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Research article

Formulation and Effectiveness Test of Analgesic Patch from Itchy Leaves *(Laportea decumana* (Roxb.) Wedd)

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Abstract

The leaves of the Itchy leaves plant (*Laportea decumana* (Roxb.) Wedd) are considered very effective in Papuan traditional medicine as a natural anti-pain (analgesic) treatment. This study aimed to determine the quality and effectiveness of the analgesic patches made from the Itchy leaves plant. Three formulas were used with the composition of the simplicia in the formula; FI 0.38% (w/v), FII 1.11% (w/v), and FIII 1.80% (w/v). The patch quality evaluation included organoleptic qualities, weight variation, folding endurance, thickness, drying loss, percent elongation, and an irritation test. In the analgesic effect test, the wriggling method was used on mice, and induced intraperitoneally with acetic acid. The mice were divided into five groups: negative control, positive control, and three groups receiving doses using patches FI, FII, and FIII. The observation of wriggling was calculated in 5-min intervals for 1 h. Data were analyzed statistically using the one-way ANOVA test and the least significant difference (LSD) test with a significant level of 5% ($p \leq 0.05$). The results showed that patches had an imperfect round shape, distinctive odor, green color, consistent weight, consistent thickness, flexibility, elasticity, and produced a little irritation, which was not harmful. The results of the statistical analysis of FI, FII, and FIII of the Itchy leaf patch (*Laportea decumana* (Roxb.) Wedd) showed significant differences in analgesic effects. The analgesic effect test results showed that patch FII with a crude drug composition of 1.11% (w/w) had the best reduction in wriggling responses in mice, with a protective power of 68.69%.

1. Introduction

Itchy leaves (*Laportea decumana* (Roxb.) Wedd) are shrubs/herbs that grow wild in East Indonesia's forests (Papua, Maluku). The plant is efficacious as a medicine for stiffness, stomach

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aches, sprains, rheumatism, muscle pain, back pain, headaches, and malaria [1]. The Papuan community uses this plant as a natural treatment. Itchy leaves are used by rubbing the leaves directly on the body part that feels sore or painful. Itchy leaves are used to eliminate dizziness by attaching some leaves to the forehead until the dizziness goes away [2].

Based on previous research on the use of Itchy leaves , ethanol extracts of *Laportea aestuans* (Linn.) Chew were assessed for a range of characteristics including toxicity, antioxidant, analgesic, and anti-inflammatory properties [3, 4]. Other researchers reported that there was an insignificant comparative analysis of the effectiveness of anti-pain ointments from two different leaf samples (mountain and coastal) [5]. Moreover, the physical qualities of an Itchy leave ointment formulation (*Laportea decumana* (Roxb.) Wedd.) was tested and revealed that the ointment was stable [6-8]. Both types of these Laportea had trichomes that could be used to overcoming pain relief.

Pain is an unpleasant sensory and emotional experience that arises due to tissue damage, either actual or potential, as described in Meliala [9] or due to tissue that tends to be damaged [10]. Non- Steroid Anti - Inflammatory Drugs (NSAIDs) can be used as the primary drug in managing pain.

Currently, various types of dosage forms for pain relief are available, such as injections, solutions, tablets, capsules, gels, creams, ointments, and patches. The fact that the treatment of pain with oral preparations can cause inconvenience because not all patients like oral dosage forms requires pain treatments to be more practical. In previous studies, pain relief from the use of Itchy leaves that had been made in topical ointments, and the physical qualities of the ointments were tested [5-7]. In this study, the treatment with Itchy leaves as anti-pain made in the preparation of patch analgesics is one form of a drug delivery system involvingh placement on the skin.

The patch is an adhesive preparation with layer adhesive containing the drug and placed on the skin to deliver a specific medication through the skin. Drug therapy in this system can be easily terminated if drugs are no longer desired. A layer of adhesive on the patch that attaches to the skin can ensure analgesic activity [11].

The patch type delivery system has some advantages. The patch can easily deliver the drug at a controlled rate, can easily be applied to the skin, and can be removed easily to terminated drug administration in case of toxic effects. Somehow, patches have become an alternative route of administration for drugs because they can avoid the occurrence of gastrointestinal disorders that can arise as a result of drugs given orally [12]. The dermal patch was formulated by adding enhancers (penetration enhancing agents) that help the penetration of active substances through the layers of the skin as well as having active compounds that provide analgesic effects. The composition of the patch was formulated with enhancers such as HPMC so that the penetration power would also increase [11, 12].

