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Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Biomedicine

journal homepage: www.elsevier.com/locate/apjtb

Original article http://dx.doi.org/10.1016/j.apjtb.2016.11.029

The synergistic effect of honey and cinnamon against *Streptococcus mutans* bacteria

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ARTICLE INFO

Article history:
Received 31 Aug 2016
Received in revised form 7 Oct 2016
Accepted 20 Nov 2016
Available online 12 Jan 2017

Keywords:
Synergistic effect
Honey
Cinnamon
Streptococcus mutans

ABSTRACT

Objective: To investigate the effect of Iranian honey, cinnamon and their combination against *Streptococcus mutans* bacteria.

Methods: Nine experimental solutions were examined in this study, including two types of honey (pasteurized and sterilized), two types of cinnamon extract (dissolved in distilled water or dimethyl sulfoxide) and five different mixtures of cinnamon in honey (prepared by admixing 1%–5% w/w of cinnamon extract into 99%–95% w/w of honey, respectively). Meanwhile, each of mentioned agent was considered as the first solution while it was diluted into seven serially two-fold dilutions (from 1:2 to 1:128 v/v). Therefore, eight different concentrations of each agent were tested. The antibacterial tests were performed through blood agar well diffusion method, and the minimum inhibitory concentration (MIC) was determined. Ultimately, the data were subjected to statistical analysis incorporating Two-way ANOVA and Bonferroni *post hoc* tests ($\alpha = 0.01$).

Results: The highest zone of inhibition was recorded for the mixtures of honey and cinnamon while all the subgroups containing 95%–99% v/v of honey were in the same range ($P < 0.01$). The MIC for both honey solutions were obtained as 500 mg/mL whereas it was 50 mg/mL for both cinnamon solutions. Moreover, the MIC related to all honey/cinnamon mixtures were 200 mg/mL.

Conclusions: A profound synergistic effect of honey and cinnamon was observed against *Streptococcus mutans* while there was no significant difference among extracts containing 99%–95% v/v of honey admixing with 1%–5% v/v of cinnamon, respectively.

1. Introduction

Dental caries is an infectious disease that is started by biofilm formation on tooth surface [1]. Among various causative bacteria in this biofim, *Streptococcus mutans* (*S. mutans*) has been proved to be the main corresponding species for carious lesion [2]. Therefore, any antibacterial agents against *S. mutans* could be incorporated as a preventive strategy against dental caries [3]. Although various antibacterial compounds such as chlorhexidine mouth rinse have been prescribed broadly, several side effects have been reported for these chemicals [4]. For that reason, many investigations have been performed to seek for adjunctive materials that could prevent plaque formation on tooth surfaces [3,5,6].

In the wake of increasing interest in complementary and alternative medicine, herbal extracts are attracted recently [7,8]. Appropriately, numerous literatures have reported a strong antibacterial effect for different plants and natural products against *S. mutans* [3,5,6]. Among these natural antibiotics, the unique potential of either honey or cinnamon has been documented frequently [9–14]. However, to the best of our knowledge, there is no available data about incorporating the combination of honey and cinnamon on cariogenic bacteria.

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Foundation Project: Supported by Dental Research Center of Shahed Dental School, Tehran, Iran (Grant No. 41/41).

Peer review under responsibility of Hainan Medical University. The journal implements double-blind peer review practiced by specially invited international editorial board members.

On the other hand, mixing different plants against the target bacteria were encouraged drastically in previous publications because the combination would assure the exposure of any microorganism to various chemical compounds and lead to profoundly enhanced activity [15,16]. Accordingly, it was argued that the combined treatment with honey and some plants showed enormous synergism effect against bacterial species comparing to their pure extracts [11]. Therefore, since both honey and cinnamon extracts are strongly effective against *S. mutans* [9–14], it could be hypothesized that the honey/cinnamon mixture would be more favorable.

Moreover, the broad-spectrum antibacterial potential of honey is directly depended on its component which is vastly affected by the type of producer bee and its geographic condition; because each type of bee would provide different additional factors available in its honey [17,18]. In view of that, some studies obtained that local honey products have more antibacterial efficacy comparing to commercially available ones [19].

Therefore, this lack of adequate data on the honey/cinnamon synergism as well as the variations in honey extracted from different regions has prompted us to investigate the effect of Iranian honey, cinnamon and their combination against *S. mutans* bacteria.

