

Optimization of HPMC as Gelling Agent in Gel Formula of Etanol Extract of Bangun-Bangun Leaves (*Plectranthus amboinicus* (Lour) Spreng)

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ARTICLE INFO

Keywords:

Bangun-bangun leaves,
gel,
HPMC.

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ABSTRACT

Hydroxy Propyl Methyl Cellulose (HPMC) is a semi synthetic cellulose derivative gelling agent and can form a clear and neutral gel and has a stable viscosity in the long run. This study aims to determine the concentration of how much HPMC can form ethanol extracts of bangun-bangun leaves (*Plectranthus amboinicus* (Lour) Spreng) and stability of gel extract preparations. This research is an experimental study, in which the ethanol extract gel formulation of bangun-bangun leaves (*Plectranthus amboinicus* (Lour) Spreng) was conducted, by varying the concentration of HPMC at concentrations of 3%, 4% and 5%. Bangun-bangun leaves extract obtained from the maceration process and formulated in gel form. Furthermore, physical properties were evaluated, which included tests of adhesion, dispersion, pH, and viscosity on the bangun-bangun leaves extract gel. The evaluation results are then presented in tabular form. The optimum formula of the bangun-bangun leaves extract gel is a formula that contains 4% HPMC. Based on the results of the study is known that the results of the evaluation of the physical properties can be said to be stable after 4 weeks of storage.

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1. INTRODUCTION

One of the most common skin problems is acne. Acne is a chronic inflammatory process of the pilosebaceous glands. This situation is often experienced by teenagers and young adults who start to appear acne on their own. Acne is usually associated with high sebum secretion [1].

Treatment of acne with other alternatives is by using natural ingredients and for example, Bangun-bangun leaves [2], [3]. Bangun-bangun leaves contain saponins, flavonoids, polyphenols, potassium and 0.2% essential oil containing carvacrol, phenol, sineol [4]. Polyphenol and flavonoid compounds can kill bacteria by denaturing proteins and reducing surface tension.

Anti-acne preparations circulate in the form of gels, creams and lotions. However, most people like gel preparations [5], because it has several advantages including non-sticky, does not contain oil, besides that it can convey medicinal ingredients well and will also cause acne to dry quickly because the gel has volatile properties [2]. In gel formulation, the gelling agent component is a critical factor that can affect the physical properties of the resulting gel.

Hydroxy propyl methyl cellulose (HPMC) is a semi-synthetic cellulose-derived gelling agent that is resistant to phenol and stable at pH 3 to 11. HPMC can form clear and neutral gels and has a stable viscosity in the long term [6].

In addition, HPMC expands limited in water so that it is a good hydrogel forming material. Hydrogels are very suitable for use as topical preparations with excess sebaceous gland function, where this is one of the factors causing acne [7].

Based on the advantages of gels and research on bangun-bangun plants that are good for acne, researchers are interested in conducting research on the formulation of ethanol extract gel preparations in bangun-bangun leaves (*Plectranthus amboinicus* (Lour) Spreng). This research is different from the research conducted [3]. Where this study uses HPMC as a gelling agent.

2. METHOD

This research was conducted from February to May 2019 at the Pharmacy Technology Laboratory of Mitra Bunda Persada College of Health Sciences, Batam. This research begins with plant identification and the preparation of ethanol extract bangun-bangun leaves by maceration, making bangun-bangun leaves gel preparations with HPMC concentrations of 3%, 4% and 5%. After that, the gel preparation was evaluated.

Digital scale, Sieve, blender, Oven (Drying oven), Maceration bottle (brown). Water bath, dropper pipette, petri dish, vernier caliper, viscometer, vaporizer cup, measuring cup, pH meter (Hanna Instruments), rotary evaporator (Haake D), aluminum foil, parchment paper, tissue, mortar, stamfer and glassware in the laboratory. Thick extract of bangun-bangun leaves (*Plectranthus amboinicus* (Lour) Spreng), distilled water, HPMC, Propylengicol, Glycerin, Methyl paraben, Propylenglycol, and 70% ethanol.

bangun-bangun leaves were obtained in the Bengkong area, Batam, Riau Islands. Plant collection is done purposively without comparing with the same plants from other areas. The leaves taken are old leaves that are dark green in color. Plant identification was carried out at the Herbarium of Andalas University, Padang, West Sumatra. The collected bangun-bangun leaves are washed thoroughly with running water. The leaves are then aerated and then weighed as a wet weight of 10 kg, then dried in the oven at 40-60°C until dry, where if the simplisia is dry and the simplisia is squeezed, the simplisia will disintegrate (to find out that the simplisia has dried, the determination of the water content of the simplisia), then weighed as a dry weight of 870 g (dry leaves that have not been mashed), then the simplisia is powdered using a blender, stored in a tightly closed plastic container, protected from heat and sunlight.

