VT INTERNATIONAL PRESS
VTIPJMRR | Journal of Multidisciplinary Research & Review
www.journal.vtinterpress.com

(Research Article)

Formulation and Evaluation of Herbal Transdermal Patch for Treatment of Rheumatoid Arthritis

Sagar Sanap[1], Vaishnavi Wagh[2], Krushana Jaybhaye[3], Arti Gawali[4], Rohit Gulve[5], Prathamesh Dhumal [6]

[1-5]U.G. Students, *Department of Pharmaceutics, Matoshri Miratai Aher College of Pharmacy, Karjule Harya, Maharashtra, India*

[6]Assistant Professor, *Department of Pharmaceutics, Matoshri Miratai Aher College of Pharmacy, Karjule Harya, Maharashtra, India*

Corresponding Author Email: sagarsanap575@gmail.com

Received: 20.05.2026	Accepted: 25.05.2026	Published: 27.05.2026

ABSTRACT

The purpose of this study was to evaluate two formulations of herbal transdermal drug delivery system (H-TDDS). Each H-TDDS contains; Menthol, Camphor, Eucalyptus Oil and Curcuma longa (Turmeric) extract as active ingredients which are known for its analgesic and anti-inflammatory properties. These ingredients are combined within hydroxy propyl methyl cellulose (HPMC) and poly vinyl alcohol (PVA) films, along with glycerine as a plasticizer. Physically each H-TDDS has a uniform thickness, weight, and appearance. They both have adequate flexibility so they can be folded repeatedly without cracking or breaking apart. Each patch has an acceptably low moisture content. The surface pH of each H-TDDS is approximately neutral. Each H-TDDS has sufficient mechanical strength to withstand normal handling conditions. The total amount of active ingredient contained in each H-TDDS is uniform. A significant proportion of the active ingredient is released over a period of at least 8 hours after application. Therefore it appears that H-TDDS may represent a useful noninvasive alternative to traditional oral dosage forms for providing relief from the symptoms of rheumatoid arthritis.

Keywords: *transdermal patch; herbal formulation; rheumatoid arthritis; curcumin; ginger extract; solvent casting; sustained release; HPMC; PVA.*

I. INTRODUCTION

Although conventional pharmacological treatments for rheumatoid arthritis (RA) provide relief from pain and inflammation, they also cause numerous side-effects which can limit treatment duration and patient compliance. In addition to limiting the length of time patients may be able to use these medications due to gastrointestinal upset and liver toxicity, the need to administer many of these drugs orally means that first pass through the liver occurs. This results in lower levels of medication reaching the body where it is needed (i.e., reduced bioavailability), and as a result, patients are forced to take much larger doses than would otherwise be required. Because patients often experience unpleasant side effects associated with high dose regimens, this further limits patient compliance. Therefore, there is a clear need for a new class of RA medications that can avoid the problems currently experienced with oral formulations. Drug delivery systems (DDS) that deliver medications across the skin represent a promising technology that could address some of the limitations currently encountered with oral RA treatments. Transdermal drug delivery systems (TDDS) allow medications to enter the bloodstream via the skin. By avoiding first pass metabolism, TDDS can increase the bioavailability of drugs compared to oral formulations. Also, because topical formulations do not require ingestion of a medication, TDDS formulations can reduce the potential for gastrointestinal side effects. As well, DDS formulations typically consist of a backing material that holds a reservoir containing the drug. This design feature allows DDS products to be easily terminated if necessary. Another benefit of DDS products relates to dosing frequency; once applied to the skin, DDS products can maintain consistent blood levels over several days. Consequently, DDS products can potentially reduce dosing frequency and improve patient compliance.

II. LITERATURE REVIEW

A. Transdermal Drug Delivery Systems

Transdermal drug delivery has been around since 1979 when it was first approved by the U.S. FDA through approval of a scopolamine patch for motion sickness. The area of transdermal drug delivery is now much broader than its beginnings. It has grown to include other forms of drugs such as nicotine, estrogen, fentanyl, diclofenac, and rivastigmine systems [11]. Barry [12], created an initial classification of permeation pathways — transcellular, intercellular, and transappendageal and found that the stratum corneum is the primary limiting factor to how fast the skin can allow substances to be delivered. Kalia and Guy [13] developed a mathematical model of transdermal

flux that showed that physicochemical properties of drugs are critical factors that affect their ability to cross the skin. Molecular weight (<500 Da) of a molecule affects its ability to move across the skin. Log P values of molecules (lipophilic) that are 1-3 will also enhance movement. Molecules with low melting points tend to penetrate better into the skin [13]. Prausnitz and Langer [14] discussed recent developments in various ways of enhancing permeability. These enhancements included chemical agents that aid in permeating the skin; iontophoresis; use of microneedles; and use of ultrasound. They noted that all of these methods have been used in some form or another in commercially available products, but that chemical penetration enhancers are still the most commonly used method of permeability enhancement in commercial products today. Singh et al. [15] studied terpenes (such as menthol and eucalyptus oil) as potential penetration enhancers. Their results indicated that menthol and eucalyptus oil cause disruption to the organized lipid layers within the stratum corneum.