2. Materials and methods

2.1. Preparation of experimental agents

2.1.1. Honey

The honey was harvested by hand in spring season from beehives situated in Hajiabad area, a region situated in Ghom Province that is roughly situated in the center of Iran. The collected honey was diluted by distilled water to produce a 200 mg/mL solution. In order to avoid bacterial or yeast contamination, we had to pasteurize or sterilize the honey. However, for evaluating the effect of these process in the antibacterial effect of honey, we conducted the study in two separate groups of honey, including pasteurized (30 min at 65 °C) and sterilized (autoclaved at 121 °C and 15 atm for 20 min) honey.

2.1.2. Cinnamon

Ethanolic extract of cinnamon was prepared by immersing 200 g of cinnamon in 1000 mL of ethanol (70%) prior. After 72 h, the whole solution was filtrated using Whatman No. 1 paper (150 μm diameter hole). Subsequently, the ethanol was evaporated by means of water bath device (Gesellschaft für Labortechnik mbH, Burgwedel, Germany) while the extract was lyophilized and stored at 4 °C until the test was performed. Since the obtained extract was not soluble in water, we incorporated dimethyl sulfoxide (DMSO) (Merck Co., Darmstadt, Germany) to produce 20 mg/mL solution of cinnamon hydro-alcoholic extract for the rest of the study.

2.1.3. Honey/cinnamon mixtures

Five different mixtures of honey and cinnamon were prepared by admixing 1%–5% w/w of cinnamon extract into 99%–95% w/w of honey respectively.

2.1.4. Preparation of the dilutions

Ultimately, each of the mentioned agent was considered as the first solution while it was diluted into seven serially two-fold dilutions (from 1:2 to 1:128 v/v). Therefore, eight different concentrations of each agent were tested. However, it should be emphasized that the honey extract was diluted into distilled water while the cinnamon into DMSO and their mixture, respectively.

2.2. Antibacterial tests

2.2.1. Bacterial strain and growth condition

S. mutans PTCC 1683 (Persian Type Culture Collection, IROST, Iran) was employed in this study. The bacteria were cultured overnight in 5 mL of Mueller–Hinton broth (Liofilchem, Roseto Degli Abruzzi, Italy) at 37 °C. Ultimately, the bacterial suspension was adjusted to 0.5 McFarland's standard incorporating the sterile normal saline.

2.2.2. Susceptibility test

The susceptibility test was accomplished via blood agar well diffusion method. In this process, 200 μL of bacterial suspension was spread on each plate of blood agar medium by means of a sterile swab and the plates were put on the bench for 1 h prior to punch some wells with the dimension of 6 mm diameter × 8 mm depth using the sterile cork-borer while the wells were at least 30 mm apart from each other. Consequently, each well was filled with 30 μL solution and the plates were incubated at 37 °C and the inhibition zone around them was measured in mm scale after 24 h.

2.2.3. Minimum inhibitory concentration (MIC)

Briefly, 1 mL of the prepared bacterial suspension (~1.5 × 10^8 bacteria/mL) was inserted into the tubes containing 1 mL of nutrient broth (Merck Co., Darmstadt, Germany). Afterward, 1 mL of each mentioned two-fold dilutions (ranged from 1:1 to 1:512 v/v) were added into the tubes and incubated at 37 °C for 24 h. Finally, the minimum concentration which inhibited bacterial growth (according to the liquid turbidity) was considered as MIC for each agent.

2.3. Statistical analysis

After exploring the normal distribution using Kolmogrov–Smearnov test, the data were subjected to Two-way ANOVA in order to evaluate the effect of the agent as well as its concentration simultaneously on the zone of inhibition. Meanwhile, Bonferroni *post hoc* test was incorporated for pairwaise comparisons while the level of significance was adjusted as 0.05.

3. Results

3.1. Susceptibility test

The mean amount of inhibition zone and the SD related to all subgroups are depicted in Table 1. It showed that the highest value was recorded for the mixtures of honey and cinnamon while all the subgroups containing 95%–99% v/v of honey were in the same range. Therefore, honey and cinnamon showed strong synergistic antibacterial effect against *S. mutans* because their pure solutions were not as much effective comparing to their combination.

The pairwise *P* values of serially two-fold dilutions of each agent are demonstrated in Tables 2–6. As it is evident, the least

Table 1

Zone of inhibition for each subgroup.