A lot of current research on Itchy leaves has been concerned with two products (ointment and powders). However, in this study, the dermal patch was made to increase ease of use and to improve the penetration of the active compounds from the leaf into the skin.

2. Materials and Methods

2.1 Collecting, determination, and preparation of Itchy leaves

These leaves were determined with code 06/UN42.15.2/PP/VI/2018. Samples of Itchy leaves were obtained from the Paniai District, Papua Province. The process of simplicia started by taking the required sample, namely the leaves (the large and the old leaves), and then drying them with the help of sunlight. The dry Itchy leaves simplicia was blended then mashed into a powder.

The simplicia powder was sieved using a 60 mesh (180 μm) sieve. Sieving was aimed to obtain a fine crude drug powder that still provided a therapeutic effect. The fine crude drug powder obtained was stored in a closed container. The weight of the fine crude powder was 400 g.

The smooth crude drug was made into three variant dosage formulas. The dosage of the crude drug used was based on the number of Itchy leaves used by the community for treatment. Empirically, one 3 gram Itchy leaf can provide an analgesic treatment effect. The dose used after being converted to a dose for the mice was 7.8mg/20g BW; 23.4mg/20g BW; and 39mg/20g BW.

2.2 Formulation of Itchy leaf analgesic simplicia patch preparations

The composition of the patch formulations is shown in Table 1. The HPMC (hydroxypropyl methylcellulose) bases were developed with 5 ml of aquadest (mixture 1). In a different container, methylparaben was dissolved in propylene glycol (mixture 2). Mixture 2 was added to mixture 1, then crushed until homogeneous. Simplicia was added to the solution and crushed until homogeneous. Ethanol (96%) was added to the mixture and ground until homogeneous. The remaining aquadest was added to make up the weight to 10 g. Next, it was kept for 24 h at room temperature and poured into molds of 3g. Then, it was placed in an oven at 50°C, until dry, then put in a desiccator for 20 h. The patch was then removed from the mold and stored in a closed container [13]. The composition of the patch formulation was made into 10 g for each fomula by calculation.

Table 1. Itchy leaf crude drug patch formula

Material	Base (w/v)	F I (w/v)	F II (w/v)	F III (w/v)
Crude drug	-	0.38	1.11	1.80
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

2.3 Evaluation of Itchy leaf crude drug analgesic patches

2.3.1 Organoleptic examination

The organoleptic examination included observing the shape, color, and smell of the resulting patch.

2.3.2 Weight uniformity

Each patch was weighed using an analytical balance, and the average value and standard deviation were determined for every three patches [14-16].

2.3.3 Folding power resistance

The folding resistance tester was carried out by flopping the patch about 300 times repeatedly manually in the same position until the patch broke. The folding resistance was considered the value of resistance to folding [14, 15].

2.3.4 Thickness

The patch thickness in each formula was measured using micrometer that had an accuracy of 0.01 mm. Measurement was tested on four different points of the patch [14-16].

2.3.5 Drying shrinkage

Each patch was weighed and stored in a desiccator containing silica for 24 h. After 24 h, the patches were re-weighed, and the percentage of drying loss was determined [14-16].

2.3.6 Percent elongation

Percent elongation is the maximum length change that a material can experience when stretched until it is broken. Length change could be seen when the patch was torn [13, 16].

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

Remarks:

a = initial length
b = length after breaking

2.3.7 Irritation test

The irritation test can be performed using a patch test on the skin of the test animals (mice) [17]. All the mice were 3-4 months old, averaging 32 g in weight and 20 cm in height. They were prepared in 5 groups for irritation testing, namely group I as the control without treatment, group II using the base, groups III, IV, and V sequentially using patch FI, FII, and FIII. The abdominal hair was shaved to apply a patch and covered with a gauze bandage. After 24 h, the plaster bandage was opened, left opened for an hour, and observed. Furthermore, for each skin condition, the values are given [16] as follows:

