IJPSR (2024), Volume 15, Issue 12 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 28 June 2024; received in revised form, 28 November 2024; accepted, 29 November 2024; published 01 December 2024

FORMULATION & EVALUATION OF HERBAL TRANSDERMAL PATCH OF *CENTELLA ASIATICA* & *LIQUORICE* TO STUDY WOUND HEALING ACTIVITY

Siddhi S. Gavali, Hrishikesh M. Lawate, Siddhi A. Hadke, Siddhant M. Gaikwad, Mitt R. Jain, Pallavi M. Suryawanshi *, Amit A. Jagtap and Sanjay R. Chaudhari

At KJ's Educational Institutes, Trinity College of Pharmacy, Kondhwa-Saswad Road, Bopdev Ghat, Pune - 411048, Maharashtra, India.

Keywords:

Centella asiatica, Liquorice, Wound healing, Hemostasis, TDDS

Correspondence to Author:
Prof. Pallavi Mohan Suryawanshi

Assistant Professor,
Department of Pharmacology,
Trinity College of Pharmacy,
Kondhwa-Saswad Road, Bopdev Ghat, Pune - 411048, Maharashtra, India.

E-mail: shelkepallavi01@gmail.com

ABSTRACT: Wound healing remains a significant challenge in modern medicine, necessitating the exploration of innovative therapeutic strategies. *Centella asiatica*, a widely recognized medicinal herb, has garnered attention for its potential wound healing properties. This study aimed to investigate the efficacy of a *Centella asiatica* transdermal patch in promoting wound healing. These results suggest that the *Centella asiatica* transdermal patch holds promise as a novel therapeutic intervention for promoting wound healing. Further research is warranted to elucidate the underlying mechanisms of action and optimize the formulation of the patch for clinical application. This study contributes to the growing body of evidence supporting the use of herbal remedies in wound management and underscores the potential of *Centella asiatica* as a valuable adjunctive therapy in wound healing. This study investigates the wound healing activity of a transdermal patch containing a combination of *Centella asiatica* and *Liquorice* extracts. The patch was formulated and evaluated for its efficacy in promoting wound healing using *in-vitro* and *in-vivo* assays. Overall, this study suggests that the *Centella asiatica* and *Liquorice* combination transdermal patch holds promise as a therapeutic option for promoting wound healing.

INTRODUCTION: The transdermal drug delivery technique has been around for a long time. Historically, creams and ointments were the most often used treatments for dermatological problems. The possibility of systemic adverse effects with certain of these formulas is a good indicator of skin absorption. Many medications have been injected topically to treat the entire body.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.15(12).3673-78

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.15(12).3673-78

Transdermal delivery systems, broadly speaking, refer to any drug compositions applied topically with the goal of delivering the active component into the general circulation. Transdermal drug delivery is topically applied and release pharmaceuticals for a systemic effect at a predefined and controlled rate.

Transdermal medication delivery is a method of administering pharmaceuticals through the epidermal layer of skin. The medicine enters the bloodstream through the skin and circulates throughout the body before reaching its intended target spot [1, 2]. One of the human body's most intricate processes is wound healing. It involves a range of cell types that play different roles in the

phases of hemostasis, inflammation, growth, re-epithelialization, and remodeling synchronizing both spatially and temporally. In terms of surface area, the human skin is the largest organ. It is the vital component that protects internal tissues from ultraviolet light, microbes, and mechanical harm. Because of this, it is extremely prone to injury, which could have a serious effect on both individual patients and the cost of healthcare. Several cell types within epidermis, dermis and hypodermis layers must work together at specific times to promote healing when the skin is injured. These phases of inflammation and hemostasis Growth, angiogenesis, re-epithelialization, re-modeling, maturation, and re-growth occur in a sequential sequence but also overlap [3]. The purpose of these research work was to develop and evaluate a transdermal medication delivery system for ayurvedic drugs containing Asiatic acid and Glycyrrhiza glabra. Solvent casting using polymers like HPMC and Carbopol 934 improves drug absorption and reduces harmful effects. Asiatic acid is a natural aglycone of pentacyclic triterpenoids, a common ingredient in *Centella asiatica* which is a well-known herb for wound healing.

