Clinical and microbiological effects of 1% *Matricaria chamomilla* mouth rinse on chronic periodontitis: A double-blind randomized placebo controlled trial

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**Abstract:**

**Background:** Several herbal mouth rinses are assessed in the literature as an adjunct to scaling and root planning (SRP) for the treatment of periodontal diseases. The objective of this study was to evaluate and compare the clinical and microbiological effects of *Matricaria chamomilla* (MTC) mouth rinse with chlorhexidine (CHX) and placebo mouth rinse for the management of chronic periodontitis.  

**Materials and Methods:** This double-blind, randomized, placebo controlled, clinical trial involved seventy five patients, suffering from chronic periodontitis, which were randomly divided into three groups: negative control (SRP + placebo), positive control (SRP + 0.12% CHX), and test group (SRP + 1% MTC mouth rinse). Mouth rinsing (adjunctive therapy) was continued for 1 month while clinical parameters (plaque index, gingival index, sulcus bleeding index, probing pocket depth [PPD], clinical attachment level, gingival recession [GR], stain index) and microbial colony forming units were evaluated at base line, 6 weeks, and 3 months.  

**Results:** All groups showed a significant change in parameters (except GR for placebo group) between base line and 3 months. MTC mouth rinse suggested added significant benefits over placebo group over the study period. However, it determined more but nonsignificant improvement in PPD (3.68 mm vs. 3.36 mm) and CAL (3.00 mm vs. 2.72 mm) as compared to CHX rinse at 3 months’ period as compared to baseline.  

**Conclusion:** Advantages of using test group were comparable to CHX associated group; therefore, MTC mouth rinse can be used as an effective adjunct during nonsurgical periodontal therapy for chronic periodontitis.  

**Key words:** Chronic periodontitis, mouth rinse, nonsurgical periodontal therapy, scaling and root planning

**INTRODUCTION**

Chronic periodontitis is a common destructive inflammatory disease of the periodontium. Biofilm is a critical factor for the initiation and development of destructive periodontal diseases. Periodontal microorganisms in biofilm are responsible for the immune inflammatory cascade in host tissue that lead to both soft and hard tissue loss.[1,2]

Removal of etiological agent, i.e., bacterial plaque is the main goal for the management of periodontal diseases. Although mechanical plaque control is of prime importance, but chemical plaque control forms an ideal adjunct to mechanical therapy.[3,4] Several chemical agents in adjunct with scaling and root planning (SRP) are used in the literature for the prevention, treatment and maintenance of periodontal destruction. Mouth rinsing with chlorhexidine (CHX), an extensively studied chemical agent for plaque control, considered as the gold standard for reducing the pathogenic microbial load and maintaining the periodontal health due to its antimicrobial and anti-plaque properties. However, tooth staining and taste alteration are the common reversible side effects of the long-term use of CHX rinse.[6-8]

Recent oral researches pull the attention toward the possible role of phytomedicines for combating with oral and periodontal inflammatory conditions.[9-12] *Matricaria chamomilla* (MTC)
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(commons commonly known as chamomile), an ancient medicinal plant of daisy (Asteraceae) family, whose flower extracts and oil are commonly known for its wide therapeutic properties. Active components of this plant extract are terpenoids (α-bisabolol, chamazulene, and sesquiterpenes), coumarins (umbelliferone), flavonoids (luteolin, apigenin, and quercetin), and spiropoetan. Previous literature proposed anti-inflammatory, antimicrobial, antiseptic, antioxidant, and wound healing properties of MTC. The MTC oral rinse showed improvement in plaque accumulation, gingival inflammation, recurrent stomatitis, and oral mucositis. However, no study in literature is found regarding the use of MTC mouth rinse for the management of chronic periodontitis.

The objective of this randomized clinical trial was to evaluate the null hypothesis that there are no added clinical advantages of 1% MTC mouth rinse as an adjunct to SRP compared with 0.12% CHX mouth rinse for the management of chronic periodontitis.

MATERIALS AND METHODS

Seventy-five individuals (39 males and 36 females) suffering from chronic periodontitis (age group of 30–65 years) were assigned in this randomized controlled clinical trial from the outpatient department of Periodontics. The research protocol was approved by the institutional ethical committee and review board. All examinations, treatments and procedures associated with this study followed the Helsinki Declaration of 1975, as revised in 2000. Written informed consent was taken from all participants recruited in the study.

