Jurnal Natural
Vol.19, (2) 2019
DOI 10.24815/jn.v19i2.12151
Published June 2019
pISSN 1411-8513
eISSN 2541-4062

FORMULATION DOSAGE FORM OF TABLET CONTAINING KEPEL LEAF EXTRACT *(Stelechocarpus burahol* (Blume) Hook.f & Thomson*)* AS AN ANTIMICROBIAL AGENTS

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Abstract. Pharmaceutical dosage form that contains herbal materials has been developed in order to make it easy to consume. Tablet is one of pharmaceutical dosage form that generally used. A formulation and antimicrobial test of tablet containing extract of Kepel leaf with different concentration of diluents, binders, and disintegrants has been studied. The evaluation test showed that formulation consist of 25% of Kepel leaf extract, 64.5% of avicel PH 102, 2% of PVP, 7% of amprotab, 0.5% of aerosil, and 1% of talcum are better than the others. The experimental method used in this study was wet granulation. From the result of the mass granulation evaluation, it was obtain that speed flow without vibration was 2.53 s, with vibration was 2.83 s, bulk density was 0.329 g/mL, taped density was 0.376 g/mL and compressibility was 12.65 %. The result of tablet evaluation obtained that the average weight was 498 mg, with the average hardness was 4 kg/cm^2 and disintegration time was 2.36 mins. Antimicrobial test showed that in the concentration of 50 mg/mL, had average inhibitory diameter against S. aureus of 12.96 mm, P. aeruginosa 12.7 mm, and against B. subtilis was 12.53 mm. Whereas, concentration of 62.5 mg/mL had average inhibitory diameter against S. aureus was 13.5 mm, P. aeruginosa was 13.56 mm, and against B. subtilis was 13.43 mm. Both concentrations did not have antimicrobial activity against E.coli.

Keywords : tablet, Kepel leaf extract, antimicrobial

I INTRODUCTION

Tablets are the most popular dosage form because they are easy to use, relatively low production costs, relatively precise dosages, and physically more durable in storage, chemically and physically stable. The release of active substances can be regulated, the volume is small and compact and make it easy to package [1]. Along with technological developments, herbal or natural ingredients can also be made in pharmaceutical dosage forms with nutritious ingredients derived from plant extracts, a tablet dosage form for example. Kepel (*Stelechocarpus burahol* (Blume) Hook.f & Thomson) is one type of fruit that has not been widely cultivated. Kepel is a rare plant in Indonesia. Kepel or burahol leaves can be used to prevent body odor, especially those caused by microorganisms. The research showed the extracts and fractions of the kepel leaves which inhibited the growth of microbes that cause body odor include *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Candida albicans* [2]. Methanol extract from Kepel leaves gave inhibitory to *Staphylococcus aureus* with the Minimum Inhibitory Concentration (MIC) obtained at a concentration of 25% b/v with a inhibitory diameter of 14. 465 mm.

II METHODOLOGY

Tools and materials used

The tools used are digital scales (Mettler Toledo), Analytic Scales (Monobloc, AB 104-S type), Dryer Cabinets, Stopwatch (Q & Q), Sieves, flow velocity gauges, Single punch (Hanjuang) tablet machines, Friabilator, Desintegration Tester Unit, Calipers, Hardness Tester, Spectrophotometer (Shimadzu, UV-160 U type), Autoclaves and petri dishes. The materials used in this study were: Kepel leaf extract, methanol, Avicel PH 102 (PT. Brataco Chemika), PVP (Polyvinyl Pirolidone)

(PT. Brataco Chemika), 95% alcohol, amprotab (PT. Brataco Chemika), aerosil (PT. Brataco Chemika), talkum (PT. Brataco Chemika). For testing the preparation was used: Nutrient Agar, Tetracycline HCl (Ningxia Qiyuan Pharmaceutical Co.Ltd), cultures of *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa*, and *Bacillus subtilis.*

Extraction

As many as 3000 g of fresh Kepel leaves are washed, then dried by aerated. The leaves are dried and then crushed using a blender to form a powder. The simplicia powder is then extracted by maceration using methanol. After obtaining the filtrate then evaporated until a thick extract was obtained.

Formulation

Three formulas were prepared based on differences in fillers of Avicel PH 102, PVP as a binder and Amprotab as a desintegran. These three formulas, it is then processed in wet granulation, then evaluated to find out the best formula (Table 1).

Table 1 Tablet Formulation

Compound	F I (%)	F II (%)	F III (%)
Kepel Extract	25	25	25
Avicel PH 102	62.5	62.5	64.5
PVP	5	2	2
Amprotab	6	9	7
Aerosil	0.5	0.5	0.5
Talcum	1	1	1
Total	**100**	**100**	**100**

Wet Granulation Method

The extract was added with avicel PH 102 filler crushed until mixed, then added with PVP binder, mixed until homogeneous. Then the mixture is moistened with 95% alcohol by spraying it to form a mass that can be clenched. The tablet mass was granulated using a sieve then the formed granules were dried in a drying cabinet at 40^{o}C for 24 h. The dried granules are then sifted back to get a smaller granule size. The granules that have been sieved are then added to the outer phase (amprotab, talc and aerosil), mixed until homogeneous [1]

Granule Evaluation

Granule evaluation is done to ensure that the granule meets the requirements for tableting proces. Granule evaluation includes flow time test, compressibility and rest angle test.

Tablet Evaluation

Appearance

Tablets observed in general include homogeneity, tablet form, color and texture.

Uniformity of weights

Each tablet was weighed 20 tablets. Calculated average weight of tablets and average deviations. If weighed one by one, it should not be more than two tablets with each weight deviating from 5%, and not a single tablet whose weight deviates from 10% [4].

