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The Effects of a Toothpaste Containing the Active Ingredients of *Galla chinensis* and Sodium Fluoride on Dentin Hypersensitivity and Sealing of Dentinal Tubules: An *In Vitro* Study and an Eight-Week Clinical Study in 98 Patients

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Background: This study aimed to evaluate the desensitizing effect of toothpaste containing the active ingredients of an extract of *Galla chinensis*, both *in vitro* and in patients with dentin hypersensitivity.





Material/Methods: Ninety-eight patients with dentin hypersensitivity were divided into two study groups and given toothpaste containing either the active ingredients of *Galla chinensis* extract and sodium fluoride, or a control toothpaste containing only sodium fluoride. Assessments included the tactile stimulation test and the Schiff cold air sensitivity scale, which were conducted at the baseline examination and after 4 and 8 weeks of dental brushing. Twenty-five intact human premolars from 24 patients with dentin hypersensitivity were prepared and randomly divided into four groups, the untreated baseline group, the study group, the positive control group, and the control group. After brushing with different toothpaste for 7 days, the effects on dentinal tubule sealing in each group was determined by scanning electron microscopy (SEM), and the degree of dentinal tubule plugging and diameter of the open dentinal tubules were calculated.

Results: Toothpaste containing the active ingredients of *Galla chinensis* and sodium fluoride significantly reduced the degree of dentin hypersensitivity when compared with toothpaste containing sodium fluoride alone after 4 weeks and 8 weeks of use. Toothpaste containing the active ingredients of *Galla chinensis* significantly reduced the number and diameter of the open dentinal tubules.

Conclusions: Toothpaste that contained the active ingredients of *Galla chinensis* and sodium fluoride reduced the symptoms of dentin hypersensitivity by sealing the dentinal tubules.

MeSH Keywords: **Dentin • Medicine, Chinese Traditional • Sodium Fluoride • Toothpastes**

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Background

Dentin hypersensitivity is a common condition associated with pain from hot and cold food and drinks, and to physical and osmotic pressure, and is associated with the porosity of the dentin tubules. Dentin adhesives and desensitizers are now added to toothpaste to relieve the pain of dentin hypersensitivity [1–3]. Loss of enamel and gingival recession caused by abrasions, wear, acid erosion, and fracture can all lead to dentin exposure [4]. Worldwide, the prevalence of dentin hypersensitivity is between 1.3–92.1%, with an average prevalence of 33.5% [5]. Dentin hypersensitivity frequently occurs in women aged between 20–40 years, and occurs most often in the pre-molar and canine teeth [6,7]. The symptoms associated with dentin hypersensitivity, such as pain and soreness, often influence the choice of diet and may reduce the quality of life.

The pathogenesis of dentin hypersensitivity remains unclear. The representative theories include fluid dynamics, nerve terminal conduction, and odontoblast conduction. Nerve terminal conduction theory believed that nerve endings extended to the enamel-dentin boundary through the dental pulp and dentin [8]. Odontoblast conduction theory believed that odontoblasts are the receptors of external stimuli and transmit signals to nerve endings [9]. The hydrodynamic theory proposed by Brännström [10] is the most widely accepted theory used to explain dentin hypersensitivity. This theory proposes that when dentin is exposed due to various reasons, external stimulation causes excessive fluid flow in the dentinal tubules, which causes the relaxation or compression of odontoblast processes, which affects the peripheral nerve endings to generate pain and other sensations [10,11].

Therefore, the current treatment of dentin hypersensitivity aims to block the dentinal tubules, isolate the external stimuli, prevent the flow of tubular fluid, and reduce the pulp nerve fiber reactivity. The active ingredients of desensitized toothpaste include fluoride, arginine, calcium-containing compounds, and strontium chloride compounds [12,13]. Laser and periodontal soft tissue treatment, and the use of diffuse depolarizing agents, such as potassium ions, may reduce the activity of the pulpal nerve [14]. Although these methods have some effect on reducing dentin hypersensitivity, the long-term therapeutic effect is unsatisfactory [15]. Therefore, there remains a need to identify safe and effective treatments for dentin hypersensitivity.

