frequency of application and the composition of panels of human subjects such as people with high and low rates of plaque growth.

Sanguinarine is a benzophenanthridine alkaloid extract from the plant Sanguinaria Canadensis, commonly referred to as "bloodroot". It has been incorporated in cough syrups and cold remedies as an expectorant (Southard, et al., 1984). A similar compound called fagaronine in the form of a chew stick has been used by African natives to aid in their oral hygiene (Odebiyi & Sofowara, 1979).
Sanguinarine is obtained in a relatively stable quaternary iminium ion form after the extraction process from Sanguinaria Candadensis. This iminium ion may possess a cationic nature accounting for its retentive properties and resulting antiplaque efficacy (Southard, et al., 1984). The iminium ion of sanguinarine has been shown to bind and neutralize substrates such as cysteine, hydrogen sulfide, and methyl mercaptan (Walterova, et al., 1981; Boulware and Southard, 1984). This is important since hydrogen sulfide has been shown to cause solubilization of gingival collagen and may alter the permeability of the crevicular epithelium.

Mouse calvaria bone cultures treated with parathyroid hormone stimulate collagenase activity and cause subsequent bone resorption. The parathyroid stimulated bone resorption can be inhibited by 20 μM/L of sanguinarine. Therefore, the concentration of sanguinarine retained in dental plaque may inhibit bone resorption (Sakamoto, 1986).

The inhibition of plaque formation by sanguinarine may be due to inhibition of bacterial adherence to the pellicle and by promotion of bacterial aggregation, which permits mechanical flushing of microorganisms by saliva and natural muscle action (Babu, et al., 1986).

Dzink and Socransky, (1985), claim that between 1 and 16 mg/ml of sanguinaria is the minimum inhibitory concentration needed for 98% of 52 bacterial oral references and 129 fresh isolates from dental plaque. At 12 mg/ml sanguinarine completely
inhibits salivary glycolysis (Yankell, 1984). Two strains each of Wolinella succinogenes and Peptococcus prevotii require an elevated minimum inhibitory concentration of 32 mg/ml to inhibit growth (Dzink & Socransky, 1985). Two hours after rinsing, sanguinarine concentration in plaque is well above the minimal inhibitory concentration while the level of sanguinarine in saliva is 10-100 times lower than plaque levels. The retention of sanguinarine is highly specific for dental plaque and may be responsible for this antiplaque activity (Southard, et al., 1984).

Viadent* oral rinse containing 0.1% sanguinarine and zinc reduces plaque formation and gingivitis in patients who do not practice oral hygiene measures for two weeks (Lindhe, 1984; Wennstrom & Lindhe, 1985). When patients are allowed to use a sanguinarine dentifrice with their normal daily oral hygiene it results in a 68% reduction of plaque and 89% decrease in sulcular bleeding (Klewansky & Vernier, 1984).

Warbington, et al., (1985), claim that a sanguinarine rinse is effective in inhibiting plaque deposition and inhibits streptococcus mutans colony forming units. As a result, plaque growth and gingivitis is significantly reduced in patients using sanguinarine as a rinse or in an irrigation system (Parsons, et al., 1986).

*Vipont Laboratories, Fort Collins, Colo. 80522.
Viadent has been found to be significantly superior to Lavoris*, Hibitane**, (0.033%) and Cepacol*** in inhibiting salivary glycolysis (Yankell, 1984). It is also superior to Listerine in inhibiting salivary glycolysis after addition of glucose 15, 45 and 90 minutes after rinsing. Even 2-6 hours after rinsing Viadent is still significantly better.

Sanguinarine and chlorhexidine both have been shown to reduce plaque accumulation supragingivally but fail to reduce inflammation and bleeding (Wennstrom & Lindhe, 1986). The reason may be that the drugs do not penetrate into the gingival pocket to interfere with the subgingival microflora. Abbas, et al., state that a chlorhexidine rinse resulted in significantly lower plaque scores than Viadent in a short-term, no oral hygiene study.

