

Development of a Natural Analgesic Patch for External Application

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Abstract

Pain-related conditions such as muscular strain and joint discomfort significantly interfere with routine activities and physical performance. Although commonly used analgesic drugs provide quick relief, their repeated or prolonged use may be associated with undesirable effects. This limitation has encouraged the exploration of natural formulations that can provide localized pain relief with better safety. The present work describes the development of an herbal-based pain relief patch intended for external application. Medicinal plants including Ashwagandha (*Withania somnifera*), Nirgundi (*Vitex negundo*), Ginger (*Zingiber officinale*), and Turmeric (*Curcuma longa*) were selected due to their traditional relevance and reported anti-inflammatory and analgesic potential. Menthol and camphor were incorporated to enhance sensory action and immediate comfort at the site of application. A suitable polymer matrix was used to prepare a flexible and skin-adherent patch. The formulated patch exhibited uniform texture, good flexibility, and satisfactory adhesion to the skin. The combined action of herbal constituents is expected to reduce localized inflammation, muscle stiffness, and pain. This study emphasizes the relevance of integrating medicinal plant knowledge with topical delivery systems to develop user-friendly pain management options. Herbal pain relief patches may serve as a practical and non-invasive alternative for managing mild to moderate musculoskeletal pain.

INTRODUCTION

Transdermal drug delivery systems (TDDS) have drawn a lot of interest as a substitute for traditional parenteral and oral drug delivery methods. These systems provide a number of benefits, including as preventing hepatic first-pass metabolism, maintaining regulated plasma drug levels, lowering the frequency of doses, and enhancing patient compliance. Although the stratum corneum functions as the main barrier preventing medication penetration through the skin, the skin provides a practical and accessible route for both local and systemic therapy (Cruz *et al.*, 2024). Permeation improvement techniques and different formulation approaches have been developed to get around this obstacle. Polymers, adhesives, plasticizers, backing membranes, and permeation enhancers are

commonly found in transdermal patches, which work together to control drug release and absorption. Transdermal system success is dependent on the active compound's molecular weight, lipophilicity, solubility, partition coefficient, and dosage. To guarantee efficient penetration through the layers of the skin, drugs meant for transdermal administration should ideally have the right physicochemical characteristics (Ignacyk *et al.*, 2023). Herbal medications' therapeutic efficacy and generally positive safety ratings have led to a growing focus on integrating them into cutting-edge drug delivery systems. Traditional Ayurvedic medicine makes extensive use of *Withania somnifera* (Ashwagandha), also referred to as winter cherry or Indian ginseng. The bioactive components found in ashwagandha roots,

including flavonoids, steroidal lactones, alkaloids, and withanolides, are what give it its wide range of pharmacological effects (Bhalla *et al.*, 2013). Pain represents a significant global health concern that affects individuals across all age groups and substantially compromises physical functioning and overall quality of life. It interferes with routine activities, reduces productivity, and imposes an increasing burden on healthcare systems worldwide. Conventional pharmacological management of pain commonly involves non-steroidal anti-inflammatory drugs (NSAIDs) and opioids; however, prolonged administration of these agents is frequently associated with adverse effects such as gastric irritation, renal toxicity, systemic complications, tolerance, and dependence (Patel *et al.*, 2013).

Owing to these limitations, there has been a growing shift toward the exploration of safer and more sustainable therapeutic alternatives derived from natural sources. Herbal formulations, particularly polyherbal combinations, have gained considerable scientific attention due to their multi-target mechanisms of action, improved biocompatibility, and long-standing traditional usage in pain management systems. The present study focuses on the development of a polyherbal transdermal pain-relief patch incorporating Ashwagandha, Nirgundi, Ginger, Curcumin, Menthol, Camphor, Aloe vera gel, and Glycerin, each selected based on documented pharmacological evidence supporting analgesic and anti-inflammatory activity (Farooqui *et al.*, 2019).

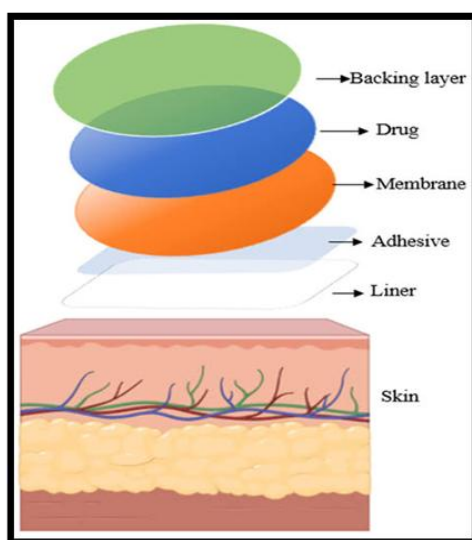


Fig.1. Pain relief patches (31)

Curcumin, the principal bioactive constituent of *Curcuma longa* (turmeric), is one of the most extensively researched natural anti-inflammatory compounds. Aloe vera exhibits soothing, wound-healing, and anti-inflammatory effects that maintain skin integrity during prolonged patch application. Aloe vera exhibits soothing, wound-healing, and anti-inflammatory effects that maintain skin integrity during prolonged patch application (Hasanah *et al.*, 2023).

