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FORMULATION AND CHARACTERIZATION EFFERVESCENT TABLETS OF GAMBIER LEAF EXTRACT (*Uncaria gambier* Roxb)

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ABSTRACT

Background: Gambier, also known as the term (*Uncaria gambier* Roxb), is a plant that has long been cultivated in Indonesia. The components of flavonoid compounds in gambier plants have been widely reported as antioxidants. Using the gambier plant will be more accessible and more practical if it is made in dosage form, one of which is in the form of effervescent tablets. **Objective:** To determine the physical and chemical characteristics of effervescent tablets of gambier leaf extract (*Uncaria gambier* Roxb). **Methods:** Descriptive design, which includes phytochemical screening research, extract quality test, physical and chemical characteristics test of effervescent tablets formulation. **Results:** Positive gambier leaf extracts contain flavonoid compounds, alkaloids, tannins, and saponins. The average weight uniformity test of the tablet is 1.57 ± 0.02 grams, the average tablet thickness test of the tablet is 0.5±0 cm while a tablet's average diameter is 1.6±0 cm, the fragility test obtained <1%, the average hardness test of the tablet is 4.34±0.02 kg, the solubility time of the tablet obtaining is 1.6 ±0.4 minutes and tablets pH is 5.5±0.2. **Conclusion:** It is possible to draw the conclusion that the positive gambier leaf extract includes flavonoid components, alkaloids, tannins, and saponins based on the findings of the data previously gathered. The quality test of gambier leaf extract is already qualified, and the test of the characteristics of the physical and chemical properties produced is suitable based on Pharmacopeia Indonesia Standard.

Keywords: Gambier; Extract; Tablet Effervescent

INTRODUCTION

Gambier (*Uncaria gambier* Roxb) is a plant that has been cultivated for a long time and is a smallholder plantation crop focused on exports in Indonesia. Gambier plants grow the most significantly in Kalimantan and Sumatra. Even though Gambier is not as familiar as other herbal plants, it has been proven to have many benefits for body health. However, in Indonesia, gambier is often used for betel nut. Apart from that, gambier can also be used to treat headaches, burns, dysentery, diarrhea, mouthwash, canker sores, a mixture of medicines for skin diseases, and textile dyes[1]. The gambier plant is a shrub whose height ranges from 1.5 to 2 m. Gambier plants can grow to climb other plants by wrapping a small, flat hook between two opposite leaf stalks. The gambier plant has sympodial branches with rounded leaf stalks, ranging from light brown to dark brown, smooth, and large round leaf stalks[2].

The flavonoid compound components in the gambier plant have been widely reported

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as antioxidants, one of which is catechin. There has been a lot of research related to Gambier's pharmacological activity, namely the methyl compound of ethanol extract of gambier leaves, which has antioxidant and antibacterial properties that inhibit the formation of fatty acids. Catechins are polyphenolic substances that have inherent antibacterial and antioxidant properties. High-quality plants have a catechin content of 73.3%[3]. If processed as a food additive, the catechin of the gambier plant has excellent potential as an antioxidant, antimicrobial, and fiber[4]. Effervescent tablets are compressed active components in the form of an acid source and a base source (carbonate), for example, citric or tartaric acid and sodium bicarbonate, used to make uncoated tablets[5]. In general, effervescent tablets are tablets that, when placed in water, produce carbon dioxide (CO2) gas bubbles, which are caused by chemical reactions.

Solid dosage form was chosen as the vehicle for this extract because of its ease of distribution, packaging, and application. Effervescent tablets were chosen because they can provide a fresh effect after drinking due to the gas produced. This effect cannot be obtained if made in ordinary tablets. Chewable tablets and lozenges were not chosen because there is a possibility that gambier extract will leave a colored residue on the teeth and mouth, which may be less popular with the public. The urgency of this research is to find out whether gambier extract can be made into effervescent tablets to produce good effervescent tablet characteristics.

METHODS

1. Tools

The instruments used are analytical scales, UV-Vis spectrophotometry, oven, friability tester, vernier caliper, stirring rod, dropper pipette, measuring cup (PYREX®), Erlenmeyer (PYREX®), filter paper, aluminum foil, glass jar, plastic wrap, glass funnel, porcelain cup, stamper mortar, 16 mesh and 12 mesh sieve, hardness tester, moisture analyzer, pH meter.

