Halitosis Control Effects of a Dentifrice Containing Resveratrol, Catechin, and Baicalin

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Objective: The purpose of this study was to investigate the change in bad breath when resveratrol, catechin, and baicalin were used as the main ingredients.

Methods: After using the experimental dentifrice, bad breath odor was measured using a sensory test. A visual analog scale was also used, and the following results were obtained.

Results: No significant differences were found between the 4 groups after 1 and 2 weeks ($p > 0.05$); after 4 weeks, the level of bad breath was significantly lower in the experimental and positive control groups compared to the level for the negative control group ($p < 0.05$). The sensory evaluation of halitosis was also significantly lower for the experimental and positive control groups compared to that for the negative control group after 4 weeks ($p < 0.05$).

Conclusion: The results of this study confirmed that foamed formulations containing resveratrol, catechin, and baicalin have halitosis reduction effects similar to those of conventional mouthwash solutions.

Keywords: baicalin, Catechin, Dentifrices, Halitosis, Resveratrol

Introduction

The World Health Organization (WHO) defines health as “a complete state of physical, mental and social wellbeing and not merely the absence of disease or infirmity.” Halitosis is not just an oral problem; it also affects people mentally and socially, hindering the healthy life of modern people with a high need for quality of life [1,2].

Halitosis is the odor blowing out of one’s mouth, and it significantly influences the daily lives of many people because of its effects on the image of an individual [3].

More than 85% of halitosis cases occur in the oral cavity. The causes of halitosis are mostly oral, such as coated tongue, periodontal disease, dental caries, stomatitis, and poor prostheses [4]. It has been found that halitosis resulting from oral causes is primarily expressed by bacterial decay and volatile sulfur compounds (VSCs) [5]. The mechanism by which VSCs are produced has been reportedly achieved through the decaying action of gram-negative anaerobic bacteria to substrates consisting of sulfur-containing amino acids, peptides, and proteins [6].

To prevent halitosis, brushing within 3 minutes of every meal, before food residues begin to cure and decay, is advised. However, it is not easy to brush after all meals or snacks for a variety of

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reasons besides the nature of one's profession. Mun et al. [7] reported that the average number of daily brushings among Korean adults was 2.39 times, indicating that brushing may be neglected after meals. Therefore, halitosis can be eliminated by replacing brushing with simple methods such as chewing gum, eating candy, using mouth spray, and gargling.

Resveratrol is an antioxidant a polyphenol-based, and grape and germinated peanut extract. This phytoallencin compound is emitted for self-defense when plants are exposed to external stresses, such as ultraviolet rays and pathogens. It has anti-cancer, antiviral, anti-aging, anti-inflammatory, and longevity effects. Cho et al. [8] traced a substance showing activity in the extract of the most cultivated Campbell Early grape variety in Korea and found that the resveratrol content was high. It has been suggested that resveratrol can effectively control inflammation and itching.

Green tea catechin is also a polyphenol with anti-carcinogenic, arteriosclerotic, antiviral, anti-obesity, anti-diabetic, antibacterial, detoxifying, and anti-inflammatory properties. It is especially effective in preventing dental caries and halitosis. Min et al. [9] confirmed that green tea extract can effectively suppress the inflammatory reaction of gums caused by *Prevotella intermedia*.

Baicalin is one of the flavonoids contained in honeyweed and roots, and it has been used in various forms in vivo for its antibacterial, anti-inflammatory, and antioxidant effects. Cho and Kim [10] showed that cell contents were eluted due to the destruction of the cell membrane function of monocytogenes strains and treatment of golden extracts on a transmission electron microscope (TEM) when observing cell morphology changes.

In previous studies, the anti-inflammatory and antibacterial effects of resveratrol and catechin were thought to be effective in preventing halitosis. Therefore, the aim of this study was to investigate and evaluate halitosis changes through the use of an experimental dentifrice.

It was thought that maintaining a satisfactory oral environment would be possible by including a component with a halitosis-preventing effect in a foam-type dentifrice that can be conveniently used by busy, modern people.

