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Original Article

Optimization of PEG 400 and PEG 6000 in Simplicia Ointment of *Laportea Decumana* (Roxb.) Wedd

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Abstract

Introduction: The Papuan people have utilized the native herb *Laportea decumana* (Roxb.) Wedd for centuries to treat aches and pains. *L. decumana* is used by attaching leaves to the body area affected by the illness. Methods:This study aimed to test the optimal composition of PEG 400 and PEG 6000 in the *L. decumana* simplicia ointment formula to produce a good physical quality ointment. This study employed three formula designs made up of a mixture of PEG 400 (A) and PEG 6000 (B) in ratios of 65%:35%, 50%:50%, and 35%:65%, respectively, using the simplex lattice design approach. Physical qualities of the created ointment, such as organoleptic, homogeneous, miscibility, stickiness, pH, and acceptability tests, were performed on it. Next, the results of the physical properties test and response calculated were used to obtain the optimum formula. The one-sample T-test with a 95% confidence level was used to compare the experimental findings of the optimal formulation ointment with the results expected by the optimization approach. Result: The results indicated that the optimum composition was PEG 400: PEG 6000 by 60%: 40% which physical quality of 3.63 cm; pH 9.2 test, and a stickiness of 7.5 seconds. The results of the one-sample T-test showed that there was a non-significant difference between the experimental results and the predicted $p>0.05$. Conclusion: The ointment for itchy leaves can be formulated with a specific composition and has good physical quality.

Keywords:- *Laportea decumana* (Roxb.) Wedd, Ointment, Optimization, PEG

Introduction

Many plants in world can be used as medicinal plants (Mangiwa *et al.*, 2021; Sun *et al.*, 2022; Wang *et al.*, 2022).In Indonesia, every region has medicinal plants that are used in ethnopharmacology (Atanasov *et al.*, 2021; Simaremare *et al.*, 2021a, Simaremare *et al.*, 2021b; Subaryanti *et al*, 2022). One of them is the *Laportea decumana* (Roxb.) Wedd (Thalib *et al*, 2021) in Figure 1, was known as a native Papuan plant (Simaremare *et al.*, 2022). Papuans have utilized itchy leaves as a painkiller, which they have been using for generations (Simaremare *et al*, 2020).

One of the alternative preparations that can be developed for topical preparations is ointment (Maru & Lahoti, 2018). The ointment is a semi-solid remedy that is applied externally and is simple to use. The drug substance is dissolved or homogeneously dispersed in a suitable ointment base (Maesaroh *et al*, 2020). To increase the effectiveness of using *L. decumana* simplicia on the skin, an ointment formulation with a water-soluble base was used. The water-soluble base ointment formulation used was a combination of PEG 400 and PEG 6000 (Simaremare *et al*, 2019; Tanjung*et al*, 2019).

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Figure 1.: *Laportea decumana* (Roxb.)Wedd plant

PEG 400 with a low molecular weight and PEG 6000 with a high molecular weight will produce an ointment product with a soft consistency that melts on the skin (Putri *et al*, 2018). Because the PEG 400 form is a viscous liquid, the combination in greater quantities than PEG 6000 will result in a softer ointment mass, so it is easy to take from the container and has good dispersion and adhesion (Goldsmith, 1946).

PEG has the benefit of not irritating the skin, having good adherence and dispersion on the skin, and not inhibiting gas exchange or sweat generation, so its efficacy is prolonged. PEG is also hydrophilic, so it is easily washed with water and can be used on hairy body parts (Goldsmith, 1946; Mahato & Narang, 2020).

Itchy leaf ointment is very good to develop so it is necessary to optimize the composition of PEG 400 and PEG 6000 using the Simplex Lattice Design (SLD) method (Crespo *et al*, 2019). This method makes it possible to obtain compositions by predicting the response profile of a mixture of materials at various variations in the amount of material composition expressed in several parts, where the total amount is equal to one part (Lu *et al*, 2021).

