

EFFECTS OF A TRADITIONAL CHINESE MEDICINE BASED DESENSITIZING GEL ON DENTIN  
HYPERSENSITIVITY

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## Abstract

**Background and Objective:** Bamboo salt, Calcined oyster, *Drynaria fortunei*, *Indigo naturalis* and *Rehmannia glutinosa* have been the main ingredients of many formulations in Chinese medicine for the treatment of toothache. This study evaluated the effect of a new desensitizing gel on dentin hypersensitivity (DH).

**Materials and Methods:** The desensitizing gel was prepared through a confirmed prescription of ingredients mentioned above and Poloxamer 407 (P407). The best concentration of P407 in prescription was screened according to the gelatin temperature of gel. Scanning electron microscopy (SEM) was used to evaluate the dentinal tubule occlusion of 32 human premolars under various treatments including the desensitizing gel. Randomized controlled clinical trials were conducted to evaluate the clinical effect of the desensitizing gel.

**Results:** The best concentration of P407 in prescription was 0.30g/ml. Scanning electron micrographs of the cross-sectional and longitudinal dentin surfaces revealed most of the dentinal tubules were occluded by sedimentation after desensitizing gel treatment, and significant difference existed compared to the control groups. Randomized clinical trials showed 173.72% and 270.07% mean relative improvements on tactile hypersensitivity at one-month and two-month follow-ups, and 54.11% and 90.91% mean relative reductions on air blast hypersensitivity at one-month and two-month follow-ups ( $p < 0.05$ ). There was no statistical difference between the desensitizing gel and Duraphat group at different time intervals ( $p > 0.05$ ).

**Conclusions:** Based on these findings, the desensitizing gel exhibits an obvious effect on dentinal tubule occlusion. Besides, data of the randomized clinical trials indicate a potential role for the desensitizing gel in managing DH.

**Keywords:** Traditional Chinese medicine; Bamboo salt; Dentin hypersensitivity; Thermosensitive gel; Scanning electron microscopy; Clinical trials

**Abbreviations:** DH: Dentin hypersensitivity; P407: Poloxamer 407; SEM: Scanning electron microscopy.

## Introduction

DH is characterized by short, sharp pain arising from exposed dentin in response to stimuli, typically thermal, evaporative, tactile, osmotic or chemical and which cannot be ascribed to any other dental defect or pathology (Dababneh RH et al., 1999). It is a common problem found mainly in adult populations, however, with huge variations in prevalence, ranging from 1% to 98% (Mantzourani M and Sharma D, 2013; Splieth CH and Tachou A, 2013; Rahiotis C et al., 2013; Scaramucci T et al., 2014; Cunha-Cruz J et al., 2013; Wang Y et al., 2012). At present, the most widely accepted explanation for DH is hydrodynamic theory (West NX et al., 2013). This theory considers stimulus caused a fluid flow via the dentinal tubules, which triggered the pulpal nerves. This theory was determined by Gysi A (1900) in the nineteenth century, and then supported by the precious studies of Brännström M (1963, 1965, 1966) and his partners many years later. In further studies, Absi EG (1987) examined hypersensitive and non-sensitive teeth via SEM. Hypersensitive teeth has highly obviously increased numbers of tubules per unit area (approximately 8×) and significantly wider tubule diameters (approximately 2×), compared to non-sensitive teeth. Therefore the basic principle of treating DH has been occluding the open tubules on the exposed dentin. To date, there are a variety of desensitizing agents on the basic of this treatment principle having achieved good efficacy (Ozen T et al., 2009; Paes Leme AF et al., 2004). However, some agents, for example Duraphat, can just be utilized by the professional operation of dentists, rather than by patients' own.

Recently, attention has been turned towards traditional Chinese medicine which is known for lower price and little side effects (Huang Guangwei et al., 2013). Bamboo salt, which has been commonly utilized in various health products such as toothpaste, is prepared through calcining sea salt with a series of procedures (Zhao X et al., 2013). Studies have shown that bamboo salt can significantly increase the level of the surface hardness and decrease mineral loss of the artificial caries-like enamel lesions cooperated with fluoride (Choi CH et al., 2012). Calcined oyster (commonly known as Duanmuli) is made by calcining *Ostrea gigas thunberg* at a temperature of 200-400°C for 1-3h. *Drynaria fortunei* (commonly known as Gusuibu) is a kind of Eufilicales, Davalliaceae ferns. *Indigo naturalis* (commonly known as Qingdai) is the dried pigment of *Baphicacanthus cusia* (Nees) Bremek, *Indigofera tinctoria* Linn, and so on. *Rehmannia glutinosa* (commonly known as Shengdihuang) is the dried root of *Rehmannia*. *Indigo naturalis* and *Rehmannia glutinosa* are rich in fluorine element, Calcined oyster and *Drynaria fortunei* are rich in calcium element, and especially the calcium content of Calcined oyster is 35.1% (Zhao Yuying et al., 2014). In addition, *Drynaria fortunei*, *Indigo naturalis*, and *Rehmannia glutinosa* contain alkaloids, volatile oil and quebrachol (Li Gengsheng, 2004; Zhang Ziqiang et al., 2008). These compounds have an effect of nerve paralysis, and volatile oil can lead to the denaturation of protein in dentin (Huang Guangwei, 2013). These four materials have been used to treat toothache in ancient prescriptions of Chinese traditional medicine.

As such, we developed a new desensitizing gel which is convenient to carry and use for patients. Its effective components are bamboo salt and traditional Chinese medicine Calcined oyster, *Drynaria fortunei*, *Indigo naturalis*, and *Rehmannia glutinosa*. The objectives of this study were to evaluate the effect of the new desensitizing gel on dentinal tubule occlusion, and its clinical effectiveness in treating DH.

## Materials and Methods

### Preparation of the Desensitizing Gel

The qualities of the drugs were identified by the hospital experts according to macroscopic and microscopic approaches. Raw materials were weighed according to a confirmed prescription: 32g of Calcined oyster, 2g of *Drynaria fortunei*, 32g of *Indigo naturalis* and 2g of *Rehmannia glutinosa*. Hydrochloric acid extract of Calcined oyster and ethanol extracts of *Drynaria fortunei*, *Indigo naturalis* and *Rehmannia glutinosa* were combined and concentrated until 800ml medicine liquid was achieved (Wei Yingjie et al., 2004; Song Zirong et al., 2006; Wang Xinchun et al., 2001). Then 32g of bamboo salt (Zhejiang Lin'an Sanheyuan Bamboo salt food Co., Ltd., Lin'an, Zhejiang, China) and 0.1g of Sweetener Neotame (Jinan Sweet Biotechnology Co., Ltd., Jinan, Shandong, China) were added into the medicine liquid and heated to dissolution. P407 (Jinan Weidu Chemical Industry Co., Ltd., Jinan, Shandong, China) were then slowly added to the solution got from the last step to prepare the desensitizing gel. (Choi HG et al., 1998; Schmolka IR, 1972).

