

Formulation and Physicochemical Characterization of *Euphorbia tirucalli* Broken Twig Extract Gel

Formulasi dan Uji Karakterisasi Fisikokimia Gel Ekstrak Ranting Patah Tulang (*Euphorbia tirucalli*)

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Abstract

Euphorbia tirucalli L. twigs contain various secondary metabolites, including alkaloids, flavonoids, tannins, saponins, and steroids, which have potential antibacterial activity. This study aimed to evaluate the effect of different concentrations of *Euphorbia tirucalli* twig extract on the physicochemical characteristics of gel formulations. Three gel formulations containing 15% (F1), 20% (F2), and 25% (F3) extract were prepared and evaluated for organoleptic properties, pH, spreadability, adhesiveness, homogeneity, and irritation potential. Quantitative data were analyzed using One-Way ANOVA at a 95% confidence level ($\alpha = 0.05$). The results showed that all formulations produced homogeneous, semi-solid gels with a soft texture and did not cause skin irritation. The pH values ranged from 5.14 ± 0.193 to 5.67 ± 0.011 , which were within the physiological skin pH range. The spreadability values ranged from 5.08 ± 0.310 to 5.19 ± 0.209 cm, meeting the acceptable criteria for topical gel preparations. All formulations exhibited good adhesiveness, with adhesion times exceeding 4 seconds (4.45 ± 1.673 to 4.46 ± 1.075 seconds). Statistical analysis indicated that variations in extract concentration had no significant effect on pH, spreadability, adhesiveness, homogeneity, or irritation parameters, with all p-values greater than 0.05. However, increasing extract concentration resulted in a visually darker gel color. In conclusion, all gel formulations fulfilled the physicochemical requirements for topical preparations, and extract concentrations ranging from 15% to 25% did not significantly affect the physicochemical characteristics of the gel, indicating their potential for further development as a natural topical dosage form.

Keywords: *Euphorbia tirucalli*, formulation gel topical, physicochemical characteristics, and extract concentration variation.

Abstrak

Ranting patah tulang (*Euphorbia tirucalli* L.) mengandung berbagai senyawa metabolit sekunder seperti alkaloid, flavonoid, tanin, saponin, dan steroid yang berpotensi sebagai antibakteri. Penelitian ini bertujuan untuk mengevaluasi pengaruh variasi konsentrasi ekstrak ranting patah tulang terhadap karakteristik fisikokimia sediaan gel. Gel diformulasikan dalam tiga variasi konsentrasi ekstrak, yaitu 15% (F1), 20% (F2), dan 25% (F3), kemudian dilakukan pengujian organoleptis, pH, daya sebar, daya lekat, homogenitas, dan iritasi. Data dianalisis menggunakan uji One-Way ANOVA pada tingkat kepercayaan 95% ($\alpha = 0,05$). Hasil penelitian menunjukkan bahwa seluruh formulasi menghasilkan gel yang homogen, bertekstur semi padat, lembut, dan tidak menimbulkan iritasi pada kulit. Nilai pH sediaan berada pada rentang $5,14 \pm 0,193$ hingga $5,67 \pm 0,011$ yang masih sesuai dengan pH fisiologis kulit, sedangkan daya sebar berada pada rentang $5,08 \pm 0,310$ hingga $5,19 \pm 0,209$ cm dan memenuhi persyaratan sediaan topikal. Daya lekat seluruh formulasi berada di atas 4 detik, yaitu antara $4,45 \pm 1,673$ hingga $4,46 \pm 1,075$ detik yang menunjukkan kemampuan adhesi yang baik pada permukaan kulit. Hasil analisis statistik menunjukkan bahwa variasi konsentrasi ekstrak tidak memberikan pengaruh yang signifikan terhadap pH, daya sebar, daya lekat, homogenitas, maupun iritasi dengan nilai signifikansi seluruh parameter $p > 0,05$. Meskipun demikian, peningkatan konsentrasi ekstrak menyebabkan warna gel menjadi lebih pekat secara visual. Berdasarkan hasil penelitian dapat disimpulkan bahwa seluruh formulasi gel ekstrak ranting patah tulang memenuhi persyaratan fisikokimia sediaan topikal dan variasi konsentrasi ekstrak 15–25% tidak memengaruhi karakteristik fisikokimia gel secara signifikan, sehingga berpotensi untuk dikembangkan lebih lanjut sebagai sediaan topikal berbahan alam.

