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Evaluation of Clinical Efficacy of Biodegradable Chip Containing *Salvadora persica* Extract in Chitosan Base as an Adjunct to Scaling and Root Planning in the Management of Periodontitis

***Fouad H. Al-Bayaty,[1] Azwin A. Kamaruddin,[2] Mohd A. Ismail,[3] Mazen M.J. Al-Obaidi[4]**

[1]Faculty of Dentistry, Department of Periodontology, MAHSA University, Selangor, Malaysia; [2]Faculty of Dentistry, Department of Comprehensive Care, Universiti Teknologi MARA, Selangor, Malaysia; [3]Klinik Pergigian Merlimau (Principal), Melaka, Ministry of Health, Malaysia; [4]Science Department, University of Technology and Applied Sciences, Rustaq, Oman.
**Corresponding Author's e-mail: drfouadhm@gmail.com*

Abstract

Objective: The objectives of this study were to develop two biodegradable periodontal chips containing *Salvadora persica* or Benzyl isothiocyanate (BITC) extract and evaluate its clinical effectiveness in managing periodontitis. ***Methods:*** Chips were formulated from *Salvadora persica*, Benzyl isothiocyanate (BITC) and chitosan; twelve patients with periodontal pockets measuring ≥5 mm participated in this study. Overall, 240 periodontal pockets were evaluated. All patients were treated with full mouth scaling and root planning (SRP) at baseline. Periodontal pockets were divided into four groups. One of which is the control group, while group two received plain chitosan chip. Group three received chips containing *Salvadora persica* extract, and group four received chips containing BITC. Plaque index (PI), bleeding on probing (BOP), periodontal probing pocket (PPD) depth, and clinical attachment levels (CAL) using acrylic stents were recorded at days 0 and 60 only. ***Results:*** Data were statistically analysed; Chi-square t-test and an ANOVA were used. Results showed

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significant improvement in plaque index, bleeding on probing, and reduction in periodontal pocket depth in all four groups ($p<0.05$). The gain in clinical attachment level was significantly higher ($p<0.005$) among the group receiving *Salvadora persica* chips compared to the control and other chip-treated groups. ***Conclusion:*** Periodontal chips containing *S. persica* can be used as adjuncts to treat patients with periodontitis.
Keywords: Chitosan; Periodontal chip; Miswak extract; Benzyl isothiocyanate; Periodontitis.

Advances in Knowledge:

- The use of Miswak-based periodontal chips has shown a significant decrease in bleeding on probing (BOP), plaque index (PI), and periodontal pocket depth (PPD). Furthermore, they have shown a more significant rise in clinical attachment level (CAL) in comparison to the control group.
- The results indicate that using Miswak-based periodontal chips might be a beneficial additional method for treating patients with periodontitis, especially during follow-up appointments for maintenance. The available data supports the efficacy of Miswak-based therapies in enhancing periodontal health and justifies the need for more investigation into their therapeutic capabilities in periodontal care.

Application to Patient Care:

- The Miswak-based periodontal chip is sourced locally, made with natural ingredients, and offers a cost-effective alternative to PerioChip®. Research shows that Miswak reduces plaque, improves gingival health, and promotes wound healing.
- Likewise, the biodegradable chip, containing thymoquinone, has shown promising results in reducing plaque, improving gingival health, and promoting wound healing. This suggests Miswak-based periodontal chips as a viable and economical alternative for managing periodontal disorders.

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Introduction

Periodontitis is an inflammatory condition that affects the periodontium, which is the supporting structure of the teeth. It goes beyond the gingiva and causes damage to the connective tissue that holds the teeth in place. The bacteria found in dental plaque are commonly acknowledged as the primary cause of inflammatory periodontal diseases.[1,2] Traditionally, periodontal therapy aims to modify the periodontal environment to create conditions that facilitate the removal of dental plaque by patients.

Treatment routines include providing oral health guidance to achieve sufficient oral hygiene, performing scaling to remove plaque and tartar, correcting any faulty dental restorations, doing root planing to smooth the tooth roots, and surgically addressing pockets or anatomical flaws.[3] Nevertheless, as knowledge and understanding of the bacterial causes of periodontal disease have grown, the use of antibacterial medicines has become a crucial component of periodontal treatment.[4] Moreover, the care of periodontitis involves preventing the further decline of periodontal support by eradicating certain pathogenic bacteria present in the periodontal pocket. This can be achieved through the process of mechanical scaling and root planning (SRP). However, the depth of the periodontal pockets can lead to significant differences in the efficiency of SRP. This highlights the importance of using antimicrobial medicines with these procedures to better manage periodontitis.[5] Antimicrobial drugs can be transported to affected areas through either systemic or local application.[6] The periodontal pockets serve as a natural liquid enclosure filled with gingival crevicular fluid, facilitating convenient access for the introduction of delivery devices. The gingival crevicular fluid serves as a vehicle for the medicine to be discharged and distributed throughout the periodontal pocket. The aforementioned features render the periodontal pocket an ideal location for the administration of medication via a localised sustained-release delivery system.

