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Research Article

Formulation and Evaluation of Gel Containing Carbomer 940 with Combination of betel Leaf (*Piper Betle L.*) Extract with Gambier (*Unchariagambir Roxb.*) Extract Against Gram Positive Bacteria

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ABSTRACT

Teeth are important parts of human body. Daily consumption of food by mouth, food stay and stick to tooth creates various problem like decay and microbial contamination on teeth and also plaque. Plaque buildup on teeth is a result of the proliferation of oral microorganisms. Streptococcus mutans is responsible for bacterium in plaque production and caries progression. The common name for this gel concoction is "toothpaste." It has been shown that both betel leaf extract and gambier extract have antibacterial activity against Streptococcus mutans, however it is unknown whether or not the combination of the two extracts also has antibacterial activity against Streptococcus mutans. This research article mainly focused on combine substances in an effort to produce an antibacterial agent with synergistic properties that may be included into a gel for cleaning one's teeth. Twenty percent gambier and two percent betel extracts were utilized to make the gel. The combined inhibition zone is 3.09 mm, which is still sufficient for stop the growth and kill the bacteria.

Keyword: Antibacterial, Betel extracts, Gel, Streptococcus mutans, Gambier**ARTICLE INFO:** Received 27 Dec. 2023; Review Complete 24 Jan 2024; Accepted 19 Feb. 2024; Available online 15 April. 2024**Cite this article as:**

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INTRODUCTION

Streptococcus mutans is the most important bacterium in plaque production and caries progression. Plaque control refers to the measures used to eliminate and prevent the formation of plaque on teeth. Mechanical or chemical methods may be used for this. Lack of expertise means that mechanical discharges like brushing and flossing teeth don't always gives the best outcomes. Chemicals added to dental products may help in plaque reduction. Products containing active herbs are becoming popular in the healthcare, cosmetics, and disease prevention industries as a result of rising interest in using natural materials or going "back to nature." Reasons for this include the fact that they cost less and have less side effects than their synthetic counterparts. Betel is a kind of plant used in medicine because of its antibacterial properties (*Piper betle Linn.*). Because of the betel phenol concentration in its essential oil, extract of betel leaves has been demonstrated to be effective against Streptococcus mutans.^{1,2,3,4,5,6} In addition to betel, gambier is

another medicinal plant with shown antibacterial efficacy against Streptococcus mutans (*Uncariagambir Roxb.*). A dried extract of gambier, called a gambier block, is commercially available. Catechins, either in their pure form or as the intermediate metabolite catechol, make up the bulk of the active component content. Also, catechins have the ability to attach to other chemical substances, particularly proteins. The bacterial cells leak and die as a result of the complexes formed between catechin and proteins. You may get a dental cleaner in a variety of forms, from gel to colored paste to powder to liquid. Gel preparation is more popular than others because to its improved visual appeal. The common name for this gel concoction is "toothpaste." It has been shown that both betel leaf extract and gambier extract have antibacterial activity against Streptococcus mutans, however it is unknown whether or not the combination of the two extracts also has antibacterial activity against Streptococcus mutans. Because of this, in this study we combine substances in an effort to produce an

antibacterial agent with synergistic properties that may be included into a gel for cleaning one's teeth.^{7,8,9,10,11}

MATERIAL AND METHOD

"*Streptococcus mutans* ATCC 31987, Water Sterile for Irrigation (Otsuka), NaCl (0.9%) (Otsuka) and Zinc Chloride (Merc). Glycerine 87% (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 menthane (Quadrant), betel leaf, gambier block (Quadrant)." All ingredients are analytical grades.

Plant Identification and Betel Leaf Extraction

Plant determination was done at Department of Botany, University of Rajasthan, Jaipur. Maceration in 95% ethanol pearut to prepare the extract. Simplisia betel leaf as much as 1.7 kg, Maceration time periods 24 hours with three times solvent replacement quantity of solvent 1:10 (simplisia: ethanol) (simplisia: ethanol). The muscles are collected and then evaporated in a rotating evaporator. The acquired yield was determined by comparing the two yields in terms of the mass of the crude drug powder, and the difference was expressed as a percentage (w/w).

