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EVALUATION OF THE KRATOM ACTIVITY (*MITRAGYNA SPECIOSA*) EXTRACT VASELINE CREAM ON PSORIASIS PROFILES IN IMIQUIMOD-INDUCED WISTAR RATS

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ABSTRAK

Psoriasis merupakan penyakit kulit inflamasi kronis yang ditandai dengan hiperproliferasi keratinosit dan peradangan epidermis. Penggunaan bahan alami sebagai alternatif terapi topikal menjadi fokus pengembangan sediaan yang lebih aman. *Mitragyna speciosa* (*M. speciosa*) diketahui memiliki senyawa aktif seperti mitragynine dan flavonoid yang berpotensi sebagai agen antiinflamasi. Penelitian ini bertujuan untuk memformulasikan dan mengevaluasi sediaan krim vaselin ekstrak etanolik *M. speciosa* terhadap model psoriasis pada tikus Wistar yang diinduksi imiquimod 5%. Tiga formula diuji (F0–F2) dengan variasi konsentrasi ekstrak (0%, 0,1%, dan 0,5%). Evaluasi meliputi uji organoleptik, pH, daya sebar, daya lekat, serta efektivitas in vivo berdasarkan skor PASI dan histopatologi. Hasil menunjukkan bahwa seluruh formula memiliki karakter fisik yang stabil dan pH dalam rentang aman. Formula 0,5% (KMG2) menunjukkan skor PASI terendah dan struktur epidermis yang mendekati normal pada hari ke-12. Kesimpulan: Krim vaselin ekstrak *M. speciosa* mampu menurunkan keparahan psoriasis secara topikal dan menunjukkan potensi sebagai kandidat fitoterapi antiinflamasi

ABSTRACT

Evaluation Of The Kratom Activity (Mitragyna Speciosa) Extract Vaseline Cream On Psoriasis Profiles In Imiquimod-Induced Wistar Rats. *Psoriasis is a chronic inflammatory skin disease characterized by keratinocyte hyperproliferation and epidermal inflammation. The use of natural ingredients as alternative topical therapies has become a focus in developing safer dermatological formulations. Mitragyna speciosa (M. speciosa) contains active compounds, including mitragynine and flavonoids, with potential anti-inflammatory properties. This study aimed to formulate and evaluate a vaseline-based cream containing ethanolic extract of M. speciosa in a psoriasis model induced by 5% imiquimod in Wistar rats. Three formulations (F0–F2) were tested with extract concentrations of 0%, 0.1%, and 0.5%, respectively. Evaluations included organoleptic properties, pH, spreadability, adhesiveness, and in vivo efficacy assessed through PASI scores and histopathological analysis. The results showed that all formulations exhibited stable physical characteristics and acceptable pH levels. The 0.5% formula (KMG2) demonstrated the lowest PASI score and the epidermal structure most similar to the normal group on day 12. Conclusion: The vaseline cream containing M. speciosa extract effectively reduced psoriasis severity when applied topically and shows promise as a candidate for anti-inflammatory phytotherapeutic development.*

INTRODUCTION

Mitragyna speciosa Korth. (M. speciosa), commonly known as kratom, is an endemic plant species from West Kalimantan with significant economic and social value. Kapuas Hulu Regency serves as the primary cultivation center for kratom in Indonesia, with an estimated cultivation area of 11,384 hectares and a population of approximately 49 million trees [1]. More than 18,000 households in this region depend on this plant as their primary source of livelihood, and it has become a leading export commodity to several countries, including the United States, Canada, and India [2]. Nevertheless, *M. speciosa* faces regulatory challenges and controversies over its legal status, underscoring the need for further research to optimize its potential sustainably.

Based on empirical evidence, *M. speciosa* has demonstrated multiple therapeutic benefits, particularly as an analgesic and anti-inflammatory agent. Its major bioactive constituents, including mitragynine and 7-hydroxymitragynine, have been reported to suppress the production of pro-inflammatory cytokines such as TNF-α and IL-6 through modulation of macrophage-mediated inflammatory pathways[3]. This effect positions *M. speciosa* as a promising candidate for herbal-based therapy in chronic inflammatory conditions, particularly as a potential anti-psoriatic agent.

Psoriasis is a chronic inflammatory skin disease that exerts not only local but also systemic effects, thereby increasing the risk of metabolic complications, including type 2 diabetes mellitus. Experimental studies have demonstrated that psoriasis-induced skin inflammation may trigger a prediabetic phenotype through the secretion of pro-inflammatory cytokines, including TNF-α and IL-17A, which affect metabolic tissues such as adipose tissue and the pancreas. This mechanism supports the hypothesis that cutaneous inflammation in psoriasis contributes to systemic metabolic dysfunction and diabetes development, independent of obesity-related factors[4]. In vitro studies have demonstrated that mitragynine, a major bioactive compound in *M. speciosa*, exhibits promising anti-inflammatory activity. However, its effectiveness as a topical therapy for psoriasis still requires validation in vivo. To date, most studies have primarily focused on the systemic effects of *M. speciosa*, while investigations regarding its topical application for psoriasis remain limited.

