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Optimization of Flocel 101 and Amylum as Fillers in Sambiloto (*Andrographis paniculata* (Burm.f.) Nees.) Capsules Formulation

Optimasi Flocel 101 dan Amilum sebagai Bahan Pengisi pada Formulasi Kapsul Sambiloto (*Andrographis paniculata* (Burm.f.) Nees.)

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ABSTRACT

Sambiloto (*Andrographis paniculata* (Burm.f.) Nees.) is an herbal plant that is beneficial for health due to its main chemical component, andrographolide. Sambiloto can be formulated into capsules to make it more practical and comfortable for consumption, mask the bitter taste, and guarantee dosage accuracy. This research aimed to determine the optimal concentration of Flocel 101 and amylum as capsule fillers to achieve the best physical properties of Sambiloto extract capsules. The study was conducted experimentally using 5 (five) formulas (F1, F2, F3, F4, and F5) with various concentrations of Flocel 101 and amylum. A series of tests were conducted on the physical properties of the capsule powder: organoleptic tests, water content, flowability, disintegration time, and average capsule weight. Additionally, quality control was performed by checking for microbial contamination through total plate count (TPC) and yeast and mold count (YMC) tests. The results of this research indicated that the F1 formula provided the best physical properties and met the requirements, with the appearance of a greenish-gray dry powder, water content of 6.88%, flow rate of 20 g/s, disintegration time of 15.5 minutes, average weight of 0.55 g, TPC 250 cfu/g, and YMC <10 cfu/g.

Keywords: Amylum, Capsule, Flocel 101, Sambiloto.

ABSTRAK

Sambiloto (*Andrographis paniculata* (Burm.f.) Nees.) adalah tanaman herbal yang bermanfaat bagi kesehatan karena komponen kimia utamanya, andrographolide. Sambiloto dapat diformulasikan menjadi kapsul agar lebih praktis dan nyaman dikonsumsi, menutupi rasa pahit, dan menjamin akurasi dosis. Penelitian ini bertujuan untuk menentukan konsentrasi optimal Flocel 101 dan amilum sebagai bahan pengisi kapsul untuk mencapai sifat fisik terbaik dari kapsul ekstrak sambiloto. Penelitian dilakukan secara eksperimental menggunakan 5 (lima) formula (F1, F2, F3, F4, dan F5) dengan berbagai konsentrasi Flocel 101 dan amilum. Serangkaian pengujian dilakukan pada sifat fisik serbuk kapsul: uji organoleptik, kadar air, daya alir, waktu hancur, dan berat rata-rata kapsul. Selain itu, kontrol kualitas dilakukan dengan memeriksa kontaminasi mikroba melalui uji *total plate count* (TPC) dan *yeast and mold count* (YMC). Hasil penelitian ini menunjukkan bahwa formula F1 memberikan sifat fisik terbaik dan memenuhi persyaratan, dengan tampilan serbuk kering berwarna abu-abu kehijauan, kadar air 6,88%, laju alir 20 g/s, waktu hancur 15,5 menit, berat rata-rata 0,55 g, TPC 250 cfu/g, dan YMC <10 cfu/g.

Kata Kunci: Amilum, Flocel 101, Kapsul, Sambiloto

INTRODUCTION

Sambiloto (*Andrographis paniculata* (Burm.f.) Nees.) is a herbal plant originating from India, but has spread widely in Indonesia (Widiyastuti et al., 2017). Sambiloto is included in the Acanthaceae family with the main chemical content of diterpene lactones including andrographolide, deoxyandrographolide, neoandrographolide, andrografisid, deoxyandrografisid, and andropanoside (KEMENKES, 2017). Sambiloto was known as the "king of bitter" because of its famous bitter taste (Nyeem et al., 2017). There are various health benefits of Sambiloto and the most prominent is its anti-diabetic activity. According to Nugroho et al. (2012), andrographolide contained in Sambiloto reduced blood glucose levels by increasing GLUT-4 mRNA and protein levels. Its antidiabetic activity is reported to be related with antioxidant activity and inhibition of NF-κB. This compound can also stimulate insulin release and inhibit glucose absorption through inhibiting the enzymes α-glucosidase and α-amylase. According to research Hidayat & Hayati (2020), ethanolic Sambiloto extract at a dose of 100 mg/kgBW (conversion to human dose assuming a body weight of 70 kg = 1120 mg) in Wistar rats induced diabetes significantly reduced serum blood sugar levels. This is in line with an increase in GLUT-4 levels, thereby increasing glucose intake by cells. In other research by Jayakumar et al. (2013), both Sambiloto and andrographolide were declared non-toxic through various administration routes.