Size uniformity

A total of 10 tablets from five parts each of two tablets. Measure with caliper length, the tablet diameter is not more than three times and not less than one third thick of the tablet [4].

Tablet hardness

Performed using a hardness tester of 20 tablets. The average hardness and standard deviation are calculated.

Friability

A total of 20 tablets are cleaned from dust and then weighed (Wo). The tablet is inserted into the friabilator device. The appliance is switched on for 4 mins. Tablets cleaned and weighed (Wt). A good tablet has less than 1% friability [3]. Friability is calculated using the formula in Eq. (1).

$$f = Wo - Wt \times 100\% \quad (1)$$

where *W*o is the initial weight and *W*t is the final weight

Desintegration Test

The time trial was carried out using the Desintegration tester tool, by inserting six tablets into the basket, raising the basket regularly 30 times per minute. Tablets are declared desintegrated if there is no part of the tablet left over the screen, except for fragments from coating agents [3].

Antimicrobial activity of tablet preparations

Prepared test media in the form of Nutrient to be liquid at 50^{o}C. Then poured 20 mL into a petri dish that has been filled with 0.1 mL bacterial suspension. homogenized by swaying slowly then allowed to solidify. After making a compact, then perforated using a perforator. Each dose of tablet

preparation was dissolved in methanol. Then 50 µL is taken using a micropipette, put in a hole that has been made in the cup. After that, it was incubated for 18-24 h at 37°C. It was measured the diameter of the inhibitory zone formed using a Caliper.

III RESULTS AND DISCUSSION

In general, the extract is hygroscopic, so in the preparation of the preparation it is necessary to carry out the granulation process. In addition, the humidity of the room also needs to be considered to prevent water withdrawal. The selection of ingredients that can reduce hygroscopicity such as Aerosil can be an option [5]. Of the three formula orientations, formula III is considered to be the best in terms of compressibility, hardness, and disintegration time of tablets. Increased levels of Avicel PH 102 are expected to increase the compressibility of the tablet so that the tablet is not brittle.

Granule Mass Evaluation

Granule testing needs to be done to determine the feasibility of the granule mass to further be able to do the tableting process. And from the evaluation results indicate that the granule mass is feasible to be punch into a tablet (Table 2). From the evaluation results, it can be seen that the granule mass has a good flowing which is shown by rest angle of 24.48° with vibration and 25.21^{o} without vibration based on the good Carr index. A good flow rate determines the ability of the granules mass to flow well into the mold.

Tablet Evaluation

Tablet evaluation is done to determine the quality of a tablet. Tablet appearenced showed on figure 1, has a good shape and brown color. Good tablet hardness of at least 4 kg, then the tablet produced is still acceptable.

Figure 1 Tablet appearance

Friability shows the ability of the tablet to survive shocks or slamming. This test can also be a measure of the hardness of a tablet. Fructility or abrasion shows the tablet's ability to withstand friction. Good Friability and Fractivity is less than 1%. Disintegration time determines the dissolving speed of a tablet, from the evaluation results, the disintegration time of the tablet has met the predetermined requirements of not more than 15 mins.

Table 2 Granule Evaluation

Parameter	Result
Flow Time	Without Vibration = 2.83 s Vibration = 2.53 s
Break Angle	Without vibration = 24.48° Vibration = 25.21^{o}
Bulk Density	0.329 g/mL
Taped Density	0.376 g/mL
Compressibilty	12.65 %

Table 3 Tablet Evaluation

Characteristic	Average
Weight	498 mg ± 0.033
Diameter	12.2 mm ± 0.000
	3.43 mm ± 0.008
Hardness	4 kg ± 0.000
Friability	0 %
Fractivity	0.21 %
Disintegration	First Tablet = 2.36 mins Last Tablet = 4.39 mins

Antimicrobial Test Results for Tablet Preparations

From the results of the study, it can be seen that the inhibition of the growth of bacterias is thought to be caused by antibacterial compounds contained in the methanol extract of kepel leaves. Kepel's leaf it known contains terpenoids and flavonoids as the secondary metabolites [6]. Leaves extracts of kepel contains flavonoids include auron, flavanones and flavanols that can be used for antibacterial agent [7]. The action mechanism of flavonoids as antibacterial is by denaturing bacterial cell proteins and damaging cell membranes so as to cause nucleotides and amino acids out of cells and makes the bacterial cell death [8] Based on observations, kepel leaf extract in tablet preparations provides the best activity in P. aeruginosa. Tablet preparations do not provide inhibitory zones in *E. coli*. This is probably due to the fact that *E. coli* is more resistant to the antibacterial compounds contained in kepel leaf extract, *E. coli* is a gram-negative bacterium that can stay alive even in media with low nutritional content [9].

Table. 4 Antimicrobial Test Results

Bacteri Test	Average of Inhibitory Diameter (mm)		
	37.5 (mg/mL)	50 (mg/mL)	62.5 (mg/mL)
Staphylococcus aureus	-	12.96	13.50
Bacillus subtilis	-	12.53	13.43
Pseudomonas aeruginosa	12.03	12.7	13.56
Escherichia coli	-	-	-

CONCLUSION

The results of the tablet evaluation showed that formula 3 was the best, with the composition of 25% kepel leaf extract, avicel PH 102 64.5%, PVP 2%, amprotab 7%, aerosil 0.5%, and 1% of talcum. Tablet preparations containing methanol extract of kepel leaves had antimicrobial activity against *Staphylococcus aureus, Bacillus subitilis* and *Pseudomonas aeruginosa*.

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