Traditional Chinese medicine has the advantage that medicines are based on natural compounds that are widely available and are simple to manufacture. *Galla chinensis* is an astringent that is commonly used in Chinese herbal medicine. The active ingredients of *Galla chinensis* are tannic acid and gallic acid. Tannic acid, also known as gallotannic acid, is a polymer of gallic acid,

both of which are polyphenols. Polyphenols contain abundant hydroxyl and carboxyl, can interact with collagen fibers in the dentin, forming large side chains of amino acids through multiple hydrogen bonds, after cross-linking among them, the mechanical and chemical properties and structural stability of the dentin were enhanced [16–19]. Also, polyphenols bind strongly with metal ions such as Ca^{2+} , which can promote the formation of minerals with hydroxyapatite, which is the main component of dentinal tubules. Hydroxyapatite can combine with negatively charged tannic acid to seal the dentinal tubules [19–22]. Tannic acid also has a strong affinity for gallic acid and protein and can precipitate protein [23,24]. *Galla chinensis* may reduce dentin hypersensitivity due to multiple effects.

Therefore, this study aimed to evaluate the desensitizing effect of toothpaste containing the active ingredients of an extract of *Galla chinensis*, both *in vitro* and in patients with dentin hypersensitivity.

Material and Methods

Study ethics and approvals

Based on the standard method for evaluating dentin sensitivity in the Guidelines for design and conduct of clinical studies on dentin hypersensitivity [25], originally compiled in the Netherlands, two independent clinical stimuli were used to assess the degree of dentin hypersensitivity. This study was conducted for 8 weeks and was approved by the Clinical Ethics Committee of the Affiliated Stomatological Hospital of Chongqing Medical University, China (Approval No. 2018-1). All study participants provided signed written informed consent.

Materials and instruments

In the study group, the main ingredients of the toothpaste were the active ingredients of *Galla chinensis* (concentration 2%) and sodium fluoride (fluorine content 1,450 ppm). In the control group, the main ingredient of the toothpaste was sodium fluoride (fluorine content, 1,450 ppm). The toothpaste used in both groups was packed in a white tube without a commercial label. The type 2000A Yeaple Electronic Force-Sensing Probe (Yeaple, Pittsford, NY, USA) was calibrated according to the manufacturer's instructions before use.

Study participants

Inclusion criteria

Participants were included in the study who were in good general health and had no systemic disease. The study participants were aged between 18–70 years, were able to participate in

the study, had complete medical records, and were able to sign written informed consent. The study participants had at least one tooth (bicuspid or anterior tooth) that was affected by dentin hypersensitivity, and showed tooth neck abrasion or gingival retraction and with a tactile stimulation test score of 10–30×g of force using the Yeaple probe and a cold air stimulus score of ≥ 2 .

Exclusion criteria

Individuals were excluded from the study who were pregnant or breastfeeding, who had physical disabilities, or who were unable to brush their teeth, or who had a history of allergies to any personal oral care product or ingredient, or who were taking anticonvulsants, antihistamines, antidepressants, sedatives, tranquilizers, and anti-inflammatory drugs within the previous month. Severe dental, periodontal, and mucosal diseases, and a history of periodontal treatment, including periodontal surgery, in the past year, excluded individuals from the study. Individuals who had sensitive teeth but with one of the following conditions were excluded from the study, teeth with large restorations, abutment of teeth of removable partial dentures, dental caries, enamel cracks, leakage of fillings or other restorations, cracked teeth, dental pulp lesions, dental abscesses, pulpitis, and atypical facial pain. Any individual was excluded from the study who was currently or who had recently participated in studies to investigate desensitizing toothpaste, used desensitizing toothpaste daily in the past three months, or who were participating in other clinical studies.

Clinical examination at baseline and the study protocol

After each subject signed informed consent, they were asked about their medical history and drug use. All subjects were given an oral soft and hard tissue examination and a dentin hypersensitivity assessment. The levels of dentin hypersensitivity in the affected teeth were assessed by two methods, the tactile stimulation test with an electronic pressure-sensitive probe, the Yeaple probe, and the thermally controlled Schiff cold air sensitivity scale. In accordance with the inclusion criteria and the exclusion criteria, eligible study participants were randomly divided into the study group and the control group. The study participants brushed their teeth only with the provided toothpaste and soft toothbrush, once in the morning and once in the evening, for 2 minutes each time. The toothpaste was squeezed onto the end of the toothbrush.

The study participants did not eat or drink within 30 minutes after brushing. The toothbrush and toothpaste used in this study were not shared with other study participants. Otherwise, the subjects maintained their usual personal oral hygiene habits, daily diet, and smoking habits, but could not use other dental care products such as toothpaste, mouthwash, floss, and

toothpicks. All subjects were re-examined after 4 weeks and 8 weeks of continuous use of the toothpaste. Subjects were asked to refrain from any oral hygiene measures or chewing gum within 4 hours, and not to eat or drink within 2 hours before the examination.