MATERIAL AND METHODS: Herbal extract powders of *Centella asiatica* and *Liquorice* are obtained from the process of extraction of dry leaves and roots respectively. Hydroxypropyl Methylcellulose (HPMC), Carbopol 934, Methanol, Propylene Glycol, Glycerol were purchased from P. H Gandhi chemicals, Pune. The other equipment used in the formulation of herbal patches were petri dish, electronic balance, hot water bath, hot air oven, magnetic stirrer, vernier caliper, UV-spectrophotometer and dissolution apparatus, *etc*.

Plant Authentication: The both plants are authenticated by Botanical Survey of India, Western zone, Pune (Authentication No:BSI/WRC/PI Id.2024/NS/01) and it is found that plant specimen is of *Centella asiatica* (L.) Urb. belonging to family Apiaceae& Second plant specimen is of *Liquorice* belonging to family Fabaceae. The process of confirming that a plant specimen is accurately identified is known as plant authenticity. This is crucial for our research since it guarantees that the right plant species are used in tests.

Experimental Methodology: Fresh *Centella asiatica* plants were used in this study, which were collected from the local market. *Centella asiatica* plants were cleaned with running tap water and rinsed in distilled water. Then the plant is shade dried for four days and grinded into fine powder by using manual technique. About 10 g of *Centella asiatica* plant power were extracted with 200 ml of Methanol solvent using Soxhlet apparatus **Fig. 1.** After that, the extract is evaporated to produce crude drug, which is then preserved in vials for further use [4, 5].

Process of Extraction:

- Start by placing the powdered material in a thimble, then heat the solvent to its boiling point.
- The solvent vapor rises through the distillation arm and enters the chamber containing the solid material.
- The solid gradually absorbs the warm solvent, causing the desired compound to dissolve.
- Once the chamber is nearly full, the solvent is siphoned out, returning to the distillation flask.
- This cycle repeats over several hours, with some of the compound dissolving in the solvent during each cycle.
- After approximately 72 hours, the desired compound becomes concentrated in the distillation flask.
- Finally, the solvent is evaporated to leave behind the extracted compound [6].

FIG. 1: SOXHLET EXTRACTION ASSEMBLY

Preparation of Transdermal Patch: Hydroxypropyl Methylcellulose (HPMC) and Carbopol 934 were used as a skeletal type of polymer material. Propylene glycols were used as a penetration enhancer and as a plasticizer.

HPMC (0.50g) and Carbopol 934 (0.25g) were measured in the necessary ratios and combined with 10ml solvent containing distilled water: methanol in the ratio of (1:1). Until the mixture dissolves, stir it over a hot water bath. Once the mixture had reached a temperature of 25°C, the pharmaceutical (*Centella asiatica*) CA+ (*Liquorice*) LI in the ratio of 50:50, 70:30 was incorporated.CA is highly effective than LI for wound healing activity, that's why to enhance the formulation efficacy, drug combination ratio 70:30 is selected not 30:70. Nextly the glycerol and propylene glycol (0.5ml) both were added.

Then the mixture was transferred into a glass petri dish and kept for about 24 hrs without any disturbance **Table 1, Fig. 2**.

Transdermal patches were carefully removed from the petri dish without rupturing and cut into small pieces of 2×4cm. The patch was collected and stored in desiccator until further use. The drug (Asiatic acid and Glycyrrhizin) was selected on the basis that they show a wound healing property and are time tested and proven safe [7, 8] **Fig. 2.**

TABLE 1: FORMULATION DESIGN

Ingredients	F1	F2
HPMC	500mg	500mg
Carbopol 934	250mg	250mg
Propylene Glycol	0.5ml	0.5ml
Glycerol	0.5ml	0.5ml
Methanol :Water	10ml	10ml
Drug CA+LI(mg)	50:50	70:30

FIG. 2: FORMULATION OF TRANSDERMAL PATCH USING SOLVENT CASTING METHOD

Evaluation of Transdermal Patch:

Organoleptic Characteristics: The physical appearance of the patch was analysed by its appearance, colour, clarity, flexibility and smoothness.

