Abstract  Background and aim: Compliance in the use of daily oral antiseptics can probably be enhanced by prescribing easily-applied bioadhesive tablets which slowly release chlorhexidine (CHX). This could also be of use in patients with difficulties in rinsing or performing mechanical plaque control. The aim of the present study was to evaluate the capacity of bioadhesive tablets containing either 30 mg or 40 mg of CHX to inhibit de novo plaque formation. Method: In this single, examiner-blinded, crossover study, 22 volunteers between 21 and 25 years of age refrained from oral hygiene for 4 days. Bioadhesive mucosal tablets containing 30 mg or 40 mg of CHX were applied in the canine region. Rinses with a 0.2% CHX solution and placebo tablets served as controls. Plaque regrowth was evaluated with the Quigley-Hein Index modification of Turesky and by an automatic image analysis system (AIA) using slides of stained plaque. Rinsing and application of the tablets were done under supervision twice daily. Results: According to the plaque index, plaque regrowth was significantly inhibited by CHX rinses ($P<0.001$) and by tablets with 40 mg of CHX ($P<0.02$) for all teeth and surfaces. Placebo tablets and 30-mg CHX tablets had no plaque-inhibiting effect. For taste, the subjects preferred the placebo and the 30-mg tablets more than the rinses and 40-mg tablets. In 3/22 of the subjects, superficial mucosal lesions were found at the side of application of the 40-mg tablets. Using the AIA system for evaluation of plaque regrowth, similar results for plaque inhibition were found. Conclusion: It can be concluded that bioadhesive mucosal tablets containing 40 mg of CHX can inhibit plaque regrowth as well as 0.2% CHX rinses. However, unpleasant taste and superficial mucosal lesions are local side effects to be considered.

Keywords  Bioadhesive tablet · Chlorhexidine · Dental plaque

Introduction

Antiseptic agents have been widely used in the prophylaxis of gingivitis and periodontal disease, and much experience has been gained with chlorhexidine (CHX) through almost 30 years of research and clinical use. The ability of chlorhexidine to prevent dental plaque formation and inhibit the development of gingivitis has been well documented [30, 35]. Chlorhexidine is considered the gold standard for comparison and study of other potential antiplaque agents [3, 22].

Numerous studies have confirmed the plaque-inhibiting effect of CHX [3, 22] rinses used alone or in combination with mechanical tooth cleaning [1, 23, 29, 34]. Antiseptics delivered as a rinse are not distributed equally to all areas of the mouth [24]. Therefore, in some studies, CHX has been incorporated in pulsating jet irrigation [12], sprays [20, 21], dentifrices [17, 22, 29, 43], strips, varnishes, and chewing gum [6, 40]. Attempts to prolong the effect by incorporating CHX into a gel did not improve the clinical outcome significantly [27, 32]. For the treatment of subgingival areas, sustained-release devices with antiseptics, mainly CHX, have been used [2, 37]. For subgingival application, CHX has been incorporated in solid thin biodegradable membranes in combination with scaling and root planing, providing better clinical results [36, 37].

The plaque inhibitory action of CHX is dose-dependent [13, 14, 25], increasing with dose, with a plateau effect occurring between twice-daily doses of 10 mg and
20 mg. At even higher doses, further small improvements in plaque inhibition have been found, although the side effects such as staining, mucosal erosion, and taste disturbance become more important [4, 31]. Because of this dose response, concentrations can be varied in different vehicles. Long-term use of CHX is not advocated because of the side effects [19].

The use of slow-release devices becomes more important if CHX is used as a replacement for mechanical plaque removal and not merely as an adjunct to toothbrushing. Dentures or orthodontic appliances can create a problem for efficient mechanical plaque removal. After oral or periodontal surgery, brushing is suspended or at least hampered for some time. In some special patient groups, even rinsing can be difficult or impossible: hospitalized, mentally and physically handicapped, geriatric, and terminally ill patients. Chlorhexidine spray has been used in terminally ill patients with some benefit but still had considerable disadvantages in daily application [26]. According to conclusions of the First European Workshop on Periodontology, the most valuable uses of chemical plaque control are in the short-to-medium term and by active CHX products, particularly when mechanical tooth cleansing is impossible, difficult, or inadequate [7].

