World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(Research Article)

Check for updates

# Formulation and evaluation of transdermal patches of leaf ethanol extract *Lantana Camara* Linn with ethyl cellulose-poly vinyl pyrolidone polymer variations

Magfirah Magfirah [1]* and Indah Kurnia Utami [2]

[1] *STIFA Pelita Mas Palu, Department of Pharmaceutical Technology, S1 Pharmacy, Central Sulawesi 94111, Indonesia.*
[2] *STIFA Pelita Mas Palu, Department of Pharmacy Clinic, S1 Pharmacy, Central Sulawesi 94111, Indonesia.*

World Journal of Advanced Research and Reviews, 2022, 15(03), 284–289

Publication history: Received on 10 August 2022; revised on 18 September 2022; accepted on 20 September 2022

Article DOI: https://doi.org/10.30574/wjarr.2022.15.3.0915

## Abstract

*Lantana camara* Linn is one of the plants that can help the wound healing process because it contains phenolic, flavonoids, and alkaloids that have antibacterial abilities against *Staphylococcus epidermidis*. but its use is still very simple, therefore it is necessary to develop traditional medicinal preparations in the transdermal patches with a combination of EC (Ethyl Cellulose) and PVP (Poly Vinyl Pyrolidone) polymers. This study aims to see the effect of using ethyl cellulose and polyvinyl pyrrolidone based on the physical characteristics of the Formulation. *Lantana camara* Linn leaf ethanol extract was obtained by maceration method using 96% ethanol solvent. The transdermal patch formulation was made with 7 formulations with a combination of EC: PVP based on a simple lattice design. Evaluation of the physical properties of the transdermal patch consisted of patch weight test, thickness test, folding endurance test, loss on drying, and moisture uptake. It can be concluded that the results of the evaluation of the preparation showed that F1 was the best preparation with polymer variations EC: PVP: PEG (200 mg: 250 mg: 50 mg) with a patch weight of 1.2213 ± 0.040; patch thickness 6.76 ± 0.251; folding endurance 310.33 ± 6.80; loss on drying 2.37 % ±0.36 and moisture absorption 3.68 % ±0.68.

**Keywords:** *Lantana camara* Linn; Transdermal patches; Formulation and evaluation; Ethyl Cellulose; Poly Vinyl Pyrolidone

## Introduction

Infectious diseases and skin disorders that are harmful to human health can be caused by gram-positive bacteria, one of which is *Staphylococcus epidermidis* (1,2). One of the natural ingredients used as medicinal ingredients is a sore that can help the wound healing process because it has antibacterial activity(3). *Lantana camara* Linn has many chemical constituents including essential oils, phenols, flavonoids, alkaloids, glycosides, phenyl ethanoids, quinines, saponins, steroids, triterpenoids, sesquiterpenoids, and tannins(4,5). The use of herbal medicines in recent times has begun to increase in the world, especially in various countries such as Indonesia, China, and India. The use of herbal medicines has increased because they have a pharmacological effect on almost all diseases with mild side effects. Common problems in herbal medicine are bioavailability, solubility, absorption of active substances, and low stability(6). In the context of developing traditional medicinal preparations, further research is needed in the form of transdermal patches (7)

A transdermal patch is a topical preparation in the form of a patch where the drug substance can penetrate the skin tissue and the drug is available systemically. The transdermal patch is one of the local preparations that can deliver drugs to the wound site. The transdermal drug delivery system has many advantages, namely providing a constant release, easy to use, reducing the frequency of drug administration, eliminating first-pass metabolism, reducing side effects of gastric irritation, and increasing the need for medication. patient. The manufacture of extract preparations in