Greenfield and Green** (1984), upon comparing Viadent toothpaste and oral rinse to Zendium toothpaste "Zendium"**** and a water rinse claim that Viadent is more effective than the enzyme system in controlling dentin caries. The Viadent group appears to result in a noticeable reduction in inflammation and longer residual effect than the enzyme system.

*Vicks Oral Health group, Richardson-Vicks, Inc., Danbury, CT 06810.

**Imperial Chemical Industries Ltd., Marclesfield, Enland.

***Merrell Dow Pharmaceuticals, Inc., Cincinnati, OH 45220.

Sanguinarine also effectively neutralizes volatile s.

****Cooper Care, Inc., Palo-Alto, CA 94304.
Sanguinarine also effectively neutralizes volatile sulfur compounds by 71.8%. This result is due to neutralization of the volatile sulfur compounds not antimicrobial action. A combination sanguinarine and zinc mouthrinse also proves to be more effective than a zinc mouthrinse in reducing volatile sulfur compounds (Boulware, et al., 1984).

Conflicting results exist on whether zinc enhances sanguinarine antiplaque effectiveness. When zinc is combined with sanguinarine (Klewansky & Roth, 1985) there is less plaque reduction and gingivitis than a rinse containing only sanguinarine. However, Eisenberg, et al., (1985), claim that the zinc ion has a synergistic effect with sanguinarine resulting in an enhanced antiplaque effect. Viadent incorporates both sanguinarine and zinc in its formulation.

Patients undergoing orthodontic treatment may have a higher than normal incidence of caries and periodontal disease due to the restriction in their ability to remove dental plaque. In these cases sanguinarine products reduce plaque formation and gingival swelling after a few months (Davison, et al., 1985; Palcanis, et al., 1986).

Viadent mouthrinse is used in a variety of periodontal procedures. Bhaskar (1984), uses sanguinarine as an antiplaque agent after periodontal maintenance procedures, prophylaxis, suture removal, prior to periodontal surgery, irrigation of periodontal pockets after scaling and root planing and during non-surgical management of periodontal disease.
Unfortunatley, sanguinarine has no adverse effect on the colony forming units of saliva, tongue, and buccal mucosa, but a reduction of colony forming units in plaque does occur. No resistant strains or crossover resistance to tetracycline or erythromycin occurs after use of sanguinarine rinses (Palcancis, et al., 1986), and when used in normal or exaggerated dosages sanguinarine does not induce animal or human mucosal irritation or sensitization. Nor does there appear to be mutagenic activity, anaphylaxis, cardiac problems or respiratory difficulties (Schwartz, 1986). In a small segment of the population, Viadent mouthrinse may cause a slight burning sensation and altered taste sensation. This problem is reversed after discontinuation or dilution of the mouthrinse (Bhaskar, 1984). Other clinical trials have not shown any detrimental effects (Palcancis, et al. 1986; Davison, et al. 1985; Lobene, et al. 1986; Southard, et al., 1984).

It appears that of the antiplaque agents tested, sanguinarine, chlorhexidine and antibiotics hold the most promise. If these agents are used post-operatively, they may enhance the surgical results by reducing plaque organisms which are known disease producing organisms. Because of sensitivity problems, antibiotics medication may be contraindicated as a routine procedure. Chlorhexidine effect at a 0.2% concentration is well documented. However, the 0.12% solution is the only FDA approved chlorhexidine concentration for antiplaque uses. Insufficient research has been done at this concentration to document its
effectiveness and long-term side effects. Therefore, at this time, sanguinarine may be the agent of choice for antiplaque action following periodontal surgery.
MATERIALS AND METHODS

Thirty patients, 25-65 years of age with localized moderate to advanced periodontitis who required periodontal surgery, were selected from the graduate periodontics clinic at the University of Kentucky College of Dentistry and participated in a parallel double blind study. Patients who were (1) taking antibiotics, steroidal or non-steroidal anti-inflammatory agents up to two weeks before the study, (2) had an acute illness, (3) were pregnant (4) were in orthodontic bands, (5) used Viadent mouthrinse thirty days prior to the surgery, or (6) had a known sensitivity to or a history of oral mucosal tissue reactions, or allergies to mouthrinses or any of the ingredients in the study material were excluded from the study. During initial therapy, prior to surgery, patients received oral hygiene instructions and scaling and root planing. Six weeks after the completion of initial therapy, a presurgical baseline was established which consisted of a plaque index (PI), a modified gingival index (GI) and a gingival exudate measurement (GE).

