International Journal of Pharmacy and Pharmaceutical Science

ISSN Print: 2664-7222
ISSN Online: 2664-7230
IJPPS 2025; 7(2): 134-140
www.pharmacyjournal.org
Received: 18-05-2025
Accepted: 21-06-2025

SS Naik
Department of Pharmaceutics, PSGV Institute of Pharmacy, Shahada, Maharashtra, India

SG Patil
PSGVPM's College of Pharmacy, Shahada, Maharashtra, India

SP Pawar
PSGVPM's College of Pharmacy, Shahada, Maharashtra, India

Corresponding Author:
SS Naik
Department of Pharmaceutics, PSGV Institute of Pharmacy, Shahada, Maharashtra, India

Transdermal patch: A potential application for pain management

SS Naik, SG Patil and SP Pawar

DOI: https://doi.org/10.33545/26647222.2025.v7.i2b.204

Abstract
Pain relief is still a key challenge in clinical medicine, especially in acute and chronic diseases with lasting needs Transdermal drug delivery systems (TDDS) as patches are increasingly utilized as non-invasive therapeutic interventions that provide drugs with extended release, avoid the hepatic first-pass effect, and enhance patient compliance. The review takes into account the promise of transdermal patches as an effective and safe delivery system of analgesic drugs. It opens with an overview of transdermal patch design, highlighting important formulation considerations like drug reservoirs, polymeric matrices, and permeation enhancers. Drug transport through the skin layers and the factors affecting transdermal absorption are addressed with special reference.
Specific focus is on the physico-chemical characteristics of drugs most widely utilized in transdermal patches for analgesic purposes, including opioids (fentanyl, buprenorphine), non-steroidal anti-inflammatory drugs (NSAIDs), and local anesthetics. In addition, new patch technologies—iontophoresis, microneedles, and nanocarrier-based systems—are assessed in order to determine their ability to penetrate the skin barrier and enhance therapeutic performance. Marketed and regulatory products are stressed to accentuate clinical translation. Safety profile, side effects, and limitations of TDDS in pain relief are rigorously assessed.
In total, transdermal patches are a valuable tool in pain treatment with targeted, continuous, and patient-tolerable drug delivery. Advances in formulation technology and delivery improvement technology in the near term will continue to broaden their therapeutic uses and make them a foundation stone in personalized treatment of pain.

Keywords: Transdermal drug delivery system (TDDS), pain management, controlled release, opioid patches, NSAIDS, microneedles, permeation enhancers, chronic pain, drug delivery and patient compliance

1. Introduction
Pain is one of the body's alarm systems with the capability of limiting patients from deleterious effect. On the other hand, excessive pain creates psychological distress and bodily damage. Pain, by duration and pathology, is either nociceptive or neuropathic. Nociceptive pain, traditionally defined as acute pain, ordinarily less than 12 weeks, is classified as those occurring because of mechanical injury, heat or chemical inflammation [1]. Examples would include pain endured as a result of a sports trauma, dental surgery, or arthritis compared to the activation of nociceptors. Neuropathic pain, in general chronic, has a more prolonged time course and is more prone to be due to injury to the somatosensory nervous system, for example, diabetic neuropathy or post-herpetic neuralgia. Diseases with both kinds of pain are also prevalent like cancer pain and post-COVID pain. Not only the choice of active pharmaceutical ingredient (API), but also the pathogenesis of the disease influences and needs to be taken into consideration for the route of administration [2].
Transdermal drug delivery system, popularly called patches recently, is a drug delivery process without puncturing the skin by utilizing the dermis or the exterior of the skin. It can be employed as an alternative means of delivering oral form of drugs and hypodermic injections. Transdermal drug delivery system can deliver an analgesic in a controlled fashion through the skin to establish a systemic or a local effect. Transdermal patches are not new. It first found its use in systemic administration, three day patch, scopolamine for the treatment

of motion sickness, which was approved in the United States in 1979 [3]. A decade later, success with nicotine patches increased more interest and use of transdermal medications. More than 35 drugs are currently utilized in the form of transdermal patches, at least 13 approved drugs. The therapeutic applications of transdermal patches are now extended to hormone replacement, analgesic, relief from angina pain due to heart disease, suppression of smoking, and neurologic diseases [4]. Figure 1 gives an overview of mechanism of action of Transdermal patches.