Materials and Methods

Materials

The material consisted of HPMC, methyl paraben, propylene glycol, ethanol, and aquadest. Itchy leaves were taken from Naramben Village, Keerom Jayapura, Indonesia, and determined in the Herbal Materia Medica Batu Laboratory with ethical approval number LB.02.02/ 2/ KE. 597/ 2021 from the Health Research and Development Agency of the Ministry of Health.

Methods

Formulation of L. decumana Simplicia Ointment

Samples *(Laportea decumana)* were dried in the oven at 40 °C. These leaves were blended until smooth, then sieved using a sieve with 125 m pores, and then stored in a place with a tight lid.

Preparation of Ointment

The *L. decumana* simplicia was put into a warm mortar, then PEG 400, PEG 6000, and propylene glycol were melted in a porcelain dish over a water bath. After being melted, the base was poured in equal amounts of L.decumana simplicia and stirred until homogeneous. Then the remaining base was

carefully mixed and stirred until a smooth and homogeneous ointment mass was formed. Finally, the ointment was packaged in a tightly closed container (Table 1).

Table1. Formulation of *L.decumana* simplicia ointment

Material	Composition (w/v), n=3		
	F (I)	F (II)	F (III)
Simplicia of Itchy leaves	2	2	2
PEG 400	42.8	32	22.4
PEG 6000	22.4	32	42.8
Propylene glycol	34	34	34
Add to Total		100	

Description:

Formulation with 50 grams of ointment preparation

F I : Formula I (PEG 400 65% : PEG 6000 35%)
F II : Formula II (PEG 400 50% : PEG 6000 50%)
F III : Formula III (PEG 400 35% : PEG 6000 65%)

Physical Quality Evaluation of Ointment

a. Organoleptic test.

Organoleptic testing was performed by examining the ointment preparation's appearance, aroma, and color (Anindhita & Arsanto, 2020).

b. pH test.

0.5 grams of ointment that has been diluted with 5 mL of distilled water was used to dip a pH meter to measure the pH value. The pH level of a good ointment was 4.5-6.5 or following the pH value of human skin (Kartini *et al*, 2017).

c. Determination of Test of homogeneity.

On a glass plate, the top, middle, and bottom ointments were removed and examined by rubbing and touching (Carneiro & Poppi, 2012).

d. Measures of spreadability.

A total of 0.5 g of ointment was placed on a glass plate with another glass placed on it and left for 1 minute. The diameter of the spread of the ointment was measured then added a load of 100 g, allowed to stand for 1 minute, and then the constant diameter was measured (Setyawaty, 2020).

e. Adhesion Test.

The ointment was measured on a glass item with a maximum weight of 0.5 grams that had been selected by the location. Another glass object is placed on a glass object containing a sample with a load of 500 grams for 1 minute. The glass object was attached to the test apparatus and a weight of 65 grams was removed. The time was recorded for the two glass objects to come off (Kartini *et al*, 2017).

Data analysis

a. The identification of the mixture's property profile.

Using data from the ointment's physical property tests and the equation, the profile was created based on SLD (Crespo et al., 2019):$Y = a(A) + b(B) + ab(A)(B)$

Note:

Y = Response (experimental result)

a, b, ab = Coefficients obtained from the three experiments

(A) (B) = The size of part A (PEG 400) and component B (PEG 6000),

with the sum of A+B always one.

The coefficient a was determined from experiments using 65% PEG 400 and 35% PEG 6000, coefficient b was determined from experiments using 35% PEG 400 and 65% PEG 6000, and to determine coefficient ab required experiments using a mixture of 50% PEG 400 and 50% PEG 6000. So that the profile of the theoretical characteristics of the mixture using different ratios of PEG 400 and PEG 6000 may be deduced from the given equations.

b. Optimal blend formula selection

The overall reaction was sought after collecting a profile of each ointment's physical characteristics (the total of the reactions to the ointment's physical characteristics)(Crespo *et al*, 2019). The formula was used to determine the total response:

R total = R1 + R2 + R3…Rn ...

