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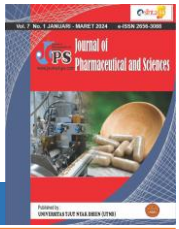

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Formulation of Transdermal Patch Nanoemulgel of Dadap Serep Leaves (*Erythrina subumbrans* (Hassk.) Merr.) and Sand Ginger (*Kaempferia galanga* L.) as Candidate Herbal Lactagogum Based on Usadha

Formulasi Transdermal Patch Nanoemulgel Ekstrak Dadap Serep *(Erythrina subumbrans (Hassk.) Merr.)* dan Rimpang Kencur *(Kaempferia galanga L.)* sebagai Kandidat Laktagogum Herbal Berbasis Usadha

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Abstract

Success rates of exclusive breastfeeding remain low due to breast engorgement and insufficient milk production. Traditional Usadha-based herbal lactagogues, such as *Erythrina subumbrans* and *Kaempferia galanga*, are used by lactating mothers; however, their delivery in practical, standardized forms is limited. This study aimed to formulate a nanoemulgel transdermal patch containing *E. subumbrans* extract and *K. galanga* extract, evaluate its physicochemical properties, and assess its safety for skin irritation as a potential herbal lactagogue. Extracts of *E. subumbrans* and *K. galanga* were added to the nanoemulsion base. The nanoemulsions were incorporated into HPMC/PVP-based transdermal patch matrices by solvent casting. The resulting patches were evaluated for physicochemical properties and tested for skin irritation. Phytochemical screening confirmed the presence of flavonoids, tannins, triterpenoids, saponins, and alkaloids in both extracts. The total flavonoid contents were 47.44 mg QE/g for *E. subumbrans* and 36.79 mg QE/g for *K. galanga*. The nanoemulsion exhibited greater than 90% transmittance, mean droplet size of 7.79 nm, and polydispersity index (PDI) of 0.193. The patches met acceptable physical criteria, including a thickness of 0.20 mm, weight variation with %CV less than 10%, and folding endurance over 300. pH values ranged from 6.00 to 6.58. In a human patch test, no erythema or edema was observed; only mild pruritus (mean = 0.2) was reported in two participants. The formulated nanoemulgel transdermal patches demonstrated favorable physicochemical properties and were non-irritating. These patches show potential as a herbal lactagogue delivery system; further studies on lactation efficacy and long-term stability are recommended.

Keywords*: *Erythrina subumbrans; Kaempferia galanga; Nanoemulsion; Transdermal patch; Lactagogum.

Abstrak

Rendahnya capaian ASI eksklusif di Bali disebabkan oleh terhambatnya produksi ASI oleh berbagai faktor, salah satunya pembengkakan payudara. Penggunaan pelancar ASI (laktagogum) herbal berbasis Usadha diterapkan secara luas, namun bentuk dan standar penggunaannya belum optimal. Potensi aktivitas laktagogum pada ekstrak daun Erythrina subumbrans dan rimpang Kaempferia galanga perlu diaplikasikan pada pengembangan sediaan topikal herbal nanoteknologi yang praktis digunakan, memiliki manfaat terapeutik maksimal dengan efek samping minimal. Penelitian ini bertujuan memformulasikan patch nano-emulgel transdermal yang mengandung ekstrak E. subumbrans dan K. galanga, mengevaluasi kualitas fisik, stabilitas, dan keamanannya sebagai laktagogum herbal. Ekstrak diperoleh melalui maserasi, kandungan fitokimia dianalisis secara kualitatif dan kuantitatif. Ekstrak ditambahkan pada basis nanoemulsi, dikarakterisasi berdasarkan parameter transmitansi, ukuran partikel, dan indeks polidispersitas. Nanoemulsi diformulasikan dalam matriks patch berbasis HPMC/PVP melalui metode casting pelarut. Patch diuji untuk sifat organoleptik, karakter fisikokimia, dan uji iritasi dengan metode human patch test. Terdapat flavonoid, tanin, triterpenoid, saponin, dan alkaloid pada kedua ekstrak. Kandungan flavonoid total E. subumbrans dan K. galanga sebesar 47,44 mg QE/g dan 36,79 mg QE/g. Nanoemulsi menunjukkan transmitansi > 90 %, ukuran partikel rata-rata 7,79 nm, dan PDI 0,193. Patch memenuhi standar mutu fisik (ketebalan 0,20 mm, variasi berat <10 %, ketahanan lipat >300) dengan pH 6,00–6,58. Pada uji iritasi kulit, tidak ditemukan eritema, edema, atau sensasi terbakar, hanya pruritus ringan (rerata = 0,2). Patch nanoemulgel transdermal ekstrak *E. subumbrans* dan *K. galanga* memiliki karakteristik fisik yang baik dan aman untuk aplikasi topikal, serta berpotensi menjadi sistem penghantaran laktagogum herbal modern.

