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Formulation And Evaluation Of *Centella Asiatica*, L. Urban Gel Preparation As An Anti-Acne Agent

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Abstract:
Background*: Centella asiatica L. Urban extract has the potential to inhibit the growth of Propionibacterium acne bacteria. Centella asiatica extract is prepared as a gel to make it easier and more convenient to use in the treatment of acne.*
Materials and Methods*: Centella asiatica L. Urban extract was made into the gel in 5 formulas by varying the concentration of each extract, 0% (F0) as a control; 1.25%(F1); 2.5%(F2); 5.0%(F3); and 10.0%(F4). The gelling agent used was Carbopol. Organoleptic, pH, viscosity, spreadability, adhesion, stability using the freeze-thaw technique, and syneresis, antimicrobial activity were all assessed in gels.*
Results*: The results showed a homogeneous gel preparation, spreadability 4.90-5.17 cm, adhesion 3.64-4.96 seconds, pH 5.85-5.91, viscosity 31186-34933 cP. In the freeze-thaw cycling test, neither pH nor viscosity significantly decreased (p>0.05). The results of the antimicrobial activity test against P. acne bacteria showed that the inhibition zone of F0 - F4 was 0; 9.66; 9.66; 10; and 10.33 cm.*
Conclusion: *Centella asiatica L. Urban extract can be made into gel preparations and shows a stable preparation and has activity against P. acne bacteria.*
Key Word*: Centella asiatica; Gel; Anti-acne*

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I. Introduction

Acne vulgaris or what is usually called acne is a chronic obstructive and inflammatory skin disease that occurs in pilosebaceous and often occurs in adolescents[1]. Acne vulgaris (henceforth acne) was determined to be the eighth most prevalent skin disease in the 2010 worldwide Burden of Disease Study, with an estimated global prevalence (for all ages) of 9.38%. Acne prevalence varies by country and age group, with estimates ranging from 35% to close to 100% of adolescents with acne at some point[2]. *Propionibacterium acne* is one of the bacteria that causes acne. This bacterium is a normal flora found on the skin but can cause opportunistic infections which will produce lipase as a contributor to the formation of acne[3].

Antibiotics may be employed to treat acne[4]. However, the antibiotic class has disadvantages. One of them may result in bacterial resistance[5] as well as expensive pricing. Therefore, to avoid the disadvantages of using antibiotics, natural ingredients such as *Centella asiatica* are used as an alternative in treating acne[6]. *Centella asiatica* extract can inhibit the growth of bacteria such as *P acne*[7]. *Centella asiatica* extract can be used for acne treatment in the gel dosage form.

Gel dosage forms have been widely used to deliver drugs such as antibiotics in treating acne[8–11]. This is because the gel dosage form has several advantages including being comfortable, not sticky, and a cold sensation on the skin; easy to spread [12]. One of the most widely used gelling agents is Carbopol[13–16]. Therefore, in this study, *Centella asiatica* extract was prepared in a gel dosage form using a Carbopol base by varying the concentration of *Centella asiatica* extract.

II. Material And Methods

The step of the research included material collection, extract characterization, formulation, and evaluation including organoleptic tests, physical tests (viscosity, pH, spreadability, adhesion), stability tests (Freez-Thaw method), and antimicrobial activity tests.

Materials: *Centella asiatica* extract obtained from PT. Lansida. While the excipients were obtained from PT. Kimia Market and PT. Subur Kimia Jaya with pharmaceutical grade quality. *Propionibacterium acne* bacteria were obtained from the UNPAD microbiology laboratory.

Methods: Research using experimental methods in the laboratory which consists of formulation and evaluation

Extract characterization: *Centella asiatica* extracts were characterized using standard procedures[17] to determine of phytocompound group in the extract which included tannins, saponins, and flavonoids.

