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Formulation and Evaluation of Granul Effervescent of Catechin from Gambier *(Uncaria gambier (Hunter)* Roxb)

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ABSTRACT

Extract of Gambier (*Uncaria gambir* (Hunter) Roxb) contains catechin compounds with antioxidant, antimicrobial, and antihelminthic activities. This study aims to determine whether the catechin gambier can be formulated as a foamy granule preparation and know whether the evaluation of the quality of the effervescent granules meets the criteria for suitable granules. The effervescent granule formula was made by the wet granulation method with two procedures with different levels of active substances. In formula 1 (F1), the level of catechins is 12%. In formula 2 (F2), the levels of catechins are 8%. Although effervescent granule evaluation tests such as compressibility test, flow rate, angle of repose, pH, and dispersion time, F1 and F2 meet the criteria of effervescent granules, testing the water content of the effervescent granules in F1 and F2 did not meet the suitable measures.

Keywords*: Catechin, Gambier, Granule effervescent, Thin layer chromatography.*

Introduction

Gambier (*Uncaria gambier (Hunter) Roxb*) is a specific plant and is a superior commodity from West Sumatera, Indonesia. However, until now, the gambier plant has not been used optimally by the people of Indonesia as herbal medicine. Gambier's superior varieties, according to the Agriculture Department, are shrimp varieties (Murapati, Lima Puluh Kota, Indonesia), Riau Varieties (Siguntur, Pesisir Selatan, Indonesia), and Cubadak variety (Siguntur, Pesisir Selatan, Indonesia). Most of the Gambier is grown outside Java, Indonesia, especially in West Sumatera Indonesia, South Sumatra and Bengkulu, Indonesia. Nearly 90% of gambier production was produced in West Sumatera, Indonesia (Isnawati *et al*., 2012).

Gambier is one of Indonesia's only commodities. In the international market, Indonesia has been ranked third for exports of raw gambier and seventh place for exports of processed gambier. Indonesian Gambier was sold at a low price as a superior product because it was only sold in raw gambier extract. Otherwise, gambier has a high selling value if it was sold as a derivative product as pure gambier lozenges, diarrhea core tablets, kate it is a free radical health drink, anti-aging gels and creams, toothpaste, transparent soap, a mixture of cosmetics and tanners (Widiyarti *et al.,* 2014).

The use of gambier can be seen traditionally as a complement to eating betel and drugs, as in Malaysia Gambier is used for burns medicine, besides the young stew and shoots used as a medicine for diarrhea and dysentery and as a mouthwash in sore throats. In modern terms, gambier is widely used as raw material for the pharmaceutical and food industries, including raw materials for liver disease drugs

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with the patent "Catergen," a candy ingredient that soothes the esophagus. In Singapore, gambier was used as raw material for stomachache and toothache medicine (Chabib *et al.,* 2010).Catechins are flavonoids, including natural polyphenol compounds that have potent antioxidants and bioactivity as a drug. Catechins function as natural antioxidants are usually more desirable because of their better safety and importance against free radicals (Rini *et al.*, 2013).

Catechins have great potential for medicinal raw materials because of their proven antibacterial effect, antivirus, and antidyslipidemic (Kurniatri *et al.*, 2019). It was known that the catechin gambier has activity against Shigella Flexner, which is the bacteria that causes diarrhea (Putri, 2010). Catechins have many benefits, including antioxidants, antibacterial properties, and antiatherosclerosis (Kurniatri *et al.*, 2015).

Effervescent granules are coarse to very coarse granules or powder and contain medicinal elements in a dry mixture, usually consisting of sodium bicarbonate, citric acid and tartaric acid. When added with acidic and alkaline water, it reacts to free carbon dioxide, thus producing foam. The resulting carbonate solution may mask the medicinal substance's salt taste or other unwanted tastes (Ansel, 1989).

Based on this background, the researchers are interested in formulating the catechin gambier (*Uncaria gambier (Hunter) Roxb)* in the form of effervescent granules, besides giving a pleasant taste and flavor because carbonation masks the unpleasant taste of the active substance and in this form the drug does not require a process of disintegration and dissolution before being absorbed so that the adequate level of the drug in the blood is achieved.

