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Original Article

EFFECT OF MALTODEXTRIN RATIO TO *KLUTUK BANANA* FRUIT EXTRACT (*MUSA BALBISIANA* COLLA) COMBINED WITH ITS PSEUDOSTEM EXTRACT ON ANTI-DYSENTERY GRANULE PERFORMANCE AND EFFECTIVITY

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ABSTRACT

Objective: The objective of this study was to determine the best ratio of maltodextrin and extract concentration on performance of anti-dysentery granule containing Klutuk banana fruit extract (*Musa balbisiana* Colla) as an effective antimicrobial to treat dysentery caused by *Shigella dysenteriae* and combined with its pseudostem extract to supply potassium needed for supporting dehydration impact caused by dysentery.

Methods: The dried fruit and pseudostem of the Klutuk banana plant were each extracted by maceration method. Each granule formula was optimized in different ratio of extract and maltodextrin concentration (1:2 (F1); 1:3 (F2); and 1:4 (F3) respectively. Then, the anti-shigellosis granule were formulated using the wet granulation method and evaluated for 30 d. The appearance of the granule, weight variation, loss on drying value, flowability, granule solubility, disintegration time, pH, and anti-dysentery activity of each formula was observed. The potassium content determination of each granule formula was done using an atomic absorption spectrophotometer method.

Results: All formulated granules showed good flow properties and antidysentery activity. Concerning to the solubility, maltodextrin addition showed the increasing solubility of all formulated granule. The F3 achieved the best-improved granule characteristic and had good anti-dysentery effectivity, but had the lowest potassium content (0.362 g/l) among all formulas. The potassium content of F1 and F2 were 0.625 g/l and 0.444 g/l, respectively.

Conclusion: Maltodextrin can improve the usefulness of granule that containing the Klutuk banana fruit and its pseudostem extracts in dysentery treatment and the dehydration impact.

Keywords: *Musa balbisiana* Colla, fruit, extract, granule, maltodextrin, anti-dysentery

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INTRODUCTION

Dysentery is a common gastrointestinal disorder primarily caused by *Shigella dysenteriae* but can potentially associate several systemic complications. *S. dysenteriae* is easily spread and found in an overcrowding population with malnutrition condition and poor of waste management and healthy water supplies [1]. The characterization of bacillary dysentery is diarrhea mixed with mucus and blood, accompanied by fever, tenesmus and abdominal cramps [2]. In children at age under 5 y old, for about 10 % of all diarrhea cases are dysentery, and is reported to cause a higher mortality rate of 15% [3]. This data is synchronized with bacillary dysentery cases in Indonesia that 29% of deaths caused by dysentery occurred at age 1-4 y old [4]. The most causes of mortality that resulting from dysentery is dehydration. Because of diarrhea in high frequency, patients develop potassium depletion, called hypokalemia. The hypokalemia was signed with general muscular weakness, paralytic ileus and cardiac arrhythmias [5].

The dysentery must be treated by clinical improvement, avoiding the causative agent to limit pathogen transmission, preventing dehydration by administering appropriate fluids and food [3]. In addition, WHO also recommend antimicrobials such as amoxicillin, trimethoprim-sulfamethoxazole (TMP/SMX) for treating dysentery [6]. But it is very important to detect the sensitivity of Shigella clinical isolates because antimicrobial resistance was reported. A number of antimicrobials such as ceftriaxone (fluoroquinolones group) and azithromycin were considered to treat resistant shigella [7]. Newer fluoroquinolones, such as norfloxacin and ciprofloxacin are also effective for bacillary dysentery, but the price is very expensive. Beside that, the resistance of *S. dysentery* type 1 to quinolone antibiotics has been reported [8, 9]. Therefore, a need of a new antibiotic candidate that effective and cheaper in prices leads scientists to explore new antimicrobial substances from medicinal plants [10, 11]. The WHO has constituted a program to control diarrheal disease include the use of traditional medicines that combined with health education improvement and prevention method [12, 13].