A study by Tuntiyasawasdikul *et al.*, 2024 reported that the ethanolic extract of *M. speciosa* demonstrated favorable skin penetration properties and low toxicity toward skin cells, indicating its potential as a topical anti-inflammatory agent. Based on these findings, the present study aimed to formulate and evaluate a cream containing the ethanolic extract of *M. speciosa* as a candidate topical anti-inflammatory therapy by assessing its physical characteristics, including homogeneity, pH, spreadability, and adhesiveness, to ensure formulation stability and potential effectiveness for dermatological applications.

METHODS

This study employed a true experimental design using a pre- and post-test control group approach to compare baseline and post-treatment outcomes across experimental groups. A total of 30 female Wistar rats were divided into five groups in this study. Psoriasis-like skin inflammation was induced using 5% imiquimod (IMQ 5%). The instruments and materials used included a digital caliper, pH meter, microscope, camera, 90% ethanol, lanolin, stearic acid, methylparaben, propylparaben, liquid paraffin, propylene glycol, white petrolatum, female Wistar rats, standard feed, and hematoxylin-eosin staining reagents.

M. speciosa leaf simplicia was obtained from a supplier in Pontianak City. Prior to extraction, botanical identification was conducted at the Biology Laboratory, Faculty of Mathematics and Natural Sciences, Tanjungpura University. The leaves were then dried and ground into powdered simplicia. A maceration technique was used to produce a concentrated extract. Briefly, 200 g of *M. speciosa* powder was soaked in 2 L of 96% ethanol, gently stirred, and incubated for 3 × 24 hours. The mixture was subsequently filtered to obtain the filtrate. The residue was re-macerated and incubated for the same duration, and the filtration process was repeated three times. The combined filtrates were then evaporated to obtain a concentrated extract.

Phytochemical screening of *M. speciosa* extract was conducted by adopting previously established methods to identify secondary metabolite groups[6]. Phenolic compounds were tested by reacting 1 mL of extract with two drops of 5% $FeCl_3$ solution; a positive result was indicated by a blue-black or greenish color change. Flavonoid analysis was performed using the Shinoda test by adding approximately 0.1 g of magnesium powder, concentrated HCl, and 96% ethanol, where the appearance of yellow to red coloration indicated the presence of flavonoids.

Saponin testing was carried out by mixing 2 mL of extract with 5 mL of distilled water, followed by vigorous shaking for 30 seconds; the formation of stable foam lasting ≥10 minutes indicated a positive result. For triterpenoid analysis, 1 mL of extract was dissolved in 3 mL of chloroform, followed by the gradual addition of concentrated sulfuric acid along the wall of the test tube. Color changes in the lower layer were then observed, where a red color indicated the presence of sterol compounds, while a golden-yellow color suggested triterpenoids.

Tannin testing was performed by reacting 1 mL of extract with 5 mL of hot water, followed by cooling and centrifugation. The formation of a blue-black or greenish color after the addition of 1% $FeCl_3$ indicated the presence of tannins. Alkaloid testing was conducted by heating 5 mL of extract in 2 M HCl, followed by the addition of NaCl and filtration. The filtrate was then treated with 2 M HCl and divided into two test tubes; the addition of Wagner's reagent to the first tube produced a brown precipitate, indicating the presence of alkaloids. All tests were performed with solvent controls and evaluated visually for qualitative confirmation.

The psoriasis cream formulation method was adapted from previous studies with modifications based on material availability[6]. The oil phase was prepared by heating white petrolatum and stearic acid at approximately 70°C until a homogeneous mixture was obtained, followed by the addition of *M. speciosa* extract according to the formulation shown in Table 1. The aqueous phase was prepared by dissolving methylparaben in hot distilled water (approximately 70°C), followed by the addition of propylene glycol and triethanolamine (TEA). Emulsification was carried out by gradually adding the aqueous phase into the oil phase while continuously stirring at approximately 70°C for 15 minutes. The mixture was then manually stirred until it reached room temperature and subsequently packaged under sterile conditions. The final cream formulation was further subjected to physical characterization tests. The organoleptic test in this study was conducted to evaluate the sensory characteristics of the formulated cream preparations with different concentration variations (F0–F2). Observations were performed visually by assessing three main parameters, namely color, homogeneity, and aroma.

Table 1. Formulation of *M. speciosa* Extract Vaseline Cream

Compounds	F0 (0%)	F1 (0,1%)	F2 (0,5%)
M. speciose extract (g)	–	0,05	0,25
Album Vaseline (g)	8	8	8
Stearic Acid (g)	7,5	7,5	7,5
TEA (g)	0,75	0,75	0,75
Glycol Prophylene (g)	4	4	4
Nipagin (methyl paraben) (g)	0,075	0,075	0,075
Aquadest (ml)	q.s. ad 50	q.s. ad 50	q.s. ad 50

A total of 0.5 g of cream was weighed and placed at the center of a glass slide, then covered with another glass slide. After being left undisturbed for 1 minute, the spread diameter of the cream was measured horizontally and vertically. Subsequently, a 150 g load was applied to the upper glass slide for 1 minute, and the spread diameter was remeasured with a caliper. The entire procedure was performed in triplicate to obtain representative results. The pH of the cream formulation was measured by weighing 1 g of cream and dissolving it in 10 mL of distilled water until a homogeneous solution formed. The pH was then measured using a previously calibrated pH meter to ensure accuracy. Each sample was tested in triplicate, and the obtained values were averaged to determine the representative pH of each formulation.