B. Herbal Anti-inflammatory Agents for Transdermal Use

Curcuma longa's major phenolic compound, curcumin, has received extensive study concerning its anti-inflammatory activity; however, it was found that curcumin suppresses COX-2 expression, pro-inflammatory cytokines and NF-kappa B signaling [16]. However, despite this wide range of activities, curcumin had a very poor absorption rate when taken orally (less than one percent), due to rapid metabolism and very low water solubility. Therefore, topical delivery of curcumin would be beneficial for increasing bioavailability [17]. Ginger (Zingiber officinale) is primarily comprised of two active compounds 6-gingerol and 6-shogaol. These are responsible for the inhibition of both prostaglandins and leukotrienes. In addition to their inhibitory actions on these enzymes they also have similar anti-inflammatory and analgesic actions as nonsteroidal anti-inflammatories (NSAID) in many animal studies [18]. The use of camphor and menthol in combination can enhance skin permeability through counter irritation mechanisms and provide localized analgesia by stimulating TRPM8 channels thereby causing a temporary sensation of coolness [19].

C. Polymer Systems for Transdermal Matrix Patches

Hence HPMC is one of the most commonly used water soluble cellulose polymer used for formation of transdermal patches due to its good film forming property, compatibility with biological system and controllable release rate from drug [20]. The PVA can improve the mechanical strength and clarity of films made by casting. The blending of these polymers in various ratio will control the swelling behavior, mechanical strength and permeability of drugs [6]. The glycerine is used as a plasticizer having hydrophilic nature which reduces the glass transition temperature of polymer matrix so that it will be easy to apply on skin comfortably and increase the flexibility of patch [5].

III. MATERIALS AND METHODS

A. Materials

The various herbal bioactive ingredients used in this study were as follows; Curcuma longa or Curcumin, Eucalyptus Oil, Ginger Extract, Camphor, Menthol. The film forming polymers that we have utilized are HPMC K4M and PVA. In addition to these two film forming polymers, our other excipient ingredients were Glycerol (Plasticizer), Ethanol, Propylene Glycol, Polyethylene Glycol 400, DMSO Dimethyl Sulfoxide, Tween 80 and Span 80, Distilled Water. Unless otherwise stated all reagents were of analytical purity.

B. Formulation Composition

Two patch formulations (F1 and F2) were prepared with varying HPMC: PVA ratios to study the effect of polymer blend on physicochemical properties and drug release. The composition per patch is presented in Table 1.

Table 1. Formulation Composition Per Patch.

Ingredient	F1 (HPMC:PVA 2:1)	F2 (HPMC:PVA 1:1)
Ginger Extract	30 mg	30 mg
Curcumin	50 mg	50 mg
Eucalyptus Oil	5 drops	5 drops
Menthol	10 mg	10 mg
Camphor	5 mg	5 mg
HPMC	500 mg	375 mg
PVA	250 mg	375 mg
Glycerin	1 mL	1 mL
Ethanol	q.s.	q.s.
Distilled Water	q.s.	q.s.

C. Method of Preparation: Solvent Casting

The patch was produced using the solvent casting technique. Solutions of HPMC and PVA were created separately by dissolving each in deionized water while being agitated continuously using a magnet stirrer until they became clear solutions. The solutions of both polymers were then thoroughly blended together. Glycerine was used as a plasticizer and ginger extract and curcumin were mixed into the polymer mixture and blended continuously.

Menthol and Camphor were dissolved in Ethanol and added to the polymer mixture. Eucalyptus Oil was slowly dripped into the mixture to create a penetration enhancer. After adding all ingredients to the mixture it was agitated at 400 RPM for 30 minutes to eliminate trapped air bubbles. Once there were no bubbles in the mixture, it was poured onto aluminum foil lined glass Petri dishes and dried for 24 hours in a hot air oven set at 40 ± 2°C. After drying, the film was carefully removed from the foil and cut into individual patches measuring 4cm x 4cm for testing [6,20].

Figure 1. Preparation of herbal transdermal patch by solvent casting method.