Kata Kunci: *Euphorbia tirucalli*, formulasi gel topikal, karakteristik fisikokimia, dan variasi konsentrasi ekstrak.



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Introduction

A wound is a condition characterized by damage to body tissues caused by physical, chemical, or biological trauma and remains a common health problem worldwide. Improper wound management can delay the healing process and increase the risk of infection, potentially leading to more severe complications [1]. In clinical practice, 0.9% sodium chloride (NaCl) solution is commonly used as a wound-cleansing agent; however, it lacks antimicrobial activity and therefore cannot eliminate microorganisms present in the wound area [2]. Consequently, there is a growing need for alternative therapeutic agents that not only facilitate wound cleansing but also possess antimicrobial properties.

In Indonesia, injuries remain a significant public health concern. Based on the 2018 Basic Health Research (Riskesmas), the prevalence of injuries reached 8.2%, with open wounds being among the most frequently reported cases [3]. Limited access to healthcare services in certain regions has encouraged the utilization of traditional medicinal plants as alternative treatments. The use of traditional medicine in developing countries is estimated to account for 70–95% of healthcare practices, highlighting its important role in community-based healthcare systems [4].

One medicinal plant that has been widely used in traditional wound treatment is *Euphorbia tirucalli* L., commonly known as the pencil tree or milk bush. Traditionally, its sap and twigs have been applied directly to wounds and bone injuries to promote healing [5]. Phytochemical studies have demonstrated that *Euphorbia tirucalli* contains various bioactive compounds, including alkaloids, flavonoids, tannins, saponins, and steroids [6]. Among these constituents, saponins exhibit antibacterial activity by disrupting bacterial cell membrane permeability, whereas tannins inhibit microbial growth through protein precipitation and membrane contraction mechanisms [7].

Previous studies have reported that *Euphorbia tirucalli* extract exhibits antimicrobial activity against several pathogenic microorganisms, including *Escherichia coli* and *Staphylococcus aureus*, as well as antifungal activity against dermatophytes [8]. In vivo investigations have also indicated its potential to accelerate wound healing, although the observed effects were not always statistically different from those of the control group [9]. These findings suggest that *Euphorbia tirucalli* possesses promising pharmacological properties that warrant further development into suitable pharmaceutical dosage forms.

Among topical dosage forms, gels are widely preferred because of their ease of application, cooling effect, non-greasy nature, and favorable drug-release characteristics [10]. Furthermore, gel systems provide good spreadability and adhesion on the skin surface, enhancing patient comfort and therapeutic effectiveness [11]. The quality and performance of a topical gel are strongly influenced by its physicochemical characteristics, including pH, spreadability, adhesiveness, homogeneity, and irritation potential [12]. Variations in the concentration of active ingredients may alter these properties and consequently affect the stability and acceptability of the formulation.

Although numerous studies have focused on the biological activities of *Euphorbia tirucalli*, research concerning the formulation and physicochemical characterization of its gel preparations remains limited. Most published studies emphasize antimicrobial and wound-healing activities without comprehensively evaluating formulation parameters. Therefore, this study was conducted to formulate *Euphorbia tirucalli* twig extract into a topical gel and investigate the effect of different extract concentrations on its physicochemical characteristics, including organoleptic properties, pH, spreadability, adhesiveness, homogeneity, and irritation potential. The findings are expected to contribute to the development of safe, effective, and stable herbal-based topical preparations for wound management.

