

## The Effect of Locally Delivered Xanthan-Based CHLO-SITE Gel with Scaling and Root Planning in the Treatment of Chronic Periodontitis: Microbial Findings

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### ABSTRACT

**Background:** This study was designed in order to evaluate the microbiological effectiveness of a locally delivered xanthan-based CHLO-SITE gel as an adjunctive therapy to scaling and root planning in the treatment of moderate-advanced chronic periodontitis.

**Methods:** In a randomized controlled split-mouth clinical trial, 20 patients with chronic periodontitis and pocket depth of 4-6 mm were selected. One side of the mouth served as control where scaling and root planning was performed as routine while the other side of the same mouth (experimental site) was treated by an extra injection of xanthan-based CHLO-SITE gel. Samples were taken from both sites on baseline, 1 month and 3 months post-treatment periods. Samples were exposed to nutrient material followed by colony counts. Data were then analyzed using Wilcoxon signed ranks and Friedman tests.

**Results:** At baseline, there was no significant difference in colony counts between the control and the experimental sites ( $P = 0.36$ ). However, after 1 month follow up, the mean colony count was  $13850 \pm 2253$  and  $151610 \pm 11248$  at experimental and control sites, respectively, with a significant difference between the two sites ( $P < 0.05$ ). A significant difference was also found in colony count between the two groups in 3 months follow up episode ( $P < 0.05$ ).

**Conclusion:** It seems that subgingival injection of xanthan-based CHLO-SITE gel could cause a significantly higher decrease in colony count than that of scaling and root planning therapy alone in chronic periodontitis.

**Keywords:** Drugs, gels, periodontitis, xanthan gum.

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### Introduction

Antibiotics are locally and systemically administered to reduce microbial plaque in the patients with periodontitis. Local administration of antibiotics is commonly preferred as provides a higher controlled dosage of the drug beneath the gingivae, therefore decreasing its' unfavorable systemic side effects. Effective and safe drugs are usually injected into the periodontal pocket in this method to

limit and even eliminate the pathologic microorganism encouraging inflammatory response and restricting tissue destruction. The penetration of the mouthwashes into the pocket depth is estimated at 4% only, while antibiotics can enter up to 29%-70% of shallow pockets and 44%-68% of moderate and deep pockets by means of supragingival washing; this rate can be increased to 75%-93% in sub-

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gingival washouts.<sup>1</sup> Restrictions in administration of antibiotics include lower efficiency of the drug in the mouthwash form and subgingival washouts of antibiotics. Researchers aimed at developing drugs with controlled slow delivery system. Furthermore, as the systemic prescription of 1 mg antibiotic drug is equal to local administration of 4-8 micrograms into pockets, its local administration seems to be theoretically successful.<sup>2</sup> In this regard, some products including doxycycline gel 10%, minocycline 2% and more recent one, CHLO-SITE (xanthan gel) have been introduced to the markets allowing less invasive characteristics as the drug is locally delivered in the region.<sup>1</sup> Higher concentration of the drug is seen in gingival sulcus fluid than that of mouthwash. A reduced need for periodontal surgeries could be seen following the use of antimicrobials accompanied with scaling and root planning. Chlorhexidine is widely known as an effective antiseptic agent used for over 30 years in management of periodontal diseases.<sup>3</sup> This agent contains a wider spectrum of local antimicrobial agent; it is safe, effective and has no toxicity;<sup>4</sup> however, tooth discoloration and oral tissue pigmentations are inevitable following its long term use.<sup>5</sup> CHLO-SITE is an agent containing 1.5% chlorhexidine of xanthan type introduced by Ghimas Company, Italy. Xanthan gel is a saccharide polymer, which constitutes of a three-dimensional mesh mechanism, released gradually when synthesized with water. Xanthan is considered as an appropriate substance to form a resistant gel due to its molecular and physical properties being easily injectable through a syringe. It is considered as a biocompatible introduced as the best carrier of the chlorhexidine. The gel will be vanished from the pocket within 10-30 days of injection and no mechanical remove is needed there after. With the use of CHLO-SITE, effective concentration of chlorhexidine against microorganisms is established for at least 15 days in the region.<sup>6</sup> Daneshmand et al. (2002) assessed the effect of chlorhexidine gel on the management of periodontal disease as a non-surgical subgingival path to reduce the pocket depth with an increase in clinical attachment level.<sup>6</sup> It seems therefore, that the use of xanthan gel is widely preferred in the process of surgical management.<sup>5</sup> Loe and Schiot (1970) evaluated the local administration of chlorhexidine-based gel Chlosite (Ghimas s.p.a., Italy) in the management of dental plaque and periodontal dis-