Physico-Chemical Evaluation:

Thickness of Patch: The thickness of each patch was measured at five distinct locations using a screw gauge or vernier caliper, and the average was determined.

The weight variation is calculated by weighing five patches and calculating their average.

Weight Uniformity: Take 5 randomly prepared patches from same batch and dry them at 60ºC for 4 hours.

The patch is then put on a computerized balance, which determines its average weight.

Folding Resistance: A patch of length 2×4cm were cut and folded multiple times at the same spot until it breaks. The number of folds before breaking determines the folding endurance.

pH: The pH of the film was tested using a pH meter. The prepared solution of patch is used for determination of pH, where a 2×4 cm area of patch was dissolved in distilled water and solution is prepared. LT-5001 tabletop pH meter is used to determine the pH.

Moisture Content: The films were weighed, placed in a desicator with calcium chloride for 24 hr **Fig. 3**, and then reweighed to calculate the percentage moisture content by using the formula mentioned below.

%Moisture content = (Initial weight - Final weight) / Initial weight × 100

FIG. 3: DETERMINING MOISTURE CONTENT USING DESICCATOR

Moisture uptake: The films were weighed and kept in desiccators with a saturated potassium chloride solution to maintain 84% relative humidity for a full day at room temperature.

The films were weighed again after a day, and the following formula was used to calculate the percentage of moisture uptake.

%Moisture uptake = (Final weight - Initial weight) / (Initial weight × 100)

Drug Content: A 2×4 cm area of the patch was dissolved in a phosphate buffer solution. The solution was stirred to dissolve the film and then transferred to a volumetric flask. The absorbance of the solution was measured at a wavelength of 253nm to determine the drug content [9-12].

Drug content (%) = Absorbance / Total amount of drug × 100

***In-vitro* Study:**

Franz Diffusion Cell Method:

1. In this this franz diffusion cell apparatus is used **Fig. 4**.
2. Which consist of two chambers, the first one is donar chamber and second is a receptor chamber.
3. The transdermal system is placed between these two chambers and a skin is placed below this transdermal patch.
4. The two chambers are tightly held together with the help of clamp.
5. The donar chamber is filled with phosphate buffer solution.
6. On starting the experiment donar chamber diffuses through membrane into receptor chamber.
7. From the receptor chamber a solution is removed for analysis from sampling port.
8. The samples are measured by using a UV-spectrophotometer in every 30 minutes.
9. This test determines the amount of diffusant that has permeated the membrane [13, 14].