Experimental Section

Materials and Equipment

Plant material used in this study was *Euphorbia tirucalli* twigs. Species identification and authentication were performed at the Center for Information and Development of Traditional Medicine, University of Surabaya (UBAYA), Indonesia, prior to extraction no. 1528/D.T/VII2023, sodium carboxymethyl cellulose (CMC-Na) as a gel base, glycerin as a humectant, propylene glycol as an additional solvent, methyl paraben as a preservative, and distilled water as the main solvent. All chemicals used had a pro analysis (pa) purity level and were obtained from trusted chemical distributors.

The equipment used included an analytical balance (Ohaus, USA), a digital pH meter (Hanna Instruments, HI2211), a hot plate stirrer (IKA C-MAG HS 7), a Pyrex beaker, a mortar and stamper, a spatula, a slide, and a spreader and adhesiveness meter. All equipment was calibrated before use to ensure the accuracy of the measurement results.

Sample Preparation and Extraction

Samples of *Euphorbia tirucalli* (bone-breaking plant) twigs were obtained from the surrounding area and identified to confirm species identity. The samples were cleaned of dirt, washed with running water, and then dried at room temperature until the water content reduced.

The dried sample was then cut into small pieces and extracted using a maceration method with 96% ethanol as a solvent. The maceration process was carried out for 3 x 24 hours with occasional stirring. The resulting filtrate was then filtered and evaporated using a rotary evaporator to obtain a thick extract. The extract was stored in a closed container at room temperature before use in the formulation.

Gel Preparation Formulation

The gel preparation is made in three variations of extract concentration, namely:

Table 1. Gel Formulation of Bone Fracture Plant Branch Extract

Material	Function	Range %	Gel Formulation %		
			F1	F2	F3
Bone Fracture Twig Extract	Active Ingredients		15	20	25
CMC-Na	Gelling Agent	3-6	5	5	5
Glycerin	Humectant	5-15	10	10	10
Propylene glycol	Preservative	15-30	15	15	15
Aquades ad	Solvent		50 ml	50 ml	50 ml

F1: 15% extract

F2: 20% extract

F3: 25% extract

The concentration of CMC-Na (5%) was selected based on preliminary formulation studies, which produced a gel with optimal viscosity, consistency, and spreadability characteristics suitable for topical administration (data not shown). The gel base was prepared by dispersing CMC-Na in distilled water until complete hydration was achieved. Methyl paraben was used as a preservative and was initially dissolved in propylene glycol at 60°C to enhance its solubility before incorporation into the gel matrix. Subsequently, glycerin and the methyl paraben-propylene glycol solution were added to the gel base and stirred continuously until a homogeneous mixture was obtained. The *Euphorbia tirucalli* twig extract was then gradually incorporated into the gel base under continuous stirring to ensure uniform distribution throughout the formulation. The entire mixture was further stirred until a smooth and homogeneous gel preparation was formed.

Characterization of Gel Preparations

The physicochemical characterization of the developed gel formulations encompassed a comprehensive panel of evaluative parameters to ascertain their quality, stability, and dermatological safety. Organoleptic assessment was performed qualitatively through visual and olfactory examination, with particular attention directed toward macroscopic attributes including coloration, odor profile, and textural consistency, all of which are critical determinants of patient acceptability and product elegance. The pH of each gel formulation was determined potentiometrically at ambient temperature using a pre-calibrated digital pH meter, with

triplicate measurements conducted to ensure analytical precision and reliability, given that pH values within the dermal-compatible range (typically 5.5–6.5) are imperative to prevent cutaneous irritation and maintain stratum corneum integrity.