Because of the great potential of Sambiloto, especially to help reduce hyperglycemia and to cover the bitter taste, Sambiloto is formulated in capsule preparation. Capsule was chosen because it was considered more practical and comfortable to consume, and ensured accurate dosage (Gadri & Priani, 2012). In capsule formulation, various excipients are needed, including fillers. Fillers function to add mass and fill the weight of the preparation (Van der Merwe et al., 2020). In this research, filler materials were used in the form of Flocel 101 and starch.

Flocel 101 is a trademark of microcrystalline cellulose which is included in the cellulose group. Flocel 101 is a white crystalline powder, odorless and tasteless. In the pharmaceutical industry, Flocel 101 can be used as a filler, binder, glidant and disintegrant in oral tablets and capsules. (Saigal et al., 2009). Flocel 101 as a capsule filler can be used in a concentration range of 20-90% (Rowe et al., 2009). Meanwhile, starch is an excipient that is commonly used as a filler and disintegrant in tablets and oral capsules. Starch is in powder form, tasteless and odorless, with a white to pale white color. Starch as a filler can be used in a concentration range of 3-20% (Rowe et al., 2009).

The use of a combination of Flocel 101 and starch fillers is expected to be an alternative capsule filler material so that good physical properties of herbal powder are produced and meet the safety and quality requirements for traditional medicines as stated in BPOM RI Regulation Number 29 of 2023. Flocel 101 is a filler that can absorbs moisture, so it is suitable for use as a filler for herbal medicine powders containing hygroscopic extracts. However, Flocel 101 has a weakness, namely poor flowability, while natural starch tends to be weaker in its ability to absorb moisture. Based on this background, this research aims to evaluate the effect of Flocel 101 and starch on the physical properties of Sambiloto herbal medicine powder, as well as to determine the optimum concentration of the combination of Flocel 101 and starch which can produce the best Sambiloto capsules and fulfill the requirements for the physical properties of the powder.

MATERIALS AND METHODS

1. Types of research

This research was carried out experimentally using 5 (five) formulas (F1, F2, F3, F4, and F5) with varying concentrations of Flocel 101 and different starch.

2. Research Variables

In this research there were 3 (three) variables, namely independent, dependent and controlled variables. The independent variables in this study were the concentration of Flocel 101 and starch as a filler for the Sambiloto herbal medicine powder. The dependent variable was the physical properties of the Sambiloto herbal medicine powder (organoleptic, water content, flowability, disintegration time, average weight, YMC, and TPC). The controlled variables in the form of the total amount of Sambiloto extract and excipients in each formula, methods of producing herbal powder, and herbal powder various physical property parameters.

3. Materials

Sambiloto extract powder of (*A. paniculata* (Burm.f.) Nees.) was extracted by the percolation method using 70% ethanol solvent (Borobudur Extraction Center), Flocel 101 (Gujarat Microwax Pvt. Ltd), starch (Ubon Sunflower Company Limited), magnesium stearate (FACI Asia Pacific Pte Ltd), aerosil (Wacker Chemicals (China) Co. Ltd), distilled water, Soybean-Casein Digest Broth, Soybean-Casein Digest Agar (Oxoid Limited), and Sabouraud Dextrose Agar (Oxoid Limited).

4. Tools

Analytical balance, moisture analyzer, disintegration tester, flow tester, stopwatch, incubator, and glassware.

5. Herbal Powder Formulation

In this study, a capsule formulation with a weight of 550 mg was carried out. The Sambiloto extract used in each was 60% (330 mg), where this dose refered to research Hidayat & Hayati (2020) was already in the effective range in helping lower blood sugar and meets toxicity requirements. All ingredients were weighed using an analytical balance. Then all the ingredients were mixed, stirred until homogeneous. The formula was presented in **Table 1.**

Table 1. Sambiloto Herbal Powder Formula

Material	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
Sambiloto extract	60	60	60	60	60
Starch	37	27	18.5	10	0
Flocel 101	0	10	18.5	27	37
Magnesium stearate	2	2	2	2	2
Aerosil	1	1	1	1	1