Separation of Insoluble Ethanol from Gambier Block

Ethanol 95% was used during the extraction to separate the insoluble material from the Gambier block (solubility extract Gambier 1: 1.9). After preparing a 1.9-kilogram block of gambier, we dissolved it in 3.4 liters of 95% ethanol and used another 3.1 liters to wash it. A concentrated extract was obtained by straining and boiling the liquid. Yield was determined using the w / w method of calculating percentages.^{12,13,14,15}

Antibacterial Activity Test

Betel leaf extract and gambier extract were used as test samples in this investigation, with the following concentrations used for each: 2%, 4%, 6%, 8%, 10%, and 12% for gambier extract and 2%, 4%, 6%, 8%, 10%, and 12% for betel leaf extract (% b/V). The extract was produced at a final concentration of 10% in a glycerin solution; the positive control (PC) was 0.6% ZnCl₂ (w/v); and the negative control (NC) was the same glycerin solution. There were two sets of tests conducted, one comparing the antibacterial effects of betel extract and gambier extract at a 2:1 ratio (2%: 10%, 4%: 12%, 6%: 14%, 8%: 16%, 10%: 18%, 12%: 20%) and the other at a 1:1 ratio (12%: 10%, 10%: 12%, 8%: 14%, 4%: 18%, 2%: 20%). The agar diffusion technique is used to test for antibacterial activity; Blood Agar is the medium of choice, and *Streptococcus mutans* is employed to achieve a turbidity of 0.5 MacFarland in the medium before being incubated for 24 hours at 37 degrees Celsius.^{16,17,18}

Formulation of Dental Cleansing Gel

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 2.5% carbomer concentration where the stirring speed in gel making process was 50 RPM.^{19,20,21}

Table 1: Dental-Cleansing Gel

Sr No.	Composition	BF %	F1(%)	F2(%)	F3(%)
1	Glycerin 86 %	10	10	10	10
2	Propylene glycol 99%	30	30	30	30
3	Sodium saccharin	0.1	0.1	0.1	0.1
4	Methylparaben	0.35	0.35	0.35	0.35
5	Carbomer 940	---	1.0	1.5	2.5
6	Tea	Adjust pH 7	Adjust pH 7	Adjust pH 7	Adjust 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	0.65	0.6
10	Oil peppermint	0.5	0.5	0.6	0.5
11	Betel leaf extract	0	2.0	2.0	2.5
12	Gambier extract	0	20	20	25

Evaluation of Dental-cleansing Gel

The organoleptic, homogeneity, pH, dispersion, viscosity, and flow characteristics of dental-cleansing gel are evaluated. Spindle number 6 was utilized on the Brookfield viscometer at speeds of 1, 2, 3, 4, and 5 revolutions per minute to measure viscosity and flow characteristics.

Stability Test

There were three months of stability tests conducted at four different temperatures: ($4^{\circ}\text{C} \pm 2^{\circ}\text{C}$), room temperature ($27.5^{\circ}\text{C} \pm 2^{\circ}\text{C}$), and ($40^{\circ}\text{C} \pm 2^{\circ}\text{C}$). The organoleptic, homogeneity, pH, and viscosity of the preparation were evaluated to determine its stability.

Mucosal irritant Test

Mele syrian hamsters (*Mesocricetus auratus*) weighing between 86 and 108 gm were used for the oral mucosal irritation test following ISO 10993-10: 201020. There were six different groups employed for testing: a 0.9% NaCl control, a 1% sodium lauryl sulphate positive control, a betel and gambier extract (K) combination, and two different formulas (1 and 2). Table 2 shows the degree of irritation and erythema on the mucosal surface of each animal. Treatment and control groups were compared for their sensitivity to the test substance.^{22,23}

Table 2: The level of irritation of oral mucosal

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

RESULTS

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
1	Rendemen	8.92 %	52.66%
2	Color	Dark green	Chocolate
3	Odour	Typical betel	Sense of chelity
4	Flavors	Spicy	Bitter
5	pH	5.21	6.3
6	Specific gravity	1.16	1.09
7	Water Content	8.2%	5.8%
8	Drying Losses	10.44%	6.90%
9	Total ash content	0.34%	0.46%
10	Ash content insoluble in acid	0.13%	0.27%
11	Residual solvent	No	---
12	Essential oil content	0.24%	---
13	Total catechin	---	61.00%

The properties of betel and gambier extracts as determined by testing are shown in Table 3. Results from an acid soluble ash test showed that both extracts had levels of ash that were higher than the 0.1% threshold set by the Indonesian Herbal Pharmacopoeia. One of the best ways to evaluate the potency and safety of herbal remedies is by testing them for ash content and acid insoluble ash. Both "non-physiological ash," or ash that is likely the result of environmental pollution, and "physiological ash," or ash that originates from the plant itself, were counted toward the total ash. The content gambier that catechins may bind metal ions^{22, 23} is one reason for the high amounts of acid insoluble ash that exceeds the requirement. To remove any metal ions that may have been introduced into the recipe from the water or

equipment used to create the gambier blocks, Na₂-EDTA was included.