A modification of the plaque index by Silness and Loe (1964) was used for plaque assessment. The canine through the second molar was dried with pressurized air and the plaque assessed by scraping an explorer along the mesial, distal, facial and lingual surface of the tooth. A score of 0 was recorded if no soft matter adhered to the explorer. For a score of 1, the plaque was not visible on the tooth surface but was seen on the explorer after it was moved across the tooth surface at the entrance of
the gingival crevice. A score of 2 was recorded when the gingival area was covered with a thin to moderately thick layer of plaque that was visible to the naked eye. A score of 3 was assigned when a heavy accumulation of soft matter was observed at the gingival area of the tooth. Each of the four gingival areas of the tooth was scored. The scores were added and divided by four to determine the plaque index for the tooth. The individual PI scores for the teeth in the quadrant were added and divided by the number of teeth present to determine the PI for the quadrant. The plaque index was also taken on the opposite nonsurgical quadrant for the first premolar and molar.

A modification of the gingival index (GI) by Loe and Silness (1963) identified clinical characteristics of inflammation on the mesial, distal, facial and lingual aspect of each tooth evaluated. A score of 0 was assigned to healthy gingiva. A score of 1 was assigned when the gingival margin had a slight color change and slight edema. A score of 2 was recorded when the gingiva was red, edematous and glazed. A score of 3 denoted gingival tissue that had marked redness, edema, glazing. A GI score for the quadrant was calculated in the same manner as the PI. To eliminate disruption of the healing attachment area of the gingival tissues, probing was not done in this study. The gingival index was also taken on the opposite nonsurgical quadrant for the first premolar and molar.
The Periotron* was used to measure gingival crevicular fluid. The Periotron was calibrated with known volumes of 0.1, 0.2, 0.3, 0.4 and 0.5 mg of sterile saline solution. Sulcular fluid was collected on the midfacial aspect of the gingiva in two contralateral pairs of first premolars and first molars. The teeth and surrounding tissues were gently dried with pressurized air and kept dry using cotton rolls in the vestibule. Strips of filter paper (Munktel No. 3) cut 2.2 mm x 15 mm were used for the sampling of gingival fluid. The strips were placed parallel to the surface of the tooth at the entrance to the gingival sulcus. A strip of filter paper was placed for 27 seconds at the crevice entrance to empty the crevicular pool and then discarded.

At the end of this time, another strip was inserted in the sulcus for 3 seconds. The strip was then carefully placed between the jaws of the instrument and the value was obtained on the readout screen after 20 seconds.

All parameters were recorded by one investigator. To avoid intraexaminer bias, calibration and reproducibility in the use of the various indices were standardized prior to beginning the study. Four randomly selected teeth in each of seven subjects with periodontal disease were scored three times each, in random order, to determine examiner variability. The calibration was repeated until a reproducibility of at least 80% was maintained by the examiner.

*Harco Electronics Ltd., Winnipeg, Canada
Six weeks after completion of the initial therapy, the patient's oral hygiene and extent of periodontal disease was assessed, which established a data baseline. If the patient's oral hygiene was acceptable, surgery was scheduled. A plaque index of one or less represented an acceptable level of oral hygiene.