### Measurement of Gelation Temperature

The gelation temperature was measured by a test tube tilting method (TTM). A 10ml glass tube containing 6g of desensitizing gel was placed in a low-temperature thermostat water bath (Shandong Provincial Key Laboratory of Oral Biomedicine, China) equipped with a temperature controller. A thermometer was immersed in the gel. The temperature was increased at a slow rate of 0.1 °C per minute. Through visual inspection, if the desensitizing gel started flowing when tilting the tube, the temperature displayed on the thermometer was determined as a gelation temperature. Tests were done in triplicate, and the mean of the gelation temperature was calculated (Bhowmik M et al., 2013).

### SEM Observation of Dentinal Tubule Occlusion

The effect of dentinal tubule occlusion was observed by SEM (Delgado RJ et al., 2013; Al-Fouzan K et al., 2012; Burnett GR et al., 2013; Susin AH et al., 2008). 32 caries-free human premolars extracted from orthodontic patients between 18-25 years old were collected. All soft tissue deposits and calculus were removed from the teeth with a periodontal scaler. The teeth were preserved in a 0.2% thymol solution at 4°C after rinsing with running tap water. The teeth were randomly divided into four groups according to the agents (tests and controls) used, each containing 8 teeth: a. Physiological saline group (blank control); b. Mouthwash slobber group (test); c. Duraphat group (positive control); d. Desensitizing gel group (test). All the teeth were sectioned horizontally below the cemento-enamel junction using a water-cooled diamond. The cervical regions were cut into about 2-mm-thick dentin disks. These disks were wet ground tangentially using grindstones on a polishing machine to expose the dentin surface, and then cut into about 3-mm square dentin areas (9mm<sup>2</sup>) of 2mm thickness. The sectioned disks were bisected in a mesiodistal direction to obtain two slices from each disk. All slices were etched with hydrofluoric acid for 1 min to open the dentinal tubules completely and ultrasonically cleaned in distilled water for 15 minutes to remove the residual smear layer. Prior to application of the agents, the slices were marked on the buccofacial or linguofacial side and the opposite side with a diamond saw in order to facilitate their fracturing for SEM observation. The experimental agents were respectively applied onto corresponding groups for 5 minutes. This procedure was repeated in every 6 hours for a month. After each daily treatment, the specimens were preserved in distilled water. After all the treatment, the specimens were ultrasonicated for 20min in distilled water and then fractured carefully on the middle. After drying in a 60°C oven for 24h, each specimen was mounted on metal holders. Half of the slices were positioned in a way that then could be observed in a cross-sectional view, while the others were positioned to permit a longitudinal view. These specimens were sputter-coated with gold and observed under an SEM (Analysis and Test Center of Shandong University Institute of Materials) (×2000 magnification).

### Randomized Clinical Trials

To determine the effectiveness of the desensitizing gel, this clinical investigation was designed as a double-blind, randomized controlled trial according to the criteria described by Holland GR et al. (1997). 123 subjects who demonstrated one hypersensitive tooth that satisfied the evaporative and tactile hypersensitivity enrolment criteria were included in the trial, and consent was obtained. All the subjects were randomly divided into four groups according to the treatments used: Test-A: Desensitizing gel (32 subjects). Test-B: Mouthwash slobber (29 subjects). Test-C: Duraphat (31 subjects). Control: Gel without desensitizing bamboo salt (31 subjects). All subjects were given the corresponding agents to use three times a day for 5 timed minutes during 2 months, without additional treatment being allowed. The entire study was blinded. The groups were not known by the examiners or subjects. DH measurements included tactile hypersensitivity and air blast hypersensitivity according to the methods described by Neuhaus KW et al. (2013) in their double-blind randomized controlled trial to determine the effectiveness of a prophylaxis paste. These assessments were performed by one examiner at baseline, one-month and two-month after the application. The assay was carried out according to the "Study guide of traditional Chinese Medicine" (Ministry of Health of the People's Republic of China, 1994), followed guidelines of the declaration of Helsinki and Tokyo for humans, approved by the institutional human experimentation committee of College of Stomatology, Shandong University, and undertaken with the understanding and written consent of each subject.

### Statistical Analysis

All statistical analysis was performed by SPSS software version 13.0 for Windows (SPSS, Inc., USA). Statistical significances were calculated by analysis of variance (ANOVA) for multiple comparisons, followed by individual comparisons between different groups at the same time point by LSD *t*-test. *P*<0.05 was utilized to confirm the presence of a significant difference in randomized clinical trials.

## Results

### Gelation Temperature of the Desensitizing Gels

Gelation temperature is the temperature at which gel phase converts to liquid. The suitable gelation temperature range for desensitizing gel would be 38-42°C. Thus, the gel will be a gel form in oral cavity and turn to liquid phase when gargling with warm water above the temperature of oral cavity. The results of gelation temperature measurements were shown in Table 1. As the concentration of P407 increasing, the gelation temperature raised markedly. Solutions containing at or below 0.18g/ml of P407 could not form gel. The gelation temperature of solutions containing 0.19-0.26g/ml of P407 was 16-37°C, whereas desirable gelation temperature could not be obtained among these formulations. The concentration formulations of P407 in desirable gelation temperature range were 0.27-0.30g/ml (gelation temperature 38-42°C). Finally, formulation containing 0.30g/ml of P407 was selected.

### SEM Observation of Dentinal Tubule Occlusion

The analysis of cross-sectional and longitudinal specimens under SEM indicated that tested agents caused dentinal tubule occlusion in varied degrees. Figures 1 to 8 showed SEM images of the dentinal tubules after application of corresponding agents.

The blank control group (Figs 1, 5) which was treated with physiological saline showed the expected pattern of dentin, with most distinct open dentinal tubules. This group would be used as parameter for comparison to the other groups. All tested groups in this study were effective in occluding dentinal tubules. Figs 2,3,4 showed scanning electron micrographs of the cross-sectional dentin surfaces. In mouthwash slobber group (Fig 2), the presence of opened and partially occluded dentinal tubules was observed. Duraphat group (Fig 3) and desensitizing gel group (Fig 4) showed similar effects on occlusion of the dentinal tubules, better than the effect of mouthwash slobber group, with most of the tubules occluded. Fig 6,7,8 showed scanning electron micrographs of the longitudinal dentin surfaces. In the longitudinal views, intertubular occlusion by sedimentation composed of very small particles could be observed in all the tested groups. The depth of intertubular occlusion in mouthwash slobber group (Fig 6) was smaller than those in Duraphat group (Fig 7) and desensitizing gel group (Fig 8), whereas the last two groups showed a similar intertubular occluding effect.

