

**The effect of sodium lauryl sulfate on  
recurrent aphthous stomatitis**

**Young Joo Shim**

**The Graduate School  
Yonsei University  
Department of Dental Science**

**The effect of sodium lauryl sulfate on  
recurrent aphthous stomatitis**

A Masters Thesis

Submitted to the Department of Dental Science

And the Graduate School of Yonsei University

in partial fulfillment of the  
requirements for the degree of  
Master of Dental Science

**Young Joo Shim**

December 2010

**This certifies that the masters thesis  
of Young Joo Shim is approved.**

---

**Thesis Supervisor : Prof. Jong-Hoon Choi**

---

**Thesis Committee Member : Prof. Hyung-Joon Ahn**

---

**Thesis Committee Member : Prof. Jeong-Seung Kwon**

**The Graduate School**

**Yonsei University**

**December 2010**

## 감사의 글

어느덧 2010 년의 마지막인 12 월입니다. 절대적인 시간은 누구에게나 같이 주어지지만, 시간의 상대적인 느낌은 다를 것입니다. 지금 현재의 이 12 월이 저에게는 아주 소중한 시간들입니다. 구강내과 수련을 마무리함과 동시에 석사논문을 마무리하며, 또한 다가올 전문의 시험을 준비하는 시간이기도 합니다. ‘마무리를 잘해야 한다’ 라고 생각하면서도 막상 준비하는 과정에서는 쉽지 않은 것 같습니다. 그 만큼 마무리에는 많은 노력과 정성이 필요한 시간들이겠지요.

혼자했다면 못했을 일들을 교수님들의 가르침과 동료들의 도움으로 마무리를 할 수 있었다고 생각합니다. 이번 석사논문을 준비하는 과정에서 지도해주신 최종훈 교수님께 먼저 감사드립니다. 수련기간 동안에도 항상 배려와 자애로움으로 저희를 대해주셔서 사람을 대할 때의 자세도 많이 배울 수 있었습니다. 그리고 조언을 아끼지 않으셨던 김성택 교수님, 안형준 교수님, 논문 인쇄하는 마지막까지 꼼꼼하게 살펴주시고, 지도해주신 권정승 교수님께도 감사한 마음을 표합니다. 그리고 임상시험과정에서 자신의 일처럼 도와주고 챙겨줬던 구강내과 전공의 선생님들께도 고마운 마음을 표합니다. 항상 응원과 지지를 아끼지 않는 부모님과 언니, 형부, 그리고 조카 서연이, 수련기간 동안 의지가 되었던 두영언니에게도 감사의 마음을 표합니다. 마지막으로 항상 자신의 일처럼 도와주고 챙겨주시며 힘들 때마다 멘토가 되어주시는 최정규님께도 항상 고마운 마음과 존경의 마음을 전합니다.

다가오는 2011 년에도 더 발전된 모습으로 여러 교수님들과 전공의 선생님들께 보답하는 사람이 되겠습니다.

2010 년 12 월

심 영 주

# TABLE OF CONTENTS

LIST OF TABLE.....	ii
ABSTRACT (ENGLISH) .....	iii
<b>I . INTRODUCTION</b> .....	1
<b>II . MATERIALS AND METHODS</b> .....	6
1. Subjects .....	6
2. Dentifrices and Toothbrushes .....	6
3. Study design.....	8
4. Ulcer diaries .....	9
5. Statistical analysis .....	10
<b>III. RESULTS</b> .....	11
<b>IV. DISCUSSION</b> .....	17
<b>IV. CONCLUSION</b> .....	22
REFERENCES .....	24
APPENDIX .....	29
ABSTRACT (KOREAN).....	31

## LIST OF TABLES

<b>Table 1.</b> Main components of dentifrices .....	7
<b>Table 2.</b> Clinical parameters.....	9
<b>Table 3.</b> Demographic characteristics of subjects .....	11
<b>Table 4.</b> Results for the parameters in group I .....	12
<b>Table 5.</b> Results for the parameters in group II .....	13
<b>Table 6.</b> Results for the parameters in group III.....	14
<b>Table 7.</b> Demographic characteristics of infrequent and frequent group .....	15
<b>Table 8.</b> Results for the parameters in infrequent group .....	16
<b>Table 9.</b> Results for the parameters in frequent group.....	16

## **Abstract**

### **The effect of sodium lauryl sulfate on recurrent aphthous stomatitis**

**Young Joo Shim**

Department of Oral Medicine/Dental Science,

The Graduate School, Yonsei university

Sodium lauryl sulfate (SLS) is an anionic detergent that has been used as the major or sole surfactant in most dentifrices. But it is local irritating factor to oral mucosa and result in many side effects. This study was to compare the effects of SLS-free dentifrice with that of SLS-containing dentifrice on recurrent aphthous stomatitis (RAS) and figure out the effect of SLS on incidence of RAS.

The ninety volunteers were divided into three groups by random and they used two dentifrices among a commercially available SLS-free dentifrice (SLS-free), a commercially available SLS-free dentifrice containing 1.5% SLS (SLS-A), and a commercially available 1.5% SLS-containing dentifrice (SLS-B). They used each dentifrice for 8 weeks and there was a 2-week washout period during which the subject used the same dentifrice as they used before this study. We compared with clinical parameters – the number of ulcers, the number of episodes, the duration of ulcers, mean pain score at tooth brushing, the feeling of dry mouth after tooth brushing, and the change of sensitivity to sour taste – between two phases in each group.

