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Pegagan Extract Anti-inflammatory Gel Formulation

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ABSTRACT: Pegagan (Centella asiatica L) is empirically used in the community as an anti-inflammatory. This study aims to formulate Pegagan extract in a gel preparation and determine the anti-inflammatory effect of the preparation based on the reduction in the volume of rat paw edema induced by carrageenan. Inflammation that occurs is measured using a plethysmometer. The results of the evaluation of preparations with organoleptic parameters, pH, viscosity, and dispersion at room temperature for 28 days for the 3 formulas made met the requirements. The results of the anti-inflammatory activity test on F3 with an extract concentration of 10% gave the best results with an inflammation percentage of 25.55%.
KEYWORDS: Antiinflammatory, Formulation, Gel, Pegagan.

I. INTRODUCTION

Inflammation is the body's natural response against harmful impulses and pathogens.The two stages of inflammation are acute inflammation and chronic inflammation.Acute inflammation, which is a component of innate immunity, is swiftly initiated by immune cells.But the second stage, chronic swelling, will develop if the edema doesn't go away.[2]Inflammation typically manifests as heat (color), swelling (tumor), pain (dolor), redness (rubor), and loss of organ function (functiolaesa).

Steroids and non-steroidal anti-inflammatory medications can be used clinically to treat inflammation (NSAIDs). The major medications for minimizing the negative consequences of inflammation are NSAIDs. Chronic NSAID use may have harmful consequences on the heart, gastrointestinal tract, and kidneys. Similar negative consequences such as hypertension, hyperglycemia, osteoporosis, and growth problems are brought on by corticosteroid medication therapy. Major issues with using synthetic medications that are now available are toxicity and recurrence. This makes it vital to hunt for safer medications. Nature has provided a variety of plants with therapeutic properties for a number of ailments, including inflammation.

[3]Pegagan is one of the plants with anti-inflammatory properties (Centella asiatica). A tropical plant called Pegagan can be found in lowlands as well as highlands that are 2500 m above sea level. Pegagan can grow in rice fields, damp fields, plantations, on the side of the road, and in other places. Depending on the area or nation in which it is found, the pegagan plant is known by a variety of names. [4,5]Pegagan has a number of active compound and performs a variety of functions, including antimicrobial, antidiabetic, antihyperuricemia, wound healing, and antioxidant. [6]This plant is used as a medicine because it has anti-inflammatory properties, boosts intelligence, and heals burns. Previous studies on gel formulations with 5% [7]Pegagan extract offered the best physical stability and satisfied the criteria for gel formulation evaluation. Another study has papaya leaves and gotu kola ethanol extract combined in a gel mixture as a wound healer. The findings demonstrated that mice's burn wounds healed more quickly the higher the extract content (.

Combining Pegagan and aloe vera extracts in wound healing gels for mice. The quickest rate of wound healing activity was at a concentration of 15%. Researchers now have the chance to create anti-inflammatory gel compositions using pegagan extract thanks to the numerous studies on the plant's extracts. [8]By choosing this topical preparation, you can avoid first-past metabolism, avoid stomach irritation, and avoid passing through the digestive system.[9]When compared to ointments, gel preparations have advantages as topical medications since the gel has good aesthetics, stable and isn't really sticky. [10]Drug components can be effectively delivered using gels.Additionally, the benefits of gel preparations include not leaving scars on the

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skin, giving off a cooling sensation, and being simple to apply uniformly.In this investigation, a gel preparation from the Pegagan extract (Centella asiatica L) will be developed as an anti-inflammatory preparation based on the description given above.

II. MATERIAL

Pegagan, 70% ethanol, carbopol, DMDM hydantoin, TEA, propylene glycol, aquadest, 1% carrageenan, and diclofenac Na gel were the substances utilized. Test animal: male rats (150–300 g).

Plant Determination

The purpose of the determination is to ensure that the pegagan sample obtained is true Centella asiatica. The determination process was carried out at the Plant Taxonomy Laboratory, Padjadjaran University.

