

Nanoparticle Patches of Itchy Leaves (*Laportea decumana* (Roxb.) Wedd)

Siti Aprilia Susanti¹, Eva Susanty Simaremare¹ , Rani Dewi Pratiwi¹, Elsy Gunawan¹ ,
Nur Fadillah Bakrie¹

¹ Department of Pharmacy, Faculty of Mathematics and Sciences, University of Cenderawasih, Jayapura, Indonesia

* Correspondence: evasmare13@gmail.com (E.S.S);

Received: 21.03.2023; Accepted: 28.05.2024; Published: 20.12.2025

Abstract: Itchy leaves (*Laportea decumana*) are endemic plants found in Papua with pain-relieving properties. This occurs through widening the pores of blood vessels in the human body, resulting in relief of aches and pain. This study aims to determine the quality of preparation by assessing the effectiveness of itchy leaf nanoparticle patch preparations. Itchy leaves were processed into patch preparations and tested for nanoparticle patch quality evaluation, an irritation test, and analgesic effect testing in mice used as test animals. This test was to measure the amount of wriggling in mice, with observations made every 5 minutes for 1 hour. The itchy leaf simplisa nanoparticles obtained were of good quality, as evidenced by physical weight, folding power resistance, thickness, drying, and irritation tests. The effectiveness of itchy leaves showed that F3 was the best formula, with an average of 105.4 ± 19.66 , a protection percent of 78.77%, and a percent effectiveness of 147.64%. The average analgesic activity data from the positive groups (F1 and F2) differed significantly. The itchy leaf simplicia nanoparticle patch is twice as effective as a patch of micro simplicia.

Keywords: Itchy leaf (*Laportea decumana* (Roxb.) Wedd); analgesics; nanoparticles; patches

© 2025 by the authors. This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The authors retain copyright of their work, and no permission is required from the authors or the publisher to reuse or distribute this article, as long as proper attribution is given to the original source.

1. Introduction

Itchy leaves (*Laportea decumana*) are one of the Genus *Laportea* [1]. In the world, the genus *Laportea* has been used as a traditional medicine because it has many pharmacological activities, such as analgesic [2], anti-inflammatory [3], antioxidant [4], anti-hyperuricemia [5], and reduction of hyperglycemia [6]. Itchy leaves are endemic plants of Papua with jagged leaves and fine fur (hair) along the leaves and stems. This hair is called a trichome, which can relieve pain by widening the pores of blood vessels [7]. Itchy leaves are used by the community as an anti-fatigue and soreness medication.

This plant contains amino acids, trichomes, and other chemical compounds containing formic acid that can relieve pain [8]. That is believed to work after being applied to the body within five minutes, leaving no hurts, aches, or stiffness, and will soon heal. The mechanism is that when leaves are applied to the skin's surface, the trichomes stick to the skin's epidermis. The release of formic acid from the hair (trichome) will dilate blood vessels' pores, facilitating blood circulation and relieving pain [9].

Based on empirical data, people used itchy leaves as analgesics [10] when tired or sore after activities such as gardening, fishing, or other activities. If the leaves were taken and, after several days, they had faded. Some product pharmacy technologies have been developed, such

as ointment, powder [11], and dermal patch. However, the patch dermal distribution did not show effective activity. It was assumed that the particle of simplicia was big so that the active compound did not have maximal penetration [12]. This itchy leaf innovation is expected to be a solution for creating the simplest and most effective nanotechnology product. Therefore, this research aimed to determine the analgesic efficacy of itchy leaf simplicia nanoparticle patches.

2. Materials and Methods

2.1. Materials.

The material consisted of HPMC, methylparaben, propylene glycol, ethanol, and Aquadest. Itchy leaves were collected from Naramben Village, Keerom, Jayapura, Indonesia, and determined at the Herbal Materia Medica Batu Laboratory, with ethical approval number LB. 02.02/2/KE. 597/ 2021 from the Health Research and Development Agency of the Ministry of Health.

2.2. Methods.

2.2.1. Preparation and evaluation of a patch of simplicia nanoparticles of itchy leaf (Figure 1).

2.2.1.1 Simplicia of itchy leaf

The sample was collected and dried in an oven at 40 °C. The simplicity of itchy leaves was achieved using the high-speed top-down milling method. The nanoparticles were made by grinding the starting material with a 60-mesh (180 µm) sieve into ball-milled particles with a size of 288nm. The ratio used was 1:8 each time to mill itchy leaf simplicia, up to 4.84 grams, with 11 pieces of milling balls that weighed 3.52 grams each, and the mixture was placed in a tube (jar). The milling process lasted 6 hours at 1000 rpm. The tubes and balls were washed with ethanol before use. The tool for analyzing particle size was the Beckman Coulter Delsa Nano Particle Analyzer, measured at room temperature (25 °C) with water as the solvent [7].