The duration of ulcers, and mean pain score were significantly decreased during the period using SLS-free compared to the period using SLS-A. And in infrequent group

which defined as the number of days to experience ulcers was 15 and under during the period using SLS-free, the number of ulcers, the number of episodes, the duration of ulcers, and mean pain score significantly decreased during the period using SLS-free compared to the period using SLS-A. The number of episodes, the duration of ulcers, and mean pain score were significantly decreased during the period using SLS-free compared to the period using SLS-B. The number of ulcers, the number of episodes, the duration of ulcers, and mean pain score were decreased during the period using SLS-A compared to the period using SLS-B, but there was no significant difference in all parameters. Subjects felt less dry mouth after tooth brushing when they used SLS-free. Subjects reported that they were more sensitive to sour taste right after using SLS-A or SLS-B than SLS-free.

It is not sure that SLS is initiating factor of RAS, but we found out that the number of ulcers, the number of episodes, and the duration of ulcers were increased during the period using SLS-containing dentifrice. Therefore, SLS is thought to be perpetuating factor of RAS.

---

Key words: Sodium lauryl sulfate (SLS), recurrent aphthous stomatitis (RAS), dentifrice

# **The effect of sodium lauryl sulfate on recurrent aphthous stomatitis**

**Young Joo Shim, D.D.S.**

Department of Oral Medicine/Dental Science,

The Graduate School, Yonsei university

(Directed by Professor **Jong-Hoon Choi**, D.D.S., M.S.D., Ph.D.)

## **I. INTRODUCTION**

Recurrent aphthous stomatitis (RAS), or recurrent aphthous ulcer is painful, recurring solitary or multiple ulcerations that is mainly formed on the non-keratinized oral mucosa. RAS affects at least 10% of the population, and there is a slight female predilection. The ulcers have well-circumscribed margins, erythematous halos, and yellow or gray floors, appearing first in childhood or adolescence, and heal naturally in seven to fourteen days (Scully 2008, 151).

The etiology of RAS is unknown, but etiologic consideration based on local and systemic factors have been reported. Systemic factors are genetic predisposition,

psychological stress, menstrual cycle, immune dysregulation, and nutritional and hematinic deficiencies such as iron, folic acid (folate) or vitamin B deficiencies. Local factors include sodium lauryl sulfate (SLS) in dentifrice, trauma of the oral tissues, smoking, infection, and hypersensitivities to food such as gluten, whole wheat, chocolate, nuts, shell-fish, soy, cheese, or other food items. These are thought to be the initiating factors and precipitating factors of chronic aphthous stomatitis (Ibsen, and Phelan 1992, 148-153). Scully and Porter (1989) suggested that RAS results from a hypersensitive host response to exogenous bacterial, viral, or dietary antigens which penetrate the oral mucosa.

Sodium lauryl sulfate (SLS) is an anionic detergent that has been used as the major or sole surfactant in most dentifrices for more than 20 years. It solubilizes flavor oils and lipid-soluble anti-bacterial agents in dentifrice (Waalder et al. 1993), and it has a direct anti-microbial effect (Waalder et al. 1993; Giertsen et al. 1989; Wade, and Addy 1992). It includes reduction of surface tension, and enhancement of foaming action (Wilkins 1994, 368). Because it aids in spreading the dentifrice throughout the mouth, it creates the impression of cleanliness, and a mouthful of foam just feels cleaner.

But, SLS may cause adverse effects. It is well known that SLS is an irritant to skin at high concentration and that its repeated application results in a dose-dependent contact dermatitis (van der Valk et al. 1984; Willis, Stephens, and Wilkinson 1989). Siegel and Grodon (1985; 1986) found that SLS reduce the protective barrier function of the oral epithelium. Widening of the stratum corneum, due to separation and loss of surface epithelial layers by SLS in an experimental model was observed (Herlofson, and Barkvoll 1996). Flores de Jacoby et al. (1975) said that dentifrice surfactants are responsible for a reduction in the keratinization index of the human oral epithelium, probably due to

rupture of intercellular junctions. SLS may have affinity for proteins and cause denaturation of many proteins (Tsuchumi et al. 1982). In addition, oral epithelial sloughing, ulcerations and inflammation (Rubright et al. 1978; Searls, and Berg 1986; Herlofson, and Barkvoll 1993) caused by SLS were observed. In Eva and Torstein's study, the oral mucosa is found to be much more sensitive to low concentration of SLS than skin in animal models (Anlfors, and Lyberg 2001). Researchers show that SLS dries out the protective mucous layer lining of the mouth, leaving the gingival and buccal mucosa vulnerable to irritants (Barkvoll, and Rølla 1989) and put the oral mucosa more dry environments.

Sodium lauryl sulfate also alters taste perception. It can break down phospholipids that inhibit taste receptors for bitterness, giving food a bitter taste. It is also thought to inhibit sweet receptors (John, Gerard, and Linda 1980). Upayakti, Anis, and Jenny (2008) compared detergent dentifrice with nondetergent dentifrice about sour taste sensitivity. They reported that SLS affects the change of sour taste sensitivity. Heesen and Schaupp (1973) reported that 24 commercial dentifrices decreased threshold taste acuity for as long as 75 minutes and noted that SLS, a surfactant contained in most dentifrices impairs taste.

There were some studies presenting that SLS might be a predisposing factor of RAS. Barkvoll and Rolla (1991) reported a possible association between the usage of SLS-containing dentifrice and RAS. They reported a mean decrease in ulcer incidence of 71.5% in a group of 10 RAS patients during a 3 month experiment period using SLS-free dentifrice when compared to the incidence experienced during a period of the same duration when SLS – containing toothpaste was used (Healy et al. 1999). And Chahine et al. (1997) studied the relationship between the incidence of RAS and the presence of SLS

in dentifrices with 23 volunteers. There was an 81% reduction of incidence when SLS-free dentifrice was used compared to the use of SLS-containing dentifrice.