6. Evaluation of Physical Properties

a. Organoleptic Test

The physical appearance and particle size of the Sambiloto herbal medicine powder were observed before and after being exposed to air at room temperature (27°C) and 60% humidity for 3x24 hours. Exposure for 3x24 hours was carried out as a simulation of the capsule filling process in the Production section which takes 1-3 days.

b. Water Content Test

The water content test was carried out using a moisture analyzer. Capsule water content requirement was ≤10% (BPOM, 2023).

c. Flowability Test

Flowability testing was carried out using a flow tester. Flow time was calculated by the formula:

$$Flow\ rate = \frac{w}{t}$$

Information:

w = powder weight

t = time for all the powder to flow

The flow rate was good if the capability of flowing was ≥ 10 g/s for 100 g of powder, therefore the flow rate was ≤ 10 s (Cahyani et al., 2021).

d. Disintegration Time Test

The disintegration time test was carried out using a disintegration tester. Capsule disintegration time requirement was ≤ 30 minutes (BPOM, 2023)

e. Yeast and Mold Count (YMC) and Total Plate Count (TPC) Test

The sample was prepared by dissolving the powder of the Sambiloto herbal medicine to be tested (usually 1 in 10) into Soybean-Casein Digest Broth, if necessary, adjust the pH to 6-8. Prepare samples for each medium in at least 2 (two) petri dishes for each dilution level. Incubate Soybean-Casein Digest Agar plates at 30°-35°C for 3-5 days for TPC, and Sabouraud Dextrose Agar plates at 20°-25°C for 5-7 days for YMC in the incubator. Select the plate from the one dilution level with the highest number of colonies. Calculate the average number of colonies in the culture medium and the number of colonies per gram or per milliliter of preparation (KEMENKES, 2020). YMC requirements were not more than 10^3 colonies/g and TPC were not more than 10^5 colonies/g (BPOM, 2023).

RESULTS AND DISCUSSION

According to BPOM RI Regulation Number 29 of 2023 concerning Safety and Quality Requirements for Natural Medicines, capsules were traditional medicine preparations that were wrapped in a hard shell. Capsule shells were generally made from gelatin, starch, or other suitable soluble materials (KEMENKES, 2020). In this research, optimization of Flocel 101 and starch as fillers for herbal medicine powder for Sambiloto capsules was carried out from various concentrations in 5 (five) different formulas. The purpose of this variation in concentration was to determine the effect of variations in concentration between the two materials and obtain the optimal concentration so that the best physical properties were produced.

In this research, optimization was carried out from 5 (five) formulas with varying concentrations of Flocel 101 and starch fillers, namely F1 (0:37), F2 (10:27), F3 (18.5:18.5), F4 (27:10), and F5 (37:0). The concentration of fillers in herbal medicine powder refered to Rowe et al. (2009) whereas a filler Flocel 101 should be in the concentration range of 20-90%, while starch was 3-20%. In each formula, concentration

variations were made with a ratio of Flocel 101 and starch of 0:100, 25:75, 50:50, 75:25, and 100:0. After formulation, organoleptic evaluation, particle size and water content were carried out for each formula. Formulas that were declared to have good results in organoleptic testing, particle size and water content will be continued to the next evaluation. The results of the initial evaluation of the Sambiloto herbal medicine powder before exposure presented in **Table 2**, and after exposure in **Table 3**. The organoleptic appearance of the herbal medicine powder presented in **Figure 1** (before exposure) and **Figure 2** (after exposure). The percentage increase in water content before and after exposure can be seen in **Figure 3**.

Based on **Table 2**, the five formulas had a powder appearance before exposure. After exposure, F1, F2, and F3 had a moist, slightly lumpy appearance, and were darker in color, while F4 and F5 had a slightly lumpy appearance. A darker color indicates that the herbal powder was moister than one with a lighter color.