A total of 0.5 g of cream formulation was weighed and placed on a glass slide, then covered with another glass slide until both surfaces adhered. The two glass slides were then subjected to a 1 kg load for 5 minutes. After the load was removed, an 80 g weight was attached to one end of the glass slides. The time required for the two glass slides to separate was recorded as the adhesion value. The procedure was repeated three times.

This study received ethical approval from the Health Research Ethics Committee of Pontianak Health Polytechnic of the Ministry of Health with certificate number 017/KEPK PK.PKP/VII/NP/2025. Prior to induction, the purchased rats were acclimatized for 14 days. Following the acclimatization period, the rats were divided into five groups as presented in Table 2. Psoriasis induction was performed using imiquimod (IMQ) for 5 days, followed by observational assessment. After the psoriasis model was confirmed, treatment with *M. speciosa* extract petrolatum cream was administered for 7 days.

Table 2. Experimental Group Design of Rats

Groups (n=6)	Interventions
Normal	No treatments
Kloderma	IMQ 5% + klobetasol propionat 0,01% cream
KMG 0	IMQ 5% + *M. speciosa* 0% vaseline cream
KMG 0,1	IMQ 5% + *M. speciosa* 0,1% vaseline cream
KMG 0,5	IMQ 5% + *M. speciosa* 0,5% vaseline cream

Ket: IMQ 5% (Imiquimod 5%)

The parameters evaluated in this study included PASI scores and tissue lesion characteristics assessed through histopathological examination. PASI scoring was determined through direct

observation by calculating lesion severity based on the established scoring formula. On day 8, the rats were euthanized via cervical dislocation. Skin tissues were then collected and fixed in 5% formaldehyde solution. The fixed skin samples were processed into histological slides using Hematoxylin and Eosin (H&E) staining. The prepared slides were subsequently examined under a microscope at 40×–100× magnification and further analyzed using ImageJ software.

RESULTS

The *M. speciosa* plant material was taxonomically identified by a biologist, Mukarlina, S.Si., M.Si., under certificate number 179/A/LB/FMIPA/UNTAN/2025. From 2 L of *M. speciosa* extract subjected to evaporation, a total of 22.6 g of concentrated extract was obtained. The extract exhibited a thick, semi-solid consistency resembling a dense paste, with a relatively high score of 4, indicating good texture suitability for further topical formulation (see the Table 3).

The color was observed as dark black and received a moderate score of 3. In terms of odor, the extract showed a strong characteristic leafy aroma that was slightly pungent, resulting in a lower score of 2. A bitter taste, likely associated with alkaloid compounds, was also recorded, with a score of 2. Overall acceptability was rated moderate (score 3), suggesting that despite the strong odor and bitter taste, the extract maintained a favorable consistency characteristic.

Table 3. Organoleptic Evaluation Results of *M. speciosa* Extract

Parameters	Observation Results	Score (1–5)
Form / Consistency	Thick, semi-solid extract (dense paste)	4
Color	Dark black	3
Odor	Strong, characteristic leafy odor (slightly pungent)	2
Taste	Bitter (associated with alkaloid content)	2
Overall Acceptability	Moderate acceptability; good texture but strong odor and taste	3

Phytochemical Screening

Phytochemical screening of *M. speciosa* extract revealed the presence of phenolic compounds, flavonoids, saponins, and alkaloids, as indicated by the characteristic color changes observed in each respective test. In contrast, the tannin and sterol tests were negative, with no significant color change detected.

Table 4. Phytochemical Screening of *M. speciosa* Extract

Test Type	Observation Results	Status
Phenolic Compounds	Dark green color	(+)
Flavonoids	Red color	(+)
Saponins	Stable foam for 10 minutes	(+)
Alkaloids	Orange precipitate	(+)
Tannins	No color change	(-)
Sterols	No color change	(-)

Figure 1 and Table 5 present the organoleptic evaluation results of *M. speciosa* extract vaseline cream formulations (F0, F1, and F2). Visually, F0 appeared milky white with a semi-solid consistency and good homogeneity. F1 showed a slightly greenish color and a characteristic extract

odor, with a soft texture and uniform consistency. Meanwhile, F2 exhibited a slightly dull transparent appearance with a stronger extract aroma and a slightly thicker texture, while remaining homogeneous without any phase separation. These findings indicate good physical stability across all formulations.

