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Formulation Dental-Cleansing Gel of Combination Betel Leaf (*Piper betle* L.) Extract with Gambier (*Uncharia gambir* Roxb.) Extract and Activity Test to *Streptococcus mutans*

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ABSTRACT

Betel leaf and gambier are traditional medicinal plants that have antibacterial activity against *Streptococcus mutans*, a combination of these two plants has not been known for its activity against these bacteria. The purpose of this research was to formulate dental-cleansing gel, combination of betel leaf extract and gambier which has antibacterial activity against *Streptococcus mutans*. The antibacterial activity test of betel leaf extract and gambier using agar diffusion method was carried out. Thereafter, a dent cleaning gel formulation was prepared using a 940 carbomer as a gelling agent of concentration 1; 1.5 and 2%. Test parameters for dental-cleansing gel includes organoleptic, pH, dispersion, viscosity, mucosal irritation test and stability test. The results of this study showed that betel and gambier extracts had antibacterial activity. Antibacterial activity combination of betel leaf extract and gambier is not synergistic. For the formulation materials, the concentration chosen is 2%: 20% (betel leaf: gambier) because in that combination the value of the resistor area is still categorized well. The result of irritation test of combination extract and dental-cleansing gel did not cause irritation. The stability test results stated that all the formulas were changed when they were stored at 4±2ºC and 40 ± 2ºC, while at room temperature with 1% carbomer, on the viscosity, spreadability and homogeneity parameters can be stated to have better stability than the formula with carbomer 1, 5% and 2%.

INTRODUCTION

One of the problems of oral and dental health is the growth of oral microflora that causes dental plaque. The bacteria that play a dominant role in plaque formation and caries development are *Streptococcus mutans*[1]. Plaque control is an effort to remove and prevent plaque buildup on tooth surfaces. These efforts can be done either mechanically or chemically. Mechanical discharges may include tooth brushing and dental floss use often do not produce maximum results due to lack of skills.

Therefore, the addition of chemicals to dental preparations can be used as a means of supporting plaque control. Increasing people's desire to use natural materials or "back to nature" is responded by the many products made from active herbs used for healthcare, cosmetics, and disease prevention. This is because natural products are considered safer, cheaper and have fewer side effects[3]. One of the medicinal plants that have antibacterial activity is betel (*Piper betle* Linn.). Betel leaf extract has been shown to have activity against *Streptococcus mutans* because it has the essential oil content of the main component bethel phenol[4,5].

In addition to betel plants, medicinal plants known to have antibacterial activity against *Streptococcus mutans* is gambier (*Uncaria gambir* Roxb). Gambier is available in the market in the form of a dried extract known as gambier block. The main active ingredient content is catechins, either in the form of pure catechins or catechol[6,7]. In addition, catechins are able to bind to other organic compounds, especially proteins. The formation of catechin and protein complexes causes leakage and death of bacterial cells[8].

Dental cleansers form in the market are found in many forms such as gel, colored paste, powder or liquid. The gel preparation is generally preferred because it has a better appearance. The gel preparation by the community is known as toothpaste[9].

Based on the above statement betel leaf extract and gambier extract have been shown to have antibacterial activity against *Streptococcus mutans*, but the antibacterial activity of the combination of both extracts against *Streptococcus mutans* is not yet known. Therefore, in this research combination is done in the hope that antibacterial activity can be obtained which is synergistic and can be formulated into dental-cleansing gel.

MATERIALS AND METHODS

Material

Streptococcus mutans ATCC 31987, Water Sterile for Irrigation (Otsuka), NaCl 0.9% (Otsuka) and Zinc Chloride (Merc).Glycerine 86% (Brataco), propylene glycol 99% (Brataco), sodium saccharin (Quadrant), methylparaben (Clariant), Carbomer 940 (Quadrant), Triethanolamine (Quadrant), Na2-EDTA (Brataco), cocamidopropyl betaine (Quadrant) Sodium lauryl sulfate (Quadrant), Oleum menthae (Quadrant), betel leaf, gambier block (Quadrant).

Plant Identification and Betel Leaf Extraction

Plant determination was done at Herbarium Bogoriense, LIPI Biology Research Center, Bogor, West Java. Preparation of the extract using a maceration method with 95% ethanol pearut. Simplisia betel leaf as much as 1.7 kg, maseration time times 24 hours with three times solvent replacement amount of solvent 1:10 (simplisia: ethanol). Mascles are collected and evaporated using rotary evaporator. The yield obtained was calculated by the percentage weight (w / w) between the yields by weight of crude drug powder[10.]