2.2.1.2. Formulation of simplicia nanoparticles of itchy leaf patches

The nanoparticle patch was made by formulation in Table 1. HPMC's basic manufacturing process was developed with 5 mL Aquadest (mixture 1). In different jars, methyl parabens are dissolved in propylene glycol (mixture 2). Mixture 2 was added to mixture 1, mixed, and eroded until homogeneous. Then, simplicia was added and ground until homogeneous. After the mixture was fully homogeneous, ethanol was added, and it was finally filled with Aquadest to 100 (w/v). It was left at room temperature for ±24 hours and coated to a thickness of ±3 g. The coating was dried in the oven at 50 °C and then placed in a desiccator for ±20 hours. The patch was removed from the mold and stored in a sealed container [7].

Table 1. Nanoparticle patch formulation

Material	Base (w/v)	FI (w/v)	FII (w/v)	FIII (w/v)
Simplicia in nanoparticle	-	0.36	1.1	1.8
HPMC	3	3	3	3
Methyl Paraben	0.3	0.3	0,3	0.3
Propylene Glycol	10	10	10	10
Ethanol	40	40	40	40
Aquadest	Ad 100	Ad 100	Ad 100	Ad 100

2.2.2. Evaluation of patches

2.2.2.1. Organoleptic examination

The organoleptic examination consists of the shape, color, and smell of the patch produced.

2.2.2.2. Uniformity of weight

Patch weights were weighed using analytical balance sheet scales, which were used to weigh each of the 3 patches. Then, researchers determined the average weight and standard deviation [8].

2.2.2.3. Folding power resistance

The folding power resistance was tested by folding the patch several times in the same position. The number of folds was considered a measure of resistance to folding [9-10].

2.2.2.4. Thickness

The patch thickness tester in each formula was used to measure the patch thickness. Measurement of patch thickness was performed using a micrometer tool at 4 different points [11].

2.2.2.5. Drying shrinkage

The patch was weighed and stored in a desiccator for 24 hours. After 24 hours, the patch was reweighed, and the percentage of drying shrinkage was determined [12].

2.2.2.6. Lengthening percentage

Percent of lengthening is the maximum length change that the material can take at the time of stretching or being pulled before it is torn. Length changes can be seen when the patch is torn [7, 13].

$$\% \text{ Elongation} = \frac{b-a}{a} \times 100\% \quad (1)$$

a: initial length; b: after breaking length

2.2.3. Evaluation and anesthetic test of a patch of simplicia nanoparticles of itchy leaf.

2.2.3.1. Test animal preparation

The test animals used consisted of 30 mice (*Mus musculus* L). Test animals were prepared and matured for 1 week by being fed and given ample water. Otherwise, healthy animals were used in the study, for example, animals that during maintenance did not exhibit changes in weight exceeding 10% and exhibited normal behavior [8]. Before testing, the mice were rested for ± 12 hours while still given a drink. Test animals were divided into 5 groups.

Irritation testing was conducted simultaneously with the analgesic effect test, so there were four common control groups: one control group without treatment for irritation testing and one positive control group for analgesic effect testing. The total number of test animals

used in the study was 30 [14]. Test animals were divided into each testing group using the Complete Randomized Design (RAL) method: each test animal was assigned a number, followed by a randomized draw (Figure 2).

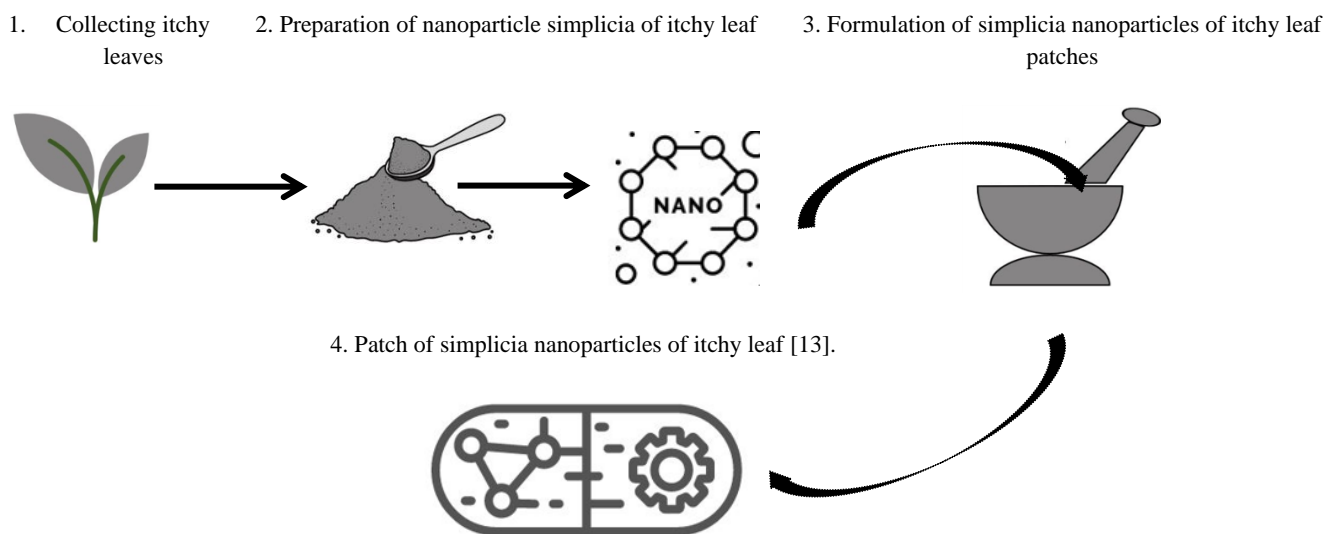


Figure 1. Procedure of an analgesic patch.