Each osseous surgical procedure consisted of inverse bevel incisions and full thickness flaps from canine to second molar. Granulation tissue was removed and all roots were planed. The flaps were apically positioned and sutured in place. Palatal flaps were designed to attain a similar flap relationship. No surgical dressings were placed. The post surgical analgesic was standardized with patients receiving Vicodin*, (1 tablet every four hours). Patients that were intolerant to Vicodin were given a different acetaminophen combination medication. The day after surgery, the first fifteen patients resumed oral hygiene routines followed by rinsing with either 15cc of Viadent mouthrinse or a control oral rinse for 15 seconds twice at bedtime for 26 days. The mouthrinse began after the first postoperative day and ended with the eve of the 28th day evaluation. The remaining fifteen patients followed the same regimen as the first fifteen patients, except they also rinsed in the morning. The active mouthrinse was Viadent mouthrinse which contained the active antiplaque agents, sanguinarine and

*Knoll Pharmaceutical Co., Whippany, N. J.
zinc chloride. The control rinse was identical except that it did not contain sanguinarine. The control rinse was colored to resemble the Viadent oral rinse so that subjects were more likely to remain blind. A double-blind methodology was used. The mouthrinses were placed into identical bottles by a disinterested third party and coded. Either the active or the control rinse was distributed to the patients following surgery. Fifteen patients received the active mouthrinse and fifteen patients received the control mouthrinse. Patients did not eat or drink thirty minutes after mouthrinsing. The operator had no knowledge as to which rinse the patient used following the surgical procedure. Patients recorded the mouthrinse code daily on a worksheet that was given to them. Data was collected on the seventh, fourteenth, twenty-first and twenty-eighth days post-surgically. Patients were given a one week supply of the mouthrinse. The empty bottle was collected each week and the patients given a new bottle of the mouthrinse. The code was readily accessible in case of an emergency. Upon completion of the clinical part of this study, the clinical code was broken and the results collected and tested statistically.

The statistical test consisted of a three-factor repeated measure analysis of covariance with the repeated measures occurring on the time factor and the covariate being the baseline score for the given dependent variable. All tests were performed using the statistical analysis system computer software package. Specifically, the repeated measures analysis included the use of
the general linear model procedure.
RESULTS

Twenty-six out of the initial thirty patients completed the study. Two patients were dropped because antibiotics were required after surgery. One patient was dropped because of an injury obtained in an automobile accident. Another patient failed to return for her final fourth week post-surgical evaluation.

There was a statistically significant difference between the baselines of the Viadent and placebo groups. All dependent variables were adjusted by using the appropriate baseline scores as a covariate.

Surgical Site (Figures 1-4)

There were no statistically significant differences between the groups as a main factor for the Gingival Index (GI) (p=0.6), Plaque Index (PI) (p=0.45), Premolar Crevicular Fluid (PCF) (p=0.65) or between group interactions with time GI (p=0.14), PI (p=0.77), PCF (p=0.25). There was also no statistically significant differences for group interactions in the number of rinses GI (p=0.42), PI (p=0.98), PCF (p=0.90). (See tables 1, 3, & 5).

Statistically significant differences were found for the Molar Crevicular Fluid (MCF) between groups as a main factor (p=0.04) and between rinses as a main factor (p=0.03). The interactions of groups with time (p=0.47) or number of rinses (p=0.32) was not statistically significant. (See table 7).
There was a statistically significant time effect across group and number of rinses (p=0.0001) for the GI, PCF, and MCF (Tables 1, 5, & 7). The Duncan's multiple range test indicates that the GI, PCF, and MCF at the first week post surgically was higher than all other time periods. However, no statistically significant time effect was found for the PI across the groups and number of rinses (p=0.07) (Table 3).

It should be noted that the three-way interaction of group by time, by number of rinses was not statistically significant for any of the surgical or nonsurgical dependent variables.

**Non Surgical Sites**

**Premolar** (Figures 5, 6, and 9)

No statistically significant differences were found between the groups as a main factor for the premolar's GI (p=0.16), PI (p=0.44), PCF (p=0.51) or between the group interactions with time GI (p=0.29), PI (p=0.95), PCF (p=0.10). There were also no significant differences for group interactions in the number of rinses: GI (p=0.65), PI (p=0.71) and PCF (p=0.52). (See tables 9, 11, & 17).

There was a statistically significant time effect across groups and number of rinses for the premolar GI (p=0.007) (Table 9). The Duncan's multiple range test indicated unlike the previous significant time effects the first week post surgically was only greater than the third post surgical week and not all other time periods. There was no statistically significant time
effect for the PI (p=0.52) (Table 11) and PCF (p=0.08) (Table 17).