2. Material

The materials used in the research were gambier leaf extract (*Uncaria gambier* Roxb), which was taken from Sumatra Agro-Industry, 96% ethanol, citric acid, tartaric acid, sodium bicarbonate, PEG 6000, PVP, and lactose.

3. Procedure

A. Phytochemical Screening

a. Flavonoid Test

Sample the test solution as much as 2 ml, add enough hot water, boil for 5 minutes, then filter. 0.05 mg Mg powder, 1 ml concentrated HCl, and 5 ml filtrate were added, and the mixture was stirred vigorously. A change in color to red, yellow, or orange indicates that it contains positive flavonoid compounds[6].

b. Saponin Test

The test tube contains 2 ml of the test solution, which is then filled with 10 ml of hot water, cooled, and shaken vigorously for 10 seconds. Finally, add one drop of 1 N HCl, and if foam forms for at least 10 minutes, it rises to a height of 1 to 10 cm[6].

c. Tannin Test

1 ml of test solution is added with drops of 1% $FeCl_3$. If a dark blue or greenish-black color forms, it indicates that there are tannin compounds[6].

d. Alkaloid Test

Take 2 ml of the test solution and evaporate it in a porcelain cup 5 ml of 2N HCl was then used to dissolve the remainder. The 3 test tubes were then filled with the solution obtained. Three drops of 2 N HCl were added to the first

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tube to serve as a blank. Three drops of Dragendroff's reagent were added to the second tube, and three drops of Mayer's reagent were added to the third tube. If Dragendorff's reagent forms an orange precipitate, while a white precipitate is formed in Mayer's reagent, it is a sign that it contains an alkaloid compound[6].

B. Formulation of Effervescent Tablets

Table 1. Tablet Formulation

Formulation				
Number	**Ingredient**	**F I 5%**	**F II 10%**	**F III 15%**
1	Gambier extract	5%	10%	15%
2	Citric acid	8,8%	8,8%	8,8%
3	Tartrat acid	25,4%	25,4%	25,4%
4	Bicarbonat Sodium	33,8%	33,8%	33,8%
5	PEG 6000	5,3%	5,3%	5,3%
6	PVP	4%	4%	4%
7	Lactosa	22,4%	22,4%	22,4%

The process of making effervescent tablets is carried out in two stages, namely, making the acid component and the alkali component. Citric acid, tartaric acid, and gambier leaf extract are combined to create an acid component. After that, make a binding solution by gradually integrating the water and acid components until a wet mass is formed that can be clenched while continuing to stir the PVP powder until it dissolves. After that, sift with sieve No. 12 mesh and oven for three hours at 50°C. Dry, then sift with sieve no. 12 mesh while adding PEG 6000. After that, make the base component by gradually mixing the sodium bicarbonate with the binding solution until a solid mass is formed that can be held. Sift with sieve No. 12 mesh after drying. The mass was then sieved with 12 mesh sieve and placed in the oven at 50ºC for 3 hours. Once dry, sift with a 12-mesh sieve. The acid and base components were mixed and sieved with a 12-mesh sieve. The granules formed were evaluated for granules including tests for flow properties, angle of repose, moisture content, and mass density. The granule mixture was printed using a tablet printing machine with a weight of 1500 mg per tablet.

C. Evaluation of Physical Quality of Effervescent Granules

a. Organoleptic

Carrying out organoleptic testing includes observing the shape, color, and aroma of the granule preparation.

b. Granule Moisture Test

Weigh 5 grams of granules and then heat them in an oven or drying cabinet at a temperature of 105ºC for 2 hours. The requirement for the moisture content of effervescent granules is no more than 2 to 4%[19].

Granule moist formula:

c. Flow Time Test

When the funnel lid or flowbility tester is opened, the mass is allowed to flow, and the time is measured using a stopwatch. Grains are weighed up to 100 grams and placed in closed conditions. Do three tries, then average the results. The requirement for a good flow time is ≤ 10 seconds[19].

d. Repose Angle Test

The granules are weighed as much as 100 grams and then entered into the flow time test funnel. The funnel cover is opened, allowing the granules to exit and be placed on a flat surface. The height and diameter of the pile of granules exiting at the mouth of the funnel are measured to calculate the angle of repose and record the flow time of the granules. Flow times are required with angles of repose between 20 and 45 degrees, with lower angles indicating better properties.

