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Optimization of Hydroxypropyl Methylcellulose (HPMC) and Glycerine in Essence of Sheet Mask Containing *Centella asiatica* (L.) Urb. Extract and Snail Mucus (*Achatina fulica*) as A Moisturizer

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Abstract: Various natural ingredients have been formulated as moisturizers in cosmetics, both from natural and animal raw, especially *Centella asiatica* (L.) Urb. Extract and snail mucus (*Achatina fulica*). However, further research is needed to determine the synergistic effect of these two ingredients in one cosmetic preparation, namely sheet masks. The mask sleeve, which is a sheet mask applicator, will dry longer than other masks, therefore the penetration shown as a moisturizer is better. Gelling agents (such as *hydroxypropyl methyl cellulose* (HPMC)) and humectants (such as glycerine) are important ingredients in sheet masks. This research aims to optimization HPMC and glycerine in a sheet masks *Centella asiatica* and snail mucus. Optimization of HPMC and glycerine with a ratio of 0.3–3% was carried out using the Software Design Expert Stat-Ease® version 10 with *Simplex Lattice Design* method. The responses from optimization of the preparation were pH, viscosity, absorption ability and skin moisture. The optimum formula was obtained at a concentration of 0.589% HPMC and 2.711% glycerine with pH of 5.64 ±0.02; viscosity of 4581.8± 59.80 cPs, absorption power in scale of 4.6±0,55 , and skin moisture of 32.09%±3.21. The irritation test has a score of 0 or does not cause irritation.

Keywords: *Centella_asiatica*, snail_mucus, glycerine, HPMC, sheet_mask

1. INTRODUCTION

While Indonesia boasts abundant natural resources, the country suffers from significant environmental damage, contributing to climate change. Climate change leads to a rise in air temperature, which can result in quicker skin dryness and paleness [1]. One of the innovations to overcome this is to use a moisturizer in a sheet masks. Sheet masks are a form of moisturizing cosmetics that are currently popular because they are hygienic and practical to use. Sheet mask preparations are considered more profitable because they can be used more easily than other masks such as peel-off, organic, or paste masks. In addition, the mask sleeve, which is a sheet mask applicator, will dry longer than other masks so that the penetration shown as a moisturizer is better [2] [3].

Various natural ingredients have been formulated as moisturizes, both from plants and animals. *Centella asiatica* (CA) is a plant material that contains asiaticoside. This group will stimulate the formation of the extracellular matrix so that it will increase the percentage of collagen and strengthen the skin [4]. Other sources are also obtained from animals, namely snails which have mucus. The mucus in snails contains allantoin, collagen, elastin, and glycolic acid. Allantoin is a secure and efficient substance for safeguarding the skin, aiding in the prevention of skin damage by promoting cell growth and facilitating the healing of wounds [5]. Moreover, it enhances the moisture level in the extracellular matrix and creates compounds with substances that can cause irritation and sensitivity [6].

Based on the description, researchers are interested in combining CA and snail mucus as an essence in sheet mask. The important excipients require additional ingredients to become preparations with good physical characteristics so as to support the function of these preparations. Gelling agent is an important material because it will affect in physical characteristics such as pH, viscosity, absorption of the preparation [7]. Besides HPMC, humectants are another component that is influential because they can retain water in the skin so that moisture activity is obtained in the skin. In this study, HPMC K4M was used as a gelling agent and glycerine as a humectant. The optimization of HPMC and glycerine used in this study used a range of 0.3%-3%. This was referred to from the concentration of glycerine as a humectant in the range of 0.2-65.7% [8] and the concentration of HPMC used for gelling agent was 0.25%-5% [9].

The purpose of this study was to determine the effect of combination of HPMC and glycerine on the chemical and physical characteristics of the essence sheet mask containing CA and snail mucus. Furthermore, this study found out the optimum ratio of HPMC and glycerine on the physical characteristics and moisture activity of the essence sheet mask containing CA and snail mucus.