Experimental

Instruments and Materials

The tools used in this research are spectrophotometer UV-Vis (Shimadzu 1800), moisture balance analyzer (Sartorius MA 30), rotary evaporator (IKA Hb 10), sieving device, incubator, pH meter (Hanna), Tap volumeter modification, granule evaluation funnel, Oven (memmert).

The materials used in this research are: Gambier extract, ethyl acetate (Bratachem), aqua dest (CV. Novalindo), toluene P: ethyl acetate P: methanol P: formic acid P, lactose (PT. Dwilab Mandiri scientific), PVP K30 (PT.Brataco), citric acid (CV. Novalindo), aspartame (Planet Kimia), tartaric acid (PT. Brataco), sodium bicarbonate (Marck).

Procedure of analysis

Sampling

The sample used in this study was the Gambier obtained from the Pesisir Selatan area, West Sumatra, Indonesia.

Sample Preparation

In this study, gambier, which is still solid, is mashed or blended until it becomes a powder. Then, the gambier powder was stored in a tightly closed dry container.

Isolation of Gambier Catechins

The powdered Gambier was weighed 100 g, and the powder was macerated with ethyl acetate solvent for 24 hours. The results of the macerate were filtered and then evaporated with a rotary evaporator. after thick, add it with aquadest and heat it at a temperature of 70 °C for 15 min while stirring. Then put it in the refrigerator to form a paste, filter with a Buechner funnel, then dry it at 50 °C after dry crushed finely and carry out identification.

Thin Layer Chromatografi (TLC) Test

a. Saturation of the Vessel

Place the filter paper in the chromatography vessel. The report is 8 cm high, and the width is the same as the vessel's width. Enter several developer solutions into the chromatography vessel to a height of 0.5 to 1 cm from the vessel's bottom. Cover tightly and leave it until the filter paper is thoroughly wet. Filter paper must always be immersed in the developer solution at the bottom of the vessel.

b. TLC Test Solution

Weigh approximately 1 g of the sample carefully and soak while shaking it over a water bath with 10 mL of the appropriate solvent for 10 min. Enter the filtrate into the flask, determine 10 ml, add solvent to mark the limit.

c. Motion phase

Toluene P: ethyl acetate P: Methanol P: formic acid P

d. Silent phase

Silica Gel 60 F_{254}

e. TLC Procedure

Catechins were dissolved in ethyl acetate and then spotted on silica gel 60 F_{254}. A bottle of standard catechins dissolved with ethyl acetate in addition to the catechin isolate spots and let it dry. Insert the plate into the vessel filled toluene P: ethyl acetate P: Methanol P: formic acid P (4:6:1:1), which has been previously saturated first, then close the vessel tightly. Then remove the silica plate and let it dry. Observe spots on the visible scale, ultraviolet (254 nm) light. Measure and record the distance of each site from the dot and then determine the value of Rf (Ministry of Health Republic of Indonesia, 2017).

Effervescent Granule Formulation

1. Citric acid, tartaric acid, half the lactose content, half the aspartame content, PVP solution) are mixed with all the ingredients until smooth/form a dough. This mixture is sifted through 12 mesh and dried in an oven at 40 °C for 18 hours (acid mixture).
2. Sodium bicarbonate, half the lactose content, half the aspartame content, PVP solution) are mixed with all the ingredients until smooth/form a dough. This mixture is sifted through 12 mesh and dried in an oven at 40 °C for 18 hours (base mixture).
3. Enter the dry acid granule into the plastic, then the alkaline granule into the plastic, shake it gently, then evaluate the granule.

Effervescent Granule Evaluation

Organoleptic Test

This is done by looking at the shape, smell, color, and homogeneity of the dosage felt by the sense of touch.

Water Content Test

Test the moisture content using a Moisturizer balance, weigh 1 g of granule, set the scale to zero (Voight., 1994).

Compressibility test

Weigh 100 g of granule into a measuring cup and record the volume. Then, the granule is compressed by tapping 1250 times with the test instrument, record the test volume before being compressed and the volume after being compressed by tapping 1250 times (Halim, 2012).

Flow rate test

Done by weighing 100 g of granules, put into a funnel whose stem is closed. The funnel cover was opened, and the granules were allowed to flow until they ran out. Then, the flow time of the granules was calculated. A good granule flow time is no more than 10 s in 100 g (Halim, 2012).