### Randomized Clinical Trials

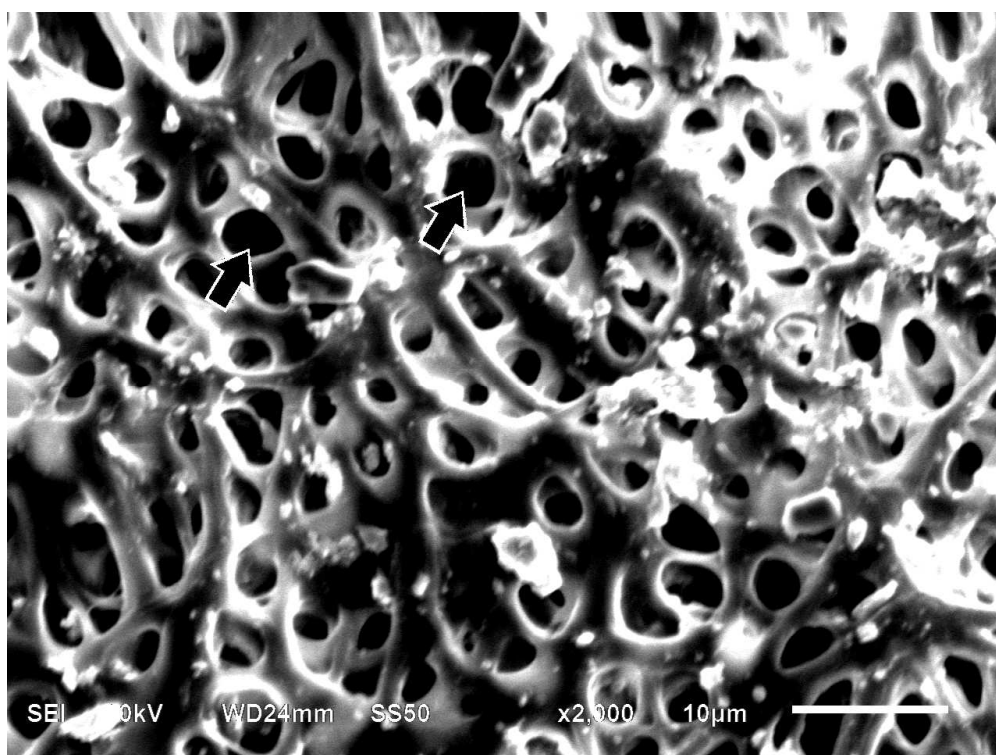
Tactile hypersensitivity scores were presented in Table 2. Subjects (n=123) of the four groups were evenly balanced with no statistically significant differences at baseline ( $p>0.05$ ). Mean values ranged from 13.13 (Test-A) to 13.55 grams (Control). As respected, there was nearly no statistical change ( $p>0.05$ ) at different time intervals in the control group which would be used as parameter for comparison to the other groups. At one-month, the mean values showed statistically significant improvements ( $p<0.05$ ) for all the test groups compared to the control. The mean relative improvements from baseline after one-month were 173.72% for Test-A, 79.48% for Test-B and 192.59% for Test-C. At two-month, the mean values of all the test groups resulted in more statistically significant improvements ( $p<0.05$ ) compared with the control. The mean relative improvements from baseline after two-month were 270.07% for Test-A, 149.96% for Test-B and 290.10% for Test-C. There was no statistical difference between Test-A and Test-C at one-month and two-month ( $p>0.05$ ), but both of them showed statistically more significant improvements than Test-B at different time intervals ( $p<0.05$ ).

Air blast hypersensitivity scores were presented in Table 3. All the subjects (n=123) were evenly balanced with no statistically significant differences at baseline ( $p>0.05$ ). Mean values ranged from 2.26 (Control) to 2.34 (Test-B). There was no statistically change ( $p>0.05$ ) in the control group at time interval during experiment. After one-month, air-blast hypersensitivity scores for all the test groups were significantly lower than the control ( $p<0.05$ ). The mean relative reductions from baseline at one-month were 54.11% for Test-A, 41.45% for Test-B and 69.40% for Test-C. After two-month, the mean values resulted in more statistically significant reductions for all the test groups compared with the control ( $p<0.05$ ). The mean relative reductions from baseline at two-month were 90.91% for Test-A, 58.97% for Test-B and 97.41% for Test-C. Duraphat was comparatively more efficient on all tests at any stage of study. The desensitizing gel showed no statistical differences from Duraphat at different time intervals ( $p>0.05$ ). Hypersensitivity measurements indicated a considerable clinical efficiency of the desensitizing gel.

**Table 1:** Gelation temperatures of desensitizing gels

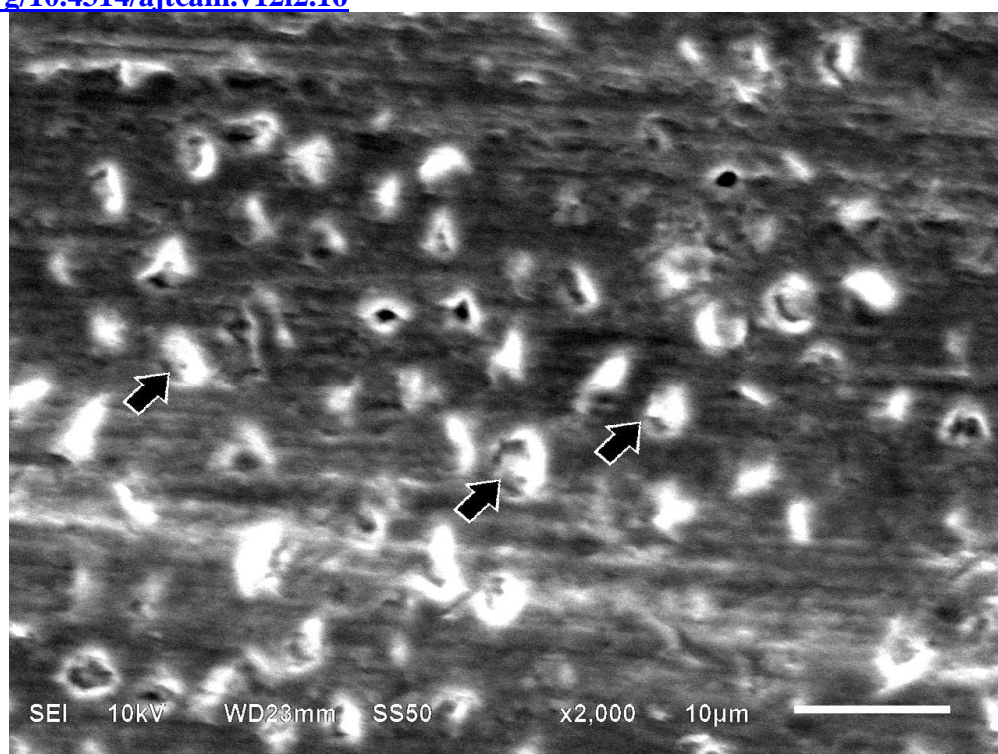
Groups	Concentration of P407 (g/ml)	Gelation temperature(°C)
1	0.16	Could not form gel
2	0.17	Could not form gel
3	0.18	Could not form gel
4	0.19	16°C
5	0.20	21°C
6	0.21	23°C
7	0.22	27°C

8	0.23	30 <sup>0</sup> C
9	0.24	33 <sup>0</sup> C
10	0.25	35 <sup>0</sup> C
11	0.26	37 <sup>0</sup> C
12	0.27	38 <sup>0</sup> C
13	0.28	40 <sup>0</sup> C
14	0.29	41 <sup>0</sup> C
15	0.30	42 <sup>0</sup> C