Molar (Figures 7, 8, & 10)

No Statistically significant differences were found between the groups as a main factor for the molar GI (p=0.68), PI (p=0.72), or MCF (p=0.30) or between group interactions with time GI (p=0.85), PI (p=0.60), MCF (p=0.73). There was also no significant difference for group interactions in the number of rinses GI (p=0.44), PI (p=0.96) and MCF (p=0.40). (See tables 13, 15, & 19)

A statistically significant time effect was found across groups and number of rinses for the GI (p=0.001). (Table 13). Except for the baseline GI, the Duncan's multiple range test indicated a significantly higher time effect at the first week after surgery than all other post surgical time periods.

There was no statistically significant time effects across group and number of rinses for the PI (p=0.40) (Table 15) or MCF (p=0.07) (Table 19).
### Table I

Gingival Index Surgical Site: Statistical Analysis

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<tr>
<th>Source</th>
<th>Degrees of Freedom</th>
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<th>Probability</th>
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Table 2

Gingival Index Surgical Site: Mean Values

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Plaque Index Surgical Site: Statistical Analysis

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Table 4

Plaque Index Surgical Site: Mean Values

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Table 5
Gingival Crevicular Fluid Premolar Surgical Site: Statistical Analysis

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Table 6
Gingival Crevicular Fluid Premolar Surgical Site: Mean Values

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Table 8
Gingival Crevicular Fluid Molar Surgical Site: Mean Values

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Table 9
Gingival Index Premolar Nonsurgical Site: Statistical Analysis

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Table 11

Plaque Index Premolar Nonsurgical Site: Statistical Analysis

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Table 12

Plaque Index Premolar Nonsurgical Site: Mean Values

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<td>0.36</td>
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<td>Probability</td>
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Table 14
Gingival Index Molar Nonsurgical Site: Mean Values

<table>
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<tr>
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<tr>
<td></td>
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<td>B  1  2  3  4</td>
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<td>0.92 0.75 0.42 0.38 0.50</td>
<td>0.32 0.50 0.21 0.21 0.42</td>
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Table 15

Plaque Index Molar Nonsurgical Site: Statistical Analysis

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<th>F ratio</th>
<th>Probability</th>
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Table 16

Plaque Index Molar Nonsurgical Site: Mean Values

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<td>B 1 2 3 4</td>
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Table 17
Gingival Crevicular Fluid Premolar Nonsurgical Site: Statistical Analysis

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<th>Sum of Squares</th>
<th>F ratio</th>
<th>Probability</th>
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Table 18

Gingival Crevicular Fluid Premolar Nonsurgical Site: Mean Value

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Table 19
Gingival Crevicular Fluid Molar Nonsurgical Site: Statistical Analysis

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<th>F ratio</th>
<th>Probability</th>
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Table 20

Gingival Crevicular Fluid Molar Nonsurgical Site: Mean Values

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<td>4.86</td>
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FIGURE 1
COMPARISON OF GINGIVAL INDEX AT POST
SURGICAL SITES FOR ACTIVE VS. PLACEBO BY
NUMBER OF RINSES AND TIME PERIODS

LEGEND

--- ACTIVE - 1 RINSE
- - - ACTIVE - 2 RINSES
- - - - PLACEBO - 1 RINSE
- - - - - PLACEBO - 2 RINSES
FIGURE 2
COMPARISON OF PLAQUE INDEX AT POST SURGICAL SITES FOR ACTIVE VS. PLACEBO BY NUMBER OF RINSES AND TIME PERIODS

LEGEND

- ACTIVE - 1 RINSE
- ACTIVE - 2 RINSES
- PLACEBO - 1 RINSE
- PLACEBO - 2 RINSES

MEAN PLAQUE INDEX

0 1 2 3 4 5 6 7 8 9 1.0
TIME PERIODS

B 1 2 3 4 5 6
FIGURE 3
COMPARISON OF GINGIVAL CREVICULAR FLUID AT
POST SURGICAL PREMOLAR SITES FOR ACTIVE VS.
PLACEBO BY NUMBER OF RINSES AND TIME PERIODS