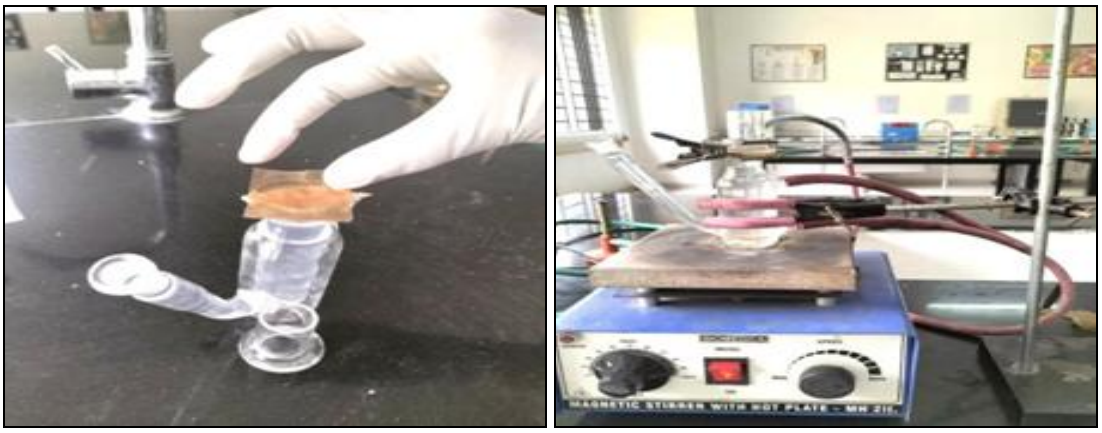

FIG. 4: FRANZ DIFFUSSION ASSEMBLY

RESULT & DISCUSSION: Using the solvent casting process, a transdermal patch containing *liquorice* and Asiatic acid was successfully created with the goal of increasing the combined bioavailability of herbal medications. It was discovered that the prepared film was clear, smooth, flexible, and uniform [15, 16]. **Table 2** displays the findings from thickness experiments conducted on various formulations. These results demonstrate that all of the created formulations' thicknesses (0.523 and 0.520 mm) were determined to be uniform. It was found that the weights had low standard deviation values and were consistent across all created formulas [17, 18]. **Table 2** displays the findings from folding endurance tests conducted on various formulations. The created formulations were found to be uniform in terms of folding endurance (136 and 142 folds), as evidenced by the aforementioned statistics. The mechanical properties of the patches are shown by their folding endurance number; a high folding endurance number signifies a high mechanical characteristic of the patches. The pH of each patch is around neutral at 6. Thus, the skin won't become irritated in any way [19].

TABLE 2: EVALUATION OF HERBAL TRANSDERMAL PATCH (CA+LI)

Formulation code	Thickness (mm)	Weight Uniformity (gm)	Folding Endurance (n)	Surface pH
F1	0.522±0.001	1.35±0.16	153±3.9	6
F2	0.524±0.009	1.37±0.07	152±3.6	6

Values are expressed as the mean±SD, where (n=3).

The moisture content in prepared formulation F1, F2, was found as shown in **Table 3**. The formulations low moisture content keeps them from becoming a totally dry and brittle layer and helps them stay stable. The patches are shielded from microbial contamination by limited moisture absorption [20, 21]. Studies on moisture absorption and content offer insights about the formulation's stability.

The percentage moisture uptake was found by placing a patch in Desicator in presence of potassium chloride solution and results are obtain as shown in **Table 3**. It shows that the drug content percentage for CA + LI patches in different formulation ratio codes ranged from 86.45% to 96.86% [22, 23].

Drug content (%) = Absorbance / Total amount of drug × 100

TABLE 3: EVALUATION OF HERBAL TRANSDERMAL PATCH (CA+LI)

Formulation code	%Moisture Content	%Moisture Uptake	Drug (%) Content
F1	3.13±0.012	5.77±0.04	89.32±0.12
F2	4.11±0.008	5.67±0.12	90.2±0.31

Values are expressed as the means ± SD, where (n=3).

***In-vitro* Franz Diffusion Cell Method:** By using a Franz diffusion apparatus, a test has been carried out and the amount of drug diffused through the membrane is calculated [24, 25] **Table 4**.

TABLE 4: *IN-VITRO* DRUG RELEASE STUDY OF PREPARED TRANSDERMAL PATCH

Formulation code	F1	F2
30 min	0.2631	0.352
60 min	0.4869	0.5385
90 min	0.6136	0.7255
120 min	0.8752	0.9334
150 min	0.946	1.063

Values are expressed as the means.

CONCLUSION: According to the result, it can be concluded that transdermal drug delivery system for *Centella asiatica* + *Liquorice* with HPMC and Carbopol 934 meet the ideal requirement for transdermal devices which can be an effective means to bypass the first past metabolism and increase bioavailability. CA + LI transdermal patches are useful for treating wounds because they offer continuous transdermal administration over extended period of time. It has been discovered via the current experiment that the medications of ayurvedic origin can be used by incorporating in modern dosage form with enhanced efficacy.