D. Evaluation Parameters

Prepared patches were evaluated for the following parameters:

The physical characteristics of the film were evaluated based on visual examination to evaluate color, smoothness of surface, elasticity, transparency, and absence of air bubble formation. Film thickness was determined by measuring the film thickness at five different points using a digital vernier caliper (Mitutoyo, Japan). The average thickness (mean ± SD) is reported. The weight variation among individual film samples was assessed by weighing (n=5) film samples individually on an analytical balance. The percent weight variation was then calculated. Folding endurance of the films was tested as follows: a single fold was made at one specific location on each film sample and repeated until the film ruptured. The number of folds before rupture was recorded. Moisture content of the films was determined as follows: film samples were first weighed and then placed into a desiccator containing calcium chloride for 24 hours. After drying, the film samples were removed from the desiccator and re-weighed. Moisture content (%) was then calculated as: ((initial wt – final wt)/initial wt) x 100. Moisture uptake by the films was also studied. Film samples were exposed to a saturated NaCl solution (approximately 75% relative humidity) for 24 hours. Moisture uptake (%), similar to that used above to determine moisture content, was calculated as: ((initial wt – final wt)/initial wt) x 100. Surface pH of the films was assessed as follows: the surface of each film was moistened with deionized water. A calibrated digital pH meter was immediately placed against the moistened film surface for 30 seconds. The pH reading obtained during this time period represented the pH of the film surface. Uniformity of drug loading throughout the films was assessed by dissolving each film sample in 100 ml of phosphate buffer (pH 7.4) and determining the amount of curcumin present by spectrophotometry at 425 nm [17]. Tensile properties of the films were evaluated according to ASTM method D882 using a texture analyzer. Tensile strength was defined as (max load/cross-sectional area).

In vitro release profiles of curcumin from the films were evaluated in a Franz diffusion cell using an egg membrane as a semi-permeable membrane separating the donor compartment (containing a phosphate buffer solution, pH 7.4 at 37 ± 0.5°C) from the receptor compartment. Aliquots (1 ml) were taken at times t = 1 hour, t = 2 hours, t = 4 hours, t = 6 hours, and t = 8 hours. Spectrophotometric analysis [13] was performed to determine the concentration of curcumin released into the receptor compartment.

E. Stability Studies

Short-term stability testing was conducted at 40 ± 2 °C / 75 ± 5% RH for three months (ICH Q1A guidelines). Patches were examined at 0, 1, 2, and 3 months for physical appearance, drug content, and in vitro drug release.

IV. RESULTS

Both formulations (F1 and F2) were successfully prepared by the solvent casting method. A comprehensive summary of the physicochemical evaluation data is presented in Table 2.

Table 2. Physicochemical Evaluation Results (Mean ± SD, n = 3).

Evaluation Parameter	F1 (HPMC:PVA 2:1)	F2 (HPMC:PVA 1:1)	Inference
Physical Appearance	Smooth, uniform, yellowish	Off-white, transparent	Excellent
Thickness (mm)	0.38 ± 0.02	0.41 ± 0.03	Uniform
Weight Variation (mg)	312 ± 4.2	318 ± 3.8	Uniform
Folding Endurance	>200 folds	>200 folds	Excellent
Moisture Content (%)	2.1 ± 0.3	2.4 ± 0.4	Acceptable
Moisture Uptake (%)	3.5 ± 0.5	3.8 ± 0.6	Acceptable
Surface pH	6.6 ± 0.1	6.7 ± 0.1	Skin-compatible
Drug Content (%)	98.2 ± 1.1	97.8 ± 1.3	Uniform
Tensile Strength (N/mm²)	2.8 ± 0.2	2.6 ± 0.3	Good
Cumulative Release (8 h, %)	82.4 ± 2.1	78.6 ± 2.4	Sustained

The two formulations had a surface that was smooth, even and completely crack-free and bubble-free. F1 (which had a greater percentage of HPMC) seemed to have a yellow colour whereas F2 was more transparent. All samples were similar in thickness which indicated an even polymer cast throughout. The weight variance was ± 5% which is in compliance with acceptable standards as stated by the relevant pharmacopeia and confirmed that there are no uneven distributions of drugs. Both formulation could fold over 200 times without breaking which proved they will be mechanically flexible enough for use clinically. The moisture content of both formulations were less than 3% and the moisture uptake was less than 4%. This proves that the formulations should store well at room temperature regardless of relative humidity. The surface pH of both formulations were measured at approximately 6.6 and 6.7 for F1 and F2 respectively. These values lie within the normal pH levels found on healthy skin (4.5 – 7.5). Therefore, these products are unlikely to cause irritation to the skin [7]. Curcumin was found to have been uniformly distributed throughout both formulations; Drug Content Uniformity (DCU) values were 98.2 ± 1.1% for F1 and 97.8 ± 1.3% for F2, which are well within the limits of DCU (90 – 110%) [21]; Controlled Release profiles indicated that both formulations provided extended duration drug delivery; F1 released 82.4 ± 2.1% of Curcumin and F2 released 78.6 ± 2.4% of Curcumin over an eight-hour period. Slightly higher release rates from F1 can likely be attributed to the greater amount of HPMC present in this formulation as it would form a more hydrophillic matrix with increased ability to absorb solvents, which allows for drug to diffuse into solution. Three months of stability testing at 40°C / 75 % RH showed no statistically significant changes in physical characteristics, drug content (>95%) or release profile; thus showing that these formulations had good stability properties.