Formulation: extract gel is made in 5 formulas as shown in Table 1. Extracts and excipients were weighed according to the formula. Carbopol 940 was dissolved in water and then trietanolamine was added until a gel mass was formed. Glycerin and DMDM hydantoin were added to the gel mass that had been formed, then distilled water was added and stirred until homogeneous[13]

Table no 1: *Centella asiatica* extracts formulas's

No	Ingredient	Formula				
		F0	**F1**	**F2**	**F3**	**F4**
1	Extractct (%)	-	1,25	2,5	5,0	10,0
2.	Carbopol 940 (%)	2	2	2	2	2
3.	Trietanalamine (%)	1	1	1	1	1
4.	Glicerine (%)	20	20	20	20	20
5.	DMDM Hydantoin	1	1	1	1	1
6.	Aquades	add. 100 ml	add. 100 ml	add. 100 ml	add. 100 ml	add. 100 ml

Evaluation: *Centella asiatica* extract gel was evaluated including organoleptic, physical properties, stability, and antimicrobial activity.

Organoleptic: The *Centella asiatica* extract gel was observed visually including consistency, color, and odor[18]

Physical properties: The physical properties of *Centella asiatica* extract gel were measured including pH, viscosity, spreadability, and adhesion force. The pH of *Centella asiatica* extract gel was determined using a pH meter (Metler Toleddo®). The viscosity of *Centella asiatica* extract gel was measured using a Brookfiled viscometer. Spreadability study: the gel (500 mg) was placed right in the middle of the glass, then a coverslip was placed on it and left for 60 seconds, then the diameter of the gel was measured. Furthermore, the weight (50 g) was placed on the glass and allowed to stand for 60 seconds, then the diameter of the gel was measured. The procedure was repeated with increasing weights of 100 g, 150 g and 200 g[19]. Adhesion force study: the gel was placed between two glass objects and then pressed on top using a weight weighing 1 kg for 5 minutes. The glass object is mounted in the test apparatus and released using an 80 g weight. The time the two glass objects were released was recorded[20].

Stability test: Samples were stored in the oven (45±2°C) for 24 hours then transferred to the refrigerator (4±2°C) for 24 hours. The procedure was repeated for the same sample for 3 cycles. The physical properties of the gel were measured for each cycle

Antimicrobial activity study: The bacterial suspension (0.1 ml) was put into a petri dish and then Mueller-Hinton added evenly over the entire surface of the petri dish. Gel samples 50 mg (F0, F1, F2, F3, F4, and clindamycin gel) were dissolved in 5 ml of DMSO. Sterile disc paper that had been immersed in the sample was placed on the surface of solid agar media (Mueller-Hinton). Petri dishes were incubated for 18-24 hours at 37°C. The inhibition zone formed was measured[21].

III. Result

Extract characterization: The results of extract characterization were shown in table 2

Table no 2: Extract characteristic

Phytocompounds groups	Reaction with	positive reaction	Results
Flavonoid	+ Amil alcohol	The orange color on the amyl alcohol layer	+
Saponin	+ HCl 2 N	Stable Foam	+
Tannin	+ $FeCl_3$	Black Green Color	+

Organoleptic: The results of organoleptic observations were shown in table 3

Table no 3: Organoleptic properties of *Centella asiatica* extract gel

Parameter	F0	F1	F2	F3	F4
Color	-	+	++	++	+++
Odor	-	-	+	+	+
The cold sensation when polished	+	+	+	+	+
semisolid consistency	+	+	+	+	+

Physical properties: The results of physical properties were shown in table 4

Table no 4: Physical properties of *Centella asiatica* extract gel

Physical properties	Formula					References
	F0	F1	F2	F3	F4	
pH	5.85 ± 0.47	5.95 ± 0.54	5.67 ± 0.44	5.85 ± 0.29	5.91 ± 0.53	4.5 – 6.5[22]
Viscosity (cP)	34066 ± 2497	34843 ± 1486	31186 ± 5300	34453 ± 254	34933 ± 1205	2000 - 50000[23]
Spreadability (cm)	4.90 ± 0.17	4.90 ± 0.26	4.97 ± 0.15	5.13 ± 0.15	5.17 ± 0.21	5 – 7[20]
Adhesion (s)	3.64 ± 0.99	4.45 ± 0.71	5.43 ± 1.64	4.60 ± 2.33	4 96 ± 1.48	more 1 s[20]