Where R1 + R2 + R3 + … + Rn is the response of each of the physical properties of the ointment.

Every response was assigned a weight, totaling one. Three responses—dispersion with a value of 0.4, adherence with a quantity of 0.4, and a pH test with a mass of 0.2—were used in this investigation as the primary parameters. The units of each response were standardized and the response assessment was calculated with the following formula:

$$N = \frac{X - Xmin}{Xmax - Xmin}$$

X = Value shown after the experiment

Xmin = Minimum desired response

Xmax = Maximum desired response

N = Response standardization value (Bolton, S, 1997)

Consequently, by dividing N by the weight, R can be computed. that has been determined.

The total of all responses:

R total = (weight x NpH) + (weight x NpH) + (weight NpH).

The total value of each greatest answer was examined to pick the best formula(Crespo *et al*, 2019).

Results and Discussion

Evaluation of The Ointment of Itchy Leaves Simplicia

Organoleptic Test

An initial step in assessing a formulation's quality is to conduct organoleptic testing on an ointment. By contrasting it with three formulations, the quality of this ointment is determined(Farhan *et al*, 2021). Table 2 displayed the results of the organoleptic test.

Table 2. Organoleptic test results

Organoleptic test	Formula		
	I	II	III
Colour	Dark green	Dark green	Dark green
Odor	Specific	Specific	Specific
Texture	Soft	Soft	Soft
Form	Semi-solid	Semi solid	Semi solid

Homogeneity Test of L. decumana Ointment

The homogeneity of a semi-solid ointment affects its application to the skin. All of the ingredients in a good ointment must be well combined, and it shouldn't leave any harsh particles on the skin (Yankey & Isaacson, 2018). Homogeneity was proven by the absence of rough particles when the ointment was applied to the slide and the uniformity of color, so this fulfills the homogeneity requirements. In this study, all of the formulas were homogenous (Table 3).

Table 3. Homogeneity Test

Type of test	FI	FII	FIII
Homogeneity	Homogenous	Homogenous	Homogenous
Spreadability (cm) ± SD	3.56 ± 0.28	3.4 ± 0.2	3.36 ± 0.30
pH	8.8	9.0	8.4
Adhesion (second) ± SD	5.63 ± 1,04	7.69 ± 3.53	14.54 ± 3.23

Spreadability Test Results

The spreadability profile of various compositions of PEG 400 PEG 4000 exposed the ointment to FI, which was higher than FIII (Table 3). PEG has a significant effect on the spreadability of the ointment (Inoue *et al*, 2013). The following equation was created after the spreadability data from the three formulae (Figure 2) were processed using the simplex lattice design (Crespo *et al*, 2019) approach:

Y = 4,22 (A) + 3,53 (B) – 1,86 (A) (B)