Simplicia

[11]In order to get rid of any dirt on the plants, the process starts with wet sorting and washing, draining, and allowing them to dry at 50°C for five days.

Extraction

[11]Simplicia was blended and put through a 60 mesh sieve. Using a ratio of 1:10 (w/v) and 70 percent ethanol, the products were macerated for 36 hours. A rotary evaporator was used to filter and concentrate the maceration extract.

Extract Gel Formulation

The process of making Pegagan extract gel begins with weighing the ingredients according to table 1. Carbopol was dispersed in distilled water and crushed slowly until homogeneous. This mixture is added triethanolamine (TEA) slowly and crushed together until clear. DMDM hydantoin was added and ground until homogeneous. Propylene glycol is also added little by little, then crushed and added with distilled water simultaneously until a gel base is formed. In the last aqueous phase, Pegagan extract was added to the gel base and then ground until homogeneous.

Preparation Evaluation

Organoleptic Test

This is accomplished by observing the odor, texture, color.

Test of Homogeneity

The prepared gel is placed to the slide, covered with another slide, and checked for lumps or granules afterwards. [7]A excellent gel preparation has no lumps or grains and is uniformly spread.

Test of pH

An instrument called a pH meter is used to measure pH. An electrode is inserted into the sample, and the pH value measured by the pH meter is used to conduct the test. Gel formulations for topical application have a pH range of 4.5 to 6.5.

Spreadability Test

A good gel has a spread of 5-7 cm

Test for Viscosity

A viscometer is used to determine the viscosity value. The preparation's viscosity value will influence how it should be used on the skin as well as when it is taken out of the packaging. For easy-to-use preparations, a good viscosity ranges from 50 to 50 000 cP

Anti-Inflammatory Activity

This test was run to see how well the gel formulation inhibited the inflammatory process. Male rats weighing between 150 and 300 grams were the test subjects. Three groups of animals, each with three rats, were used. A Pegagan extract gel test group, a negative control group, and a positive control group of diclofenac sodium gel each made up the animal group. The animals were weighed and marked on the left leg prior to testing. The rat's left leg was then used as V0 to measure using a plethysmometer. The rat's left paw was then intraplanarly injected with 0.1 mL of 1 percent carrageenan. According to the group, the therapy was administered topically after an hour. For 360 minutes, the volume of the rats left leg was measured every 60 minutes with a Plethysmometer (Vt). [8]Following measurement, the method below is used to determine the percentage of inflammation. [13]The amount of inflammation created can be used to determine the effectiveness of antiinflammatory activity; the lower the amount of inflammation, the more effective the antiinflammatory activity.

$$\textbf{Inflammation percentage} = \frac{\textbf{Vt} - \textbf{V0}}{\textbf{V0}} \textbf{ x 100}\%$$

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III. RESULTS AND DISCUSSION

The results of the study showed that the sample was Centella asiatica (L.) Urb, a member of the Apiaceae family. This process is used to ensure that the plants being utilized have the proper identification and to guard against errors when gathering plant raw materials.

Producing simplicia has the dual goals of extending shelf life and maintaining the level of metabolites in plants so that they are resistant to damage. The obtained Pegagan plants are next subjected to wet sorting. In order to achieve the best materials, this technique is used to separate dirt and other foreign contaminants from simplicia materials. Additionally, the wet sorting procedure has the ability to lower the initial microbial population in simplicia. The following step is washing the plants under clean flowing water to remove any dirt or foreign objects. After being rinsed, pegagan is drained and cut. To minimize the particle size and hasten the drying process, chopping is used.

