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Original Article

UTILIZATION RED DRAGON FRUIT PEEL (*HYLOCEREUS POLYRHIZUS*) ETHANOL EXTRACT IN ORAL THIN FILM STRIP AS A MOUTH FRESHENER

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ABSTRACT

Objective: The aim of this study was to formulate an oral thin film strip (OTFS) contained the red dragon fruit peel (RDFP) ethanol extract (*Hylocereus polyrhizus*) and evaluate the characteristic, stability and antibacterial activity against *Streptococcus mutans (S. mutans)*.

Methods: The film was made using the solvent casting method by adding a variety of concentration ethanol extract of red dragon fruit peel (5%, 10%, and 15%). The films were evaluated in organoleptic test, weight, thickness, pH, disintegration time, folding endurance, stability test and antibacterial activity.

Results: The results showed that the film provided a distinctive color, aroma, and taste of the extract. The result of film evaluation had weight between 0.07-0.21 g, thickness between 0.10-0.20 mm, pH between 5.70-5.99, disintegration time between 34.99-49.13 s, and folding endurance between 321.00-812.83 times. The films were stable for 2 mo at a variety storage temperature (4±2 ℃, 28±2 ℃, and 40±2 ℃). The films showed antibacterial activity for 5%, 10% and 15% with the diameter of inhibition 8.5 mm, 10.8 mm, and 12.9 mm, respectively.

Conclusion: Ethanol extract of RDFP can be utilized as a mouth freshener film that is stable for 2 mo and has antibacterial activity against *S. mutans*.

Keywords: Red dragon fruit peel, OTFS, Stability, Antibacterial activity

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INTRODUCTION

Oral administration route is the most preferred route of administration compared to the other drug administration. This route is related to an easy administration, suitable for drug formulation in solid form, and associated with compliance and convenience of administration to patients [1].

Based on the study that was conducted by 17% of the population studied (without disease and complaints of dysphagia) had difficulty swallowing drug in tablet form [2]. So, it is necessary to choose the right dosage form to facilitate drug administration to the patients. Oral film is one of the most widely alternative dosage forms to replace conventional tablets or capsules. The US FDA defined oral film as an oral soluble solid dosage form which can dissolve rapidly when it placed on the tongue [3]. Oral film is one of the oral route administrations which can increase patients' acceptance through its rapid solubility administration without water to assist swallowing [4]. Oral films can be made by five methods such as solvent casting, semi-solid casting, hot-melt extrusion, solid dispersion extrusion, and rolling method. The most preferred use method is solvent casting method [5]. This method is considered simpler than others; thereby, water-soluble materials are dissolved to a thick and clear solution [6, 7]. Then, the other additive materials are dissolved in other suitable solvents until the desired mass is formed. Then, the two masses are mixed and poured in to the cast, dried it into the oven and then a thin film is formed [8]. Some drugs that had applied oral film for drug delivery such as felodipine [9], amlodipine besylate [10], Glimipiride [11] or naproxen sodium [12].

Halitosis, also known as bad breath, is a medical condition that can affect peoples of all ages. In dental health practitioners, bad breath is the third most common problem that patients complaining about after cavities and periodontal disease [13]. One of the sources of this problem is due to bacterial activity in the oral cavity, such as *S. mutans* [14].

Red dragon fruit (*Hylocereus polyrhizus*) which is later mentioned as *H. polyrhizus* is one of the fruits which contains many secondary metabolites and have a very good antibacterial activity [15, 16]. The skin of the red dragon fruit accounts for approximately 30-35% of the fruit, which is still limited to be used and frequently discarded as waste [17]. This is very unfortunate because the red dragon fruit peel has many benefits, including high contained of vitamin C, flavonoids, tannins, alkaloids, steroids, and saponins [18]. Therefore, the study aimed to formulate an oral strip film contained of RDFP ethanol extract and to evaluate the characteristics, stability and antibacterial activity against *S. mutans*.

MATERIALS AND METHODS

Materials

Red dragon fruit peel (*H. polyrhizus*) was collected from a plantation at Simpang Empat District (3 °07'22.0"N/98 °25'24.3"E, 1200 m asl, Karo, North Sumatra). The sample was determined by Herbarium Medanense, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Sumatera Utara, Indonesia with the identification number: 6519/MEDA/2021. HPMC, glycerol and ethanol 96% were purchased from Smart Lab Company (Medan, Indonesia). Distilled water, dimethyl sulfoxide (DMSO), menthol, peppermint oil, Mueller Hinton agar (MHA), nutrient agar, nutrient broth, sodium benzoate, sucrose, corn starch, sorbitol and citric acid were purchased from CV Rudang Jaya (Medan, Indonesia). All chemical reagents used were analytical grade and applied without further purification.