1. Erythema
   a. No erythema (not visible) = 0
   b. Erythema very mild (barely visible; 25 mm diameter) = 1
   c. Mild erythema (clearly visible; 25-30 mm diameter) = 2
   d. Moderate erythema (30-35 mm diameter) = 3
   e. Erythema severe (dark red; forms an eschar; 30 mm in diameter) = 4
2. Edema
   a. No edema (not visible) = 0
   b. Edema very mild (almost imperceptible) = 1
   c. Edema mild (clearly visible margins; thickness of 1 mm) = 2
   d. Edema (1 mm margin) = 3
   e. Edema severe (margins 1 mm and extends beyond the test area) = 4

The irritation index was calculated by adding up each test animal's values after 24 h and 72 h of giving the sample, then dividing it in half. Rate irritation is as follows:

0.00 = No irritation
0.04-0.99 = Slight irritation
1.00-2.99 = Mild irritation
3.00-5.99 = Irritation
6.00-8.00 = Severe irritation

2.4 Preparation of test animals

The test animals used were mice *(Mus musculus*) consisting of as many as 30 mice. The test animals were prepared and acclimatized for one week with sufficient food and drink. Only mice that were declared healthy were used in the study. During maintenance, the mice that had the weight change not exceeding 10% and showed normal behavior, were selected [13]. Before testing, the mice were put on a water fast for 18 h. The test subjects used in the irritation and analgesic activity testing were grouped into five groups. The minimum number of samples per test group was determined according to Federer's formula for experimental tests:

$$(t-1)\,(n-1) \geq 15 \quad (2)$$

in which (t) was the treatment groups and (n) is the number of samples for treatment.

$(t-1)\,(n-1) \geq 15$
$(5-1)\,(n-1) \geq 15$
$4\,(n-1) \geq 15$
$4n-4 \geq 15$
$4n \geq 19$
$n \geq 4.75$

Based on the calculations, the minimum number of test animals used per treatment group was five mice. The irritation test was carried out simultaneously with the analgesic effect test. Four control groups were the same for the two tests, one untreated control group was used for the irritation test, and one positive control group for the analgesic effect test. The tested animals were divided into each test group using the Completely Randomized Design (CRD) method, namely by giving each animal a number, then drawing a random drawing.

2.5 Analgetic activity test

Tests were carried out using the wriggling method. The abdominal hair of the mice was shaved beforehand according to the size of the patch. Furthermore, the mice were given pain induction using acetic acid intraperitoneally, then the test patches were attached. The mice were divided into five groups: group I as negative control using patches without Itchy leaf crude drug (base), group II as a positive control using conventional patches, groups III, IV, and V sequentially using the Itchy leaf simplicia patches FI, FII, and FIII. Observation of the amount of wriggling was calculated every 5 min for 1 h. During the early test, the test animals were given the same food to avoid each test animal's internal variability. The data calculated was on the percentage of protection of the test material that we called the test material's ability to reduce the wriggling response of mice due to acetic acid induction [16, 18].

$$\% \text{ Protection} = \frac{\text{Mean of wriggle amount (negative control group} - \text{material test group)}}{\text{Mean of the wriggle amount in the negative control group}} \text{ x } 100\% \quad (3)$$

The percentage of data for protecting the test material was then calculated by comparing the ratio of protection in the positive control group:

$$\% \text{ Effectiveness} = \frac{\%\text{Protection of material test group}}{\%\text{Protection of positive control group}} \text{ x } 100\% \quad (4)$$

2.6 Data analysis

Data analysis consisted of a one-way analysis of variance (ANOVA) to determine whether there were significant differences between the test groups. The difference was significant if the p-value was <0.05, and the difference was insignificant if the p-value was > 0.05. If there was a significant difference in the results, it was followed by a test of the Least Significant Difference (LSD) with the level of significant difference of 5% ($p \leq 0.05$). The software used to analyze statistical data was SPSS Statistics 20.

3. Results and Discussion

3.1 Formulation of analgesic simplisia Itchy leaves patch preparations

The leaves of Itchy leaves plants have secondary metabolites such as alkaloids, glycosides, and terpenoids. In addition, the leaves have defensive structures, which are stiff hairs or bristles (trichomes) that contain formic acid. These leaves are believed to be hereditary that are affixed to a person feeling sore or stiff, and the pain or stiffness will then decrease. When trichomes are applied to the body, formic acid comes out through enzymatic processes. Formic acid widens blood pores so that blood flows smoothly. This mechanism reduces pain and stiffness in the body or in muscles [7]. Itchy leaves are considered very useful in treatment, so the previously mentioned Papuan community uses them as a natural antipain (analgesic) treatments [8].