The second clinical screen, the tactile stimulation test, and the Schiff cold air sensitivity test

After the baseline measurements and at 4 weeks of continuous use of the toothpaste, the second screen was performed. Subjects underwent oral soft tissue and hard tissue examination, the tactile stimulation test, and the Schiff cold air sensitivity test. After the baseline measurements and 8 weeks of continuous use of the toothpaste, the third examination was performed. Subjects underwent oral soft tissue and hard tissue examination, the tactile stimulation test, and the Schiff cold air sensitivity test. The interval between the tactile stimulus and the cold air blast test was not less than 5 minutes [26]. The tests for all subjects were performed by two dentists with standardized training and experience in dentin hypersensitivity assessment. One dentist completed the tactile stimulation test, and the other dentist completed the Schiff cold air sensitivity test. Before the beginning of each test, the examiner conducted a reproducibility test ($\kappa > 0.9$).

The tactile stimulation test using a Yeaple probe

An electronic pressure-sensitive probe, the Yeaple probe, was calibrated before each use. Tactile hypersensitivity was evaluated as previously described [27]. Subjects were instructed to respond when they first experienced discomfort when the tip of the Yeaple electronic pressure-sensitive probe contacted the exposed dentin area of the sensitive teeth. The probe was vertically pressed to the examined tooth surface beginning at a preset force of 10×g, which increased by 10×g increments until the subjects experienced discomfort or until 80×g of force was applied. The corresponding force value was recorded when the subject responded, and if the subject did not respond at 80×g, the pressure was recorded as $>80\times g$. Higher Yeaple probe test scores indicated less tooth sensitivity.

The Schiff cold air sensitivity test

Air was delivered from a standard dental unit air syringe with a pressure of 60 psi and a temperature of 19–21°C. Air was directed at the exposed dentin surface of the sensitive tooth for one second. Cotton balls were used to isolate the adjacent teeth during the air blast to prevent inaccurate results. Each tooth was examined once. The Schiff cold air sensitivity scale [28] was used to evaluate the air blast hypersensitivity score, as follows: 0, the tooth/subject did not respond to the air stimulus; 1, the tooth/subject responded to the air

stimulus, but did not request suspension of the stimulus; 2, the tooth/subject responded to the air stimulus and asked to stop or remove the stimulus; 3, the tooth/subject responded to the air stimulus, which caused pain, and the subject requested discontinuation of the stimulus.

Safety assessment

At baseline, and after 4 weeks and 8 weeks of toothpaste use, all subjects were required to undergo a safety assessment to evaluate the biological safety of the test toothpaste and the control toothpaste, including the oral soft tissue and hard tissue. Health checks were performed of the soft and hard palates, gingival mucosa, buccal mucosa, tongue, sublingual and submandibular areas, salivary glands, tonsils, and pharynx. These tests were performed to document the occurrence and causes of any adverse events.

Establishment of the *in vitro* dentin hypersensitivity model

The method of establishment of the *in vitro* dentin hypersensitivity model was as previously described [29]. The study included 25 premolars extracted during orthodontic procedures, which had no caries, no cracks, and no defects. The extracted teeth were immersed in 0.05% thymol solution (0.5 g/L), and stored in a 4°C refrigerator for no more than one month.

The soft tissues on the root surface were removed, and a dental hard tissue cutter was used to cut the crown and root of each tooth at 1 mm above and below the cemento-enamel junction. The tooth block at the neck of the tooth was retained and the cemento-enamel junction was in the middle of the tooth block. The tooth blocks are cut into two sections at the labial side and the lingual side. Silicon carbide sandpaper (No. 600, No. 1200, No. 3000, No. 5000) (MATADOR, Remscheid, Germany) was used to remove tooth enamel on the buccolingual side under running water, and the dentine at 1 mm below the enamel-dentinal junction was retained. There were 50 dentin sections obtained. All samples were incubated in 0.5 M of ethylenediamine tetra-acetic acid (EDTA) solution for 0.5 hours and washed using an ultrasonic cleaner (KQ-SOB) (Kunshan Ultrasonic Instruments Co., Ltd., Kunshan, China) for 2 h. Under a polarizing microscope, 24 dentin slices with no cracks, and open dentinal tubules were selected and placed in deionized water for future use.