Transdermal patches also have several merits when compared with oral and hypodermic injections. It is more biocompatible in first pass hepatic metabolism. Simpler administration of the drug by patch removal, painless application, and extended application for 1 week are some merits. But this drug delivery system has not yet been utilized to its maximum potential because of extremely limited constraints [5]. Local irritation and skin sensitization can restrict the quantity of drugs. Effective transdermal drugs are of molecular weights no larger than a few hundred Daltons, thereby restricting the dosage of drugs as well. Difficulty in delivery of hydrophilic drugs, cost of medicines, and delayed rate of absorption are some other constraints.

Transdermal medications will also have increased demand with additional developments for better safety and efficacy. Another giant step ahead would be the development of patches to deliver peptide and even protein drugs such as insulin, growth hormone, and vaccines. Transdermal patches are divided into three generations - first generation, second generation, and third generation [6].

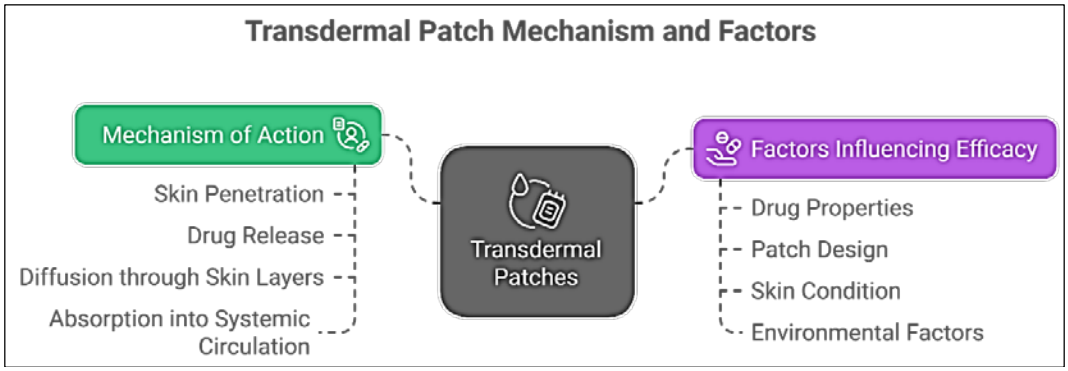

Fig 1: Mechanism of action of Transdermal Patches

A. First Generation Transdermal Patches

The first-generation transdermal drug delivery systems (TDDS) were mainly formulated to administer low-dose, lipophilic, and small molecules through the skin barrier with minimum damage to it. They utilized passive diffusion and contain traditional products such as nicotine, scopolamine, and nitro-glycerine patches. Their biggest limitation was that they could not provide hydrophilic or macromolecular drugs and hence had limited applications

B. Second Generation Transdermal Patches

In order to address the limited property of passive systems, improvement strategies like chemical enhancers, iontophoresis (electrically mediated delivery), and non-cavitational ultrasound were introduced in the second-generation TDDS. These strategies enhanced the permeability of stratum corneum, facilitating the delivery of medium-sized molecules. Though enhanced, they were hampered by the risk of skin irritation and variable drug delivery rates.

C. Third Generation Transdermal Patches

Third-generation TDDS represent a quantum leap that provides sophisticated physical techniques such as microneedles, thermal ablation, microdermabrasion, electroporation, and cavitational ultrasound. These techniques cross the stratum corneum barrier in a reversible and safe way and enable delivery of biologics, vaccines, and macromolecules. Microneedle arrays, in particular, have been of interest since they are painless and minimally invasive drug delivery.

Also on the horizon within this category are intelligent patches with biosensors and feedback-regulated systems that are providing real-time therapeutic adjustments [7-8]. Table I summarizes the generation features of Transdermal Patches.