Solution	CD	CW	HS	HP	H95%	H96%	H97%	H98%	H99%
1:1	17.00 ± 1.00	23.33 ± 2.30	25.00 ± 0.00	25.00 ± 1.00	36.66 ± 7.57	40.00 ± 1.00	40.00 ± 0.00	40.00 ± 0.00	40.00 ± 0.00
1:2	17.00 ± 0.00	12.66 ± 1.15	20.33 ± 2.51	20.00 ± 0.00	30.00 ± 1.00	30.00 ± 1.00	26.33 ± 2.08	29.00 ± 2.64	30.00 ± 1.00
1:4	10.00 ± 6.90	11.66 ± 3.05	17.66 ± 1.15	16.00 ± 2.64	26.00 ± 1.00	26.00 ± 1.00	23.00 ± 2.64	24.66 ± 2.30	26.00 ± 1.00
1:8	11.33 ± 2.08	15.00 ± 2.64	14.66 ± 3.05	14.00 ± 1.00	20.00 ± 1.73	22.66 ± 1.15	18.00 ± 1.00	18.66 ± 4.93	22.00 ± 1.00
1:16	13.00 ± 1.73	9.00 ± 1.00	13.00 ± 1.00	14.00 ± 1.00	19.00 ± 1.00	15.00 ± 0.00	15.00 ± 0.00	12.66 ± 2.08	12.00 ± 2.64
1:32	12.00 ± 1.00	8.00 ± 0.00	12.66 ± 0.57	12.33 ± 0.57	15.00 ± 2.64	12.00 ± 1.00	12.00 ± 1.00	12.33 ± 0.57	12.00 ± 1.00
1:64	12.00 ± 0.00	8.00 ± 1.15	11.00 ± 0.00	12.66 ± 2.00	12.00 ± 1.00	12.00 ± 0.00	12.00 ± 2.00	11.66 ± 1.73	12.00 ± 0.57
1:128	11.00 ± 0.00	8.00 ± 0.00	10.00 ± 1.00	12.00 ± 0.00	12.00 ± 0.00	11.66 ± 0.57	12.00 ± 0.00	11.66 ± 0.57	12.00 ± 0.00
DW	11.00 ± 0.00	8.00 ± 0.00	8.00 ± 0.00	8.00 ± 0.00	11.00 ± 0.00	11.00 ± 0.00	11.00 ± 0.00	11.00 ± 0.00	11.00 ± 0.00

Data were expressed as mean ± SD. DW: Distilled water; CD: Cinnamon dissolved in DMSO; CW: Cinnamon dissolved in water; HS: Sterilized honey; HP: Pasteurized honey; H95%–H99%: Honey and cinnamon complex containing 95%–99% v/v of honey.

Table 2

Pairwise comparison of *P* values related to different dilutions of cinnamon dissolved in DMSO (above the diagonal) and cinnamon dissolved in water (below the diagonal).

	1:1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	DW
1:1		1.00	0.01	0.60	1.00	1.00	1.00	0.25	0.25
1:2	0.000		0.01	0.60	1.00	1.00	1.00	0.25	0.25
1:4	0.000	1.00		1.00	1.00	1.00	1.00	1.00	1.00
1:8	0.000	1.00	1.00		1.00	1.00	1.00	1.00	1.00
1:16	0.000	1.00	1.00	0.25		1.00	1.00	1.00	1.00
1:32	0.000	1.00	1.00	0.01	1.00		1.00	1.00	1.00
1:64	0.000	1.00	1.00	0.01	1.00	1.00		1.00	1.00
1:128	0.000	1.00	1.00	0.01	1.00	1.00	1.00		1.00
DW	0.000	1.00	1.00	0.01	1.00	1.00	1.00	1.00	

DW: Distilled water.

Table 3

Pairwaise comparison of *P* values related to different dilutions of pasteurized honey (above the diagonal) and sterilized honey (below the diagonal).

	1:1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	DW
1:1		1.00	0.000	0.000	0.000	0.000	0.000	0.000	0.000
1:2	1.00		1.00	0.25	0.25	0.002	0.006	0.001	0.000
1:4	0.006	1.00		1.00	1.00	1.00	1.00	1.00	0.001
1:8	0.000	0.60	1.00		1.00	1.00	1.00	1.00	0.25
1:16	0.000	0.006	1.00	1.00		1.00	1.00	1.00	0.25
1:32	0.000	0.002	1.00	1.00	1.00		1.00	1.00	1.00
1:64	0.000	0.000	0.04	1.00	1.00	1.00		1.00	1.00
1:128	0.000	0.000	0.002	1.00	1.00	1.00	1.00		1.00
DW	0.000	0.000	0.000	0.04	1.00	1.00	1.00	1.00	

DW: Distilled water.