Inclusion criteria included systemically healthy individuals of >30 years of age with previously untreated generalized chronic periodontitis, having minimum 15 teeth, minimum of six teeth with at least one interproximal site with probing pocket depth (PPD) between 5 and 7 mm, and clinical attachment level (CAL) between 5 and 10 mm, at least 30% of the sites with PPD and CAL ≥5 mm and presence of bleeding on probing.

Exclusion criteria were any systemic disease, use of any medication in the previous 6 months, subjects wearing partial dentures or complete dentures, patients allergic, alcoholics, smokers or tobacco users in any form, mentally retarded individual, pregnant, or lactating females.

This prospective study was designed as a randomized, double-blind, three arms longitudinal, placebo-controlled clinical trial. One hundred and thirty-five individuals were examined for eligibility, out of which 75 individuals satisfying the inclusion criteria were randomly recruited to one of the three groups using a computer generated random allocation sequence. Group sample sizes were decided by power analysis with 95% power and a significance level of 0.05.

1. Group 1 – Twenty-five individuals (14 males and 11 females): SRP + placebo mouth rinsing (negative control group)
2. Group 2 – Twenty-five individuals (12 males and 13 females): SRP + 0.12% CHX mouth rinsing (positive control group)
3. Group 3 – Twenty-five individuals (13 males and 12 females): SRP + 1% MTC mouth rinsing (test group).

The primary outcome of this study was CAL, while PPD and microbial colony forming units (CFUs) were the secondary outcome measures. A single clinician who was blinded to the groups assigned to the individuals, recorded all the parameters, i.e., plaque index (PI), gingival index (GI), sulcus bleeding index, PPD, CAL, gingival recession (GR), stain index (SI) at baseline (prior to the treatment), 6 weeks and 3 months after therapy. PPD, CAL, and GR were recorded at the six sites per tooth in every tooth, except third molar, with a manual UNC-15 periodontal probe (Hu-Friedy, Leimen, Germany) to the nearest millimeter. For recording of parameters at different periods, patients were instructed to refrain from any oral hygiene procedure for 8 h prior to the evaluation. The staining of the six maxillary anterior teeth was assessed using the Lobene index.

For subgingival plaque collection, the teeth were isolated with cotton rolls, and a plaque sample was obtained by the introduction of sterile paper cones inside the pocket for 30 s. The sample was placed in a vial containing 10 ml of transport medium. The samples were placed into the petridishes containing blood agar under anaerobic environment (5%–10% carbon dioxide) at 35°C–37°C. After 5–7 days of incubation period colonies of the selected anaerobic microorganism (Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola) were identified and counted. The results were converted into logarithm values for better understanding and statistical analysis. Plaque samples were collected at baseline, 6 weeks, and 3 months of postoperative period.

The mouth rinse was prepared in the laboratory of the Department of Pharmacy, MJP Rohilkhand University, Bareilly, by an experienced pharmacologist. The batch number for this mouth rinse is CMA-0801–1001. 50 g dried CML flower [Figure 1] was taken and was crushed with the help of mortar and pestle to powder form. This powder was mixed with 500 ml of boiled water in a conical flask and suspension was prepared by shaking flask in a shaking incubator (200 rpm) at 37°C temperature for 4 h. This flask was then brought to room temperature and was filtered using Whatman paper under suction and then passed through 0.22 µ filter paper (Millipore, Billerica, MA) to obtain uniform aqueous extract. After discarding residual flash and evaporation, the remaining extract was 250 ml consisting of appropriate concentration. This extract was freeze dried at −20°C until utilized. The standardization of concentration for mouth rinse was determined by titration. From that extract, 2.2 ml volume of the was diluted using pipette with 220 ml of distilled water to prepare 1% v/v mouthwash solution and 0.05% peppermint oil was also add as a flavoring agent.

All participants received full mouth SRP by manual and ultrasonic scalers and dental polishing by a periodontist, unaware to the study protocol, in a single visit. According to their groups, patients were asked to rinse with 15 ml of assigned medication two time in a day till 30 days for 1 min, i.e., in the morning 30–45 min after brushing and were instructed not to rinse or eat anything for 30 min after using mouthwash and at night before going to sleep. Mouthwashes were put in three identical opaque bottles coded with A, B, or C [Figure 4]. Another clinician distributed the bottles to the patients according to the randomization and allocation list.