Kata kunci*: *Erythrina subumbrans; Kaempferia galanga; Nanoemulsi; Transdermal patch; Laktagogum.

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Introduction

Optimizing child growth and development through exclusive breastfeeding is essential for fostering high-quality human resources. According to the Indonesian Health Survey, the exclusive breastfeeding rate in Bali is 65.7%, which remains below the national average. Furthermore, only 57.7% of infants receive exclusive breastfeeding for a full 6 months [1]. This low rate of exclusive breastfeeding among infants aged 0-6 months contributes to the persistently high prevalence of stunting in toddlers.

Breast engorgement and hypogalactia are significant barriers to successful exclusive breastfeeding [2]. In response to the growing back-to-nature movement and concerns about potential side effects, the use of herbal lactagogues has increased [3]. Lactagogues are substances that stimulate, enhance, or facilitate breast milk production [4]. Among the 26 types of Usadha-based herbal lactagogues, dadap serep leaves (*Erythrina subumbrans* (Hassk.) Merr) and sand ginger rhizome (*Kaempferia galanga* L.) are notable examples [5]. The alkaloids, flavonoids, tannins, and polyphenols found in dadap serep leaves possess analgesic, antipyretic, and anti-inflammatory properties, which can help alleviate breast swelling [6].

Sand ginger is empirically used to make "boreh basanbuat" to stimulate breast milk production [7]. Sand ginger rhizome contains compounds such as alkaloids, flavonoids, saponins, and steroids that have the potential to stimulate the hormone oxytocin. Oxytocin plays a crucial role in stimulating the production of prolactin, the hormone responsible for breast milk production [8]. Sand ginger ethanol extract has a significant effect on the histology of mammary glands, particularly in relation to milk production [9].

The use of boreh is outdated in today's world, therefore, it is important to develop a new form of boreh by creating a topical herbal formulation in the form of a transdermal nanoemulgel patch. A transdermal drug delivery system (TDDS) was selected to enable sustained drug delivery while bypassing gastrointestinal degradation and hepatic first-pass metabolism. Depending on formulation design, transdermal systems may produce systemic or localized effects. In this study, systemic absorption is targeted for lactation stimulation, whereas localized dermal retention is intended for antiinflammatory activity to prevent breast engorgement. The research question is whether dadap serep leaf extract (*Erythrina subumbrans* (Hassk.) Merr) and sand ginger rhizome (*Kaempheria galanga* L.) can be combined into a nanoemulgel transdermal patch that meets quality and physical stability standards and is safe for use as a breast milk stimulant in nursing mothers. The goal of this study is to develop a nanoemulgel transdermal patch containing dadap serep leaf extract and sand ginger rhizome that adheres to quality and stability criteria and is safe for use as a herbal lactagogue in nursing mothers.

Experimental Section

Materials and Apparatus

Leaves of *Erythrina subumbrans* (Hassk.) Merr. were collected from Badung Regency, Bali, while rhizomes of K*aempferia galanga* L. were obtained from Karangasem Regency, Bali. The solvents and excipients used in the study included 96% ethanol (Bratachem), n-hexane (Bratachem), distilled water, polyethylene glycol 400, Tween 80 (Merck), virgin coconut oil (Bali Coconut), methyl paraben (Bratachem), hydroxypropyl methylcellulose (Bratachem), polyvinylpyrrolidone (Bratachem), and propylene glycol (Bratachem). The instruments used were overhead stirrer (Scilogex), Analytical balance (Fujitsu), oven (Memmert), desiccator (Normax).