PerioChip® is an innovative biodegradable delivery system designed to reduce pocket depth in chronic periodontitis. It is intended to be used as an adjunct treatment with SRP.[7] The chip is a compact, orange-tan, rectangular object with one end rounded, designed to be put into periodontal pockets. The weight of each PerioChip® is approximately 7.4 mg and it contains 2.5 mg of chlorhexidine gluconate, which is an

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antimicrobial agent. The chlorhexidine gluconate is held in a biodegradable matrix made of hydrolysed gelatin that is cross-linked with glutaraldehyde. Multiple studies have demonstrated the clinical efficacy of dental practitioners and their patients in effectively managing periodontitis over an extended period of time.[8–10] Nevertheless, the utilisation of PerioChip® has demonstrated little negative consequences in previous instances. This may be attributed to the primary constituent, namely chlorhexidine gluconate. This hypothesis is substantiated by the observation of brown discoloration of teeth, certain restorative materials, and mucosa, as well as the presence of a bitter taste. Additionally, in some cases, the use of chlorhexidine in mouth rinses has been associated with the sloughing of oral mucosa.[11–13] In order to mitigate these detrimental effects, numerous researchers are currently exploring the potential utilization of natural products, such as plant extracts and herbs, as viable alternatives. Previous studies have examined the efficacy of plant extracts and herbs such as *Myrtus communis*,[14] *Arnica montana*, and *Hamamelis virginiana* against periodontopathic bacteria, revealing their potential antibacterial activity.[15,16]

Salvadora persica is an evergreen tree with medicinal properties that has been utilised for over ten centuries by various populations, particularly Islamic communities residing in Arabia, India, and Africa. Many products have been developed from this medicinal tree, such as toothbrushes made from the roots and small branches of this tree. Miswak (Miswak, Sewak, Siwak) is a chewing stick obtained from the roots of the *S. persica* tree, otherwise known as the Arak tree or Peelu tree. According to research findings, *S. persica* has been found to contain substances with plaque-inhibiting properties and antibacterial effects against various cariogenic bacteria commonly present in the oral cavity.[16] The therapeutic applications of *S. persica* have been identified in dental hygiene products such as toothpaste, mouth rinses, and endodontic irrigation solutions.[17] The steam-distillable oil derived from the root of *S. persica* consists of 10% benzyl nitrate and 90% Benzyl isothiocyanate (BITC).[17] It exhibits a diverse array of bactericidal properties.[16–19]

BITC is a naturally-occurring compound found in plant tissue. The compound is present in Indian cress (*Tropaeolum majus* L.), garden cress (*Lepidium sativum* L.), and significant quantities can be found in cruciferous vegetables such as cabbages, Brussels sprouts, cauliflower, and broccoli.[20]

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Chitosan has gained more attention as a carrier for medication delivery because of its stability, ability to break down naturally, lack of toxicity, and impressive characteristics in adhering to mucus and improving permeability.[13,21] There is currently a lack of research studies investigating the potential development of a periodontal chip incorporating *S. persica* (Miswak) for the treatment of chronic periodontitis. The objective of this study is to develop a periodontal chip that incorporates *S. persica* and assess the efficacy of a biodegradable periodontal chip, that contains *S. persica* in a chitosan base, as a targeted drug delivery system for the treatment of periodontitis.

Materials and Method

Study Design

A clinical trial investigation, lasting for 60 days, was conducted at the Faculty of Dentistry, Universiti Teknologi MARA Shah Alam. The study was randomised and single-blind. The ethics committee approved the research approach involving human subjects (600-RMI (5/1/6/01)), with all participants providing written informed consent to participate in the research endeavour. The study is comprised of two distinct components: a laboratory process and a clinical trial. The laboratory technique includes the manufacture of periodontal chips, while the clinical trial involves the implementation of periodontal therapy and the insertion of the chips.

Study Populations

A total of twelve male individuals diagnosed with periodontitis, ranging in age from 35 to 56 years (with a mean age of 41.8 ± 5.6), were selected to participate in this randomised clinical trial. All participants had at least four nonadjacent teeth with periodontal pockets measuring ≥ 5 mm. A total of 1656 periodontal pockets were assessed, but only 240 periodontal pockets with a measurement of ≥ 5 mm were identified and analysed. The exclusion criteria for patients consisted of a medical history of systemic disease that could potentially affect the progression of periodontal disease or necessitate prophylactic antibiotics prior to dental treatment, recent use of antibiotics or any form of periodontal treatment within the previous three months, the presence of overhanging restorations, pregnancy, smoking habits, and allergy to *S. persica*. The clinical trial was registered in the international database (Current

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Controlled Trials Limited) Registration no: ISRCTN, ISRCTN 29742423. DOI 10.1186/ISRCTN29742423.

Laboratory Procedure

Preparation of *S. persica* Extract

The *S. persica* (Miswak) sticks utilised in this study were bought from a local store in Malaysia, specifically AL KHAIR, B.NO.AK. The material was subsequently crushed into nanoparticle powder utilising a Hammer Mill blender. The particle size of the powder was analysed using the Master sizer 2000 instrument in order to verify the particle size. The powder was subsequently extracted using ethanol. A total of 200 grams of *S. persica* powder resulted in a yield of 15 grams of dry extraction.