* Corresponding author: Magfirah
STIFA Pelita Mas Palu, Department of Pharmaceutical Technology, S1 Pharmacy, Central Sulawesi 94111, Indonesia

the form of patches is an innovation in the manufacture of preparations to modify the preparation to increase compliance, safety, and comfort for patients. One of the basic components of a patch is a polymer (7). Polymers play an important role in producing patch preparations with good physical characteristics. Polymers are substances made from a polymerization process that can be divided into two groups, namely water-soluble polymers and water-insoluble polymers. Water-soluble or hydrophilic polymers can swell and form a gel-like consistency. When this happens, a natural layer is formed for drug diffusion to occur (8). This natural layer is like open pores making it easier for molecules or drug substances to diffuse. An example of a water soluble polymer is polyvinyl pyrrolidone (PVP). PVP as a polymer is based on the properties of providing a good film shape, non-irritating, and easily soluble in skin-safe solvents, PVP is used as a hydrophilic polymer, disintegrant, suspending agent, carrier for drugs with a concentration of 10-25%, dispersing agent and suspending agent. in pharmaceutical preparations (9). Water insoluble polymers are affected by the ratio of the crystalline form to the amorphous form of the polymer (10). These crystals cause the formation of a barrier for the movement of molecules, an example of a water insoluble polymer is ethyl cellulose. Ethyl cellulose (EC) is a hydrophobic cellulose derivative, has good hardness and flexibility, and functions to increase the viscosity of the patch, ethyl cellulose as a coating agent, tablet binder, tablet filler, viscosity-increasing agent, and sustained-release tablet coating is used in concentrations 3.0 – 20.0% (11). The combination of these two polymers is expected to produce good physical characteristics for the patch (8,9).

## Material and methods

### 1.1. Material

*Lantana camara* Linn ethanol extract leaves, ethanol 96% (Merck), ethyl cellulose (Merck), Poly Vinyl Pyrrolidone Merck), propylene glycol (Merck), ethanol absolute (Merck)

### 1.2. Methods

#### *1.2.1. Preparation and manufacture of extracts*

The dried *Lantana camara* Linn leaves were powdered and sieved through a 60 mesh sieve. Simplicia powder as much as 800 g, macerated with 96% ethanol for 3 days and then filtered, the liquid extract obtained was evaporated with a rotary evaporator followed by an evaporation process with a water bath so that a thick extract was obtained and the percent yield was calculated. After that, phytochemical screening was carried out including alkaloid, flavonoid, saponin, and tannin tests according to the procedure.

#### *1.2.2. Formulation of Patch*

The patch Formulation containing *Lantana camara* Linn ethanolic extract leaves was designed with seven formula designs with varying concentrations of PVP and EC polymers. The concentrations of PVP and EC used were obtained from the simple lattice design method. The total weight of the polymer mixture was 500 mg. The design of the formula can be seen in table 1.

**Table 1** *Lantana camara* Linn Ethanol Extract leaves Patch Formula Design

| Formulation | *Lantana camara* Linn ethanolic extract leaves | Excipients | | | |
|---|---|---|---|---|---|
| | | ethyl cellulose | Poly Vinyl Pyrolidone | propylene glycol | ethanol absolute |
| F1 | 100 mg | 200 | 250 | 50 | 10 ml |
| F2 | 100 mg | 300 | 150 | 50 | 10 ml |
| F3 | 100 mg | 350 | 100 | 50 | 10 ml |
| F4 | 100 mg | 100 | 350 | 50 | 10 ml |
| F5 | 100 mg | 350 | 100 | 50 | 10 ml |
| F6 | 100 mg | 400 | 50 | 50 | 10 ml |
| F7 | 100mg | 50 | 400 | 50 | 10 ml |

Ethyl cellulose was dissolved in ±2 mL of 96% ethanol followed by the addition of PVP and stirred until dissolved. The ethanolic extract of *Lantana camara* Linn leaves was dissolved in Propylene glycol and ±3 mL of ethanol then added to the polymer base, made up to 10 mL with 96% ethanol. Then homogenized with a magnetic stirrer for 20 minutes. The mixture was then poured into a petri dish and evaporated to dryness at room temperature (10).

*1.2.3. Evaluation Of Patch*

Weight uniformity

The patch weights were weighed using an analytical balance, where for every 3 patches, the average weight and standard deviation were determined (7,11–14).

Thickness

The patch thickness tester in each formula is to measure the thickness of 3 patches one by one. Patch thickness measurements using a micrometer and carried out at 3 different points.

Folding endurance

Testing of Folding endurance is carried out with the patch repeatedly in the same position until the patch. The number of folds is considered as the value of resistance to folding (7,11–14).

Loss of drying

The patches were weighed and stored in a desiccator for 24 hours containing silica. After 24 hours, the patch was reweighed and the percentage of Loss on drying was determined (7,11–14).