Separation of Insoluble Ethanol from Gambier Block

To perform the separation of insoluble material from Gambier block ethanol extraction was carried out using ethanol 95% (solubility extract Gambier 1: 1.8)[11.] Prepared gambier block 1.9 kg which then dissolved in 3.5 liters 95% ethanol, and 3 liters to rinse. The extract was strained and steamed until a thick and condensed extract was formed. The yield obtained was calculated by the percentage weight (w / w).

Examination of Characteristics and Quality of Extracts

Examination of characteristic and quality of extract include: organoleptic, pH, type weight, total ash content, acid unsaturated ash content, moisture content, drying shrinkage, essential oil content and total catechin content. Quality inspection of extract was performed by using parameters as per the procedure of General Standards Medicinal Plant Extracts[10] and the Indonesian herbal pharmacopoeia[12.13.] Determination of catechins was done following the procedures of Indonesian National Standard SNI01-3391-2000[14].

Antibacterial Activity Test

The test samples in this study were betel leaf extract and gambier extract, the concentration order of gambier extract test (% w / v) were: 10%, 12%, 14%, 16%, 18%, 20% and betel leaf extract (%b/V) are: 2%, 4%, 6%, 8%, 10%, 12%. The whole concentration of extract prepared in a solution of glycerin 10%, while the positive control (PC) used was $ZnCl_2$ 0.6% (w / v), and a negative control (NC) was a solution of glycerine 10% (v / v). Tests of antibacterial activity of combination of betel extract and gambier extract were arranged in parallel (2%: 10%, 4%: 12%, 6%: 14%, 8%: 16%, 10%: 18%, 12%: 20%) and (12%: 10%, 10%: 12%, 8%: 14%, 6%: 16%, 4%: 18%, 2%: 20%). The test method of antibacterial activity using agar diffusion method, the medium used is Blood Agar, *Streptococcus mutans* which is applied to the media turbidity is equivalent to 0.5 *Mac-Farland*, incubated for 24 hours at 37°C. To view the antibacterial strength by Xiaodong Pan et.all [15] responses categorized into weak barriers (0-3 mm), fine (3-6mm) and strong (> 6 mm).

Formulation of Dental-cleansing Gel using Combination of Betel and Gambier Extract

Formulation of dental-cleansing gel with the combination of betel leaf extract and gambier extract was done based on Table 1. The gel formula of tooth cleaning was made variation of 1%, 1.5% and 2% carbomer concentration where the stirring speed in gel making process was 100 RPM.

Table 1. Dental-cleansing gel[16, 17]

Sr. No.	Composition	BF (%)	Formula		
			F1 (%)	F2 (%)	F3 (%)
1	Glycerin 86%	10	10	10	10
2	Propylen Glycol 99%	30	30	30	30
3	Sodium saccharin	0.1	0.1	0.1	0.1
4	Methylparaben	0.3	0.3	0.3	0.3
5	Carbomer 940	*	1	1.5	2
6	TEA	Ad pH 7	Ad pH 7	Ad pH 7	Ad pH 7
7	Na_2 -EDTA	0.1	0.1	0.1	0.1
8	*Cocamidopropyl betaine*	4	4	4	4
9	Sodium Lauryl Sulphate	0.5	0.5	0.5	0.5
10	Oil pipermin	0.5	0.5	0.5	0.5
11	Betel leaf extract	0	2	2	2
12	Gambier extract	0	20	20	20
13	Water	Ad 100			

Description: * BF (Blanko Formula) 1%; 1.5% and 2%

Evaluation of Dental-cleansing Gel

Evaluation of gel dental-cleansing gel includes: organoleptic, homogeneity, pH, dispersion, viscosity and flow properties. Determination of viscosity and flow properties using Brookfield viscometer, used spindle number 6, with rotation speed 1; 2; 2.5; 4; 5 RPM.

Stability Test

Stability testing was performed on the storage temperature 4 ± 2^{o}C, room temperature (27.5 ± 2^{o}C) and a temperature of 40±2^{o}C for 3 months. The measured stability parameters were organoleptic, homogeneity, pH, and viscosity of the preparation[18.19].