Preparation of the Biodegradable Chitosan Chip

A solution containing 1% acetic acid was prepared by adding it to 2.5 grams of chitosan powder obtained from Sigma Germany. The mixture was allowed to stand overnight. Subsequently, it was dissolved in water and subjected to sonication to achieve a uniform mixture, which was then put into specially designed rectangular glass molds that were lined with aluminum foil. After being let to dry overnight at room temperature, the resulting film was divided into small rectangular chips measuring 0.5 x 0.5 sq cm and having a thickness of 0.16 ± 0.02 mm. Subsequently, the chips were enveloped with aluminum foil and stored in aseptic vials at ambient temperature.[22]

Preparation of S. persica Chips Containing Biodegradable Chitosan

The *S. persica* (2.5 mg; 100%w/w) was fragmented and mixed with chitosan that had been steeped in 1% acetic acid overnight. Both components were subjected to sonication to produce a uniform combination and then transferred into a specially designed rectangular glass mold that was lined with aluminium foil. Following an overnight drying period at room temperature, the resulting film was divided into small rectangular chips of 0.5 x 0.5 square centimetres. A content uniformity test was conducted on a few randomly selected chips to confirm the precise amount of medication delivered in each chip. Subsequently, the chips were transferred into aseptic vials and stored at ambient temperature. The identical protocols were

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replicated using 0.25 mg of BITC, which was obtained from Sigma Germany. This was done to fabricate chitosan chips that incorporate the active component *S. persica*.

In Vitro Release Study

A 'vial' method was utilised for the in vitro release study. Ten chips made of *S. persica*, measuring 0.5 x 0.5 sq cm and with a thickness of 0.16 ± 0.02 mm, were inserted into glass vials. Each vial contained 5 mm of phosphate buffer saline. At intervals of 2 to 6 hours, samples (1.0 ml) were periodically taken. Additionally, samples were taken at 1, 2, 3, 5, 7, 9, 11, and 15 days. Each time, the sample was replaced with fresh phosphate buffer saline to ensure that there was enough media for proper breakdown. The samples were examined utilising a spectrophotometer set at a wavelength of 350 nm. The concentration of *S. persica* was determined using the calibration curve established in phosphate buffer saline. An in vitro release was constructed from the data obtained.[22]

Clinical Trial

Before commencement of the clinical trial, patients were given a subject information sheet to explain the research procedures in detail, including using training model to show how the chips will be inserted (Figure 1A) and each patient signed a consent form. An alginate impression was taken for both arches, and a soft transparent acrylic stent was constructed. The acrylic stent was used to precisely identify the specific location and ensure consistent measurements were taken at each visit (Figure 1B). At first, the examination involves a comprehensive assessment of the periodontal condition. All patients underwent for full mouth scaling and polishing. They were also given instructions to follow a normal and effective oral hygiene regimen that includes brushing. A sole examiner (M.A.I), who was uninformed of the therapies administered to each participant, conducted all clinical measurements. The clinical parameter was measured on day 0 and day 60 after treatment.

Plaque index (PI),[23] bleeding on probing (BOP),[24] and the periodontal probing pocket depth (PPD) were all assessed using a UNC periodontal probe, while the presence or absence of BOP was categorised as 0 or 1. BOP received a favorable rating if bleeding manifested within 20 seconds following pocket probing.

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Following the collection of baseline measures, all study pockets underwent root planing using Gracey curettes (Hu-Friedy, Chicago, IL, USA) under local anaesthesia. The procedure was performed by a single investigator (A.A.K.).

In addition, chips were administered inside the periodontal pockets following SRP in groups 2, 3, and 4 (Figure 1C).

Prior to baseline, the 240 periodontal pockets were randomised into four groups.

Group 1:- (control group):- Consisted of 60 sites, received SRP alone.

Group 2:- Consisted of 60 sites, received SRP with chitosan chip insertion.

Group 3:- Consisted of 60 sites, received SRP followed by *S. persica* chip insertion.

Group 4:- Consisted of 60 sites, received SRP followed by insertion of the chip containing BITC.

Patients underwent examination 48 hours after the insertion of chips for evaluation. Patients were advised to refrain from using dental floss, mouth rinses, or oral irrigation devices for a duration of 10 days in order to prevent any movement of the chip throughout the study period. On day 14, patients were recalled for second chip insertion, and the PI and BOP were checked. All the clinical parameters were re-recorded on the last day of a clinical trial (day 60). CAL was measured by comparing the PPD before and after treatment. A reduction in the PPD indicated a gain in CAL and an increase will denote worsening of the PPD. CAL is measured by subtracting the distance between the cementoenamel junction and the free gingival margin from the PPD value.[25]

Intra-examiner Agreement

Measurements of PLI, BOP, and PPD were used to calibrate the examiners internally. A total of 180 sites were assessed on a single patient, and the data was documented. After two hours, the examiner proceeded to re-measure the 180 pockets. The measurements were replicated twice on the identical patient. Data were inserted into Statistical Package for Social Science (SPSS), and Cohen's kappa coefficient was used. The analysis result was Kappa = 0.81 ($p<0.001$), which shows almost perfect agreement.