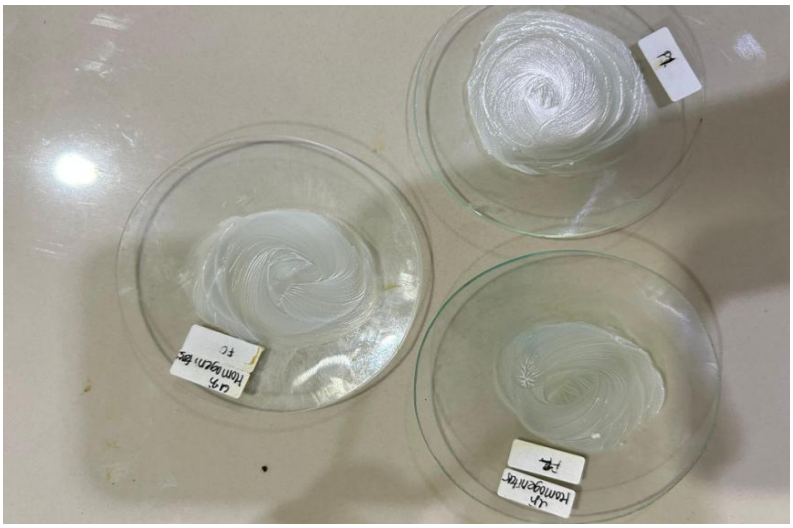

Figure 1 Organoleptic Analysis of *M. speciosa* extract

Table 5. Organoleptic Evaluation of *M. speciosa* Extract Vaseline Cream

Formula	Color	Odor	Consistency / Texture	Homogeneity
F0	Milky white	Odorless (neutral)	Soft, semi-solid	Homogeneous, no clumps
F1	Slightly cloudy white	Slight characteristic extract odor	Soft, slightly thick	Homogeneous, well blended
F2	Slightly dull transparent white	Stronger characteristic extract odor	Slightly thicker	Homogeneous, no phase separation

The spreadability test results of *M. speciosa* extract vaseline cream showed that all formulations (F0–F2) exhibited relatively similar spreading capacities, with average values ranging from 3.78 to 4.00 cm. Formula F1 demonstrated the highest horizontal spreadability at 3.92 ± 0.41 cm, while Formula F2 showed the highest vertical spreadability at 4.00 ± 0.28 cm. The base formulation without extract (F0) also showed stable results, with spreadability values of 3.89 ± 0.10 cm (horizontal) and 3.91 ± 0.43 cm (vertical).

Table 6. Spreadability Test Results of *M. speciosa* Extract Vaseline Cream

Formula (n=3)	Mean of Spreadibility Test (cm)	
	Horizontal	Vertical
F0	3,89 ± 0,10	3,91 ± 0,43
F1	3,92 ± 0,41	3,78 ± 0,41
F2	3,86 ± 0,28	4,00 ± 0,28

Note: The spreadability test was performed in triplicate

The pH evaluation results of *M. speciosa* extract vaseline cream showed that all formulations (F0–F2) had pH values within a neutral to slightly alkaline range. Formula F0, which served as the control without extract, exhibited an average pH of 7.64 ± 0.05, while Formula F1 (containing a lower extract concentration) showed the lowest pH value at 7.48 ± 0.26. Formula F2, containing a higher extract concentration, demonstrated the highest average pH value of 7.67 ± 0.09.

Table 7. The pH Average of *M. speciosa* Extract Cream

Formula (n=3)	Mean of pH Results
F0	7,64 ± 0,05
F1	7,48 ± 0,26
F2	7,67 ± 0,09

Note: pH level analysis was conducted in triplicate

The adhesion test results of *M. speciosa* extract vaseline cream demonstrated differences in adhesion time among formulations based on the average of three repetitions. Formula F1 showed the highest average adhesion time at 5.33 minutes. Meanwhile, Formula F0 (control without extract) exhibited an adhesion time of 3.83 minutes. Formula F2 recorded the lowest average adhesion time at 1.17 minutes. All tests were conducted in triplicate for each formulation to ensure the consistency and validity of the results.

Table 8. Average Adhesion Test Results of *M. speciosa* Extract Vaseline Cream

Formula (n=3)	Mean of Minutes
F0	3,83
F1	5,33
F2	1,17

Note: The adhesion test was performed in triplicate

The PASI score analysis using the Kruskal–Wallis test demonstrated a significant difference among groups on day 5, whereas no significant difference was observed on day 12 (p-values: 0.003 and 0.068, respectively). Complete measurement data are presented in Table 9. Based on the Mann–Whitney post hoc test, on day 5 (before treatment with *M. speciosa* extract cream), significant differences were observed (Figure 2) between the Normal and Kloderma groups (p=0.002), Normal and KMG0 (*M. speciosa*-free cream) (p=0.002), Normal and KMG1 (0.1% extract cream) (p=0.002), as well as Normal and KMG2 (0.5% extract cream) (p=0.002). Meanwhile, on day 12 (after treatment with *M. speciosa* extract cream), no significant differences were found among all groups (p=0.065).