The purpose of this study was determine the effectiveness for preventing halitosis by using resveratrol, catechin, and baicalin in a dentifrice formulated as a foam tablet.

Materials and Methods

1. Subjects

1) Research subjects

The study was approved by the Institutional Review Board of the Dankook University (IRB no. DKU 2017-09-004-004). The subjects of this study were 120 people who brushed regularly more than twice a day; the number of residual teeth without dental caries or restorations was 24 or more. The study participants were adult males and females in their 20s and 40s who signed the consent form; their composition by gender and age is shown in Table 1.

2) Research subject: dentifrices

In this study, an experimental dentifrice, as well as a comparative dentifrice, standard dentifrice, and control gargle dentifrice were used. The experimental dentifrice contained xylitol, sodium hydrogen carbonate, calcium carbonate, magnesium carbonate, malic acid, stevia, magnesium stearate, hydroxypropyl methylcellulose, and fragrance powder. Resveratrol (0.05%), catechin (0.3%), and baicalin (0.1%) were the main ingredients in this effervescent tablet dentifrice. The comparative dentifrice contained xylitol, sodium hydrogen carbonate, calcium carbonate, magnesium carbonate, malic acid, stevia, magnesium stearate, hydroxypropyl methylcellulose, and fragrance powder in an effervescent tablet. It differed from the experimental dentifrice in that resveratrol, catechin, and baicalin were not ingredients. The standard dentifrice was a cream with the usual components (primarily dental-type silica). The control gargle dentifrice contained only basic ingredients, such as wetting and foaming agents and fragrances (Table 2).

Table 1. Gender and age distribution of subjects

Sex	Age			Total
	20s	30s	40s	
Male	14	14	5	33
Female	57	15	15	87
Total	71	29	20	120

Values are presented as number.

Table 2. Main ingredient content of target toothpaste

Toothpaste	Ingredient		
	Resveratrol	Catechin	Baicalin
Toothpaste 1*	0.05	0.3	0.1
Toothpaste 2**	0	0	0
Toothpaste 3***	0	0	0

Values are presented as percent (%). *Toothpaste 1: experiment toothpaste. **Toothpaste 2: comparative toothpaste. ***Toothpaste 3: standard toothpaste.

2. Methods

1) Assignment of research subjects

This study was designed for a four-week, parallel comparison, randomized trial. If an applicant who voluntarily signed the test agreement was registered, a visit evaluation was used to judge whether the selection criteria was met. The selected test subjects were assigned randomly to either the experimental group, comparative group, negative control group, or positive control group in the order of registration following 1 week of the run-in period. Thirty study subjects per group were distributed.

2) Training in dentifrice use

(1) Experimental group

In the experimental group, brushing was performed with the rotation method using the standard dentifrice for 3 minutes each morning and after dinner. After lunch, the mouth was cleaned using the experimental dentifrice.

Participants using the experimental dentifrice placed 1 tablet in the mouth, chewing and crushing it with the teeth and rubbing it on the gums, teeth, and tongue prior to gargling and

spitting out the residue. Additional brushing was avoided.

(2) Comparison group

After breakfast and dinner every day, participants in the comparison group performed the same procedure carried out by the experimental group and brushed with a standard dentifrice for 3 minutes using the rotation method. After lunch, they used the comparative dentifrice to clean the mouth.

The comparative dentifrice was made by placing 1 tablet in the mouth, chewing and crushing it with the teeth, then rubbing it on the gums, teeth, and tongue prior to gargling and spitting out the residue. Additional brushing was avoided.

(3) Negative control group

After breakfast and dinner each day, participants in the negative control group used the standard dentifrice for 3 minutes in the same manner as that used by the experimental group. Brushing was performed using the rotation method, and no special oral cleaning was performed after lunch.

(4) Positive control group

After breakfast and dinner each day, participants in the positive control group used the standard dentifrice for 3 minutes in the same manner as that used by the experimental group. Brushing was performed using the rotation method. Participants used a control dentifrice for the mouthwash, spitting 10 cc of the proper amount within 1 minute after eating lunch.