2. MATERIALS AND METHODS

2.1. Material and Tools

Materials used in this study were *Centella asiatica* (L.) Urb. (B2P2TOOT, Tawangmangu, Indonesia), snail mucus (CV. Keong Sumber Makmur, Indonesia), allantoin (Sigma Aldrich, catalague no 102505490), compressed paper masked (Fresca, Indonesia), HPMC K4M (Dow Chemical), glycerine (Brataco Chemical), propylene glycol (Brataco Chemical), DMDM-hydantoine (Clariant), perfume and aqua destillata.

Instruments used in this study were rotary evaporator (Heidolph), glass funnel, hotplate, magnetic stirrer, digital balance (Ohaus), Brookfield viscometer (DV-1 Prime), pH meter (Trans Instruments Walklab Series), infra red spectrophotometer (Agylent), and Skin Analyzer Moisture (BIA Skin Moisture Analyzer series ZL201430286553.9).

2.2. Methods

2.2.1. Identification and Determination

Determination to obtain certainty about the plants used in this research. Identification and determination of *Centella asiatica* was carried out at the Laboratory of the Research and Development Center for Medicinal Plants and Traditional Medicine Tawamangu, Karanganyar, Central Java. Snail determination was carried out in the Ecology and Biosystematics laboratory, Department of Biology, Faculty of Science and Mathematics, Dipenogoro University, Semarang.

2.2.2. Extraction *Centella asiatica* (CA) and identification active substance

Extraction was carried out using the remaceration method by soaking dried CA herb powder in 70% ethanol in a ratio of (1:7) for 4 days, with solvent replacement every 24 hours. The extract obtained was followed by a qualitative analysis test using thin layer chromatography (TLC) to determine the active substance content in the extract. The Rf obtained in the TLC test is compared with the Rf in the reference [10].

2.2.3. Analysis of allantoin compound in snail mucus sample

Identification of allantoin compound in snail mucus obtained from CV. Keong Sumber Makmur was carried out with FTIR instrument and compared with allantoin standard spectrum [11].

2.2.4. Optimization HPMC and glycerine in sheet mask containing *Centella asiatica*

Manufacturing begins by developing HPMC into a gelling agent in aqua distillate at a temperature of 70°C then leaving it overnight. In the subsequent stage, glycerine and propylene glycol were added and mixed on a hot plate at 70°C at a speed of 200-400 rpm until homogeneous, then mixed with HPMC gel. DMDM-hydantoin as a preservative was added until homogeneous. The active ingredients (CA and snail mucus) are weighed and added gradually. Finally, fragrance was added and the remaining solvent was added up to 60 grams. A sheet mask sleeve was prepared and then 15 grams of the preparation was placed in the sleeve, which was then placed in a tightly closed foil bag. The optimization used in this research was used range of 0.3%-3%, this is referred to from the concentration of glycerin as a humectant in the range of 0.2-65.7% [12] and the concentration of HPMC used for gelling agent is 0.25%-5% [9]. As for the optimization composition from Software Design Expert Stat-Ease® version 10 for each run can be seen in table 1.

Table 1. Formulation Essence Sheet Mask with Different Concentrations of HPMC and Glycerin

Formula / **Ingredients** (%$^w/_w$)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
CA Extracts	3	3	3	3	3	3	3	3	3	3
Snail mucus	9	9	9	9	9	9	9	9	9	9
Propilenglycol	10	10	10	10	10	10	10	10	10	10
HPMC	**0.3**	**3**	**0.975**	**0.3**	**2.325**	**1.65**	**1.65**	**3**	**0.3**	**3**
Glycerinee	**3**	**0.3**	**2.325**	**3**	**0.975**	**1.65**	**1.65**	**0.3**	**3**	**0.3**
DMDM-*hydantoine*	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Perfume	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Aquadest (ad)	100	100	100	100	100	100	100	100	100	100

2.2.5. Chemical and physical characteristic test of essence sheet mask [13] [14]

a. Organoleptic test

The organoleptic test is a physical test of the essence sheet mask that has been made which includes observing the smell, color and shape.

b. pH test

The pH test is a constant pH check by a pH meter after calibration with pH 4 and pH 7 buffer solutions. The electrode was immersed in the preparation, and the recorded pH value was noted.

c. Viscosity test

Viscosity test is a viscosity test that is carried out using a Brookfield viscometer. This test uses a spindle diameter of 62 mm and speed of 4 rpm.

d. Absorption ability test

The absorption ability test was carried out by weighing 15 grams and then placing it in a porcelain cup, then inserting the mask sleeve. The time required for the preparation to absorb into the mask sleeve is given the appropriate score. The researcher has formulated their own range for the data to facilitate assessment. This custom range was designed to simplify evaluation (table 2).