Mucosal Irritant Test

The oral mucosal irritation test was performed on mele syrian hamster (*Mesocricetus auratus*) weight 86- 108 grams, the number of test animals used was 3 for each test group established ISO 10993-10: 2010[20]. The test group used were 6 test groups: negative control of NaCl 0.9%, positive control of 1% sodium lauryl sulfate, combination of betel and gambier extract (K), formula 1, 2 and 3.

To view the picture of each animal irritation and erythema reaction grade mucosal surface can be seen in Table 2. The level of irritation was compared between the treatment group and control group[20.]

Table 2. The level of irritation of oral mucosal[20]

The reaction forms erythema and wounds	Score
No erythema	0
Erythema is very light (barely visible)	1
Light erythema	2
Moderate erythema	3
Severe erythema (red bits) with mucosal exfoliation.	4

RESULTS

Extraction Results, Extract Quality Examination and Phytochemical Screening

Table 3. Examination of the quality of extracts of betel leaf (*Piper betel*) and extract gambier (*Gambir Uncaria*)

Sr. No.	Parameters	Betel Leaf Extract	Gambier Extract	Terms Extract Sirih [13]	Terms Extract Gambier [12, 14]
1	Rendemen	9.80%	51.74%	5%>	-
2	Organoleptic: a. Color b. Aroma c. Flavors	Dark green Typical Betel Spicy bit bitter	Chocolate Typical Sense of chelity bit bitter	Green Typical Spicy bit bitter	Chocolate Typical Sense of chelity, bit bitter
3	pH	5.20	6.40	-	-
4	Specific gravity	1.15	1.011	-	-
5	Water content	8.00%	5.33%	≤ 10%	≤ 14%
6	Drying losses	10.33%	6.00%	≤ 10%	-
7	Total ash content	0.33%	0.47%	≤ 0.30%	≤ 0.50%
8	Ash content is not soluble acid	0.12%	0.29%	≤ 0.10%	≤ 0.10%
9	Residual solvent	There is no	-	-	-
10	Essential oil content	0.33%	-	-	-
11	Total catechin	-	60.74%	-	≥ 60%

Table 3. shows the test results of betel and gambier extract characteristics. The test of acid soluble ash content of both extracts exceeds the limit required in the Indonesian Herbal Pharmacopoeia that is no more than 0.1%. Determination of ash content and acid insoluble ash is an important index to describe the quality and purity of herbal medicine. Ash total included "physiological ash", which is derived from plant tissue itself, and "non-physiological ash", which is likely to come from environmental contamination[21.] One cause of the high levels of acid insoluble ash that exceeds the requirement is because of the content

gambier that catechins can bind metal ions[22, 23]. The metal ions can be derived from water or tools used during the manufacturing process gambier blocks, so the formula is added Na_2-EDTA as metal ion chelating agent.

Levels of essential oils derived from betel leaf extract thick were 0.3%, previous studies Triana H and Lovely P[24] states that the oil content of betel leaf of some areas in Yogyakarta, through solvent extraction using maceration with 95% ethanol concentration obtained Essential oil ranges from 1.5 to 8.3%. Meanwhile, according to Pradhan et.al [25] levels of essential oil on betel leaf is from 0.08 to 0.2%. The small volumes of essential oils may be affected by plant growth and treatment at the time of extract preparation, especially during extract concentration, the use of high temperatures is a major cause of reduced essential oils.

Antibacterial Activity Test Results

Based on Table 4. gambier extracts have antibacterial activity against *Streptococcus mutans* in the concentration range tested gambier is 10-20%.The addition of gambier concentration is directly proportional to the inhibitory diameter. According to the Xiaodong Pan et.all [15] responses categorized into weak (0-3 mm), fine (3-6 mm) and strong (> 6 mm). Gambier extract concentration 16%-20% belong to the good response in which the diameter of inhibitory zone is highest at concentrations of 20%.