Moisture uptake

Patches that have been stored at room temperature in a desiccator for 24 hours are weighed first, then exposed to a temperature of 40◦C in a climatic chamber for 24 hours and weighed again. The percentage of moisture absorption is calculated using the following formula:

$$\text{Moisture uptake} = \frac{initial\ weight - final\ weight}{final\ weight} \text{ x } 100\ \%\ (7,11\text{–}14).$$

### 1.3. Analysis

Determination of physically stable patch preparations by looking at the standard deviation between formulas, and comparing them with the standard

## Results

### 1.4. Extraction

Extraction of 800 g of Simplicia leaves of *Lantana camara* Linn using 3000 ml of 96% ethanol as solvent including remaceration solvent, with the maceration method produces a thick extract of 50 g (6.25%). Tembelekan leaf Simplicia was extracted by maceration method using 96% ethanol solvent for 5 days then evaporated to obtain a thick extract. The maceration method was chosen because it can avoid the risk of losing the active substance due to the influence of heat during the extraction process (10). The process of making the formula is preceded by a preliminary test to determine the chemical content in the thick extract of *Lantana camara* Linn leaves, the tests carried out are flavonoid, saponin, and tannin tests. The results of qualitative identification of the ethanol extract of *Lantana camara* Linn leaves obtained positive results can be seen in table 2.

**Table 2** The results of the identification of the chemical of *Lantana camara* Linn ethanol extract leaves

| **Chemical** | **Reagent** | **Hasil** | **Keterangan** |
|---|---|---|---|
| Alkaloid | HCl 2 N + Dragendroff | Red precipitate | Presence of Alkaloids |
| Flavonoid | HCL+ Mg powder | Reddish yellow solution | Presence of flavonoid |
| Saponin | Boiling water +HCL | Foam formed ± 2 cm | Presence of saponin |
| Tannin | Boiling water + FeCl3 | Dark blue solution | Presence of Tannin |

Testing the identification of alkaloids, flavonoids, saponins, and tannins, is by the literature which states that the ethanolic extract of *Lantana camara* Linn leaves contains compounds belonging to the Alkaloid, flavonoid, saponin, and tannin groups (1).

### 1.5. Patch Characteristic Evaluation

Evaluation of the physical characteristics of the patch which includes; Patch weight, thickness, folding endurance, loss of drying, and moisture uptake. Of the seven formulas made by varying the concentration of PVP and EC all formulas can be removed from the mold. Test data were obtained by replicating all formulas 3 times. Patch evaluation test results can be seen in table 3.

**Table 3** Patch Evaluation *Lantana camara* Linn

| Formulation | Evaluation Of Patch | | | | |
|---|---|---|---|---|---|
| | **Patch of weight (mg)** | **Thickness (mm)** | **Folding endurance (kali)** | **Loss of drying (%)** | **Moisture uptake (%)** |
| F1 | 1.2213 ± 0.040 | 6.76 ± 0.251 | 310.33 ± 6.80 | 2.37±0.36 | 3.68±0.68 |
| F2 | 1.2768 ± 0.082 | 8.76 ± 0.208 | 301 ± 4.58 | 3.53±0.88 | 4.53±0.69 |
| F3 | 1.2738 ± 0.042 | 7.73 ±0.208 | 304 ± 13.07 | 5.95±0.60 | 5.19±0.83 |
| F4 | 1.3884 ± 0.049 | 11.7 ± 0.300 | 349.66 ± 4.50 | 2.30±0.26 | 2.65±0.47 |
| F5 | 1.2438 ± 0.039 | 8.10 ± 0.360 | 313.66 ± 5.13 | 7.63±0.69 | 5.38±0.80 |
| F6 | 1.1166 ± 0.007 | 6.86 ± 0.152 | 343.33 ± 5.77 | 11.23±0.30 | 10.88±0.52 |
| F7 | 1.6040 ±0.006 | 13.7 ± 0.200 | 325 ± 8.66 | 2.17±0.21 | 2.86±0.42 |

## Discussion

### 1.6. Patch of Weight

The patch weights in the 7 formulas are in the range of 1.1166-1.6040 with a small standard deviation (SD) value indicating the uniformity of the weight of the patch made. The same formula weights indicate that the patch formulations have the same number of components or do not differ much. If the number of components weighed in the same formula is expected in one formula to have a uniform weight, this indicates the Weight of the active substance content. The results in Table 3 show that the weight of the patch will increase according to the number of PVP polymers, which is the highest value in F7 with polymer content of EC: PVP: PG, namely 50 mg: 400 mg: 50 mg. This shows that the weight of the patch is influenced by the hygroscopic PVP polymer which binds water vapor in the environment during storage, thereby increasing the weight of the patch.(7,11,12,15–17).