ease with their report suggesting no significant difference between those of the agent compared with the control.<sup>6</sup> With the introduction of chlorhexidine-based xanthan gel under the commercial name of CHLO-SITE Chlosite® (Ghimas s.p.a., Italy), the present study was designed to compare the microbial colony count changes found following scaling and root planning when a local delivery of CHLO-SITE was performed in patients with moderate to advanced chronic periodontitis.

## Materials and Methods

A split mouth randomized controlled clinical trial was performed on 20 patients who were suffering from chronic periodontitis. Cases were selected from those referred to the Department of Periodontology, Dental School, Shahid Beheshti University of Medical Sciences during 2006-2007. Individual examinations, both clinical and radiographic, were obtained in order to diagnose and allocate each case appropriately. Written consent form was obtained from patients following thorough information being given to each case. All selected patients had demonstrated at least two discrete regions with pocket depth of 4-6 mm bleeding during probing in two symmetrical teeth being assigned to case and control groups. All regions were restricted to molar teeth and each tooth was positioned in one quadrant apart from the other. None of the selected teeth had any large cavity or restorations, restoration with overhang and or any type of full crown restoration. All patients were confirmed fit and healthy with no signs of any systemic disease. Cases with any periodontal treatment during the past 3 months were excluded even those used any drugs effective on periodontium such as cyclosporine, sodium dilantin, phenytoin, or anti-inflammatory drugs, i.e., estrogens. In addition, pregnant or breast feeding mothers were excluded too. As two control and case regions were symmetrically and randomly selected in single specimen with split-mouth technique, the effects of intervening variables were matched and removed. The specimens were obtained from case and control pockets by a sterile swap. The swap containing the specimens were placed in appropriately designated transport media and transferred to microbiology laboratory at Shahid Beheshti Medical School soon after sample taking. The slides of specimens were prepared and stained subsequently, using a gram staining. Specimens were then incubated (Termos-

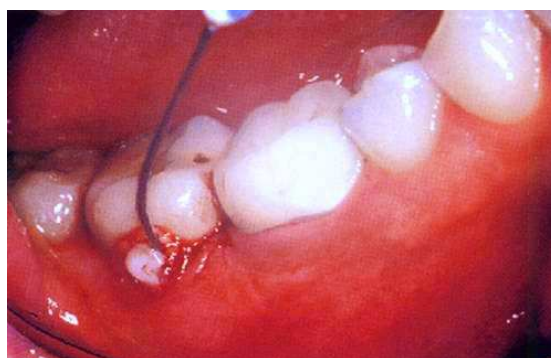
tat 380 Bacterio Brand: Joaun) at 37°C for 24 hours while in transport media. Specimens were then subjected to a culture in blood agar + simple gelose and MacConkey and the colony count of the microorganisms were done. Culture media included nutrient agar with the followings for gram positives:

Pepton: meat extracts 3.0, agar, agar 12.0, meat 5.0 (Merck, KGaA, Dermstadt, Germany).

The culture media for gram negatives was however the MacConkey with the following structures: Pepton from casein – peptone from meat – sodium chloride – lactose – bile salt mixture - neutral red – crystal violet and agar – agar (kGaA, MERCK, Germany).

The plates were stored at 37°C for 48 hours and studied in terms of bacterial colony count. The specification of each bacteria was also, identified at this stage. Both control and case sites were subjected to standard scaling and root planning while additional administration of CHLO-SITE xanthan-based gel was performed in the case site as intervention. The two phases of microbial assessment was carried out at 1 and 3 months follow-up. Specimens of control and case sites were collected at both 1 and 3 months follow-up episodes using a sterile swap and then, followed a cutting as the first phase. Patients received a unique oral hygiene instruction by operator; they were asked to use soft bristled toothbrush to brush their tooth through the Bass technique. In order to assess the solo effect of CHLO-SITE gel on microbial colony count, patients were asked not to use any mouthwash due to their chemical effects and interference with results. Patients were subjected to a nonsurgical periodontal treatment by supragingival and subgingival scaling using Ultrasonic Scaler, (VGE 3025 K). Root planning of each site was then performed under a lidocaine gel local anesthesia (Etkal-Tehran, Iran). Gracey curettes (Hufriday, USA) were employed to yield smooth and clear surfaces. All surfaces were washed with sterile water and subsequently dried using cotton pallets. Each case site was treated by the injection of chlorhexidine-based CHLO-SITE gel while the control sites received no additional management. A round, blunt tipped syringe containing the gel was placed into the pocket progressing into its depth so that the gel encompassed the overall pocket wall with its excess coming out of the pocket opening (Figure 1). The syringe and its tip both were exclusively produced by