Herlofson and Barkvoll (1994) had shown that 10 patients using SLS-free dentifrice obtained 70% reduction in the number of ulcers compared to the pre-study period using their regular dentifrice and 60% reduction compared with the patients who used a 1.2% SLS-containing dentifrice.

On the other hand, in a double-blind crossover clinical trial by Healy et al. (1999), the ulcer parameters - number of ulcer days, total pain scores, number of ulcer episodes, and number of ulcers- measured were not significantly affected by the use of SLS-free dentifrice compared to the use of SLS-containing dentifrice.

Some studies reported that there were reduction of incidence or the number of ulcers when SLS-free dentifrice was used compared to the use of SLS-containing dentifrice, and others reported that there were no significant differences in ulcer number or incidence between the period using SLS-free dentifrice and the period using SLS-containing dentifrice.

On the basis of these previous studies, there has been a lot of controversy over the effect of SLS on RAS, but we supposed that SLS might be a local irritant to RAS. The aim of this study is to compare the effects of SLS-free dentifrice with that of SLS-containing dentifrice in a population of patients suffering from RAS and figure out the effect of SLS on RAS. In previous studies, they assessed only one clinical parameter such as the number of ulcers or the incidence of ulcers except Healy's study. And they had only one control and the studies were single-blind crossover trials except Healy's study. In this study, the number of ulcers, the frequency, duration of ulcer, and pain at tooth brushing were compared using double-blind crossover trial and we also analyzed the effect of SLS according to the

number of days to experience ulcers. And we had set two control dentifrices on the supposition that other ingredients of dentifrice except SLS would affect RAS. In addition, we identified the effect of SLS in dentifrice to the change of sensitivity to sour taste and the feeling of dry mouth after tooth brushing.

## **II. MATERIALS AND METHODS**

### **1. Subjects**

Subjects for this study were recruited either by poster canvassing for RAS sufferers in Yonsei university health system (medical and dental hospital) and Yonsei university college of dentistry, or by referral from the department of oral medicine and oral diagnosis, Yonsei university dental hospital, from January 2010 to August 2010. Volunteers who had a history of regular recurrent oral ulcerations with at least 6 months duration, and more than one episode per month were included. The volunteers in the following situations were excluded: those using SLS-free dentifrice now; those who take medications affecting the oral ulcers (ex, corticosteroids); those who have chronic oral mucosal disease (lichen planus, pemphigus vulgaris, pemphigoid, and etc.); those who have allergies to food or medications; those who are pregnant.

Each volunteer was interviewed by clinician and the age, gender, medical history, and drug histories were documented at the first visit. Detailed information about the study was given by the clinician, and informed consent was obtained from all subjects prior to the start of the study. The subjects were instructed not to change their oral hygiene habits, eating habits, or lifestyle during the study. They were requested not to take any other treatment or medication to heal or relieve the oral ulcers during the entire study period.

### **2. Dentifrices and toothbrushes**

The subjects were asked to brush their teeth using their usual tooth brushing method with supplied dentifrice and toothbrush. Three dentifrices were used for this study. SLS-

free dentifrice (SLS-free) (Wiconi<sup>®</sup> dentifrice) is a commercially available SLS-free dentifrice, and SLS-A dentifrice (SLS-A) is a 1.5% SLS-containing dentifrice (Wiconi<sup>®</sup> dentifrice + 1.5% SLS), and SLS-B dentifrice (SLS-B) is a commercially available 1.5% SLS-containing dentifrice. All dentifrices were packed in the same plain white tubes labeled with the identification number of subject. Both the clinicians and subjects were blind as to the type of dentifrice. The main components of dentifrices were shown in table 1.

**Table 1. Main components of dentifrices**

	<b>SLS-free</b>	<b>SLS-A</b>	<b>SLS-B</b>
<b>Abrasives</b>	Silicon dioxide	Silicon dioxide	Silicon dioxide Precipitated calcium carbonate
<b>Humectants</b>	D-sorbitol syrup	D-sorbitol syrup	D-sorbitol syrup / Glycerin
<b>Sweeting agents</b>	Xylitol	Xylitol	Sodium saccharin
<b>Additional Agent</b>	Propolis	Propolis	Propolis / Ginseng extract
<b>Flavouring agent</b>	Phytoncide oil / Spearmint oil	Phytoncide oil / Spearmint oil	DL-menthol Sodium benzoate
<b>Surfactants</b>	Not contained	1.5% sodium lauryl sulfate	1.5% Sodium lauryl sulfate

### **3. Study design**

The design of this study was a double-blind crossover trial. This study was carried out with the approval of Institutional Review Board(IRB) of the Yonsei university dental hospital (IRB number : 2-2009-0012). The subjects were divided into three groups. Each group included thirty subjects. The group I used SLS-free and SLS-A, the group II used SLS-A and SLS-B, and the group III used SLS-free and SLS-B. The subjects were randomly allocated to one of the group. They used one dentifrice for 8 weeks, and then they used the other dentifrice for additional 8 weeks. The order of dentifrice used was selected at random. Between the two phases there was a 2-week washout period during which the subject used the same dentifrice as they used before this study.

We compared two phases in each group with the clinical parameters. The clinical parameters are shown in Table 2.

To evaluate the effect of SLS between the subjects who experience ulcers frequently and the subjects who experience ulcers infrequently, we divided the group I into two subgroups by duration of ulcers when they used SLS-free dentifrice and compared two phases between the subgroups. The duration of ulcers less than or equal to 15 days was defined as infrequent group and the duration of ulcers greater than 15 days was defined as frequent group. We compared with the number of ulcers, the number of ulcer episodes, the duration of ulcers, and mean ulcer pain between the period using SLS-free dentifrice and the period using SLS-A dentifrice.