Preparation of artificial saliva

The method of preparation of artificial saliva was as previously described [30]. The chemical composition of the artificial saliva included 1.5 mmol/L CaCl₂, 130 mmol/L KCl, 0.9 mmol/L KH₂PO₄, 20 mmol/L HEPES, 1 mmol/L NaN₃, and 2% bovine serum

albumin (BSA). Artificial saliva was adjusted to pH 7.0 using 2 mol/L of NaOH solution. Artificial saliva was prepared daily.

Sample processing

The 24 dental samples were embedded in paraffin wax, and the labial or lingual dentine on both labial and lingual sides were exposed. The samples were randomly divided into the untreated baseline group, the study group (desensitizing toothpaste containing active ingredients of *Galla chinensis*), the positive control group (toothpaste containing sodium fluoride alone), and the control group (deionized water). The baseline group received no treatment. The study group and the positive control group were brushed with 1.0 g of desensitizing toothpaste containing the active ingredients of *Galla chinensis* and sodium fluoride, and toothpaste containing sodium fluoride alone, respectively, using an electric toothbrush. The control group was brushed with deionized water using an electric toothbrush. The sample was brushed twice a day at 9:00 a.m. and 18:00 p.m. for 3 minutes each time. After brushing, the samples were rinsed with demineralized water for 30 s, placed in artificial saliva, and stored at a 37°C constant temperature water bath. The artificial saliva was changed every 24 h. Samples were treated continuously for 7 days, and then ultrasonically washed for 1 min, and immediately placed in glutaraldehyde fixative solution (Beijing Solarbio Science & Technology Co., Ltd., Beijing, China) at 4°C for 24 hours. The samples were dried at the critical point and coated with gold in an MC1000 Ion Sputter Coater for scanning electron microscopy (SEM). Each sample was observed and photographed at ×1,000 and ×5,000 by scanning electron microscopy (SEM) using a TM3030 scanning electron microscope (Hitachi, Tokyo, Japan).

Scanning electron microscopy (SEM)

The 24 samples were ultrasonically washed for 1 min, and immediately placed in glutaraldehyde fixative solution and fixed at 4°C for 24 hours. The samples were dried at the critical point and coated with gold in an MC1000 Ion Sputter Coater. Each sample was observed and photographed at ×1,000 and ×5,000 by SEM.

Image processing

The SEM images of the samples in each group were stored and imported into Image-Pro Plus version 6.0 image analysis software (Media Cybernetics, Rockville, MD, USA). According to the correction software scale on the image, the gray value was defined to distinguish the area of the open dentinal tubules, and to mark the boundary of the open dentinal tubules (excluding tubules with incomplete edges). The mean area (S_0) and mean diameter (d_0) of dentinal tubules in the untreated baseline samples, and the mean area (S_1) and the

Table 1. Baseline clinical data of the 98 patients with dentin hypersensitivity included in this study.

Group	Age (years)*			Average age (age range)	Number of men* (%)	Number of women* (%)	Total number
	18–35	36–45	>45				
Study group	9	16	22	45.06 (28–68)	20 (42.55%)	27 (57.45%)	47
Control group	5	10	32	48.83 (28–69)	18 (38.30%)	29 (61.70%)	47

* There was no significant difference in age and gender constituent ratio between the study group and the control group.

average diameter (d_1) of the open dentinal tubules in the other study groups were calculated. The plugging rate (PR,%) of the dentinal tubules in each group was calculated by the formula: $(1 - S_1/S_0) \times 100\%$.

Statistical analysis

The efficacy variables for the reduction of dentin hypersensitivity were the change from the baseline in the tactile stimulation test and the Schiff cold air sensitivity scale after 4 weeks and 8 weeks of treatment. All data were analyzed using SPSS version 22.0 software (IBM, Chicago, IL, USA). The gender difference between the study groups and the control groups was analyzed using the chi-squared (χ^2) test. Age difference, the change in values of the tactile stimulation test and the Schiff cold air sensitivity scores between the groups were analyzed using one-way analysis of variance (ANOVA). The significance level (two-sided) was $\alpha=0.05$. The difference in the dentinal tubule sealing effect between the groups was compared with the rank-sum test. Statistical significance was set to $\alpha=0.05$. A P-value <0.05 was considered to be statistically significant.

Results

Baseline clinical data

After baseline examination and according to inclusion and exclusion criteria, 98 eligible subjects were included in this study. There were 94 subjects who completed 8 weeks of treatment. Four subjects who received baseline examination but did not receive 4-week and 8-week examinations, withdrew from the study. The reasons for the withdrawal were not associated with the products used in this study and their data were not included in the statistical analysis. The age and gender of the subjects who completed the study are shown in Table 1. The mean age of the subjects in the study group and the control group was 45.06 years (range, 28–68 years) and 48.83 years (range, 28–69 years), respectively. There was no significant difference in the age and the gender ratio between the two groups. No adverse reactions or side effects caused by the test toothpaste or control toothpaste occurred in the study subjects.