Spreadability, a key rheological property influencing dose uniformity and therapeutic efficacy, was evaluated by quantifying the diameter of spread exhibited by a 0.5 g sample subjected to a standardized compressive load between two glass slides, thereby providing an indirect measure of the gel's ease of application and its potential for forming an even film over the application site. Adhesive strength, which reflects the formulation's residence time on the skin surface and consequently its drug bioavailability, was determined by measuring the detachment time of two slides separated by a 0.25 g gel layer under a fixed gravitational load, with a longer separation time denoting superior mucoadhesive or dermo-adhesive properties. Homogeneity assessment was conducted via macroscopic inspection of a thin gel layer spread over a clean glass slide, permitting the detection of any undissolved particulates, agglomerates, or phase separation that would compromise product uniformity and dosing accuracy.

Finally, a prospective dermal irritation study was performed on healthy human volunteers, wherein a defined quantity of the gel was applied to the volar forearm for a 60-minute observation period, with clinical monitoring for erythema, pruritus, and edema. This protocol was rigorously reviewed and approved by the institutional ethics committee, and written informed consent was obtained from all participants prior to enrollment, thereby ensuring adherence to the ethical principles delineated in the Declaration of Helsinki and safeguarding volunteer welfare throughout the investigative procedure.

Data analysis

The test data were analyzed using SPSS software with the One-Way ANOVA method to determine the effect of variations in extract concentration on the physicochemical characteristics of the gel. The significance value was set at $p < 0.05$.

Results and Discussion

Formulation and characterization of gel preparations

A gel preparation of bone-breaking twig extract was successfully formulated in three concentration variations: 15%, 20%, and 25%. The differences in extract concentration affected these physical characteristics of the preparation, particularly its organoleptic aspects.

Organoleptic test results showed that all formulations were semi-solid with a soft, homogeneous texture. The most visible differences were in color, with increasing extract concentration resulting in a more intense gel color. The odor produced by all formulations was relatively similar, possessing the distinctive aromatic odor of plant extracts.

Table 2. Organoleptic Test Results

Formula	Characteristics		
	Color	Smell	Texture
F1	Green	Aromatic Characteristics	Soft, cool, and non-sticky
F2	Green Brown	Aromatic Characteristics	Soft, cool, and non-sticky
F3	Chocolate	Aromatic Characteristics	Soft, cool, and non-sticky

These results are consistent with previous research which stated that increasing the concentration of plant extract in topical preparations can affect color and aroma intensity without changing the basic form of the preparation [1]. This indicates that *Euphorbia tirucalli* extract can be formulated in gel form without causing significant physical changes.

Physicochemical properties of gel preparations

pH test

The pH measurement results showed that all formulations had a pH ranging from 5.14 to 5.24. This value is still within the normal skin pH range (4.5 to 6.5), making it safe for topical use. There were no significant differences between formulations based on statistical analysis ($p > 0.05$), indicating that variations

in extract concentration did not significantly affect the pH of the preparations. This is likely due to the buffering properties of the gel base, which is able to maintain pH stability.

Table 3.pH Test Results

Formula	pH			Average + SD
	R1	R2	R3	
F1	5.37	5.05	5.02	5.14±0.193
F2	5.68	5.68	5.66	5.67±0.011
F3	5.20	5.06	5.48	5.24±0.213

This finding is consistent with other studies which reported that the addition of plant extracts in certain concentrations does not always significantly affect pH when using a stable gel base [2]. Although no statistically significant differences were observed among the formulations ($p > 0.05$), the higher pH value observed in F2 suggests a potential trend that should be further evaluated using a larger sample size and additional replicates to confirm its significance.

Spreadability test

Table 4.Spreadability Test Results

Formula	Spread Power			Average + SD
	R1	R2	R3	
F1	5.43	5.03	5.12	5.19±0.159
F2	5.42	5.01	4.81	5.08±0.110
F3	5.32	5.03	5.04	5.13±0.164

The spreadability test results showed that all formulations had a spread diameter ranging from 5.08–5.19 cm. This value meets the requirements for a good topical preparation, which is in the range of 5–7 cm. Good spreadability indicates that the gel is easy to apply and spreads evenly across the skin surface. The absence of significant differences between formulations indicates that increasing the extract concentration does not significantly affect viscosity. This is supported by previous research which states that spreadability is influenced by the viscosity of the preparation, and as long as the concentration of the active ingredient does not significantly change the base structure, the spreadability tends to remain stable [3].