Preparation of RDFP extract

The peel of red dragon fruit was cleaned in the water, then drained and weighed the peel of the red dragon fruit. The peel of red dragon fruit was drained in drying cabinet at a temperature 40-60 °Cuntil it dry. After drying process, the RDFP simplicia was powdered using mixer. The extract was made from dry simplicia powder by maceration method using ethanol 96% as the solvent. Ten parts of simplicia was put into a vessel with 75 parts of the solvent, cover it, then leave it for 5 d, protected from the light white stirring often. After that, squeeze, washed the pulp with the solvent until it 100 parts. Moved to the other vessel, and did the same steps for 2 d, and then filtered it. Then, concentrate the filtrate with rotary evaporator until the extract reached [19].

Methods of OTFS formulation

The formulation of oral film was made in four formulations, F1 (without extract), F2 (5% extract), F3 (10% extract), and F4(15% extract). OTFS of RDFP (*H. polyrhizus*) ethanol extract formula can be seen in the table 1.

Preparation of OTFS

A polymer solution was made by dissolving corn starch into beaker with 20 parts of distilled water by weight of polymer, then stirred for 2 min, then added HPMC into the same beaker stirred it for 5 min. Sodium benzoate was dissolved in 7 ml of hot water in a different beaker glass, then added citric acid, sucrose, and menthol. All the materials were stirred until completely mixed. The solution mixture was added to the polymer solution stirred until homogeny. Then, 4 drops of peppermint oil and distilled water were added.

The solution was slowly stirred until completely mixed to avoid the bubbles. After all the ingredients were mixed, put the solution into the mold, then dried at the oven with a temperature 37 ℃for 24 h. After it dry, the film was carefully removed from the mold and then cut to size 2x3 cm [17].

Table 1: Formulation of OTFS ethanol extract of RDFP

Ingredients	Formula				Function
	F1	F2	F3	F4	
Ethanol extract of RDFP	-	5%	10%	15%	Active Ingredient
Corn Starch	3%	3%	3%	3%	Polymer
HPMC	3%	3%	3%	3%	Polymer
Glycerol	2%	2%	2%	2%	Plasticizer
Citric Acid	0.5%	0.5%	0,5%	0.5%	Saliva Stimulating Agent
Sorbitol	0.5%	0.5%	0,5%	0.5%	Plasticizer and Sweetener
Sucrose	1%	1%	1%	1%	Sweetener
Menthol	0.1%	0.1%	0.1%	0.1%	Flavoring Agent
Sodium Benzoate	0.1%	0.1%	0.1%	0.1%	Preservative
Peppermint Oil	q. s	q. s	q. s	q. s	Essence
Distilled water	ad 150 ml	ad 150 ml	ad 150 ml	ad 150 ml	Solvent

Oral films characterization evaluations

Organoleptic test

Organoleptic test was carried out by visual observation, included homogeneity, color, texture, aroma, and taste [21].

Weight test

Six films were random selected and their average weight was calculated using an analytical balance. One film was taken randomly and then weight and compare it with the average weight to get the deviation value [21].

Thickness test

Measurement of film thickness using a micrometer screw was carried out on 6 films of each formula in 5 different places, upper and lower right corners; upper and lower left corners; and the middle. Then, all of the measurements were added and divided to find the average of the thickness [20].

pH test

The pH test was carried out using a pH meter. The instrument was first calibrated using a neutral pH buffer solution (pH 7) and an acidic pH buffer solution (pH 4) until the instrument showed the pH value. Then, washed the electrode with distilled water and then dried with a tissue. A film in a beaker glass was dissolved with 10 ml of distilled water. Then, the electrode was dipped in the solution and wait until the instrument showed the pH value. The test was carried out on 6 films [21].

Disintegration time test

The disintegration time was measured using the petri dish method. Three ml of distilled water was placed in a petri dish and one film was added to the surface of the water and the time required for the film to dissolve was calculated as disintegration time of the film [22].