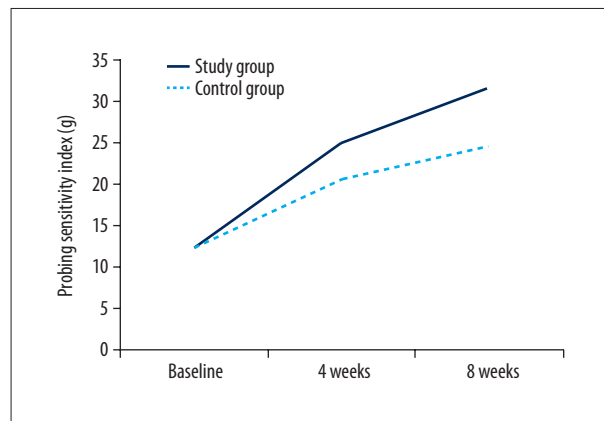


Figure 1. Changes in the tactile stimulation test score in the study group and the control group at baseline and at 4 weeks and 8 weeks after the use of the toothpaste.

The tactile stimulation test

Table 2 and Figure 1 show the tactile stimulation test scores of the two groups and the change from baseline in the scores at 4 weeks and 8 weeks after toothpaste use. At baseline, there was no significant difference in the tactile stimulation test score between the two groups. At 4 weeks and 8 weeks after the toothpaste use, the tactile stimulation test score was significantly higher in the study group than in the control group (Table 2), and the tactile stimulation test score showed an increasing trend from 4 weeks to 8 weeks (Figure 1). These findings indicated that the hypersensitivity of the teeth was reduced in the study group.

Air blast hypersensitivity assessment

Table 3 and Figure 2 show the air blast hypersensitivity score and change from baseline in the score at 4 weeks and 8 weeks after toothpaste use. At baseline, there was no significant difference in the air blast hypersensitivity score between the two groups. At 4 weeks and 8 weeks after toothpaste use, the air blast hypersensitivity score was significantly lower in the study group than in the control group (Table 3), and the air blast hypersensitivity score showed a decreasing trend from 4 to 8 weeks (Figure 2), suggesting that the sensitivity of teeth caused by the cold air stimulus was reduced after treatment.

Table 2. The tactile stimulation test scores in the study group and the control group at baseline and at 4 weeks and 8 weeks after the use of the toothpaste.

Group	Baseline (mean±SD)	4 weeks (mean±SD)	Change in the score *% and P-value	8 weeks (mean±SD)	Change in the score *% and P-value
Study group	12.55±2.70	25.31±5.50	101.67%, P<0.05	31.70±6.13	152.59%, P<0.05
Control group	12.23±3.06	20.74±4.84	69.58%	24.68±4.66	101.80%

* Change in the score=(tactile stimulation test score at 4 weeks or 8 weeks – tactile stimulation test score at baseline)/tactile stimulation test score at baseline×100%

Table 3. The air blast hypersensitivity scores in the study group and the control group at baseline and at 4 weeks and 8 weeks after the use of the toothpaste.

Group	Baseline (mean±SD)	4 weeks (mean±SD)	Change in the score *% and P-value	8 weeks (mean±SD)	Change in the score *% and P-value
Study group	2.309±0.365	1.543±0.323	-33.17%, P<0.05	1.223±0.369	-47.03%, P<0.05
Control group	2.383±0.33	2.011±0.379	-15.61%	1.734±0.307	-27.23%

* Change in the score=(Air blast hypersensitivity score at 4 or 8 weeks–Air blast hypersensitivity score at baseline)/Air blast hypersensitivity score at baseline×100%.

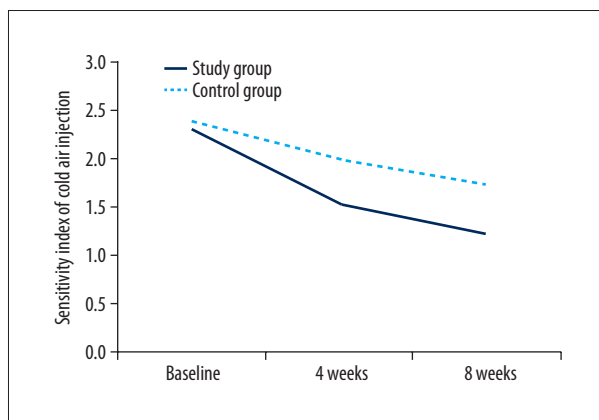


Figure 2. Change in the Schiff cold air sensitivity score in the study group and the control group at baseline and at 4 weeks and 8 weeks after the use of the toothpaste.