Previous research found that the levels of essential oils produced from betel leaf extract were just 0.3%. The oil content of betel leaf from certain regions in Yogyakarta was recovered by solvent extraction via maceration with 95% ethanol concentration, as stated by Triana H and Lovely P²⁴. From 1.5% to 8.3% is where you'll find essential oil. Meanwhile, the essential oil concentration on betel leaf ranges from 0.08 to 0.2%, as reported by Pradhan et.al. High temperatures used during the extraction process, particularly during the concentration of the extract, are a key contributor

to the depletion of essential oils that might occur as a result of the plant's development and care.¹⁰

Antibacterial Activity Test Results

The numbers are from Table 4. The concentration range of gambier extracts examined shows antibacterial action

against *Streptococcus mutans* (10-20%). An increase in gambier concentration correlates positively with a decrease in inhibitory diameter. All 15 answers were divided into three categories by Xiaodong Pan et al.: weak (0-3 mm), fine (3-6 mm), and strong (> 6 mm). The optimal response is shown at Gambier extract concentrations between 16 and 20 percent, with the maximum width of the inhibitory zone being seen at 20 percent.^{11,16}

Table 4: Diameter of the inhibitory area of gambier extract

Concentration (%)	Repeat (mm) 1	Repeat (mm) 2	Repeat (mm) 3	Average (mm)	Standard Deviation	Response
8	1.80	2.22	1.50	1.80	0.19	Weak
10	1.90	2.20	1.60	1.90	0.20	Weak
12	2.60	2.60	2.20	2.40	0.15	Fair
14	3.95	3.90	3.95	3.90	0.17	Good
16	5.35	5.10	4.95	5.15	0.15	Good
18	5.90	5.60	5.70	5.73	0.15	Good
NC	0.00	0.00	0.00	0.00	0.00	No
PC	5.60	5.70	5.80	5.70	0.10	Good

Description: NC (Negative Control) Glycerin 10%; PC (Positive Control) ZnCl₂ 0.6%;

Table 5: Diameter of inhibition area of betel leaf extract

Concentration (%)	Repeat (mm) 1	Repeat (mm) 2	Repeat (mm) 3	Average (mm)	Standard Deviation	Response
2	1.10	1.10	1.20	1.10	0.06	Weak
4	1.50	1.80	1.60	1.63	0.35	Weak
6	2.80	3.20	2.70	2.93	0.49	Fair
8	3.70	4.20	4.00	3.96	0.37	Good
10	5.70	5.80	5.90	5.66	0.21	Good
12	6.20	5.60	5.70	5.73	0.15	Very Good
14	6.40	5.40	5.70	5.73	0.15	Good
NC	0.00	0.00	0.00	0.00	0.00	No
PC	5.60	5.70	5.80	5.70	0.10	Good

Description: NC (Negative Control) Glycerin 10%; PC (Positive Control) ZnCl₂ 0.6%;

Diameter of paper disc 6mm

The combined antibacterial activity was evaluated once the individual extracts' efficacy was established. There are two types of concentration tests for determining the efficacy of a mixture of extracts, namely, parallel and crossing concentrations. The goal of these cross-combinations is to

compare the effect on antibacterial activity of varying the amounts of gambier extract and betel extract concurrently. The antibacterial activity of betel and gambier is almost equivalent when evaluated alone, therefore learning about their combined effects on the inhibitory zone is the goal of this parallel combination. To achieve the combination shown in Tables 11 and 12, respectively.