Table 4. Diameter of the inhibitory area of gambier extract

Concentration (%)	Repeat (mm)			Average (mm)	Standard Deviation	Response
	1	2	3			
10	1.90	2.10	1.70	1.90	0.20	Weak
12	2.60	2.50	2.30	2.47	0.15	Weak
14	3.10	3.10	2.80	3.00	0.17	Weak
16	5.30	5.10	5.00	5.13	0.15	Good
18	5.90	5.60	5.70	5.73	0.15	Good
20	6.20	6.10	5.80	6.07	0.23	Good
NC	0.00	0.00	0.00	0.00	0.00	There is no
PC	5.80	5.60	5.70	5.70	0.10	Good

Description: NC (Negative Control) Glycerin 10%; PC (Positive Control) $ZnCl_2$ 0.6%;

Diameter of paper disc 6 mm

Previous research by Rindit Pambayun et.Al.[8] that gambier extract has antibacterial activity against *Streptococcus mutans* that has a bactericidal effect. This is caused by the gambier polyphenol compounds as catechins which are natural compounds of plants that have the ability as antibacterials due to polyphenols easily bind to other organic compounds, especially proteins. The formation of complex compounds causes the function and role of these compounds to be reduced, even causing leakage and cell death.

The test results of betel leaf extracts for antibacterial activity against *Streptococcus mutans* can be seen in Table 5. Extract betel possesses antibacterial activity in the concentration range tested, namely 2- 12%. The extract of the sisih at concentrations of 8-12% having inhibition zone is included in the good response where the highest inhibition zone value at a concentration of 12%. Results of previous studies by Nur Indriyani Syarifuddin[26] ethanol extract of the betel leaves have antibacterial activity. Besides betel contains essential oil component is eugenol which has a cell wall degradation activity and cell lysis thereby causing cell death[27.28.]

Table 5. Diameter of inhibition area of betel leaf extract

Concentration (%)	Repeat (mm)			Average (mm)	Standard Deviation	Response Barriers
	1	2	3			
2	1.00	1.10	1.10	1.07	0.06	Weak
4	1.30	2.00	1.60	1.63	0.35	Weak
6	2.60	3.50	2.70	2.93	0.49	Weak
8	3.70	4.40	3.80	3.97	0.38	Good
10	5.60	6.00	5.70	5.77	0.21	Good
12	6.20	6.10	6.30	6.20	0.10	Good
NC	0.00	0.00	0.00	0.00	0.00	There is no
PC	5.80	5.70	5.50	5.67	0.15	Good

Description: NC (Negative Control) Glycerin 10%; PC (Positive Control) $ZnCl_2$ 0.6%;

Diameter of paper disc 6 mm

After the antibacterial activity of each extract was then tested the antibacterial activity in combination. The activity test of the combination of extracts is divided into two: parallel concentrations and crossed concentrations. The aim of cross-combinations is to see the response of antibacterial activity if one of the extract concentrations is lowered and the other is raised simultaneously from gambier extract with betel extract. While the purpose is done parallel combination is to know the antibacterial activity between betel with gambier on inhibition zone which is almost the same when tested singly. So as to obtain the combination as seen in Table 6 and 7.

Table 6. Diameter of inhibition area of betel leaf extract combination and gambier extract with parallel concentration

Code	Concentration (%)		Repeat (mm)			Average	Standard
	Betel	Gambier	1	2	3	(mm)	Deviation
P1	2	10	0.00	0.00	0.00	0.00	0.00
P2	4	12	0.00	0.00	0.00	0.00	0.00
P3	6	14	0.00	0.00	0.00	0.00	0.00
P4	8	16	0.00	0.00	1.00	0.30	0.33
P5	10	18	1.60	1.00	1.50	1.40	1.38
P6	12	20	2.30	1.60	2.40	2.10	2.10
NC	0	0	0.00	0.00	0.00	0.00	0.00
PC	0	0	6.20	6.10	5.80	6.00	6.03

Information :

NC: Negative Control (10% Glycerin)

PC: Positive Control ($ZnCl_2$ 0.6%)

Diameter of paper disc 6 mm

Table 6 shows that the parallel combination of P1 to P4 no antibacterial against *Streptococcus aktivitas mutans.*While the combination of P5 and P6 showed a weak activity with inhibition zone successively 1.40 ± 1.38 mm and 2.01 ± 2.01 mm. The result of the combination in parallel yields the diameter of the resistor area which is smaller than its sole concentration. This shows that the combination of the extract is not synergistic. Table 7 shows that the

crossed combination has a decreasing inhibition zone compared to a single extract, but in combination, S6 inhibition zone has a well-categorized.