Angle of repose formula[19]:

$$(repose\ angle) = \frac{h\ (height)}{r\ (circle\ radius)}$$

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e. Compressibility Test

Put 100 ml of granules into the measuring cup, then tap the tube 500 times using a tap density volumeter. Record the test volume before compression (V0) and the volume before compression (V1)[7].

D. Evaluation of Effervescent Tablets

a. Organoleptic

The test was carried out by observing the shape, taste, smell, and color of the tablets being made.

b. Weight Uniformity Test

Twenty randomly selected pills underwent individual examination and weighting. Tablets whose weight deviation from the average weight exceeds the price listed in column A cannot be more than two tablets, and there cannot be more than one tablet where the deviation in weight means the average weight exceeds the price listed in column B[19].

c. Size Uniformity Test

A total of 20 tablets were taken randomly, and their diameter and thickness were measured. Unless otherwise stated, the diameter of the tablet should not be more than three times the thickness of the tablet and should not be less than 1 1/3 the thickness of the tablet. The diameter and thickness of the tablets were measured using a caliper[19].

d. Friability Test

Tablet friability is a parameter that describes the resistance of the tablet surface to various treatments that result in abrasion on the tablet surface. The tool used to carry out fragility tests was a friability tester. If tablet friability is high, this will affect the amount of active substance in the tablet. If the tablet's friability value is less than 0.8%, the tablet is considered good enough[8].

e. Hardness Test

The tablet is inserted into a hardness tester, which is then turned on to provide hardness results. Twenty replications of each formulation were carried out. For effervescent pills, an acceptable hardness of at least 4 kg is required[9].

f. Solubility Time Test

The effervescent tablet was placed in 200 ml of distilled water for a solubility time test. After the effervescent tablets are soaked, the time until all the tablets disintegrate and dissolve is measured using a timer. Excellent effervescent pills dissolve in one to two minutes[8].

g. pH Test

pH testing needs to be done because if the effervescent solution formed is too acidic, it can irritate the stomach, whereas if it is too alkaline, it will cause a bitter and unpleasant taste. If the pH of the effervescent solution is close to neutral, then the measurement results are said to be good[10]. The measurement results are said to be good if the pH of the effervescent tablet solution is close to neutral, namely pH 6-7.

4. Data analysis

The results of the data that have been obtained are analyzed descriptively arranged in tables and fit in graphical form.

RESULTS AND DISCUSSION

1. Phytochemical Screening

Phytochemical screening was a simple method for qualitatively analyzing compounds found in plants and observing color reactions using reagents that function to show color changes. The results of the screening test for gambier

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leaf extract (Uncaria gambier Roxb) stated that gambir leaf extract was positive for containing flavonoids, alkaloids, saponins, and tannins. Gambier leaf extract (*Uncaria gambier* Roxb) was declared positive for containing flavonoid compounds because it showed a change in color to orange or yellow. Positive for containing alkaloid compounds because it shows a color change to orange or there is an orange precipitate if Dragendorff's reagent is used. Positively containing saponin compounds is indicated by the formation of stable foam for approximately 7 minutes. Meanwhile, if it is positive for tannin compounds, it will show a color change to blackish green or blackish blue. This is in line with previous research conducted by Amos[20], Nurliayana[21], and also Anggraini[22], where positive results were found for the content of flavonoids, alkaloids, Saponins, and tannins.

2. Evaluation of the Physical Quality of Effervescent Granules

This evaluation is based on the Pharmacopeia Indonesia Standard and compares it to other research that used extract as an active ingredient in effervescent tablet formulation[19].

A. Organoleptic

This organoleptic test is carried out using the five senses method, which aims to determine the shape, color, aroma, and taste of the effervescent granules that have been made. The results obtained are in the form of granules, brownish white color, sour taste, and a distinctive gambier aroma.

B. Moist Granules

The average results obtained from evaluating the moisture content of effervescent granules using a moisture tool were control formula I 2.5%, formula II 3.4%, and formula III 2.4%. These results are in line with research[11], which obtained results ranging from 2-4%, which means that the water content of the granules produced met the requirements. Based on research results obtained, the range was 3.36-3.45%[12]. Meanwhile, the results of research by Karmini et al.[13] were around 3%.