Table 2. Absorption Ability Test Scores

Score	Time
5	0 second – 1 minutes 59 seconds
4	2 minutes – 3 minutes 59 seconds
3	4 minutes – 5 minutes 59 seconds
2	6 minutes – 7 minutes 59 seconds
1	8 minutes – 10 minutes

e. Skin moisture test

The moisture test was carried out on 12 volunteers and it was confirmed that they did not have skin diseases. This test already has an Ethical approval from Stifar Yayasan Pharmasi Semarang, Indonesia with number permit 427/YP/NA/KEPK/STIFAR/EC/XI/2023. The test used a skin moisture analyzer with the pre-post-test group design method. The test preparation was applied to the panelists on the upper arm, measuring 3x5 cm in the morning and evening. Determination of the percentage of skin moisture was carried out for 2 hours, 3 days and 7 days after using the preparation [15] using BIA Skin Moisture Analyzer series ZL201430286553.9. The results are then calculated:

$$\%Mositure\ activity = \frac{(volunteers'\ skin\ moisture\ scores - n) - (volunteers'\ skin\ moisture\ scores\ day - 0)}{volunteers'\ skin\ moisture\ scores\ day - 0}\ x\ 100\% \quad .....(1)$$

When the moisture score is in the range of 0-45%, then the skin is categorized as dry skin; a score of 46-55% is categorized as moist skin; and 56-100% is categorized as very moist skin (BIA Skin Moisture Analyzer).

f. Skin irritation test

This test has already received ethical approval from Stifar Yayasan Pharmasi Semarang, Indonesia, under permit number 427/YP/NA/KEPK/STIFAR/EC/II/2023. The irritation test employed a specific method, which involved conducting an open patch test on the inner forearm of ten panelists. In this procedure, 1 mL of the prepared solution was applied to a designated area (measuring 2.5 x 2.5 cm), typically on the inner left arm. The arm was left exposed for approximately 24 hours, and any skin reactions that occurred were carefully observed. The presence of redness, itching, or swelling on the treated inner forearm skin indicated a positive irritation reaction [16].

Table 3. Grading of Erythema and Oedema [17]

Erythema and Eschar Formation	Score	Oedema formation	Score
No erythema	0	No oedema	0
Very slight erythema (barely perceptible)	1	Very slight oedema (barely perceptible)	1
Well-defined erythema	2	Slight oedema (edges pf area well defined bu definte raising)	2
Moderate to severe erythema	3	Moderate oedema (raised approximately 1 mm)	3
Severe erythema (beef redness) to eschar formation preventing grading of erythema	4	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4