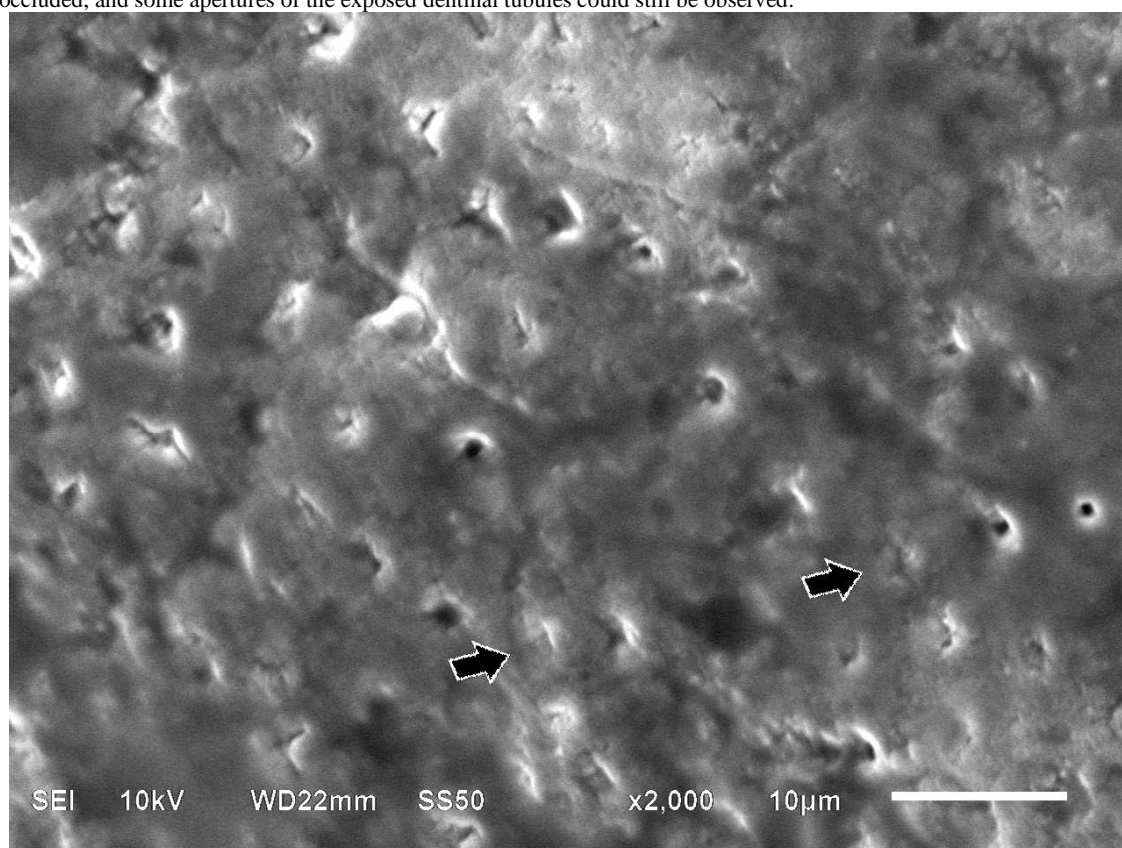


**Figure 1:** Scanning electron micrograph of physiological saline group (blank control)- Cross-sectional view of dentinal tubules. The dentinal tubules were completely opened, and the dentin surface free of smear layer and ope tubules could be observed clearly.

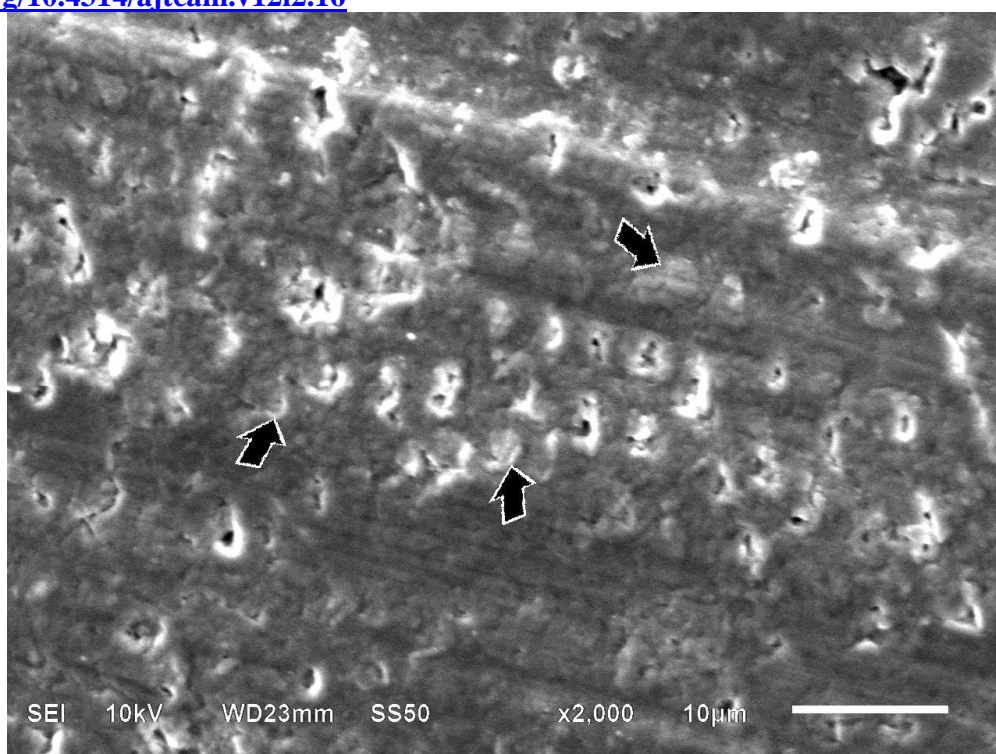




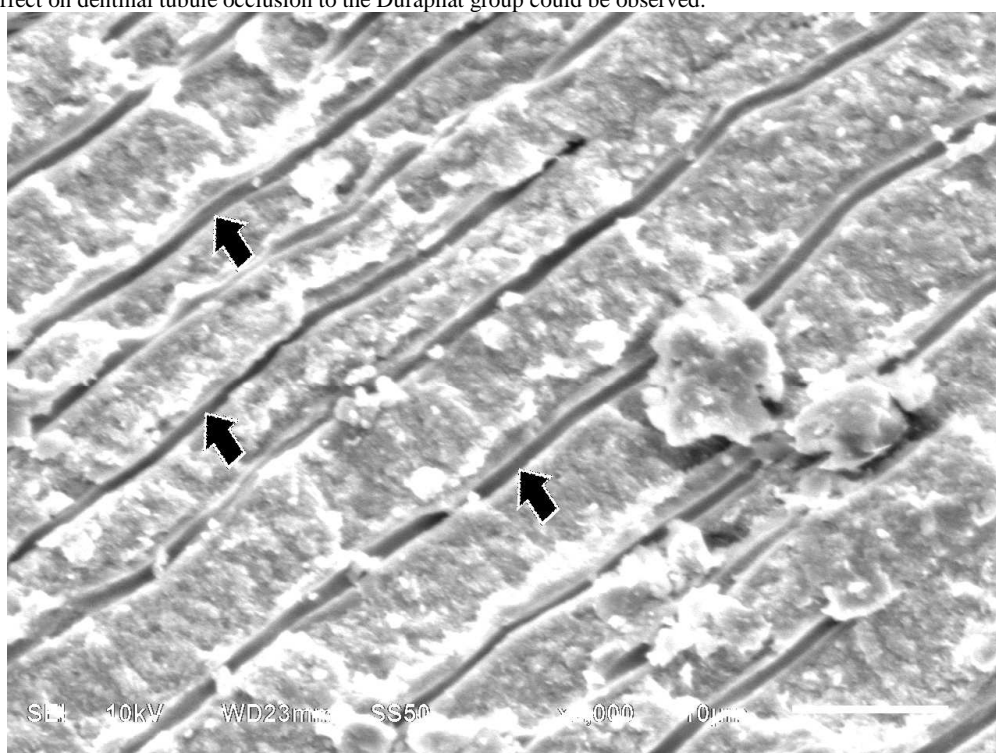
**Figure 2:** Scanning electron micrograph of mouthwash slobber group (test control)- Cross-sectional view of dentinal tubules. The dentinal tubules were partially occluded, and some apertures of the exposed dentinal tubules could still be observed.