The effects on dentinal tubule sealing

Table 4 and Figure 3 show that after the dentin samples were treated with different toothpastes, the plugging rate of dentinal tubules and the diameter of the open dentinal tubules were reduced to different degrees. The significant differences were found between the study group and the control group. Also, sealing of dentinal tubules was more pronounced for toothpaste containing active ingredients of *Galla chinensis* and sodium fluoride compared with the toothpaste containing sodium fluoride alone. Compared with the baseline group, the plugging rate of dentinal tubules and the diameter of the open dentinal tubules were also statistically reduced in the control group.

Table 4. Comparison of the mean area, plugging rate, and diameter of the dentinal tubules between the baseline group, the study group, the positive control group, and the control group.

Groups	Mean area (µm ²)	Plugging rate	Mean diameter (µm)
Baseline group	11.75±3.64 ^{b,c,d}	–	3.78±0.59 ^{b,c,d}
Study group	5.01±2.42 ^{a,c,d}	57.36% ^{a,b,d}	2.36±0.59 ^{a,c,d}
Positive control group	6.67±2.48 ^{a,b,d}	43.23% ^{a,b,d}	2.77±0.55 ^{a,b,d}
Control group	8.82±2.79 ^{a,b,c}	24.94% ^{a,b,d}	3.26±0.51 ^{a,b,d}

^a P<0.05, vs. the baseline group; ^b P<0.05 vs. the study group; ^c P<0.05 vs. the positive control group; ^d P<0.05 vs. the control group.

