Formulation and Evaluation of Gel Containing *Barringtonia Racemosa* L.Spreng Kernel Extract for Topical Application

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Abstract: Medicinal plants are now widely used by the community as an effort to tackle health problems amid advances in science and technology. A natural material that can be used as an alternative biological therapy for wound management is a putat air (*Barringtonia racemosa*). The phytochemical content of this plant is in the form of saponins, flavonoids, and terpenoids. The research objective was obtained physical test data of wound gel formula with ethanol extract of putat air. The research design is experimental. In this research, four wound gel formulas containing putat air kernel extract were evaluated for organoleptic, pH, homogeneity and viscosity. The formula designed was corbopol 940 2% with kernel extract of putat air 1%, 3%, 5% and 7%. Based on the organoleptic test, the four formulas are semisolid, yellowish-white, thick and odorless. Homogeneity testing, homogeneous preparations but there are bubbles. The higher the concentration of putat air (*B. racemosa*) extract, the more bubbles as well as the color of the yellowish gel. This is also due to high saponin levels. The pH test shows it is ideal for topical preparations, which is between pH 6-6.2. The highest pH is found in formulas with a concentration of putat air (*B. racemosa*) extract 1%. Viscosity measurement results for the entire formula, resulting in a value that is included in the standard that is 9000-10500 cP. Based on the physical essence, this gel preparation is still suiTable for treating wounds on the skin.

1 INTRODUCTION

Indonesia has various types of medicinal plants. Medicinal plants are now widely used by the community as an effort to tackle health problems amid advances in science and technology. A natural material that can be used as an alternative biological therapy for wound management is a putat air (*Barringtonia racemosa*). Based on proven research that this plant has been prescribed in the Ayurvedic literature of traditional Indian medicine for the treatment of dog and snake bite wounds. The phytochemical content of this plant is in the form of saponins, flavonoids, and terpenoids (Ojewele et al., 2004: Gowri.et.al.2009; Musman, 2010). The *B.racemosa* plant is a type of local mangrove known as a putat air. One species in the kingdom of Plantae of the genus Barringtonia which is classified under the family Lecythidaceae.

The taxonomic hierarchy of *B.racemosa* can be arranged in the following order: Kingdom: Plantae; Subkingdom: Viridiplantae; Infracingdom: Streptophyta; Superdivision: Spermatophytina; Class: Magnoliopsida; Superorder: Asteranae; Order: Ericales; Family: Lecythidaceae; Genus: Barringtonia; Species: Barringtonia racemosa (L.). (Osman et al., 2015).

Phytochemical constituents found in putat air (B. Racemosa) include saponins, sterols and phenolics. Saponins for instance are classified as triterpene glycosides which are very well known to be inherently present in B. racemosa. The presence of such compounds had been acknowledged to be the reason of its suitability to be used as cleaning agents due to its surface-active properties and may produce long-lasting foam (Chen.et.all.,2010; Makkar., 2007).

Plant sterols are the components occur in plant cells which are generally functions to control membrane fluidity and permeability. The presence of sterol in plants is associated with a number of benefits for instance it has the potential to be used as natural preventive dietary product in lowering plasma

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cholesterol level (Piironen., 2000). Phenolics are compounds possessing one or more aromatic rings with one or more hydroxyl groups. They are broadly diversified ranging from simple molecules to highly polymerized substances with more than 8000 compounds being categorized into the group. Plant phenolics can be further classified into several sub-groups which are phenolic acids, flavonoids, tannins (non-flavonoid polyphenols), stilbenes and lignans. Phenolic compounds are frequently associated with antioxidative properties and being recognized as natural antioxidants (Dai and Mumper., 2010). Flavonoids are reported to have 3 mechanisms of inhibition of microorganisms, namely by (1) destruction of the cytoplasmic membrane, (2) inhibition of nucleic acid synthesis, and (3) inhibition of metabolic energy (Cushnie, 2011).

Pharmacological activity of *B.racemosa* contains antimicrobial, antibacterial against strains of both gram positive and gram negative bacteria, namely staphylococcus aureus, staphylococcus epidermidis, Eschericia coli, shigella dysentriae, vibrio cholerae and Proteus sp. This plant also contains antinociceptive (analgesic), antioxidants, anti-inflammatory and anti-fungal (Khan, 2001).