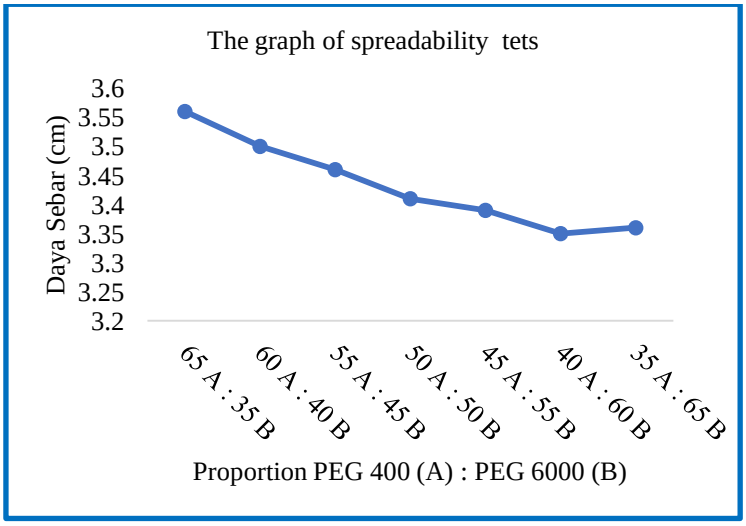

Figure 2. The result of the spreadability test

pH Test Results

The test of pH data obtained from the three formulas was then processed using the Simplex Lattice Design method (Fig. 3) and the following equation was obtained:Y = 6,44 (A) + 5,10 (B) + 12,90 (A) (B).

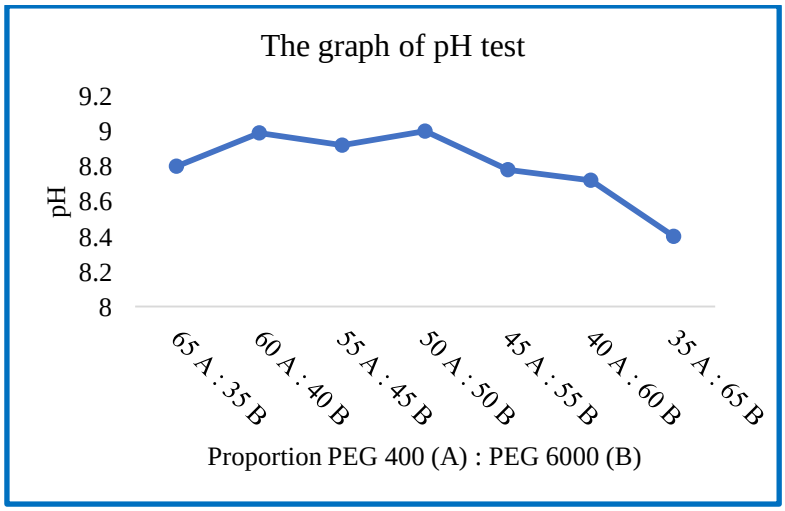

Figure 3.The result of *the* pH test

Based on Fig. 3, the information provided in the respective compositions of PEG 400 and PEG 6000 did not affect the pH. However, the average pH results from the composition of PEG 400 and PEG 6000 were higher than the quality standard pH range of 4.5–6.5.

Adhesion Test Results

The ability of ointment to stick longer to the skin allows the active substance to have a more effective effect. The general nature of ointment is that it can adhere to the surface of the skin several times before it is washed or cleaned (Setyawaty, 2020). Viscosity has a direct relationship with adhesiveness. Greater adhesion will happen if the viscosity is high.

The result indicated that the evaluation of the three formulas was different, but all of the formulas had a good quality that was higher than standard (more than 4 seconds). The results of the analysis showed that the FI, FII, and FIII had significant values ($p < 0.05$) so there was a significant difference between the test groups (Table 3).

The following equation was created after processing the adhesion data from the three formulae by using the simplex lattice design approach: Y = 10,13 (A) + 39,83 (B) – 67,68 (A) (B). The adhesion profiles of various compositions of PEG 400: PEG 6000 are shown in Fig. 4.