Table I: Summary Table of Generational Features [7]

Generation	Key Features	Limitations	Examples
1st	Passive diffusion, lipophilic drugs	Low drug variety	Nicotine, Nitroglycerin
2nd	Chemical/physical enhancers (e.g., iontophoresis)	Skin irritation risk	Fentanyl patches with iontophoresis
3rd	Microneedles, electroporation, smart patches	Cost, complexity	Vaccine patches, insulin microneedles

2. Factors Involved With Transdermal Drug Delivery

Transdermal drug delivery is controlled by a complex system of factors that all contribute to the rate, extent, and predictability of drug absorption across the skin. Key determinants are the drug's physicochemical properties—e.g., small molecular size, medium lipophilicity (log P 1-3), and potency at doses below 1 mg/kg—which offer adequate permeability through the stratum corneum. Skin condition itself is important; conditions such as hydration, temperature, location of application, age, and whether there is skin disease or injury present or not can enhance or inhibit absorption [9]. The design type of the formulation—matrix or reservoir—is also important, along with whether permeation enhancers are present or absent, how sticky it is, and what the backing material is. All these directly affect drug release and bioavailability. Environmental factors like exposure to

heat, sweat, exercise, and application methods can modify drug kinetics or decrease patch adhesion. Transdermal delivery avoids first-pass hepatic metabolism, but cutaneous metabolism affects drug stability. The standards of regulations also regulate the effectiveness of patches by necessitating strict tests for content uniformity, adhesion, permeation, and environmental stability. Lastly, successful transdermal pain relief treatment relies on optimising these factors to induce controlled, safe, and extended drug release [10].

3. Transdermal Patches for Pain Management

Transdermal patches are now are used in pain management for both acute and chronic pain. They are available in various forms which include non-steroidal anti-inflammatory drug patches (NSAID), opioid patches, local anesthetic patches, capsaicin, and nitroglycerine. They are commonly used in pediatric practice.

A. NSAID Transdermal Patches

Nonsteroidal anti-inflammatory drug (NSAID) therapy continues to be the standard in pain and inflammation management of musculoskeletal trauma, arthritis, and soft tissue injury. Standard oral NSAID therapy, however, is well recognized to induce severe systemic side effects like gastrointestinal hemorrhage, renal toxicity, and cardiovascular disease [11]. To avoid these complications, transdermal NSAID patches have been developed as a new option with regional drug delivery and decreased systemic exposure. NSAIDs block the activity of the cyclooxygenase (COX) enzymes—mainly COX-2 in inflamed tissues—to inhibit prostaglandin formation and alleviate inflammation and pain. Perceptually administered in the form of transdermal patches, NSAIDs escape first-pass hepatic metabolism and directly reach inflamed tissues without traversing the general circulation, resulting in lower systemic levels but locally active concentrations [12]

Example of important NSAIDs in Transdermal Patches

A number of NSAIDs have been successfully incorporated into transdermal patches, most extensively used and researched being ibuprofen, diclofenac, and ketoprofen.

- Diclofenac Epolamine Patch (Flector Patch®): It was approved in most countries to manage acute pain due to minor sprain, strain, and contusion. The patch delivers 1.3% diclofenac epolamine. It was found to decrease pain severity scores by a clinically significant amount and enhance function in soft tissue injury patients.
- Ketoprofen Patches: Due to increased skin penetration and high lipid solubility, ketoprofen has been found extremely effective in myofascial and cervical syndromes of pain, even being more effective than oral NSAIDs in localized treatment.
- Ibuprofen Patches: Although still in the process of formulating improvements, ibuprofen patches are already available for purchase in a few nations and show reliable pain relief with optimal tolerability, especially for post-traumatic inflammation [13-14].