The various parts of *Barringtonia racemosa (B. racemosa)* are known to possess multiple biological activities (Khan and Omoloso., 2002). Extracts prepared from different parts of *B. racemosa* possess analgesic, antitumor and antimicrobial activities (Thomas and Panikkar., 2002; Muse and Ahmad.,2008). The aqueous bark extract of *B. racemosa* exerted significant and dose-dependent antinociceptive activity in experimental animals. This activity is attributed to the presence of opioids or opiodiomimetics as well as phenolics and steroidal con- stituents in *B. racemosa* (Husein.at el., 2009). Anti-oxidant and anti-inflammatory ef- fects of *B. racemosa* leaves ar attributed to its lycopene content . This extract exerted *in vitro* nitric oxide synthase inhibitory and antioxidant activity in RAW cells (Muse and Ahmad., 2008). Methanolic, ethanolic and boiling water extracts of *B. racemosa* leaves, sticks and barks at the concentration of 50 mg/mL were found to possess antifungal activity against *Fusarium* sp., *Tricoderma koningii*, *Penicillium* sp., *Ganoderma tropicum*, *Ganoderma lucidum*, *Aspergillus* sp. and *Rhizopus* sp (Osaman.et.al.,2015).

The extracts obtained from the aerial parts of this plant demonstrated *in vitro* antioxidant activity *B. racemosa* leaves demonstrated higher antioxidant activities than the stems, owing to its antioxidant content (Patil.et.al.,2011).

Effectiveness and comfort in the use of putat air extract (*B.racemosa*) on a skin can be improved by formulating it into gel dosage forms. Topical gel preparations can increase the effectiveness and comfort in its use which is able to deliver medicinal ingredients well, easily spread evenly when applied to the skin, giving a cold sensation, and does not cause marks on the skin (Madan and Singh, 2010). Carbopol is a hydrophilic gel, so it is easily dispersed in water and in small concentrations can function as a gel base with a fairly good thickness at pH 6-11. Carbopol is white, has a texture like feathers, acids, hygroscopic powder with a slight characteristic odor. Carbopol is a strong gel base has a high acidity so that in its use as a gelling agent it only takes around 0.5-2.0% (Melani et al., 2005; Rowe et al., 2009). This is the advantage of using carbopol compared to other ingredients Ideally, gelling agents are the basis of gel preparations that are inert, safe and not reactive with other components of the gel formula. The characteristics of the gelling agent used must be adjusted to the dosage form. Gel preparations must be well formulated to meet safe, effective and stable. Until now there has been no reference that found wound gel formula using extracts of putat air (*B.racemosa*) (Scopus, 2019; Web of Science, 2019; PubMed, 2019).

2 RESEARCH METHODS

The aim of this study was to conduct a physical test of a watertight wound gel formula (*B. Racemosa*). The research design is experimental. The stages of the formulation were carried out by designing four types of formulas, from which the four formulas were tested physically, namely organoleptic, viscosity, homogeneity and pH.

Material

Sample Preparation

The putat air fruit (*B.racemose*) was taken from the village of Gampong Pulo.Kec. Peudada. Bireuen Regency. Fruit taken is old and fell on the ground. The water drops are immediately put into a sealed plastic bag. Before it is sealed, it expels air from the plastic bag. Then the plastic bag is placed in a cool place (4° C) (Table 1).

Table 1. Preparation of Carbopol 940 gelling agent formula

Material	Base Formula (% b/b)				
	F1	F2	F3	F4	F5
Carbopol	2	2	2	2	2
TEA	2	2	2	2	2
Glycerin	1	1	1	1	1
Propylene Glycol	6	6	6	6	6
Nipagin	0.2	0.2	0.2	0.2	0.2
Aquadest	Ad 100	ad 100	Ad 100	Ad 100	Ad 100
Putat extract (gr)	0	1	3	5	7

The part of the putat air used is the white inside seeds. The putat air is peeled and the seeds are taken. Brown seeds are washed without peeling the brown skin. Brown skin is left to peel itself during drying. Then the putat air seeds are cut into small pieces and then dried in a drying chamber at 40 ° C for one week. Wet material is 4 kg and after drying becomes 1.5 kg. Simpisia Extraction is removing the first and second metabolites from putat air tissue cells using solvents. The solvent used is 70% ethanol. The concentration of ethanol solvent 70% more dissolved flavonoids than pure ethanol solvents. Ethanol polarity increases and more easily penetrates cell membranes with the addition of 30% water (Musman, 2013).