3. RESULTS AND DISCUSSION

3.1. Extract Centella asiatica

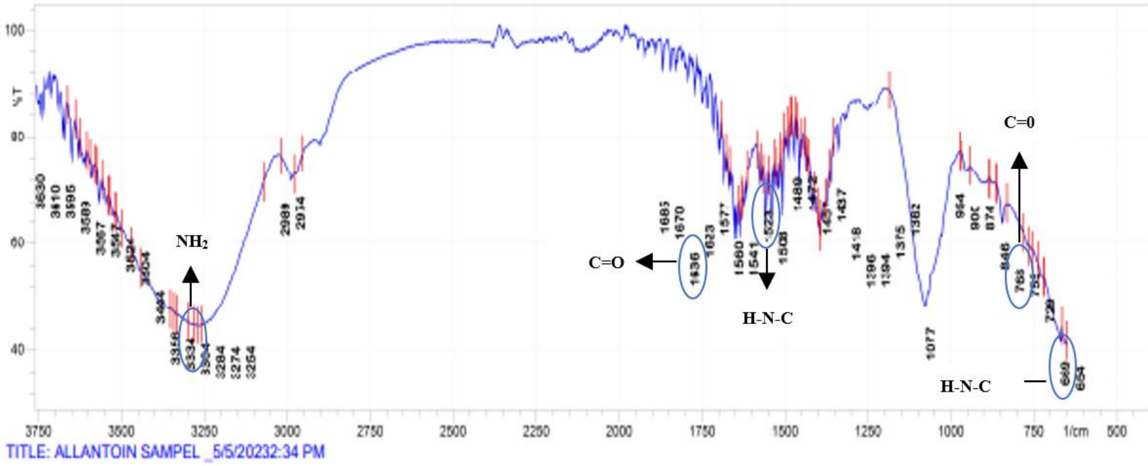
The extract obtained from 200 grams of *Centella asiatica* herba is 38.5300 grams (the yield percentage produced was 19.26%). The choice of the remaceration method was based on previous research of Rahimah et al., 2021 [18] using the remaceration method to extract CA and obtained a yield of 30.1%, while compared the research of Hapsari et al., 2017 [10] which used the maceration method to obtain a yield of 5.9%. The solvent used in the extraction this time was 70% ethanol because research stated that asiaticoside was mostly found in 70% ethanol extractor compared to 30% and 50% ethanol. An ethanol free test was also carried out on the extract to ensure that the extract was free from ethanol solvent. A positive ethanol-free result is indicated by the absence of ester odor from the ethanol extract which has been reacted with concentrated sulfuric acid and 1% acetic acid [19]. The results of a qualitative analysis with TLC showed that the extract contained asiaticoside, flavonoids, tannins, saponins and steroids (Table 5).

Table 5. Qualitative Analysis with TLC Result of *Centella asiatica* [10, 20]

Compounds	Research Results	Reference Results	Conclusion
Asiaticoside	Purple Staining at UV 254 nm; Rf: 0.25	Blue or purple staining; Rf: 0.24	Positive
Flavonoids	Brownish yellow stain; Rf : 0.66	Yellow or yellow-brown stain; Rf: 0.5-0.7	Positive
Alkaloids	No stains are formed	Brown or orange stains; Rf: 0.2-0.8	Negative
Saponin	Yellow stain; Rf: 0.46	Blue to blue violet stains, sometimes in the form of red, yellow, dark blue, purple, green or yellow-brown spots in visible light; Rf: 0.11-0.40	Positive
Tannin	Blackish purple stain; Rf: 0.78	Blackish purple stain; Rf: 0.66-0.79 (Fatih, 2016)	Positive
Steroids/terpenoids	Purple stain; Rf: 0.30	Red, violet, green or purple stains; Rf: 0.06-0.70	Positive

3.2. Snail Mucus Analysis

Allantoin in snail mucus sample was identified by using FTIR. The spectra analysis in Figure 1 reveals that the allantoin present in snail mucus closely resembles the spectra profile of the allantoin standard used as a reference. However, the allantoin in snail mucus exhibits a reduced intensity. This disparity in intensity can be attributed to the impurities present in the snail mucus sample, implying that the purity level of the sample is inferior to that of the standard allantoin [21].



_______ : Snail Mucus Spectra (sample)

_______ : Allantoin Spectra (sigma)

Figure 1. Comparison of Spectra Results between Snail Mucus Sampel and Allantoin Standard (Sigma no 102505490)

Based on previous research, bands within the range of 3500–3350 cm^{-1} and 3450–3150 cm^{-1}, which correspond to the asymmetric and symmetric stretching vibrations of amino groups, were discernible. Additionally, bands associated with the vibrations of H-N-C groups were detected in the range of 1550–1500 cm^{-1}. Absorption bands around 1636–1640 cm^{-1} were likely attributed to stretching vibrations of C = O and C = C groups, particularly associated with amidic groups. A stretching vibration of low intensity in the range of 1120–910 cm^{-1} was observed, likely originating from the C-NH_2 aliphatic amine group. Bands spanning from 860–510 cm^{-1} and a separate band at 450 cm^{-1} were indicative of N-H out-of-plane bending vibrations. Bands at 1840–1640 cm^{-1} and 780–760 cm^{-1} could be linked to C = O vibrations. Notably, the bands identified in each sample exhibited variations from the characteristic functional group bands of the allantoin standard, suggesting the presence of allantoin compounds in the analyzed samples of snail mucus.