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

Code	Concentration (%)		Repeat (mm)			Average (mm)	Standard Deviation	Finding
	Betel	Gambier	1	2	3			
P1	2	8	1.00	1.00	1.00	1.00	0.07	Fair
P2	4	10	1.10	1.20	1.08	1.12	0.38	Good

P3	6	12	1.60	1.80	1.60	1.66	0.59	Good
P4	8	14	4.50	4.60	3.70	4.26	0.70	Good
P5	10	16	6.10	6.50	5.70	6.10	0.89	Fair
P6	12	18	6.30	6.00	5.90	6.30	0.86	Fair
NC	0	0	0.00	0.00	0.00	0.00	0.00	No
PC	0	0	5.80	5.80	5.70	5.76	0.72	Good

NC: Negative Control (10% Glycerin), PC: Positive Control (ZnCl₂ 0.6%)

Diameter of paper disc 6 mm

The width of the inhibitory zone was lower when betel and gambier extracts were combined, with both concentrations running in parallel and the two species being crossbred. Therefore, it may be concluded that there is no synergy between the two extracts. There are various phytochemical components in the crude extract, and this may account for the lower antibacterial activity of the combined extracts, as reported by G. Adwan and M. Mahanna.

The bactericidal is sometimes used with a bacteriostatic medication (one that blocks protein synthesis in bacteria). Not only that, but many of the chemicals in crude extract are reactive, meaning that they may alter activity and physical and chemical stability when mixed together. However, more research reveals that betel leaf extract and extract gambier do the same bactericidal action, with the primary component being essential oil from betel and catechins from gambier, respectively. These substances operate by destroying cells and causing cell lysis. The chemical reactions of the phytochemical components of each extract may be to blame, rather than the extract's actual operating mechanism. A combination of S6 extract and 2% betel and 20% gambier

concentration was achieved for gel formation; this combination of S6 extract may be classified as having excellent activity when compared with P6 combination, which was used in the original formulation of the components. As a result, the 20% gambier concentration was chosen above the 2% betel concentration because of the superior economic, raw material availability, and percent (%) yield.

Formulation of Dentistry Gel Preparation

Dental-cleansing gel formulation has the form of a semi-solid, reddish brown color and a aroma with a slight typical mint 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 a soluble auxiliary extract also contributes to a sweet taste to dental-cleansing gel. Cleansing gel for teeth has a pH of 7.18 0.04 to 7.28 0.08. Carbomer 940's viscosity is very pH dependent, with optimal viscosity at pH 7.3 and acceptable viscosity across the range of 4.5 to 11. Triethanolamine was used into the formulation of the dental-cleansing gel to achieve a pH balance.

Table 7: Characteristics of gel densifier preparations of betel extract and gambier extract

Characteristics	F1	F2	F3
Form	Semisolid	Semisolid	Semisolid
Homogeneity	Homogeneous	Semisolid	Semisolid
Color	Brown – red	Brown – red	Brown - red
Aroma	Min	Min	Min
Flavors	Sweat	Sweat rather spicy	Sweat rather spicy
pH	7.24±0.04	7.27±0.08	7.28±0.04
Spreading power	51.04±0.50	49.04±0.50	51.24±0.30
Viscosity	39333,33cp	52333,33cp	54333,3cp

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.^{8,9}

Stability Test Result of the Parameters Organoleptic and Homogeneity

Brown particles developed in formulas 1 and 2 after 3 months of storage at 4°C, as shown in Table 14, but in

formula 3 particles formed after 2 months of storage. Lower extract solubility during 40°C storage might lead to the formation of insoluble particles. These results show that the solubility of the extract is affected by the concentration of

the gelling agent at low temperatures of 4°C, where a concentration of 2% of carbomer 940 in formula 3 leads to fast precipitation of the extract. Formulas 1 and 2 are found to be more stable than formula 3 when stored at 4°C.^{10,16}

Table 8: 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	There are particles	Clear	Clear
	3	Clear	Clear	Clear
F2	0	Clear	Clear	Clear
	1	Clear	There are particles	Clear
	2	Clear	Clear	Clear
	3	Clear	Clear	Clear
F3	0	Clear	Clear	Clear
	1	Clear	Clear	Clear
	2	Clear	Clear	There are particles
	3	Clear	Clear	Clear

CONCLUSION

A cross combination of betel leaf extract and gambier extract results in synergistic action. Concluded that twenty percent gambier and two percent betel extracts were utilized to make the gel and given the combined inhibition zone is 3.09 mm against gram positive bacteria, which is still sufficiently distinct for solve the teethest problem. Gel viscosity and spreading are both affected by the amount of carbomer 940 added to the mixture. Formula 1 with 1% carbomer is the most stable dental-cleansing gel since the concentration of 940 carbomer has no influence on stability.

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