Since the incorporation of an antiseptic agent into a certain vehicle does not guarantee in vivo availability and efficacy, clinical testing is essential [33]. Van der Ouderaa [35] suggested a number of basic requirements for the delivery of antiplaque agents in a certain vehicle: stability of the product, optimal bioavailability, no adverse reactions, simplicity of use, and a good cost:benefit ratio. In the absence of oral hygiene, primary in vivo testing of new products or application formulations can be done in a plaque regrowth model over a limited time period [5]. Bioadhesive mucosal tablets containing fluorides have been used successfully in the past as slow-release devices [10, 11]. To our knowledge, they have not been used for supragingival chemotherapeutic plaque control.

The aim of the present study was to evaluate clinically and with computerized image analysis (CIA) the inhibition of de novo plaque formation by adhesive tablets containing CHX compared to 0.2% rinses with CHX twice daily in a 4-day plaque regrowth model.

**Material and methods**

Twenty-two young, healthy volunteers (nine males, 13 females, average age 23.4 years, range 20–25) were selected for this single, examiner-blinded, crossover study. All were Caucasians and the majority were nonsmokers (n=16). None of them used antibiotics, corticosteroids, or drugs influencing plaque formation, nor had they used another antimicrobial product within 2 weeks before or during the study. They had no restorations in the upper front region, no crown or bridgework, and no orthodontic appliances. They had a minimum of 24 natural teeth. Probing depth never exceeded 3 mm.

Two weeks prior to the start of the study, all subjects were enrolled in an oral hygiene program to achieve clinically healthy gingival conditions. Volunteers were subjected to four different regimens on alternate weeks: 0.2% CHX rinse, bioadhesive slow-release tablets containing 30 mg of CHX, tablets containing 40 mg, and placebo tablets. The sequence of the four different products was random. Between experiments, there was a washout period of 10 days. During the washout period, all subjects used the same type of toothbrush (Sensodyne) and sodium laurylsulphate-free toothpaste (Sensodyne).

The tablets were fabricated in the Laboratory of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences, Gent University. In essence, they consisted of drum-dried cornstarch, carbopol 974P, and doses of CHX acetate. The CHX acetate dosage was equivalent to a 30-mg or 40-mg CHX gluconate dose in a rinse. The rinse was a commercial solution of 0.2% CHX (Corsodyl).

At the beginning of each test period, zero plaque scores were obtained by thorough professional prophylaxis. Plaque removal was carefully checked using a 0.5% erythrosine dye. The subjects were instructed not to perform any oral hygiene for 4 days and not to change their normal diet and eating habits.

The tablets were placed in the apical region of the upper left or right canine alternately twice daily, under supervision. At day 4, plaque accumulation along the gingival margin at the mesial, distal, buccal, and lingual/palatal surfaces of all teeth was evaluated after staining with 0.5% erythrosine dye using the Turesky et al. modification [39] of the Quigley-Hein plaque index [41]. The intraexaminer reliability for plaque scoring was 94%. All scoring was done by the same blinded investigator.

Standardized photographs were taken of the six upper front teeth using a reproducible method [18]. For this purpose, a stent in acrylic was made for each subject, perfectly fitting the upper jaw. This stent was then fixed to the camera, providing a constant distance and inclination to the upper front teeth. The area of plaque on the buccal and interproximal surfaces of two upper front teeth (21 and 13), expressed in percentage of the total tooth surface, was then calculated using CIA. Based on gray levels, each image was digitized. Relative to a standard reference, the percentages of total surface and of stained plaque surface were computed. The intraexaminer reproducibility of the measurements, which were all performed by a single investigator, was 97.8% [18].

On day 4, the subjects rated taste, taste disturbance, and user friendliness on a visual analogue scale (VAS) from 0 (no taste) to 10 (worst possible taste imaginable). For user friendliness, 10 was considered “very friendly and easy to use.” For mucosal lesions, a score of 10 was considered to be extremely painful and irritative, while no pain at all was 0 on the VAS. At day 4 after data collection, professional cleaning was performed. All volunteers completed the study.