Stability test: The results of the stability studies were shown in table 4

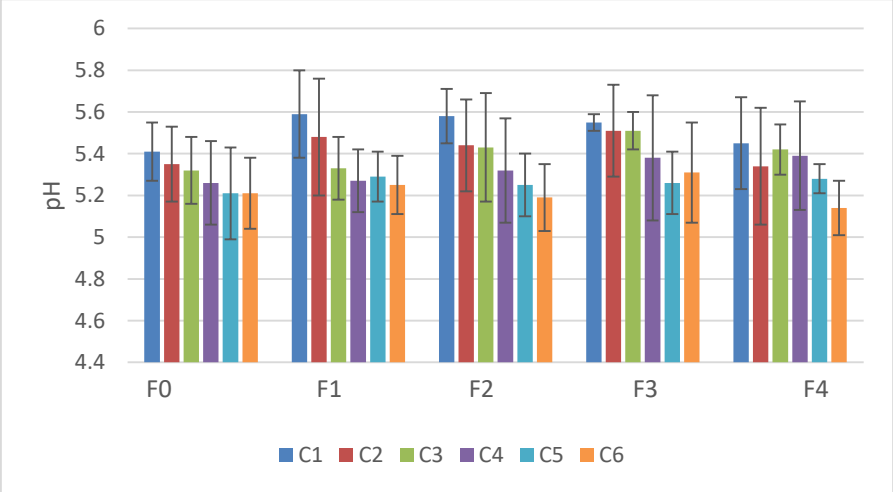

Fig. 1: Trend of change in pH from1st cycle (C1) to 6th cycle (C6) for each formula

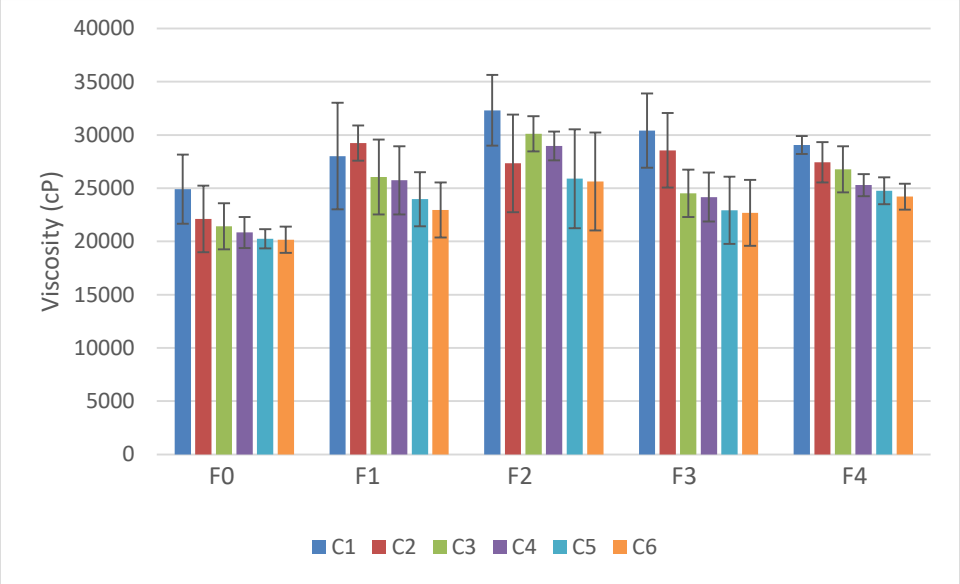

Fig.2: Trend of change in viscosity from 1st cycle (C1) to 6th cycle (C6) for each formula

Antimicrobial activity study: The results of the antibacterial activity test of Centella asiatica extract gel are shown in table no 5