The granule moisture test was carried out to determine the water content of effervescent granules made after undergoing the drying process. Drying the granules is done to control the mass of the effervescent granules so that microbes or fungi do not easily grow. Powders with high water content are difficult to compress because the mass will stick to the molding machine and cause capping. On the other hand, if the water content of the granules is low, tablets will easily become brittle because the binding force between the tablets is too weak[14].

C. Flow Time

The results obtained were for formula I 5.11 grams/second, formula II 4.94 grams/second, and formula III 5.67 grams/second, where these results showed that the granules had met the flow time test requirements as stipulated namely less than 10 grams/second. The flow rate will influence the granules flowing from the hopper to the die hole in the tablet pressing machine. It can be seen that the effervescent granules produced are considered good. This greatly influences the uniformity of filling the granules into the tablet molding holes to produce tablets with a uniform weight. Flow time is the time it takes for the granule to flow through the funnel. Good flow properties are required for the uniform filling of tablets into the molding holes of the tablet machine and also to facilitate material

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movement around the production facility[15].

D. Angle of repose

Testing the angle of repose of gambier leaf extract effervescent granules obtained results, namely formula I 34.45º, formula II 33.04º, and formula III 30.46º. It can be concluded that the granules have good flow properties. Testing the angle of repose will influence the printing process so that the tablet product that will be produced, namely effervescent tablets, is included in good quality effervescent tablets. This condition is because the lower the value of the angle of repose, the better the characteristics, namely, the easier it is for the granules to flow. These results were in line with research[9], where the results obtained ranged from 26.6º-31º, where these results met the standard angle of the repose test.

E. Compressibility

The results of testing the compressibility index of gambier leaf extract effervescent granules showed that formula I was 9.30%, formula II was 9.75%, and formula III was 12.5%. Where the granule has good compressibility and meets the requirements, if the value is less than 10%, indicating good flow. In comparison, the compressibility index value above 38% suggests inferior flow. A good compressibility value will show uniform granule shape and size. It will make the process of pressing effervescent tablets easier. The purpose of carrying out a compressibility test is to determine the ability of a granule to be compressed.

3. Evaluation of Effervescent Tablets

A. Organoleptic

The results of the organoleptic evaluation of gambier leaf extract (Uncaria gambier Roxb) using the five senses, including shape, aroma, color, and taste, can be seen in Table 1.

Table 2. Organoleptic result

Formula	Shape	Color	Taste	Smell
F I	Round	White with a brown spot	Acid	Gambier Typical
F II	Round	White with a brown spot	Acid	Gambier Typical
F III	Round	White with a brown spot	Acid	Gambier Typical

Table 3. Weight Uniformity Result

Formula	Average (gr)	A (5%)	B (10%)
F I	1,55	1,47-1,63	1,39-1,70
F II	1,58	1,50-1,66	1,42-1,74
F III	1,59	1,50-1,66	1,42-1,74
SD	0,02	-	-

Based on the weight uniformity test results in Table 3 for formula I, formula II, and formula III, none of the tablet weights deviated more than column A (5%). Column B (10%), and all effervescent tablet weights were declared to have passed the weight uniformity requirements, based on pharmacopeia Indonesia states that there are no more than two tablets whose weight each deviates from the average weight by more than the price set in column A (5%) and not a single tablet whose weight deviates from the average weight by greater than the price set in column B (10%). The factor that influences weight uniformity is the uniformity of filling when pressing the granules into tablets (die), and this is also closely related to the mass flow properties of the tablet[15].

Table 4. Size Uniformity Result

Average Size Uniformity (cm)		
Formula	Tablet Thick	Tablet Diameter
F I	0,5	1,6
F II	0,5	1,6
F III	0,5	1,6
SD	0	0

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Based on the results of the size uniformity test, it is known that the size uniformity of formula I, formula II, and formula III effervescent tablets meets the requirements of Pharmacopeia Indonesia.