Table 4

Pairwise comparison of *P* values related to different dilutions of the honey and cinnamon complex containing 95% v/v (above the diagonal) and 96% v/v (below the diagonal) of honey.

	1:1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	DW
1:1		0.42	0.000	0.000	0.000	0.000	0.000	0.000	0.000
1:2	0.000		1.00	0.000	0.000	0.000	0.000	0.000	0.000
1:4	0.000	1.00		0.25	0.01	0.000	0.000	0.000	0.000
1:8	0.000	0.006	1.00		1.00	1.00	0.001	0.001	0.000
1:16	0.000	0.000	0.000	0.002		1.00	0.01	0.01	0.001
1:32	0.000	0.000	0.000	0.000	1.00		1.00	1.00	1.00
1:64	0.000	0.000	0.000	0.000	1.00	1.00		1.00	1.00
1:128	0.000	0.000	0.000	0.000	1.00	1.00	1.00		1.00
DW	0.000	0.000	0.000	0.000	1.00	1.00	1.00	1.00	

DW: Distilled water.

Table 5
Pairwise comparison of *P* values related to different dilutions of the honey and cinnamon complex containing 97% v/v (above the diagonal) and 98% v/v (below the diagonal) of honey.

	1:1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	DW
1:1		0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
1:2	0.000		1.00	0.000	0.000	0.000	0.000	0.000	0.000
1:4	0.000	1.00		1.00	0.001	0.000	0.000	0.000	0.000
1:8	0.000	0.000	0.25		1.00	0.25	0.25	0.25	0.01
1:16	0.000	0.000	0.000	0.25		1.00	1.00	1.00	1.00
1:32	0.000	0.000	0.000	0.10	1.00		1.00	1.00	1.00
1:64	0.000	0.000	0.000	0.01	1.00	1.00		1.00	1.00
1:128	0.000	0.000	0.000	0.01	1.00	1.00	1.00		1.00
DW	0.000	0.000	0.000	0.002	1.00	1.00	1.00	1.00	

DW: Distilled water.

Table 6
Pairwise comparison of *P* values related to different dilutions of the honey and cinnamon complex containing 99% v/v of honey.

	1:1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	DW
1:1		0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
1:2			1.00	0.001	0.000	0.000	0.000	0.000	0.000
1:4				1.00	0.000	0.000	0.000	0.000	0.000
1:8					0.000	0.000	0.000	0.000	0.000
1:16						1.00	1.00	1.00	1.00
1:32							1.00	1.00	1.00
1:64								1.00	1.00
1:128									1.00
DW									

DW: Distilled water.

effective agent included cinnamon diluted by DMSO because none of its experimental concentrations had significant difference with distilled water (Table 2). Conversely, the mixture containing 95% v/v of honey and 5% v/v of cinnamon was the strongest agent because it showed significantly higher zone of inhibition comparing to distilled water even in sixteenth fold dilution (1:16 represented in Table 4).

On the other hand, as shown in Table 3, the sterile honey could be considered more effective than the pasteurized one because its eighth fold dilution (1:8) was significantly differed with distilled water; while in pasteurized subgroup the least concentration which showed noticeable difference with distilled water included the fourth fold dilution (1:4).

The pairwise *P* values comparing different agents with the same concentrations were displayed in Tables 7–10. Accordingly, in the first four concentrations (1:1, 1:2, 1:4 and 1:8 represented in Tables 7 and 8, respectively), although there was no significant difference between the five subgroups containing 95%–99% v/v of honey, all of them are statistically distinguishable from other agents. Moreover, pasteurized and sterile honeys did not have significant difference with cinnamon diluted by water while all of these three subgroups were noticeably different from the DMSO diluted cinnamon.

In contrast, in the latter four concentrations (1:16, 1:32, 1:64 and 1:128 represented in Tables 9 and 10, respectively), almost all the agents in any subgroups did not have significant difference with each other. It meant that in very low concentrations, all the experimental solutions showed weak antibacterial capacity.

3.2. MIC

In our experiment, the MIC of both types of pure honey (sterilized and pasteurized), pure cinnamon extract dissolved in

Table 7
Pairwise comparison of *P* values related to same dilution of different experimental solutions, 1:1 dilution (above the diagonal) and 1:2 dilution (below the diagonal).