Utilization of natural materials has been proven to be used as a natural antibiotic, especially for bacillary dysentery treatment. In Indonesia, bananas are an abundant agricultural commodity. Empirically, banana fruits have been used in the dysentery treatment and diarrhea disease [14, 15]. Our previous research showed that fruit of Klutuk banana possessed a potential antimicrobial activity against *S. dysenteriaea*. The ethanolic extract of banana fruits contains flavonoid and tannin compounds that proved as the antibacterial agent against *S. dysentriae*. In addition, the pseudostem part of Klutuk banana also has a weak antimicrobial activity but has potassium content that is higher than the fruit. Therefore, in this study, the extracts of fruits and pseudostem combined to be formulated into anti-dysentery preparations that are also able to prevent hypokalemia.

Development of drugs containing plant extracts involves stability problems and technological because of the certain characteristics of extract that causing difficulties during pharmaceutical processing [16]. The active substances in extract often at low concentration as well as the rendemen. Whereas to produce an effective preparation, it required extract in large quantities to achieve an effective dose [17, 18]. Therefore, the granulation technique was needed to improve dosage uniformity by inhibiting particle segregation [19, 20]. Granules are one of the drug form that more convenient in application than powder drug. The granules can swallow easily and they do not atomize nor adhere to the mucous membranes of the throat or the oral cavity [21]. The other advantages of granule preparation are chemically stable compared to the liquid form, convenient and suitable for large dosage preparations, and the rate of disintegration can be faster than that of tablets or capsules in oral administration [22]. The granules can also be given to pediatric patients who are still unable to swallow capsules or tablets properly. Generally, the use of granules may be administered to children by dissolving granules in water or by mixing them into semi-solid food [23]. However, the problem is that both of these test extracts are difficult to dissolve in water. For that, it is a necessary addition of excipients that can increase the solubility of the extract to develop improved granule with effective anti-dysentery activity. Maltodextrin is an adjuvant which is known to increase the solubility of the preparation and the active substance due to it is more likely hydrophilic in nature, thereby enhancing the water solubility of extract. Therefore, in this study, maltodextrin was added in the granular formulation that containing dissoluble extract to enhance the extraction solubility, so that anti-dysentery granule containing Klutuk banana fruits and its pseudostem ethanolic extract can be developed well and work effectively.

MATERIALS AND METHODS

Materials

The unripe fresh fruits and pseudostem of Klutuk banana (*Musa balbisiana* Colla) were collected from Cimincrang village, Gede Bage district, West Java, Indonesia. The identification of the plant was confirmed at the Institute of plant determination in the Department of Biology, Faculty of mathematics and natural sciences, Padjadjaran University, Jatinangor, Indonesia. The specimen number of the klutuk banana plant was HB/04/2016. The tested bacteria used in this study was *Shigella dysenteriae* ATCC 13313, obtained from the Laboratory of Microbiology, Faculty of Medicine, University Maranatha Kristen, Bandung, Indonesia. The growth medium used were Shigella-Salmonella agar (SS-Pronadisa), Mueller Hinton Agar (MHA-OXOID) and Mueller Hinton Broth (MHB-OXOID). The chemicals used were ethanol, 10% ammonia, amyl alcohol, 2N hydrochloric acid, iron (III) chloride, ether, chloroform, anhydrous acetic acid solution in concentrated H2SO4, 1% gelatin, reagent Dragendorff (potassium bismuth iodide solution). Mayer reagents (potassium mercury iodide solution), 10% vanillin solution in concentrated H2SO4, 1N sodium hydroxide, potassium permanganate powder, magnesium powder, and sterile physiological sodium chloride, maltodextrine, demineralized water, PVP, stevia sugar, aerosil and chocolate flavor.

Extraction

The fruits and banana pseudostem were washed with tap water, chopped and dried. Then each (500 g) of dried material was ground into a fine powder and soaked in bottle maceration with 3 L of 70% ethanol. Solvent replacement was done for 3 times every 24 h in the same amount of solvent. All these maceration results were then concentrated using a rotary evaporator until viscous extracts of each material were obtained. Each extraction yield was calculated by dividing the viscous extract weight obtained by the of the dried material weight. The moisture content determination of each extract was analyzed using the distillation of toluene. The 2 g of thick extract was put into a clean and dry flask, then a volume of 200 ml toluene was added. The flask was heated for 14 m carefully. After all the water had been distilled, the tube was allowed to cool at room temperature, then the volume of water was observed.