Folding endurance test

This test was carried out by folding the film in the same layer continuously until it breaks. The number of folds without breaking was calculated as the value of the film folding endurance [21].

Stability test of OTFS

The film was wrapped using aluminum foil, packed in a tightly close container. The films were stored at cold temperatures (4±2 ℃, room temperatures (28±2 ℃, and hot temperatures (40±2 ℃ for 8 w. Then, characterization evaluation was carried out, which included organoleptic, weight, thickness, pH, disintegration time, and folding endurance of the film. Each evaluation was carried out with an interval of 2 w [21].

Antibacterial activity of RDFP ethanol extract and oral films test

The microorganism tested was *S. mutans* ATCC 25175 bacteria isolated from Microbiology Laboratory of the Faculty of Pharmacy, Universitas Sumatera Utara. The bacterial inoculum (0.1 ml) was put into a sterile petri dish, and pour with 15 ml of MHA at a temperature of 45-50 ℃The petri dish was shake on the table surface until mixed homogeneously. On the solid media, discs were placed which had been soaked with a concentration of red dragon fruit peel ethanol extract of test solution and DMSO as a negative control, and the film which has been formed in a circle was placed, then incubated for 24 h at a temperature of 35±2 ℃ Then, the bacterial growth was observed and the diameter of the inhibition was measured, marked by the presence of a clear area, indicating that the area was not overgrown with bacteria [23].

RESULTS

Extraction of RDFP

In the manufacture of the extract, RDFP was dried in drying cabinet at a temperature of 40-60 ℃to dry. The results of extraction by maceration method from 1000 g simplicia powder with ethanol 96% give a concentrate extract of 103.7494 g.

OTFS characterization

The oral film's organoleptic test was measured by using sense perceptions. The result of oral film's organoleptic test can be seen on the table 2 and the other evaluation, such as weight, thickness, pH, disintegration time, and folding endurance can be seen on the table 3.

In organoleptic evaluation, based on the homogeneity category, there were no difference between four formulas. In the texture category, there were a difference between F1, F2, F3 and F4, where the higher concentration which added makes the texture of oral film becomes slightly oily and with the addition of 15% extract, the film has a sticky texture. In color category, there were a difference between each formula, where the addition of extract makes the color of the film was derived from the extract's color. The higher concentration of the extract, make a film's color become darker. In the category of aroma, F1 was different with F2, F3, and F4, where

the addition of extract gives a distinctive aroma from the extract in the film. In the category of taste, there were a distinctive taste from the extract. The higher concentration provides a strong taste of the extract.

Table 2: The result of oral film's organoleptic

Parameter	F1	F2	F3	F4
Homogeneity	Homogenous	Homogenous	Homogenous	Homogenous
Texture	Dry and Smooth	Dry and Smooth	Dry and slightly oily	Oily and slightly sticky
Color	No color and transparent	Light Brown	Brown	Dark Brown
Aroma	Peppermint	Extract Aroma and Peppermint	Extract Aroma and Peppermint	Extract Aroma and Peppermint
Taste	Peppermint with a little sour	Peppermint with a little sour and extract's taste	Peppermint with a little sour and extract's taste	Peppermint with a little sour and extract's taste

Table 3: The result of OTFS's evaluation

Formula	Weight (g)	Thickness (mm)	pH	Disintegration time (s)	Folding endurance (times)
F1	0.0700±0.0081	0.1026±0.0058	5.70±0.0319	34.99±0.3760	812.83±21.4431
F2	0.1083±0.0177	0.1303±0.0100	5.79±0.0256	39.65±0.3808	703.33±42.3701
F3	0.1566±0.0170	0.1683±0.0076	5.89±0.0226	44.34±0.4124	526.83±24.0307
F4	0.2066±0.0137	0.2023±0.0050	5.99±0.0368	49.13±0.4893	321.00±13.2035

Data in mean±SD, (n=6)

Based on the results obtained, all formula showed a good weight in the range of 70-206 mg. The results of the film thickness of each formula meet the thickness requirements and standard deviation requirements of<5%, where the oral film thickness requirement was less than 0.25 mm [20]. The pH value shows that each formula did not have a much different value. The pH of the film from each formula met the requirements for the pH of the oral film, namely 5.5-7.9 [21]. The formula with the highest extract concentration (F4) had the greatest disintegration time and the lower extract concentration had the faster time for the film disintegrate. The disintegration time of the resulting films still meets the disintegration time requirements which was less than 1 min [24]. Folding endurance was a test to estimate the mechanical properties or flexibility of the film. The measurement of folding endurance by folding at the same point repeatedly until the film breaks [25]. Based on the results, the folding endurance of the resulting preparations met the requirements for good folding resistance, i.e., a film that does not break with a number of folds 300 times was considered to have good flexibility [26].