The extraction method used is homogenization of sympathies. Dried fruit that has been dried in a dryer (temperature 40 ° C) is ground in a blender. The putat flour is stored in a container and 70% ethanol is poured and 30% water is left for 24 hours. Every 1x24 hours the solvent is replaced until the solvent is no longer colored. Then the mixture is filtered.

The obtained filtrate is dried with a rotary carrier. Dehydrated ethanol extract was dissolved in 10 ml of ethanol and 20 ml of aquades, and placed in a separating funnel and then mixed with 100 ml of n-hexane solvent until colorless. The residues were mixed with ethyl acetate and ethanol, and then the fraction was evaporated. The resulting solution was stored in a vial for phytochemical filtration.

2.1 Preparation of Carbopol 940 Gelling Agent Formula

The gel base consisting of carbopol, TEA, propylenglycol, glycerin and aquades was made into 4 different formulas, namely by varying the concentration of putat air (*B.raccemosa*) seed extract 1%, 2%, 3%, 5% and 7%. The gel preparation on the basis of 940 carbopol is done by means of carbopol 940 developed in 10 parts of distilled water in a beaker, left to stand for 1 x 24 hours. Then added TEA then homogenized.

Then propylene glycol and methyl paraben were added, which were previously dissolved in 900C hot distilled water, stirring until homogeneous. The extract was mixed with glycerin, mixed into the base, added the remaining water to the base, and stirred until homogeneous.

3 RESULT

3.1 Organoleptic Test

Organoleptic test results of Formula shown on the Table 2:

Table 2: Organoleptic test results

No	Formula	Color	Smell	Consistency
1	F1	Clear	Distinctive smell	Thick
2	F2	Yellowish white	Typical odor of putat air extract	Thick
3	F3	Yellowish white	Typical odor of putat air extract	Thick
4	F4	Yellowish white	Typical odor of putat air extract	Thick
5	F5	Yellowish white	Typical odor of putat air extract	Thick

Based on Table 2. Data obtained formulas F2, F3, F4 and F5 are yellowish, have a distinctive odor and have a thick consistency as shown in Figure 1:

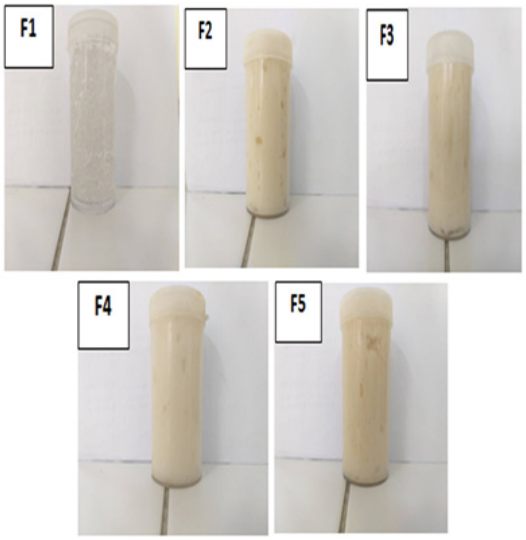

Figure 1: Result of Homogenity test

3.2 Viscosity Test

Viscosity is a statement of the resistance of a liquid to flow. The higher the viscosity, the higher the prisoner (Sinko, 2011). Viscosity of the preparation should not be too high and should not be too low, because if it is too high (thick), the gel will be difficult to remove from the package, whereas if the viscosity is too low it will reduce the length of time to stay on the skin when used.

Gel viscosity (Table 3) was measured using a Brookfiled cone and plate viscometer (Engineering Laboratories INC, Stoughton MA, USA). Gel flow is measured at room temperature. The sample is placed about 1 g in the cone. Measurements are made by increasing the shear rate from 0.5 / sec to 100 / sec and viscosity is read at each rotation per minute.