Phytochemical screening

The purposed of preliminary phytochemical analysis was to identify the secondary metabolites that present in fruit and pseudostem of Klutuk banana ethanolic extract. The phytochemical screening of alkaloids, flavonoids, polyphenols, tannins, monoterpenoids, sesquiterpenoids, steroids, triterpenoids, quinones, and saponins was carried out by following standard method [24].

Granule formulation

Based on our previous study, the best combination of both extracts as antidysentery and for hypokalemia prevention was 60% w/v: 7 %w/v for fruit and pseudostem extract, respectively. In this study, all granule formulations with different maltodextrin ratio were made. The total weight of each formula was 5 g. In this granule formula, some of the excipient components were used, as follows: stevia sweetener, polyvinylpyrrolidone (PVP) was used as a binding agent, aerosil as adsorbent and disintegrant, maltodextrin was used to increase granule solubility, chocolate flavor was used for coloring granules, and 95% ethanol was used as granulation solvent. The detail of extract granule formulas could be seen in table 1.

Table 1: Formulation of granule

Composition (%w/w)	Formula 1	Formula 2	Formula 3
Fruit extract	60	60	60
Pseudostem extract	7	7	7
Sweetener (Stevia)	5	5	5
PVP	1	1	1
Aerosil	1	1	1
Maltodextrin	1:2	1:3	1:4
Chocolate Flavor	qs	qs	qs
95% Ethanol	qs	qs	qs

The Klutuk banana ethanolic extracts of fruit and pseudostem were dried using aerosil and maltodextrin. Then stevia, chocolate flavor, and PVP were added to the extraction mixture. The mixture was stirred until homogeneous, crushed and sprayed with 95% ethanol gradually to form a mass that can be clinched. The mass was then sieved using mesh no. 10 to form granules, then the granules were dried in an oven at 40-50 °C for 18 h. The dried granules were sieved again using a sieve no.16. The final granules formed were stored in a desiccator containing silica gel to avoid air humidity.

Granule physical examination

Physical appearance of granule was observed at room temperature (27 °C) at 75% RH for a month, with interval observation every 3 d [25].

Loss on drying test

2 g of granules was inserted in the moisture balance tool; then the moistures value was measured at 105 °C until constant weight was achieved. The percentage value of loss on drying can be seen on the screen [26].

Flowability test

The angle of repose and the Hausner ratio are conventionally used to characterize granule flow. The flowability test and angle of repose of the granule were conducted using flow tester equipped in the funnel with the nozzle. The angle of repose of the granules was evaluated by introducing a granule of 20 g into the flow tester, then the bottom of the funnel was opened so that the granules can flow. The time required by all the granules to pass through a funnel was calculated using a stopwatch. The flow rate is expressed as the number of g of granules passing through the funnel per second. The angle of repose can be calculated by measuring the average diameter and peak height.

Granule compressibility

The compressibility of granules was determined using a bulk density tester. A weight of 20 g granule was poured slowly into a measuring cup and recorded as Vo. Then the granule in the measuring cup was tapped, and the volume change was recorded as Vt. The bulk density is calculated by dividing the granule weight by volume (V_0). Meanwhile, the tapped density is calculated by dividing the granule weight by volume (Vt). After that, the granule compressibility was calculated by the Carr index method and the Hausner ratio of how to divide the granule weight by volume.

Granule solubility

The solubility test of the granule is determined according to the solubility term which can be seen in table 2.

Granule disintegration time

A weight of 8 g granules was dissolved in 200 ml of distilled water. The test was performed using a magnetic stirrer at a temperature of 50 °C with a speed of 120 rpm. Then, the granules were inserted and the granule-dissolving time was calculated using a stopwatch. The best preference time required to dissolve granules was less than 5 min [28].

Table 2: Solubility of substance in a solvent [27]

Term solubility	The amount of solvent part is required to dissolve one part of the material
Highly soluble	<1
Easily Soluble	1-10
Soluble	10-30
Nearly difficult to dissolve	30-100
Difficult to dissolve	100-1000
Very difficult to dissolve	1000-10000
Practically insoluble	>10000

pH solution

Granule weighed as much as 5 g then dissolved in 100 ml distilled water. Then a pH measuring device that has been calibrated using buffer pH 4 and pH 7 was fed into the granule solution, and the measured pH was recorded.