2.2.3.2. Irritation test

Irritation testing can be done with a patch test on the skin of a test animal. The test animals were arranged into 5 irritant testing groups: group I was a treatment control; group II used bases; groups III, IV, and V sequentially used FI, FII, and FIII patches. The hair of mice was shaved on the abdomen to affix the patch. It was then covered using a plaster bandage and left for 24 hours. After 24 hours, the plaster bandage was opened and left for 1 hour, then observed (Figure 2). Once observed, the section was re-closed and re-observed after 72 hours [15].

2.2.3.3. Analgesic activity test

Testing was done using the squirm method on male mice. After shaving their hair, the mice were given pain induction with acetic acid intraperitoneally. The mice were divided into five groups: group I as a negative control using patches without itchy leaves (base), group II as a positive control using conventional patches, and groups III, IV, and V sequentially using itchy leaf simplicia patches. FI, FII, and FIII were observed for the number of squirms calculated per 5 minutes for 1 hour [10].

Data were calculated as the percentage of protection of test materials, namely the ability of test materials to reduce the pain response of mice induced by acetic acid [14].

$$\% \text{ Protection} = \frac{\text{the mean number of stretches (control negative group-test group)}}{\text{the mean number of wriggles in the negative control group}} \times 100\% \quad (2)$$

The next test material protection percentage was calculated by comparing the protection percentage in the positive control group.

$$\% \text{ Efectivity} = \frac{\% \text{ Test group protection}}{\% \text{ Positive control group protection}} \times 100\%$$

2.2.4. Data Analysis

The data were analyzed using ANOVA to determine whether there were any meaningful differences across the test groups. It can be expressed meaningfully differently: if the value $p < 0.050$, it can be stated that there is a difference; if the value $p > 0.050$, it can be stated that there is no difference. Then, if there was a meaningful difference, the data analysis would continue with the Smallest Real Difference (BNT) test to determine and show meaningful differences within each specific test group. It can be expressed meaningfully differently when the value $p < 0.050$ and no difference when the value $p > 0.050$.

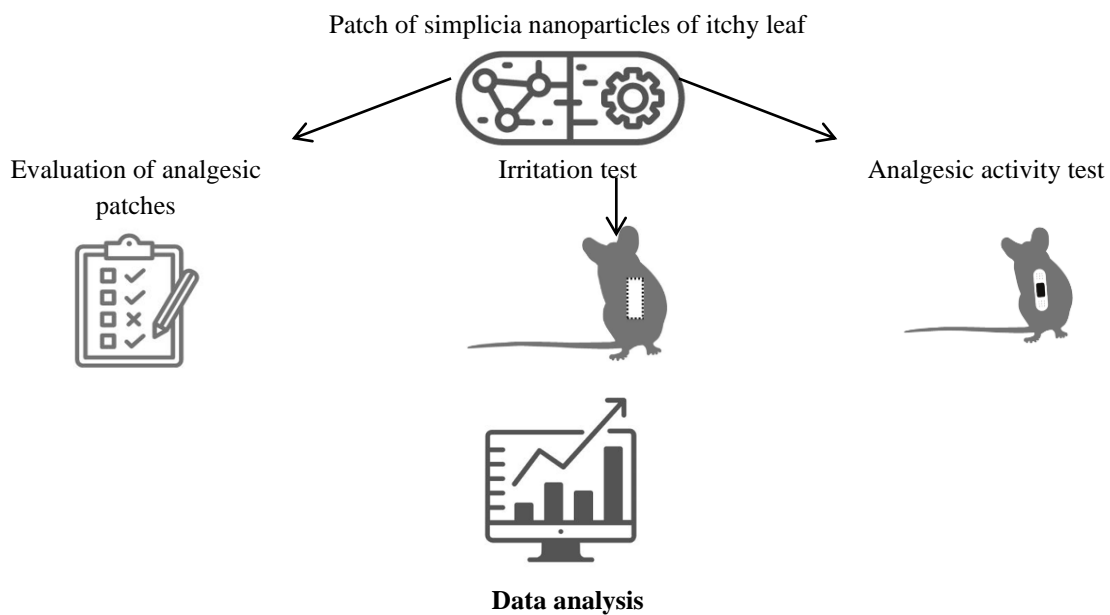


Figure 2. Procedure of an *in vivo* analgesic patch.