OTFS stability test

The stability evaluation film was measured for 2 mo includes at three variant temperatures (4±2 °C, 28±2 °C and 40±2 °C). The characterization of film was evaluated, includes organoleptic, weight, thickness, pH, disintegration time, and folding endurance. The result of weight stability test can be seen in table 4.

Table 4: Results of weight stability evaluation

Parameters	Weight (g)				
	0 w	2 w	4 w	6 w	8 w
Cold conditions (4±2 °C)					
F1	0.0700±0.0081	0.076±0.0074	0.078±0.0150	0.076±0.0094	0.073±0.0110
F2	0.1083±0.0177	0.118±0.0106	0.115±0.0125	0.120±0.0810	0.118±0.0068
F3	0.1566±0.0170	0.165±0.0125	0.166±0.0137	0.158±0.0068	0.155±0.0138
F4	0.2066±0.0137	0.213±0.0074	0.208±0.0106	0.205±0.0125	0.210±0.0153
Room temperature (28±2 °C)					
F1	0.0700±0.0081	0.07±0.0082	0.071±0.0146	0.07±0.0081	0.065±0.0125
F2	0.1083±0.0177	0.106±0.0124	0.108±0.0146	0.110±0.0115	0.093±0.0094
F3	0.1566±0.0170	0.155±0.0095	0.156±0.0074	0.153±0.0110	0.146±0.0074
F4	0.2066±0.0137	0.205±0.0076	0.202±0.0157	0.195±0.011	0.193±0.0094
Hot temperature conditions (40±2 °C)					
F1	0.0700±0.0081	0.063±0.0047	0.063±0.0137	0.060±0.0100	0.055±0.0095
F2	0.1083±0.0177	0.101±0.0106	0.100±0.0141	0.092±0.0089	0.090±0.0082
F3	0.1566±0.0170	0.148±0.0134	0.143±0.0074	0.136±0.0094	0.132±0.0068
F4	0.2066±0.0137	0.196±0.0179	0.192±0.0121	0.184±0.0110	0.176±0.0074

Data in mean±SD (n=6)

Based on the length of storage time, the films did not show a big difference from each formula at 0 w, 2 w, 4 w, 6 w, and 8 w. Based on the data, it can be seen that the weight of the film at 4±2 °Cwas higher than the films which stored at a temperature of 28±2 °Cwhile at a temperature of 40±2 °Clower than the weight of the film stored at a temperature of 28±2 °Cand 4±2 °C

Table 5: Thickness stability of OTFS for 2 mo

Parameters	Time (weeks)				
	0	2	4	6	8
Cold conditions (4±2 °C)					
F1	0.1026±0.0058	0.109±0.0090	0.106±0.0094	0.099±0.0149	0.096±0.0121
F2	0.1303±0.0100	0.137±0.0121	0.138±0.0100	0.131±0.0110	0.126±0.0026
F3	0.1683±0.0076	0.174±0.0035	0.176±0.0079	0.169±0.0100	0.162±0.0130

Parameters	Time (weeks)				
	0	2	4	6	8
F4	0.2023±0.0050	0.207±0.0122	0.210±0.0149	0.204±0.0097	0.197±0.0072
Room temperature (28±2 ℃)					
F1	0.1026±0.0058	0.103±0.0561	0.100±0.1000	0.096±0.0129	0.093±0.0110
F2	0.1303±0.0100	0.132±0.0175	0.133±0.0130	0.126±0.0056	0.118±0.0054
F3	0.1683±0.0076	0.169±0.0044	0.168±0.0093	0.164±0.0088	0.156±0.0077
F4	0.2023±0.0050	0.202±0.0442	0.201±0.0074	0.194±0.0078	0.189±0.0066
Hot temperature conditions (40±2 ℃)					
F1	0.1026±0.0058	0.097±0.0170	0.093±0.0139	0.091±0.0122	0.089±0.0130
F2	0.1303±0.0100	0.126±0.0060	0.125±0.0110	0.116±0.0038	0.110±0.0791
F3	0.1683±0.0076	0.163±0.0100	0.161±0.0091	0.155±0.0076	0.151±0.0049
F4	0.2023±0.0050	0.191±0.0060	0.189±0.0140	0.187±0.0053	0.185±0.0059

Data in mean±SD, (n=6)

Based on the table 5, the measurement of film thickness at storage temperature of 4±2 ℃was slightly higher than temperature of 28±2 ℃ while at storage temperature of 40±2 ℃ was decreased. The results of the film thickness stability test based on the length of storage time showed no difference at 8 w measurements.