Table 9. The result of PASI Score based on Kruskal-Wallis Analysis

Groups (n=6)	PASI Score			
	Pre Treatment	P-*Value*	Post Treatment	P-*Value*
Normal	0,00 ± 0,00		0,00 ± 0,00	
Kloderma	5,33 ± 1,37		0,67 ± 0,52	
KMG 0	5,67 ± 0,52	0,003*	0,83 ± 1,60	0,068
KMG 1	6,00 ± 1,26		0,33 ± 0,52	
KMG 2	6,67 ± 1,37		0,00 ± 0,00	

Note: PASI: *Psoriasis Area Severity Index,* * indicates significance (p < 0,05)

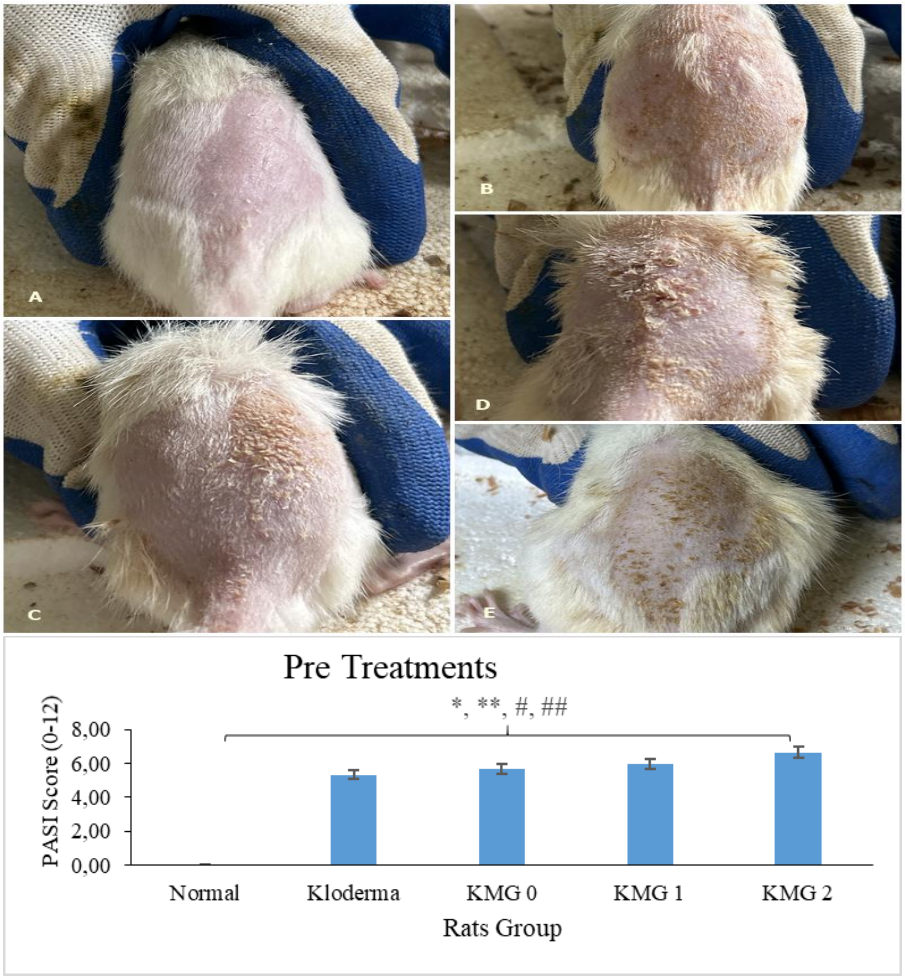

Figure 2. Psoriatic conditions on day 5 across treatment groups: (A) Normal, (B) Kloderma, (C) KMG 0, (D) KMG 0.1, and (E) KMG 0.5 *indicates a significant difference between the Normal and Kloderma groups; ** indicates a significant difference between the Normal and KMG0 groups; # indicates a significant difference between the Normal and KMG1 groups; and ## indicates a significant difference between the Normal and KMG2 groups based on the Mann–Whitney test (p < 0.05).

Based on Figure 2, a clear visual difference was observed between the normal group (A) and the psoriasis-induced groups (B–E) on day 5 prior to treatment with *M. speciosa* extract cream. The normal group exhibited smooth skin surfaces without erythema or scaling, whereas the Kloderma and KMG (0–2) groups showed noticeable skin thickening, erythema, and scaling, indicating

successful induction of psoriasis-like lesions. These observations were supported by PASI score measurements, which showed significantly higher scores in all treatment groups compared to the normal group ($p < 0.05$). These findings confirm that the psoriasis model was successfully established pathologically before treatment initiation.