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No professional supra gingival debridement and polishing was performed after baseline scaling or before the end of the study. All patients were prescribed by the same dentifrices (Colgate Strong teeth, Colgate-Palmolive, India), toothbrushes (Colgate Sensitive Ultra Soft, Colgate-Palmolive, India) and were instructed in the use of the dentifrice to use during the period of the study. Patients were advised to minimize colored beverage (i.e., tea, coffee, and fruit juice) consumption during the study.

The patient’s compliance was assessed every week at the time of recall visits. In these visits, patients exchanged their old bottles with new bottles of medication/placebo. Each bottle contained 220 ml of solution, sufficient for 7 days of rinsing. Subjects were also asked about the self-reported complications. The entire study design is shown with the help of a consort flowchart in Figure 5.

Descriptive statistics were computed for each analyzed variable within each study group. The normality of the distributions was assessed by Shapiro–Wilk test. As the data were not normally distributed, nonparametric statistical test were used for analysis. Friedman test was used to compare the periodontal parameters at different time intervals within each of the study group. After applying the Bonferroni correction, post hoc comparison was done using Wilcoxon signed rank test. Krystal–Walli’s anova was used for intergroup comparison.

RESULTS

Demographical data for the study are in Table 1. For all the three rinses, in intragroup comparison, mean values of PPD, PI, GI, GBI, SI demonstrated significant (P < 0.05) improvement (throughout the study) between any two prospective time period [Table 2]. While for CAL all groups proposed significant benefit (within groups) at all time frame except for CHX and MTC between 6 weeks and 3 months [Table 3].

On intergroup comparison, mean values of all parameters except SI showed nonsignificant (P > 0.05) difference at base line. Both CHX and MTC showed significant difference in mean values of all the parameters (except GR) as compared to placebo group at 6 weeks’ period. While between CHX and MTC, mean values of all the parameters investigated in nonsignificant difference at 6 weeks after base line [Table 4].

For mean change in parameters both CHX and MTC showed significant more improvement (except in GR, SI) as compared to placebo group between base line-6 weeks. However, between CHX and MTC, all parameters improved in nonsignificant manner [Table 5]. Table 6 shows the frequency distribution of CAL gain.

Three patients in CHX group evident with teeth staining and one patient with taste alteration. Apart from this, no adverse effects or complications were reported by any group during the study.

Microbiological parameter was improved for all three groups during the study. MTC group showed significantly less (P < 0.05) CFUs than placebo but comparable (P > 0.05) to CHX group [Tables 7 and 8].

DISCUSSION

Our findings proposed that all three treatment groups presented with significant changes in parameters at different time periods (except GR for placebo and MTC, and CAL for CHX and MTC). However, on intergroup comparison, mean of parameters determined nonsignificant differences between CHX and MTC at 6 weeks and 3 months’ period. Both combined therapies showed significant differences, in mean of parameter, as compared to placebo at 6 weeks and 3 months’ period (except PPD at 6 weeks, and GR at 3 months between CHX and placebo and GR at 6 weeks and 3 months between MTC and placebo).

In addition to above, observation of this trial also demonstrated that both MTC and CHX rinses suggested similar advantages in reduction of PPD, CAL, PI, GI, and MBI after 3 months of base line period, while for same comparison both oral rinses were significantly more beneficial than SRP/placebo.
Ample amount of evidence is present in the literature regarding the positive outcomes of CHX in adjunction with SRP for the management of periodontal disease.\[6-8,11\] Therefore CHX mouth rinse was taken as a positive control in this study. However, certain disadvantages of CHX like unpleasant taste and staining of teeth always seeking for the use of any new herbal mouth rinse. The placebo group was included as the negative control in this study because it was supposed to show no additional benefit with SRP. These two well-design controls curtailed the effects of variables other than the independent variables.