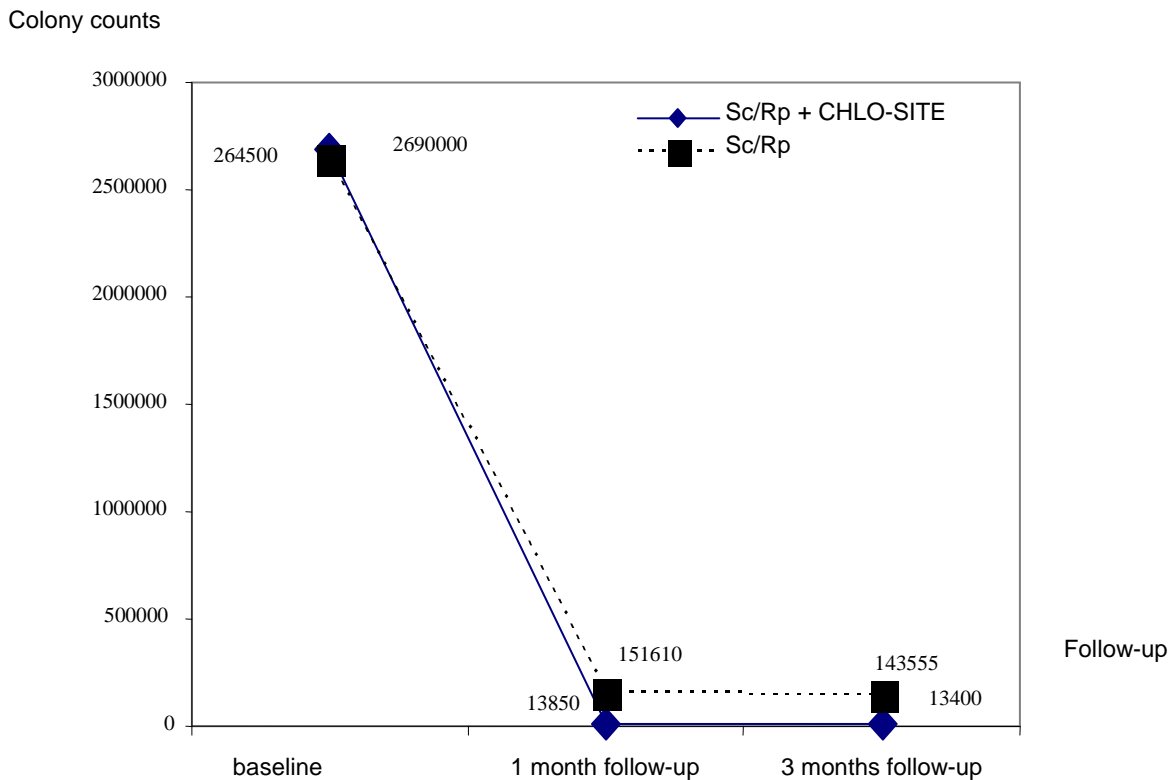
the Ghimas company (Bologna, Italy). This round tipped syringe is equipped with lateral opening at the ending part for the emersion of gel excess. Finally, the case surfaces were covered with co-packed in order to prevent any unwanted loss of the gel. The co-pack dressing as then removed in 7-10 days of the treatment and dental surfaces were cleansed with rubber cap and prophylaxis pumice powder. Oral hygiene promotion was reassessed again and necessary instructions were insisted. Specimens were followed up regularly once a week up to the end of study period, to reassure maintenance of suitable oral health care of patients. Sample plaque was taken from both case and control sites using a sterile swap at 1 and 3 months follow-up. This was followed by the microbial assessments, and the colony counts were means of colony forming units compared to the baseline values. The data were analyzed using the Wilcoxon signed ranks and the Friedman tests.