LEGEND

ACTIVE - 1 RINSE
ACTIVE - 2 RINSES
PLACEBO - 1 RINSE
PLACEBO - 2 RINSES
FIGURE 4
COMPARISON OF GINGIVAL CREVICULAR FLUID AT POST SURGICAL MOLAR SITES FOR ACTIVE VS. PLACEBO BY NUMBER OF RINSES AND TIME PERIODS

LEGEND

--- ACTIVE - 1 RINSE
--- ACTIVE - 2 RINSES
----- PLACEBO - 1 RINSE
----- PLACEBO - 2 RINSES

MEAN GCF, MOLAR

TIME PERIODS
FIGURE 5
COMPARISON OF GINGIVAL INDEX AT PREMOLAR NON SURGICAL SITES FOR ACTIVE VS. PLACEBO BY NUMBER OF RINSES AND TIME PERIODS

LEGEND
-—— ACTIVE - 1 RINSE
-—— ACTIVE - 2 RINSES
-—— PLACEBO - 1 RINSE
-—— PLACEBO - 2 RINSES
FIGURE 6
COMPARISON OF PLAQUE INDEX AT PREMOLAR NON SURGICAL SITES FOR ACTIVE VS. PLACEBO BY NUMBER OF RINSES AND TIME PERIODS

LEGEND

- ACTIVE - 1 RINSE
- ACTIVE - 2 RINSES
- PLACEBO - 1 RINSE
- PLACEBO - 2 RINSES

MEAN PLAQUE INDEX PM NON-SX

TIME PERIODS
FIGURE 7
COMPARISON OF GINGIVAL INDEX AT MOLAR NON SURGICAL SITES FOR ACTIVE VS. PLACEBO BY NUMBER OF RINSES AND TIME PERIODS

LEGEND
--- ACTIVE - 1 RINSE
--- ACTIVE - 2 RINSES
--- PLACEBO - 1 RINSE
--- PLACEBO - 2 RINSES

MEAN GINGIVAL INDEX MOLAR NON-SX

TIME PERIODS
FIGURE 8
COMPARISON OF PLAQUE INDEX AT MOLAR NON-SURGICAL SITES FOR ACTIVE VS. PLACEBO BY NUMBER OF RINSES AND TIME PERIODS
FIGURE 9
COMPARISON OF GINGIVAL Crevicular Fluid at PREMOLAR NON SURGICAL SITES FOR ACTIVE VS. PLACEBO BY NUMBER OF RINSES AND TIME PERIODS

LEGEND

- - - - - - ACTIVE - 1 RINSE
- - - - - - ACTIVE - 2 RINSES
- - - - - - PLACEBO - 1 RINSE
- - - - - - PLACEBO - 2 RINSES

MEAN GCF PM NON-SX

TIME PERIODS

0 1 2 3 4
FIGURE 10
COMPARISON OF GINGIVAL CREVICULAR FLUID AT
MOLAR NON SURGICAL SITES FOR ACTIVE VS.
PLACEBO BY NUMBER OF RINSES AND TIME PERIODS

LEGEND

- ACTIVE - 1 RINSE
- ACTIVE - 2 RINSES
- PLACEBO - 1 RINSE
- PLACEBO - 2 RINSES

MEAN GCF MOLAR NON-SX

TIME PERIODS
DISCUSSION

The study was designed to evaluate the effects of a sanguinarine mouthrinse on gingival inflammation, plaque accumulation and gingival crevicular fluid (GCF) following periodontal surgery.

The surgical and nonsurgical GI, PI, and GCF, were not statistically significantly different between the groups and there was not a group interaction with time or number of rinses.