The results of the pH stability test showed that there was a difference in the pH value based on the length of storage time. The changes in pH values were seen at storage temperatures of 28±2 ℃ 4±2 ℃and 40±2 ℃ But, the change in pH value still indicates that the pH value meets the pH requirements of oral film that are safe for the oral cavity (fig. 1-3).

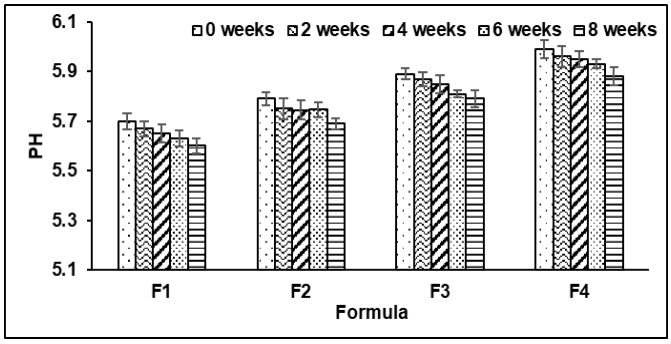

Fig. 1: The pH of the films after saving 2 mo in 4±2 ℃. Data in mean±SD (n=6)

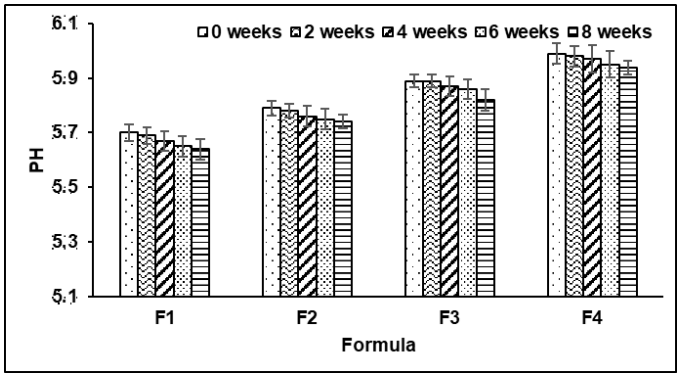

Fig. 2: The pH of the films after saving 2 mo in 28±2 ℃. Data in mean±SD (n=6)

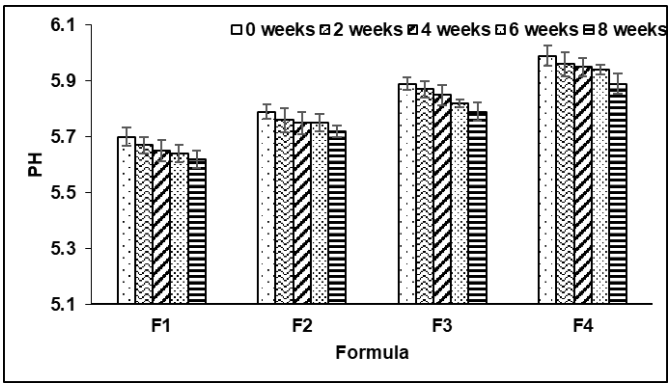

Fig. 3: The pH of the films after saving 2 mo in 40±2 ℃. Data in mean±SD (n=6)

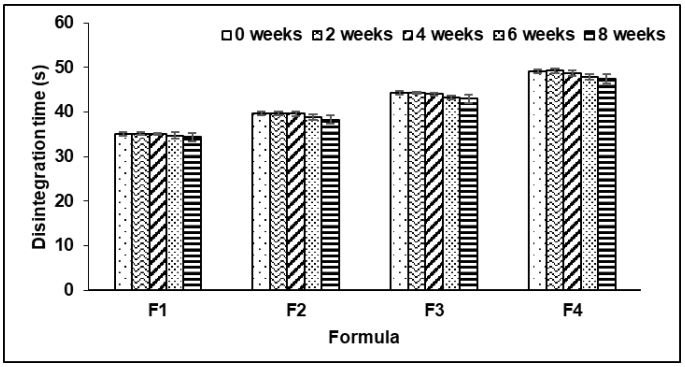

Fig. 4: Disintegration time stability evaluation in 4±2 ℃. Data in mean±SD (n=6)