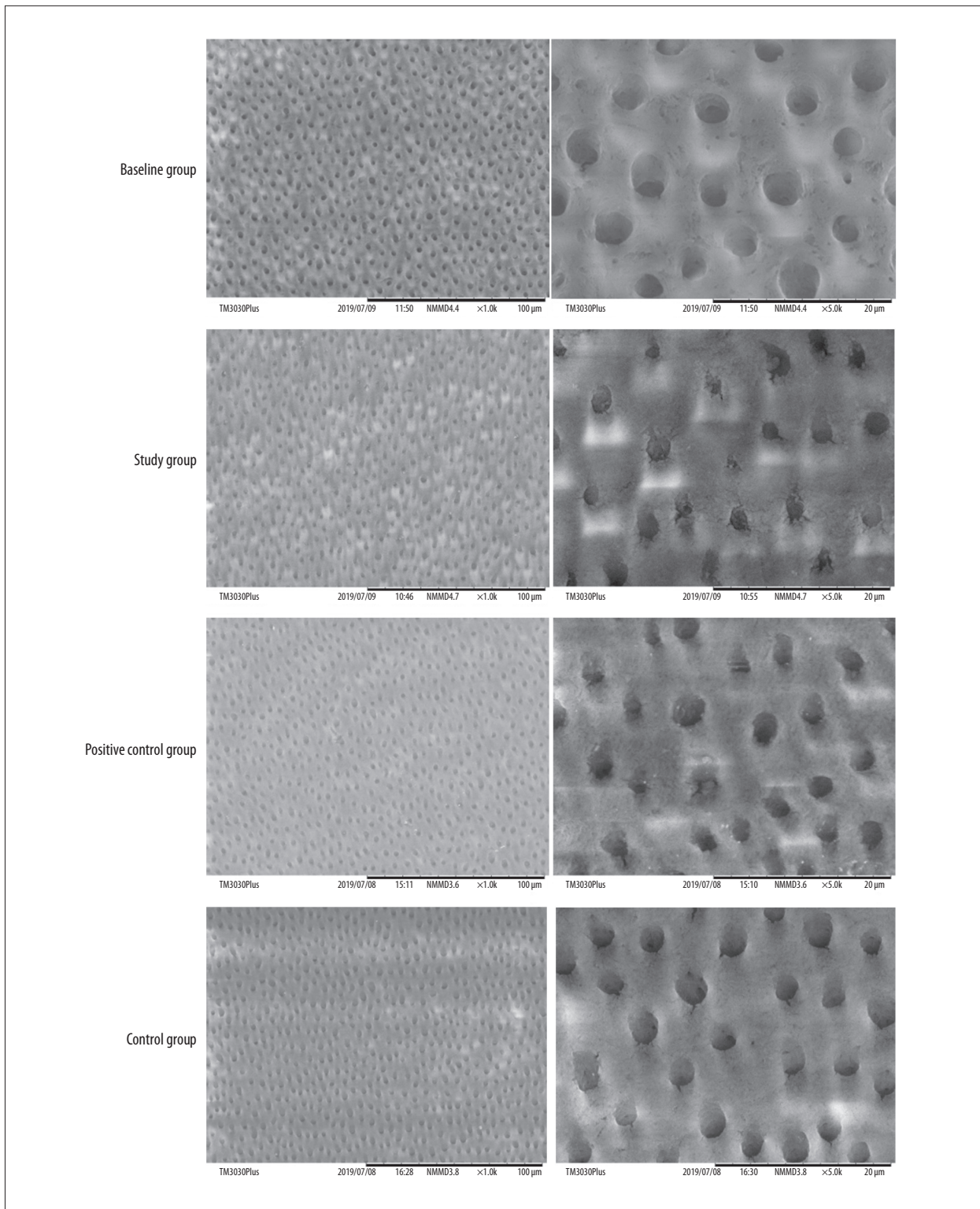


Figure 3. The scanning electron microscopy (SEM) results.

Discussion

Dentin hypersensitivity is a subjective perception of pain caused by external stimuli to the exposed dentin. However, pain has different characteristics, from mild discomfort to severe pain [7,31,32]. Patients do not necessarily have pain responses to all stimuli, and different patients experienced different degrees of pain to the same external stimulus [33–35]. Therefore, two different external stimuli are usually used to evaluate dentin hypersensitivity [36]. According to the guidelines for evaluating the efficacy of desensitizing toothpaste [25], in the present study, dentin hypersensitivity was assessed using the tactile stimulation test with an electronic pressure-sensitive Yeaple probe, and the Schiff cold air sensitivity scale.

In the present study, 94 subjects completed 8 weeks of treatment. All subjects were randomly divided according to gender and age at baseline so that the two groups of subjects were comparable. Compared with baseline, dentin hypersensitivity in response to the tactile stimulus and the air blast was significantly reduced after the use of the toothpaste containing the active ingredients of *Galla chinensis* and sodium fluoride toothpaste for 4 and 8 weeks. Toothpaste containing the active ingredients of *Galla chinensis* showed significantly reduced hypersensitivity compared with sodium fluoride toothpaste. The sealing effect of toothpaste containing both the active ingredients of *Galla chinensis* and sodium fluoride on dentinal tubules was significantly better when compared with the toothpaste containing sodium fluoride alone. Compared with the baseline group, deionized water used in the control group also sealed the dentinal tubules, indicating that saliva may have a dentinal tubule sealing effect.

Dentin contains about 70% minerals, 20% organic matrix, and 10% water by weight. The main ingredient of the dentin organic matrix is type I collagen fibers (90%), which form the scaffold for the deposition of mineral crystals and filling the non-collagen matrix [37]. The active ingredients of *Galla chinensis* are tannic acid and gallic acid, which can cross-link the collagen fibers in dentin [16–19], promote the deposition of minerals with hydroxyapatite as the main ingredient [19–22], and precipitate protein [23,24] to seal dentinal tubules, thereby reducing dentin hypersensitivity. Our previous study showed that open dentinal tubules could be sealed to varying degrees after treatment with tannic acid, gallic acid, and remineralized fluid circulation for 7 days [38]. The results in the present study are consistent with the findings from previous studies. Prajatelista et al. found that gallic acid/metal ion (including Ca^{2+}) was a simple, rapid, and effective method for the treatment of dentin hypersensitivity [22]. Oh et al. showed that the tannin/iron complex had a better effect on dentin tubule sealing than Gluma (a dense polymer resin primarily composed of glutaraldehyde and hydroxyethyl-methacrylate solution),

which could reduce the permeability of dentin tubules and reduce dentin hypersensitivity [39]. However, the disadvantage was that the tannin/iron complex deposited on the surface of dentin turned the dentin purple, which was not an acceptable cosmetic side effect [20].