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A laboratory-based experimental method was employed to isolate active compounds from *Erythrina subumbrans* leaves and *Kaempferia galanga* rhizomes, formulate them into a nanoemulgel transdermal patch, evaluate the physical quality and stability of the formulation, and conduct an irritation test to obtain a herbal topical preparation that met quality and safety standards.

Extraction of *E. subumbrans* leaves and *K. galanga* rhizomes

A total of 250 g of *Erythrina subumbrans* leaf simplicia powder was extracted using 96% ethanol at a ratio of 1:10. Likewise, 250 g of *Kaempferia galanga* rhizome powder was macerated with 96% ethanol at a ratio of 1:5 until fully submerged. Maceration and remaceration were carried out for 5 days. The filtrate was then evaporated using a rotary evaporator at 50 °C until a crude extract was obtained.

Phytochemical screening of *E. subumbrans* leaf extract and *K. galanga* rhizome extract

Phytochemical screening of the extracts was conducted qualitatively to determine the presence of alkaloids, flavonoids, phenolics, terpenoids/steroids, and saponins.

Determination of flavonoid content in *E. subumbrans* leaf extract and *K. galanga* rhizome extract

The flavonoid content, which is linked to anti-inflammatory activity for managing breast swelling, was measured using a spectrophotometric method using the $AlCl_3$ colorimetric assay with quercetin as the reference standard [10]. A quercetin calibration curve was prepared at concentrations of 20, 40, 60, 80, and 100 ppm. A total of 10 mg of extract was dissolved in 10 mL of 96% ethanol to obtain a stock solution with a concentration of 1000 ppm. Then, 1 mL of the solution was transferred into a test tube and mixed with 1 mL of 10% $AlCl_3$ and 8 mL of 5% acetic acid. The mixture was incubated for 30 minutes, and the absorbance was measured at 415 nm using a UV-Vis spectrophotometer.

Formulation of nanoemulsion containing *E. subumbrans* leaf extract and *K. galanga* rhizome extract

The nanoemulsion was prepared using an overhead stirrer. In the first step, Tween 80 and PEG 400 were homogenized at 500 rpm for 30 minutes. Virgin coconut oil (VCO) and the extract, previously dissolved in 96% ethanol, were then added to the mixture and further homogenized using the overhead stirrer for 30 minutes. Methyl paraben, dissolved in 96% ethanol, was added gradually while continuously stirring for an additional 30 minutes. The process temperature was maintained at a stable room temperature, and no pressure degradation treatment was applied during the preparation process. The nanoemulsion was characterized by measuring its percent transmittance using a UV-Vis spectrophotometer at a maximum wavelength of 650 nm. Particle size analysis was carried out using a Particle Size Analyzer (PSA).

Formulation of transdermal patch nanoemulgel containing *E. subumbrans* leaf extract and *K. galanga* rhizome extract

The transdermal patch nanoemulgel was prepared using a solvent evaporation method. HPMC was dissolved in hot distilled water at a ratio of 1:40. A PVP solution previously prepared in hot distilled water at a ratio of 1:10 was then added. The nanoemulsion was incorporated into the HPMC:PVP base and stirred until homogeneous. Propylene glycol and PEG 400 were added, followed by 96% ethanol to a final volume of 100 mL. Approximately 3 g of the mixture was cast into a 5 cm diameter petri dish and evaporated in an oven at 40–60 °C for approximately 6 hours.

Physical stability evaluation of transdermal patch nanoemulgel containing *E. subumbrans* leaf extract and *K. galanga* rhizome extract

The physical stability of the formulation was evaluated through organoleptic assessment, pH measurement, weight uniformity test, thickness test, and folding endurance test. These evaluations were conducted to ensure that the nanoemulgel transdermal patch formulation containing *Erythrina subumbrans* leaf extract and *Kaempferia galanga* rhizome extract met the required quality standards.

