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Formulation and Activity of Gel Containing Nanoparticles of Javanese Turmeric Extract as Antiacne

(Formulasi dan Aktivitas Gel yang Mengandung Nanopartikel Ekstrak Temulawak sebagai Antiacne)

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Abstract: Javanese turmeric is one of the Indonesia's authentic plant that has many benefits, antimicrobial effect is one of them. Curcuminoid and xanthorrhizol contents are responsible for its antimicrobial activity. Acne vulgaris is one of skin's disorder that caused by bacteria, the major cause is *Propionibacterium acnes.* This study aimed to compare antimicrobial activity difference between nanoparticle and extract gel. Javanese turmeric was extracted and then formulated into nanoparticles. Javanese turmeric extract and its nanoparticles were then formulated in gel preparation. Gel preparations were evaluated physically (organoleptic, homogeinity, spreadibility, and viscosity and rheology), chemically (pH value), and tested for their antimicrobial activity. Gel evaluations showed that both formula (nanoparticle and extract gel formula) did not show any discoloration and still homogeny. Extract gel formula had viscosity about 1540–1600 Ps, while nano extract gel had viscosity in the range of 487.63–501.01Ps. Extract gel formula had spreadability in the range of 51.75-53.35 mm, while nano extract gel has viscosity in the range of 65.125-72.75 mm. Extract gel formula had pH value in the range of 5.98–6.02, while nano extract gel had pH value in the range of 5.88–5.93. Extract gel formula has inhibition zone in the range of 10.0 mm–10.3 mm, while nanoextract gel has inhibition zone in the range of 13.0 mm–13.4 mm. Based on statistical paired sample t-test analysis, nano extract gel formula was significantly different from extract gel formula in antimicrobial activity.

Keywords: nanoparticle, javanese turmeric, gel, antiacne, *Propionibacterium acnes.*

Abstrak: Temulawak adalah salah satu tanaman asli Indonesia yang memiliki banyak manfaat, salah satunya adalah efek antimikroba. Kandungan curcuminoid dan xanthorrhizol bertanggung jawab atas aktivitas antimikroba. Acne vulgaris adalah salah satu kelainan kulit yang disebabkan oleh bakteri, penyebab utamanya adalah *Propionibacterium acnes*. Penelitian ini bertujuan untuk membandingkan perbedaan aktivitas antimikroba antara nanopartikel dan ekstrak gel. Temulawak diekstraksi dan kemudian diformulasikan menjadi partikel nano. Ekstrak temulawak dan nanopartikelnya kemudian diformulasikan dalam sediaan gel. Sediaan gel dievaluasi secara fisik (organoleptik, homogenitas, spreadibility, dan viskositas dan reologi), secara kimiawi (nilai pH), dan diuji aktivitas antimikroba nya. Evaluasi gel menunjukkan bahwa kedua formula (nanopartikel dan ekstrak ekstrak gel) tidak menunjukkan perubahan warna dan masih homogen. Formula gel ekstrak memiliki viskositas sekitar 1540–1600 Ps, sedangkan gel ekstrak nano memiliki viskositas pada kisaran 487,63-501,01Ps. Formula gel ekstrak memiliki daya sebar dalam kisaran 51,75-53,35 mm, sedangkan gel ekstrak nano memiliki viskositas pada kisaran 65,125-72,75 mm. Formula gel ekstrak memiliki nilai pH di kisaran 5,98-6,02, sedangkan gel ekstrak nano memiliki nilai pH di kisaran 5,88-5,93. Formula gel ekstrak memiliki zona hambat pada kisaran 10,0 mm - 10,3 mm, sedangkan nanoextract gel memiliki zona hambat pada kisaran 13,0 mm - 13,4 mm. Berdasarkan analisis uji-t sampel berpasangan statistik, formula gel ekstrak nano berbeda secara signifikan dari formula ekstrak gel dalam aktivitas antimikroba.

Kata Kunci: nanopartikel, temulawak, gel, antiacne, *Propionibacterium acnes.*

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INTRODUCTION

THE USE of natural medicines has long been known and used by the people of Indonesia long before the introduction of modern medical systems. With the increasing price of chemical drugs and the increasing number of antibiotics that are resistant to many microbes, the public begins to look back to natural medicines which are considered to have a more affordable price and smaller side effects compared to chemical drugs, and can be used as an alternative to finding new antibiotics which is not resistant[1,2].

Temulawak is one of the many medicinal plants found in Indonesia, and the only part of the plant that is used for treatment is the rhizome. According to several studies that have been carried out, ginger rhizome has potential as an active antimicrobial agent against several Gram-positive and Gram-negative bacteria, so it is interested in conducting further research on the antibacterial activity possessed by ginger rhizome[3]. Several studies have shown the phenol component in ginger to have antibacterial activity acting on the membrane and cell wall of bacteria.