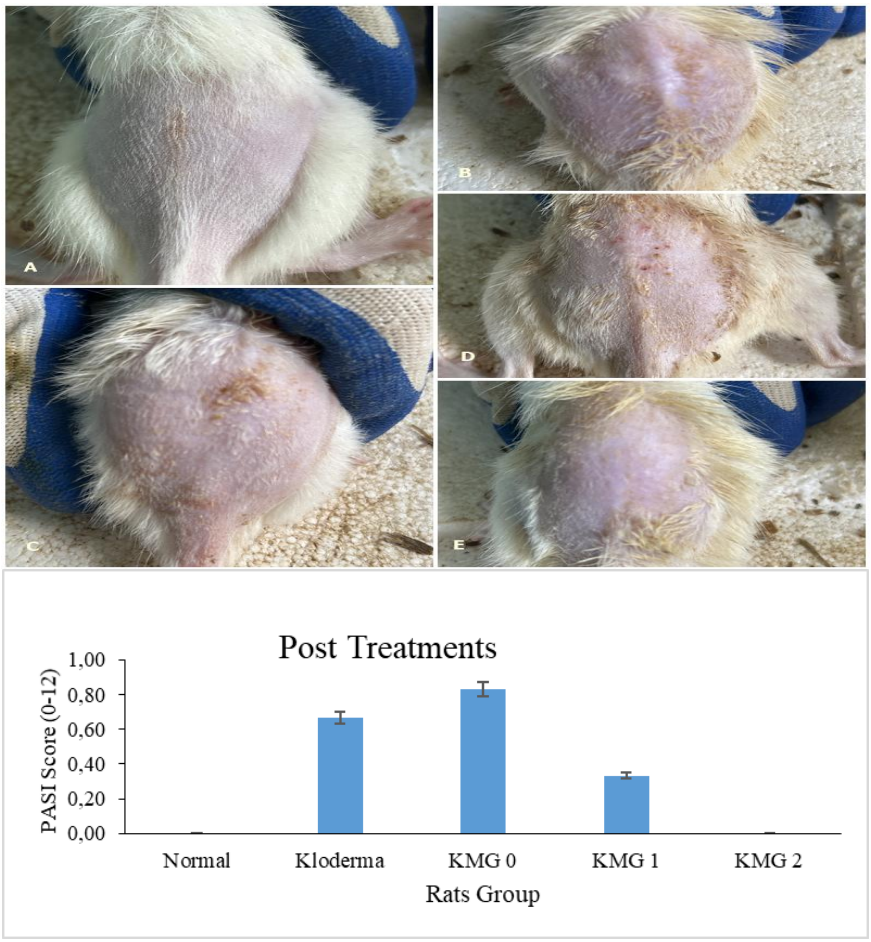

Figure 3 Psoriatic conditions on day 12 across treatment groups: (A) Normal, (B) Kloderma, (C) KMG 0, (D) KMG 1, and (E) KMG 2. The Kruskal–Wallis test showed no significant differences in psoriasis scores among the groups. Similarly, the Mann–Whitney test indicated no significant differences on day 12 ($p = 0.05$)

Histopathological evaluation of skin tissue on day 12 demonstrated notable differences in epidermal and dermal architecture among the treatment groups. Group A (Normal) exhibited intact epidermal layers with well-arranged keratinocytes and no evidence of inflammation. In contrast, group B (Kloderma) showed inflammatory cell infiltration, although marked epidermal thickening, acanthosis, and parakeratosis were not clearly observed. Group C (KMG0) displayed characteristic psoriasis-like lesions, including epidermal hyperplasia and Munro's microabscesses. Group D (KMG1) showed a reduction in epidermal thickness, indicating partial improvement. Notably, group E (KMG2) demonstrated substantial restoration of skin structure, with epidermal morphology closely resembling the normal group and reduced inflammatory manifestations. The complete histopathological observations are presented in Figure 2.