3. Results and Discussion

3.1. *Simplicia itchy leaves (L. decumana) nanoparticles.*

Samples of itchy leaf plants were obtained from Naramben Village, Keerom Regency, Papua Province. The manufacturing of simplicia began with leaf sampling, followed by drying in an oven at 40 °C and blending to make a powder [17]. Simplicia was sieved using a 60-mesh (180 µm) sieve and then reduced to nanoparticle size. The study used the high-speed milling method with the Beckman Coulter Delsa Nano Particle Analyzer, which measured at room temperature (25 °C), and used water as the solvent [18]. The measurements obtained an average diameter of 266.8 ± 60.1 nm. The ratio used was 1:8 each time to mill simplicia of the itchy leaf as much as 4.84 grams with 11 pieces of milling balls that weighed 3.52 grams (each ball) and put in a tube (jar). The milling process continued for 6 hours at 1000 rpm, and the tubes and balls were first washed with ethanol. The particle size results showed that the particles were nanoparticle-sized according to the standards [19,20].

3.2. Evaluation of patches.

3.2.1. Organoleptic.

The evaluation results of the itchy leaves simplicia nanoparticle patch showed an irregular, round shape across all preparations (Table 2). Base and FI preparations had a base odor because there were no additives. However, F2 and F3 had a distinctive smell of simplicia due to the higher number of simplicia nanoparticles. The base formula had a clear color, F1 had a light green color, and F2 and F3 were dark green [21].

Table 2. The measurement of itch results in a nanoparticle.

Cumulants Results	
Diameter (d)	: 2029.2
Polydispersity Index (P.I.)	: 0.666 nm
Diffusion Const. (D)	: 2.424e-009 cm ² /sec
Measurement Condition	
Temperature	: 25.0 °C
Diluent Name	: Water
Refractive Index	: 1.3328
Viscosity	: 0.8878 cP
Scattering Intensity	: 11960 cps

3.2.2. Uniformity of weights.

Based on Table 3, the evaluation results for itchy leaf simplicia nanoparticle patches showed uniform weight, with an average weight of 0.52 ± 0.22 . FI had an average weight of 0.44 ± 0.04 , F2 was 0.64 ± 0.06 , and F3 was 0.47 ± 0.05 . All formulation uniformity weights were suitable because they were smaller than the standard value (<5%) [22].

Table 3. Results of Evaluation of Simplicia Nanoparticle Patch of Itchy Leaves

Physical Evaluation	Base	F1	F2	F3
Shape	Round and smooth	Round and must be	Round and soft	Round and Soft
Smell	Base	Base	Typical simplicia	Typical simplicia
Color	Clear	Light green	Dark green	Dark green
Uniformity of Weight (g)	0.52 ± 0.22	0.44 ± 0.04	0.64 ± 0.06	0.47 ± 0.05
Folding Power Resistance	> 200	>200	>200	>200
Thickness (mm)	0.2 ± 0.005	0.2 ± 0.005	0.2 ± 0.005	0.2 ± 0.006
Drying Shrink	4.41 ± 0.992	12.8 ± 0.652	1.56 ± 0.162	11.71 ± 0.452
Elonging Percentage	75 %	100%	100%	87%
Irritation Test	0.00 ± 0.000 Not irritating	0.00 ± 0.000 Not irritating	0.1 ± 0.223 Slightly irritating	0.1 ± 0.223 Slightly irritating

3.2.3. Folding power resistance.

Folding power resistance aims to determine the elasticity of the nanoparticle patch after folding to the same position until it breaks [23]. The standard of folding power resistance is >200 folds [24]. The results obtained for Itchy leaf nanoparticle patches showed a folding power of >200 folds, so the formulas were compiled according to the established standard (Table 3).

3.2.4. Thickness.

Evaluation of the patch preparation thickness aims to determine the uniformity of the formula's thickness. Based on Table 3, the thickness of the four formulas was 0.2 mm. Thus, the patch of three formulas had a thickness that suited the standard (>1mm) [23].

3.2.5. Drying shrinkage.

Drying stacking aims to determine the moisture content during patch preparation. The result showed that the drying shrinkage of the formula was 4.41%, 12.8%, 1.56%, and 11.71% (Bases, F1, F2, and F3, respectively). The requirement for the standard value is < 9.29%, so that the base and F2 complied with the standard (<10%). However, F1 and F3 are not eligible because the drying shrinkage value exceeded 10%.

3.2.6. Lengthening percentage.

Percent of lengthening is the maximum length change that the material can take at the time of stretching or being pulled before it is torn. Length changes can be seen when the patch is torn [15]. Percent of lengthening is the maximum length change that the material can make when stretching or being pulled before the material is torn. Based on Table 3, the base, F1, F2, and F3 formulas meet the standard requirements of > 33% [23].

3.3. Irritation test.

Irritation testing aims to show whether the preparations made have an irritating effect on the skin. Table 3 shows that the base and F1 do not show irritation (0.00), and F2 and F3 show irritation (0.1) but do not show severe irritation. This can occur due to the itchy effects of itchy leaf nanoparticles.

3.4. Analgesic test.

3.4.1. Preliminary test.

A preliminary test for acetic acid concentration was conducted to determine the concentration required to induce a writhing response in mice. Mice test animals exhibited a writhing response, including licking their feet, extending both legs forward and backward, and pressing their stomachs down (stretching the body).