ACKNOWLEDGEMENT: The authors would like to thank the Principal of KJEI's Trinity College of Pharmacy, Pune for providing all necessary facilities and encouragement.

CONFLICTS OF INTEREST: The authors declare that they have no conflicts of interest.

REFERENCES:

1. Apoorv Tripathi and Sameer Rastogi: Fast disintegrating tablets over other solid dosage form. a comprehensive review. International Journal of Science & Engineering Development Research 2023; 8(6): 598-607. Available from:http://www.ijrti.org/papers/IJRTI2306095.pdf
2. Arribas-López and Elena: A Systematic Review of the Effect of *Centella asiatica* on Wound Healing. Int J of Env Res and Public Health 2022; 19(6): 3266 -69.
3. Saundharya P, Jerrine Joseph, Rajalakshmi G and Mary Shamya: Formulation of Wound Healing Transdermal Patch from Tubers Extract of *Momordica cymbalaria* and its *In-vitro* Evaluation. Haya: The Saudi Journal of Life Sciences 2022; 7(7): 224-233.
4. Pandian GS: Ultraviolet spectrum of extract of *Centella asiatica* (Vallarai) in edible oil as supplement. Asian J of Pharma and Clinical Research 2018; 11(4): 425-26.
5. Shelke PS and Jagtap PN: Formulation and *in–vitro* evaluation of transdermal patches of anti–arthritic ayurvedic medicinal plants. Biosc Biotech Res Comm 2020; 13(2): 803-808.
6. Wong WF, Ang KP, Sethi G and Looi CY: Recent Advancement of Medical Patch for Transdermal Drug Delivery. Medicina (Kaunas) 2023; 59(4): 778. Available from:https://doi.org/10.3390/medicina59040778
7. Cherukuri S, Batchu UR, Mandava K, Cherukuri V and Ganapuram KR: Formulation and evaluation of transdermal drug delivery of topiramate. Int J Pharm Investig 2017; 7(1): 10-17.
8. Long Mo, Guijing Lu, Xiping Ou and Dongsheng Ouyang: Formulation and development of novel control release transdermal patches of carvedilol to improve bioavailability for the treatment of heart failure. Saudi Journal of Biological Sciences 2022; 29(1): 266-272.
9. Reddy DP, Bhanja SB, Chauhan AK, Kumar BK, Panda DS and Panigrahi BB: Methanolic Extraction, Formulation and Evaluation of Herbal Transdermal Patches of *Azadira chtaindica.* A Juss Research Journal of Pharmacy and Technology 2021; 14(7): 3709-5.
10. Liji Jacob, Manju Salim S and Jilby Saju: Formulation and evaluation of transdermal patches of selegiline. Asian Journal of Pharmacy and Technology 2022; 12(2): 96-100.
11. Sheba R, Nakka D, Rajan R and EuSheau Z: Development and *in-vitro* evaluation of self-adhesive matrix-type transdermal delivery system of ondansetron hydrochloride. Trop J Pharma Res 2015; 14(2): 211-18.
12. Cherukuri S, Rajeswari B and Kiranmai M: Formulation and evaluation of transdermal drug delivery of topiramate. Int J Pharma Invest 2017; 7(1): 1-8.
13. Ramadon and Delly: Enhancement Strategies for Transdermal Drug Delivery Systems: Current Trends and Applications. DDTR 2021; 12(4): 758–91.
14. LalitaChauhan: Formulation and evaluation of Novel herbal antidiabetic transdermal patch. Inno Pharm Pharmacother 2018; 6(4):61-64.
15. Anukunwithaya T, Tantisira MH, Tantisira B and Khemawoot P: Pharmacokinetics of a standardized extract of *C. asiatica* ECa 233 in rats. Pl Me 2017; 83(8): 710-17.