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Statistical Analyses

Mean values per patient of the clinical parameters were ascertained for every treatment group at the examination. Updates in the clinical parameters were computed for each site in test and control groups. Updates in PLI, BOP, PPD, and CAL between baseline and day 60 were analysed among the treatment groups. The data was gathered and analysed using SPSS Version 26.0; statistical significance of differences was tested with a paired sample t-test, Chi-square and one-way ANOVA. Significance was accepted at the probability level $p<0.05$.

Results

In Vitro *S. persica* Release Study

An in vitro release research is crucial since it has the ability to forecast and replicate in vivo settings. Figure 2 depicts the progressive and continual release of *S. persica* over a span of 11 days. Starting from day 11, the discharge from the *S. persica* chip steadily decreases till day 15. At the conclusion of this time frame, there was a complete release of drugs, totalling 100%. This finding forms the rationale for re-inserting the periodontal chip after the 15th day.

Mean PI Pre and Post Treatment

Each of the four groups showed a decrease and enhancement in the number of sites with evident supragingival PI, before and after the therapy. The groups treated with *S. persica*, BITC, and chitosan chips exhibited a notable enhancement in PI after the therapy. However, the PI for the control group did not show a significant change before and after treatment, with a p-value of less than 0.05 (Table 1).

Mean BOP Pre- and Post-Treatment

Regarding BOP, there was a notable improvement in all groups after therapy. The improvements in BOP were somewhat uniform across all groups after two months, with a p-value of 0.05 (Table 2).

Mean PPD Pre- and Post-Treatment

The average periodontal pocket was measured before and after the treatment. The findings demonstrated statistically significant reductions (PPD) after SRP across all four groups ($p=0.01$). Table 2 displays the average differences in PPD before and

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after therapy. Each group experienced a significant change in PPD after a duration of two months (p=0.01). After two months, the PPD decreased to 4.52 mm in the group treated with SRP alone. In the group receiving SRP combined with chitosan, the PPD reduced to 5.27 mm. Similarly, the SRP combined with *S. persica* chip group showed a reduction to 5.60 mm, while the SRP combined with BITC chip group had a reduction to 4.63 mm. These measurements were compared to the pre-treatment records. The average reductions in PPD were as follows: 0.82 mm for the group that received SRP alone, 1 mm for the group that received SRP in combination with chitosan, 1.55 mm for the group that received SRP in combination with *S. persica*, and 1.27 mm for the group that received SRP in combination with the BITC chip. The group that received SRP plus the *S. persica* chip demonstrated more noticeable improvements in PPD, as indicated in Table 3, in comparison to the other groups.

The Measurement of Clinical Attachment Levels (CAL)

The findings indicated an increase in CAL within all four groups. The group treated with *S. persica* demonstrated a notably greater improvement, exhibiting the highest gain of 1.52 mm (Figure 3). This was followed by the BITC group, which showed a gain of 1.25 mm. The chitosan group displayed a gain of CAL of 1.00 mm, while the control group had a gain of 0.82 mm.

Discussion

The objective of our research was to develop and assess a biodegradable chip that contains an extract from the *S. persica* plant in a chitosan basis. This chip is intended to be used as a targeted medication delivery system for the treatment of periodontitis. The roots of the *S. persica* have been demonstrated to possess an antimicrobial effect.[11] The primary antibacterial component found in *S. persica* extracts is BITC.

The utilisation of *S. persica* extracts and commercially synthesised BITC exhibited a rapid and robust bactericidal effect against oral pathogens implicated in periodontal disease, as well as various Gram-negative bacteria.[17] Moreover, *S. persica* has demonstrated its efficacy as an anti-inflammatory and antioxidant agent through multiple trials, exhibiting therapeutic properties.[26] It modifies the structure of nitric oxide synthase isoforms and reduces the levels of pro-inflammatory cytokines such as IL-1, IL-6, IL-8, TNF, and IFN.[27,28] Additionally, it enhances the anti-inflammatory

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and antioxidant effects at the site of inflammation.[17] These characteristics prove that *S. persica* extracts may have an important role in the management and progression of periodontal disease.

Prior research has demonstrated that including a biodegradable chlorhexidine chip as an adjunct to treatment resulted in significant enhancements in probing depth and attachment level, in comparison to using SRP alone.[29,30] The present study demonstrated the noticeable impact of the treatments on all groups. Specifically, the group receiving SRP plus *S. persica* chip exhibited a greater decrease in PPD compared to the other groups. The reduction in PPD (1.55 mm) seen in this group was more substantial compared to prior studies[4,18] using SRP and other chips like chlorhexidine chips. The findings were consistent with studies conducted by researchers[22,29,30] who utilised periodontal chips containing chlorhexidine as a local delivery method for treating periodontitis. These previous studies demonstrated that when a biodegradable chlorhexidine chip is utilised as an adjunct to conventional periodontal therapy, it leads to critical enhancements in periodontal probing depth and attachment level compared to SRP alone. In addition, they found that the clinical sign of periodontitis also significantly improved when a periodontal chip is used as an adjunct compared to SRP alone. The current study observed a significant improvement in CAL gain in the group treated with *S. persica* chips, as compared to the other groups. This phenomenon may arise from the cumulative influence of the antibacterial properties resulting from the controlled release of *S. persica* and chitosan, or potentially from the synergistic interactions among the constituents of *S. persica*. The study aims to utilise a concentration of 2.5 mg, which is consistent with the concentration found in chlorhexidine chips. In contrast, a dosage of 0.25 mg of the BITC was employed. It can be speculated that increase in the concentration of BITC may yield for more favourable outcomes. Results showed the improvement in gingival inflammation throughout the study, as evidenced by the significant changes in BOP before and after treatment in all groups. These findings are consistent with the results of several prior studies.[22,30]