Adhesion test

Table 5.Adhesion Test Results

Formula	Adhesive Power			Average + SD
	R1	R2	R3	
F1	06.37	03.30	03.68	4.45±1.673
F2	03.55	04.20	05.65	4.46±1.075
F3	04.68	05.61	03.38	4.45±1.120

The adhesion test results showed that all formulations had an adhesion time of more than 4 seconds. This indicates that the gel preparation has good adhesion to the skin surface. High adhesion is crucial in topical preparations because it can increase the contact time between the drug and the skin, thereby increasing therapeutic effectiveness. The absence of significant differences between formulations indicates that the extract concentration does not affect the gel's adhesive properties.

Homogeneity test

The homogeneity test results showed that all formulations contained no coarse particles and were evenly distributed. This indicates that the mixing process was successful. Homogeneity is a critical parameter in pharmaceutical preparations because it influences dosage uniformity and drug effectiveness. These results indicate that the formulation method used was optimal

Table 6. Homogeneity Test Results

Formula	Homogeneity		
	R1	R2	R3
F1	Homogeneous	Homogeneous	Homogeneous
F2	Homogeneous	Homogeneous	Homogeneous
F3	Homogeneous	Homogeneous	Homogeneous

Irritation test**Table 7.** Irritation Test Results

Formula	Irritation				
	1	2	3	4	5
F1	-	-	-	-	-
F2	-	-	-	-	-
F3	-	-	-	-	-

The irritation test results showed that all formulations did not cause irritation reactions such as redness, itching, or burning after 1 hour of application. This indicates that the gel preparation is safe for use on the skin. These results support previous research that found *Euphorbia tirucalli* extract at certain concentrations is relatively safe for topical use and does not cause skin irritation [4].

Analysis of the effect of concentration on gel characteristics**Table 2.** Effect of Concentration on Gel Characteristics

Parameter	p-value (Sig.)	Information
pH	> 0.05	Not Significant
Spread Power	> 0.05	Not Significant
Adhesive Power	> 0.05	Not Significant
Homogeneity	> 0.05	Not Significant
Irritation	> 0.05	Not Significant

Statistical analysis using the One-Way ANOVA method showed that variations in extract concentration (15%, 20%, and 25%) did not significantly affect all tested physicochemical parameters ($p > 0.05$). This indicates that increasing the extract concentration within this range did not change the basic properties of the gel preparation. Thus, the gel formulation of the bone-breaking twig extract has good physicochemical stability at various concentrations.

However, visually, there is a color difference that becomes more intense with increasing extract concentration. This can be a consideration for aesthetics and user preference. Overall, the results of this study indicate that *Euphorbia tirucalli* extract has the potential to be developed as a topical gel preparation. Compared with previous studies that focused more on biological activity, this study provides novel contributions in the formulation and physicochemical characterization of the preparation.

Conclusion

This study successfully formulated a gel preparation of *Euphorbia tirucalli* twig extract in three concentration variations, namely 15%, 20%, and 25%, with physicochemical characteristics that met the requirements for topical preparations. All formulations showed satisfactory results in organoleptic evaluation, pH, spreadability, adhesiveness, homogeneity, and irritation tests, indicating that they were safe and stable for topical application. Variations in extract concentration did not significantly affect the physicochemical parameters evaluated; however, they influenced the color intensity of the gel formulation. These findings suggest that *Euphorbia tirucalli* twig extract has potential for development as an active ingredient in topical gel preparations for wound care. A limitation of this study was the absence of accelerated stability testing and in vitro antibacterial activity evaluation. Therefore, further studies are recommended to assess the

pharmacological activity in vivo, conduct accelerated and long-term stability studies, and optimize the formulation to improve therapeutic efficacy and user acceptability.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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