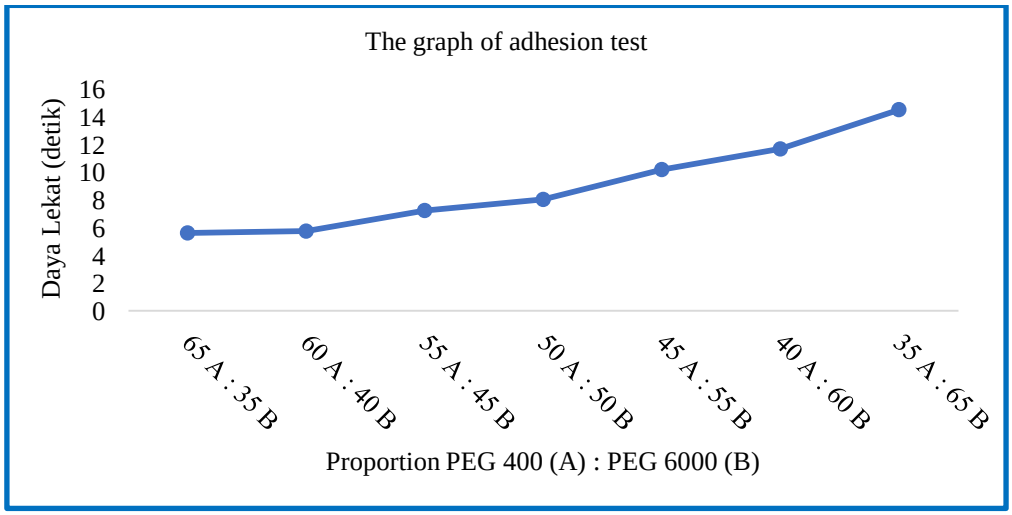

Figure 4.The result of the adhesion test

The Optimization of Formula Profile

Fig 5 concluded that the optimal formula ointment was the ointment containing 60% PEG 400 and 40% PEG 6000 which received the most responses overall.

Table 4. The Results of optimization testing for *L.decumana* ointment (60% PEG 400 & 40% PEG 6000)

Test		Result
Organoleptic	Colour	Dark green
	Odor	Specific
	Texture	Soft
	Form	Semi-solid
Homogeneity		Homogenous
Spread power		3.63
pH		9.20
Adhesion power		7.50

The usage of PEG 400 35% and PEG 6000 65% showed a significant graphic decrease, where the test values for dispersion, adhesion, and pH affected the consistency of the resulting ointment. The best ointment recipe was then created in the same manner and put to the test to ensure accuracy (Table 4).

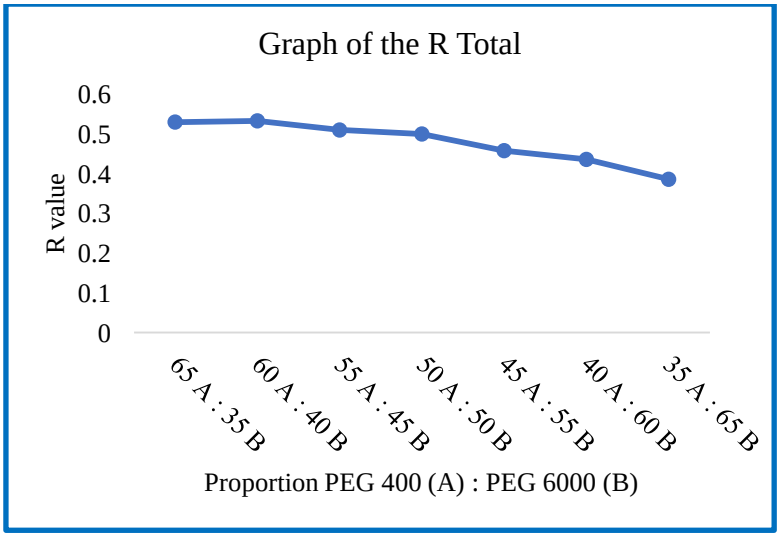

Figure 5. Total of the R graph

The confirmed physicochemical characteristics test results were compared to the outcomes that the theoretical SLD technique had anticipated(Maesaroh *et al*, 2020). To establish the statistically significant difference between the two findings, this prediction employed the One-Sample *t*-test with a 95% confidence level (Table 5).