Table 7. Diameter of inhibition zone of betel leaf extract combination and gambier extract with crossed concentration

Code	Concentration (%)		Repeat (mm)			Average (mm)	Standard Deviation
	Betel	Gambier	1	2	3		
S1	12	10	1.40	1.80	1.70	1.63	0.21
S2	10	12	0.20	0.60	0.00	0.27	0.31
S3	8	14	0.60	0.60	0.00	0.40	0.35
S4	6	16	1.90	1.70	0.60	1.40	0.70
S5	4	18	2.60	2.60	1.60	2.27	0.58
S6	2	20	3.20	3.40	2.60	3.07	0.42
NC	0	0	0.00	0.00	0.00	0.00	0.00
PC	0	0	6.00	6.10	6.20	6.10	0.10

Information :

CN: Negative Control (10% Glycerin)

PC: Positive Control ($ZnCl_2$ 0.6%)

Diameter of paper disc 6 mm

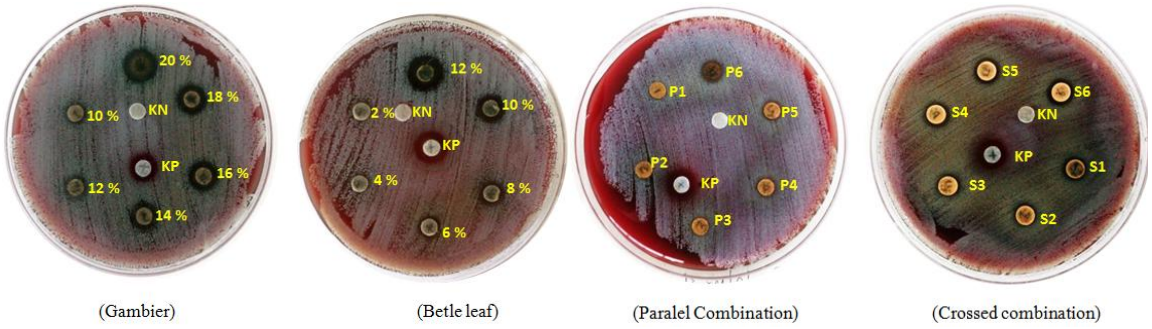

Figure 1. Test result of antibacterial activity

The diameter of the inhibition zone in the combination of betel and gambier extracts, both concentrations in parallel and crossbreed resulted in a smaller inhibition zone compared to a

single extract inhibition cona from betel leaf extract and gambier. So it can be stated that the two extracts are not synergistic. According to G. Adwan and M. Mahanna[28] reduced the antibacterial activity of the combination of extracts can be caused crude extract which contains many phytochemical components that may have a different mechanism. For example, one drug is bacteriostatic (inhibit protein synthesis in bacteria) that is given with the bactericidal[29.] In addition, there are a lot of crude extract compounds that allow to react with one another so as to affect the activity and the physical and chemical stability when combined[28.] However, if explored further betel leaf extract and extract gambier have the same work that is bactericidal with the main component of essential oil of betel and catechins from gambier which has a working mechanism destroy cells and cause cell lysis[8.28.] So that the cause is not synergistic possibly not because of the working mechanism of the extract, but the chemical reactions of the phytochemical components of each extract.

For the formulation of the ingredients, a combination of S6 extract with 2% betel and 20% gambier concentration was obtained for gel formulation, in which the combination of S6 extract can be categorized as having good activity when compared with P6 combination. In addition, if viewed in terms of economic, availability of raw materials and percent (%) yield is better still better gambier extract than dengangan betel extract so that the selected gambier concentration 20% and betel 2%.

Fromulasi Dentistry Gel Preparation

Dental-cleansing gel formulation has the form of a semi-solid, reddish brown color and aroma with a slight aroma typical *minnt* gambier and betel. Then the gel has a sweet taste derived from sodium saccharin added to improve the taste of bitter extracts. In addition, glycerin as soluble auxiliary extract also contributes sweet taste to dental-cleansing gel.

Table 8. Characteristics of gel dentifier preparations of betel extract and gambier extract

Characteristics	F1	F2	F3
1. Organoleptic:			
a. Form	Semisolid	Semisolid	Semisolid
b. Homogeneity	Homogeneous	Homogeneous	Homogeneous
c. Color	Brown-red	Brown-red	Brown-red
d. Aroma	*Min*	*Min*	*Min*
e. Flavors	Sweet, rather spicy	Sweet, rather spicy	Sweet, rather spicy
2. pH	7.24 ± 0.04	7.28 ± 0.08	7.18 ± 0.04
3. Spreading power	51.03 ± 0.50mm	46.14 ± 0.29mm	43.72 ± 0.3mm
4. Viscosity (5 RPM)	39333,33 cP	52333,33 cP	54333,3 cP

Dental-cleansing gel has a neutral pH that is in the range of 7.18 ± 0.04 to 7.28 ± 0.08. The viscosity of carbomer 940 highly influenced by pH, where pH 4.5 to 11 showed good viscosity and a maximum viscosity of 940 carbomer achieved at pH 7[30.] In the dental-cleansing gel formula, neutral pH was obtained by addition of Triethanolamine.