**Figure 3:** Scanning electron micrograph of Duraphat group (positive control)- Cross-sectional view of dentinal tubules. Most of the tubules were completely occluded. The dentin surface covered by sedimentation and more occluded tubules than mouthwash slobber group could be observed.

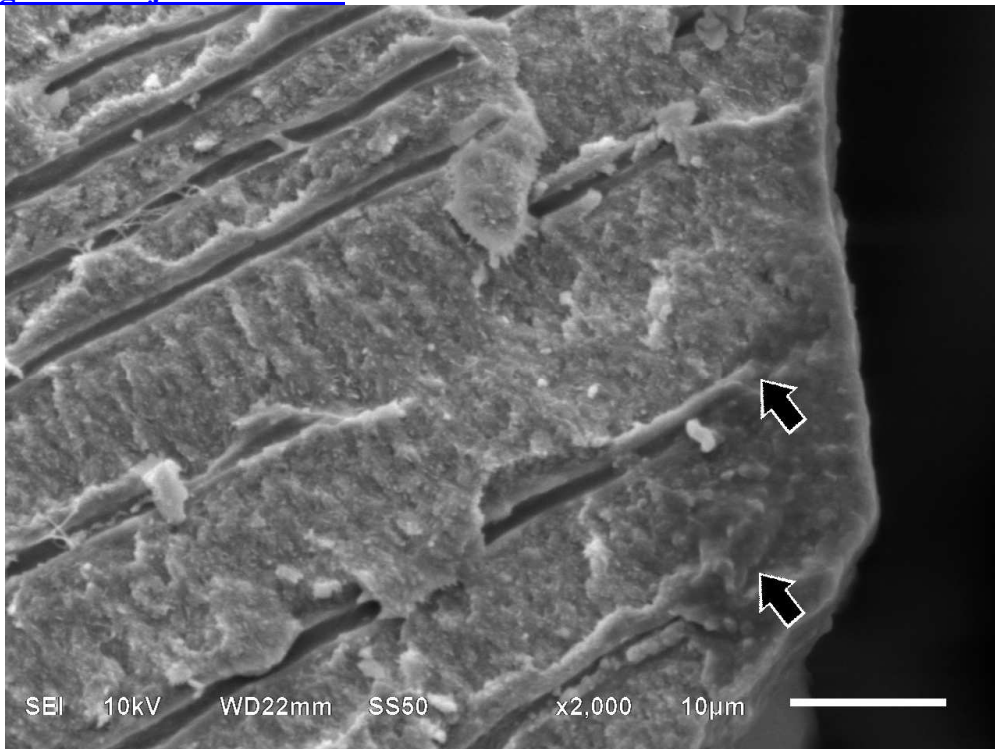


**Figure 4:** Scanning electron micrograph of desensitizing gel group (test control)- Cross-sectional view of dentinal tubules. Most of the tubules were occluded. A similar effect on dentinal tubule occlusion to the Duraphat group could be observed.

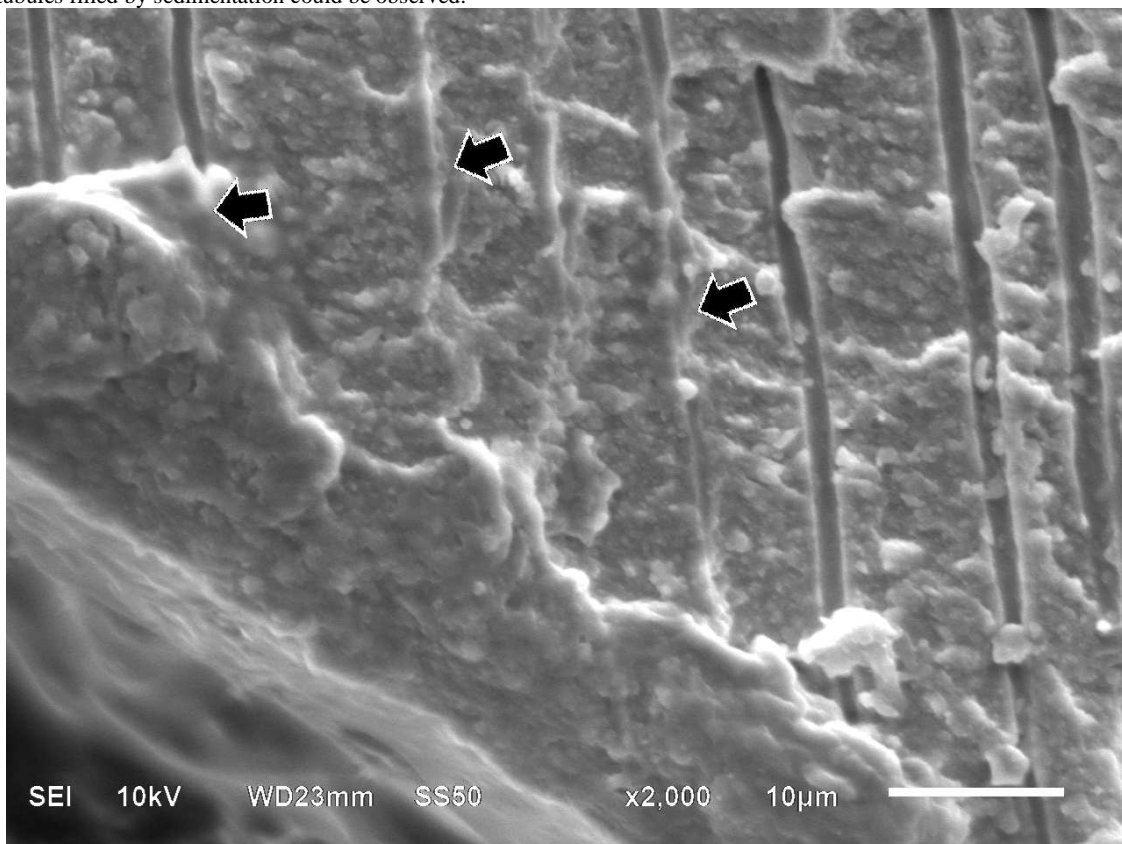


**Figure 5:** Scanning electron micrograph of physiological saline group (blank control)- Lateral view of the dentinal tubules. The dentin surface free of smear layer and totally opened dentinal tubules could be observed clearly.