In this study, no visible discoloration of the crowns of the teeth was found *in vivo*. *Galla chinensis* has previously been reported to inhibit the formation of bacterial biofilms formed by *Streptococcus mutans*, *Streptococcus sanguis*, *Actinomyces viscosus*, and *Lactobacillus lactis* and the formation of acid in the biofilm [39,40]. Also, *Galla chinensis* has previously been reported to inhibit the dissolution of Ca^{2+} and PO_4^{3-} during the development of enamel caries, inhibits enamel demineralization [39,40]. Also, *Galla chinensis* forms a complex with Ca^{2+} in the enamel micropore, resulting in remineralization and promotes the formation of reparative components on the enamel surface at the early stage of the development of dental caries [39,40]. Therefore, *Galla chinensis* may inhibit the development of enamel caries [41–44]. *Galla chinensis* also inhibits dentin demineralization and promotes remineralization. The possible mechanisms may include inhibition of the dissolution of Ca^{2+} in the dentin, stabilizing collagen fibers, and inhibiting the degradation of collagen fibers [45,46]. Also, tannic acid can reduce periodontal tissue damage by inhibiting dental plaque formation, reducing periodontal tissue inflammation by inhibiting inflammatory factors, and promotes periodontal tissue regeneration and repair [47]. However, the role of the toothpaste containing tannic acid, gallic acid, and other bioactive substances in controlling periodontal tissue growth and reducing dentin hypersensitivity requires further investigation.

Fluoride in toothpaste can reduce dentin hypersensitivity to some extent, by the effects of the fluoride ion that seals the dentinal tubules and blocks liquid flow in the dentinal tubules by precipitation of calcium fluoride and fluorapatite [48–50]. A study published by Chatas et al. showed that the application of prophylactic professional polishing paste containing a calcium sodium phosphosilicate formula (Novamin) as an in-office procedure effectively reduced the symptoms of dentin sensitivity after one week of use [51]. In the present study, we used toothpaste containing *Galla chinensis* ingredients and sodium fluoride to reduce dentin hypersensitivity. The results showed that when compared with the toothpaste containing sodium fluoride alone, the sealing effect of the toothpaste containing the active ingredients of *Galla chinensis* and sodium fluoride on dentinal tubules increased and had a greater effect in reducing dentin hypersensitivity. These results suggested that active ingredients of *Galla chinensis* and sodium fluoride in the toothpaste have a synergistic effect. No adverse reactions or side effects were caused by the test toothpaste or the control toothpaste, which indicated that the toothpaste containing the active ingredients of *Galla chinensis* was safe.

In addition to *Galla chinensis*, Chinese herbal medicines, such as *Zanthoxylum nitidum*, *Pinus massoniana*, paeonol, *Angelica dahurica*, asarum, galangal, pepper, *Murraya exotica*, and *Piper longum* have been reported to reduce dentin hypersensitivity [52,55]. Chinese herbal medicines contain a variety of alkaloids, tannins, and volatile oils. Alkaloids have anti-inflammatory, analgesic, and mild local anesthesia effects, and can reduce the sensitivity of dentin and pulp nerve endings. Tannins have a strong astringent effect, which can coagulate proteins in the dentinal tubules to gradually seal them and paralyze nerve endings. Volatile oil also has mild analgesic, nerve paralysis, anti-inflammatory, and analgesic effects. These traditional Chinese active substances can treat dentin hypersensitivity by blocking nerve conduction in the dentinal tubule and paralyzing dental pulp nerve [53–55]. Traditional Chinese medicine has a long history and cultural tradition, and herbal medicines are simple to harvest or produce and do not generate drug resistance [56–58]. Also, the natural compounds used in traditional Chinese medicine have fewer adverse reactions during long-term use [59,60].

Recent studies have shown that 25–46% of people aged between 18–70 years have dentin hypersensitivity [61,62]. In the present study, subjects in the age range of 18–70 years with

dentin hypersensitivity were included. However, we did not divide all subjects into different age groups, and we also did not analyze the effects of the toothpaste containing active ingredients of *Galla chinensis* and sodium fluoride on dentinal tubule sealing and dentin hypersensitivity on different types of teeth. Therefore, further studies are needed to compare the effects of *Galla chinensis* on different age groups and different types of teeth.

Conclusions

This study aimed to evaluate the desensitizing effect of toothpaste containing the active ingredients of an extract of *Galla chinensis* both *in vitro* and in patients with dentin hypersensitivity. Toothpaste that contained the active ingredients of *Galla chinensis* extract and sodium fluoride reduced the symptoms of dentin hypersensitivity by sealing the dentinal tubules. However, the long-term effects of *Galla chinensis* on dentin hypersensitivity remain to be investigated.

Conflict of interest

None.

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