NSAID transdermal patches are are mostly indicated for the management of musculoskeletal conditions like osteoarthritis—of the knee and hand—bursitis, tendonitis, post-operative orthopaedic pain, and soft tissue trauma, including athletic trauma. These patches are particularly useful in the management of chronic pain, with evidence, including a recent meta-analysis by Sánchez *et al*. (2024), showing them to be more effective than placebo and as effective as compared to oral NSAIDs, but with significantly fewer gastrointestinal side effects. NSAID patches have been superior to oral treatments and topical gels [15]. Transdermal products have been demonstrated by clinical trials to provide more consistent and greater drug penetration compared to gels, along with controlled delivery for 12 to 24 hours. The longer action is especially useful for the patient who would benefit from long-term pain relief without frequent dosing, such as the elderly or patient with polypharmacy. Some patients develop cutaneous manifestations of erythema, rash, or pruritus in localized areas. Drug absorption and therapeutic reliability are also influenced by variations in skin hydration, anatomical location, and patient age [16]. NSAID patches are not appropriate for the management of systemic inflammation or extensive arthritic disease that requires elevated levels of drug in the body system. They are also contraindicated in patients with a history of NSAID hypersensitivity or impaired skin integrity. Even with such constraints, NSAID patches are safer compared to oral NSAIDs in most patients with much less risk of side effects from the systemic route [17].

B. Opioid Transdermal Patches

Pain management is an integral aspect of management in oncologic and non-oncologic chronic illness, where administration of opioids systemically over time usually leads to problems with tolerance, addiction, and systemic toxicity. In these situations, transdermal opioid patches have now become a non-invasive, long-term mode of delivery, providing continuous analgesia with better compliance and fewer side effects [18]. Opioid patches administer medications such as fentanyl or buprenorphine through the skin into the systemic circulation for an extended period of time, generally 72 hours. These lipophilic opioids are ideal candidates for transdermal delivery because of the characteristics like high potency, low molecular weight and lipid solubility. This route avoids first-pass hepatic metabolism, enables steady plasma concentrations, and reduces peak-trough fluctuations, which are common with oral or parenteral opioid regimens [19].

Major Opioid Patches in Use

a. Fentanyl Patches

Fentanyl is the most commonly used opioid in transdermal patches. A typical fentanyl patch delivers 12 to 100 µg/hour and is replaced every 72 hours. It is particularly effective for chronic pcancer pain, advanced rheumatoid arthritis and postoperative and palliative care. Clinical studies have demonstrated fentanyl's ability to significantly reduce pain scores and improve quality of life for patients with previously uncontrolled pain, often achieving complete relief.

b. Buprenorphine Patches

Buprenorphine, a partial µ-opioid receptor agonist and κ-antagonist, provides effective analgesia with reduced risk of respiratory depression. The buprenorphine patch, changed every 3-7 days, is approved in many countries for moderate to severe chronic pain and has shown promise in geriatric populations and opioid-naïve patients due to its safer profile [20-21].

Opioid patches are recommended in the treatment of chronic cancer pain, especially in patients who are unable to take oral medications or with swallowing difficulties. These patches are also given in the treatment of patients suffering from chronic pain due to disorders like osteoarthritis, neuropathic pain, and failed back surgery syndrome. The patches are also recommended in the palliative care treatment where non-invasive, long-duration analgesia is preferable. Studies have reported the effective use of fentanyl patches in patients with chronic soft tissue cancers, noting significant improvements in both pain control and sleep quality [22].

The use of opioid patches offer number of advantages to the patients like improved patient compliance, which can be seen especially among elderly or cognitively impaired patients. The other advantages are minimal gastrointestinal side effects, reduced dosing frequency and non-invasive and discrete which is ideal for outpatient and home-based care. These features make opioid patches especially suitable in long-term pain control settings, with enhanced convenience and fewer fluctuations in analgesic effect [23].

Although useful, opioid patches have their own restrictions and side effects. First among these is the risk of respiratory depression, especially in opioid-naïve individuals, such that even therapeutic doses have the potential to lead to life-threatening hypoventilation. Skin reaction at the site of application, for instance, erythema, rash, or pruritus, is another frequent grievance that can reduce compliance [24]. Additionally, delayed onset and slow titration reduce the utility of opioid patches in the context of rapidly increasing or acute pain. Additionally, accidental overdose is also a risk, particularly if the patch comes into contact with extrinsic sources of heat, for example, fever or heating pads, which dramatically enhance drug absorption. Finally, issues of physical dependence and tolerance persist, requiring proper patient selection, dose adjustment, and frequent monitoring during the treatment period to minimize risk and maximize safety [25].