**Table 2. Clinical parameters**

<b>Parameter</b>	<b>Explanation</b>
<b>The number of ulcers</b>	Sum of the number of ulcers for 8 weeks
<b>The number of episodes</b>	Sum of the number of episodes which subject experiences ulcers for 8 weeks
<b>The duration of ulcers</b>	Sum of days which subject experiences ulcers for 8 weeks
<b>Mean pain score</b>	The mean scores of pain (NRS*) experienced at tooth brushing while ulcers exist
<b>The taste change</b>	The change of sensitivity to sour taste after tooth brushing
<b>The feeling of dry mouth</b>	The feeling of dryness (NRS) after tooth brushing

\* NRS : numerical rating scale

#### **4. Ulcer diaries**

The subjects asked to keep a diary to record the presence of ulcers. The ulcer diary which the subject used during study period was shown in appendix A. When ulcers were developed subjects recorded the first and the last day of each episode, the number of ulcers, and pain score at tooth brushing. Pain score was chosen from a scale of zero to 10, where zero represented 'no pain' and 10 represented 'the worst pain they had ever experienced' (numerical rating scale, NRS).

After each phase, the subjects visited us and brought their diaries. We checked the diaries and oral examination was carried out by clinician. The clinician asked following questions: the taste change after tooth brushing; the feeling of dry mouth after tooth brushing; any discomforts related to dentifrices.

## **5. Statistical analysis**

The differences in clinical parameters between the two phases were analyzed by non-parametric Wilcoxon signed-rank test. SPSS Version 12.0 statistical package (SPSS<sup>®</sup> Inc., Chicago, IL, USA) was used for all statistical analyses. P values less than 0.05 were considered to be statistically significant.

## III. RESULTS

### 3.1 Subject demographics

Sixty of the 90 volunteers completed the study. During the experimental period, many of the subjects could not complete this study due to the unbearable pain. They wanted to take medications to relieve the symptoms. That's why the expulsion rate was high. 23 in group I, 18 in group II, and 19 in group III were enrolled in the study. The demographic characteristics of the Group I, Group II and Group III were shown in Table 3.

**Table 3. Demographic characteristics of subjects**

	<b>Group I (n=23)</b>	<b>Group II (n=18)</b>	<b>Group III (n=19)</b>
<b>Age*</b>	41.13±15.66	44.22 ± 11.70	45.89 ± 8.49
<b>Male</b>	8 (34.8%)	9 (50%)	10 (52.6%)
<b>Female</b>	15 (65.2%)	9 (50%)	9 (47.4%)

\* Values are given as mean ± standard deviation (SD)

### 3.2 Results for the parameters in group I

Data for the parameters in group I were described in Table 4. The duration of ulcers, mean pain score, and the feeling of dry mouth were significantly decreased during the period using SLS-free compared to the period using SLS-A ( $p < 0.05$ ). There was no significant difference in the number of ulcers, and the number of episodes. The presence of taste change after tooth brushing was 8.7% in SLS-free and 73.9% in SLS-A. There were no reported discomforts associated with dentifrices.

**Table 4. Results for the parameters in group I**

Parameters	SLS-free	SLS-A	P-value**
The number of ulcers*	4 (0~20)	4 (0~20)	0.066
The number of episodes*	3 (0~8)	3 (2~8)	0.138
The duration of ulcers*	17 (0~46)	21 (7~52)	0.038**
Mean pain score*	2 (0~7)	4 (0~8)	<0.0001**
The feeling of dry mouth*	0 (0~6)	2 (0~7)	0.042**
The taste change	Yes (8.7%) No (91.3%)	Yes (73.9%) No (26.1%)	

\* Values are given as median (minimum ~ maximum)

\*\* Statistically significant at significant level of 95%

### 3.3 Results for the parameters in group II

Data for the parameters in group II were described in Table 5. The number of ulcers, the number of episodes, the duration of ulcers, mean pain score, and the feeling of dry mouth were decreased during the period using SLS-A compared to the period using SLS-B, but there was no significant difference in all parameters. The presence of taste change after tooth brushing was 55.6% in SLS-A and 72.2% in SLS-B. There were no reported discomforts associated with dentifrices.

**Table 5. Results for the parameters in group II**

<b>Parameters</b>	<b>SLS-A</b>	<b>SLS-B</b>	<b>P-value**</b>
<b>The number of ulcers*</b>	4 (0~11)	5.5 (0~12)	0.289
<b>The number of episodes*</b>	3 (0~7)	3 (0~9)	0.159
<b>The duration of ulcers*</b>	14.5 (0~51)	22 (0~47)	0.069
<b>Mean pain score*</b>	3.5 (0~8)	5 (0~8)	0.237
<b>The feeling of dry mouth*</b>	2 (0~5)	2 (0~6)	0.478
<b>The taste change</b>	Yes (55.6%) No (44.4%)	Yes (72.2%) No (27.8%)	

\* Values are given as median (minimum ~ maximum)

\*\* Statistically significant at significant level of 95%

### 3.4. Results for the parameters in group III

Data for the parameters in group III were described in Table 6. The number of ulcers, the number of episodes, the duration of ulcers, mean pain score, and the feeling of dry mouth were significantly decreased during the period using SLS-free compared to the period using SLS-B ( $p < 0.05$ ). There was no significant difference in the number of ulcers. The presence of taste change after tooth brushing was 15.8% in SLS-free and 78.9% in SLS-B. There were no reported discomforts associated with dentifrices.