Nanotechnology is technology that allows an object to be nano-sized. Today, nanotechnology is used as a sensor, delivering drugs to targets, and introducing gene systems[4]. The benefits of nanoparticles are mainly in the pharmaceutical world as drug delivery so that the drug will be absorbed in a specific place or directly to the expected target cell. Extract nanoparticles are extracts that are modified in such a way with certain carriers so that they have better properties, for example providing the desired therapeutic effect more quickly. Extract nanoparticles provide a solution to the problem of low drug efficacy due to the inability of the active substance to reach the therapeutic site of the organ[5,6].

Acne vulgaris (acne) is one of the skin problems that is often experienced by humans, especially in adolescents and adults. The emergence of acne starts from inflammation of the skin, where the oil glands produce excess sebum and blockage of the oil gland and the formation of blackheads (whiteheads). When blackheads enlarge, open blackheads (blackheads) will form and emerge to the surface of the skin opening pores and then interact with the bacterias that cause acne, namely *Propionibacterium acnes, Staphylococcus aureus, and Staphylococcus epidermidis*.

Antibacterial activity of extracts and nanoparticles of Javanese turmeric (temulawak) extract were compared and then formulated into gel preparations on the basis of carbopol 940 so that it can be applied to treat acne and gel preparations were tested for their activity in inhibiting the growth of *Propionibacterium acnes*. Temulawak extract concentration was chosen for gel preparations by 0.5%.

MATERIAL AND METHODS

MATERIAL. Javanese turmeric (*Curcuma xanthorrhiza* Roxb), etanol 96% and 70%, chitosan (Sigma Aldrich), natrium tripolyphosphate, carbopol 940, triethanolamine, prophylenglicol, dinatrium EDTA, methyl paraben, prophyl paraben, natrium metabisulfit, NaCl 0.9% steril solution, aquadest, bacteria of *Propionibacterium acnes*, chloramphenicol **Instrument.** Glassware, analytical scales, socket number 4 and 18, macerator, filter paper, vacuum rotavapor, Transmission Electron Microscope (JEOL 1080), Particle Size Analyzer, Zetasizer, homogenizer, viskometer (Brookfield DV II+ PRO), pH meter (Hanna Instrument), inkubator (Memmert), vortex, autoclaf, anaerobic jar (Oxoid), LAF room, sterile disc paper, sterile swab.

METHODS. Javanese Turmeric Extract Preparation. Temulawak rhizome extract was prepared by maceration technique, using 96% ethanol solvent. A total of 900.80 grams of ginger rhizome simplicia powder macerated by stirring with 96% ethanol for the first 6 hours, then allowed to stand for 18 hours. The filtrate obtained was filtered then collected. The process was repeated 10 times then the collected filtrate was concentrated with a vacuum evaporator until a thick extract was obtained.

Nanoparticles Preparation. One gram of chitosan was dissolved in 100 mL of 1% glacial acetic acid using a magnetic stirrer to obtain a chitosan concentration of 1%. As much as 500 mg of temulawak ethanol extract added mixed solvent (5 mL Capmul, 10 mL 70% ethanol, 10 mL propylene glycol, 5 mL glycerin), 5 mL tween 80, and 5 mL aquadest. Then 5% chitosan solution was added as much as 5 mL so that the concentration of chitosan was 0.1%. The mixture is stirred using a magnetic stirrer for 10 minutes. Furthermore, dropping with 5 mL of 0.2% Na-TPP drops at a rate of 1 drop / 3 seconds with a burette and in a magnetic stirrer rpm 300 to form nanoparticles which are characterized by homogeneous turbidity. Then stay on the magnetic stirrer for 15 minutes to obtain a stable solution of temulawak extract nanoparticles.).

Formulation of Gel. Carbopol 940 was developed in 30 mL of distilled water for 24 hours, then added triethanolamine gradually while homogenized with a homogenizer to form a gel base. Methylparaben and prophylparaben were dissolved in a portion of prophylene glycol, then added with sodium EDTA and sodium metabisulphite which had previously

been dissolved in part of the aquadest, then put into a mixture of gel bases. Temulawak ethanol extract or the extract nanoparticles were added to the mixture while stirring with homogenizer until homogeneous at a speed of 200 rpm. Formulation of gel shown in Table 1.

Tab1e 1. Gel Formulation.

Excipient	Bobot (% b/b)		
	Blank gel	Formula with extract	Formula with nanoextract
Ethanol extract of Java turmeric	-	0.5	-
Nanoparticle Java turmeric extract*	-	-	50 mL
Carbopol 940	0.75	0.75	0.75
Propylen glikol	15	15	15
Triethanolamin	0.75	0.75	0.75
Natrium metabisulfit	0.1	0.1	0.1
Dinatrium EDTA	0.05	0.05	0.05
Metil paraben	0.03	0.03	0.03
Propil paraben	0.01	0.01	0.01
Aquadest ad	100	100	100

*50 mL of temulawak nano extract is equivalent to 0.5% of ginger extract

Gel Evaluation. The gel that has been made is evaluated at room temperature for 4 weeks of storage (0, 1, 2, 3, and 4 weeks), which includes: phsycal evaluation (organoleptic, homogenity, viscosity dan rheology, spreading coefficience and pH). .