The formula consisted of ingredients including HPMC, methylparaben, propylene glycol, ethanol, and aquadest [19]. Orientation was carried out first to obtain the appropriate composition of the ingredients. A physically good patch must be flexible, thin, and homogeneous. Based on the results of the orientation, it was found that the formula in 10 g contained a composition of 3% HPMC, 0.3% methylparaben, 10% propylene glycol, and 40% ethanol. Based on the calculation, the formula was made in three formulas (FI, FII, and FIII) with the composition of Itchy leaves crude drug in 10 g containing the formula of 36 mg, 111 mg, and 180 mg, respectively.

3.2 Evaluation of Itchy leaf crude drug analgesic patches

A physically good patch must be flexible, thin, homogeneous, and have low drying shrinkage and moisture absorption. The standard used in this study is shown in Table 2.

3.2.1 Organoleptic examination

Based on Table 2, the shapes of the base patches, FI, F II, and F III were irregularly round. This shape was due to the fact that the size of the printed area did not match the size of the desired patch area resulting in a patch that was not perfectly round. The shape and width of the print can affect the shape and size of the patch.

Table 2. Evaluation results of Itchy leaf analgetic patches

Evaluation	Base	FI	FII	FIII
Organoleptic				
Shape	Irregular round	Irregular round	Irregular round	Irregular round
Smell	Typical base	Typical base	Typical simplicia	Typical simplicia
Color	Clear	Light green	Dark green	Dark green
Uniformity of weight (g)	0.36±0.01	0.36±0.01	0.43±0.02	0.43±0.02
Folding power	> 200	> 200	> 200	> 200
Thickness (mm)	0.20±0.00	0.20±0.00	0.20±0.00	0.20±0.00
Shrink drying	7.46±1.53	5.51±0.23	5.45±1.19	3.29+1,48
Percent elongation	122.22%	129.73 %	25.00 %	15.38 %
Irritation test	0.00±0.00	0.00±0.00	0.30±0.55	0.40±0.45
	Not irritating	Not irritating	Slightly irritating	Slightly irritating

n=4

The smell of the patch preparations in the base was unique because the base consisted of additional ingredients for making the patch without using active ingredients, namely the fine crude drug of Itchy leaves. In FI, the smell of the patch preparations was typical of the base'smell because the amount of Itchy leaf crude drug powder composition was still small. However, the odor of the FII and FIII patch preparations was characteristic of the crude drug because of the greater amount of Itchy leaf fine crude drug powder used in the composition.

The color of the patch in the base looked clear because it did not contain colored ingredients. The color of th FI patch preparation was light gree, while the FII and FIII patches were dark green. This was because the amount of the Itchy leaf crude drug powderwas higher in patches II and III than in patch FI. The greater the amount of Itchy leaf crude drug powder in the composition, the more greenish the patch color was [15].

3.2.2 Weight uniformity

Weight checking, aimed at determining the uniformity of the weight of each patch, was performed to confirm that the patch-making process had produced a relatively uniform product The patch weight uniformity had a standard deviation value that did not deviate more than 5%. Based on Table 2, the smaller standard deviation values (<5%) indicated the uniformity of the patches' weights made in the three replications. This showed that the amount of material deposited in three replications in each formula was uniform. The uniform weight formula showed that the formulation of the patch had the same material composition or did not differ much. This indicated the uniformity of the active substance content in the formula [20].

3.2.3 Folding power resistance

The folding resistance evaluation was aimed to determine the patch's flexibility and elasticity after being folded in the same position until broken. The fold resistance that meets the standard was > 200 folds [21]. Based on Table 2, the bases, and the FI, FII, and FIII patches had folds > 200, and this meant that each formula had power-folding endurance. This was influenced by the use of propylene glycol as plasticizer, which was able to increase flexibility [15].

3.2.4 Thickness

The evaluation of the thickness of the patches was aimed at determining the thickness uniformity for each formula. The thicker the patch the more the diffusion power of penetration will affect the active compounds in the patch. On the contrary, thin patches tend to be easily torn. Based on Table 2, the thickness had an average of 0.21 mm. From this data, the patch's thickness that had been formulated met the requirements for the thickness of the patch, which was > 1mm [15, 22].