Ashwagandha (*Withania somnifera*), a renowned Rasayana herb in Ayurveda, is recognized for its adaptogenic and rejuvenating properties. Contemporary pharmacological studies highlight its analgesic, anti-inflammatory, muscle relaxant, and neuroprotective effects. Ashwagandha contributes to modulation of inflammatory mediators and reduction of oxidative stress through bioactive constituents such as withanolides. Its incorporation into a polyherbal patch enhances therapeutic efficacy by simultaneously addressing

inflammation, muscular discomfort, and physiological stress associated with chronic pain conditions (Baghel *et al.*, 2021). Ginger (*Zingiber officinale*) possesses well-documented analgesic, antioxidant, and anti-inflammatory activities attributed to active constituents such as gingerols, shogaols, and zingerone (Langer *et al.*, 2008). These phytochemicals inhibit cyclooxygenase (COX) and lipoxygenase (LOX) pathways, thereby suppressing inflammatory mediator synthesis (Frondoza, 2005). Clinical evidence supports the effectiveness of ginger in reducing exercise-induced muscle soreness and inflammatory pain. Additionally, its ability to enhance peripheral circulation and mitigate oxidative stress further supports its application in topical transdermal systems for musculoskeletal pain relief (Black, 2010). Menthol and camphor function as counter-irritants widely utilized in topical analgesic preparations. Menthol activates transient receptor potential melastatin 8 (TRPM8) channels,

producing a cooling sensation that modulates nociceptive signalling pathways. Camphor interacts with sensory nerve endings, including TRPV1 and TRPM8 receptors, generating a warming and mild aesthetic effect that distracts pain perception. Menthol and camphor are commonly used counter-irritants in topical pain-relief formulations. They produce cooling and warming sensations on the skin that help reduce pain by stimulating thermoreceptors, distracting pain signals, and improving localized blood flow. Menthol activates TRPM8 receptors, creating a cooling effect, while camphor stimulates sensory nerves to provide warming relief. Clinical studies confirm their effectiveness in relieving muscle and joint pain, making them essential components in modern herbal patch formulations (Hoang, 2023). Collectively, evidence from preclinical, formulation-based, and clinical investigations

supports the therapeutic potential of polyherbal transdermal patches in managing osteoarthritis, back pain, and other musculoskeletal disorders. Systematic reviews indicate that such formulations are generally safe, well-tolerated, and suitable for long-term application (Ding, 2014).

2. MATERIALS AND METHODS

2.1 Herbs used for preparation of polyherbal pain relief patches

2.1.1 *Ashwagandha*:

Family: Solanaceae

Biological Name: *Withania somnifera*

Biological Source: Dried roots

Chemical Constituents: Withanolides, withaferin A, alkaloids

Uses: Anti-inflammatory, analgesic, muscle relaxant (Dharmasiri, *et al.*, 2003).



Fig. 2. *Withania somnifera* (Ashwagandha)



Fig. 3 Nirgundi

2.1.2 *Nirgundi*:

Family: Verbenaceae

Biological Name: *Vitex negundo*

Biological Source: Leaves

Chemical Constituents: Flavonoids, iridoid glycosides, terpenoids

Uses: Reduces pain, swelling, joint stiffness (Frondoza, *et al.*, 2005).

2.1.3 *Ginger*:

Family: Zingiberaceae

Biological Name: *Zingiber officinale*

Biological Source: Rhizomes

Chemical Constituents: Gingerols, shogaols, zingerone

Uses: Anti-inflammatory, improves circulation, relieves muscle pain (Hewlings, *et al.*, 2017).



Fig. 4 Ginger



Fig. 5 Curcumin

2.1.4 Curcumin (Turmeric):

Family: Zingiberaceae

Biological Name: Curcuma longa

Biological Source: Dried rhizomes

Chemical Constituents: Curcuminoids, volatile oils

Uses: Anti-inflammatory, antioxidant reduces swelling (Eccles, *et al.*, 1994).

2.1.5 Menthol:

Family: Lamiaceae

Biological Name: Mentha arvensis / Mentha piperita

Biological Source: Mint leaf oil crystals

Chemical Constituents: Menthol, menthone

Uses: TRPM8 activation, cooling, pain-relieving, permeation enhancer (Chen, *et al.*, 2013).