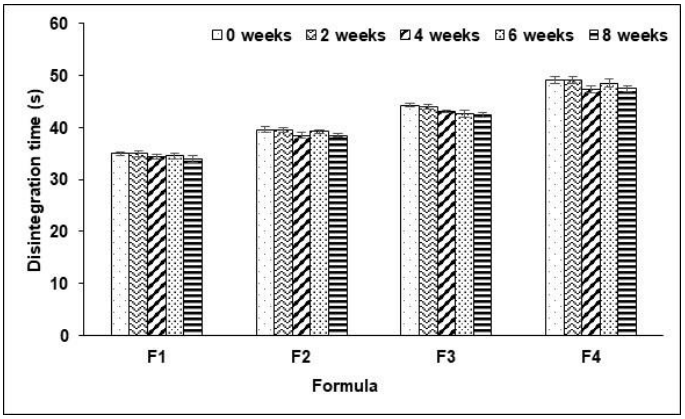

Fig. 5: Disintegration time stability evaluation in 28±2 ℃. Data in mean±SD (n=6)

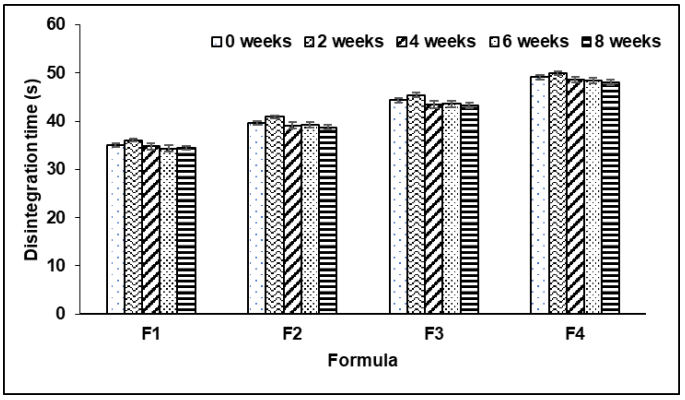

Fig. 6: Disintegration time stability evaluation in 40±2 ℃. Data in mean±SD, (n=6)

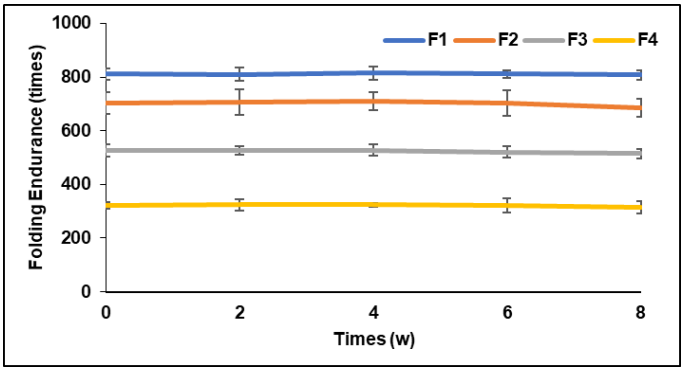

Fig. 7: Folding endurance stability evaluation at 4±2 ℃. Data in mean±SD, (n=6)

Based on the results of the disintegration time stability test during 8 w of storage at temperatures of 4±2 ℃, 28±2 ℃ and 40±2 ℃, there were differences at 4±2 ℃and 40±2 ℃temperatures. On the test, the storage temperature of 4±2 ℃for 8 w slightly increase. In measuring the disintegration time of the films with a temperature of 40±2 ℃, it can be seen from the data that there was a slight decrease in the value of disintegration time (fig. 4-6).

The differences in the value of folding endurance can be seen from the difference in the storage temperature of the film, where the preparations stored at a temperature of 40±2 ℃ have a smaller folding endurance than the films that stored at a temperature of 28±2 ℃ Meanwhile, at a storage temperature of 4±2 ℃, the folding endurance value was greater than the film which stored at 28±2 ℃ (fig. 7-9).