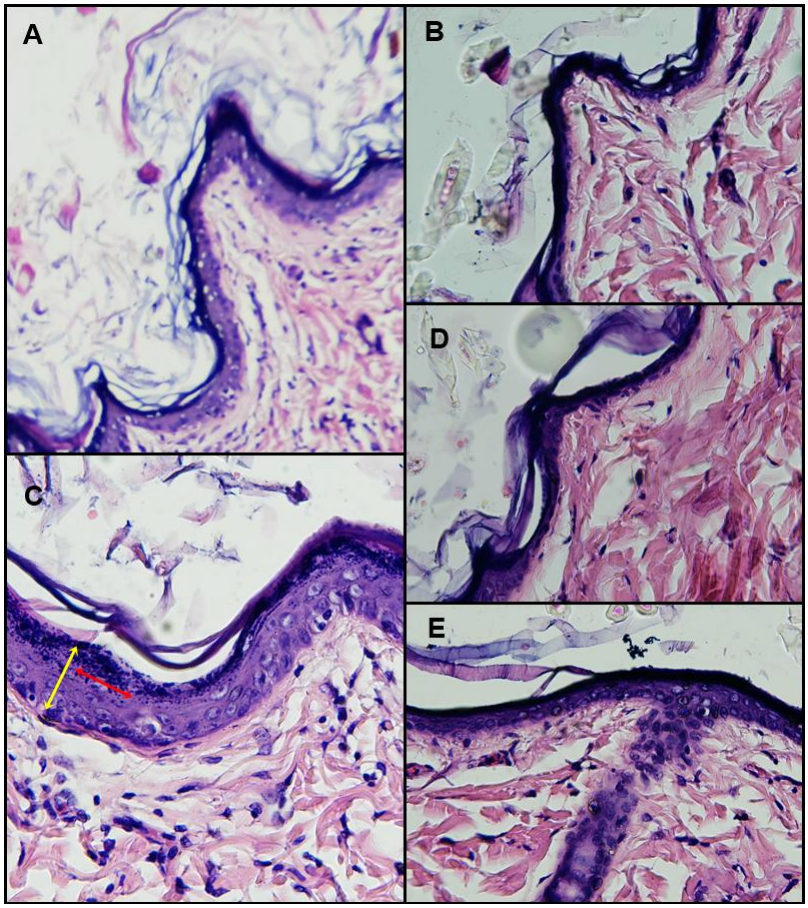

Figure 4 Histological features of skin tissue in psoriasis-induced rats: (A) Normal, (B) Kloderma, (C) KMG0, (D) KMG1, and (E) KMG2. The figure demonstrates the most preserved epidermal architecture in groups A (Normal) and E (KMG2). Psoriasis-related features, including epidermal hyperplasia (yellow arrows) and Munro's microabscesses (red arrows), remained clearly evident in group C (KMG0), while group D (KMG1) showed moderate histological improvement

DISCUSSION

The taxonomically verified ethanolic leaf extract of *M. speciosa* yielded 22.6 g of concentrated extract from 2 L of filtrate following evaporation. Organoleptic evaluation (Table 3) revealed a thick consistency, dark black color, a strong characteristic leafy odor, and a bitter taste, which may be attributed to its alkaloid content. These characteristics are consistent with previous reports describing *M. speciosa* as rich in bioactive alkaloids, particularly mitragynine and 7-hydroxymitragynine [7]. The moderate overall acceptability score (3) indicates that despite its strong odor and bitter taste, the extract demonstrated suitable consistency and homogeneity for topical formulation. These physical properties support its potential application as an active ingredient in anti-inflammatory cream formulations due to its compatibility with semisolid dermatological bases [8].

Phytochemical screening further confirmed the presence of phenols, flavonoids, saponins, and alkaloids, all of which may contribute to the extract's biological activity. Phenolic and flavonoid compounds are known to exert antioxidant effects through free radical scavenging and inhibition of lipid peroxidation [9]. In addition, alkaloids, particularly mitragynine and 7-hydroxymitragynine have been reported to exhibit anti-inflammatory activity by suppressing pro-inflammatory mediators such as TNF-α and IL-6 [7].

The presence of saponins may enhance the solubility of other active compounds, thereby potentially improving the extract's overall pharmacological activity. The absence of tannins and sterols suggests that ethanol extraction was more selective toward polar compounds. Overall, this phytochemical profile supports the potential of *M. speciosa* as a natural active ingredient with antioxidant and anti-inflammatory properties relevant for topical applications. Organoleptic evaluation is essential to assess the physical quality of cream formulations, including color, odor, consistency, and homogeneity.

The results demonstrated that incorporating M. speciosa extract altered the appearance of the formulations from milky white in F0 to slightly greenish in F1 and dull, translucent white in F2, accompanied by the emergence of a characteristic herbal odor. These findings are consistent with the presence of bioactive constituents in *M. speciosa*, such as alkaloids and flavonoids, which possess distinctive color and aroma characteristics [10]. The F2 formulation exhibited a slightly thicker texture than F1, likely due to the higher extract concentration, which increased formulation viscosity. All formulations remained homogeneous without phase separation, indicating good compatibility between the active extract and the vaseline-based cream. This physical stability is critical for topical efficacy and user acceptability [11].

The spreadability test demonstrated that all *M. speciosa* vaseline cream formulations exhibited good and relatively uniform spreading capacity, with values ranging from 3.78 to 4.00 cm. This consistent spreadability indicates an appropriate balance between viscosity and cream softness, with increasing extract concentration not significantly reducing the formulation’s ability to spread. These findings suggest that the formulations possess suitable physical characteristics for topical application, as adequate spreadability facilitates easier application and enhances the contact area of active compounds on the skin surface [12].

Furthermore, these results align with the principle that spreadability is inversely related to the yield stress of semisolid formulations [13]. A previous study by Manian et al. (2022) also reported that consistent spreadability values reflect proper physical stability and uniform distribution of active ingredients in topical preparations [14]. Therefore, the spreadability of the M. speciosa cream indicates that the formulation meets key physical requirements for dermatological use, particularly regarding ease of application and potential absorption efficiency.

The pH evaluation showed that all *M. speciosa* vaseline cream formulations were within a neutral to slightly alkaline range, with values between 7.48 and 7.67. Formula F1 exhibited the lowest pH value (7.48 ± 0.26), while F2 showed the highest pH (7.67 ± 0.09). The relatively low standard deviations indicate good formulation consistency across repeated measurements. These pH values remain within the acceptable safety range for topical cream products. According to the Indonesian National Agency of Drug and Food Control (BPOM), the permissible pH range for topical preparations generally falls between 4.5 and 8.5, depending on the product type and intended use. Therefore, all tested formulations fulfilled the pH safety requirements for topical applications [15].

From a dermatological perspective, normal human skin typically has a pH ranging from 4.1 to 5.8. Although products with a neutral to slightly alkaline pH can still be safely used, formulations closer to the physiological skin pH are generally preferred because they help maintain microbiome balance and preserve skin barrier function[16]. Previous studies have also reported that topical formulations with pH values higher than normal skin pH do not necessarily cause irritation, particularly when the base materials are mild and physically stable[17]. Therefore, the *M. speciosa* cream formulations demonstrated acceptable pH stability and remained within regulatory safety limits, supporting their further development as herbal topical preparations.