3) Halitosis test

Subjects were tested for halitosis 4 times before dentifrice use and 1, 2, and 4 weeks after use. The halitosis test was performed using BB checker (Plustech, Daejeon, Korea). An additional sensory test was performed using the visual analog scale. At the first visit, the base was measured (before dentifrice use); 1 week after the first visit, adverse reactions were confirmed and halitosis test indicators were measured. Adverse reactions were confirmed 2 weeks after the first visit (at the third visit) and halitosis test indicators were measured. The last visit confirmed adverse reactions 4 weeks after the first visit; additionally, halitosis test indicators were measured.

Figure 1. Changes in Organoleptic test by group and measurement period. E1: experimental group, E2: comparison group, NC: negative control group, PC: positive control group.

Table 3. Changes in Organoleptic test by group and measurement period

Group	N	Base	1 week	2 weeks	4 weeks
		M±SD	M±SD	M±SD	M±SD
E1	30	4.63±0.67	4.47±0.78	4.53±0.73	4.27±0.83
E2	30	4.67±0.66	4.57±0.57	4.50±0.68	4.30±0.79
NC	30	4.60±0.67	4.50±0.63	4.73±0.78	4.60±0.56
PC	30	4.53±0.68	4.60±0.50	4.37±0.67	4.37±0.76
p-value*		0.885	0.838	0.266	0.305

M±SD: mean ± standard deviation, E1: experimental group, E2: comparison group, NC: negative control group, PC: positive control group. *by one way ANOVA.

4) Data analysis

The experimental results of this study were analyzed using the IBM SPSS Statistics ver. 24.0 (IBM Co., Armonk, NY, USA) statistical program. Intergroup comparisons were analyzed with a one-way ANOVA (Scheffe post-analysis) and the Kruskal-Wallis test, among others. Intra-group comparisons were analyzed with a paired t-test, Wilcoxon's signed rank test, et cetera, and a repeated measure analysis was performed to compare intergroup differences between time points. The correlation between continuous variables was analyzed using Pearson's correlation coefficient.

Results

1. Bad breath sensory test

In the bad breath sensory test, the experimental group decreased by 0.36 to Base 4.63 ± 0.67 and 4 weeks after 4 weeks to 4.27 ± 0.83 , the comparison group decreased by 0.37 to Base 4.67 ± 0.66 to 4.30 ± 0.79 after 4 weeks, and there was no differ-

Figure 2. Changes in BB checker value by group and measurement period. E1: experimental group, E2: comparison group, NC: negative control group, PC: positive control group.

ence between the base and the negative control group after 4 weeks, the positive control group decreased by 0.16 to 4.53 ± 0.68 at Base and 4.37 ± 0.79 after 4 weeks. The experimental group and the control group decreased more than the negative and positive control groups, but there was no significant difference (Figure 1, Table 3).

2. BB checker test

In the halitosis test using the BB checker (Plustech), after 4 weeks, the experimental group decreased to 7.36 ± 14.1 , the comparative group 78.5 ± 13.0 , and the positive control group 72.8 ± 13.3 , but the negative control group increased to 87.3 ± 13.3 ($p < 0.05$), and after 4 weeks, each group. There was a significant difference between the 2 groups ($p < 0.05$) (Figure 2, Table 4).

Discussion

More than 85% of halitosis cases occur in the oral cavity. Therefore, to prevent halitosis, systemic health management is important, but oral health management is particularly important [11]. The best way to keep the oral cavity clean and healthy is brushing right after eating. Brushing removes plaque, prevents dental caries and periodontal disease, and eliminates halitosis. Conventional brushing involves the use of a cream dentifrice with a toothbrush [12]. To help manage halitosis with only the most basic brushing, it is necessary to educate regarding the proper brushing technique and develop a variety of dentifrices that combine ingredients for eliminating halitosis. Many such efforts have already been made.