Noticeable alterations in visible plaque were observed in all treatment groups that were administered chips, except for the control group that solely underwent SRP. These changes were observed both before and after the treatment. One of the

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limitations of this study is the inability to compare it with chlorhexidine chips due to financial constraints, as the acquisition of chlorhexidine chips was deemed costly. Additional research is required to evaluate the efficacy of the chips through an extensive clinical trial, enhance the concentration of BITC, and conduct a comparative analysis with chlorhexidine chips that are currently available in the market. Moreover, periodontal chips containing *S. persica* can be used on the same appointment for SRP or during periodontal maintenance appointments. Based on the findings of this study, it can be concluded that the utilisation of periodontal chips made from *S. persica* and BITC, incorporated in a chitosan base for targeted drug delivery, offers clinical advantages. These chips can be effectively used as an adjunct to conventional SRP in the treatment of patients with periodontitis. Significant changes in visible plaque were found before and after treatment in all treatment groups that received chips except the control group, which received SRP alone. Periodontal chips containing *S. persica* can be used on the same appointment for SRP or during periodontal maintenance appointments. In view of this research, the periodontal chips formulated from *S. persica* and BITC incorporated in chitosan base as a target drug delivery provide clinical benefits achieved with these chips as an adjunct to conventional SRP in the management of periodontitis patients.

Conclusion

Based on the findings of this study, it can be concluded that the utilisation of periodontal chips derived from *S. persica* and BITC integrated into a chitosan base as a means of targeted drug delivery offers clinical advantages. These chips can be used as an adjunct to conventional SRP in the treatment of patients with periodontitis.

Authors' Contributions

The research was designed by FHA who also prepared the chips and drafted the initial manuscript. MMJ played a key role in analyzing the results, performing the antibacterial procedures, and editing the final draft. AAK and MAI both contributed significantly by conducting the clinical trial.

Conflicts of Interest

The authors declare no conflict of interests.

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1. References

[1] Noor E, Al-Bayaty FH. A review on predisposing and modifying factors of periodontal disease. J Adv Med Res 2015; 5(1):5–23.

[2] Al-Bayaty FH, Baharuddin NA, Abdulla MA. The relationship between serum cotinine levels and periodontal status. Online J Biol Sci 2010; 10(2):54–9. https://doi.org/10.3844/ojbsci.2010.54.59.

[3] Lang NP, Bartold PM. Periodontal health. J Clin Periodontol 2018; 45(Suppl 20):S9–S16. https://doi.org/10.1111/jcpe.12936.

[4] G. Caton J, Armitage G, Berglundh T, Chapple ILC, Jepsen S, S. Kornman K, et al. A new classification scheme for periodontal and peri-implant diseases and conditions – Introduction and key changes from the 1999 classification. J Clin Periodontol 2018; 45(Suppl 20):S1–S8. https://doi.org/10.1111/jcpe.12935.

[5] Vinholis AHC, Figueiredo LC, Marcantonio Junior E, Marcantonio RAC, Salvador SLS, Goissis G. Subgingival utilization of a 1% chlorhexidine collagen gel for the treatment of periodontal pockets. A clinical and microbiological study. Braz Dent J 2001; 12(3):209–13.

[6] Gao W, Chen Y, Zhang Y, Zhang Q, Zhang L. Nanoparticle-based local antimicrobial drug delivery. Adv Drug Deliv Rev 2018; 127:46–57. https://doi.org/10.1016/j.addr.2017.09.015.

[7] Puri K, Dodwad V, Bhat K, Puri N. Effect of controlled-release Periochip™ on clinical and microbiological parameters in patients of chronic periodontitis. J Indian Soc Periodontol 2013; 17(5):605–11.

[8] Basher SS, Saub R, Vaithilingam RD, Safii SH, Daher AM, Al-Bayaty FH, et al. Impact of non-surgical periodontal therapy on OHRQoL in an obese population, a randomised control trial. Health Qual Life Outcomes 2017; 15:225. https://doi.org/10.1186/s12955-017-0793-7.

[9] Stabholz A, Shapira L, Mahler D, Gellman Y, Ramon T, Dolev E, et al. Using the PerioChip in treating adult periodontitis: an interim report. Compend Contin Educ Dent 2000; 21(4):325–8.

Accepted Article

[10] Heasman PA, Heasman L, Stacey F, McCracken GI. Local delivery of chlorhexidine gluconate (PerioChip™) in periodontal maintenance patients. J Clin Periodontol 2001; 28(1):90–5. https://doi.org/10.1111/j.1600-051X.2001.280114.x.

[11] Al-Bayaty FH, AI-Koubaisi AH, Ali NAW, Abdulla MA. Effect of mouth wash extracted from Salvadora persica (Miswak) on dental plaque formation: A clinical trail. J Med Plants Res 2010; 4(14):1459–67.