In the best of our knowledge, MTC and CHX rinses were not compared before for the management of chronic periodontitis. Therefore, direct verification of the results was not possible. The observations for placebo and CHX groups of our study are in the accordance with previous studies.\[7,29,30\] Our study follows the results of other trials involving herbal rinse in which test group demonstrated with no additional benefits as compared to CHX oral rinse.\[12,31,32\] Variability in the magnitude of results was observed in the literature for the adjunctive use of CHX rinse with SRP in the management of chronic periodontitis. The disparity in patient selection, base line parameters, and follow-up period might influence the observed heterogeneity in the findings.

| Comparison          | Placebo (n=25) | CHX (n=25) | MTC (n=25) |
|---------------------|----------------|-----------|------------|
| PPD (n=25)          | 0.000*         | 0.000*    | 0.000*     |
| CAL (n=25)          | 0.000*         | 0.000*    | 0.000*     |
| GR (n=25)           | 0.034          | 0.001*    | 0.059      |
| GI (n=25)           | 0.000*         | 0.000*    | 0.000*     |
| PI (n=25)           | 0.000*         | 0.000*    | 0.000*     |
| SBI (n=25)          | 0.000*         | 0.000*    | 0.000*     |
| SI (n=25)           | 0.000*         | 0.000*    | 0.000*     |

Wilcoxon signed-ranks test, *P<0.002 – statistically significant. PPD – Probing pocket depth; CAL – Clinical attachment level; GR – Gingival recession; GI – Gingival index; PI – Plaque index; SBI – Sulcus bleeding index; SI – Staining index; CHX – Chlorhexidine mouth rinse group; MTC – Matricaria chamomilla (MTC) Mouth Rinse Group; SD – Standard deviation; n – Number of patients; P – Significance level; GBI – Gingival bleeding index
is listed on the FDAs Generally Recognized as Safe List; however, persons with known hypersensitivity to plants of the Asteraceae (Compositae) family such as arnica flower, marigold, ragweed, should avoid its use.

The main mechanism of action is anti-inflammatory property due to apigenin, chamazulene, and bisabolol present in MTC extract that inhibit nitric oxide (NO) production, activities of hyaluronidase, collagenase, cyclooxygenases enzymes, prostaglandin E2, interleukin-1β, -6, -12, and tumor necrosis factor-alpha.\[16,17\]

Goes et al.\[22\] evaluated a significant improvement in PI, and GBI for both CHX and MTC mouth rinse after 15 days of the study in gingivitis patients. Both CHX and MTC groups determined more significant benefits as compared to placebo. However, no significant differences found between the above said two medicated mouth rinses. No adverse event presented with MTC rinse as similar to our study. An another cross over design study also elucidated significantly more improvement in mean plaque and gingival score after 4 weeks of chamomile mouth rinse intervention, as compared to control, in gingivitis patients with no adverse effects throughout the study.\[18\]

A previous double-blind, placebo-controlled clinical trial detected nonsignificant benefits of chamomile mouth rinse for chemotherapy induced stomatitis.\[33\] Please change it as Mazokopakis EE et al also advocated the role of CMT m/w for the management of methotrexate-induced oral mucositis.\[34\]

Whenever microbial assessment used in conjunction with clinical trials, it tributes and nourishes the inferences of the research because certain pathogens have a positive correlation

We use chamomile rinse for the management of chronic periodontitis due to its antimicrobial, anti-inflammatory, antioxidant, immune regulatory, and superior healing properties.\[14,15\] MTC is an annual plant indigenous to Asia and Europe, possessing hollow, bright gold cones of the flowers that are packed with disc or tubular florets, and are ringed with white ray or ligulate florets. It is also known as chamomile or camomile, Italian camomilla, German chamomile, wild chamomile, and Hungarian chamomile. Chamomile is used in several countries for commercial purposes as herbal tea and for pharmaceutical and cosmeceutical uses.\[13,16,17\]

Table 4: Significance value (P) for difference in mean of parameters between the groups (within time period)

| Parameters | Time periods | Placebo - CHX | Placebo - MTC | CHX - MTC |
|------------|--------------|---------------|---------------|-----------|
| PPD        | 6 weeks      | 0.091         | 0.018*        | NS        |
|            | 3 months     | 0.000         | 0.000*        | NS        |
| CAL        | 6 weeks      | 0.017*        | 0.004*        | NS        |
|            | 3 months     | 0.041*        | 0.017*        | NS        |
| GR         | 6 weeks      | 0.018*        | 0.066         | NS        |
| GI         | 6 weeks      | 0.001*        | 0.000*        | NS        |
|            | 3 months     | 0.000*        | 0.000*        | NS        |
| PI         | 6 weeks      | 0.000*        | 0.000*        | NS        |
|            | 3 months     | 0.000*        | 0.000*        | NS        |
| GBI        | 6 weeks      | 0.000*        | 0.000*        | NS        |
|            | 3 months     | 0.000*        | 0.000*        | NS        |
| SI         | Baseline     | 0.008*        | 0.005*        | NS        |
|            | 6 weeks      | 0.000*        | 0.000*        | NS        |
|            | 3 months     | 0.000*        | 0.000*        | NS        |