**Table 6. Results for the parameters in group III**

Parameters	SLS-free	SLS-B	<i>P</i> -value**
<b>The number of ulcers*</b>	4 (1~12)	5 (2~13)	0.112
<b>The number of episodes*</b>	3 (1~9)	4 (2~11)	0.022**
<b>The duration of ulcers*</b>	15 (4~44)	21 (8~33)	0.026**
<b>Mean pain score*</b>	1 (0~8)	3 (1~8)	0.001**
<b>The feeling of dry mouth*</b>	0 (0~5)	2 (0~7)	0.035**
<b>The taste change</b>	Yes (15.8%) No (84.2%)	Yes (78.9%) No (21.1%)	

\* Values are given as median (minimum ~ maximum)

\*\* Statistically significant at significant level of 95%

### 3.5. Results for the parameters in infrequent and frequent group

Among 23 in group I, 11 in infrequent group, and 12 in frequent group were enrolled. The demographic characteristics of the infrequent and frequent group were shown in Table 7.

Data for the parameters in infrequent group and frequent group were described in Table 8 and Table 9. In infrequent group, all the parameters were significantly decreased during the period using SLS-free compared to the period using SLS-A ( $p < 0.05$ ). On the other hand, in frequent group, there were no significant differences in all parameters except mean pain score. Mean pain score was significantly decreased during the period using SLS-free compared to the period using SLS-A ( $p < 0.019$ ).

**Table 7. Demographic characteristics of infrequent and frequent group**

	Infrequent group (n=11)	Frequent group (n=12)
<b>Age*</b>	37.45 ± 15.18	44.50 ± 15.97
<b>Male</b>	2 (18.2%)	6 (50.0%)
<b>Female</b>	9 (81.8%)	6 (50.0%)

\* Values are given as mean ± standard deviation (SD)

**Table 8. Results for the parameters in infrequent group**

Parameters	SLS-free	SLS-A	P-value**
The number of ulcers*	1 (0~3)	3 (2~7)	0.003**
The number of episodes*	1 (0~3)	3 (2~4)	0.004**
The duration of ulcers*	5 (0~12)	13 (8~41)	0.003**
Mean pain score*	0 (0~3)	2 (0~5)	0.003**

\* Values are given as median (minimum ~ maximum)

\*\* Statistically significant at significant level of 95%

**Table 9. Results for the parameters in frequent group**

Parameters	SLS-free	SLS-A	P-value**
The number of ulcers*	7.5 (4~20)	7.5 (2~20)	0.675
The number of episodes*	5 (3~8)	4.5 (2~8)	0.058
The duration of ulcers*	23.5 (17~46)	27 (7~52)	0.894
Mean pain score*	0.5 (0~6)	2 (0~7)	0.019**

\* Values are given as median (minimum ~ maximum)

\*\* Statistically significant at significant level of 95%

## IV. DISCUSSION

The oral epithelium is considered to be an important physiologic barrier to the passage of potentially harmful substances through it to the underlying connective tissue. Thus the integrity of this barrier can be important to the organism and changes in the ability of this barrier to perform its function could result in harmful effects (Siegel, and Gordon 1986).

SLS may damage the mucin layer by denaturing its glycoproteins. Mucin is the principal organic constituents of mucus, the visco-elastic material that covers all mucosal surfaces, and plays an essential role in non-immune protection of the mucosal surfaces (Tabak et al. 1982). The denaturing effect of the SLS on the mucin layer with exposure of the underlying epithelium is believed to induce an increased incidence of recurrent aphthous stomatitis (Herlofon, and Barkvoll 1994). It is possible that impaired barrier function of oral mucosa by SLS in dentifrice cause enhanced penetration of exogenous antigens. This raises the possibility that SLS could play a role in the pathogenesis of RAS (Healy et al. 1999).

In group I, the duration of ulcers was significantly decreased during the period using SLS-free dentifrice (SLS-free) compared to the period using of SLS-containing dentifrice (SLS-A). But, there was no significant difference in the number of ulcers, and the number of episodes. Therefore, it is thought that SLS altered the protective barrier of oral mucosa and delayed the healing process of ulcers, although it didn't affect the number of ulcers or the number of episodes. Therefore, SLS is thought to be perpetuating factor of RAS.

In group III, the number of episodes, and the duration of ulcers were significantly decreased during the period using SLS-free dentifrice (SLS-free) compared to the period using SLS-containing dentifrice (SLS-B).

In group II, on the supposition that other ingredients in SLS-free might affect the healing process of ulcerations, we compared SLS-A and SLS-B. There were no significant differences in all clinical parameters between SLS-A and SLS-B. Although there were other ingredients which might affect the healing process of ulcerations in SLS-A, the healing time of ulcerations did not decrease in the presence of SLS.

Some subject's response produced opposite effects to what was intended. When he or she was using SLS-free, he or she had more ulcer periods. On the contrary, when he or she was using SLS-A or SLS-B, he or she had less ulcer periods. SLS is an effective anti-plaque agent and antimicrobial agent. The direct anti-microbial effect has been attributed to adsorption of SLS to bacterial cell walls interfering with cell wall integrity (Helenius, and Simons 1975), inhibition of bacterial enzymes involved in glucose metabolism and competition for tooth binding sites (Barkvoll, Embery, and Rølla 1988). It is possible that this anti-plaque action which may help to reduce secondary bacterial infection of ulcerations. Loss of this action may mask any benefit experienced through a reduced irritant effect with the use of SLS-free dentifrice in RAS patients (Healy et al. 1999). In addition to this, we might not control all local and systemic factors which are the predisposing and precipitating factors of RAS. So, the opposite effects may result from just fluctuation of disease.