Corner of rest

Weigh the granule as much as 30 g and put it into the funnel where the bottom is closed with the fingers, at the same time opening the lid of the funnel then releasing the finger from the mouth of the horn and the material is allowed to flow then freely a cone-like pile will occur, measured the height of the pile (h) and diameter (d) powder so that the radius can be are counted (r), corner of the stack (è) is the calculated landslide angle (Halim, 2012).

pH

Performed using a pH meter, the granules were weighed as much as 5 g and dissolved in 150 mL of water and then measured the pH (Noerwahid, 2016).

Dispersion time

Put 100 ml of water with different temperatures of 10 °C, 27 °C, and 60 °C into the beaker glass, then add 5 g of granule. (Noerwahid, 2016).

Results and Discussion

TLC test for catechin isolates in Gambier

The determination of the TLC profile aims to show the presence of an identity compound in the sample and describe the composition of the chemical compounds contained in the sample. The comparison used is the catechin (standard). The eluent used is toluene P: ethyl acetate P: Methanol P: formic acid P (4:6:1:1). Based on the results of the TLC, the sample produces one spot with an Rf value of 0.66. In comparison, the results obtained by the catechin comparators (standard) with an Rf value of 0.66 can be seen in the samples and comparators, proving that the catechin isolates of gambier have the same content as the comparators.

Effervescent Granule Evaluation

Effervescent granule evaluation is to determine the

Table 1. Effervescent Granule formulation for 100 g.

Material	Formula %		Uses
	F1	F2	
Catechin gambier	12%	8%	Active substance
Citric acid	9.5%	8.5%	Acid
Tartric acid	18.7 %	17.7%	Acid
Sodium bicarbonate	23.8%	25.8%	Carbonate
PVP K30	4.5%	3.5%	Binder
Lactose	30%	35%	Filler
Aspartame	1.5%	1.5%	C. saporis

quality and physical stability of the effervescent granule preparation whether it is good or not, and it is necessary to evaluate the practice consisting of organoleptic test, water content test, compressibility test, flow rate test, rest angle test, pH test, dispersion time test.

Organoleptic testing on formula 1 (F1) acid granule is yellow, the base granule is brown, formula 2 (F2) acid granule is yellow, and the baseline granule is brown (Figure 1).

They tested the moisture content of the effervescent granules using the Moisture Balance tool against two formulas consisting of acid and alkaline granules in each formula (Table 2). The F1 acid granule obtained a water content of 1.55%, in the baseline granule test 7.31%. In F2, acid granules get 1.75% content. On the baseline granule test, the moisture content was 8.58%. They were testing the water content of the granules in F1 and F2 of acid, and alkaline granules did not criteria the requirements on an excellent granule water content. According to Voight, (1994) a good granule water content is 2-5%. Recommend drying the acid granules using a modified granule incubator so that the granules are not too dry. Whereas in F1 and F2, the acid granule does not meet the requirements because the higher the use of sodium bicarbonate, the higher the moisture content of the granule.

Compressibility testing aims to determine the flow properties, which was done by setting the granules using a 100 ml measuring cup. Compressibility indicates a decrease in the volume of the granule due to tapping or vibration. Compressibility value of F1 acid granule 3.22%, F1 primary granule 3.22%, and F2 acid granules 7.69%, primary granule 7.69%. This result qualifies because the compressibility requirement is below 20% (Table 3).

The flow rate and angle of rest testing were carried out to determine the granules' flow rate, the

Fig. 1. Effervescent Granule

Table 2. Effervescent granule moisture content

Formulation	Granule Weight (g)	Water content (%)	Average	
F1	Acid granule	1.007	2.49	2.55 ± 0.05
		1.010	2.59	
		1.006	2.59	
	Alkaline granule	1.023	7.14	7.31 ± 0.29
		1.021	7.65	
		1.009	7.14	
F2	Acid granule	1.008	2.69	1.75 ± 0.05
		1.006	2.79	
		1.007	2.79	
	Alkaline granule	1.004	8.97	8.56 ± 0.47
		1.024	8.06	
		1.021	8.73	

Table 3. Compressibility testing

Formulation	Granules	Real Density	Incompresible Density	Kp (%)
F1	Acid	0.6	0.62	3.22
F2	Alkaline	0.6	0.62	3.22
F1	Acid	0.6	0.65	7.69
F2	Alkaline	0.6	0.65	7.69

homogeneity of the powder, and the uniformity of filling of a granule. The average flow rate test obtained in the F1 acid granule is 3.17 g/s, in the alkaline granule test is 3.09 g/s. In the acid granule F2 test, it was 2.74 g/s. In the base granule test, it was 2.67 g/s (Table 4).