16. Choi YM, An S and Lee J: Titrated extract of *Centella asiatica* increases hair inductive property through inhibition of STAT signaling pathway in three-dimensional spheroid cultured human dermal papilla cells. Bioscience, Biotech and Biochem 2017; 81(12): 2323–29.
17. Sh Ahmed A, Taher M and Mandal UK: Pharmacological properties of *Centella asiatica* hydrogel in accelerating wound healing in rabbits. BMC Complementary and Alternative Medicine 2019; 19(1): 213-18.
18. Kapoor A, Mishra SK, Verma DK and Pandey P: Chemical penetration enhancers for transdermal drug delivery system. Journal of Drug Delivery and Therapeutics 2018; 8(5): 62-6.
19. Doaa H. Assar, Nagwan Elhabashi, Abd-Allah A. Mokhbatly, Amany E. Ragab, Zizy I. Elbialy, Sally A. Rizk, Aishah E. Albalawi, Norah A. Althobaiti, Soad Al Jaouni and Ayman Atiba: Wound healing potential of licorice extract in rat model: Antioxidants, histopathological, immunohistochemical and gene expression evidences. Biomedicine & Pharmacotherapy 2021; 143: 112151.
20. Zabihi M, Hatefi B, Ardakani ME, Ranjbar AM and Mohammadi F: Impact of licorice root on the burn healing process: A double-blinded randomized controlled clinical trial. Complement Ther Med 2023; 73: 102941. Available from: https://doi.org/10.1016/j.ctim.2023.102941
21. Bolla SR, Mohammed Al-Subaie A, Yousuf Al-Jindan R, Papayya Balakrishna J, Kanchi Ravi P, Veeraraghavan VP, Arumugam Pillai A, Gollapalli SSR, Palpath Joseph J and Surapaneni KM: *In-vitro* wound healing potency of methanolic leaf extract of *Aristolochia saccata* is possibly mediated by its stimulatory effect on collagen-1 expression. Heliyon 2019; 5(5): 01648. Available from: https://pubmed.ncbi.nlm.nih.gov/31193473/
22. Bhardwaj A, Harinath Dwivedi, Koshi Mamman and SA Saraf: Solubility enhancement of *Boswellia serrata* Roxb. ex colebr extract through a self dispersible lipidic formulation approach. Indian Journal of Natural Products and Resources 2016; 7(1): 9-18.
23. Mohsen Zabihi, Bahareh Hatefi, Mohammad Ebrahimzadeh Ardakani, Ali Mohammad Ranjbar and Farhad Mohammadi: Impact of licorice root on the burn healing process: A double-blinded randomized controlled clinical trial. Complementary Therapies in Medicine 2023; 73:102941. Available from: https://www.sciencedirect.com/science/article/pii/S0965229923000286
24. Kyoung-Sik Park: Pharmacological effects of *Centella asiatica* on skin diseases: evidence and possible mechanisms. Evidence-based Complementary and Alternative Medicine 2021. Available from: https://www.semanticscholar.org/paper/Pharmacological-Effects-of-Centella-asiatica-on-and-Park/7c9500020063653c8f61ed8a92913482fe9f992a
25. Aszrin, Farashakira Adam, Siti Abdul Mutalib, Maisarah, Tang, Hooi, Tang and Shirley: An overview of *Centella asiatica* and its therapeutic applications. Life Sciences, Medicine and Biomedicine 2024; 8(1): 146-51.

How to cite this article:
Gavali SS, Lawate HM, Hadke SA, Gaikwad SM, Jain MR, Suryawanshi PM, Jagtap AA and Chaudhari SR: Formulation & evaluation of herbal transdermal patch of *Centella asiatica* & liquorice to study wound healing activity. Int J Pharm Sci & Res 2024; 15(12): 3673-78. doi: 10.13040/IJPSR.0975-8232.15(12).3673-78.