In analysis of the effect of SLS in infrequent and frequent group, there were some interesting results. When we divided the group I by duration of ulcers, our reference point was 15 because of most minor aphthous ulcers going away naturally in a week or

two. In infrequent group, all clinical parameters were significantly decreased during the period using SLS-free dentifrice. But in frequent group, none of all clinical parameter except mean pain score at tooth brushing was significantly decreased during the period using SLS-free dentifrice. SLS is a local factor that damages mucous protective layers of mouth. Using SLS-free dentifrice was beneficial to infrequent RAS sufferers in the incidence of RAS, but in frequent RAS sufferers, controlling the local factors such as SLS was not helpful to decrease the number of ulcers, the number of episode, and the duration of ulcers. So it is supposed that frequent RAS sufferers may be more affected by systemic factors such as the host's immune system rather than the local factors in the incidence of RAS. But in both groups, the mean pain score at tooth brushing were significantly decreased. Pain during tooth brushing or eating is the main cause that patients with RAS go to see a doctor. So, SLS-free dentifrice will be beneficial to RAS sufferers to reduce pain in their daily lives. In the future study, for the exact analysis, we should divide the subjects by the frequency of ulceration on the basis of pre-study evaluation period and we control the age, gender, and subject size between the two groups.

Our results showed that subjects felt more dryness after tooth brushing with SLS-A and SLS-B dentifrice. Because the SLS dries out the protective mucous layers of the mouth, SLS may induce the feeling of dry mouth after tooth brushing. So, it is better for patients with dry mouth or Sjögren syndrome to use SLS-free dentifrice.

About the taste change after tooth brushing, subjects reported that they were more sensitive to sour taste right after using SLS-containing dentifrice. That's because SLS blocks sweet sensors. All the other taste bud cells in mouth are firing away well, but the receptors which pick up the sweet sensors are not working anymore in the presence of

SLS. Not only does SLS block the sweet sensors, but also it enhances the sour and bitter sensors. So people get this massive influx of sour and bitter taste coming through the mouth. In addition to this, SLS destroys phospholipids. These fatty compounds act as inhibitors on bitter receptors. So SLS dulls the sweetness and promotes the sour and bitter taste after tooth brushing by inhibiting sweet receptors and destroying phospholipids (O'Hare, and Nick 2007). Our results were consistent with that of previous study, and SLS-free dentifrice will be beneficial to sommeliers or baristas who must have accurate taste sensitivity.

The change of sensitivity to sour taste is 73.9% in group I when the subjects used SLS-A and 55.6% in group II when the subjects used SLS-A. The percentage between group I and group II was different although they used the same dentifrice. The difference of percentage between the two dentifrices in group II was lower than group I and group III. Of course the individual variation results in this difference between the two groups. However, we compared SLS-free dentifrice with SLS-containing dentifrice in Group I and group III, and compared between different SLS-containing dentifrices in group II. So, the subjective feelings about change of sensitivity to sour taste were clearer in group I and group III than group II. For more accurate results, it would be better for us to analyze the change of sensitivity to sour taste by measurement of whole-mouth taste threshold in the future study.

Although we found out that SLS could delay healing process of ulcerations from this study because of SLS-free dentifrice reducing the duration of ulcers, there were some limitations to this study.

First, there was no pre-study evaluation period. In our study, there was only comparison between the period using SLS-free dentifrice and the period using SLS-

containing dentifrice. So, for the exact effect of SLS on RAS, we need to set the pre-study evaluation period.

Second there are many local and systemic factors in pathogenesis of RAS. So, there are many variables to control. These factors make it even more difficult for the researchers to conduct their study. We should try to control the variables such as hematinic deficiencies, trauma, the change of routine daily life, stressful events, and etc.

Third, recording their subjective symptoms by keeping a diary is not sufficiently accurate. So, we could not record the size of ulcers. It is difficult and bothersome for them to visit a clinician whenever ulcers develop. In the future study, we should develop a more accurate recording system that the patients can easily use.

And the last, the total subject size was small. During the study period, many of the volunteers recruited could not complete this experiment due to the unbearable pain. They said that during the ulcer period, they felt severe pain and it was very hard for them to consume any food due to ulceration, so they wanted to take the medication or to be treated. That's why the expulsion rate was high in this study.

From this data, we found that SLS might be a local irritating factor to oral mucosa and could play a role in healing process of ulceration. SLS-free dentifrice is helpful to reduce irritation to oral mucosa and decrease the pain while tooth brushing. It seems reasonable that dental professionals would recommend an SLS-free dentifrice for patients suffering from RAS, dry mouth, or other mucosa diseases such as Behçet's disease, lichen planus, pemphigus vulgaris and pemphigoid.

## V. CONCLUSION

This study was to compare the effects of SLS-free dentifrice (SLS-free) with that of SLS-containing dentifrice (SLS-A and SLS-B) on RAS, and following conclusions were drawn.

1. The duration of ulcers, and mean pain score were significantly decreased during the period using SLS-free compared to the period using SLS-A. And in infrequent group which was defined as the number of days to experience ulcers was 15 and under, the number of ulcers, the number of episodes, the duration of ulcers, and mean pain score were significantly decreased during the period using SLS-free compared to the period using SLS-A.
2. The number of episodes, the duration of ulcers, and mean pain score were decreased significantly during the period using SLS-free compared to the period using SLS-B.
3. The number of ulcers, the number of episodes, the duration of ulcers, and mean pain score were decreased during the period using SLS-A compared to the period using SLS-B, but there was no significant difference in all parameters.
4. Subjects felt less dry mouth after tooth brushing when they used SLS-free.
5. Subjects reported that they were more sensitive to sour taste right after using SLS-A or SLS-B than SLS-free.

It is not sure that SLS is initiating factor of RAS in this study, but we found out that the number of ulcers, the number of episodes, and the duration of ulcers were increased during the

period using SLS-containing dentifrice. Therefore, SLS is thought to be perpetuating factor of RAS. In the future, the systematic study by thoroughly controlling the confounding variables will be necessary.

## REFERENCES

Ahlfors Eva Elisabeth, and Torstein Lyberg. 2001. "Contact sensitivity reactions in oral mucosa". *Acta Odontol Scand*, 59 : 248-254.