In terms of water content, the results obtained for water content before exposure for F1, F2, F3, F4, and F5 (in %) were 7.11 respectively; 6.74; 5.43; 6.47; and 4.20. Meanwhile, after exposure, the water content of F1, F2, F3, F4, and F5 (in %) respectively became 11.02; 10.73; 10.17; 10.02; and 9.60. From **Tables 2 and 3** the higher the concentration of Flocel 101 was, the lower the water content. That was also proven by F4 and F5 which had a drier appearance than F1, F2, and F3 with a lower Flocel 101 concentration percentage. According to Islamiarti et al (2021), at a concentration of 20-90% Flocel 101, apart from being a filler, it could also act as an adsorbent. This was in line with research by Islamiarti et al. (2021) that Flocel was able to produce a more effective powder drying effect than starch. According to Sun (2008), Flocel 101 was microcrystalline cellulose which had many hydroxyl groups in the cellulose chain which allowed water absorption and made it had quite strong adsorption capacity. Because the five formulas were considered quite good, the physical properties evaluation was continued to the next test (flowability, disintegration time, YMC, and TPC tests).

Table 2. Organoleptic Test Results and Water Content of Herbal Powder Before Exposure

Parameter	Before showing				
	F1	F2	F3	F4	F5
Appearance	Powder	Powder	Powder	Powder	Powder
Water content (%)	7.11	6.74	5.43	6.47	4.20

Table 3. Organoleptic Test Results and Water Content of Herbal Powder After Exposure

Parameter	After being exposed				
	F1	F2	F3	F4	F5
Appearance	Moist, a bit lumpy	Moist, a bit lumpy	Moist, a bit lumpy	A bit lumpy	A bit lumpy
Water content (%)	11.02	10.73	10.17	10.02	9.60

(a) (b) (c) (d) (e)

Figure 1. Organoleptic of Herbal Powder Before Exposure to Air and Room Humidity: (a) F1, (b) F2, (c) F3, (d) F4, (e) F5

(a) (b) (c) (d) (e)

Figure 2. Organoleptic of Herbal Powder after Exposure to Room Air and Humidity: (a) F1, (b) F2, (c) F3, (d) F4, (e) F5

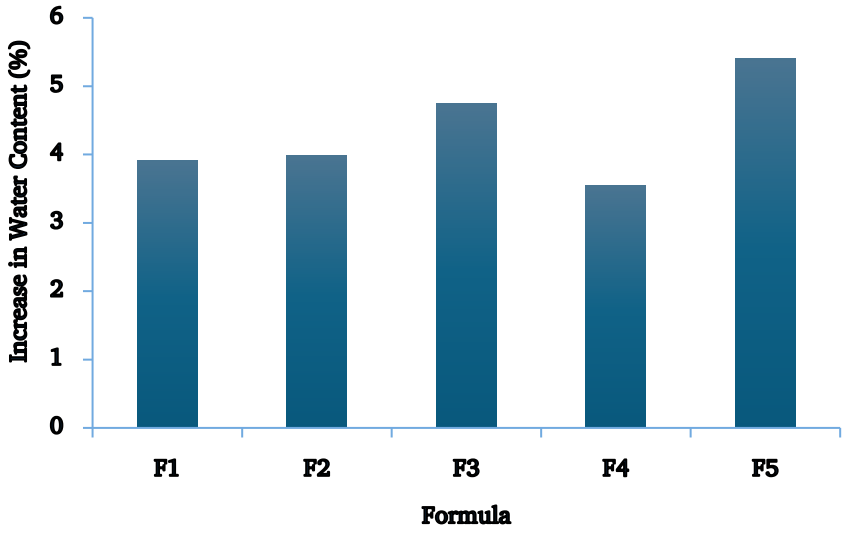

Figure 3. Graph of Increase in Water Content Before and After Exposure to Room Air and Humidity

Table 4. Complete Physical Properties Test Results

Parameter	F1	F2	F3	F4	F5
Form	Powder	Powder	Powder	Powder	Powder
Color	Greenish ash	Greenish ash	Greenish ash	Greenish ash	Greenish ash
LOD (%)	6.88	5.43	4.87	5,10	4.09
Flow rate (g/s)	20.00	5.00	5.00	5.00	5.00
Disintegration Time (min)	15.50	17.80	14.00	13.60	12.60
Average weight (g)	0.55	0.54	0.50	0.47	<0.47
TPC (cfu/g)	250	1000	1000	500	1250
YMC (cfu/g)	<10	15	40	<10	<10

The results of testing the physical properties of Sambiloto herbal medicine powder presented in **Table 4**. From further organoleptic tests carried out, it was found that the entire formula was greenish gray in color with a dry powder texture. The entire formula had a water content that met the requirements ≤10%, with the water content getting lower as the concentration of Flocel 101 in the formula increases. According to Pujiwati and Usman (2023), the drier the capsule filler powder, the better it was, because dry powder could mix better with other ingredients therefore it guaranteed the homogeneity of the capsule contents (Pujiawati & Usman, 2023). Apart from that, dry powder could also produce good flowability.