Based on Table 4, the results of the preliminary test on acid concentration indicate that an acetic acid concentration of 0.6% yields an average number of stretches of 270.33. For acetic acid concentrations of 0.8% and 1%, the average number of stretches is quite a lot, so it will be easy to observe them. 0.8% has an average of 457.00, and 1% acetic acid has an average of 412.33 stretches. Therefore, the acetic acid concentration used for the next test is 0.8% with the highest average number of stretches, so it is easy to observe.

Table 4. Results of Determination of Acetic Acid Concentration

Determination of Acetic Acid Concentration	
Acetic Acid Concentration	Average
0.6%	270.33
0.8%	457.00
1.0%	412.33

Determination of Conventional Patch Preparations

Patch size	Average
1 cm x 1 cm	257.33
2 cm x 2 cm	288.67
3cm x 3 cm	147.00
Determination of Composition of Itchy Leaf Simplicia	
Composition of simplicia	Average
F1	238.33
F2	267.33
F3	144.33

3.4.2. Determination of conventional patch sizes.

Preliminary tests were conducted to determine conventional patch sizes that could reduce the writhing response in mice. Based on the test results, a patch measuring 3cm x 3cm can already show healing activity, as it elicits the least writhing response in mice, with an average of 147.00 ± 37.21 . Patches of 1cm x 1cm elicited fewer wriggling responses, with an average of 257.33 ± 32.47 , compared to patches of 2cm x 2 cm, with an average of 288.67 ± 46.61 . Based on that, the conventional patch size used as a positive control in the next test is a patch with a size of 2cm x 2cm. A patch measuring 3cm x 3cm was not chosen because it is large and will make it difficult for mice to move.

3.4.3. Determination of the composition of itchy leaf simplicia.

Tests were carried out to determine the composition of itchy leaf simplicia in patches that can effectively reduce writhing in mice. Based on the test results, F1 showed the greatest reduction in writhing in mice, with an average of 238.33 ± 67.82 , followed by F2, with an average of 267.33 ± 50.96 , and F3, which showed the least stretched response, with an average of 144.33 ± 37.07 . So that all three can be used in the next test.

3.4.4. Analgesic activity test.

Testing was performed to determine the analgesic effectiveness of the preparations using the wriggling method in male mice [25]. Before conducting the test, the preliminary test was completed to determine acetic acid levels, the size of conventional patches, and the composition of simplicia. Based on this, it was found that the acetic acid concentration used was 0.8% because of the greatest number of wriggles [12]. The size of the conventional patch used was 2x2 cm for the base, positive control, formulas 1, 2, and 3. Data were calculated for the percentage of protection of test materials, namely the ability of test materials to reduce the mice's pain response to the mictest material and to the acetic acid-induced pain response [16]. The next test material protection percentage was calculated by comparing the protection percentage in the positive control group.

Based on the results in Figure 3, the negative group had a higher average number of wriggings because it did not contain ingredients that could reduce wriggling in mice. In the positive control, F1, F2, and F3 showed a reduction in wriggling in mice. The ANOVA test showed significant results for every formulation ($p < 0.05$). LSD test results confirmed that the average analgesic activity data for the negative groups and the F1, F2, and F3 groups differed significantly. In addition, the average analgesic activity data from the positive groups with F1 and F2 differed significantly. That means each formula had different activity values than the others.

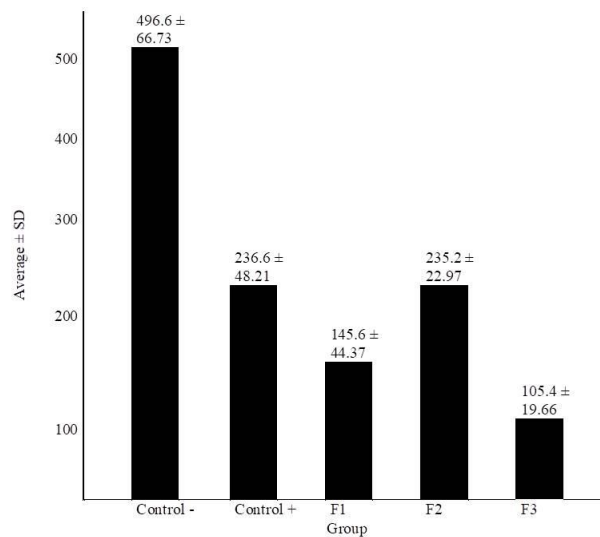


Figure 3. Results of analgesic activity test of nanoparticle simplicia *L.decumana*

Figure 4 displays the percent protection, which is the test material's ability to reduce the squeak response induced by acetic acid [16]. For the negative control, the percent protection and effectiveness were 0% because there were no simplicia or active compounds that reduced the response of wriggling in mice. The positive control had protection and effectiveness percentages of 52.35% and 100%, F1 70.68% with 135.01%, F2 52.63% with 100.53%, and F3 78.77% with 147.64%, respectively.