These findings may be attributed to several factors: (1) The placebo contained zinc which has antiplaque properties (Harrap et al, 1984, Saxton et al, 1986). Etemadzadeh and Ainamo, 1987 found that the main effect of Viadent may be due to its zinc content rather than the sanguinarine extract. (2) A PI of one or less was required prior to periodontal surgery. Gjermo and Ericksen, 1974, Fischman et al, 1975 demonstrated that only a small difference exists in plaque and gingivitis scores in oral hygiene conscious patients that used chlorhexidine or zinc mouthrinses compared to placebo mouthrinse. This study concurs with these results. However, Southard et al, 1984 found a twenty percent reduction of plaque in patients with uncontrolled oral hygiene, five rinses daily and a true placebo without zinc.

In the non surgical area the GCF at the post surgical molar site, was the only site in which there was a statistically significant difference between groups and between number of rinses as a main factor. This may be due to less than adequate oral hygiene in the posterior area where antiplaque mouthrinses
may have more effect. Saxton et al, 1986 found that an area with a rapid rate of plaque growth benefited more from the use of an antiplaque mouthrinse.

The GI and GCF at the surgical site were statistically different with time across groups and the number of rinses. These changes may be attributed to the removal of hard and soft accretions and the return to gingival health. Arnold et al, 1966 concluded that this change was due to a decreased inflammatory state and the progressive healing of the soft tissue. A direct relationship between gingival healing and gingival exudate flow was postulated. Other authors have concluded that the GCF and GI will decrease after periodontal surgery (Burgoyne, 1982, Sandalli and Wade, 1969).

The GI rose sharply during the first week post surgically except in the active group with two rinses (Fig. 1). This corresponds clinically with a rise in the GCF in all groups except the premolar placebo group with one rinse (Fig. 3, 4). The PI also increased during this period (Fig. 2). Arnold et al, 1966 found that the greatest amount of inflammation occurred at one week after surgery. He believed the large initial increase in the GCF was due to surgical trauma, plus the loss of an intact epithelial barrier. The findings in this study are in agreement with Arnold et al, 1966.

For all groups the plaque scores increased one week after surgery (Fig. 2). Patients are usually reluctant or unable to clean because of root sensitivity or soft tissue discomfort,
which may account for these findings. The slight increase in the PI at the second postsurgical week may be due to improvement of the patients' oral hygiene, or less pain and discomfort as a result of oral hygiene procedures.

An additional rinsing period was added in the middle of the study. This was done to more closely follow the recommendations of the Vipont Laboratories of having two rinsing periods per day, as shown on the product label. This additional rinsing unfortunately increased the number of groups which complicated the design of the study. A future recommendation in maintaining a uniform number of rinses for all patients should be given strong consideration.

Further research is needed with other controls (such as zinc free placebos) and larger sample sizes in order to support the use of Viadent as an effective antiplaque agent. In future studies to determine the efficacy of sanguinarine four specific groups could be used: chlorhexidine as a positive control, Viadent, zinc chloride (1000 ppm), and water as a pure placebo.
CONCLUSIONS

1. There were no statistically significant differences in the gingival index, plaque index or gingival crevicular fluid between groups as a main factor, or group interactions with time or number of rinses.

2. Statistically significant differences were found between Viadent and control mouthrinses and the number of rinses for the amount of gingival crevicular fluid flow at the surgical molar sites.

3. At the surgical site, the gingival index and the gingival crevicular fluid were significantly higher during the first week postoperatively when compared to all other time periods.

4. In this study, the Viadent mouthrinse did not demonstrate better antiplaque or antigingivitis properties after periodontal surgery, compared to the active placebo mouthrinse (Viadent without sanguinarine but containing...
REFERENCES


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VITA

Paul William Kroger was born on September 30, 1954, in Dayton, Ohio. He graduated from Chaminade High School in Dayton, Ohio in 1972.

He attended Xavier University in Cincinnati, Ohio from 1972-1976 and graduated with a Bachelor of Science in Natural Science.

He entered the University of Louisville School of Dentistry in 1976 and graduated with a Doctor of Dental Medicine in 1980.

He served in the United States Army Dental Corps at Wurzberg, Germany from 1981 - 1984 and at Fort Knox, Kentucky from 1984 - 1985.

He entered the University of Kentucky College of Dentistry Graduate Program in Periodontics in 1985 and graduate in 1987.

Paul W. Kroger, D.M.D.

Date
END

12-87

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