Irritation test of transdermal patch nanoemulgel containing *E. subumbrans* leaf extract and *K. galanga* rhizome extract

The irritation test was conducted on 10 healthy volunteers who met the inclusion criteria (females aged 18–35 years, healthy adults, with no history of severe skin allergies, not pregnant or breastfeeding, and not using specific topical medications). All experimental procedures involving human participants were

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conducted in accordance with the Declaration of Helsinki and were approved by the Health Research Ethics Committee of STIKES Bina Usada Bali (Ethics Clearance No. 296/EA/KEPK-BUB-2025). Written informed consent was obtained from all volunteers prior to participation.

A skin examination was performed on the back or upper arm to ensure the absence of wounds, rashes, or other skin conditions. The selected area was cleaned with an antiseptic and allowed to dry, then marked using a dermatological marker. The transdermal patch was applied to the designated area for 20 minutes to observe primary irritation reactions. A second observation was conducted 24 hours after patch removal to detect delayed contact allergic responses. The reactions were evaluated using a standard scoring system, such as the

Results and Discussion

Determination and Extraction of *E. subumbrans* leaves and *K. galanga* rhizomes

The leaves of *Erythrina subumbrans* (Hassk.) Merr. were identified at UPT Herbal Laboratory Materia Medica Batu, as confirmed by Determination Certificate No. 000.9.3/3316/102.20/2025. The rhizomes of *Kaempferia galanga* L. were identified based on Determination Certificate No. 000.9.3/3315/102.20/2025. Extraction of both *Erythrina subumbrans* leaf and *Kaempferia galanga* rhizome simplicia was carried out using 96% ethanol as the solvent. A total of 250 g of *Erythrina subumbrans* simplicia was macerated, resulting in 18 g of thick extract (yield value of 7.2%). Maceration of 250 g of *Kaempferia galanga* simplicia yielded 22.6 g of thick extract (yield value of 9.1%).

Phytochemical screening and determination of flavonoid content of *E. subumbrans* leaf extract and *K. galanga* rhizome extract

Phytochemical screening was conducted on the viscous extracts to qualitatively identify the classes of secondary metabolites present in the *Erythrina subumbrans* leaf extract and *Kaempferia galanga* rhizome extract. Preliminary information regarding their potential biological activities was thus obtained, serving as a basis for further pharmacological investigation. The results of the phytochemical screening are presented in Table 1.

Table 1. Phytochemical screening results of Extract of *E. subumbrans* and Extract of *K. galanga*

No	Secondary Metabolites	Reagent	Extract of *E. subumbrans*	Extract of *K. galanga*	Information
1.	Flavonoid	Mg powder & HCl + Amyl Alcohol	(+)	(+)	A red color forms.
2.	Alkaloid	H_2SO_4 & Mayer's reagent	(-)	(+)	A white precipitate is formed.
		H_2SO_4 & Dragendorff's reagent	(+)	(+)	A red precipitate is formed.
3.	Tannin	$FeCl_3$ 10%	(+)	(+)	A black colour forms.
4.	Triterpenoid/ steroid	Chloroform & Liebermann Burchard's reagent	(+)	(+)	A green-brown colour is formed.
5.	Saponin	Distilled water & HCl of 2N	(+)	(+)	A stable foam is formed.

Breast engorgement is a common physiological condition characterized by the accumulation of milk, fluid retention, and mild local inflammation within the breast tissue. This inflammatory response can exacerbate pain, edema, and impede milk flow, potentially leading to complications such as mastitis if not properly managed. Effective modulation of the inflammatory process is crucial to alleviate interstitial edema, reduce pressure on alveoli and milk ducts, and decrease capillary permeability and fluid exudation into the interstitial space. Flavonoids, a class of polyphenolic compounds, have been extensively studied for their anti-inflammatory effects. They can suppress the activation of transcription factors or regulate the expression of pro-inflammatory genes [11]. Tannins help maintain tissue integrity and reduce local edema. They may exert their anti-inflammatory effects through their astringent properties, which can influence cell membrane function and reduce vascular permeability. Saponins have potential in modulating cellular signaling pathways, enhancing the bioavailability of other compounds, and supporting lactation hormone regulation. Alkaloids can modulate the neuroendocrine system, influencing the release of hormones such as dopamine, prolactin, and oxytocin, which are crucial for milk production and ejection [12].