[12] Shakir MS, Al-Bayaty FH, Albajalan OB. Preparation and characterization of periodontal chips from egg shell membrane. J Int Dent Med Res 2019; 12(2):434–42.

[13] Al-Bayaty FH, Ismail IHB, Zain ZBM, Nasruddin NAB, Suradi NFB. Formulation and Evaluation of new biodegradable periodontal chips from Malaysian propolis in chitosan base. J Int Dent Med Res 2017; 10(2):292–8.

[14] Walid H, Fouad H. The effect of Myrtus Communis extract mouth wash on newly dental plaque. J Coll Dent, 2001; 8:41–9.

[15] Iauk L, Lo Bue AM, Milazzo I, Rapisarda A, Blandino G. Antibacterial activity of medicinal plant extracts against periodontopathic bacteria. Phyther Res 2003; 17(6):599–604. https://doi.org/10.1002/ptr.1188.

[16] Al-Bayaty FH, Razak MAA, Hussain SF, Mulok TZ, Almas K, Smith S, et al. Antibacterial Activity of Salvadora Persica and Benzylisothiocyanate against Prevotella Intermedia and Eikenella Corrodens Incorporated into Periodontal Chips. J Int Dent Med Res 2022; 15(2):498–504.

[17] Sofrata A, Santangelo EM, Azeem M, Borg-Karlson AK, Gustafsson A, Pütsep K. Benzyl isothiocyanate, a major component from the roots of Salvadora persica is highly active against Gram-Negative bacteria. PLoS One 2011; 6(8):e23045. https://doi.org/10.1371/journal.pone.0023045.

[18] Sofrata AH, Claesson RLK, Lingström PK, Gustafsson AK. Strong Antibacterial Effect of Miswak Against Oral Microorganisms Associated With Periodontitis and Caries. J Periodontol 2008; 79(8):1474–9. https://doi.org/10.1902/jop.2008.070506.

[19] Vahabi S, Najafi E, Alizadeh S. In vitro antimicrobial effects of some herbal essences against oral pathogens. J Med Plant Res 2011; 5(19):4870–8.

[20] Sahu MK, Swarnakumar NS, Sivakumar K, Thangaradjou T, Kannan L. Probiotics in aquaculture: Importance and future perspectives. Indian J

Accepted Article

Microbiol 2008; 48(3):299–308. https://doi.org/10.1007/s12088-008-0024-3.
[21] Tiyaboonchai W. Chitosan Nanoparticles : A Promising System for Drug Delivery. Naresuan Univ J 2003; 11(3):51–66.
[22] Jothi MV, Bhat KM, Pratibha PK, Bhat GS. The evaluation of a biodegradable dental chip containing chlorhexidine in chitosan base as a targeted drug delivery in the management of chronic periodontitis in patients. Drug Dev Res 2009; 70(5):395–401. https://doi.org/10.1002/ddr.20316.
[23] Löe H. The Gingival Index, the Plaque Index and the Retention Index Systems. J Periodontol 1967; 38(6):610–6. https://doi.org/10.1902/jop.1967.38.6.610.
[24] Lang NP, Nyman S, Senn C, Joss A. Bleeding on probing as it relates to probing pressure and gingival health. J Clin Periodontol 1991; 18(4):257–61. https://doi.org/10.1111/j.1600-051X.1991.tb00424.x.
[25] Glavind L, Löe H. Errors in the clinical assessment of periodontal destruction. J Periodontal Res 1967; 2(3):180–4. https://doi.org/10.1111/j.1600-0765.1967.tb01887.x.
[26] Khanam A, Ahmad A, Iftikhar N, Ali Q, Fatima T, Alswailmi FK, et al. Variation in Phenolic Profile, Antioxidant, and Anti-Inflammatory Activities of Salvadora oleoides Decene. and Salvadora persica L. Fruits and Aerial Part Extracts. Life 2022; 12(9):1446. https://doi.org/10.3390/life12091446.
[27] Bokhary T, Refaat B, Bakr ES, Baz S, Rajab B, Gadalla H, et al. Salvadora persica extract attenuates cyclophosphamide-induced hepatorenal damage by modulating oxidative stress, inflammation and apoptosis in rats. J Integr Med 2022; 20(4):348–54. https://doi.org/10.1016/j.joim.2022.05.001.
[28] Lebda MA, El-Far AH, Noreldin AE, Elewa YHA, Al Jaouni SK, Mousa SA. Protective Effects of Miswak (Salvadora persica) against Experimentally Induced Gastric Ulcers in Rats. Oxid Med Cell Longev 2018; 2018:6703296. https://doi.org/10.1155/2018/6703296.
[29] Soskolne WA. Subgingival delivery of therapeutic agents in the treatment of periodontal diseases. Crit Rev Oral Biol Med 1997; 8(2):164–74. https://doi.org/10.1177/10454411970080020501.
[30] Grisi DC, Salvador SL, Figueiredo LC, Souza SLS, Novaes AB Jr, Grisi MFM. Effect of a controlled-release chlorhexidine chip on clinical and microbiological parameters of periodontal syndrome. J Clin Periodontol 2002; 29(10):875–81. https://doi.org/10.1034/j.1600-051X.2002.291001.x.