1:1/1:2	HS	HP	CD	CW	H95%	H96%	H97%	H98%	H99%
HS		1.00	0.001	1.00	0.000	0.000	0.000	0.000	0.000
HP	1.00		0.001	1.00	0.000	0.000	0.000	0.000	0.000
CD	1.00	1.00		0.10	0.000	0.000	0.000	0.000	0.000
CW	0.002	0.006	1.00		0.000	0.000	0.000	0.000	0.000
H95%	0.000	0.000	0.000	0.000		1.00	1.00	1.00	1.00
H96%	0.000	0.000	0.000	0.000	1.00		1.00	1.00	1.00
H97%	0.25	0.10	0.000	0.000	1.00	1.00		1.00	1.00
H98%	0.000	0.000	0.000	0.000	1.00	1.00	1.00		1.00
H99%	0.000	0.000	0.000	0.000	1.00	1.00	1.00	1.00	

CD: Cinnamon dissolved in DMSO; CW: Cinnamon dissolved in water; HS: Sterilized honey; HP: Pasteurized honey; H95%–H99%: Honey and cinnamon complex containing 95%–99% v/v of honey.

Table 8

Pairwise comparison of *P* values related to same dilution of different experimental solutions, 1:4 dilution (above the diagonal) and 1:8 dilution (below the diagonal).

1:4/1:8	HS	HP	CD	CW	H95%	H96%	H97%	H98%	H99%
HS		1.00	0.002	0.25	0.000	0.000	0.01	0.01	0.000
HP	0.000		0.25	1.00	0.000	0.000	1.00	0.000	0.000
CD	1.00	1.00		1.00	0.000	0.000	0.000	0.000	0.000
CW	1.00	1.00	1.00		0.000	0.000	0.000	0.000	0.000
H95%	1.00	0.25	0.000	1.00		1.00	1.00	1.00	1.00
H96%	0.001	0.000	0.000	0.002	1.00		1.00	1.00	1.00
H97%	1.00	1.00	0.04	1.00	1.00	1.00		1.00	1.00
H98%	1.00	1.00	0.006	1.00	1.00	1.00	1.00		1.00
H99%	0.006	0.001	0.000	0.01	1.00	1.00	1.00	1.00	

CD: Cinnamon dissolved in DMSO; CW: Cinnamon dissolved in water; HS: Sterilized honey; HP: Pasteurized honey; H95%–H99%: Honey and cinnamon complex containing 95%–99% v/v of honey.

Table 9

Pairwise comparison of *P* values related to same dilution of different experimental solutions, 1:16 dilution (above the diagonal) and 1:32 dilution (below the diagonal).

1:16/1:32	HS	HP	CD	CW	H95%	H96%	H97%	H98%	H99%
HS		1.00	1.00	1.00	0.25	1.00	1.00	1.00	1.00
HP	1.00		1.00	1.00	1.00	1.00	1.00	1.00	1.00
CD	1.00	1.00		1.00	0.25	1.00	1.00	1.00	1.00
CW	1.00	1.00	1.00		0.000	0.25	0.25	1.00	1.00
H95%	1.00	1.00	1.00	0.01		1.00	1.00	0.10	0.01
H96%	1.00	1.00	1.00	1.00	1.00		1.00	1.00	1.00
H97%	1.00	1.00	1.00	1.00	1.00	1.00		1.00	1.00
H98%	1.00	1.00	1.00	1.00	1.00	1.00	1.00		1.00
H99%	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	

CD: Cinnamon dissolved in DMSO; CW: Cinnamon dissolved in water; HS: Sterilized honey; HP: Pasteurized honey; H95%–H99%: Honey and cinnamon complex containing 95%–99% v/v of honey.

Table 10

Pairwise comparison of *P* values related to same dilution of different experimental solutions, 1:64 dilution (above the diagonal) and 1:128 dilution (below the diagonal).

1:16/1:32	HS	HP	CD	CW	H95%	H96%	H97%	H98%	H99%
HS		1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
HP	1.00		1.00	1.00	1.00	1.00	1.00	1.00	1.00
CD	1.00	1.00		1.00	1.00	1.00	1.00	1.00	1.00
CW	1.00	1.00	1.00		1.00	1.00	1.00	1.00	1.00
H95%	1.00	1.00	1.00	1.00		1.00	1.00	1.00	1.00
H96%	1.00	1.00	1.00	1.00	1.00		1.00	1.00	1.00
H97%	1.00	1.00	1.00	1.00	1.00	1.00		1.00	1.00
H98%	1.00	1.00	1.00	1.00	1.00	1.00	1.00		1.00
H99%	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	

CD: Cinnamon dissolved in DMSO; CW: Cinnamon dissolved in water; HS: Sterilized honey; HP: Pasteurized honey; H95%–H99%: Honey and cinnamon complex containing 95%–99% v/v of honey.