E. subumbrans exhibits a higher total flavonoid content (TFC) compared to *K. galanga*, with an average of 47.44 mg QE/g versus 36.79 mg QE/g, respectively. Both extracts fall into the 'high' category of flavonoid

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content, indicating substantial antioxidant potential. Flavonoids, such as quercetin, can stimulate milk production by enhancing prolactin secretion and increasing the expression of milk proteins. Quercetin administration in lactating mice led to elevated prolactin levels and upregulated the mRNA expression of milk proteins like α-lactalbumin and β-casein, thereby improving lactation performance [13].

Table 2. Flavonoid's quantity of extract of *E. subumbrans* and *K. galanga*

Extract	TFC (mgQE/g)	TFC Average (mgQE/g)	SD
Extract of *E. subumbrans*	48.44	47.44	0.9
	46.70		
	47.17		
Extract of *K. galanga*	36.05	36.79	0.7
	37.48		
	36.84		

Formulation of nanoemulsion containing *E. subumbrans* leaf extract and *K. galanga* rhizome extract

The preparation of nanoemulsions from *Erythrina subumbrans* and *Kaempferia galanga* rhizome extracts is intended to enhance the solubility, stability, and bioavailability of the bioactive compounds. Through this system, biological activities such as anti-inflammatory effects are expected to be maximized via formation of droplets sized < 200 nm with a polydispersity index ≤ 0.30, high encapsulation efficiency, and superior release and penetration profiles compared with conventional extract forms. Nanoemulsions are able to improve penetration and maintain the stability of herbal active ingredients in topical application [14]. Studies on the nanoemulsification of *K. galanga* essential oil have demonstrated that the kencur essential oil can be formulated into a stable and well-characterized nanoemulsion [15].

In the initial stage of nanoemulsion preparation, a mixture of Tween 80 (surfactant) and PEG 400 (co-surfactant) was homogenized at 500 rpm for 30 minutes until a clear and homogeneous mixture was obtained. The carrier oil (VCO) together with the extracts of *E. subumbrans* (Hassk.) Merr. leaves and *K. galanga* L. rhizomes, which had previously been dissolved in 96% ethanol, were then added to produce a formulation of low viscosity that appeared more stable following further stirring with an overhead stirrer for 30 minutes. Next, methylparaben, functioning as a preservative, was dissolved in 96% ethanol and gradually incorporated into the nanoemulsion system. Continuous stirring for 30 minutes ensured uniform distribution of methylparaben throughout the formulation.

Figure 1. Nanoemulsion of *E. subumbrans's* extract and *K. galanga's* extract

The formulation results indicate that all formula variations produced nanoemulsion systems with characteristics as detailed in Table 3.

Table 3. Characteristic of Nanoemulsion's Variation

Formula	Organoleptic characteristics	pH	Homogenity	%transmittant
F0	Slightly yellow color, clear, odorless.	5.30	Homogeneous	96.4
F1	Yellowish colour, transparent, strong kencur aroma.	5.08	Homogeneous	93.9
F2	Yellowish to light brown color, transparent, dominant characteristic aroma of kencur.	5.21	Homogeneous	94.2
F3	Yellowish to light brown color, transparent, distinct aroma of kencur and dadap leaves.	5.10	Homogeneous	94.1
F4	Yellowish to light brown color, transparent, dominant aroma of dadap leaves.	5.15	Homogeneous	95.1

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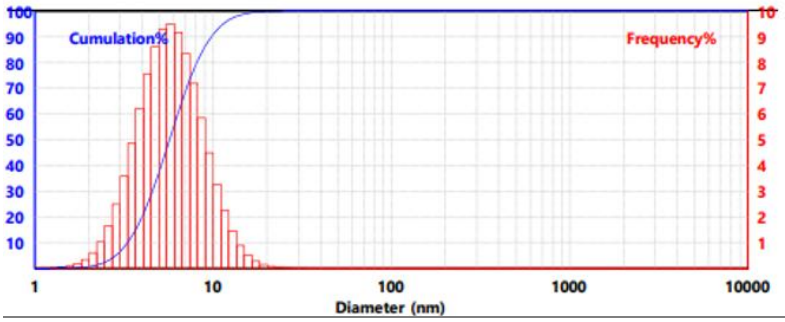
The nanoemulsion formulations exhibited a yellowish and transparent appearance with percent transmittance values above 90%, suggesting formation of droplets in the nanometer range with minimal light scattering. Similar findings were reported in *Lycium barbarum* nanoemulsions, where smaller droplet size correlated with higher transparency as surfactant ratio was optimized [16].