The optimization design used in the Design Expert version 10 software program is a design using the Simplex lattice design method. This method was chosen because SLD (simple lattice design) is an optimization method that can determine the physical properties between two or more mixtures, so it can be used on materials that can be mixed physically. Apart from that, the optimized material has the same concentration range, namely 0.3-3%.

In making an essence sheet mask containing Centella asiatica extract and snail mucus, HPMC and glycerin were optimized, these two ingredients were optimized because they can affect the physical characteristics of the preparation, especially the viscosity of the preparation.

3.3. *Physical Characteristic of Essence Sheet Mask*

Table 4. The Physical Characteristic of Essence Sheet Mask

Formula	pH	Viscosity (cPs)	Absorption Ability (minute)	Skin Moisture (%)
F1	5.18	4244	5	35.61
F2	5.42	5601	2	22.45
F3	5.34	4739	4	28.21
F4	5.22	4544	5	3636
F5	5.41	4911	2	23.61
F6	5.40	4784	3	24.39
F7	5.39	4851	3	24.44
F8	5.40	5661	1	20.83
F9	5.20	4664	5	36.36
F10	5.41	5946	2	20.83

Table 5. Anava Results

Response	p-value prob > F (Modl)	Description	p-value Prob > F *Lack of Fit*	Description
pH	<0.0001	*Significant*	0.3365	*Not significant*
Viscosity	0.0003	*Significant*	0.3022	*Not significant*
Absorption	<0.0001	*Significant*	0.8060	*Not significant*
Skin Moisture	<0.0001	*Significant*	0.0785	*Not significant*

Table 6. Equation Simplex Lattice Design

Response	Equation
pH	Y = 1.63188 (A) + 1.55610 (B) + 0.049960 (A)(B)
Viscosity	Y = 1814.26154 (A)+ 1376.42678 (B) – 175.65519 (A)(B)
Absorption	Y = 0.43712 (A) + 1.69068(B) – 0.20215 (A)(B)
Skin Moisture	Y = 6.68612 (A) + 11.98755 (B) – 2.27753 (A)(B)

The HPMC coefficients (+1.63188) and glycerine (+1.55610) showed almost the same effect of increasing pH, but the HPMC coefficient values were higher than those of glycerine (table 4). This means that HPMC has a greater effect than glycerine in increasing the pH value. The resulting pH is caused by the difference between the two ingredients, HPMC 10% used in this study has a pH of 5.07 and glycerine has a pH of 4.62. The pH value of HPMC is more alkaline than the pH value of glycerine.

The HPMC coefficient value (+)1814.26154 also indicates that the effect is greater in increasing the viscosity of the preparation compared to glycerine, which has a coefficient (+1376.42678). In this study, 10% HPMC had a viscosity of 4439 cPs and glycerine had a much lower viscosity value of 442.4 cPs. This causes a difference in viscosity resulting from the effect of adding each ingredient to each formula. HPMC is a polymer derived from cellulose. This polymer molecule enters the cavity formed by water molecules, resulting in hydrogen bonds between the hydroxyl groups (-OH) of the polymer and water molecules. Therefore, the higher the concentration of HPMC, the more hydroxyl groups are bound, so the viscosity is higher [22] [23]. This means increasing amount of HPMC, the more liquid will be retained and bound by HPMC, finally the viscosity will increase.

On the other hand, the coefficient value of HPMC (0.43712) is smaller than that of glycerine (+1.69068), this indicates that the effect of glycerine in increasing the absorption ability of the preparation is greater. this is because the high HPMC content will increase the viscosity of the preparation, the preparation becomes thicker and difficult to absorb in the sheet mask sleeve.