**Figure 1.** The injection of CHLO-SITE gel in case surfaces.

## Results

In total, twenty patients (12 males and 8 females) with mean age of 37.9 years (30-48 years) were tested in this investigation. The mean colony counts in scaling/root planning + CHLO-SITES was  $2690000 \pm 21675$  and its median was 450000 at baseline. In scaling/root planning (control) sites, the mean colony counts were  $2645000 \pm 27929$  with median of 100000. Wilcoxon signed ranks test showed no significant difference between the colony counts of two sites ( $P = 0.36$ ). At 1 month follow-up, the mean and median colony counts on scaling/root planning + CHLO-SITE surfaces were  $13850 \pm 2253$  and 1000, respectively. This was while the measurement result was  $151610 \pm 11248$  and 10000, respectively, when



**Figure 2.** The mean colony counts on both groups at baseline and the two follow-up periods.

scaling/root planning was attempted alone. Comparing the colony counts revealed significant differences between the two groups at one month follow-up stage suggesting a more decrease in colony counts of cases having extra treatment by xanthan-based CHLO-SITE gel ( $P < 0.05$ ). These figures were even more different at 3 months follow-up, with a significant difference between colony counts of the two groups ( $P < 0.05$ ). This could be explained by the efficiency of CHLO-SITE gel as its use was continued up to 3 months after baseline. However, this level of microorganism count was much less than that of 1 month follow-up. The mean colony counts in CHLO-SITE + scaling/root planning surfaces were  $13400 \pm 2304$  and the median value was 1000. The values were  $14355 \pm 3189$  and 10000 in the scaling/root planning sites alone. More decrease was noted in the number of colony counts in CHLO-SITE applied surfaces compared to scaling/root planning alone. The mean colony counts recorded in both groups at baseline and the two follow-up periods are shown in Figure 2. The total colony counts recorded in each of the two assessed surfaces were compared in baseline and the two follow-up stages using the Friedman test. Results of this test showed that changes had

occurred in the colony counts in both groups, with a significant reduction through time ( $P < 0.001$ ). This indicates the significance of colony counts decrease in both groups through the follow up periods. The decrease was more evident in 1 month follow-up while the reduction process slowed down through the 3 months recall. As the Friedman test resulted in a significant difference, Wilcoxon signed ranks test was utilized to detect the quality of differences in multiple times at both groups. The test results further revealed that significant differences are existed between baseline vs. 1 month follow-up and also, between baseline vs. 3 months follow-up ( $P < 0.001$ ). Unlike previous comparisons, when colony counts were compared in 1 and 3 months follow-up, no significant differences were noted between case and control sites with  $P = 0.71$  in control and  $P = 0.65$  in experimental sites.

## Discussion

This comparative study was conducted on the microbial findings of two groups treated by either scaling and root planning alone or CHLO-SITE xanthan gel with chlorhexidine (a recently developed formula) + scaling/root planning in moderate

to advanced chronic periodontitis. Significant differences were seen between the two groups concerning total colony counts at 1 month follow-up period. A higher decline in colony count was recorded when xanthan was applied to the treating surfaces suggesting a more efferent potential treatment when using CHLO-SITE in the management of moderate to advanced periodontitis than that of standard treatment group. Microbial findings after 3 months follow-up have also demonstrated significant differences between the two surfaces too. Results of this investigation also suggest that concentration of CHLO-SITE gel could also have a preserved effect at the 3 months follow up. However, this was decreased to some degrees when compared to observation at 1 month follow-up. No significant differences were found between both sites regarding colony counts at baseline. This could indicate that all changes at follow-up periods are directly related to the intervention performed later. The number of colony counts recorded for scaling/root planning surfaces was more than what was noted at the scaling/root planning + CHLO-SITE surfaces at both follow-up periods. These results suggest more efficiency in xanthan-based CHLO-SITE use than standard treatment due to the approved influence of bacterial colonies in the development of periodontitis. Pappalardo et al. (2006) studied the effect of a 10% doxycycline injected directly into the periodontal pocket. In their study, 50% of patients received local treatment using a chlorhexidine-based gel (1.5%) in situ; while the other half received any mechanical treatment with scaling and root planning. The crevicular fluid of the doxycycline-treated group was analyzed using high performance liquid chromatography over a period of 1 month. A reduction in attachment loss was reported in addition to a reduction in probing depth of 0.9 mm. The reduction in attachment loss and probing depth was less in the remaining half of patients when compared to those measured in the other two treatment groups.<sup>7</sup> Those areas which received CHLO-SITE gel exhibited a relatively more improvement in probing depth and clinical attachment level parameters than those of chlorhexidine and PlakOut gel. However, the differences were not statistically significant by this sample size. Similarly, the current investigation showed more improvements in CHLO-SITE + scaling/root planning surfaces than standard scaling/root planning measured areas. Two groups