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Table 1: The variations in PI that were observed between the groups before and after treatment. Every value is expressed as the mean difference, which is statistically significant at the level of $p<0.05$.

Type of Treatment	Visit	N	Pearson Chi-Square	df	Significance
Control	Pre-Treatment Post-Treatment	60	0.292	1	NS
Chitosan	Pre-Treatment Post-Treatment	60	0.031	1	S
Salvadora persica	Pre-Treatment Post-Treatment	60	0.026	1	S
BITC	Pre-Treatment Post-Treatment	60	0.009	1	S

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Table 2: Mean BOP before and after treatment. The mean difference is statistically significant at the $p<0.05$ level for all values.

Type of Treatment	Visit	N	Pearson Chi-Square	df	Significance
Control	Pre-Treatment Post-Treatment	60	0.024	1	S
Chitosan	Pre-Treatment Post-Treatment	60	0.008	1	S
Salvadora persica	Pre-Treatment Post-Treatment	60	0.024	1	S
BITC	Pre-Treatment Post-Treatment	60	0.009	1	S

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513 **Table 3:** Mean of PPD Pre- and Post-Treatment. All values are expressed as mean

514 difference is significant at ($p<0.05$) level.

Treatment	Visit	N	Mean (pre & post)	Mean difference (pre & post)	SD	T-statistics	P-value	Significance
Control	Pre-treatment	60	5.52	0.82	0.567	**11.152**	0.001	S
	Post-treatment		4.52					
Chitosan	Pre-treatment	60	6.08	1.00	0.759	**10.204**	0.001	S
	Post-treatment		5.27					
Salvadora Persica	Pre-treatment	60	7.15	1.55	0.891	**13.473**	0.001	S
	Post-treatment		5.60					
BITC	Pre-treatment	60	5.90	1.27	0.594	**10.281**	0.001	S
	Post-treatment		4.63					

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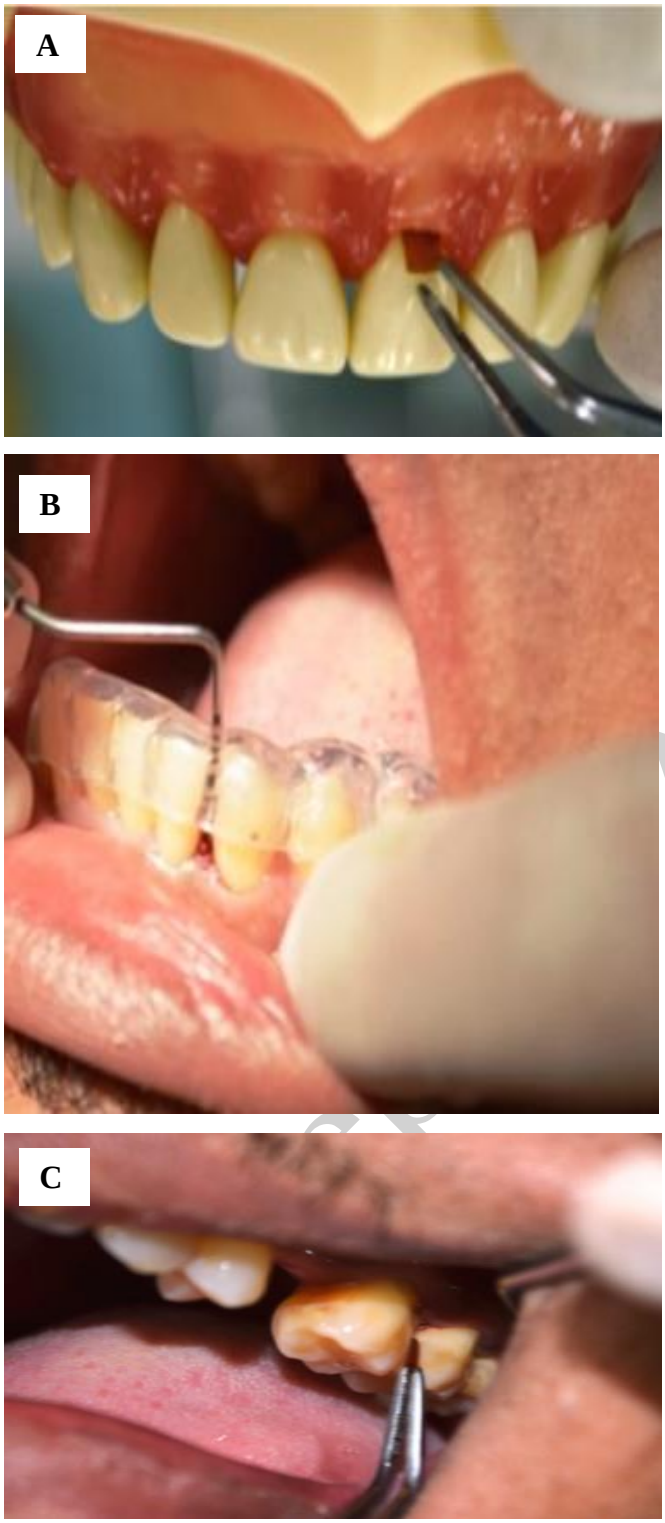

Figure 1: A: Picture showing the insertion of the Miswak chip into the pocket on a Frasaco model for patient dental education, demonstration and simulation model. **B:** Method of measuring periodontal pocket using acrylic stent pre and post treatment. **C:** Insertion of the a Miswak chip inside the periodontal pocket of a patient.