Previous studies have demonstrated that quantitative adhesion testing using texture analyzers can systematically compare the adhesive performance of different topical formulations [18]. In addition, modern pharmaceutics literature recognizes adhesion properties (tack or adhesiveness) as an important parameter in topical formulation development because they directly influence formulation retention and the efficiency of drug delivery to the skin[19]. In this study, adhesion testing showed that formula F1 had the highest average adhesion time (5.33 minutes), followed by F0 (3.83 minutes), and F2 had the lowest adhesion time (1.17 minutes). These variations reflect differences in the physical adhesive characteristics of each formulation and their ability to maintain contact with the application surface over time. The two-glass slide adhesion method measures the time required for the cream layers to separate, making it a relevant parameter for evaluating topical creams. Improved adhesion may enhance therapeutic effectiveness by allowing active compounds to remain on the skin surface for a longer period before being removed or transferred.

In this study, although *M. speciosa* extract cream had already been administered, significant differences among treatment groups were still observed on day 5 (Figure 2), indicating that the healing process had not yet reached an optimal stage during the early phase of treatment. The flavonoid and alkaloid compounds present in *M. speciosa* are known to exert anti-inflammatory effects by suppressing the expression of pro-inflammatory mediators such as TNF-α and IL-6; however, a longer treatment duration may be required to achieve significant clinical improvement[8]. By day 12 after topical application, Figure 3 showed that the KMG2 group resembled the normal skin group, with smoother skin texture, reduced erythema, and decreased scaling. In contrast, the Kloderma group still exhibited residual lesions, including mild erythema and slight skin thickening.

The comparable scores observed between the normal group and the KMG2 group suggest that the highest concentration of *M. speciosa* extract cream (0.5%) exerted a therapeutic effect that nearly restored the skin to normal homeostasis within 12 days of treatment. This finding is consistent with previous studies reporting that topical flavonoids in psoriasis models can suppress the Th17/IL-23 inflammatory pathway, reduce the expression of pro-inflammatory cytokines such as IL-17, IL-22, and TNF-α, and improve epidermal barrier integrity [20]. For comparison, previous studies using imiquimod-induced psoriasis rat models demonstrated that flavonoid compounds such as quercetin were able to reduce erythema, skin thickening, and inflammatory cell infiltration through antioxidant mechanisms and inhibition of the NF-κB and MAPK signaling pathways [21]. Furthermore, Li et al. (2020) reported that chrysin, another flavonoid compound, effectively attenuated psoriasis-like lesions by suppressing TNF-α and IL-17 expression and inhibiting the activation of the JAK-STAT and NF-κB pathways [22].

However, it should be emphasized that the optimal therapeutic effect was observed only at the highest concentration after a relatively long treatment period. These findings highlight that both dosage and treatment duration are critical factors in achieving effective and sustained psoriasis remission. Therefore, future studies are recommended to evaluate intermediate concentration ranges and extend the treatment duration beyond 12 days. Such investigations should also incorporate histopathological analysis and assessment of inflammatory biomarkers, including TNF-α, IL-17, and IL-23, to further confirm the molecular mechanisms underlying the anti-inflammatory effects of *M. speciosa* extract in psoriasis models.

Histological observations revealed that the Normal group (A) and the Kloderma group (B) maintained relatively normal epidermal architecture, with no prominent signs of acanthosis or parakeratosis. In contrast, the KMG0 group (C) continued to exhibit classic psoriasis-like lesions, including epidermal hyperplasia and Munro's microabscesses. The KMG1 group (D) demonstrated

partial improvement, with reduced epidermal thickening and the absence of marked acanthosis and parakeratosis. Notably, the KMG2 group (E) showed epidermal recovery approaching normal conditions, characterized by a thinner epidermal layer, minimal parakeratosis, and reduced inflammatory cell infiltration. Hallmark histopathological features of psoriasis, including acanthosis (epidermal hyperplasia), parakeratosis, and dermal inflammatory infiltration, are widely recognized as classic diagnostic characteristics of psoriasis vulgaris (Figure 4) [24]. Additional findings such as suprapapillary plate thinning and dilated dermal blood vessels, are also commonly reported in psoriatic lesions[25]. The observed morphological improvements, particularly in the KMG2 group, suggest the therapeutic potential of *M. speciosa* extract in reducing epidermal hyperproliferation and inflammation.

CONCLUSION

This study demonstrated that *M. speciosa* extract vaseline cream exhibited stable physical characteristics and was considered safe for topical application, as indicated by acceptable spreadability, pH, and homogeneity. The 0.5% formulation showed notable improvement in psoriasis lesions, both visually and histologically, with a return to normal skin architecture and a reduction in PASI scores. These findings support the potential of *M. speciosa* extract as a promising herbal topical anti-inflammatory candidate for managing mild to moderate psoriasis.

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