Preparation of Mc Farland solution

Preparation of Mc Farland's standard solution was done by mixing 0.05 ml of 1,175% $BaCl_2$ solution with 9.95 ml of 1% H_2SO_4 solution then it was shaken until homogeneous. Turbidity of the solution was measured at a wavelength of 625 nm using distilled water as a blank. The absorbance value of the solution should be in the range of 0.08 to 0.13. The standard McFarland 0.5 solutions are equivalent to a bacterial cell suspension that having a concentration of 1 x 10^8CFU/ml [29].

Antibacterial effectiveness test

The anti-dysentery effectivity test of the granules was assayed using the agar diffusion method with perforation technique. Granules from each formula were dissolved in sterile aquadest and diluted to achieve tested concentration, i.e. 30,40 and 50 %w/v. A total of 20 µl bacterial suspension was poured into sterile Petri dishes and suspended in 20 ml of the MHA, then homogenized. The medium was allowed to solidify to be perforated to prepare the holes for storing the extract. Each granule solution with a different concentration of 100 µL was fed into the hole. The negative and positive control was prepared, where the negative control contains only medium, meanwhile the positive control consisted of the inoculated bacterial suspension using the streak inoculation method. All test and control media were incubated at 37 °C for 24 h. The inhibitory diameter formed was measured using a caliper [30].

Potassium level measurement

Samples were prepared by dry destruction methods and analyzed using Atomic Absorption Spectrophotometry (SSA). As much as 1 g granule of each formula, weighed and heated at a temperature of 600 °C to form ash. A total of 10 ml of 6.5% HNO_3 was reacted to ash and reheated on a hot plate. The mixture was filtered and fed into a 25 ml flask, then demineralized water was added to the boundary marker. The test sample solution was ready to be measured. Before use, a 1 g of solid KCl was dried for 2 h at 100 °C and then cooled for 30 min. To prepare a standard potassium solution, KCl was weighed 25 mg and fed into a 25 ml measuring flask to obtain a standard potassium solution at 1000 µg/ml. Furthermore, demineralized water was added to the measurement marks, and shaken until all homogeneous solutions, to obtain a stock solution of 1000 ppm. The standard solution of potassium was diluted in various concentrations with the addition of demineralized water. The absorbance of the standard solution resulting from dilution was measured using atomic absorption spectroscopy. The blank used for measurement was demineralized water. The measurement was carried out by inserting a hose into the standard solution with the smallest concentration to the highest concentration. The absorbance measurement results were recorded and calculated linear regression so that a straight line equation was obtained to see the linearity [31].

RESULTS AND DISCUSSION

Extraction results

The thick extract obtained from the extraction process of 500 g of fruit and pseudostem Klutuk banana was 35.85 g and 16.54 g, respectively. Both extracts displayed the same morphological appearance of dark brown, distinctive odor, and bitter taste. The water content of both extracts was 5%. This value is in accordance with the requirements given for water content that is less than 10%. The less moisture content of the extract, the less likely the occurrence of extract contamination by microorganisms.

Phytochemical screening of extracts

Based on phytochemical screening results, it was found that ethanol extract of fruit and psedostem of klutuk banana contained the same compounds, as follows: flavonoids, polyphenols, tannins, monoterpenoids and sesquiterpenoids, quinones, and saponins. As our previous study, mentioned that the fruit ethanolic extract of klutuk banana had potent anti-dysentery activity against *S. dysenteriae*. In another study, the same secondary metabolite content in the extract of *Tabernaemontana divaricate* provides anti-dysentery activity [32]. These data showed that those metabolites responsible for the anti-dysentery activity against *S. dysenteriae*. The function of flavonoids worked by forming complex compounds against bacterial extracellular proteins that interfere with the integrity of bacterial cell membranes. Flavonoids may also interact with bacterial DNA so that it caused damage to the cell wall permeability of bacteria, microsomes, and lysosomes. Meanwhile, the polyphenols can coagulate bacterial protein and made lysis of bacterial cell membrane [33]. In addition, a research study informed that the banana fruit extract content higher total phenolic compounds than its peel [34]. The presence of saponins in the extract content also increasing the permeability and reduce the surface tension of cell walls through the interaction of saponins with lipopolysaccharide in the bacterial cell wall. This caused the cell wall lysis and disrupted the cell's metabolism [35, 36]. As an antibacterial, tannins can damage cell membranes and shrank cell walls, thus damaging bacterial cell permeability which eventually leads to bacterial death [37].