Flowability could be interpreted as the ability of powder to flow in a capsule filling machine, where powder that had good flowability could flow easily in the filling machine and produced a uniform capsule weight. Based on the flow rate test results, only F1 had a flow rate that met the requirements, namely ≥10 g/s (BPOM, 2023), while for F2, F3, F4, and F5 they did not meet the flow capacity requirements. Based on particle size measurements, a total of 90% of the powder from the entire formula passes through mesh number 60. According to Soppela et al. (2010), One of the factors that influence flowability was the size and shape of the particles. Particles larger than 250 μm could flow freely, whereas particles below 100 μm were generally cohesive and susceptible to flowability problems. Based on research conducted by Soppela et al. (2010), in particle size testing Flocel 101 had size 60.46 ± 0.16 μm. Meanwhile, based on research by Prasetia et al. (2016), the particle size distribution of natural starch without heating was very narrow where it only focuses on one point, almost all of it passes through mesh sieve no. 80 (≤ 180 μm). The research results were in accordance with theory, where the higher the concentration of Flocel 101, the worse the flow rate would be because Flocel 101 had a smaller particle size than starch.

In terms of disintegration time, the five formulas had a disintegration time that met the requirements, ≤ 30 minutes (BPOM, 2023). Based on the test results, it identified that increasing the concentration of Flocel 101 made the disintegration time faster. Starch and Flocel 101 could both act as disintegrating agents, but with different effectiveness. When in contact with water, starch grains returned to their original shape and released a certain amount of pressure, which would cause damage to interparticular hydrogen bonds and create a crushing effect. (Soedirman et al., 2009). Meanwhile, Flocel 101 worked by wicking (permeation), where water would enter through the pores, resulting in a faster disintegration effect with high effectiveness. (Kokafrinsia & Saryanti, 2021). A good disintegration time indicated that the capsule was easily destroyed and dissolved in the body after consumption, so that it can provide the desired pharmacological effect in the right time.(Dewi & Farida, 2021).

The test results for the average weight of capsules presented in **Table 4**. The average weights of F1, F2, F3, F4, and F5 respectively (in grams) were 0.55; 0.54; 0.50; 0.47; and <0.47. These results showed that as the concentration of Flocel 101 increased, the average capsule weight became lower. Weight was influenced by the density of the material, where Flocel 101 had a bulk density of 0.33 ± 0.01 g/mL (Yugatama et al., 2015), while starch had bulk *density amounted* to 0.491 ± 0.00081 g/mL (Wartana, 2019). Due to the low density of Flocel 101, the greater the concentration of Flocel 101 is, the more likely it was that the capsule would not reach the desired target weight. Weight was related to the level of active drug substance, where a lack of average capsule weight would affect the amount of active substance contained in the capsule, its efficacy will also be reduced (Gopalan and Gozali, 2018). Therefore, the closest to the target weight was F1, where the target capsule weight was 550 mg.

Based on the TPC and YMC test results, the amount of TPC in F1, F2, F3, F4, and F5 respectively (in cfu/g) was 250; 1000; 1000; 1000; 500; and 1250. Meanwhile, the number of YMC respectively (in cfu/g) was <10; 15; 40; <10; <10. The amount of YMC and TPC in the entire formula met the requirements of BPOM RI (2023), where the amount of YMC ≤ 10^3 colonies/g and TPC ≤ 10^5 colonies/g. The amount of YMC and TPC that met these requirements indicates that the entire formula was safe for consumption.

CONCLUSION

Based on research that had been carried out, variations in the concentration of Flocel 101 and starch could affect the appearance, water content, flowability and disintegration time of the Sambiloto herbal medicine capsules. Of the entire formula, F1 showed the capsule herbal powder with the best physical properties. Formula F1 had a greenish ash dry powder appearance, water content 6.88%, flow rate 20 g/s, disintegration time 15.5 minutes, average weight 0.55 g, TPC 250 cfu/g and YMC <10 cfu /g which met the requirements for traditional medicine capsules containing natural extracts.

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