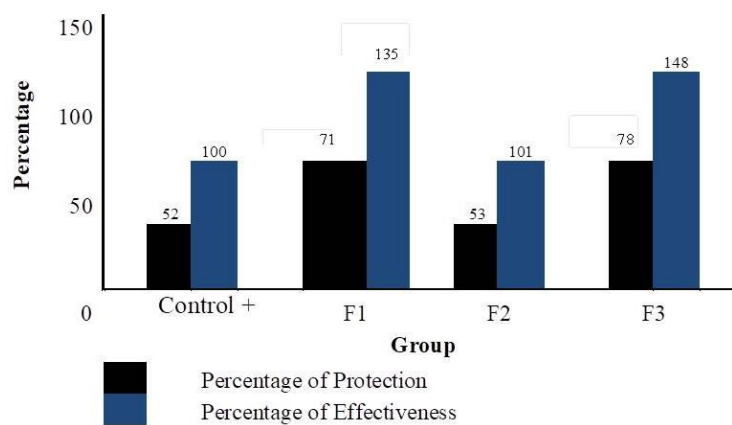


Figure 4. Test results of the protection percentage of nanoparticle simplicia *L.decumana*

In previous tests conducted at a simple size of 180 μm , the effectiveness was found to be close to that of the positive control [12]. However, in this study, the percentage and effectiveness of the patches were higher than those of the control group. The simplicia size of nanoparticles (266.8 nm) was more effective (50%) than simplicia at micrometer size (180 μm). It happened because the active compounds were more widely distributed and penetrated the skin surface [26]. These phenomena confirmed that a particle's size influenced the drug effect [27].

Itchy leaves have weapons in the form of hair or stiff fur (trichomes) that contain formic acid and methyl silicic acid. When the trichomes contact the skin, formic acid and methyl silicic acid will be released through the trichomes by applied pressure or an enzymatic process. Formic acid works by providing a sensation of decreased blood vessel sensitivity, stimulating

pain receptors so that blood can flow smoothly and reduce pain and aches in the body or muscles. Methyl salicylate gave the analgesic activity.

Nevertheless, this study was limited to a short-term in vivo evaluation using a single pain-induction model, and further investigations involving long-term safety, mechanistic studies, pharmacokinetics, and clinical evaluation are warranted. Future research should also explore formulation optimization, stability studies, and broader therapeutic applications to support the development of *L. decumana* nanoparticle patches as a viable herbal-based transdermal analgesic product.

4. Conclusions

This study demonstrates that nanoparticle-based simplicia patches of *Laportea decumana* exhibit satisfactory physicochemical quality and significantly enhanced analgesic activity compared to conventional and micro-sized formulations. Among the tested formulations, F3 showed the highest analgesic performance, with superior protection and effectiveness percentages, indicating that particle size reduction to the nanoscale improves skin penetration and therapeutic efficacy. These findings highlight the potential of nanotechnology-driven transdermal delivery systems to optimize the traditional use of itchy leaves as topical analgesics, offering a more effective, practical, and standardized pharmaceutical dosage form.

Author Contributions

Conceptualization, E.S.S.; methodology, E.G.; validation, E.S.S. and R.D.P.; investigation, S.A.S.; resources, N.F.B.; data curation, R.D.P. and N.F.B.; writing—original draft preparation, E.S.S. and S.A.S.; writing—review and editing, E.S.S. and E.G.; visualization, N.F.B.; supervision, E.S.S.; project administration, S.A.S.; funding acquisition, E.G. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement

The animal study protocol was approved by the Health Research and Development Agency of the Ministry of Health (LB.02.02/ 2/ KE. 597/ 2021).

Informed Consent Statement

Not applicable.

Data Availability Statement

Data supporting the findings of this study are available upon reasonable request from the corresponding author.

Funding

This research was funded by the Ministry of Education and Culture of the Republic of Indonesia, which provided financial support for this study.

Acknowledgments

The authors would like to thank Cenderawasih University

Conflicts of Interest

The authors declare no conflict of interest.