Solubility test result of the component formula

In drug invention, almost 70% of new drug candidates found as an insoluble drug due to perform poor water solubility [38]. These poor solubility reflects the drug dissolution in gastrointestinal fluids that can limit the *in vivo* bioavailability, especially for oral administration. Therefore, the solubility of active substances and excipients is very important in determining the solubility of a drug preparation. In this study, before formulation, all the components of the formula were tested for their solubility in water. A component of the formula was considered as a soluble component if the amount of solvent part that is required to dissolve one part of the material is not more than 30 parts. Otherwise, the substance is considered poorly soluble. Based on the results of the solubility test, it is known that both extracts were difficult to dissolve in water, while other excipient ingredients were easily soluble in water. Therefore, to attempt its effectiveness, both extracts must be formulated using excipient ingredients that can increase their solubility by the addition of maltodextrin.

Formulation and evaluation of anti-dysentery granule

The use of complexing carbohydrates agents with water was one of the recent strategies conducted to improve drug solubility by forming a water-soluble inclusion complex of the drug [39]. The complexation was purposed to stabilize the drug chemically and modified the lipid barrier to enhance the absorption of the drug [40]. Because of this complexation process, poorly soluble extract of Klutuk banana could be effectively delivered to the desired target. These supramolecular systems using carbohydrate will be developed consistently in the field of pharmaceutical and medical application. The mechanism of each carbohydrate type are varied [41]. In this study, the type of carbohydrate used as a diluent was polysaccharide namely maltodextrin. Maltodextrin is a kind of polysaccharide as a hydrolysis product of starch. In addition to its solubility effect, maltodextrin can be used in food because it has advantageous characteristics such as: fast dispersion, tasteless without having its own pharmacological activity and crystallization inhibitor. In this study, three granule formulas were obtained with variations in the concentration ratio of extract compared to maltodextrin. Maltodextrin in this formula was made to vary in order to increase the solubility of extracts in granules and accelerate the drying process of extracts [42, 43]. The color of this anti-dysentery granules was dark-brown with a characteristic odor. This anti-dysenteri granule can be applicated for all ages, especially for people who cannot swallow drugs and children.

Physical evaluation of granules

The physical appearance of granules was observed at room temperature (27 °C). The initial average weight of the granule corresponds to the total composition weight formulated. But during its storage time, the weight of the granules has increased. These can be assumed due to the moisture content increased of the granules. However, there was no physical change in the all granules of the formula. The granule observation results can be seen in table 2.

Table 2: The average of granules weight during storage time

Time of observation (day)	Granule weight (g)		
	F1	F2	F3
0	5.000±0.0000	5.000±0.0000	5.000±0.0000
3	5.083±0.0004	5.081±0.0004	5.082±0.0000
6	5.091±0.0004	5.087±0.0004	5.089±0.0004
9	5.124±0.0000	5.121±0.0000	5.122±0.0000
12	5.133±0.0004	5.128±0.0004	5.129±0.0004
15	5.151±0.0004	5.148±0.0004	5.149±0.0004
18	5.174±0.0004	5.167±0.0004	5.168±0.0004
21	5.182±0.0004	5.174±0.0000	5.176±0.0000
24	5.191±0.0004	5.183±0.0004	5.185±0.0004
27	5.233±0.0004	5.196±0.0004	5.189±0.0004
30	5.340±0.0004	5.210±0.0004	5.240±0.0004

Loss on drying result

From the results, it was known that the loss on drying granules of formula 1, 2 and 3, respectively 3.9; 2.5; and 4%. These data can be correlated with granular moisture, which causes granular weight changes for 30 d of storage. However, the percentages of loss on drying were in the normal range of requirement at range between 2-4% [44]. Percent LOD values of granule formula which comply with the requirement limits indicated the formulation content lower moisture value.

Flowability test results

All granules had excellent flow rates for all formulas, which were 19.49; 20.07 and 20.39, in accordance with the relationship between flowability and flow character which was very good, for about>10. The angle of repose measurement was aimed to determine the characteristics of the fluidity associated with the cohesiveness between the constituent particles. The angle of repose would increase if the particle size becomes smaller [45]. The angle of repose value was 25.70 (formula 1); 25.25 (formula 2) and 24.53 (formula 3). This is consistent with the results of the formula 3 flowability which was<25 g/sec thereby determining the excellent flow character of the granule. Formula 3 had good flow characteristics based on the value of repose angle and granular flowability. Therefore, it can be concluded that the higher the maltodextrin level, the better the granular flow character.