Fig. 6 Menthol



Fig. 7 Camphor

2.1.6 Camphor:

Family: Lauraceae

Biological Name: From Cinnamomum camphora

Biological Source: Wood of the tree

Chemical Constituents: Camphor, cineole

Uses: Counter-irritant, improves blood flow, reduces muscle pain (Juergens, *et al.*, 1998).

2.1.7 Eucalyptus Oil:

Family: Myrtaceae

Biological Name: Eucalyptus globulus

Biological Source: Leaves

Chemical Constituents: 1,8-cineole, α -pinene

Uses: Analgesic, anti-inflammatory, muscle relaxation (Saple, *et al.*, 2008).



Fig. 8 Eucalyptus oil



Fig. 9 Aloe-vera Gel

2.1.8 Aloe-vera:

Family: Liliaceae

Biological Name: Aloe barbadensis Miller

Biological Source: Leaf gel

Chemical Constituents: Aloin, aloesin, polysaccharides

Uses: Skin-soothing, calming, reduces irritation (Krochta, *et al.*, 2007).

2.1.9. Plastizer:

Plasticizers play a critical role in the formulation of herbal transdermal patches by enhancing the flexibility and mechanical strength of polymeric films. They minimize the risk of film cracking

during handling and storage by reducing the glass transition temperature (T_g) of the polymer matrix). This plasticizing effect improves softness, surface smoothness, and skin adhesion, thereby increasing patient comfort during application. Among various plasticizers, glycerine is most frequently employed due to its excellent compatibility with hydrophilic polymers such as HPMC, PVA, chitosan, and gelatin. The presence of three hydroxyl groups in glycerin enables the formation of strong hydrogen bonds with polymer chains, resulting in improved elasticity, tensile strength, and folding endurance of the transdermal film. Its hygroscopic nature facilitates moisture retention within the matrix, thereby preventing brittleness and preserving the physical stability of the herbal patch during storage. Furthermore, glycerin enhances drug release characteristics by promoting polymer swelling, decreasing crystallinity, and facilitating diffusion of herbal actives including menthol, camphor, curcumin, and Nirgundi. Owing to its skin compatibility, non-toxic profile, affordability, and wide availability, glycerin is considered a preferred plasticizer in herbal transdermal formulations (Assis, *et al.*, 2009).

2.1.10 Base Polymer Used in Herbal Patches:

Methyl Cellulose (MC): is extensively utilized as a base polymer in herbal transdermal pain-relief patches due to its excellent film-forming capability,

biocompatibility, and non-toxic characteristics, making it highly suitable for transdermal applications (Shingade *et al.*, 2012). MC forms smooth, uniform, and flexible films that provide structural integrity and ensure homogeneous distribution of herbal constituents such as menthol, camphor, curcumin, ginger extract, Nirgundi, and eucalyptus oil within the polymeric matrix (Chowdhary *et al.*, 2010) -retention capacity helps maintain adequate hydration of the patch and prevents cracking or excessive drying during storage, thereby improving the stability of the formulation and supporting controlled release of natural analgesic agents (Bandyopadhyay *et al.*, 2006). In addition, MC exhibits strong compatibility with plasticizers such as glycerine, enhancing elasticity, folding endurance, and overall comfort of the patch upon dermal application. The controlled swelling behaviour and moderate permeability of MC facilitate sustained release of incorporated herbal actives, contributing to prolonged therapeutic effects. Moreover, MC is cost-effective, readily available, and compatible with other excipients including PVA, HPMC, and various penetration enhancers, offering formulation versatility. These combined properties establish methyl cellulose as an ideal and dependable base polymer for polyherbal transdermal pain-relief systems (Boateng *et al.*, 2014).

2.2 Procedure:

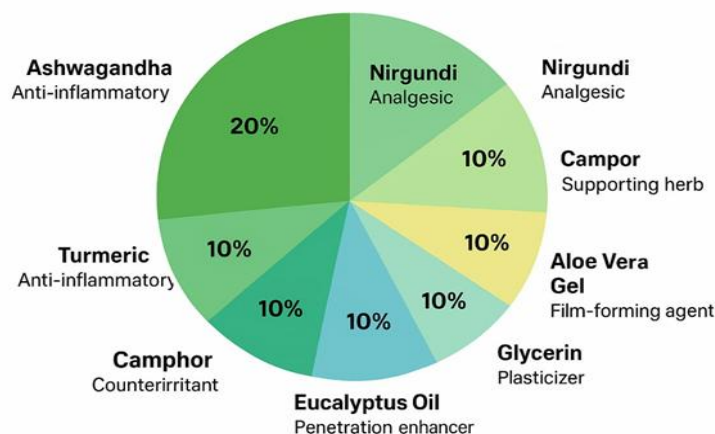


Fig.10 Composition of Patch

The polyherbal transdermal patch was prepared using a solvent casting technique to ensure uniform dispersion of active herbal constituents within the polymeric matrix.