Drying with an oven can reduce the moisture content regularly in a relatively short time. High water content can be a medium for mold growth and also certain enzymes contained in cells so that they can decompose the active compounds present in simplicia. With drying, the water content will be reduced and the reaction of enzymatic decomposition of compounds can be prevented thereby increasing the shelf life of simplicia. Pegagan was macerated for 36 hours in a solution of 70% ethanol to extract the substance because it can best extract the active components in pegagan.Because it is simpler, requires less equipment, and does not include heating, the maceration method was chosen to prevent harm to the active ingredients found in pegagan.

Figure 1. Pegagan extract

Pegagan Extract Gel

The pegagan extract gel was made by varying the concentration of the active substance, namely 3%, 5% and 10%. Carbopol was chosen as the gelling agent because it is easily dispersed in water and with a small concentration it is able to form a gel base. Carbopol can bind the active substance strongly so that it will decrease the solubility which results in the effectiveness of the active substance being reduced. [18]For this reason, propylene glycol is added as a humectant which will improve the nature of carbopol in binding the active. Propylene glycol can also maintain the stability of the preparation by absorbing moisture from the environment and preventing the evaporation of water in the preparation. Propylene glycol can also play a role in moisturizing the skin so that the skin does not dry out. TEA is used as an alkalizing agent that can provide an alkaline atmosphere to carbopol so that it forms a thick and transparent gel base. DMDM hydantoin is used as a preservative to prevent the growth of microorganisms because the gel has a high water content and water is a medium for the growth of microorganisms. In the formula, the higher the concentration of pegagan extract, the darker the color of the gel produced.

Table 1. Pegagan Extract Gel

Ingredients	F1	F2	F3
Carbopol	1	1	1
DMDM hydantoin	1	1	1
Pegagan	3	5	10
Propylene Glycol	10	10	10
TEA	0,5	0,5	0,5
Aquadest add			

The gel that has been made was evaluated in the form of organoleptic, pH, viscosity, dispersion and homogeneity. Evaluation was carried out in stages starting from the day of manufacture or day 0, day 7, day 14, day 21 and day 28 to determine the stability of the preparation at room temperature storage. The three formulas that have been made have met the requirements for the evaluation of the preparations.For 28 days of storage at room temperature, the preparation's organoleptic evaluation was visible in the preparation's color, odor, and shape. The table demonstrates that there have been no physical changes to the preparation between the first day of formulation and day 28. Color, scent, and form did not change at F1, F2, or F3. The three formulas had

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a green hue, the distinctive pegagan smell, and a dispersed phase consistency.

Table 2. Organoleptics

	Color		Odor		Texture	
	0	28	0	28	0	28
F1	green	green	specific	specific	gel	gel
F2	green	green	specific	specific	gel	gel
F3	green	green	specific	specific	gel	gel

The homogeneity test findings revealed that from the beginning of production until 28 days of storage, there were no lumps or granules. This indicates that the gel has been created has good homogeneity and is in compliance with the gel preparation standards, which state that there should be no grains visible. Figure 2 below shows the homogeneity of F, F2 and F3.

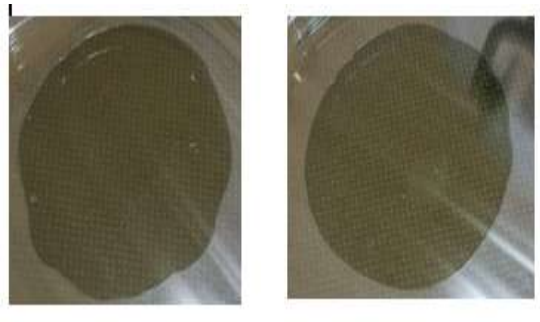

Figure 2. Homogeneity

The pH test is carried out to determine whether the preparation made has a pH that is suitable for the skin or not. In accordance with the purpose of making a gel to be applied to the skin. If the pH is too alkaline it will cause the skin to become dry and if it is too acidic it will cause irritation. The pH test results can be seen in table 3. Even though there is a change in pH in the preparations made, the 3rd formula still meets the skin pH requirements, namely 4.5-6-5 from the first day of formulation to 28 days of storage.