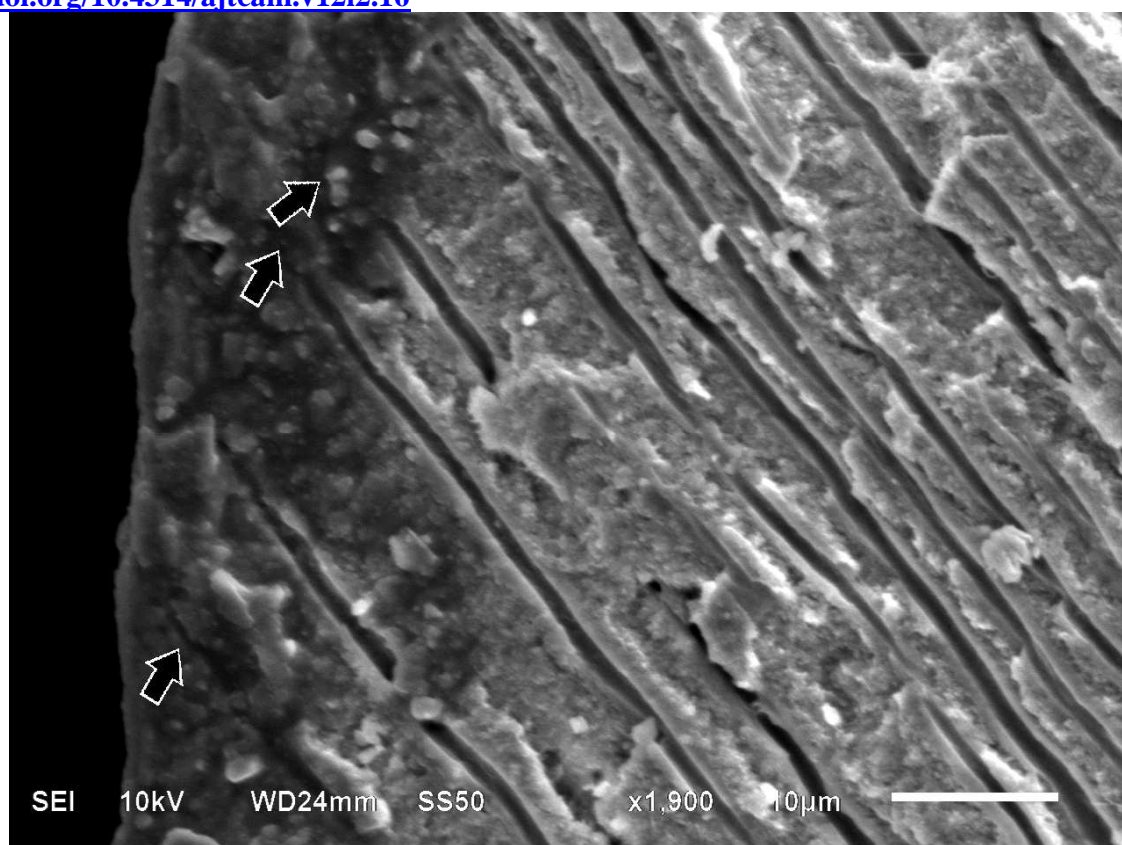




**Figure 6:** Scanning electron micrograph of mouthwash slobber group (test control)- Lateral view of the dentinal tubules. Partially intertubular occlusion and tubules filled by sedimentation could be observed.



**Figure 7:** Scanning electron micrograph of Duraphat group (positive control)- Lateral view of the dentinal tubules. Most of the dentinal tubule openings were occluded by sedimentation. More occluded tubules and deeper intertubular occlusion than mouthwash slobber group could be observed.



**Figure 8:** Scanning electron micrograph of desensitizing gel group (test control)- Lateral view of the dentinal tubules. Most of the dentinal tubule openings were occluded by sedimentation. A similar effect on intertubular occlusion to the Duraphat group could be observed.

## Discussion

In this study, we developed a new desensitizing gel with bamboo salt and traditional Chinese medicine *Calcined oyster*, *Drynaria fortunei*, *Indigo naturalis*, and *Rehmannia glutinosa*, and researched its desensitizing effect on DH. The effect of dentinal tubule occlusion was observed using SEM. SEM images showed a significant occluding effect of dentinal tubules in desensitizing gel group. Compared with mouthwash slobber, desensitizing gel had more obvious effects in views of occluded tubule numbers and intertubular occluding depth, which were close to the effects of Duraphat. The possible mechanism contains occluding dentinal tubules and anaesthetizing pulp nerves. Firstly, calcium and fluorine elements in the gel combine each other into sodium fluoride precipitation, which form a thin mineralized smear layer on the dentin surface and enter into the exposed dentinal tubules. Fluoride ion in the gel reacts with calcium salt in the tooth tissue, and forms calcium fluoride or hydroxyl fluorapatite, which reduce the diameter of the dentinal tubules (Suge T et al., 1995). Moreover, under the action of volatile oil, proteins in dentin denature and coagulate, and then deposit in the tubules (Huang Guangwei, 2013). All these reactions reduce or avoid the fluid flow via the dentinal tubules. Thus the stimulation of tubular fluid flow on dental pulps can be reduced or eliminated. Secondly, alkaloids, volatile oil and quebrachol in the medicine have certain local anaesthetic and analgesic effect, which reduces the sensitivity of dental pulp nerves (Huang Guangwei, 2013). Calcium fluoride and hydroxyl fluorapatite can promote the formation of secondary dentin which has lower permeability than primary dentin. Thereby secondary dentin increases hardness and resistance to acid of dentin, and reduces the sensitivity of dental pulp nerves likewise (Suge T et al., 1995).

**Table 2:** Tactile sensitivity scores

Assessment/Treatment		Tactile sensitivity						Between-Treatment p-value			
t		N	Mean	SD	Median	Min	Max	vs. Test-A	vs. Test-B	vs. Test-C	vs. Control
Baseline	Test-A	32	13.13	4.71	10	10	20	-	n.s.	n.s.	n.s.
	Test-B	29	13.45	4.84	10	10	20	n.s.	-	n.s.	n.s.
	Test-C	31	13.23	4.75	10	10	20	n.s.	n.s.	-	n.s.
	Control	31	13.55	4.86	10	10	20	n.s.	n.s.	n.s.	-
1-Month	Test-A	32	35.94	10.43	40	10	50	-	$p < 0.05$	n.s.	$p < 0.05$
	Test-B	29	24.14	9.07	20	10	40	$p < 0.05$	-	$p < 0.05$	$p < 0.05$



	Test-C	31	38.71	8.06	40	20	50	n.s.	$p<0.05$	-	$p<0.05$
	Control	31	14.19	5.02	10	10	20	$p<0.05$	$p<0.05$	$p<0.05$	-
<b>2-Month</b>	Test-A	32	48.59	9.77	50	20	55	-	$p<0.05$	n.s.	$p<0.05$
	Test-B	29	33.62	12.81	30	10	55	$p<0.05$	-	$p<0.05$	$p<0.05$
	Test-C	31	51.61	6.24	55	30	55	n.s.	$p<0.05$	-	$p<0.05$
	Control	31	14.84	6.26	10	10	30	$p<0.05$	$p<0.05$	$p<0.05$	-

Between-Treatment  $p$ -values were calculated by analysis of variance (ANOVA) for multiple comparisons, followed by individual comparisons between different groups at the same time point by LSD  $t$ -test. Difference was considered significant at  $P<0.05$ .

n.s. = non-significant.