Preparation of Gel Base: Methyl cellulose (MC) was gradually dispersed in cold distilled water and allowed to hydrate completely to form a uniform gel base. Glycerin was incorporated into the hydrated

polymer as a plasticizer to enhance flexibility and mechanical stability of the film.

Preparation of Herbal Solution: Standardized extracts of Ashwagandha, Nirgundi, Turmeric (Curcumin), and Ginger were dissolved in propylene glycol (PG) to obtain a homogeneous herbal solution.

Incorporation of Active Ingredients: Menthol and Camphor were separately dissolved in propylene glycol and added to the herbal solution. Aloe vera gel and Eucalyptus oil were subsequently incorporated under continuous stirring to ensure uniform mixing.

Mixing: The prepared herbal solution was slowly blended with the methyl cellulose gel base under continuous stirring to obtain a smooth and uniform formulation without air entrapment.

Casting: The final mixture was poured and evenly spread onto a clean, levelled surface lined with butter paper or aluminium foil to achieve uniform thickness.

Drying: The cast films were allowed to dry either at room temperature or in a hot air oven maintained at 40–45°C until complete solvent evaporation and film formation occurred.

Cutting and Packaging: After drying, the former films were carefully peeled off, cut into appropriate sizes, and stored in airtight pouches to prevent moisture absorption and preserve stability.

3. RESULTS AND DISCUSSION

The prepared transdermal patch was evaluated for physicochemical parameters including thickness, weight variation, folding endurance, surface pH, and moisture content to ensure uniformity, stability, and patient safety. The thickness of the patch was found to be uniform throughout, indicating consistent casting and even drug distribution. The weight variation was within $\pm 5\%$, confirming batch uniformity and reproducibility of the formulation process. Folding endurance values exceeded 200, demonstrating good mechanical strength and flexibility, which are essential for maintaining patch integrity during application and use. The surface pH was observed within the acceptable skin-compatible range (5–7), suggesting minimal risk of skin irritation upon application. Moisture content was below 5%, indicating adequate stability and reduced chances of microbial growth or formulation degradation.

Overall, all evaluated parameters complied with standard acceptable limits, confirming the prepared formulation to be stable, uniform, safe, and suitable for transdermal drug delivery applications.

The formulated polyherbal transdermal patch exhibited satisfactory film forming characteristics with uniform thickness and smooth surface texture. Thin incorporation of methyl cellulose as the base polymer provided structural integrity and consistent distribution of herbal actives within the matrix. Glycerin effectively functioned as a plasticizer by

enhancing film flexibility, preventing brittleness, and improving folding endurance. The prepared patches demonstrated good mechanical strength and adhesion, indicating suitability for topical application. The combination of Ashwagandha, Nirgundi, Ginger, and Curcumin contributed synergistic anti-inflammatory and analgesic activity. Menthol and Camphor produced immediate cooling and warming sensations through counter-irritant mechanisms, supporting rapid onset of localized pain relief. Aloe vera enhanced skin compatibility and improved permeation of active constituents. The sustained release behaviour observed from the polymeric matrix suggests prolonged therapeutic action, which may reduce the frequency of application compared to conventional topical formulations. The polyherbal approach demonstrated potential advantages over single-herb systems due to synergistic pharmacological interactions among the incorporated ingredients. Overall, the formulation successfully integrates traditional herbal therapeutics with modern transdermal drug delivery technology, supporting its potential role in managing musculoskeletal pain conditions.

4. CONCLUSION

The developed polyherbal transdermal pain-relief patch containing Ashwagandha, Nirgundi, Ginger, Curcumin, Menthol, Camphor, Eucalyptus oil, and Aloe vera demonstrated desirable physicochemical and mechanical properties, including effective film formation, adequate flexibility, and satisfactory adhesion. The synergistic interaction among the selected herbal constituents contributed to enhanced anti-inflammatory and analgesic potential. Based on the observed characteristics, polyherbal transdermal patches represent a promising and patient-friendly alternative for long-term management of musculoskeletal pain.

Author Declaration

We certify that each of the listed authors has read and approved the article, and that no other persons meet the requirements to be included as authors. We also certify that we have all approved the order of authors as stated in the manuscript.

Declaration of competing Interest

All authors declare no conflict of interest.

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