Role of Funders

The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

References

1. Mangiwa, S.; Mangiwa, S.; Mangiwa, S. Alkaloid Cytotoxic Test on Ethanol Extract from Itchy Leaves (*Laportea Decumana* (Roxb.) Wedd.). *Research and Advances in Pharmacy and Life Sciences* **2021**, *3*, 1–8, <https://doi.org/10.46610/rapls.2021.v03i02.001>.
2. Thalib, A.; Masadah, R.; Prihartono, P.; Hamid, F.; Hasan, H.; Keliwawa, S.; Labulawa, I. *Laportea Decumana* (Roxb.) Wedd. Herbal Endemic Potential from Indonesia: A Literature Review. *Open Access Macedonian Journal of Medical Sciences* **2021**, *9*, 639–643, <https://doi.org/10.3889/oamjms.2021.7759>.
3. Simaremare, E.S.; Souisa, W.V. Uji Aktivitas Antihiperurisemia Ekstrak Daun Gatal (*Laportea Decumana* (Roxb.) Wedd) Asal Papua. *Pharmauho: Jurnal Farmasi, Sains, dan Kesehatan* **2021**, *7*, 21, <https://doi.org/10.33772/pharmauho.v7i1.14966>.
4. Wang, M.M.; Li, Y.N.; Ming, W.K.; Wu, P.F.; Yi, P.; Gong, Z.P.; Hao, X.J.; Yuan, C.M. Bioassay-Guided Isolation of Human Carboxylesterase 2 Inhibitory and Antioxidant Constituents from *Laportea Bulbifera*: Inhibition Interactions and Molecular Mechanism. *Arabian Journal of Chemistry* **2022**, *15*, 103723, <https://doi.org/10.1016/j.arabjc.2022.103723>.
5. Wang, M.M.; Li, Y.N.; Ming, W.K.; Wu, P.F.; Yi, P.; Gong, Z.P.; Hao, X.J.; Yuan, C.M. Bioassay-Guided Isolation of Human Carboxylesterase 2 Inhibitory and Antioxidant Constituents from *Laportea Bulbifera*: Inhibition Interactions and Molecular Mechanism. *Arabian Journal of Chemistry* **2022**, *15*, 103723, <https://doi.org/10.1016/j.arabjc.2022.103723>.
6. Mohammed, A. Hypoglycemic Potential of African Medicinal Plants in Diabetic and Non-Diabetic Human Subjects: A Review. *Clinical Complementary Medicine and Pharmacology* **2023**, *3*, 100081, <https://doi.org/10.1016/j.ccmp.2023.100081>.
7. Simaremare, E.S.; Ruban, A.; Runtuboi, D.Y.P. Aktivitas Antibakteri Ekstrak Etanol Daun Gatal (*Laportea Aestuans* (L.) Chew). *Jurnal Biologi Papua* **2018**, *9*, 1–7, <https://doi.org/10.31957/jbp.101>.
8. Simaremare, E.S.; Suryani Worabay, P.A.; Martogi Hutapea, H. The Level of Community Knowledge on the Usage of Itchy Leaves. *Journal of Pharmacological Research and Developments* **2021**, *3*, 10–19, <https://doi.org/10.46610/jprd.2021.v03i02.002>.
9. Simaremare, E.S.; Pratiwi, R.D.; Rusnaeni, R.; Gunawan, E.; Dirgantara, S. Pemanfaatan Tanaman Daun Gatal (*Laportea Decumana*) Sebagai Obat Anti Capek. *JPPM (Jurnal Pengabdian dan Pemberdayaan Masyarakat)* **2019**, *3*, 97, <https://doi.org/10.30595/jppm.v3i1.3027>.
10. Basy, L. La; Santosa, D.; Murwanti, R.; Hertiani, T. Taylor. *Pharmacognosy Journal* **2022**, *14*, 286–295, <https://doi.org/10.5530/pj.2022.14.98>.
11. Simaremare, E.S.; D. N. Putri, C.; D. Pratiwi, R.; Gunawan, E. Itchy Leaves (*Laportea Decumana* (Roxb.) Wedd) Simplicia Loose Powder. *Malaysian Journal of Medical Research* **2022**, *06*, 09–13, <https://doi.org/10.31674/mjmr.2022.v06i01.003>.
12. Simaremare, E.S.; Tolip, M.R.Y.; Pratiwi, R.D. TAY. *Current Applied Science and Technology* **2022**, *22*, 1–13, <https://doi.org/10.55003/cast.2022.03.22.008>.
13. Zhou, B.; Liu, S.; Yin, H.; Qi, M.; Hong, M.; Ren, G. Bin Development of Gliclazide Ionic Liquid and the Transdermal Patches: An Effective and Noninvasive Sustained Release Formulation to Achieve Hypoglycemic Effects. *European Journal of Pharmaceutical Sciences* **2021**, *164*, 105915, <https://doi.org/10.1016/j.ejps.2021.105915>.
14. Suryani; Musnina, W.O.S.; Ruslin; Nisa, M.; Aprianti, R.; Hasanah, M.; Putri, F.R.; Adjeng, A.N.T.; Yuniar, N.; Sahumena, M.H.; et al. Formulation and Physical Characterization of Curcumin Nanoparticle Transdermal Patch. *International Journal of Applied Pharmaceutics* **2019**, *11*, 217–221, <https://doi.org/10.22159/ijap.2019v11i6.34780>.
15. Nurmessa, A.; Nurhabibah, N.; Najihudin, A. Formulasi dan evaluasi stabilitas fisik patch transdermal alkaloid nikotin daun tembakau (*Nicotiana Tobacum* Linn) dengan variasi polimer dan asam oleat. *Jurnal Penelitian Farmasi & Herbal* **2019**, *2*, 1–8, <https://doi.org/10.36656/jpjh.v2i1.150>.
16. Galani, V.J.; Patel, B.G. Analgesic and Anti-Inflammatory Activity of *Argyrea Speciosa* and *Sphearanthus Indicus* in the Experimental Animals. *Global Journal of Pharmacology* **2010**, *4*, 136–141, [https://idosi.org/gjp/4\(3\)10/8.pdf](https://idosi.org/gjp/4(3)10/8.pdf).
17. Kustiati, U.; Wihadmadyatami, H.; Kusindarta, D.L. Dataset of Phytochemical and Secondary Metabolite