Dav Diameter: Xav =7.79nm	Dispersion Index: PI=0.1930	Photon count = 3
D10= 3.32nm	D50 = 5.69 nm	D90 = 9.77 nm

Figure 2. Result of Particle Size Analyzer of Nanoemulsion

The particle size analysis confirmed this, with an average droplet size of 7.79 nm and a polydispersity index (PDI) of 0.193, indicating narrow distribution and good homogeneity. These observations are in line with essential oil nanoemulsions in *Persicaria minor*, which achieved PDI < 0.3 and droplet size 91 nm, showing improved kinetic stability and enhanced optical clarity when particle size is small and distribution is uniform [17]. The observed good homogeneity and stable pH helped maintain physical integrity and prevent phase separation, a factor also emphasized in studies of nanoemulsions/gels incorporating omega-3 fatty acids and inulin, where rheological stability was lost with increasing polydispersity over time [18].

Additionally, the dominant aroma of kencur and dadap leaves suggests efficient incorporation of volatile compounds, resonating with recent research on essential oil-based nanoemulsions which show better volatility retention and aroma preservation compared to conventional emulsions. Collectively, these results indicate that the developed nanoemulsion possesses desirable physical qualities high transparency, small and uniformly distributed droplet size, good homogeneity, and aroma retention all of which are favorable for physical stability and quality of nanoemulsion preparations.

Formulation and physical stability evaluation of transdermal patch nanoemulgel containing *E. subumbrans* leaf extract and *K. galanga* rhizome extract

Following the successful development of a nanoemulsion with optimal physicochemical characteristics namely high optical clarity, ultrafine droplet size, narrow polydispersity index, and preserved volatile constituents the research was extended to the formulation of a transdermal patch.

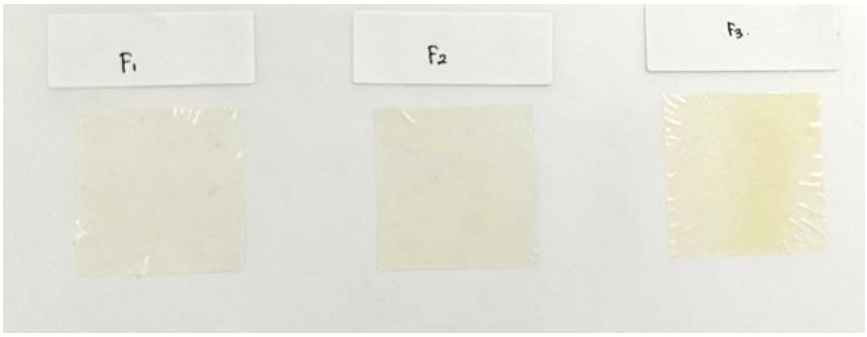


Figure 3. Transdermal Patch of Nanoemulsions

Integrating nanoemulsions into the transdermal patch matrix has emerged as an innovative strategy to enhance dermal permeation and optimize bioactive compound stability. A recent systematic review confirmed that nanoemulsion-based patches facilitate increased flux across the stratum corneum by lowering diffusional resistance, while maintaining favorable physicochemical integrity of the formulation. The dual lipophilic–hydrophilic compatibility of nanoemulsions, which enables their efficient incorporation into patch systems and augments the delivery of both hydrophilic and lipophilic actives across the skin barrier [19]. Collectively,

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these findings justify the progression from nanoemulsion to patch formulation, as the hybrid system integrates the nanoscale advantages of enhanced solubilization, homogeneity, and volatile retention with the clinical benefits of transdermal technology, such as non-invasiveness, controlled release, and improved patient compliance. This approach reflects a contemporary paradigm in nanotechnology-based drug delivery systems with promising pharmaceutical applications.