Antiacne Activity Test of Gel Containing Javanese Turmeric Extract and Its Nanoparticles. The antimicrobial activity of extract gel and temulawak extract nanoparticle gel were carried out on *Propionibacterium acnes* test bacteria. The sterile swab was dipped in a bacterial suspension and then dried by attaching the swab to the tube wall, and swabed to the blood agar. Furthermore, the test solution was made by weighing 1 gram of extract gel or ginger extract nanoparticles then dissolved in 3 mLsterile aquadest (equivalent to 0.5% extract). Sterile disc paper was immersed in the test solution. Disc paper that had been saturated with the test solution was placed on the surface of the media. After that, the media was incubated at 35-37 °C for 24 hours under anaerobic conditions. Observed and measured DDH formed. Observations were made by measuring the diameter of the inhibitory power (DDH) after incubation. The formation of DDH is marked by the formation of clear zones around the discs. From the data obtained a graph is made to see and compare the antibacterial power of the test sample in inhibiting bacterial growth[8].

Data Analysis. The data obtained were analyzed by paired t-test (paired sample t test) using the SPSS program to determine the presence / absence of significant differences between the antiacne activity of temulawak extract and temulawak extract nanoparticles when they were formulated into a gel preparation formulation.

RESULT AND DISCUSSIONS

Javanese Turmeric Extract Preparation. The produced extract was viscous with the characteristic as shown in Table 2.

Table 2. Identification of simplisia and extract Java turmeric (*Curcuma xanthorrhiza* Roxb.).

Identification	Results
Foreign organic matter	0.46 %
Determination of the degree of fine powder simplicia	qualify
Rendemen	14.36 %
DER-native	6.96

Nanoparticles Preparation. Particle size measurements are carried out to ascertain whether nanoparticles have been made to have sizes that fall within the range of nanoparticle categories. Based on the results of the examination, the nanoparticles made have an average sizeof under 100 nm. Potential measurements are carried out to determine the load that is inside the nanoparticles where this value is related to the nanoparticle system that is formed. A nanoparticle system that is approved stable has many of the same charges as the particles will replace each other and no particle aggregation occurs. If in one

nanoparticle system has a different charge between the particles, there will be an aggregation that causes these particles to become unusable nanoparticles that can be combined with the formation of aggregate deposits. Based on the examination results, the nanoparticles made have a potential zeta with negative value. Most of these nanoparticles are more neutral, but nanoparticles that are formed are relatively stable in their formula composition containing many stabilizing components.

Antiacne Activity Test. Based on the results of activity tests, ginger extract nanoparticles have better activity than temulawak extract. This is caused by nanoparticles that can diffuse better into the test microbes so that more microbes were inhibited which were marked by the clear zone produced. Antiacne activity test shown in Table 3.

Tab1e 3. Antiacne activity test.

Sample	Average of inhibition zone diameter (mm)
sitif control (kloramfenikol)	15
Java turmeric extract	9.8
Java turmeric nanoparticle extract	11.23
Blank gel	0
Gel of Java turmeric extract	10.13
Gel of Java turmeric nanopartikel extract	13.27

Organoleptic Evaluation. Organoleptic evaluation and homogeneity for 0 until 4 weeks give formulation of gel still stable. The viscosity of the extract gel is lower than the blank gel because the extract gel contained curcuma extract dissolved in propylene glycol so that it can reduce the viscosity value. In addition, Java turmeric extract has an acidic pH (extract pH = 5) so that the resulting gel preparation will have a lower pH than the blank. Nano-extract gel has the lowest viscosity than the blank gel and gel extract because nano-extract in liquid form was directly put into the gel preparation. For the gel flow characteristics, all three preparations have pseudoplastic – thixotropic flow properties. The greater the viscosity, the spread power decreases. The blank gel had the smallest dispersal power due to its high viscosity value so that its spread ability was relatively low. The pH of nano gel preparations has the lowest value compared to blank gel and gel extract. This matter was caused by the nano extracts are acidic because of the content of chitosan. Organoleptic evaluation shown in Table 4.

Tab1e 4. Identification of gel formulations.

Identification	Blank gel	Gel of Java turmeric extract	Nanoparticle gel of Java turmeric extract
Organoleptic	Semisolid, colorless, odorless	Semisolid, light yellow, odorless	Semisolid, orange yellow, odorless
Homogenitas	Homogen	Homogen	Homogen
Viskosity dan Rheology	1566.67 ± 12.47 Ps	1543.33 ± 12.47 Ps	473.21 ± 15.11 Ps
Spreading coefficience	2075.46 ± 38.54 mm^2	2259.62± 35.84 mm^2	4030.47 ± 89.69 mm^2
pH	6.10 ± 0.02	6.10 ± 0.02	5.88 ± 0.04

CONCLUSIONS

Antiacne activity of temulawak nano extract was better than temulawak extract. Temulawak extract gel and temulawak extract nanoparticle gel have better antiacne activity compared to the extract and nanoparticle extract alone. Thereby, the gel is a great potential dosage form to be developed for both the extract and the nanoparticles.

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