Compressibility index

The Compressibility index (Carr's index) is a propensity measurement of a powder to be compressed that is determined from the tapped and bulk densities. The values of the granule bulk density were 0.65 (F1), 0.57 (F2) and 0.67 (F3), while the tapped density values were 0.77 (F1), 0.71 (F2) and 0.71 (F3). Based on the results of bulk and tapped density, the granule flow character can be calculated using the Index Carr and Hausner ratio formula. Based on the Carr Index calculation, it was known that formula 3 (F3) had the lowest Carr Index value of 5.63% among all formulas. This value showed that the F3 was the most flowable granule because the less compressible a material, the more it is flowable. However, the other formulas were in a range of good flow characteristics with its Carr index value of 15.58% for F1 and 19.72% for F2. If the there is a greater difference value between tapped and bulk density, so there will be a greater inter-particle interaction and can be categorized as poor flowing granule. While the results of the Hausner ratio calculation were as follows: 1.18 (F1), 1.25 (F2) and 1.06 (F3). Thus, it can be concluded that F3 with the highest maltodextrin content produced excellent granule flow.

Granule solubility results

Formulate the poorly soluble extract and improving their bioavailability is an important effort in pharmaceutical science. Thus, the in data of *in vitro* dissolution has been an important step to be analyzed in drug development [46, 47]. In this study, the amount of water as a solvent needed to dissolve 1 part granule for formula 1 was 30 ml while of formula 2 was 25 ml and formula 3 was 20 ml. Thus, all granule formulas were performed as water-soluble preparations. This data showed that there was a significant effect by adding maltodextrin to the granule formula. Considering that both extracts as the active component were difficult to dissolve in water. The extract dissolution with a high aqueous solubility was very important to the therapeutic effect, especially for oral administration. Because this solubility parameter was one of the fundamental parameters for it's *in vivo* bioavailability that control the rate and extract absorption [48, 49].

Granule dissolution time results

The dissolution time is a very important to determine the rate of the granule to pass into the solution [50]. As expected, the granule release was dependent on the concentration of maltodextrin in all formulations. The measurement results show that formula 3 has a faster soluble time of 3.26 min compared to formula F1 (4.10 min) and F2 (3.5 min). In theory, the best time required for the granule to dissolve is less than 5 min [28].

pH granule solution

One of the critical effect after oral drug administration is a pH risk of injury on the stomach, esophagus, and duodenum. In addition, the acid or base character of the drugs was an important key that affects their biopharmaceutical properties. Therefore the pH of the pharmaceutical form must be evaluated. pH testings were carried out on the base granule solution, all formula granules, ethanol extract solution, fruit and its pseodostem of Klutuk banana. The results showed that the pH of the three granule formulas (F1 = 5.65; F2 = 5.67; F3 = 6.20), the pH of fruit banana ethanol extract (5.86) and the pH of pseudostem (5.89) was acidic, whereas the granule base had a relatively neutral pH of 7.03. Based on these pH evaluations, the higher maltodextrin concentration in formula could increase the pH of the extract to a pH corresponding to the normal range pH of the colon. However, the better pH for the base target was the base pH. Because the pH of the solid drug, have better solubility closely at range pH 7.0 for resulting in colon targeted system. The formula 3 with a highest maltodextrine concentration was hypothesized as the best formula with the increasing pH ability.

Antibacterial effectiveness result

The antibacterial activity of all granules formulas against *S. dysenteriae* examined in the present study was qualitatively assessed by the presence of inhibition zone and zone diameter measurement, as given in the tables 3.