Table 3: Gel Viscosity Test Results

No	Formula	Viscosity
1	F1	8250 cp
2	F2	9000 cp
3	F3	9500 cp
4	F4	10000 cp
5	F5	10500 cp

3.3 pH of the Preparation

The pH was measured using a pH meter (Schott, Deutschland, Belgium). 1 g of sample is dissolved in 10 ml of water at room temperature. Furthermore, the electrode will contact with the surface of the solution and leave it in balance for 1 minute (Table 4).

Table 4: pH gel test results

No	Formula	pH
1	F1	6,6
2	F2	6,2
3	F3	6,0
4	F4	6,0
5	F5	6,0

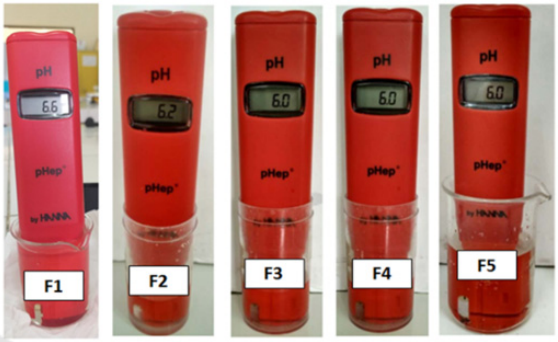

Figure 2**:** pH gel test results

3.4 Homogenity Test

Based on Table 5. the results obtained are all homogeneous formulas.

Table 5: Homogenecity Test Results Gel wound of putat air (*B.Racemosa*) extract

No	Formula	Results
1	F1	Homogeneous
2	F2	Homogeneous
3	F3	Homogeneous
4	F4	Homogeneous
5	F5	Homogeneous

4 DISCUSSION

Carbopol is a synthetic acrylic acid polymer, a white powder with a distinctive odor, very easily ionized, slightly acidic, insoluble in water and most solvents, and is hygroscopic. In neutral form, carbopol is soluble in water, alcohol, and glycerin and will form a clear and sTable gel. In acidic solutions (pH 3.5-4.0) carbopol dispersions show low to moderate viscosity and at pH 5.0-10.0 and at temperatures above 750C will show optimal viscosity. Carbopol functions as a thickener, surfactant, stabilizer, and thickener. In cosmetics, carbopol is used in a neutral form at pH

7.7 because carbopol is sTable at that pH and is incompatible with strong acids (Rowe et al., 2009).

Carbopol is a gelling agent that can modify the flow properties and viscosity and can be a stabilizing agent for a topical preparation. The use of Carbopol as a good gelling agent is in the range of 0.5% -2.0% (Rowe et al., 2009). Propylene glycol is a humectant that also affects the swelling and viscosity of the gel. Carbopol formulated in conjunction with humectants such as propylene glycol and glycerin can produce good stability at the right ratio.

Humectant propylene glycol is able to bind with water to form hydrogen bonds so that it can trap water, therefore the use of these two humectants should not be too large so that carbopol can still bind to water and can maintain gel consistency (for Propylene glycol <30%) (Islam, 2004).

According to Bakker (2012), states that gel is a heterogeneous system. In gel preparations, the solid phase is in a three-dimensional structure so that particles in the solid phase cannot move past the liquid phase. In order for a solid phase to remain sTable in a three-dimensional structure, solid phase particles must form secondary bonds with other particles (*Van der Waals* bonds). The stability of the gel preparation depends on the shape of the particles from the solid phase; physico-chemical characteristics of the solid phase and its ability to form secondary bonds; concentration of solid phase; physico-chemical characteristics of the liquid phase.

Viscosity shows the level of thickness of a gel preparation. Carbopol 940 in powder form is a polymer that forms coils so that this will limit its thickening ability, but if carbopol is dispersed into water, the carbopol will be hydrated and some of the coils will be uncoiled (Noveon, 2009). Carbopol will function well if the constituent polymers are truly uncoiled. The mechanism is the neutralization of the carboxylic acid group in the polymer chain with the appropriate base. This will result in the formation of negative charges along the polymer chain, where neutralization is done by adding TEA. The repulsion between negative charges causes carbopol 940 to make the coiled structure change to a freer structure (Garg., Et al., 2002).