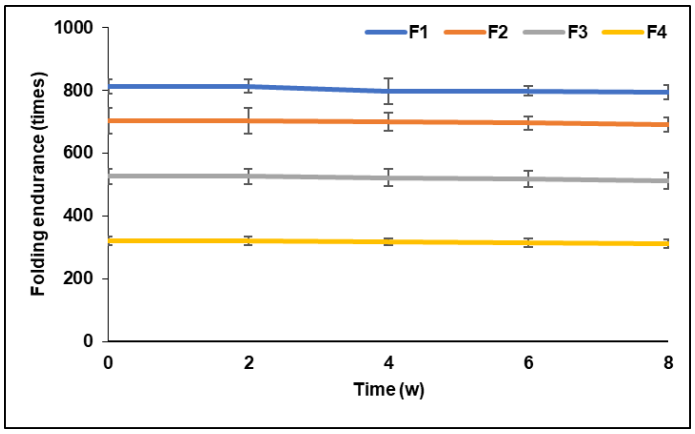

Fig. 8: Folding endurance stability evaluation at 28±2 ℃. Data in mean±SD, (n=6)

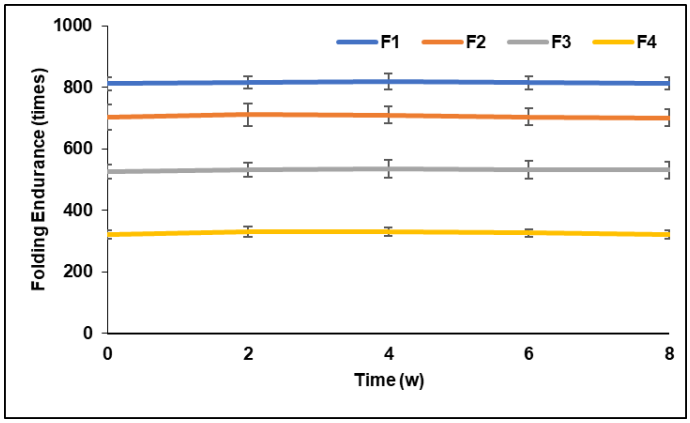

Fig. 9: Folding endurance stability evaluation at 40±2 ℃. Data in mean±SD, (n=6)

Antimicrobial activity

Antibacterial activity testing was carried out using the diffusion method with MHA media and *S. mutans* bacteria. Antibacterial activity testing was carried out on ethanol extract of RDFP and the films. The antibacterial activity produced was seen based on the diameter of the clear zone formed and it can be seen in table 6. Classification of the strength of antibacterial activity was seen based on the inhibition zone formed; if the diameter<5 mm was in the weak category, 5-9 mm was in the medium category, 10-19 mm was in the strong category, and diameter>20 mm was in the very strong category [28].

Table 6: Diameter of Inhibition zone of *S. mutans*

Sample	Diameter of inhibition zone (mm)
DMSO	-
Extract 5%	10.1±0.0577
Extract 10%	11.9±0.4372
Extract 15%	13.8±0.2333
F1	4.6±0.1201
F2	8.5±0.1856
F3	10.8±0.2404
F4	12.9±0.1155

Data in mean±SD (n=3)

DISCUSSION

The oral films were made using HPMC and corn starch as polymers. The use of HPMC and corn starch in the formulation resulted in a flexible and non-sticky film. According to the research, that using HPMC as polymer was chosen because it was able to provide the smooth and semi-transparent film [29]. The addition materials that have hydrocolloid properties, such as corn starch, has the ability to absorb water easily, so it can reduce the wetness of oral film formulation [30, 31]. The measurement of oral film characteristic was organoleptic test, weight test, thickness, pH, disintegration time, and folding endurance. In organoleptic evaluation, the result was in accordance with the research from Dewi and Mulya on 2019, that was the addition of extract into the formulas can affect the organoleptic characteristics of the film, which was the results of the formula has a distinctive's characteristics that affected by the extract [21].