The HPMC coefficient value is also smaller with a value of (+6.68612) while glycerine is (+11.98755) in increasing skin moisture. Glycerine can form a hygroscopic layer, therefore it can absorb water from the air and be able to retain it. This process can also prevent dehydration of the stratum corneum layer. The advantage of glycerine as a humectant compared to other humectant ingredients is that glycerine can maintain moisture in the skin because of the large number of hydroxyl groups, making it stronger in binding and holding water in the skin [24] [25].

Determination of the optimum formula obtained from Software Design Expert Stat-Ease® version 10 Simplex Lattice Design method with the optimum parameters of pH, viscosity, absorption ability and skin moisture. The importance of each parameter can be determined from unimportant to important, with a weight of 1 (not important, +) to most important (+++++) with a weight of 5. The importance, in this case, is determined by the parameter's influence on the preparation of the essence sheet mask.

The pH parameter was assigned a maximum target with a weight of 3 (+++). This decision was made because all pH values produced in the running formula fall within the safe range accepted by the skin. A pH that is too low can cause irritation, while a pH that is too high can cause scaly skin. The desired pH in an optimum formula must fall within the required range of 4.5-6.5.

The viscosity parameter was designated as a minimum target with a weight of 5 (+++++). This is due to viscosity being a crucial parameter in this preparation. Viscosity directly affects the dosage form produced. In this research, the aim is to obtain a liquid result to ensure that the preparation can still be absorbed by the mask sleeve. Low viscosity results in a liquid preparation that can be easily absorbed into the mask sleeve, serving as an applicator. Viscosity is a parameter directly linked to the absorption ability parameter.

The absorption ability parameter was assigned a maximum target with a weight of 5 (+++++). This choice was made because proper absorption of the essence sheet mask into the sleeve is crucial. If the preparation cannot be absorbed properly into the sleeve, it will not be evenly distributed when used. Absorption also aids in determining the effectiveness of the preparation upon application. If the preparation cannot be absorbed properly into the sleeve, it cannot be classified as a sheet mask, resulting in similar application methods to other types of masks. The moisture parameter was assigned a maximum target weight of 5 (+++++). A higher humidity level yields better moisture activity, facilitating the desired therapeutic effect.

The optimum formula obtained is a formula with a concentration of 0.589% HPMC and 2.711% glycerine with a desirability value of 0.711. The optimum formula was composed of a predetermined ratio of HPMC and glycerin. The manufacturing steps were conducted in the same manner as during the formula's preparation, and testing was performed using identical procedures.

The physical appearance of the essence sheet mask was depicted in Figure 2. The test results of the essence sheet mask were presented in Table 9.

Table 9. Optimum Formula Test Results

Response parameters	Test Result
pH	5.64 ± 0.02
Viscosity (cPs)	4581.80 ± 59.80
Absorption Ability (minute)	4.60 ± 0.55
Skin Moisture (%)	32.09 ± 3.21

(a) **(b)**

Figure 2. Optimum formula of (a) essence of sheet mask containing CA and snail mucus (b) sheet mask containing CA and snail mucus after absorption ability test

Irritation is an inflammation of the skin that occurs due to the presence of foreign compounds. Symptoms include a burning feeling that occurs due to dilation of blood vessels characterized by redness (erythema) and swelling (edema). The irritation test was carried out covered with gauze. The resulting preparations meet the cosmetic requirements that are safe for human skin, proven by a score of 0 on the irritation test for all volunteers [11]. The results of the irritation test show that the irritation score caused by the preparations is 0 or not irritating.

4. CONCLUSION

HPMC and glycerine have effect on the physical characteristics and moisture activity test of the essence sheet mask combination of CA extract and snail mucus. HPMC can increase the pH and viscosity in the preparation. Glycerine can increase the absorption ability of the essence to the mask sleeve and skin moisture.

Both HPMC and glycerine are compatible in essence with sheet masks containing CA and snail mucus with the optimum composition in the proportion of 0.589% HPMC and 2.7111% glycerine. The response results for the optimum formula were test results of pH 5.64 ± 0.02, viscosity 4581.8 ± 59.80 cPs, absorption ability 4.6 ± 0.55, and humidity 32.09 ± 3.21%.

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