Carbopol 940 polymers will be intertwined with each other by forming cross links so as to produce a three-dimensional matrix to form a gel that is very thick in a second, so the higher the viscosity value, the level of thickness of a preparation is also higher because of the number of polymers undergoing cross links and forming more and more gel bases. It cannot be said that the higher the viscosity, the better the preparation of the gel, because it will be related to the spreadability and comfort of the preparation during use. It should be noted that the value of viscosity is inversely proportional to the value of the dispersal power (Garg., Et al., 2002).

The composition of propylene glycol in the formulation is said to be good at around 15% (Rowe et.al, 2009). Another opinion states that propylene glycol can be a good humectant in the composition of 5% of the preparation. The use of humectants that are too high will cause the water in the preparation to interact entirely with propylene glycol and form hydrogen bonds, even skin moisture when applied can lose moisture and can become dehydrated. However, if the concentration of propylene glycol is too small, it can be feared that the water content in the preparation cannot be maintained (Aulton, 2007).

Based on the theories above, the optimum area of propylene glycol will be in the range of approximately 5% -30%. This study uses 6%. Other materials used this time include glycerin and nipagin as preservatives, TEA as an alkaline agent, neutralyzing agent that helps form the gel and aquadest character (Rowe et.al, 2009). Base optimization is done by organoleptic test, homogeneity test, pH test, viscosity test, and spreadability test.

Organoleptic testing is done by observing the shape, color, and odor. This test aims to see the quality and stability of the preparation which includes the shape, odor, and color of the preparation. If there is no change in shape, color and odor in the preparation for 48 hours after the preparation is made, until during one month of storage, then the preparation can be categorized as having a fairly good quality and stability (although it must be tested again at a later stage).

The results showed that all concentrations of white, yellowish, thick and odorous putat extract. The color of the gel is not clear because of the high levels of saponins. Homogeneity testing was carried out using two pieces of glass objects.

Homogeneous preparations are preparations in which there are no beads from the material used. The test results show that the preparations are homogeneous but there are bubbles generated during the manufacturing process using a stirer. The higher the concentration of putat air extract, the more bubbles. This is also due to high saponin levels.

The pH test shows that the ideal gel preparation for topical preparations according to British Pharmacopeia is between pH 6-8. The highest pH is found in formulas with a concentration of putat extract 1%. Formula with a concentration of putat extract 3%, 5% and 7%, its pH 6. This gel preparation

is still suiTable for use in treating wounds on the skin. If a topical preparation has a pH range that does not match the pH of the skin, then the preparation has the potential to cause irritation and erythema to its users.

Gel base viscosity was measured at a speed of 0.1 rpm for 30 seconds. According to Indonesian National Standars 16-4399-1996, the standard viscosity value for gel preparations is 6000-50000 cP or 6-50 Pa.S. Viscosity measurement results for the entire formula, resulting in a value that is included in the standard that is 9000-10500 cP. The research of Srividya et al (2001) describes corbopol 940 as a gel forming agent oflaxacin antibacterial agent in combination with hydroxypropyl methylcellulose (Methocel E50LV) which acts as a viscosity enhancing agent. The formulation developed is a therapy that is effective, stable, non-irritating and provides continuous drug release over an 8 hour period.

Sari's research (2016), aims to find out the right comparison between 940 carbohydrate gel base and hydroxypropyl methylcellulose (HPMC) on the stability of physical properties of extract gel and methanol fraction of kesum leaves with Simplex Lattice Design (SLD) method, there is no significant difference between the properties physical extract gel and methanol fraction of kesum leaves (*Polygonum minus* Huds.).

5 CONCLUSIONS

Based on the organoleptic test, the four formulas are semi solid, yellowish-white, thick and odorless. Homogeneity testing, homogeneous preparations but there are bubbles The higher the concentration of putat air (*B. racemose*) extract, the more bubbles as well as the color of the yellowish gel. This is also due to high saponin levels. The pH test shows it is ideal for topical preparations, which is between pH 6-6.2. The highest pH is found in formulas with a concentration of putat air (*B. racemose*) extract 1%. Viscosity measurement results for the entire formula, resulting in a value that is included in the standard that is 9000-10500 cP. Based on the physical essence, this gel preparation is still suiTable for treating wounds on the skin.

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