Table 3: Antibacterial effect of all granule formulas

Formula	Concentration (%w/v)	Inhibition zone diameter (mm)
Formula 1	30	15.50±0.0001
	40	16.53±0.0001
	50	16.86±0.0001
Formula 2	30	15.30±0.0004
	40	16.40±0.0002
	50	16.65±0.0004
Formula 3	30	15.20±0.0004
	40	15.73±0.0004
	50	16.20±0.0004

Note: perforator diameter: 8.8 mm

Among all the formula, formula 1 performed the highest anti-dysentery activity due to the lower concentration of maltodextrin in the formula, gave the higher extract portion of concentration in the ratio of extract and maltodextrine. In formula 1 content the biggest concentration of fruit extract that had been studied as the potent anti-dysentery herb candidate. As it is shown in table 3, the greater concentration of klutuk banana ethanol extract produced the bigger diameter of the inhibitory zone. Based on the inhibitory zones diameter, all tested formula could be categorized as a very active antibacterial, because they resulted in the diameter of inhibition above 11 mm [51].

Statistical analysis results

Statistical analysis was carried out to determine the effect of differences in formulas and differences in concentration as well as the possibility of interactions occurring so as to affect the diameter of the inhibition. The statistical method used was ANAVA Factorial Design in order to study the interaction between the difference in formula and an increase in concentration. Sometimes the two factors are mutually synergistic to the (positive) response. But sometimes the existence of a factor actually inhibits the performance of other factors (negative). The existence of these two mechanisms tends to increase the influence of interaction between the two factors. ANAVA test results can be seen in table 4.

Based on the factorial design results presented in table 4, there was an influence between the variations of the formula to the inhibition zone diameter. There was an effect between increasing the concentration of the inhibition zone diameter and influence between the variation of the formula and increasing the concentration of the inhibition zone diameter. This could be seen from the sig value. = 0.00 which has a smaller value than the real level (α = 0,05). Because Ho was rejected, it was necessary to do the further tests using the Tukey test to determine the differences in the effects of formula 1, 2 and 3 on the inhibitory diameter and the different effects of each concentration on ian nhibitory diameter that could be seen in table 5.

Table 4: ANAVA test results of the formula and concentration difference effect

Source	Type III sum of squares	Df	Mean square	F	Sig.
Corrected Model	20.496[a]	8	2.562	1532.093	0.00
Intercept	4549.626	1	4549.626	2720706.68	0.00
Formula	7.038	2	3.519	2104.395	0.00
Konsentrasi	12.027	2	6.014	3596.183	0.00
F*K	1.431	4	0.358	213.897	0.00
Error	0.015	9	0.002		
Total	4570.137	18			
Corrected Total	20.511	17			

Table 5: Tukey test result

(I) Formula			Mean difference (I-J)	Std. Error	Sig.	95% confidence interval	
						Lower bound	Upper bound
Tukey HSD	1	2	-.1183*	.02361	.002	-.1843	-.0524
		3	1.2633*	.02361	.000	1.1974	1.3293
	2	1	0.1183*	.02361	.002	.0524	.1843
		3	1.3817*	.02361	.000	1.3157	1.4476
	3	1	-1.2633*	.02361	.000	-1.3293	-1.1974
		2	-1.3817*	.02361	.000	-1.4476	-1.3157

Based on the results of the Tukey test, it could be seen that there were significant differences between each formula of the inhibition zone diameter. The value of p-value = 0.002<= 0.05 then H01 was rejected, meaning that there were differences in Formula 1 and 2 to the diameter of the inhibitory zone. The value of p-value = 0,000<= 0,05 then H02 was rejected, mean that there were differences in Formula 1 and 3 to the diameter of the inhibitory zone. The value of p-value = 0,000<= 0,05 then H03 rejected mean that there were differences in Formula 2 and 3 to the diameter of the inhibitory zone.

Potassium quantitative analysis

Based on the results of the potassium concentration analysis, formula 1 had a potassium content of 0.625 g/l, while formula 2 had a potassium content of 0.444 g/l and formula 3 had a potassium content of 0.362 g/l. The body needs potassium as much as 15-25 mEq which is equivalent to 0.585-0.975 g/l [7]. So that, all granule formulas comply a body potassium requirement and could be a natural anti-hypokalemia.

CONCLUSION

Anti-dysentery granules formulated from the ethanolic fruit and the pseudostem extract of Klutuk banana and optimized using different ratios of maltodextrin concentration were found to comply the standards of granule performance, had potent anti-dysentery activity and could be a strong anti-hypokalemia drug candidate.

AUTHORS CONTRIBUTIONS

All the authors have contributed equally

CONFLICT OF INTERESTS

Declared none

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