Figure 2. shows the formula 1, 2 and 3 having a thixotropic plastic stream in which graphs of formula 1, 2 and 3 form the flow curve not through the origin (0,0) but cutting the shear stress axis (Shear stress).Yield value formula 1, 2 and 3 determined by extrapolating the curve to the x-axis and yield values obtained consecutively 97922,90; 98821,25; 135355,20 dyne/cm^2. From these results, it can be concluded that the addition of 940 carbomer effect on the value of the yield value, the higher the concentration of carbomer 940, the higher its value- yield. Gel will not flow until the shear stress is concerned exceed the yield value[30.]

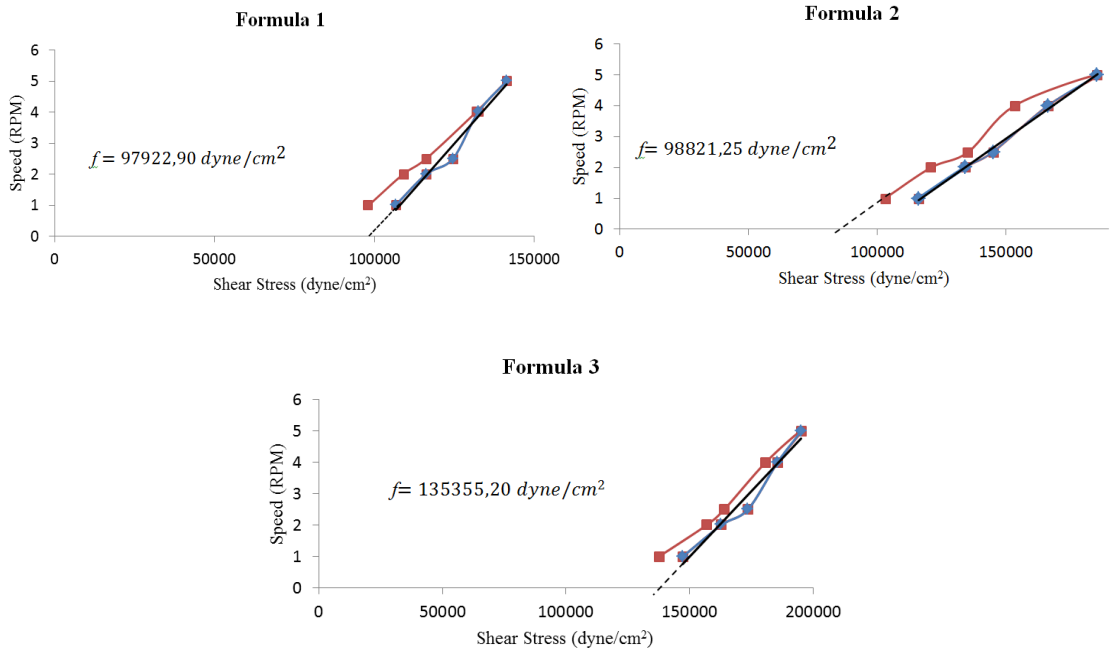

Figure 2. Curve flow properties curve

Description: ---- Extrapolation, ── curve rises, ── curve down

The gel has a thixotropic property because when the shear rate is increased then it is lowered, the curve is obtained that is not coincident or there is a difference when the shear rate is increased and decreased.This is because the structural changes do not return to their original state immediately when the pressure is reduced. This flow curve depends on the rate of shear increases and decreases along the length of experiencing substance rate of shear[33].

Test Result of Oral Mucosal Irritation

Oral mucosal irritation test conducted on syria hamster *(Mesocricetus auratus)* male weighing 86-108 grams number of test animals used were 3 for each test group. Assessment of irritation index by comparing the negative and positive control group to the test group. The test group used were 4 groups: combination of betel and gambier extract, formula 1, 2 and 3. In addition, a negative control of 0.9% NaCl, 1% sodium lauryl sulphate positive control was used. The irritation test results of formula 1, 2, 3 and combinations of extracts do not cause mucosal irritation in test animals.