V. DISCUSSION

The physical and chemical performance of the herbal transdermal patches produced in this research show comparable performance to other reported transdermal formulations of HPMC/PVA. Curcumin and ginger extracts used as dual active agents in these products will utilize different mechanisms of action. Curcumin will inhibit NF-kappa B and reduce systemic cytokine signaling [16]; Ginger derived compounds, specifically gingerols, will inhibit COX / LOX pathways on the site of inflammation [18]. Both processes are especially pertinent due to the complex pathophysiological process associated with rheumatoid arthritis (RA). In RA, both systemic and localized inflammatory cascade(s) occur. Eucalyptus oil, menthol and camphor were utilized as dual purpose agent counter irritants/analgesics and chemical permeation enhancers. It has been established that menthol increases the skin permeability to hydrophilic drugs by removal of inter cellular lipid layers. Also, disruption of ordered structure of stratum corneum lipids by eucalyptol (1,8 cineole) reduces diffusion resistance [15]. Therefore, it can be explained why greater cumulative amounts of drug release was observed from both formulation samples when compared to previously reported curcumin only patch samples. The influence of HPMC: PVA ratio on the mechanical and release characteristics of the formulations was significant. Higher concentration of HPMC in sample F1 increased its hydrophilicity and consequently increased its water absorption rate. As result of this, faster release of drugs into the vehicle occurred. On the contrary, addition of PVA in F2 improved tensile strength and decreased susceptibility to moisture. These findings agree with results obtained by Patel et al. [6] and Chien [11], who showed that optimization of ratio of cellulose-based polymers and polyvinyl alcohol based polymers is an effective method of modifying release profile without affecting amount of incorporated active substance. Important drawback of the study is lack of ex-vivo permeation studies performed using human or animal skin that would give more representative flux values than obtained in vitro. Furthermore, no in-vivo studies assessing anti-arthritic effectiveness and potential skin irritation caused by use of studied products were conducted. Therefore, further investigations should focus on these two aspects. Limited efficiency of loading of curcumin due to low aqueous solubility may also represent some limitations in presented study. Use of nanoscale encapsulating methods before integration into patch, might improve this aspect in future studies.

VI. CONCLUSION

This study developed and tested transdermal patches that contain various herbs — specifically, curcumin; ginger; eucalyptus oil; menthol; camphor — in HPMC/PVA polymer matrixes to treat rheumatoid arthritis. The results showed that both formulations exhibited acceptable physical/chemical properties; consistent drug distribution; sufficient mechanical strength; suitable skin-compatible surface pH; and slow, controlled delivery of drugs over an eight-hour period. Both formulations were also shown to be stable when stored in simulated environmental conditions for up to three months. Although there was no major difference found between the two, it appears as though F1 (HPMC: PVA 2:1), had slightly better drug release than F2 (HPMC: PVA 1:1). On the other hand, F2 (HPMC: PVA 1:1) had significantly greater tensile strength. The herbal transdermal patch represents a promising, non-invasive, and easy-to-use treatment option for patients with RA. As compared to oral analgesic treatments, this product will have less of a chance to undergo first pass metabolism; has less potential to cause gastrointestinal side effects; maintains its therapeutically active ingredient longer at the site of the disease process.

ACKNOWLEDGMENT

The authors are deeply grateful to the Department of Pharmaceutics, Matoshree Miratai Aher College of Pharmacy, Karjule Harya, Maharashtra, India, for providing the necessary infrastructure, instruments, and analytical facilities. Sincere thanks are extended to the faculty of the department for their valuable guidance and encouragement throughout this research work.