*P<0.05 – statistically significant. NS – Non significant; PPD – Probing pocket depth; CAL – Clinical attachment level; GR – Gingival recession; GI – Gingival index; PI – Plaque index; SBI – Sulcus bleeding index; SI – Stating index; CHX – Chlorhexidine mouth rinse group; MTC – Matricaria chamomilla (MTC) Mouth Rinse Group; P – Significance level; GBI – Gingival bleeding index

Figure 5: Consort flowchart of study. n – Patients analysed after followup.
Table 5: Significance value (P) for change in parameters from baseline to 3 months (inter group)

| Parameters | Placebo - CHX | Placebo - MTC | CHX - MTC |
|------------|---------------|---------------|-----------|
| PPD        | 0.027*        | 0.001*        | NS        |
| CAL        | 0.044*        | 0.011*        | NS        |
| GR         | NS            | NS            | NS        |
| GI         | 0.001*        | 0.000*        | NS        |
| PI         | 0.004*        | 0.000*        | NS        |
| GBI        | 0.003*        | 0.006*        | NS        |
| SI         | NS            | NS            | NS        |

*P<0.05 – statistically significant. NS – Non significant; PPD – Probing pocket depth; CAL – Clinical attachment level; GR – Gingival recession; GI – Gingival index; PI – Plaque index; GBI – Sulcus bleeding index; SI – Stating index; CHX – Chlorhexidine mouth rinse group; MTC – Matricaria chamomilla (MTC) Mouth Rinse Group; P – Significance level; GBI – Gingival bleeding index

Table 6: Frequency distribution of clinical attachment level gain over the study

| CAL gain (mm) | Placebo, n (%) | CHX, n (%) | MTC, n (%) |
|---------------|----------------|------------|------------|
| ≤1            | 4 (16)         | 2 (8)      | 0 (0)      |
| 2             | 13 (52)        | 7 (28)     | 8 (32)     |
| 3             | 6 (24)         | 13 (52)    | 10 (40)    |
| ≥4            | 2 (8)          | 3 (12)     | 7 (28)     |

CAL – Clinical attachment level; CHX – Chlorhexidine mouth rinse group; MTC – Matricaria chamomilla (MTC) Mouth Rinse Group; n – Number of patients

Table 7: Microbiological mean±standard deviation (colony forming units in log) for groups

| Parameters       | Baseline (n=25) | 6 weeks (n=25) | 3 months (n=25) | P   | Mean change (%) |
|------------------|----------------|---------------|----------------|-----|-----------------|
| Placebo          |                |               |                |     |                 |
| *P<0.05 – statistically significant. CFUs – Colony forming units; CHX – Chlorhexidine mouth rinse group; MTC – Matricaria chamomilla (MTC) Mouth Rinse Group; SD – Standard deviation; n – Number of patients; P – Significance level; *P<0.05 – Porphyromonas gingivalis; T. forsythia – Tannerella forsythia; T. denticola – Treponema denticola

CONCLUSION

The MTC mouth rinse was found to improve the clinical and microbiological picture of chronic periodontitis. Its outcomes commensurate the gold standard mouth wash CHX; therefore, Chamomile mouth rinse can be a potential therapeutic agent for chronic periodontitis.

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Conflicts of interest

There are no conflicts of interest.
Table 8: Significance value (P) for mean difference in parameters between the groups (within time period)

| Parameters | Time periods | Placebo - CHX | Placebo - MTC | CHX - MTC |
|------------|--------------|---------------|---------------|-----------|
| *P<0.05 – statistically significant. NS – Non significant; CHX – Chlorhexidine mouth rinse group; MTC – Matricaria chamomilla (MTC) Mouth Rinse Group; P – Significance level; P. gingivalis – Porphyromonas gingivalis; T. forsythia – Tannerella forsythia; T. denticola – Treponema denticola* |
| P. gingivalis | 6 weeks | 0.00* | 0.00* | NS |
| | 3 months | 0.00* | 0.00* | NS |
| T. forsythia | 6 weeks | 0.00* | 0.00* | NS |
| | 3 months | 0.00* | 0.00* | NS |
| T. denticola | 6 weeks | 0.00* | 0.00* | NS |
| | 3 months | 0.00* | 0.00* | NS |

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