**Table 3:** Air blast sensitivity scores.

Assessment/Treatment		Air blast sensitivity						Between-Treatment $p$ -value			
		N	Mean	SD	Median	Min.	Max.	vs. Test-A	vs. Test-B	vs. Test-C	vs. Control
<b>Baseline</b>	Test-A	32	2.31	0.78	2.5	1	3	-	n.s.	n.s.	n.s.
	Test-B	29	2.34	0.77	3	1	3	n.s.	-	n.s.	n.s.
	Test-C	31	2.32	0.79	3	1	3	n.s.	n.s.	-	n.s.
	Control	31	2.26	0.68	2	1	3	n.s.	n.s.	n.s.	-
<b>1-month</b>	Test-A	32	1.06	0.98	1	0	3	-	n.s.	n.s.	$p<0.05$
	Test-B	29	1.37	0.82	1	0	3	n.s.	-	$p<0.05$	$p<0.05$
	Test-C	31	0.71	0.74	1	0	2	n.s.	$p<0.05$	-	$p<0.05$
	Control	31	1.94	0.73	2	0	3	$p<0.05$	$p<0.05$	$p<0.05$	-
<b>2-month</b>	Test-A	32	0.21	0.75	0	0	3	-	$p<0.05$	n.s.	$p<0.05$
	Test-B	29	0.96	0.87	1	0	3	$p<0.05$	-	$p<0.05$	$p<0.05$
	Test-C	31	0.06	0.25	0	0	1	n.s.	$p<0.05$	-	$p<0.05$
	Control	31	1.97	0.98	2	0	3	$p<0.05$	$p<0.05$	$p<0.05$	-

Between-Treatment  $p$ -values were calculated by analysis of variance (ANOVA) for multiple comparisons, followed by individual comparisons between different groups at the same time point by LSD  $t$ -test. Difference was considered significant at  $P<0.05$ .

n.s. = non-significant.

Poloxamer, a copolymer of poly (oxyethylene)-poly (oxypropylene)-poly (oxyethylene), was employed as thermosensitive material for the desensitizing gel. Poloxamer solutions exhibit a thermosensitive gelling property, which means they are solutions at low temperatures but turn to gels when the temperature increasing, especially P407 (Dumortier G et al., 1991; Lenarets V et al., 1987). P407 is commonly utilized in liquid suppository not only due to the thermosensitive gelling property, but also due to low toxicity, excellent water-solubility, good drug release characteristics and compatibility with other chemicals. In our study, we measured the gelation temperature of the desensitizing gels with different concentrations of P407. Different from previous researches (Dumortier G et al., 1991; Lenarets V et al., 1987), the desensitizing gel existed as gel at low temperature but turned to liquid when the temperature increasing. Mechanism of the phenomenon needed further research. However, utilizing this novel property, the desensitizing gel was designed into a thermosensitive gel. With a suitable gelation temperature, it exists as a gel phase in oral cavity, which avoids leakage from the teeth, and becomes liquid when gargling with warm water above 37°C. Taken together, it is concluded that 0.30g·ml<sup>-1</sup> was the optimal formulation of P407 which had the suitable gelation temperature.

To evaluate the effectiveness of the desensitizing gel, clinical trials was carried out using double blind, randomized, parallel groups. Desensitizing effect was detected by DH measurements included tactile hypersensitivity and air blast hypersensitivity. The results of our study indicated all the three tested agents, mouthwash slobber, Duraphat and desensitizing gel were effective in decreasing sensitivity compared to control for all stimuli at different time intervals ( $p<0.05$ ). Duraphat was comparatively more efficient on all tests at any stage of study. The desensitizing gel showed significant improvements close to Duraphat on all tests at different time intervals ( $p>0.05$ ). Its mean relative improvement from baseline on tactile hypersensitivity was 173.72% at one-month and increased to 270.07% at two-month. The mean relative reduction from baseline on air blast hypersensitivity was 54.11% at one-month and 90.91% at two-month. Our findings showed that the desensitizing gel resulted in significant relief from hypersensitivity, indicating an immediate and long lasting effect.

On the whole, the new desensitizing gel combines the advantages of bamboo salt and traditional Chinese medicines into a whole. The present investigation confirms that the desensitizing gel possesses an obvious effect on dentinal tubule occlusion with considerable clinical effectiveness, indicating a potential role in managing DH. Moreover, the new desensitizing gel is easy to carry and use with a good taste. Further studies will be performed gradually including improvement of gel strength and bioadhesive force, antimicrobial effects of the desensitizing gel, randomized clinical trials with larger sample sizes and long-term follow-ups, drug resistance after long-term application, and so on.