REFERENCES

[1] Smolen, J. S., Aletaha, D., & McInnes, I. B. (2016). Rheumatoid arthritis. The Lancet, 388(10055), 2023–2038. https://doi.org/10.1016/S0140-6736(16)30173-8

[2] Aletaha, D., Neogi, T., Silman, A. J., Funovits, J., Felson, D. T., Bingham, C. O., III, Birnbaum, N. S., Burmester, G. R., Bykerk, V. P., Cohen, M. D., Combe, B., Costenbader, K. H., Dougados, M., Emery, P., Ferraccioli, G., Hazes, J. M. W., Hobbs, K., Huizinga, T. W. J., Kavanaugh, A., … Hawker, G. (2010). 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis & Rheumatism, 62(9), 2569–2581. https://doi.org/10.1002/art.27584

[3] Firestein, G. S. (2003). Evolving concepts of rheumatoid arthritis. Nature, 423(6937), 356–361. https://doi.org/10.1038/nature01661

[4] Wolfe, M. M., Lichtenstein, D. R., & Singh, G. (1999). Gastrointestinal toxicity of nonsteroidal antiinflammatory drugs. New England Journal of Medicine, 340(24), 1888–1899. https://doi.org/10.1056/NEJM199906173402407

[5] Ansel, H. C., Popovich, N. G., & Allen, L. V. (2021). Ansel's pharmaceutical dosage forms and drug delivery systems (11th ed.). Wolters Kluwer Health.

[6] Patel, D., Chaudhary, S. A., Parmar, B., & Bhura, N. (2012). Transdermal drug delivery system: A review. The Pharma Innovation Journal, 1(4), 66–75.

[7] Prausnitz, M. R., & Langer, R. (2008). Transdermal drug delivery. Nature Biotechnology, 26(11), 1261–1268. https://doi.org/10.1038/nbt.1504

[8] Gupta, R., Badhe, Y., & Rai, J. (2019). Herbal formulations used in pain management and inflammation. International Journal of Pharmaceutical Sciences Review and Research, 58(1), 45–52.

[9] Aggarwal, B. B., & Harikumar, K. B. (2009). Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. International Journal of Biochemistry & Cell Biology, 41(1), 40–59. https://doi.org/10.1016/j.biocel.2008.06.010

[10] Grzanna, R., Lindmark, L., & Frondoza, C. G. (2005). Ginger: An herbal medicinal product with broad anti-inflammatory actions. Journal of Medicinal Food, 8(2), 125–132. https://doi.org/10.1089/jmf.2005.8.125

[11] Chien, Y. W. (2019). Novel drug delivery systems (2nd ed.). Marcel Dekker.

[12] Barry, B. W. (2001). Novel mechanisms and devices to enable successful transdermal drug delivery. European Journal of Pharmaceutical Sciences, 14(2), 101–114. https://doi.org/10.1016/S0928-0987(01)00167-1

[13] Kalia, Y. N., & Guy, R. H. (2001). Modeling transdermal drug release. Advanced Drug Delivery Reviews, 48(2–3), 159–172. https://doi.org/10.1016/S0169-409X(01)00113-2

[14] Prausnitz, M. R., Mitragotri, S., & Langer, R. (2004). Current status and future potential of transdermal drug delivery. Nature Reviews Drug Discovery, 3(2), 115–124. https://doi.org/10.1038/nrd1304

[15] Singh, J., Tripathi, K. T., & Sakia, T. R. (1993). Effect of penetration enhancers on the in vitro permeation of ephedrine through rat skin from matrix-based transdermal formulations. Drug Development and Industrial Pharmacy, 19(13), 1623–1628. https://doi.org/10.3109/03639049309069304

[16] Aggarwal, B. B., Kumar, A., & Bharti, A. C. (2003). Anticancer potential of curcumin: Preclinical and clinical studies. Anticancer Research, 23(1A), 363–398.

[17] Anand, P., Kunnumakkara, A. B., Newman, R. A., & Aggarwal, B. B. (2007). Bioavailability of curcumin: Problems and promises. Molecular Pharmaceutics, 4(6), 807–818. https://doi.org/10.1021/mp700113r

[18] Altman, R. D., & Marcussen, K. C. (2001). Effects of a ginger extract on knee pain in patients with osteoarthritis. Arthritis & Rheumatism, 44(11), 2531–2538. https://doi.org/10.1002/1529-0131(200111)44:11<2531::AID-ART433>3.0.CO;2-J

[19] Patel, T., Ishiuji, Y., & Yosipovitch, G. (2007). Menthol: A refreshing look at this ancient compound. Journal of the American Academy of Dermatology, 57(5), 873–878. https://doi.org/10.1016/j.jaad.2007.04.008

[20] Jain, N. K. (2019). Controlled and novel drug delivery (1st ed.). CBS Publishers and Distributors.

[21] Indian Pharmacopoeia Commission. (2022). Indian pharmacopoeia. Ministry of Health and Family Welfare.