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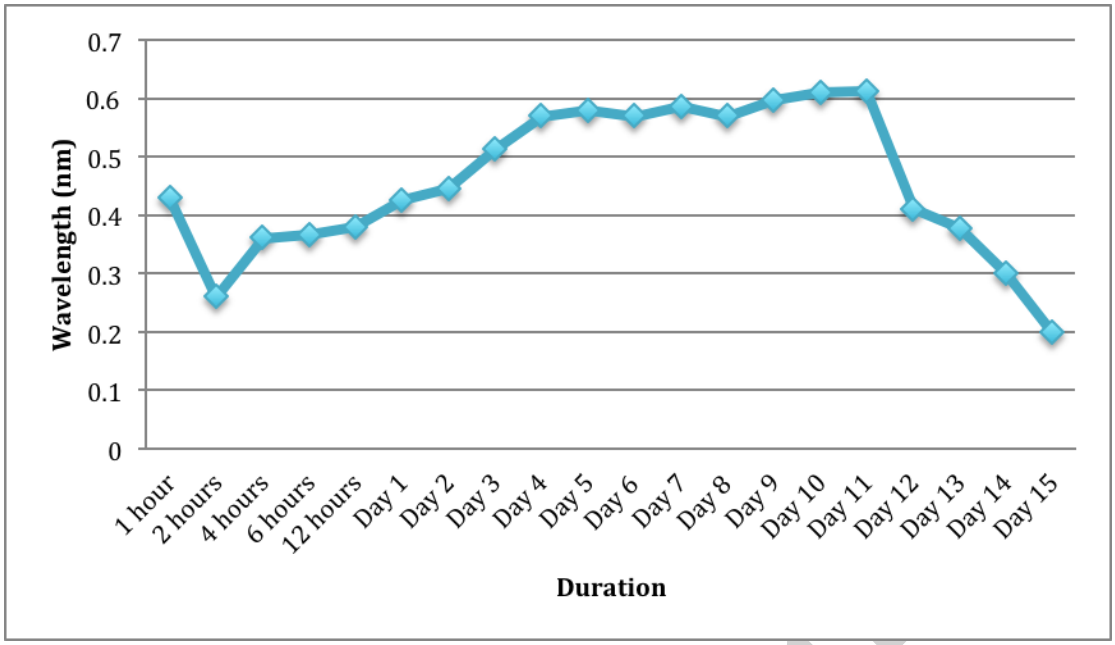

Figure 2: Research on the release of drugs by *S. persica* in vitro.

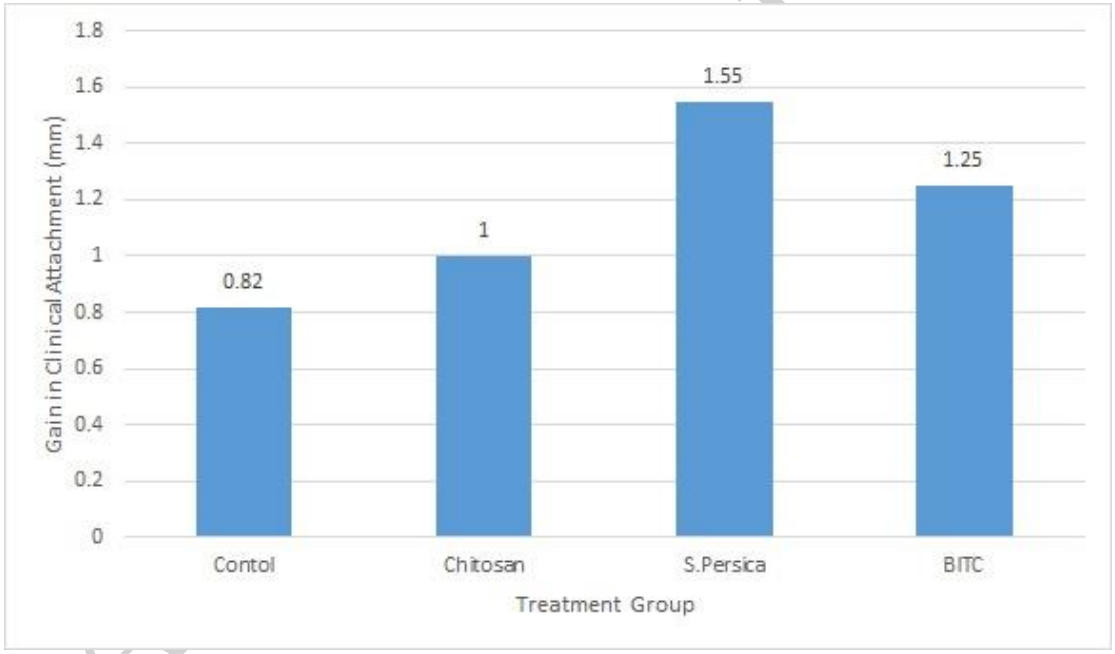

Figure 3: Comparative analysis of CAL gain in four groups measured in millimetres.