To ensure the quality and suitability of the developed transdermal patch formulation, a comprehensive characterization of its physicochemical and mechanical properties was conducted as detailed in Table 4.

Table 4. Characteristic of Transdermal Patch

	Organoleptic characteristics	pH	Patch thickness (mm)	Weight uniformity	Folding endurance
F1	Film, transparent white, characteristic aroma of E. subumbrans with a slight note of K. galanga, dry, smooth, flexible, and non-sticky.	6.00	0.2	0.077 ±0.004 (%CV=5.09)	>300
F2	Film, yellowish transparent, characteristic aroma of E. subumbrans with a slight note of K. galanga, smooth and slightly moist surface, flexible, and non-sticky.	6.50	0.2	0.098±0.003 (%CV=3.44)	>300
F3	Film, yellowish transparent, characteristic aroma of E. subumbrans with a slight note of K. galanga, smooth and slightly moist surface, flexible, and non-sticky.	6.58	0.2	0.055±0.002 (%CV=4.08)	>300

The evaluation included organoleptic observation to assess the visual appearance, color, and odor of the patch, which serve as preliminary indicators of product acceptability and stability. Measurement of pH was performed to confirm compatibility with skin physiology, thereby minimizing the risk of irritation upon application. Patch thickness and weight uniformity were examined as critical parameters to guarantee dosage consistency and reproducibility during production. Furthermore, folding endurance testing was carried out to evaluate the mechanical strength and flexibility of the patch, which are essential attributes for maintaining structural integrity during handling and prolonged use on the skin.

The three patch formulations evaluated in this study exhibited similar physical appearances and sensory properties: all were film-type matrices with a characteristic aroma of *E. subumbrans* and a slight note of *K. galanga*. Formula 1 appeared as transparent-white and dry with a smooth surface, whereas Formulas 2 and 3 were yellowish-transparent with a slightly moist but smooth surface. Such organoleptic descriptors (color, odor, surface feel, tackiness) are relevant quality attributes for herbal-based transdermal systems because they reflect the composition (extract pigments, residual solvents or oils, plasticizer content) and can influence patient acceptability and perceived quality. Studies on transdermal patches prepared from natural extracts report comparable descriptors and emphasize reporting them because they relate to formulation components (polymer type, plasticizer, extract) and manufacturing conditions.

All formulations had a measured thickness of 0.20 mm, a value within typical ranges reported for matrix-type transdermal patches. Patch thickness is an important formulation parameter: it influences drug loading per unit area, the diffusion pathlength for the active ingredient, mechanical flexibility, and ultimately the in-vitro/in-vivo release and permeation rates. Thinner matrices often permit faster drug release but may reduce mechanical robustness or adhesive capacity, whereas thicker films can slow release but improve handling.

The measured pH values were 6.00 (Formula 1), 6.50 (Formula 2), and 6.58 (Formula 3). From a dermal compatibility standpoint, topical/transdermal products are generally recommended to have a pH close to the skin surface pH to minimize irritation or disruption of the barrier. The skin surface is mildly acidic, and contemporary reviews recommend that topical formulations be formulated near this acidic range when possible, although slightly higher pH is still commonly tolerated for short-term application. Surface moisture may indicate residual solvent, plasticizer migration, or hygroscopic components in the matrix. A slightly moist surface can improve initial adhesion but may also affect tackiness over time, water vapor transmission, and microbial stability.