### 1.7. Patch Thickness

Thickness has a role in the physical properties of the patch, a thin patch will be more easily accepted in its use. Patch thickness test results, obtained in 7 formulas in the range of patch thickness are 6.86-13.7 mm. The measurement results in Table 3 show that a small standard deviation value for each patch thickness measurement provides a guarantee of uniform thickness of the patch made by the solvent evaporation method. Aesthetically thin patches are more attractive and easy to accept. The results in table 3 show that formula 7 has a greater thickness than other formulas with a thickness value of 13.7 mm. A thickness test was carried out to determine the thickness of the patch at three different points. The ideal patch has a thin thickness but does not tear quickly, so it is comfortable to use. Patch thickness is influenced by the technique of pouring the patch solution into the mold and is also influenced by the amount of patch weight formed from each formula. The greater the weight of the patch, the greater the thickness of the patch (7,11,12,15–17).

### 1.8. Patch folding endurance

Folding endurance is done by folding the patch repeatedly in the same place. If the number of folds is greater than 300, then the patch is considered to have good folding endurance. Increased folding resistance of a patch indicates that the patch has a good film consistency so that it is not easily broken or torn during storage. The results in table 3 obtained show that the folding resistance of the formula is >300. This shows that the combination of PVP-EC polymer can increase the folding resistance of the dermal patch of the *Lantana camara* L ethanol extract leaf which can be seen in all formulas that meet good patch folding endurance values. This is due to the incorporation of properties of both PVP and EC polymers. Hydrophilic PVP can increase the elasticity of the patch so that it is not easily broken while the hydrophobic EC polymer can increase the strength of the patch so that it is not easily torn (7,11,12,15–17).

### 1.9. Loss Of Drying

Loss Of Drying is a method to determine the moisture content in the patch. A good patch should not be too moist. After all, it will tear easily but also should not be too dry because it can break easily. There is no absolute value for the required amount of drying shrinkage, however, based on previous research, it was stated that a good patch drying shrinkage value was <9.29% The results of table 3, show that all formulas (F1, F2, F3, F4, F6, and F7) except F5 provide a drying shrinkage value of 11.23%, the high value of drying loss is due to the difficulty of adjusting the moisture content with the solvent evaporation method in making patches. This is because the temperature used during drying is room temperature. In addition, the hygroscopicity of the extract and the low concentration of PVP in the formula affected the high loss of drying value (7,11,12,15–17).

### 1.10. Moisture Uptake

Moisture uptake is a response parameter to determine the ability of the patch to absorb moisture. A low percentage value of absorption will produce a patch that is relatively stable and protected from microbial contamination. In general, the percent moisture absorption capacity of the film will increase if the hydrophilicity of the polymer or plasticizer, or enhancer used also increases. Based on previous research, it was stated that the percent value of moisture absorption ranged from 2-10%. The results in table 3 show that the percentage of moisture that is quite high in F7 is 10.88%, this is probably influenced by the hygroscopicity of the extract and also the low concentration of PVP in the formula affects the high fiber strength of the moisture patch (7,11,12,15–17).

## Conclusion

Based on the results of the research, it was concluded that the best formula was formula 1 with polymer variations EC: PVP: PEG (200 mg: 250 mg: 50 mg) with a patch weight of 1.2213 ± 0.040; patch thickness 6.76 ± 0.251; folding resistance 310.33 ± 6.80; drying shrinkage 2.37 % ±0.36 and moisture absorption capacity 3.68 % ±0.68.

## Compliance with ethical standards

### *Acknowledgments*

The author expresses my deep thanks to the Directorate General of Higher Education, Research, and Technology. Ministry of Education, Culture, Research, and Technology the opportunity to conduct and finance this research.