The measurement of film weight aims to determine the uniformity of film's weight. It was necessary to ensure the consistency of the film that were made [24]. The results of the uniformity of weight from each formula shows that the average of weight from each formula has difference. The difference in film weight occurred due to the differences in extract concentration that added into the formula, where was the higher concentration that was added make the greater weight of the film. An addition, the manual casting and cutting process can affect the uniformity of weight from each formula [21]. Based on

the thickness evaluation, there was a difference between four formulas. The difference in the thickness of the resulting film was due to the addition of extracts with different concentrations into the formula, where was the greater concentration of extract which added will increase the thickness of the resulting film. This was in accordance the previous research that the greater amount of extract added into the preparation make the thickness of the film will increase [20].

pH evaluation for the film aims to determine that pH of the films was in the physiological pH range of the mouth so that when consumed it does not cause irritation to the oral cavity [23]. The difference in pH occurred with the higher concentration of the extract that added into the formula. The results of the pH showed that the resulting oral film was not too acidic. If the pH of the oral film too acidic, it can irritate the oral cavity and if it was too alkaline, it can cause a dental carries [24].

Disintegration time test was carried out as the time (s) for the film to disintegrate upon it contact with saliva or water. Disintegration time was measured when the films begin to disintegrate or disperse after contact with saliva or water. There is no specific guideline that stating the disintegration time of oral film. Usually, the disintegration time for oral films is 5-30 seconds, and this time varies depending on the ingredients that contained in the formula [26]. In another study, the requirement for a good disintegration time of oral film was 1 min [25]. The results of the examination of the formula's disintegration time showed that there were differences in the average of each different formula, where in the formula with the higher addition of extract make the disintegration time of the film became longer. This is related to an increase in the thickness of the resulting film. According to previous research, the disintegration time of the preparation can be influenced by the thickness of the film, where the thicker the preparation, the longer the time required for the preparation [24].

The results of folding endurance test showed that they were differences in the folding endurance of the resulting films. This value indicates that the greater concentration of the extract that added, give the lower endurance for the films to fold. This result shows that the extract affecting the folding endurance of the oral films. The folding endurance of the oral film is directly related to the mechanical strength of the oral films, which is regulated by the concentration of the plasticizer [25].

Based on the results of the stability test, the film was still stable for 8 w of storage with different storage temperature conditions. The results obtained in the film weight stability test showed that the films which stored at temperature of 4±2 ℃increased in weight due to increased moisture. Meanwhile, the difference in weight of films stored at a temperature of 40±2 ℃experienced a decrease in weight caused by moisture loss due to high temperature during storage [21]. On film thickness, the films which stored at a temperature of 40±2 ℃ can experience a decrease in thickness due to high temperature during storage resulting in dry films, so that film's thickness can be reduced [21, 32]. Any changes in the value of the film thickness during storage will affect the value of the disintegration time and the folding endurance of the film [32-34]. The higher temperature during storage resulting the thinner film, and it will cause the film to break down more easily when it contacted with saliva or water [35]. Meanwhile, the increase in film thickness will increase the moisture content of the film and make the mechanical properties of the film more rigid [34]. Film dosage form can experience a decrease in pH during storage due to the release of H+ions from citric acid which contained in the formulation [20].

The antibacterial activity of RDFP ethanol extract showed that the inhibition diameter in accordance to the strong category [28]. The antibacterial activity was a resulted from secondary metabolites that contained in the extract, namely alkaloids, saponins, tannins, flavonoids, and triterpenoids [18]. Oral films antibacterial activity shows that F2, F3, and F4 had antibacterial activity with strong to moderate categories. This antibacterial activity derived from the concentration of the extracts which added to the formulas. Films without the addition of the extracts (F1) had antibacterial activity in weak category. It was due to the addition of antimicrobial agents or preservative, namely sodium benzoate [36]. The difference in the diameter of the bacterial inhibition zone between the four formulas was related to an increase in the concentration of the extract, where the higher the concentration of the extract, the larger diameter of the bacterial inhibition zone.

There are some good oral hygiene instructions to solve halitosis problem. Proper brush and inter-dental brush usage are very important issue. However, sometimes even if the mouth is healthy, halitosis still can be happened. Some healthy drinks consumption like kombucha maybe also contribute to halitosis [37]; even this traditional drink has antimicrobial activity and have a lot of benefit for our body [38, 39].

CONCLUSION

Ethanol extract of RDFP can be utilized as a mouth freshener film that can be stable for 2 mo at a different storage temperature (4±2 ℃, 28±2 ℃, and 40±2 ℃). The ethanol extract of RDFP and the film has antibacterial activity against *S. mutans*.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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