represent significant differences in all parameters measured at both follow-up times except bleeding on probing being changed on 3 months follow-up. Cosyn and Sabzevar (2005) assessed the effect of xanthan-based chlorhexidine gel on 20 patients with chronic periodontitis who had received CHLO-SITE or placebo gels using chlorhexidine mouthwash for 6 weeks.<sup>8</sup> It was suggested that treatment options have the capacity to improve the clinical parameters in such patients. More improvements could be seen in CHLO-SITE treated areas than the control sites regarding probing depth and clinical attachment level. However, no significant differences were found between the two groups.<sup>8</sup> The colony counts decreased in the case of present study with a higher reduction ratio in both groups after the treatment at 1 month follow-up being adjusted in the following months. Those findings maybe due to short term bacteriostatic properties of CHLO-SITE gel as injections were repeated in follow-up appointments; therefore, more improvements could be seen afterwards. The matched interfering variables for the split-mouth technique were employed for this investigation. Two groups did not show any significant differences concerning the colony counts at baseline. The mean colony counts of the two groups were however close with  $2690000 \pm 21675$  at scaling/root planning plus CHLO-SITE and  $2645000 \pm 27929$  at scaling/root planning surfaces. A further similarity was noted in the colony counts of both surfaces indicating the level of accuracy and validity of results achieved. As all patients received similar toothbrush and toothpastes with similar oral hygiene instructions, it was therefore concluded that these could have no effect on colony count outcome of the case and control sites at base line. The colony counts at CHLO-SITE + scaling/root planning and scaling/root planning surfaces decreased significantly through time indicating the effectiveness of both treatment modalities to manage periodontitis. The comparisons of multiple follow-up times showed the significant differences between baseline to 1 month and 3 months; However, no significant difference was noted between 1 and 3 months follow-up times. Daneshmand et al. (2002) evaluated the effect of subgingival application of PerioChip® (2.5 mg chlorhexidine gluconate chip) with scaling and root planning in patients with moderate to advanced periodontitis and reported no further antimicrobial effect in each

improvement in each site.<sup>6</sup> They reported no significant differences in the colony counts of specimens collected from standard and chlorhexidine treated regions. Jorgensen et al. (2004) assessed the antimicrobial effect of a subgingival doxycycline delivery in moderate-advanced periodontitis with no significant differences being found between the microbiological counts in cases and control,<sup>9</sup> although it was shown that chemical management of periodontal disease is more effective than mechanical treatment alone. Grisi et al. (2002) concluded that chlorhexidine chip application can not improve the clinical and microbiological status of the cases when associated with routine scaling and root planning.<sup>10</sup> Perinetti et al. (2004) stated the efficacy of subgingival metronidazole 1% and chlorhexidine 1% in improving clinical and microbiological outcomes of chronic periodontitis.<sup>11</sup> Some other investigators have shown a noticeable effect on the microbiological counts reduction when antimicrobial drugs are used in subgingival area to treat the chronic periodontitis.<sup>12-14</sup> It is important to note that exposure time of the drug to microorganisms is a very critical subject to be considered when assessing the effect of local administration of antibiotics in periodontal disease. According to the manufacturer's instruction, CHLO-SITE gel preserves its effective concentration within the periodontal pocket. Although a higher decrease is seen in colony counts when CHLO-SITE was used after standard root planing, such treatment option has resulted in a relatively fair decrease in number of colonies suggesting its effectiveness. Further clinical and microbiological studies are suggested with longer observation times.

## Conclusion

It seems that subgingival administration of xanthan-based CHLO-SITE gel could result in a more significant decrease in number of colonies than scaling and root planning therapy alone when treating the chronic periodontitis. The decreased colony numbers seems to be more intensive in the 1<sup>st</sup> month follow up while it is further adjusted at 3 months follow up.

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