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## References

1. Absi EG, Addy M, Adams D, (1987). Dentine hypersensitivity: A study of the patency of dentinal tubules in sensitive and non-sensitive cervical dentine. *J Clin Periodontol*, 14(5): 280-4.
2. Al-Fouzan K, Al-Garawi Z, Al-Hezaimi K, Javed F, Al-Shalan T, Rotstein I, (2012). Effect of acid etching on marginal adaptation of mineral trioxide aggregate to apical dentin: microcomputed tomography and scanning electron microscopy analysis. *Int J Oral Sci*, 4(4):202-7.
3. Bhowmik M, Kumari P, Sarkar G, Bain MK, Bhowmik B, Mollick MM, Mondal D, Maity D, Rana D, Bhattacharjee D, Chattopadhyay D, (2013). Effect of xanthan gum and guar gum on in situ gelling ophthalmic drug delivery system based on poloxamer-407. *Int J Biol Macromol*, 62: 117-23.
4. Brännström M, (1963). A hydrodynamic mechanism in the transmission of pain-produced stimuli through the dentine. In: Anderson DJ (ed), *Sensory mechanisms in dentine*. Pergamon, Oxford, pp. 73-9.
5. Brännström M, (1965). The surface of sensitive dentine. *Odontol Revy*, 16:293-9.
6. Brännström M, (1966). The sensitivity of dentine. *Oral Surg, Oral Med, Oral Path*, 21: 517-26.
7. Burnett GR, Willson RJ, Lucas RA, (2013). *In vitro* studies investigating the dentin tubule-occlusion properties of an experimental anhydrous stannous fluoride dentifrice. *Am J Dent*, 26 Spec No A: 10A-14A.
8. Choi CH, Ha MO, Youn HJ, Jeong SS, Iijima Y, Sohn W, Hong SJ, (2012). Effect of bamboo salt-NaF dentifrice on enamel remineralization. *Am J Dent*, 25(1): 9-12.
9. Choi HG, Jung JH, Ryu JM, Yoon SJ, Oh YK, Kim CK, (1998). Development of in situ-gelling and mucoadhesive acetaminophen liquid suppository. *Int J Pharm*, 165: 33-44.
10. Cunha-Cruz J, Wataha JC, Heaton LJ, Rothen M, Sobieraj M, Scott J, Berg J, (2013). The prevalence of dentin hypersensitivity in general dental practices in the northwest United States. *J Am Dent Assoc*, 144(3): 288-96.
11. Dababneh RH, Khouri AT, Addy M, (1999). Dentine hypersensitivity---an enigma? A review of terminology, epidemiology, mechanisms, aetiology and management. *Br Dent J*, 187(11):606-11; discussion 603.
12. Delgado RJ, Gasparoto TH, Sipert CR, Pinheiro CR, de Moraes IG, Garcia RB, Duarte MA, Bramante CM, Torres SA, Garlet GP, Campanelli AP, Bernardineli N, (2013). Antimicrobial activity of calcium hydroxide and chlorhexidine on intratubular *Candida albicans*. *Int J Oral Sci*, 5(1): 32-6.
13. Dumortier G, Zumer M, Couraraze G, Chaumeil JC, Grossiord JL, (1991). Rheological study of a thermoreversible morphine gel. *Drug Dev Ind Pharm*, 17: 1255-65.
14. Gysi A, (1900). An attempt to explain the sensitiveness of dentin. *Br J Dent Sci*, 43: 865-8.
15. Holland GR, Narhi MN, Addy M, Gangarosa L, Orchardson R, (1997). Guidelines for the design and conduct of clinical trials on dentine hypersensitivity. *J Clin Periodontol*, 24(11): 808-13.
16. Huang Guangwei, Liang Hong, Zhou Hui, Dai Yantao, (2013). Research status and prospect of Chinese traditional medicine toothpaste on dentin hypersensitivity. *Oral Care Ind*, 23(3): 51-2.
17. Lenarets V, Triqueneaux C, Quarton M, Falson FR, Couvreur P, (1987). Temperature-dependent rheological behavior of Pluronic F-127 aqueous solutions. *Int J Pharm*, 31: 121-7.
18. Li Gengsheng, Yu Zhen, Wang Huisen, (2004). Progress on the chemical constituents and pharmacological research of *Rehmannia glutinosa*. *Foreign Med Sci*, 26(2): 74-8.
19. Mantzourani M, Sharma D, (2013). Dentine sensitivity: past, present and future. *J Dent*, 41 Suppl 4: S3-17.
20. Neuhaus KW, Milleman JL, Milleman KR, Mongiello KA, Simonton TC, Clark CE, Proskin HM, Seemann R, (2013). Effectiveness of a calcium sodium phosphosilicate containing prophylaxis paste in reducing dentin hypersensitivity immediately and 4 weeks after a single application: a double-blind randomized controlled trial. *J Clin Periodontol*, 40(4): 349-57.
21. Ozen T, Orhan K, Avsever H, Tunca YM, Ulker AE, Akyol M, (2009). Dentin hypersensitivity: A randomized clinical comparison of three different agents in a short-term treatment period. *Oper Dent*, 34(4): 392-8.
22. Paes Leme AF, dos Santos JC, Giannini M, Wada RS, (2004). Occlusion of dentin tubules by desensitizing agents. *Am J Dent*, 17(5): 368-72.
23. Rahiotis C, Polychronopoulou A, Tsiklakis K, Kakaboura A, (2013). Cervical dentin hypersensitivity: a cross-sectional investigation in Athens, Greece. *J Oral Rehabil*, 40(12): 948-57.
24. Scaramucci T, de Almeida Anfe TE, da Silva Ferreira S, Frias AC, Sobral MA, (2014). Investigation of the prevalence, clinical features, and risk factors of dentin hypersensitivity in a selected Brazilian population. *Clin Oral Investig*, 18(2): 651-7.
25. Schmolka IR, (1972). Artificial skin I. Preparation and properties of Pluronic F-127 gels for treatment of burns. *J Biomed Mater Res*, 6(6): 571-82.
26. Song Zirong, Tan Zijun, Chen Xisong, Bai Haibo, (2006). The optimization of extraction process of *Rehmannia glutinosa*. *Chin J Exper Traditional Med Formulae*, Vol.12, No.1.
27. Splieth CH, Tachou A, (2013). Epidemiology of dentin hypersensitivity. *Clin Oral Investig*, 17 Suppl 1: S3-8.
28. Suge T, Ishikawa K, Kawasaki A, Yoshiyama M, Asaoka K, Ebisu S (1995). Effects of fluoride on the calcium phosphate precipitation method for dentinal tubule occlusion. *J Dent Res*, 74(4): 1 079.
29. Susin AH, Alves LS, Melo GP, Lenzi TL, (2008). Comparative scanning electron microscopic study of the effect of different dental conditioners on

<http://dx.doi.org/10.4314/ajtcam.v12i2.16>

- dentin micromorphology. J Appl Oral Sci, 16(2): 100-5.
- 30.Wang Xinchun, Sun Yiyi, Bi Yueqi, Hou Shixiang, (2001). The optimal extraction method of Indigo Naturalis in liquid compound preparation. West Chin J Pharm Sci, 16(3): 191-5
- 31.Wang Y, Que K, Lin L, Hu D, Li X, (2012). The prevalence of dentine hypersensitivity in the general population in China. J Oral Rehabil, 39(11): 812-20.
- 32.Wei Yingjie, Chen Ning, Wang Jing, Zhou Xumin, Yang Zhenghua, 2004. Optimum extraction on *Drynaria fortunei* (Kunze) J. Sm. by orthogonal design. Lishizhen Med Materia Medica Res, Vol.15, No.11.
- 33.West NX, Lussi A, Seong J, Hellwig E, (2013). Dentin hypersensitivity: pain mechanisms and aetiology of exposed cervical dentin. Clin Oral Investig, 17 Suppl 1: S9-19.
- 34.Zhang Ziqiang, Zhang Hulin, Zhang Xiaogang, (2008). Research progress on the effect of effective components of *Rhizoma drynariae* on proliferation and differentiation of bone marrow mesenchymal stem cell. Gansu J TCM, 21(12): 58-62.
- 35.Zhao X, Deng X, Park KY, Qiu L, Pang L, (2013). Purple bamboo salt has anticancer activity in TCA8113 cells in vitro and preventive effects on buccal mucosa cancer in mice *in vivo*. Exp Ther Med, 5(2): 549-54.
- 36.Zhao Yuying, Wei Fenghua, Wang Yingli, (2014). A comparative study on the chemical constituents of oyster shell and Calcined oysterand. Chinese J Exp Tradit Med Formulae, 20(12): 110-4.