Stability Test Result of the Parameters Organoleptic and Homogeneity

Organoleptic of dental-cleansing gel: color, taste, and flavor are not changed. The result of macroscopic homogeneity test showed that all the formula seen on the glass of the object is

homogeneous, whereas if observed under a microscope with 100 times magnification there is a difference in appearance of the preparation. The results of observations of formulas 1, 2 and 3, microscopically can be seen in Table 9.

Based on observations in Table 9 in the month 3rd formula 1 and 2 at the storage temperature of 4°C revealed that there is formation of brown particles, whereas in formula 3 particles formed after storage at month 2. The existence of possible particle resulting from reduced solubility of the extracts at low temperature storage is 4°C.

From this test, it can be observed that the concentration of the agent gelling affect the solubility of the extract in cold temperatures are 4°C, at which the temperature of formula 3 with a concentration of 2% carbomer 940 causing rapid precipitation of the extract. It can be concluded that the formula 1 and 2 is more stable than the formula 3 at 4°C in storage.

Table 9. Results of stability tests on homogeneity parameters microscopically

Formula	The month	Temperature		
		4°C	Room	40°C
F1	0	Clear	Clear	Clear
	1	Clear	Clear	Clear
	2	Clear	Clear	Clear
	3	There are Particles	Clear	Clear
F2	0	Clear	Clear	Clear
	1	Clear	Clear	Clear
	2	Clear	Clear	Clear
	3	There are Particles	Clear	Clear
F3	0	Clear	Clear	Clear
	1	Clear	Clear	Clear
	2	There are Particles	Clear	Clear
	3	There are Particles	Clear	Clear

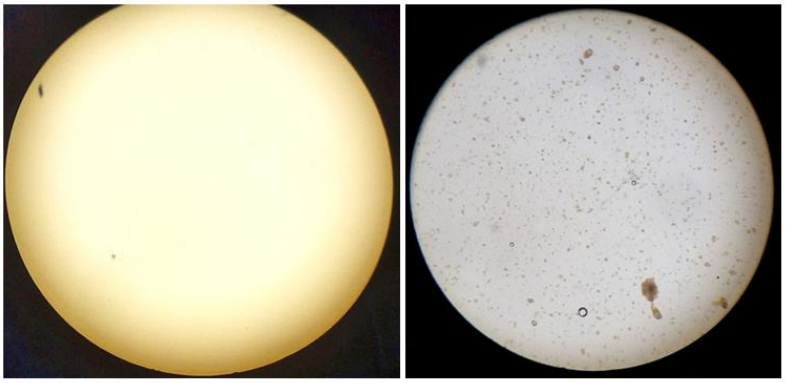

Figure 3. Test formula gel stability at temperatures of 4°C with microscopic

homogeneity parameters are viewed under a light microscope with a magnification of 100 times:

Description: (a) Appearance of gel preparation before stability test

(b) Penapilan gel after stability test at a temperature of 4°C

Observation Stability Against Spreading Power Parameters

The result of the stability test on the power parameters in Table 10. shows the change of power in the formula 1, 2 and 3, this is shown in the ANOVA test. Formula 1 and 2 were stored at cold and hot temperatures showed a difference of the spread between monthly *(p-value*<0.05). The gel is stored at room temperature showed no difference between the month *(p-value*> 0.05) in the formula 1 and 2, while in formula 3 are significant changes between the month *(p-value*<0.05). From this test can be stated formula 1 and 2 are stable at room temperature storage whereas while formula 3 is unstable.

Table 10. The average of stability test results against distribution power parameters

Formula	The month	Dispersive power ($mm^{2)}$ at a temperature of:		
		4°C	Room	40°C
F1	0	2083.94	2030.65	2023.89
	1	2017.16	2050.47	2083.94
	2	2003,80	2083.94	2070,71
	3	1873.76	2097.43	2172.52
P-value		0.000	0.236	0.013
F2	0	1668.64	1674,72	1674,72
	1	1532.76	1680.79	1585.36
	2	1464.15	1729.77	1754.29
	3	1359.04	1723,56	2348.07
P-value		0,000	0.302	0,000
F3	0	1532.76	1532.76	1586.80
	1	1498.32	1538.58	1527.23
	2	1430.36	1632.63	1620.68
	3	1380.65	1711.25	2017.16
P-value		0.001	0,000	0.000

Results of Stability Tests on Viscosity Parameters

Results of stability test data analysis with the viscosity parameter storage temperature can be seen in Table 11. Formula 1, 2 and 3 in the storage of 4 ± 2°C increase in viscosity. While at the storage at room temperature shows a stable viscosity in formula 1, 2 and 3 while a significant decrease *(p-value*<0.05). Then, at a storage temperature of 40 ± 2°C all showed a decrease in viscosity gel.