Table 5. Verification and prediction results of dispersion, adhesion, and pH tests

Parameter	Prediction	Verification	Significant (95%)	Result
Spread power (cm)	3.50	3.63	0.27	Not significantly different
Adhesion power	5.76	7.50	0.37	Not significantly different
pH	8.99	9.20	0.79	Not significantly different

Discussion

The organoleptic test indicated that Formula I, Formula II, and Formula III had a dark green color due to a mixture of PEG 400, PEG 600, and propylene glycol. This mixture, mixed with simpliciaproducesa dark green that is the same color as the itching itself. So, the ointment had a distinctive odor like simplicia leaf itching in a soft, semi-solid form.

The results of homogeneity revealed that FI, FII, and F III had homogeneous ointments. When applied to a test object—a glass—for macroscopic analysis, Table 3 was demonstrated by the uniform hue and absence of coarse particles. Homogeneous ointment indicated that there were no bubbles or uneven texture or color when itchy leaf ointment was applied to the slide (Ajhar *et al*, 2023).

Based on the spreadability profile of various compositions of PEG 400: PEG, the ointment with the addition of PEG 400 had a greater effect on spreading than PEG 6000. This also showed that the greater the proportion of PEG 400 used, the more responsive the dispersion. The higher the amount of PEG 400 in the formula, the larger the diameter of the spread of the ointment, so the wider the spread of the ointment. The ointment's viscosity was reduced, making it softer and more spreadable, which led to an increase in the ointment's spreadability(Makaba *et al*, 2021).

The spreadability test was used to calculate the ability of the ointment to spread on the skin. Spreadability determines how widely the active chemical will be dispersed. In addition, dispersion/spread power is related to viscosity; the larger the spreadability, the smaller the viscosity value. The spreadability findings (Table 3) revealed that the three ointment formulae were not significant, but the itching leaves ointment complied with the spreadability standards for semi-solids (Hartesi *et al*, 2020).

The purpose of the pH test is to evaluate the safety of the ointment when applied to the skin to prevent skin irritation. According to SNI 16-4399-1996, the pH range of the ointment on the skin is 4.5–6.5. A pH value that exceeds 7 could cause skin irritation. Based on the pH test, the pH of the three formulas produced a pH range above the standard pH. (Table 3). Theoretically, an ointment with an excessively acidic pH might irritate the skin, whereas one with an excessively alkaline pH can

cause scaly skin. The higher pH can be caused by a less stable ointment during storage. This instability could damage the product during storage or use (Hartesi *et al*, 2020).

Fig. 3 showed that PEG 6000 had a greater effect than PEG 400 in increasing the adhesion power of the ointment. That was because of the denser concentration of PEG 6000. The ointment will get denser and more viscous as PEG 6000 and PEG 400 concentrations increase, increasing its stickiness for a longer period of time. On the other hand, the lower the concentration of PEG 6000 and the high concentration of PEG 400 will make the preparation more liquid and runny so that the adhesion was faster.

Based on the combined response value of multiple test parameters, the best formula is chosen. For example, the dispersion test with a weight of 0.4 is related to the ability of the preparation to spread on the skin surface. The more widely the active chemical is dispersed, the higher the dispersion. Another example is the adhesion test with a weight of 0.4, which is related to the viscosity and ability of the ointment to adhere to the surface of the skin. The length of the ointment in the skin will penetrate the surface skin. The active substance can have an effective effect. The pH test with a weight of 0.2, which was related to the safety of the ointment on the skin, was used as an indicator if the ointment would irritate the skin. The optimal formula is the one with the highest total response value.

Based on Table 5, The three tests yielded a significant value, with a significant value of p> 0.05. It signified that the value was legitimate because the predicted value with verification showed that there was no appreciable change. Therefore, if the experiment were repeated, it would produce data that was close to or even the same as the predicted results.

Conclusions

Optimization of PEG 400 and PEG 6000 in the Laportea *decumana* (Roxb.) Wedd simplicia ointment was 60%: 40%. This ointment had good quality, with a spread of 3.63 cm; pH 9.2 test; and a stickiness of 7.5 seconds. The results of the One-sample T-test showed that there was a non-significant difference between the experimental results and the predicted p>0.05.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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