Official title: Whitening Efficacy of Dentifrice Containing 10% High Cleaning Silica, 0.5% Sodium Phytate and 0.5% Sodium Pyrophosphate

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Study Population and Design

This clinical trial was conducted at Guanghua School of Stomatology, Sun Yat-sen University, Guangzhou, China, from May to October 2018. The study protocols were approved by the institutional review board at Guanghua School of Stomatology, Sun Yat-sen University and were in good accordance with the World Medical Association Declaration of Helsinki on ethical aspects. This eight week study used a randomized, double-blind, parallel-group design.

The participants were informed of the study purposes and told that their participation was voluntary. Informed consent forms were signed. A total of 84 adults who met with the inclusion and exclusion criteria were invited to take part in the study. The inclusion criteria were: 1) aged 18 to 70 years old; 2) good general health; 3) able to attend the clinical examinations during the eight week study period; 4) possessing more than 20 natural permanent teeth that were uncrowned or not heavily filled with restorative materials, excluding third molars; 5) having a whole-mouth mean tooth composite stain index of more than 1.5 according to the Lobene Stain Index.(1) Exclusion criteria were: 1) severe oral diseases or chronic diseases; 2) advanced periodontal diseases; 3) pregnant or lactating females; 4) fluorosis or tetracycline teeth ; 5) wearing orthodontic bands or partial or removable dentures; 6) taking part in other clinical trials; 7) receiving prophylaxis during the previous 3 months or tooth whitening treatment during the past 6 months; 8) allergic to the study products.

Study procedures

Eligible patients were distributed into test and control groups randomly according to computer generated random numbers externally by a dentist. This dentist kept the randomization and group allocation information. All the other study personnel did not have access to the information during the course of the study.

The patients in the test group were given toothpaste containing 10% high cleaning silica, 0.5% sodium pyrophosphate and 0.5% phytic acid, while the patients in the control group were given a negative control toothpaste containing silica base without any active ingredient. All toothpastes were identical in appearance and taste. The

toothpaste was marked with its specific code number which represented its group allocation and this number was not decoded until the end of the study. The distribution of the toothpaste was made in a separate place to ensure that other study personnel and patients were unaware of group assignment.

The patients were asked to only use the assigned toothpaste and the same toothbrush to brush their teeth twice daily, in the morning and in the evening, for one minute. The patients were asked to maintain their other oral hygiene habits and daily eating habits. The patients were not allowed to use any other toothpastes sand oral health care products, such as mouthrinse.

The patients came to the clinic to receive clinical examinations atbaseline, 4 weeks and 8 weeks. The same examiner provided the clinical examinations during the course of the study. Firstly, evaluation of oral soft and hard tissues were performed. The examiner assessed soft and hard palate, oral mucosa, tongue, sublingual and mandibular areas, salivary glands and pharynx and larynx areas of each patient. Secondly, tooth stain of the anterior teeth were measured using the Lobene Stain Index. The index measures the area and intensity of extrinsic tooth stain on the facial and lingual surfaces of six lower anterior teeth and facial surfaces of six upper anterior teeth. The tooth surfaces were divided into two regions: body and gingival. For each part, the intensity and extent of extrinsic tooth stain were graded on a scale of 0-3. For stain intensity, the scale is scored as follows: 0= No stain; 1=Light stain (yellow to light brown or gray); 2=Moderate stain(medium brown); and 3=Heavy stain(dark brown to black). For stain area, the scale is scored as follows: 0= No stain detected; 1= stain covering up to 1/3 of the region; 2= Stain covering >1/3 to 2/3 of the region; and 3=Stain covering >2/3 of the region. Three variables on tooth stain were calculated for each patient. The mean Lobene stain area, intensity and composite scores were the sum of the scores on the the recorded regions of tooth surfaces divided by the number of regions. The stain composite score for each region of the tooth surfaces was the stain area score multiplied by the stain intensity score.

At 4 weeks and 8 weeks, during the follow up examinations, the patients were also

questioned by an investigator about if they had experienced any adverse events. The adverse events included discomfort while brushing, bitter or alteration in taste, any allergic reactions arising from the use of the toothpastes and any feeling of changes on oral soft tissues. Any changes in general health conditions of the patients were also monitored.

After the patient finished each examination session, the acquired data were collected by the facilitator who kept the data. The other study personnel had no way to access the patient data during the course of the study.

Statistical analysis

According to the data from a previous study on tooth stain removal, the sample size of this study was calculated. Based on a a standard deviation of 0.5 for tooth stain area score, a reduction in the mean stain intensity scores of 20% between the test and control groups, a power of 80%, a significance of 0.05, and an attrition of 10%, it was estimated that 40 patients needed to be included in each group.

Chi-square test and the independent *t* test were conducted to compare the differences between treatment groups on sex, age and baseline Lobene stain scores. ANCOVA with baseline Lobene score as the covariate was conducted to compare the differences between groups in follow-up Lobene area, intensity and composite stain scores. For each group, paired *t* tests were conducted to compare the differences between baseline and each of the two follow-ups in Lobene stain scores. All statistical analyses were two sided and at a significance level of $\alpha = 0.05$.

Study Protocol and Statistical Analysis Plan