Preparation of Ethanol Extract of Bangun-Bangun Leaves (*Plectranthus amboinicus* (Lour.) Spreng)

The simplisia powder was extracted by maceration using 70% ethanol solvent. Method: a total of 610 g of simplisia powder was put into a dark glass container and then macerated with 4500 ml of 70% ethanol solvent for 5 days protected from sunlight while stirring frequently, then blotted, squeezed with flannel cloth, then the pulp was added to enough liquid to obtain the entire juice as much as 6000 ml, then allowed to stand for 2 days and poured. The macerate was evaporated with the help of a rotary evaporator vaporizer at a temperature of no more than 400C and evaporated until a thick extract of 90.86 g was obtained.

Examination of the Characteristics of Bangun - Bangun Leaves Extract (*Plectranthus amboinicus* (Lour.) Spreng)

Based on Ministry Of Health Of The Republic Of Indonesia in 2000 [8]:

- Organoleptical : The thick extract obtained is observed with the five senses including shape, color, taste and smell.
- Drying Shrinkage : The viscous extract was weighed as much as 2 g and put into a porcelain crucible with a lid that had previously been heated to 105oC for 30 minutes and had been tared. Krus put into the oven in the state of the krus lid open, dry at 105oC for 30 minutes fixed weight. Then cool in a dexicator, and weigh. This is done until the weight is constant and the results are expressed in percent. The purpose is to provide a maximum limit (range) on the amount of compounds lost in the drying process. The value for drying shrinkage if not otherwise stated is less than 10%.

Formulation

Table 1. Formulation

Gel Base Formula of Ethanol Extract of Bangun - Bangun Leaves

Materials	Usability	Formula I	Formula II	Formula III
Ethanol Extract of Bangun - Bangun Leaves	Active substance	2,5%	2,5%	2,5%
HPMC	Gelling agent	3%	4%	5%

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Glycerin	Humectant	15%	15%	15%
Propylenglicol	Solvent	5%	5%	5%
Methyl Paraben	Preservative	0,2%	0,2%	0,2%
Aquadest	Solvent	Ad 100%	Ad 100%	Ad 100%

Description: Concentration of extract with HPMC 3, 4, 5%

Working Procedure: HPMC was developed with distilled water that had been heated at 100°C. Glycerin and methyl paraben were mixed with the developed HPMC, crushed to form a gel preparation. Propylenglycol was dissolved with slightly heated distilled water. Add water little by little to form a gel base, then the ethanol extract is added to the remaining hot water and added to the finished gel base and then crushed until homogeneous.

Gel Preparation Evaluation

Physical evaluation of gel preparation of ethanol extract of bangun - bangun leaves:

- Organoleptic tests include odor, color, and concentration done visually [9].
- Spreadability Test as much as 1 gram of gel preparation is placed carefully on a glass measuring 20 x 20 cm. Furthermore, it is covered with mica paper and given a weight on it until the weight reaches 125 grams, then the diameter formed after 1 minute is measured [10].
- Adhesion Test A 0.25 gram sample is placed between 2 glass objects, then pressed with a 1 kg load for 5 minutes. After that the load is lifted from the object glass, then the object glass is mounted on the test tool. The test tool was given a load of 80 grams and then recorded the time of release of the gel from the object glass [11].
- Homogeneity test is done by applying the gel on an object glass and then attached to another object glass. Visually observed the presence or absence of coarse grains [12].
- pH test is done by turning on the pH meter, then the pH meter electrode is dipped into the gel formula. Let stand for a while until the pH meter screen shows a stable number [13].
- Viscosity test is carried out by means of a rotor mounted on a test device, set until the rotor is immersed in the gel. The tool is activated, the scale shown is read until it shows a stable number [14].