Results of testing the stability of the viscosity parameter showed a significant change between the month primarily on storage temperature 4 ± 2°C and 40 ± 2°C, whereas at room temperature formula 1 stable until 3rd month and formula 2 is stable up to month 1. These test results prove that the storage temperature can affect the viscosity of the gel, which is a semi-solid viscosity decrease as the temperature is increased and the viscosity increases when the temperature lowered[26].

Table 11. Average stability test results against viscosity parameters

Formula	The month	Viscosity (cP) at temperature:		
		4°C	Room	40°C
F1	0	39333,3	41000.0	39333,3
	1	47666,7	40333,3	36666,7
	2	48666,7	39666,7	36333.3
	3	50333,3	39333,3	35333.3
P-value		0.000	0.256	0,000
F2	0	51333,3	51666,7	51333,3
	1	52333,3	51666,7	48333,3
	2	54666,7	49666,7	44333,3
	3	55333,3	49000.0	43333.3
P-value		0,000	0.003	0,000
F3	0	54333,3	52333,3	53333,3
	1	63333,3	51000.0	50333,3
	2	66333,3	50333,3	48666,7
	3	68333,3	49666,7	46333,3
P-value		0,000	0.041	0,000

Description: Viscosity = *dial reading* at 5 x factor RPM spindle

Spindle factor at RPM 5 = 2000

Results of Stability Testing Against Parameters pH.

Result of ANOVA data analysis Table 12. that formula 1, 2 and 3 significantly (p-value <0,05) decreased pH. However, if further review using the least significant difference test (LSD) / least significant differences (LSD), formula 1 at room temperature storage can be declared stable until month 1. Although the three formulas decline in pH but still within the requirements set by SNI 12- 3524-1995 that allowed pH range is 4.5 to 10.5 [14].

Table 12. Average stability test results against pH parameters

Formula	The month	PH at temperature:		
		4ºC	Room	40ºC
F1	0	7.27	7.20	7.27
	1	7.07	7.07	6.90
	2	7.00	6.97	6.87
	3	6.90	6.87	6.60
P-value		0.001	0.002	0,000
F2	0	7.27	7.27	7.20
	1	7.03	7.17	7.10
	2	6.93	6.97	6.83
	3	6.83	6.67	6.50
P-value		0,000	0,000	0,000
F3	0	7.13	7.20	7.20
	1	6.90	6.90	6.93
	2	6.90	6.93	6.83
	3	6.77	6.70	6.50
P-value		0,000	0,000	0,000

The carbomer 940 is a polymer of acrylic acid is a weak acid that when added to water will produce a pH of 2.5-3.0 at a concentration of 1%[14.] The 940 carbomer can be neutralized with triethanolamine (TEA). Triethanolamine an organic amine group is alkaline (pH 10.5 at 0.1 N), if the dispersion of carbomer was neutralized using TEA then progressively the carboxyl group of the carbomer will be ionized at[17.34] neutralizing reagent.

The pH degradation of the stability test is probably due to the hydrolysis of the carboxyl and amine bonds, wherein the salts formed from neutralizing weak acids or weak bases are easily hydrolysed. The second factor is probably caused by the acidic pH of the extract. To maintain the pH of the preparation so as to require the addition of a pH buffer to maintain the pH stability of the gel, one of the neutral pH buffers which may be used is phosphate buffer pH 7.

CONCLUSION

The combination of betel leaf extract and gambier extract have activity that is not synergistic either combination in parallel or cross. The combination of extracts used in gel preparation was 20% gambier and 2% betel. In combination, it has a 3.07 mm inhibition zone that can still be categorized well.

The carbomer 940 adductor effect on the physical properties of the gel, the higher the 940 carbomer the higher the viscosity value and the lower the spread. The addition of the 940 carbomer has an effect on the stability, the greater the concentration of the 940 carbomer, the greater the changes occurring during storage, so the formula 1 with 1% carbomer is the best dental-cleansing gel.

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