Barkvoll P., Embery G., and Rolla G. 1988. "Studies on the interaction between sodium lauryl sulfate and hydroxyapatite using Fourier transformed infrared spectroscopy". *J Biol Buccale*, 16 : 75-79.

Barkvoll P., and Rolla G. 1989. "Possible effects of sodium lauryl sulfate(SLS)". *J Dent Res*, 68 : 991.

Barkvoll P., and Rolla G. 1991. "Possible effects of sodium lauryl sulfate (SLS) on recurrent aphthous ulcers". *J Dent Res*, 70 : 549.

Chahine Lina, Nancy Semperson, and Christopher Wagoner. 1997. "The effect of sodium lauryl sulfate on recurrent aphthous ulcers : a clinical study". *Compend Contin EducDent*, Dec;18(2) : 1238-1240.

John A. DeSimone, Gerard L. Heck, and Linda M. Bartoshuk. 1980. "Surface active taste modifiers: a comparison of the physical and psychophysical properties of gymnemic acid and sodium lauryl sulfate". *Chem Senses*, 5(4) : 317-330.

Flores de Jacoby L., Thor G., and Lange D. E. 1975. "Vergleichende klinische und

zytologische Untersuchungen nach Anwendung von zwei Zahnpasten" (in Deutsche).  
*Dtsch Zahnaerztl Z*, 30 : 385-388.

Giertsen E., Scheie A. A., and Rolla G. 1989. "Plaque inhibition by a combination of zinc citrate and sodium lauryl sulfate". *Caries Res*, 23 : 278-283.

Healy C. H., M Paterson, and S. Joyston-Bechal, D. M. Williams, M. H. Thornhill. 1999. "The effect of a sodium lauryl sulfate-free dentifrice on patients with recurrent oral ulceration". *Oral disease*, 5 : 29-43.

Helenius A., and Simons K. 1975. "Solubilization of membranes by detergents". *Biochem Biophys Acta*, 415 : 29-79.

Herlofson B. Brokstad, and Barkvoll Pöl. 1993. "Desquamative effect of sodium lauryl sulfate on oral mucosa. A preliminary study". *Acta Odontol Scand*, 51 : 39-43.

Herlofson B. Brokstad, and Barkvoll Pöl. 1994. "Sodium lauryl sulfate and recurrent aphthous ulcers: a preliminary study". *Acta Odontol Scand* , 52(5) : 257-259.

Herlofson B. Brokstad, and Barkvoll Pöl. 1996. "Oral mucosal desquamation caused by two toothpaste detergents in an experimental model". *Eur J Oral Sci*, 104 : 21-26.

Ibsen Olga A. C., and Phelan Joan Andersen. 1992. *Oral pathology for the Dental hygienist*. 1<sup>st</sup> ed. Philadelphia : WB Saunders Co.

Kowitz G., F. Lucatorto, and W. Bennett. 1973. "Effects of dentifrices on soft tissues of the oral cavity". *J Oral Med*, 28 : 105-109.

Nick O'Hare. 2007. "Why does orange juice taste so awful after you brush your teeth?". *The Guardian*. 27 September.

Rubright W. C., Walker J. A., and Karlsson U. L., Diehl D. L. 1978. "Oral slough caused by dentifrice detergents and aggravated by drugs with antiseptic activity". *J Am Dent Assoc* , 97 : 215-220.

Scully Crispian, and Porter S. 1989. "Recurrent aphthous stomatitis : current concept of aetiology, pathogenesis and management". *J oral pathol med*, 18 : 21-27.

Scully Crispian. 2008. *Oral and Maxillofacial medicine. The basis of diagnosis and treatment*. 2<sup>nd</sup> ed. Toronto : Churchill Livingstone.

Searls J. C., and Berg C. A. 1986. "The influence of dentifrice detergents on oral epithelial slough". *Dent Hyg (Chic)*, Jan : 60(1) : 20-3.

Siegel Ivens A., and Herbert P. Gordon. 1985. "Surfactant-induced increases of permeability of rat oral mucosa to non-electrolytes in vivo". *Archs Oral Biol*, 30 : 43-47.

Siegel Ivens A., and Herbert P. Gordon. 1985. "Effects of surfactants on the permeability of canine oral mucosa in vitro". *Toxicol Letters* , 26 : 153-157.

Siegel Ivens A., and Herbert P. Gordon. 1986. "Surfactant-induced alternations of permeability of rabbit oral mucosa in vitro". *Experiment Molec Pathol* , 44 : 132-137.

Tabak L. A., Levine M. J., and Mandel I. D., Ellison S. A. 1982. "Role of salivary mucins in the protection of the oral cavity". *J Oral Pathol*, 11 : 1-17.

Tzutzumi M., Oyama Y., and Suda I., Watanabe T. 1982. "Action of some detergents on succinate dehydrogenase of E. coli in vivo". *Bacteriol Abstr*, 17 : 3081-J17.

Upayakti Ifarum, Anis Irmawati, and Jenny Sunariani. 2008. "Comparison of sour taste sensitivity between detergent toothpaste and nondetergent toothpaste". *Dent J* 1 : Nomor 1 : Edisi 09-2008.

Van der Valk P. G. M., Crijns M. C., and Nater J. P., Bleumink E. 1984. "Skin irritancy of commercially available soap and detergent bars as measured by water vapour loss". *Derm Beruf Umwelt*, 32(3) : 87-90.

Von Heesen W. and Schaupp H. 1973. "Gustatory changes after the use of dentifrices and related agents". *Oral Res Abs*, 8:171.

Waalder S. M., Rölla G., and Skjörland K. K., Ögaard B. 1993. "Effects of oral rinsing with triclosan and sodium lauryl sulfate on dental plaque formation:a pilot study". *Scand J Dent Res*, 101 : 192-195.