- Profiling of Holy Basil Leaf (*Ocimum Sanctum* Linn) Ethanolic Extract Using Spectrophotometry, Thin Layer Chromatography, Fourier Transform Infrared Spectroscopy, and Nuclear Magnetic Resonance. *Data in Brief* **2022**, *40*, <https://doi.org/10.1016/j.dib.2021.107774>.
18. Caputo, F.; Clogston, J.; Calzolari, L.; Rösslein, M.; Prina-Mello, A. Measuring Particle Size Distribution of Nanoparticle Enabled Medicinal Products, the Joint View of EUNCL and NCI-NCL. A Step by Step Approach Combining Orthogonal Measurements with Increasing Complexity. *Journal of Controlled Release* **2019**, *299*, 31–43, <https://doi.org/10.1016/j.jconrel.2019.02.030>.
 19. Kotsuchibashi, Y.; Nakagawa, Y.; Ebara, M. Nanoparticles. *Biomaterials Nanoarchitectonics* **2016**, *5*, 7–23, <https://doi.org/10.1016/B978-0-323-37127-8.00002-9>.
 20. Saepurahman; Hashaikeh, R. Insight into Ball Milling for Size Reduction and Nanoparticles Production of H-Y Zeolite. *Materials Chemistry and Physics* **2018**, *220*, 322–330, <https://doi.org/10.1016/j.matchemphys.2018.08.080>.
 21. Shams, M.S.; Alam, M.I.; Ali, A.; Sultana, Y.; Aqil, M. Pharmacodynamics of a Losartan Transdermal System for the Treatment of Hypertension. *Drug Development and Industrial Pharmacy* **2010**, *36*, 385–392, <https://doi.org/10.3109/03639040903188471>.
 22. Ullah, W.; Nawaz, A.; Akhlaq, M.; Shah, K.U.; Latif, M.S.; Doolaanea, A.A.; Alfatama, M. Transdermal Delivery of Gatifloxacin Carboxymethyl Cellulose-Based Patches: Preparation and Characterization. *Journal of Drug Delivery Science and Technology* **2021**, *66*, 102783, <https://doi.org/10.1016/j.jddst.2021.102783>.
 23. Mutlu, M.E.; Ulag, S.; Sengor, M.; Daglılar, S.; Narayan, R.; Gunduz, O. Electrospayed Collagen/Gentamicin Nanoparticles Coated Microneedle Patches for Skin Treatment. *Materials Letters* **2021**, *305*, 130844, <https://doi.org/10.1016/j.matlet.2021.130844>.
 24. Talib, S.; Ahmed, N.; Khan, D.; Khan, G.M.; Rehman, A. ur Chitosan-Chondroitin Based Artemether Loaded Nanoparticles for Transdermal Drug Delivery System. *Journal of Drug Delivery Science and Technology* **2021**, *61*, 102281, <https://doi.org/10.1016/j.jddst.2020.102281>.
 25. Genevois, A.L.; Ruel, J.; Penalba, V.; Hatton, S.; Petitfils, C.; Ducrocq, M.; Principe, P.; Dietrich, G.; Greco, C.; Delmas, P. Analgesic Effects of Topical Amitriptyline in Patients With Chemotherapy-Induced Peripheral Neuropathy: Mechanistic Insights From Studies in Mice. *Journal of Pain* **2021**, *22*, 440–453, <https://doi.org/10.1016/j.jpain.2020.11.002>.
 26. Trushina, D.B.; Borodina, T.N.; Belyakov, S.; Antipina, M.N. Calcium Carbonate Vaterite Particles for Drug Delivery: Advances and Challenges. *Materials Today Advances* **2022**, *14*, 100214, <https://doi.org/10.1016/j.mtadv.2022.100214>.
 27. Abdellahi, M.; Tajally, M.; Mirzaee, O. The Effect of the Particle Size on the Heating and Drug Release Potential of the Magnetic Nanoparticles in a Novel Point of View. *Journal of Magnetism and Magnetic Materials* **2021**, *530*, 167938, <https://doi.org/10.1016/j.jmmm.2021.167938>.

Publisher's Note & Disclaimer

The statements, opinions, and data presented in this publication are solely those of the individual author(s) and contributor(s) and do not necessarily reflect the views of the publisher and/or the editor(s). The publisher and/or the editor(s) disclaim any responsibility for the accuracy, completeness, or reliability of the content. Neither the publisher nor the editor(s) assume any legal liability for any errors, omissions, or consequences arising from the use of the information presented in this publication. Furthermore, the publisher and/or the editor(s) disclaim any liability for any injury, damage, or loss to persons or property that may result from the use of any ideas, methods, instructions, or products mentioned in the content. Readers are encouraged to independently verify any information before relying on it, and the publisher assumes no responsibility for any consequences arising from the use of materials contained in this publication.