Weight uniformity testing was carried out on three transdermal patch formulations. Based on these results, all three formulations exhibited %CV values below 10%, indicating that the weight uniformity of the patches was within the acceptable range according to pharmacopeial standards (for preparations weighing <300 mg, a deviation of up to ±10% is permitted) [20]. This suggests that the patch manufacturing process produced relatively consistent weights for each unit. Among the three formulations, formulation 2 demonstrated the best weight uniformity, as indicated by the lowest %CV value (3.44%). This study still has

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several limitations, particularly the absence of an in-depth ethnopharmaceutical evaluation regarding public acceptance of the modern *Usadha*-based formulation and its compatibility with the philosophy of *Usadha*. Therefore, further studies using ethnopharmaceutical and cultural approaches are recommended to evaluate community acceptance, the suitability of the modern formulation with *Usadha* principles, and user preferences for transdermal preparations compared to traditional forms such as *boreh*. Further studies are required, including accelerated stability testing, in vitro release and permeation studies using Franz diffusion cells with both synthetic and biological membranes, as well as release kinetics evaluation to ensure the stability and transdermal performance of the developed formulation.

Irritation test result of transdermal patch nanoemulgel containing *E. subumbrans* leaf extract and *K. galanga* rhizome extract

Following the evaluation of physical uniformity, a human patch test was conducted to assess skin irritation. This test involved 10 participants who met the inclusion criteria, and all procedures were ethically approved under Ethics Clearance No. 296/EA/KEPK-BUB-2025 issued by the Health Research Ethics Committee of STIKES Bina Usada Bali. Based on the results of the human patch test as describe in Table 5, no signs of irritation such as erythema, edema, or stinging sensation were observed in any participants. Only two participants (P2 and P6) reported mild pruritus (score 1), while the others experienced no discomfort. The mean score for pruritus was 0.2 ± 0.42, whereas erythema, edema, and stinging all showed 0.0 ± 0.0.

Table 5. Data of Patch Test Result

Indicator	Score (Mean ± SD)	Category
Erythema	0.0 ± 0.0	No irritation
Oedema	0.0 ± 0.0	No irritation
Pruritus	0.2 ± 0.42	Mild irritation
Stinging sensation	0.0 ± 0.0	No irritation

Overall, these findings indicate that the tested transdermal patches can be considered safe and non-irritating to the skin. The mild pruritus observed in a small subset of participants remained within physiological tolerance limits and was likely related to individual variations in skin sensitivity or response to the patch components. This result is consistent with recent literature reporting that transdermal delivery systems are generally safe and rarely cause significant irritation, particularly when formulated with biocompatible polymers and excipients. These findings suggest that the patches were well tolerated and produced no significant irritation, consistent with previous studies showing minimal irritation in transdermal drug delivery systems [21;22].

In this study, the irritation test was conducted on healthy women of reproductive age who were neither pregnant nor breastfeeding, considering the initial safety aspects of the study, limitations in research time, and ethical approval constraints during the study period. The selection of these subjects was intended as a preliminary evaluation of the topical safety of the developed nanoemulgel transdermal patch formulation. However, physiological conditions during lactation are known to potentially affect skin sensitivity and responses to topical preparations; therefore, the findings of this study may not fully represent the target population, namely breastfeeding mothers. Consequently, before clinical application in breastfeeding women, more comprehensive safety evaluations are required, including assessments of possible changes in skin sensitivity during lactation as well as the potential risk of exposure to both mother and infant resulting from the use of the transdermal preparation.

Conclusions

The ethanol extracts of *Erythrina subumbrans* and *Kaempferia galanga* were shown to contain key phytochemical classes flavonoids, tannins, triterpenoids, saponins, and alkaloids, that collectively may alleviate breast engorgement, ease pain, and support lactation. Quantitative phytochemical analysis revealed a high total flavonoid content, with *E. subumbrans* (47.44 mg QE/g) exceeding *K. galanga* (36.79 mg QE/g), suggesting a stronger antioxidant and bioactive potential. The developed nanoemulsions exhibited favorable physicochemical characteristics being transparent, homogeneous, with an average droplet size of 7.79 nm and PDI 0.192, indicative of good stability and minimal risk of phase separation. The transdermal patch formulations incorporating these nanoemulsions met pharmaceutically relevant criteria and showed no

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significant skin irritation in a human patch test. For future research, it is advisable to conduct *in vivo* studies on lactation-stimulating activity in animal models are required before clinical application, assess the long-term stability of the transdermal system, and perform detailed permeation and release kinetic studies of the active compounds under physiological conditions.

Conflict of Interest

All authors declare that there are no conflicts of interest in this study.

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