Wade W. G., and Addy M. 1992. "Antibacterial activity of some triclosan-containing toothpastes and their ingredients". *J Periodontol* , 63 : 280-282.

Wilkins E. O. 1994. *Clinical practice of the dental hygienist*. 7<sup>th</sup> ed. Baltimore : Williams & Wilkins.

Carolyn M. Willis, Catherine J. M. Stephens, and John D. Wilkinson. 1989. "Epidermal damage induced by irritants in man: a light and electron microscopic study". *J Invest Dermatol*, 93 : 695-699.

## APPENDIX

Appendix A. Ulcer diary

## 증상 기록 일기

본 일기는 피험자 분의 내원 횟수를 줄이고 증상 확인을 위하여 시행하는 것으로 빠짐없이 기입해 주시면 감사하겠습니다. **입안이 헐었을 때만 증상을 기록하시면 됩니다.**



식별번호 :

내원일 : 20    년    월    일

2010년    월    일~2010년    월    일	
♣ 아래에서 궤양이 생긴 부위를 표시해주세요. ( 괄호 안은 개수)	
윗입술 (    개)	잇몸(    개)
아랫입술 (    개)	오른쪽볼(    개)
혀 (    개)	왼쪽볼 (    개)

궤양의 크기(해당크기에 체크)



불편감 (0~10) \_\_\_\_\_  
 0 : 전혀 아프지 않다.  
 10: 상상할 수 있는 한 최대한 아프다.

2010년    월    일~2010년    월    일	
♣ 아래에서 궤양이 생긴 부위를 표시해주세요. ( 괄호 안은 개수)	
윗입술 (    개)	잇몸(    개)
아랫입술 (    개)	오른쪽볼(    개)
혀 (    개)	왼쪽볼 (    개)

궤양의 크기(해당크기에 체크)



불편감 (0~10) \_\_\_\_\_  
 0 : 전혀 아프지 않다.  
 10: 상상할 수 있는 한 최대한 아프다.

2010년    월    일~2010년    월    일	
♣ 아래에서 궤양이 생긴 부위를 표시해주세요. ( 괄호 안은 개수)	
윗입술 (    개)	잇몸(    개)
아랫입술 (    개)	오른쪽볼(    개)
혀 (    개)	왼쪽볼 (    개)

궤양의 크기(해당크기에 체크)



불편감 (0~10) \_\_\_\_\_  
 0 : 전혀 아프지 않다.  
 10: 상상할 수 있는 한 최대한 아프다.

## ABSTRACT (IN KOREAN)

### 재발성 아프타성 구내염에 대한 라우릴 황산 나트륨의 영향

라우릴 황산 나트륨 (sodium lauryl sulfate, SLS)은 치약에 흔히 쓰이는 합성 세제로, 효과적인 변성제(denaturant)이다. 그러나 구강점막에는 자극이 되는 요소로 작용하여 여러 가지 부작용을 유발하기도 한다. 본 연구에서는 재발성 아프타성 구내염 (recurrent aphthous stomatitis, RAS)이 있는 환자에서 SLS 가 있는 치약과 SLS 가 없는 치약을 사용하여 궤양과 관련된 임상 지수들을 비교하여 RAS 의 발생에 SLS 가 미치는 효과를 알아보려고 하였다. 90 명의 자원자를 대상으로 30 명씩 세 그룹으로 나누어 시중에 판매되고 있는 SLS 가 포함되지 않은 치약 (SLS-free), 시중에 판매되고 있는 SLS 가 포함되지 않은 치약에 1.5% SLS 를 첨가한 치약 (SLS-A), 그리고 시중에 판매되고 있는 1.5% SLS 가 포함된 치약 (SLS-B) 중 두 종류의 치약을 각각 8 주 동안 사용한 후 비교하였다. 8 주 간의 사용기간 사이에는 환자가 기존에 사용하던 치약을 사용하는 2 주간의 약효 세척 단계 (washout phase)를 두었으며 총궤양수, 총궤양발생빈도, 총궤양발생일수, 양치질시의 통증, 치약 사용 후 건조감, 치약 사용 후 미각변화에 대해 비교하였다. SLS-free 사용시 SLS-A 사용시에 비해 총궤양발생일수와 양치질시의 통증이 통계적으로 유의하게 감소하였다. 또한 SLS-free 사용시 총궤양발생일수가 15 일 이하인 그룹에서는 SLS-A 사용시에 비해 총궤양수, 총궤양발생빈도, 총궤양발생일수, 양치질시의 통증이 통계적으로 유의하게 감소하였고, 15 일 초과 그룹에서는 양치질시의 통증을 제외하고는 통계적으로 유의한 차이를 보이지 않았다. SLS-free 사용시 SLS-B 사용시에

비해 총궤양발생빈도, 총궤양일수, 양치질시의 통증이 통계적으로 유의하게 감소하였다. SLS-A 사용시에는 SLS-B 사용시에 비해 모든 임상 지수에서 통계적으로 유의한 차이를 보이지 않았다. SLS-free 를 사용할 때 양치질 후의 건조감이 감소되었으며, SLS-A 나 SLS-B 를 사용한 후에 신맛에 대한 민감도가 더 증가하였다. 결론적으로 SLS 가 RAS 의 유발요인인지는 확실하지 않으나 SLS 가 포함된 치약 사용시 궤양의 개수, 발생빈도, 지속시간이 증가되는 것으로 보아 SLS 가 RAS 의 악화요인으로 작용하거나 치유를 지연시키는 요인으로 작용할 것으로 생각된다.

---

**핵심되는 말** : 합성계면활성제, 재발성 아프타성 구내염, 치약