Table no 5: Inhibition zone of *Centella asiatica* extract gel and clindamycin gel

Sample	Inhibition zone (mm)	Category	Reference
F0	0		≥ 20 mm (very strong) 11-19 mm (strong) 5-10 mm (moderate) < 5 mm (weak)
F1	9.7 ± 1.15	Moderate	
F2	9.7 ± 0.57	Moderate	
F3	10.0 ± 0.57	Strong	
F4	10.0 ± 1.73	Strong	
Clindamycin gel	24.6 ± 0.05	Very strong	

IV. Discussion

Phytocompound groups responsible for the antimicrobial activity of *Centella asiatica* are tannins, flavonoids, and saponins[24]. Therefore, in this study, the presence of these phytocompound groups was characterized. The results (Table no 2) showed that the tannins, flavonoids, and saponins were positively contained in the extract .

Carbopol is a polymer that is widely used as a gelling agent[13–16]. Carbopol can swell in an alkaline environment. Therefore, in this study, a pH regulator, namely triethanolamine, was used to swell Carbopol [13]. In addition, in this study glycerin was used as a moisturizer and DMDM hydantoin as a preservative[25]. Then the difference between the formulas (Table no 1) is the concentration of the extract (0% ; 1.25%; 2.5%; 5.0%; and 10,0%).

The organoleptic, physical properties, stability, and antibacterial activities of *Centella asiatica* extract gel were all evaluated. The results of organoleptic characterization (Tabel no 3) that all formulas produce a gel with a semi-solid consistency and cold sensation when polished. This is since all formulations employ the same concentration of Carbopol and glycerin. However, each formula has a varied level of color and odor strength. The strength of the color and odor depends on the extract's concentration. While the physical properties of *Centella asiatica* extract gel from all formulas showed results (Table no 4) that met the requirements for both pH, viscosity, spreadability, and adhesion. Physical properties, namely pH, need to be characterized to assess whether the gel is acceptable to the skin[26]. Meanwhile, spreadability and viscosity are factors in how easily a gel may be applied to the skin. While adhesion evaluates how long the gel remains in contact with the skin to allow the active ingredients in the gel time to work effectively.

Furthermore, the stability of the gel was evaluated using the freeze-thaw method. The freeze-thaw method is an accelerated stability study by storing samples at two extreme temperatures, namely 40ºC and 4ºC, and is carried out for several cycles[27]. The results of the study (Fig.1 and Fig.2) showed that there was a decreasing trend in pH and viscosity from the first cycle to the sixth cycle. However, when examined

statistically there was no significant difference in either (P>0,05) pH or viscosity from the first cycle to the sixth cycle. Therefore it can be concluded that both the pH and the viscosity were stable from the first cycle to the sixth cycle.

It is well known that *Centella asiatica* has antibacterial properties[28]. One of them is that it may inhibit the acne-causing *P acne* bacteria from growing[6]. Therefore, in this research, a study was conducted on the antimicrobial activity of *Centella asiatica* extract gel against *P acne* bacteria. Antimicrobial studies used the paper disc method because it is a simple method and suitable for *P acne* bacteria[29]. the results of the antibacterial study showed that F1 did not have antibacterial activity because it did not use extracts. while F1 - F4 had activity against *P acne* bacteria although not as high as clindamycin gel as a positive control. F1 (1.25% *Centella asiatica* extract) and F2 (2.5% *Centella asiatica* extract) are classified as moderately antibacterial, whereas F3 (5.0% *Centella asiatica* extract) and F4 (10.0% *Centella asiatica* extract) are classified as strong antibacterial.

V. Conclusion

Centella asiatica extract was made into a gel using Carbopol as a gelling agent. *Centella asiatica* extract gel meets the requirements of pH, viscosity, spreadability, and adhesion for all formulas. In addition, the gel maintained its stability through six cycles of accelerated stability testing employing the freeze-thaw method. *Centella asiatica* extract gel with concentrations of 5% and 10% could inhibit the growth of *P acne* bacteria with activity in the strong category.

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