3.2.5 Drying shrinkage

The drying shringkage was performed to determine the moisture content of the patches. A good patch drying shrinkage value was <10%. Low water levels in a patch showed that the patch was stable and dry and protected from microbial contamination [23]. Based on Table 2, the FIII patch had the smallest percentage, followed by FII, FI, and the base. This meant that they all qualified, as shrinkage value were below 10%. The patch moisture was influenced by the ability of HPMC (polymer) to absorb water.

3.2.6 Percent elongation

Percent elongation is the maximum length change that a material can experience when stretched until it tears. Differences in length can be seen when the patch was torn [13]. There are no standardized requirements for percent lengthening of patch preparations, but patches with a percent lengthening > 33% are said to be good [24]. From Table 2, the base and FI had a good percentage of elongation (> 33%). In the case of the FII and FIII patches, the elongation percentage was below 33%, but the patches still showed elasticity visually. A factor that may have affected this was the level of the crude drug relative to the HPMC polymer. The FII and FIII patches contained more Itchy leaf crude drug composition than FI and the base.

3.2.7 Irritation test

According to Table 2, the base and FI had irritation indexes showing no irritation (range 0. 00), while FII and FIII had irritation indexes showing a slight irritation (range from 0.04 to 0.9). Based on observations after 72 h, the mice's skin returned to normal. This result was classified as harmless because the sensitivity of mice's skin was different from human skin. The irritation was influenced by the patch's composition containing Itchy leaf crude drug, which had an itchy effect on the skin.

3.3 Analgetic activity test

The analgesic activity testing was carried out to determine the effectiveness of analgesics on the Itchy leaf crude drug patches. This research received ethical approval from the Health Research and Development Agency of the Ministry of Health of the Republic of Indonesia with the number LB.02.021/2/KE.201/2020.

Based on the results of the preliminary test, the analgesic activity test used 0.6% acetic acid as a pain inducer, a conventional patch with a size of 2cm x 2 cm as a positive control, and three formulas (FI, FII, FIII) variants of the powder composition. There were five test groups, namely the negative control group using the base patch, the positive control using a product that contained methyl salicylate, menthol, and camphor, a group using the conventional patch, and the treatment groups using the Itchy leaf analgesic patches which was divided into three groups.

Based on Table 3, the negative control group gave the most wriggling responses. That was because the negative control used a base patch without containing active ingredients that were able to reduce the wriggling response in mice. In the positive control group and the treatment group, the three formulas showed a decrease in mice response. This showed that conventional patches and test patches with variants of Itchy leaf crude drug composition were able to reduce the wriggling response in mice that had been caused by acetic acid induction.

The test data were then analyzed using one - way analysis of variance (ANOVA) to determine whether there were significant differences between each test group (Table 4). Based on the analysis, there was a significant difference with a probability value of 0.017 (<0.05), so further analysis was carried out with the Least Significant Difference (LSD) test (Table 5).

Table 3. Analytical activity test results of the patch to the number of mice wriggles

Treatment group	Mean number of wriggles
Negative control	468.80±88.03
Positive control	150.80±53.22
FI	155.80±55.49
FII	146.80±54.97
FIII	181.80±62.27

Table 4. The result of the Anova test from analytical activity test results of the patch to the number of mice wriggles

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	409045.105	4	102261.276	3.890	0.017
Within groups	525708.895	20	26285.445		
Total	934754.000	24			

Table 5. The patch LSD test result of the number of wriggles in mice

Sig.	Negative Control	Positive Control	FI	FII	FIII
Negative Control	-	0.006*	0.017*	0.002*	0.010*
Positive control	0.006*	-	0.937	0.685	0.612
FI	0.017*	0.937	-	0.667	0.729
FII	0.002*	0.685	0.667	-	0.349
FIII	0.010*	0.612	0.729	0.349	-

(*) The mean difference is significant

Based on the results of the analysis, the positive control group, the FI, FII, and FIII groups were not significantly different based on probability values > 0.05, while being significantly different from the negative control group (patch basis) with a p-value <0.050. The data was calculated on the percentage of the protection of the test material, namely the ability of the test material to reduce the wriggling response in mice due to acetic acid induction [25]. The percentage of data for the protection of the test material was then calculated by comparing the percentage of protection in the positive control group [26].