DMSO and the combined solution containing 50:50 (v/v) honey/cinnamon was obtained as 500, 1 and 1 mg/mL, respectively.

4. Discussion

The results of the current investigation revealed the profound synergistic effect of honey and cinnamon against *S. mutans* while there was no significant difference among extracts containing 99%–95% v/v of honey admixing. Therefore, it seems that the starch of cinnamon could strongly increase the antibacterial effect of honey against *S. mutans*. Actually, we compared different amount of mixed cinnamon in honey to conclude about the best concentration of synergism, but interestingly it was revealed that the presence of cinnamon even in very low fractions would be efficient enough. Therefore, the least amount (such as 1% v/v) is preferred because the admixed cinnamon would not affect the honey taste, which is a major aspect for consumption.

Our synergism outcome is different from the study of Probst *et al.* who reported very weak antibacterial potential for the combination of propolis/cinnamon comparing to pure cinnamon or propolis [16]. However, this disagreement could be related to the difference in detailed composition of honey and propolis. In addition, they incorporated 70% ethanol in their solutions, while we used either distilled water or DMSO because it has been

documented that the ethanol could impact the antibacterial effect of each solution [12].

Moreover, the synergism antibacterial activity of honey has been proved by admixing with other plants such as ginger. In this aspect, Moussa *et al.* argued synergism of honey and ginger against some bacterial species including *Escherichia coli* and *Staphylococcus aureus* [20]. Besides that, Moussa *et al.* also concluded that "honey-ginger powder extract mixtures have the potential to serve as cheap source of antibacterial agents especially for the drug resistant bacterial strains" [20], which could confirm our results.

In contrast to our findings, Patel *et al.* reported similar zone of inhibition for *S. mutans* around honey extract comparing to the mixture of honey and ginger [11]. This controversy could be attributed to the variations in honey composition collected from different regions. Actually, the chemical ingredients of honey including the amount of trace elements, vitamins, *etc*. is directly related to the nutrition and geographic origin of the honey bee [17].

Despite 70% concentration of sugar, honey could be classified as anti-cariogenic agent as the enormous published data argued strong antibacterial potency of honey, which could surpass its cariogenicity [21]. Although the exact antibacterial mechanism of honey is not clear yet [10], the main proposed theory is related to its hydrogen peroxide content [22]. However, this theory is challenged for *S. mutans* because this species, which is categorized as viridans streptococci, produces H_2O_2 itself as alpha hemolysis [23,24]. Alternatively, the other mechanism that could contribute to the antibacterial nature of honey includes its very high osmotic pressure [22] while the enormously high sugar content would lead to lysis of the bacterial cell wall [10]. Furthermore, the chemical factors of honey such as phenolic acids, lysozyme, flavonoids, phytochemicals, antioxidants, beeswax, nectar, pollen, propolis as well as low pH and low redox potential could be corresponding to the robust antibacterial potential of honey [21,25,26]. Hence, it would be quite beneficial if the honey (instead of other types of sugar) is incorporated as a sweetener in toothpaste, gum, candy, chocolates, *etc*. [27].

On the other hand, the mechanism that is responsible for antimicrobial property of cinnamon includes its chemical active ingredients such as cinnamic aldehyde and eugenol [12]. Cinnamaldehyde is an electronegative compound that could interfere with the biologic process in microorganism specially nitrogen containing substances such as proteins and nucleic acids [28]. Furthermore, the cinnamon extract contains aromatic aldehyde which would impede the decarboxylase activity of amino acid in cell [14]. However, further studies are suggested to clarify the mechanism responsible for honey/cinnamon synergism.

Overwhelmingly, since neither the honey nor cinnamon has adverse effect on human tissues [20], they could be safely incorporated in oral environment for caries prevention. Moreover, although both of the two agents individually have considerable antibacterial potential, their tremendous synergism could simplify the adjustment of a therapeutic level against *S. mutans*.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

The authors are very grateful to Dental Research Center of Shahed Dental School, Tehran, Iran (Grant No. 41/41) for financial support of the study.

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