Table 1. pH

Day	pH		
	F1	F2	F3
0	5,32±0,04	5,50±0,01	4,90±0,05
7	5,26±0,01	5,34±0,01	4,82±0,01
14	5,23±0,01	5,35±0,04	4,77±0,02
21	5,22±0,01	5,30±0,02	4,78±0,01
28	5,21±0,01	5,29±0,01	4,80±0,005

The gel's spreadability was used to gauge how widely it would cover the skin after application. Table 4 displays the test results. For the three manufactured formulations, there was a shift in the test findings from the first day of production to the 28th day. Overall, nevertheless, the dispersion value remains within the acceptable range of 5-7 cm.

Table 2. Spreadability

Day	F1	F2	F3
0	5,93±0,09	5,03±0,05	5,20±0,08
7	5,50±0,08	5,10±0,14	5,33±0,17
14	5,33±0,05	5,10±0,08	5,03±0,05
21	5,53±0,05	5,13±0,05	5,13±0,12
28	5,40±0,08	5,07±0,09	5,20±0,16

The relationship between viscosity and dispersion value is inverse (Dambur et al., 2019). Table 5 displays the test results after 28 days of storage. The viscosity value is still within the acceptable range for gel preparations, which is between 2000
and 50,000 cP..

Table 3. Viscosity

Day	F1	F2	F3
0	10893,33	13626,67	12313
7	10813,33	13773,33	12440
14	10173,33	13780	12800
21	10240	13240	12586,67
28	9880	13413,33	12293,33

Carrageenan induction is used in anti-inflammatory research on rat paws. In cases of severe inflammation, carrageenan works as an edema-forming substance. Carrageenan stimulates inflammatory mediators that lead to inflammation when it enters the body. The body's antibodies fight the impact of the antigens that enter the body and cause this inflammation. Male rats were chosen so that the hormone estrogen wouldn't disrupt the inflammatory process (Nurcholis&Sulastri, 2018). Determination for anti-inflammatory properties was done on the three formulations. Additionally, tests using Na-diclofenac gel, a positive control that ensures anti-inflammatory action, were conducted. To guarantee that there is no anti-

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inflammatory activity, there is also a negative control. The results of the anti-inflammatory activity test can be seen in Figure 3.

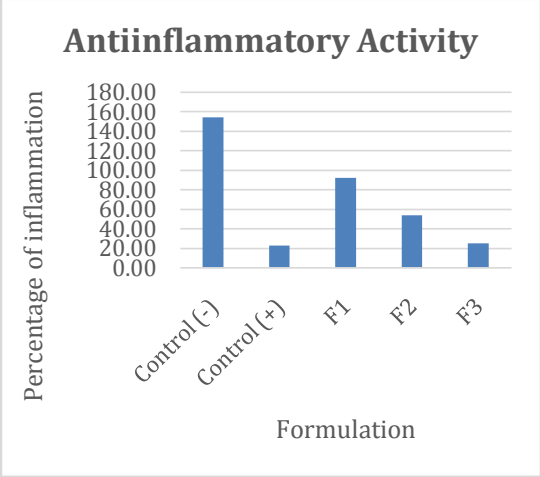

Figure 3. Antiinflammatory activity in 360 minute

The percentage of inflammation in the negative control was still significant. This is due to the absence of substances that can inhibit inflammatory mediators, so inflammation occurs significantly. When compared the formulas F1, F2 and F3 showed a decrease in the percentage of inflammation. But not as low as a positive control. This is proportional to the increased concentration of Pegagan extract from F1, F2, and F3.

IV. CONCLUSION

The Pegagan extract gel preparation that has been made shows storage stability at room temperature for 28 days of storage. This can be seen from the organoleptic parameters, pH, viscosity, dispersion, and homogeneity that meet the requirements for evaluating gel preparations. The results of the anti-inflammatory activity test showed that F3 gave the best results for anti-inflammatory activity with an inflammation percentage of 25.55%.

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