Itchy leaves have secondary metabolites such as alkaloids, steroids, triterpenoids, and glycosides [7]. However, the trichome that has a significant effect as an analgesic is formic acid and methyl salicylate. Alkaloids provide analgesic properties by acting on typical opioid receptors in the central nerve system (CNS) so that pain perception and emotional response to pain are changed or reduced. Opioids are opium alkaloids that produce analgesic effects through their action on brain regions containing peptides that have pharmacological properties resembling opioids. Analgesic and anti-inflammatory effects in methanol extract from *Laportea interrupta* were able to inhibit thermally stimulated mice pain in mice tails. Methanol extract of *L. interrupta* can inhibit pain due to the content of opioids (opium alkaloids) which can reduce pain by acting directly on the central nervous system [27].

Itchy leaves contain sterols, steroids, and triterpenoids [28]. In contrast to alkaloids, steroids cause analgesic activity by suppressing the phospholipase enzyme so that the formation of prostaglandins and leukotrienes is blocked [29]. Dongmo *et al*. [30] reported the analgesic effect of methanol extract of *Laportea ovalifolia* and they showed that the phytosterol content included steroid derivative compounds that provided an analgesic effect mediated by inhibition of prostaglandin synthesis.

Triterpenoids can inhibit the oxidation of arachidonic acid into endoperoxides and reduce the activity of the lipoxygenase enzyme. If the oxidation of arachidonic acid can be inhibited, reactive oxygen will not be formed, and pain and inflammation is reduced. Decreased activity of the lipoxygenase enzyme causes the formation of leukotrienes which can activate leukocytes that stimulate inflammation. The presence of inhibition on the oxidation of arachidonic acid and neutralization of reactive oxygen causes terpenoids to act as analgesics and anti-inflammatory [31].

Another plant in the same Urticaceae family as Itchy leaves is *Dendrocnide sinuata*. Aqueous extract of *D. sinuata* was found to contain flavonoids and saponins which were thought to have an analgesic effect. Flavonoids are known to inhibit the synthesis of prostaglandin enzymes, more specifically endoperoxides [32]. Flavonoids act as analgesics; their mechanism of action is to inhibit the action of the cyclooxygenase enzyme and arachidonic acid produced by the prostaglandins, thereby reducing pain. Furthermore, flavonoids also inhibit neutrophil degranulation which inhibits the release of cytokines, free radicals, and enzymes that play a role in inflammation [25].

The percentage of protection can be found in Table 6. The positive control had a protection percentage of 67.83%. The FI patch had a protection percentage of 66.77%, the FII had a protection percentage of 68.69%, and the FIII had a protection percentage of 69.55%. The analgesic effect with the chemical stimulation method is expressed by the percentage value of protection of ≥ 50%, meaning that all the wriggling responses due to acetic acid induction experienced by the mice in all treatment groups were reduced. In the formula group, the FII and FIII patches had greater protection than the conventional patches, and FIII was found to be the best formula as analgesic Itchy leaves patch. Based on the results for the percentage of effectiveness in Table 6, FI had an effectiveness percentage value of 98.43%, FII had an effectiveness percentage value of 101.26%, and FIII had an effectiveness percentage value of 90.25%. The three formulas showed a percentage value of effectiveness that was close to the conventional patch, meaning that the three Itchy leaves simplicia patch formulas provided analgesic effects equivalent to conventional patches.

Table 6. Results percentage of protection and percentage of effectiveness of the Itchy leaves patches

Treatment Group	Percentage of Protection (%)	Percentage of Effectiveness (%)
Positive Control	67.83	100.00
FI	66.77	98.43
FII	68.69	101.26
FIII	61.22	90.25

4. Conclusions

Simplicia leaves were formulated into Itchy leaf patches. The patches were green, of a spherical shape that was not ideal, had distinctive odor, and were of uniform weight and thickness. They were flexible, elastic, and slightly irritating but not to a dangerous extent. The FI, FII, and FIII analgesic patch preparations made from Itchy leaf crude drug did not differ significantly in analgesic treatment effectiveness. F II with a composition of 0.4% (w/v) of Itchy leaf simplicia was the best formula to reduce the wriggling response in mice. It had a 68.69% protective power and 101.26% effectiveness, which was equivalent to conventional patches.

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