3. RESULTS AND DISCUSSION

In this study, the extraction process was carried out by maceration method, namely soaking the sample with a certain solvent or a suitable solvent. The solvent used in this study is 70% ethanol. bangun - bangun leaves samples weighed 10 kg and macerated with ethanol as much as 5 L. Then vaporized using a rotary evaporator, then evaporated again using an oven so as to get the results of thick extracts and 7.5 g will be needed.

In organoleptical viscous extract evaluation, the results obtained from bangun - bangun leaves extract (*Plectranthus amboinicus* L.) have a bitter taste, dark green color, have a distinctive odor and have a thick shape or texture.

In the evaluation of drying shrinkage thick extract, the results of drying shrinkage of thick extract of bangun - bangun leaves (*Plectranthus amboinicus* L.) that have met the requirements, which is 3%.

Based on the research that has been conducted, the following results are obtained.

Organoleptic Observation

Table 2. Organoleptical Observation Results of Gel Formulas

Gel Formula	Observation					
	Color	Before Storage		After Storage		
		Smell	Shape	Color	Smell	Shape
HPMC 3%	Dark	Typical	Semi	Dark	Typical	Semi
	Green	Extract	Solid	Green	Extract	Solid
HPMC 4%	Dark	Typical	Semi	Dark	Typical	Semi
	Green	Extract	Solid	Green	Extract	Solid

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HPMC 5%	Dark Green	Typical Extract	Semi Solid	Dark Green	Typical Extract	Semi Solid
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Spreadability Observation

Table 3. Observation Results of Spreadability of Gel Formulas

Spreadability		
Formula	Formula	Formula
HPMC 3%	HPMC 4%	HPMC 5%
3.8 cm	5 cm	3.6 cm

Stickiness Observation

Table 4. Gel Formula Adhesion Observation Results

Stickiness		
Formula	Formula	Formula
HPMC 3%	HPMC 4%	HPMC 5%
2.74 seconds	3.12 seconds	3.79seconds

Homogeneity Observation

Table 5. Results of Homogentias Observation of Gel Preparation

Gel Formula	Homogeneity Observation	
	Before	After
HPMC 3%	✓	✓
HPMC 4%	✓	✓
HPMC 5%	✓	✓

Description: ✓ = No obstacles/Homogeneous

Observation of pH of Gel Preparation

Table 6. Results of pH Observation of Gel Preparations

Gel Formula	Week I	Week II	Week III	Week IV
HPMC 3%	5.02	5.27	5.36	6.10
HPMC 4%	5.06	5.42	5.64	6.20
HPMC 5%	5.13	5.53	5.78	6.40

Gel Viscosity Observation

Table 7. Viscosity Observation Result of Gel Formula (Rpm 6)

Gel Formula	Week I	Week II	Week III	Week IV
HPMC 3%	9,800 Cps	10,400 Cps	10,900 Cps	11,600 Cps
HPMC 4%	9,600 Cps	13,200 Cps	14,500 Cps	15,000 Cps
HPMC 5%	13,340 Cps	16,200 Cps	16,700 Cps	17,800 Cps

This study aims to determine at what concentration HPMC ethanol extract of bangun-bangun leaves (*Plectranthus amboinicus* L.) can form a good gel.

The sample used is bangun-bangun leaves (*Plectranthus amboinicus* L.) because it contains high antioxidants. Bangun-bangun leaves (*Plectranthus amboinicus* L.) is one of the Indonesian ethnobotanicals that has been consumed for generations by the people of North Sumatra as a vegetable food. The sample selection of bangun-bangun leaves is because many people in Batam do not know what bangun-bangun leaves are and want to inform the benefits of bangun-bangun leaves for health. Before obtaining a thick extract, the leaves of bangun - bangun that have been picked must be washed first. After being washed and dried, the leaves were dried in the sun by covering them with a black cloth so as not to be exposed directly to the sun's heat and the content in the leaves was not lost for 2 weeks.

Furthermore, the dried sample is macerated with a solvent that is suitable for compounds that cannot be damaged by heating such as antioxidants. The workmanship and tools used are also simple. Bangun-bangun leaves powder was macerated with 70% ethanol solvent for 5 days with 3 repetitions, in order to get a more optimal thick extract. The selection of ethanol solvent with a concentration of 70% in accordance with the Herbal Pharmacopoeia says the dry powder extract material of the *simplicia* to be macerated using 70% ethanol.

After the sample has been macerated, then the thick extract is taken using a rotary evaporator which functions to convert part or all of a solvent from a solution from liquid to vapor. After getting the results, it was then baked at 400C for 4 days in order to get a thick extract and the extract was not damaged.