### *Conflict of interest statement*

The authors have no conflicts of interest regarding this investigation.

## References

[1] Kumar G, Rao B. A Review on Medicinal Properties of Lantana camara . Research Journal of Pharmacy and Technology. 2012;5(6);711-715

[2] Parwanto MLE. Efficiency of Lantana camara Linn. leaf extracts ointment on dermal wound healing were infected with Staphylococcus epidermidis. Int J Basic Clinic Pharmacol. 2017;6(3):1-8.

[3] Wahyuningrum R, E G, IN P. Antimicrobial and Antioxidant Activity of Extract and Fraction of Tembelekan Leaves (Lantana camara L.). Udayana Journal of Pharmacy. 2021; 10(1);107-116

[4] Wijaya AY, Masruhim MA, Kuncoro H. Anti-Inflammatory Activity of Tembelekan Leaf Extract (Lantana Camara Linn) in White Rat (Rattus Norvegicus). Journal of Science and Health. 2016 ;1(6):284–9.

[5] Ningsi S, Ida N. Test of the Effect of Ethanol Extract Gel of Tembelekan Leaves (Lantana Camara Linn.) on Healing of Cuts in Rabbits (Oryctolagus cumiculus). JF FIK UINAM. 2015;3(2):48–53.

[6] Berlian HNP, Budiman A. Review Article: The Use of Nano Technology in Herbal Medicine Formulations. Pharmacists, Supplements . 2018 ;15(2):29–41.

[7] Kumar A, Rana M, Bisht M, Rana A. Formulation, Development and Evaluation of Herbal Transdermal Patch for Fracture Healing. Indian Drugs. 2020 ;57(09):60–6.

[8] Zakaria N, Bangun H, Vonna A, Oesman F, Khaira Z, Fajrina F, et al. The Effect of Using HPMC Polymer AND Polyvinyl Pyrolidone on Physical Character of Diclofenac Sodium Transdermal Patch. Journal of Science & Health Darussalam. 2021;1(2):58–66.

[9] Baharudin A, Maesaroh I, Kuningan SM. Formulation of Transdermal Patch Preparations From Ambon Banana Tree Weevil Extract (Musa paradisiaca var. sapientum) for Healing Cuts. Journal of Herbs and Pharmacological. 2020;2(2):55–62.

[10] Fatmawaty A, Nisa M. Mulberry Leaf (Morus Alba L.) Ethanol Extract Patch Formulation with Variations in Concentration of Polyvinyl Pyrolidone and Ethyl Cellulose Polymers. Journal of Pharmaceutical and Medical Sciences. 2017; 2(1); 17-20

[11] Rathore VPS, Tikariya K, Mukherjee J. Formulation and Evaluation of Transdermal Patch of Thiochochicoside. International Journal of Pharmaceutical Sciences and Medicine. 2021;6(12):18–28.

[12] Shivalingam MR, Balasubramanian A, Ramalingam K. Formulation and evaluation of transdermal patches of pantoprazole sodium. International Journal of Applied Pharmaceutics. 2021;13(5):287–91.

[13] Ermawati DE, Prilantari HU. Effect of Combination of Hydroxypropylmethylcellulose and Sodium Carboxymethylcellulose Polymer on Physical Properties of Ibuprofen Matrix-based Patch. Journal of Pharmaceutical Science and Clinical Research. 2019;4(2):109.

[14] Kemala N diamond widya. Formulation and Evaluation of Glibenclamide Transdermal Patch Matrix Using Hydroxy Propyl Methyl Cellulose (HPMC) K15M as a Polymer. Indonesian Islamic University; 2016.

[15] Abdul A, Sathali H, Mageshkumar L. Studies On The Development Of Transdermal Patches Of Nisoldipine. Chem Pharm Sc. 2013;3(2):146–154.

[16] Manna S, Dhanalakshmi D, Bhowmik M, Jana S, Jana S. Cellulose Derivative-Based Bioadhesive Blend Patch for Transdermal Drug Delivery. FrontMater. 2022 ;9(1):1-7

[17] Shelke PS. Formulation and In–Vitro Evaluation of Transdermal Patches of Anti–Arthritic Ayurvedic Medicinal Plants. Biosci Biotechnol Res Commun. 2020;13(2):803–8.