In testing the rest of the F1 acid granule, the rest angle is 27.55°, and the acid granule is 29.14°. In the F2 test, the acid granule can get a grade of 28.22°, and the base granule can be 29.40° (Table 5). From the results of the angle of rest obtained for the two formulas, the rest angle is very good 25° - 30° (Voight, 1994).

Table 5. The testing angle of silence

Formulation		Tan ´	Arc Tan ´(°)
F1	Acid granule	0.53	27.55
	Alkaline granule	0.56	29.14
F2	Acid granule	0.54	28.22
	Alkaline granule	0.57	29.44

The pH test aims to determine whether the effervescent granules have acidic or alkaline values. It was done by measuring the solution using a pH meter. The pH test in F1 got a value of 5.75, and the pH test of F2 got a value of 5.60 (Table 6). When viewed from this value, the effervescent catechin gambier granule solution is included in low acidic food products because the pH is still above 4.5. (Hernani *et al*., 2012).

Table 6. pH testing

Formula	pH	Average
F1	5.84	5.75±0.07
	5.72	
	5.50	
F2	5.46	5.60±0.12
	5.65	
	5.70	

Dispersion time testing is conducted to determine whether the granule can dissolve and how long the granule can dissolve. Tests are carried out using water temperatures of 10 °C, 27 °C, and 60 °C. In F1, the average dispersion time at a water temperature of 10 °C is 4.17 min, at a water temperature of 27 °C is 3.27 min, at a water temperature of 60 °C is 2.22 min. In F2, the average dispersion time at a water temperature of 10 °C is 4.35 min, at a water tempera-

Table 4. Flow rate testing

Formulation	Granule Weight (g)	Flow Rate Time (min)	Flow Rate (g/s)
F1 Acid granule	20	6.43	3.11
	20	6.17	3.24
	20	6.27	3.18
Average	6.29	3.17 ± 0.06	
F1 Alkaline granule	20	6.50	3.07
	20	6.43	3.11
	20	6.47	3.09
Average	6.46	3.09± 0.02	
Formula 2 alkaline granule	20	7.38	2.71
	20	7.16	2.79
	20	7.33	2.72
Average	7.29	2.74±0.04	
Formula Alkaline granules	20	7.53	2.65
	20	7.54	2.66
	20	7.33	2.72
Average	7.46	2.67±0.03	

ture of 27 ºC is 3.23 min, at a water temperature of 2.28 min (Table 7). Thus, this dispersion time test has met the requirements. When the granule is dispersed in water and completes the reaction in <5 minutes, the preparation is dispersed entirely. (Siregar and Wikarsa, 2010).

Table 7. Dispersion time testing

Formula	Temperature		
	10 ºC	27 ºC	60 ºC
F1	4.12 min	3.28 min	2.22 min
	4.19 min	3.27 min	2.21 min
	4.21 min	3.26 min	2.23 min
Average	4.17 min±0.04	3.27 min±0.01	2.22 min±0.01
F2	4.38 min	3.25 min	2.25 min
	4.31 min	3.21 min	2.27 min
	4.36 min	3.23 min	2.32 min
Average	4.35 min±0.03	3.23 min±0.02	2.28 min±0.03

Conclusion

The effervescent granule formula was made by the wet granulation method with two formulas with different levels of active substances. In F1, the level of catechins is 12%. In F2, the levels of catechins are 8%. Although effervescent granule evaluation tests such as compressibility test, flow rate, angle of repose, pH, and dispersion time F1 and F2 meet the criteria of effervescent granules, testing the water content of the effervescent granules in F1 and F2 did not meet the suitable measures. Based on the research results that have been done, it was concluded that catechins could be formulated into effervescent granules. On the other hand, the catechin gambier effervescent granule preparation did not meet the criteria of a suitable granule because the water content of the granule did not meet the criteria of the relevant requirements.

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