Kim et al. [13] studied the antimicrobial activity on halitosis-causing strains by a dentifrice containing sodium hydrogen carbonate and triclosan, as well as the lasting effects of halitosis formation inhibition. Effectiveness was achieved when only the basic component and sodium hydrogen carbonate were present, but it was confirmed that the dentifrice mixed with sodium hydrogen carbonate and triclosan showed excellent antimicrobial effects and could more effectively suppress the

Table 4. Changes in BB checker value by group and measurement period

Group	N	Base	1 week	2 weeks	4 weeks
		M $\pm$ SD	M $\pm$ SD	M $\pm$ SD	M $\pm$ SD
E1	30	81.4 $\pm$ 11.7	78.7 $\pm$ 16.3	77.2 $\pm$ 14.9	73.6 $\pm$ 14.1 ^{**a}
E2	30	82.3 $\pm$ 12.9	81.5 $\pm$ 12.7	82.2 $\pm$ 10.8	78.5 $\pm$ 13.0 ^{a,b}
NC	30	82.3 $\pm$ 14.1	83.8 $\pm$ 14.9	84.3 $\pm$ 9.3	87.3 $\pm$ 14.3 ^b
PC	30	81.3 $\pm$ 12.4	77.4 $\pm$ 12.4	76.7 $\pm$ 11.5	72.8 $\pm$ 13.3 ^{**a}
p-value*		0.984	0.309	0.034	0.000

M $\pm$ SD: mean $\pm$ standard deviation, E1: experimental group, E2: comparison group, NC: negative control group, PC: positive control group. *by one way ANOVA. **by paired t-test between base and after. ^{a,b,c} Same letter means no statistical difference by Scheffe test.

occurrence of halitosis. In this study, halitosis measurements showed no significant differences in the change in halitosis between the four groups after 1 and 2 weeks. After 4 weeks, the halitosis levels in the experimental and positive control groups were significantly lower than those in the negative control group. It was thought that the sodium hydrogen carbonate blended to make the experimental dentifrice a foam tablet would be helpful in reducing halitosis.

Yoo et al. [14] reported that green tea extract was effective in improving gingivitis and halitosis. In their study, a dentifrice was used in combination with resveratrol, catechin, and baicalin, and it was confirmed that catechin, which occupied the largest content, had the greatest effect on the prevention of halitosis. Thus, it was shown to be effective in improving halitosis. Bae et al. [15] confirmed the effect of preventing halitosis using a dentifrice in combination with triclozan, grapefruit seed extract, eucalyptus oil, and flavonoids. In addition, it has been reported that research and development of a dentifrice that contains ingredients with excellent antioxidant, anti-inflammatory, and antibacterial activities continues. Regarding the comparative experiments on the clinical application of the halitosis tester to several species by Lee et al. [16], the halitosis test was performed using BB checker (Plustech). In addition, a sensory test was performed using the visual analog scale to check how the subjects perceived changes in halitosis [17]. It was also confirmed that the experimental and positive control groups had significantly lower levels of halitosis than the negative control group 4 weeks after the experiment.

Every year, a lot of research is being done on resveratrol, catechins, and baicalin. However, unlike catechins, few studies have confirmed the effectiveness of resveratrol and baicalin when applied orally. Jo et al. [18] reported that resveratrol is effective in protecting cells against oxidative damage. Cheon et al. [19] confirmed that resveratrol diet suppressed inflammation and bone destruction. Yang and Kim [20] studied the antibacterial effect of baicalin. It is thought that more research is needed in the future to determine how positively these ingredients, which are excellent in anti-inflammatory and antibacterial effects, have in the oral cavity.

Conclusion

As a result of this study, it was confirmed that when dentifrice in the form of foam tablets containing resveratrol, catechin, and baicalin was used, the effect of reducing bad breath was similar to that of the existing mouthwash. In the case of using the detergent containing resveritrol, catechin, and baicalin, which were used in the experimental group and the positive control group, and the foamed form, it was found to have

an effect of preventing bad breath after continuous use for at least 4 weeks.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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