Preparation of gel preparations using a concentration ratio of HPMC ingredients in a ratio of 3%, 4%, 5% and with additional ingredients such as glycerin which is used as a humectant on the skin that can provide a soft effect on the skin [15], propylenglikol as a solvent in the gel, methyl paraben as a preservative. Preservatives in the formulation if the water content in the gel preparation is high so that microbial contamination does not occur [12], [7] and distilled water.

HPMC is developed with distilled water that has been heated at 100°C. Glycerin and methyl paraben were mixed with HPMC that had expanded, crushed to form a gel preparation. Propylenglycol was dissolved with slightly heated distilled water. Add water little by little to form a gel base, then the ethanol extract is added to the remaining hot water and added to the finished gel base and then crushed until homogeneous.

After the gel is finished, then the gel is evaluated whether the gel is good or not. The gel that has been mixed with 2.5 g of thick extract is then allowed to stand for 1 day and see if there is a color change or not. If the color of the gel changes, the gel has oxidized, meaning that the content in the gel that has been mixed with the extract has no function or little function.

Examination of the physical stability of the preparation includes organoleptical evaluation of the gel preparation carried out on changes in the shape, color and odor of the preparation. The examination was carried out visually at room temperature for 12 weeks with an inspection time span of 4 weeks. The preparation is declared stable if there is no change in shape, color and odor [16]. The results of the organoleptical stability test of all gel preparations of ethanol extract of bangun-bangun leaves did not change in shape, color and odor.

Observation of spreadability, the results of the observation of spreadability that the formula with 3% HPMC has an area of 3.8 cm, 4% HPMC has an area of 5 cm, while 5% HPMC has an area of 3.6 cm. From the profile, it is known that at the same load, the difference in HPMC concentration causes a difference in the diameter of the spread. A more dilute preparation produces a larger spreading diameter because it is easier to flow. Besides because of the lower viscosity, the diameter of the spread is wider. In contrast to the thicker, it produces a small spreading diameter because it is slow to flow. The aim is to determine the spreadability of the gel on the skin being treated. The spreadability range for a good gel is 5-7 cm [17].

Observation of Adhesive Power, the results of the observation of adhesive power that the 3% HPMC formula has a time of 2.74 seconds, the 4% HPMC formula has a time of 3.12 seconds, while the 5% HPMC has a time of 3.79 seconds. From the three concentrations, it is known that the higher the concentration, the consistency of the gel will increase and the adhesion will be greater [18]. The adhesion ability of the gel will affect the therapeutic effect. The longer the ability of the gel to adhere to the skin, the gel can provide a longer therapeutic effect.

Homogeneity observation, the results of the homogeneity check that all gel preparations meet the requirements because they show a homogeneous composition and no coarse grains are visible. This shows that the preparations made have a homogeneous composition.

The results of the pH stability test of gel preparations from ethanol extract of bangun-bangun leaves can be seen in table 6, which shows that the pH remains stable in storage because it is still within the pH requirements of the skin, namely 4.5-6.5 [19]. So the higher the concentration of HPMC in the gel extract of bangun-bangun leaves, the higher the pH. With the aim of knowing the safety of the preparation when used so as not to irritate the skin [20].

Viscosity observation, the result of an examination that aims to determine the viscosity value of the substance. The higher the viscosity value, the higher the viscosity level [23]. The ups and downs of the viscosity of each formula of bangun-bangun leaves at the concentration of HPMC used can be seen in table 7. The more HPMC that is dissolved, the thicker the liquid and forms into a gel. The viscosity required by SNI 16-4399-1996 is 2,000 cp - 50,000 cp. So from the results of the viscosity examination of the gel preparation on bangun-bangun leaves, it is still within the requirements of SNI 16-4399-1996.

4. CONCLUSION

The concentration of 4% HPMC in ethanol extract of bangun-bangun leaves (*Plectranthus amboinicus* (Lour.) Spreng) can form the optimal gel formula. The results of the evaluation of physical properties which include adhesion, spreadability, pH and viscosity tests can be said to be stable after 4 weeks of storage. It is recommended to further researchers to be able to develop gel formulations from ethanol extract of bangun-bangun leaves that are in accordance with the standards that have been set, so that the appearance of gel preparations is more attractive and further research has more variations in concentration.

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