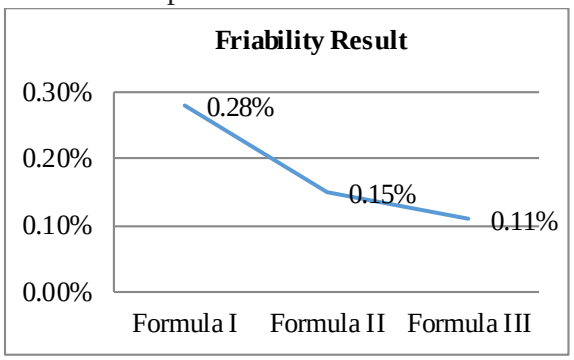

Figure 1. Friability Result

Based on the results of the friability test shown in Figure 1, it can be seen that the tablet hardness for formula I, formula II, and formula III meet the requirements, namely less than 1%. This is because the amount of binding agent used is quite good in the formula because the smaller the percentage of brittleness, the stronger the tablet is in resisting light scratches or damage during handling, packaging, and shipping. The higher the level of binding agent (PVP) in a tablet, the harder the tablet is and the less brittle it becomes. Apart from that, factors that also influence tablet fragility are room temperature and humidity because effervescent tablets easily decompose at room temperature and high humidity[12].

Table 5. Hardness Test Result

Formula	Average (kg)
F I	4,35
F II	4,37
F III	4,32
SD	0,02

Based on the test results on tablet hardness, the average is shown in Table 5. The hardness test results for formula I were 4.35 kg, formula II 4.37 kg, and formula III 4.32 kg. These results met the minimum requirements for tablet hardness, namely 4 kg[9]. The greater the hardness value of the tablet, the more excellent the tablet's resistance to mechanical pressure, shock, and tablet cracking during packaging, transportation, and distribution to consumers. The hardness of tablets is greatly influenced by the formulation ingredients, especially the addition of a binding agent, namely PVP, at 4%. An increase in PVP will result in bonds between compounds in the tablet, making the tablet harder[15].

Table 6. Dissolving Time Result

Formula	Average (S)
F I	1.43
F II	2.12
F III	1.27
SD	0.45

Based on Table 6 of the dissolving time test, it was found that the average dissolving time for formula I effervescent tablets was 1.43 minutes, formula II 2.12 minutes, and formula III 1.27 minutes. From these results, it can be stated that all tablets had a good dissolving time of less than 5 minutes. Because the faster the tablet dissolves, the faster the effervescent reaction occurs. Formula III, after replication, was 3 times faster to dissolve compared to other formulas. This difference in dissolution time is due to the fact that during the process of making effervescent tablets, there are several stages of the wet granulation method that allow reactions between acids and bases to occur, namely when adding a binder, dry sieving and also when pressing the tablets as well as room humidity conditions greater than 25%, this is due to the difficulty of controlling humidity in the room where the research was conducted. Apart from that, if the effervescent tablet is placed in a room where the humidity is high, it will cause the effervescent tablet to easily absorb water vapor and cause acids and bases to react more easily and produce CO2, and this is what causes when the tablet is dissolved the

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carbonization power is reduced and the dissolution time becomes longer[15].

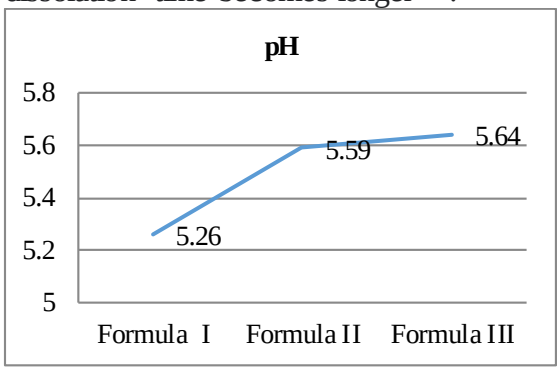

Figure 2. pH Result

The pH test results shown in Figure 2 show that all formulas have an average pH value of 5, and this value meets the requirements, namely, that they are close to neutral pH 6-7[12]. According to Apsari et al., the pH value results are acceptable for oral preparations because they are not too acidic. Things that influence the pH value of effervescent tablet preparations were the acid and base components in the formulation. However, variations of citric-tartric acid and PEG 6000 did not produce differences in the pH value of the formula[16].

CONCLUSION

Gambier leaf extract positively contains several secondary metabolite compounds such as flavonoids, alkaloids, saponins, and tannins. The physical and chemical characteristics of the gambier leaf extract effervescent tablet preparation produced were suitable based on pharmacopeia Indonesia literature. pH, dissolving time, size uniformity, weight uniformity, hardness test, and friability test all result in a good range for effervescent tablets.

CONFLICT OF INTEREST

There is no conflict of interest in this article. This article is written independently without the involvement of other parties who could improperly influence this article.

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