Transdermal systems are being explored for pediatric pain management, particularly in palliative contexts where invasive routes are undesirable. Fentanyl and buprenorphine patches have been cautiously used in children, demonstrating safety under monitored protocols [26].

C. Local Anesthetic Patches

Local anesthetic patches provide a more superior analgesia and less surgery with the noninvasive, effective, and comfortable technique of local anesthetic delivery than injectables. Transdermal drug delivery systems are particularly useful in dermatologic surgery, musculoskeletal pain, and postoperative pain management, where patient compliance and comfort are essential [27]. Local anesthetics work through amplifying the block of voltage-gated sodium channels on the neuronal membranes to impede the passage of action potentials and induce reversible loss of sensation within the area of action. As patches, the medications get diffused into stratum corneum and localized in the dermis and subcutaneous tissue to induce local analgesia without systemic effect [28].

Major Preparations of Local Anesthetic Patches

a. Lidocaine Patch (Lidoderm®)

The most popular formula, 5% lidocaine patch, is FDA approved for the treatment of postherpetic neuralgia and has also been found effective in several off-label applications like myofascial pain, neuropathic pain, and port-site laparoscopic pain [29]. The patch is applied for a period of 12 hours within a 24-hour cycle and provides topical analgesia without systemic sedation or dependence.

b. Lidocaine/Tetracaine Self-Warming Patch

This heat component-including combination patch (i.e., Synera®) capitalizes on both the use of a heat component to enhance permeability of the skin and co-delivery of tetracaine and lidocaine. It is routinely employed for cosmetic and minor dermatologic procedures such as biopsies, excision of moles, and laser resurfacing. Clinically, effectiveness has been demonstrated to anesthetize the skin within 20-30 minutes [30].

Local anesthetic patches have found widespread utility across various clinical domains due to their non-invasive nature and effective localized analgesia. In dermatology and aesthetic procedures, these patches are commonly employed to minimize discomfort associated with laser hair removal, dermal filler injections, skin biopsies, and cryotherapy or electrocautery. Their ease of application and low complication risk make them ideal for outpatient cosmetic treatments.

In chronic pain management, the Lidoderm® (5% lidocaine) patch has gained traction for conditions such as diabetic neuropathy, lower back pain, and postherpetic neuralgia. Notably, it has shown therapeutic benefit in managing myofascial trigger points and trigeminal neuralgia, with fewer systemic side effects compared to traditional oral analgesics. Local anesthetic patches offer several notable clinical advantages that make them a compelling choice in pain management [31]. Their non-invasive administration allows for easier application, particularly beneficial in outpatient and ambulatory settings. These patches provide targeted analgesia with minimal systemic absorption, thereby reducing the potential for systemic side effects. A significant benefit is the reduced reliance on opioids, which supports broader efforts to combat opioid overuse and dependence. Additionally, the convenience of use enhances patient compliance, especially among pediatric patients and those who are averse to needles. Some formulations, particularly self-warming patches, offer a faster onset of action, further adding to their practicality in clinical use [32].

Although generally well-tolerated, local anesthetic patches are not without risks. Skin reactions such as erythema, rash, and allergic contact dermatitis (ACD) have been reported, with ACD particularly associated with lidocaine sensitivity. In cases of repeated exposure, patch testing may be necessary to confirm hypersensitivity, especially in high-risk individuals [33]. Although systemic toxicity is rare, it may occur with prolonged use, especially in pediatric or thin-skinned populations where drug absorption may be higher. Another limitation is their restricted depth of drug penetration, rendering them unsuitable for deep tissue or intra-articular pain. Moreover, temperature and skin hydration levels can significantly affect drug diffusion through the skin, potentially impacting their therapeutic efficacy [34].

When compared to traditional infiltration anesthesia, local anesthetic patches provide certain advantages and limitations. Notably, they eliminate the pain associated with needle injections, which can enhance patient comfort, especially in pediatric and geriatric populations. However,

they typically have a longer onset of action, ranging from 20 to 60 minutes, as opposed to the rapid onset (1-2 minutes) seen with injectable lidocaine. Furthermore, their effectiveness is largely limited to superficial procedures due to their inability to adequately anesthetize deeply innervated tissues. Despite these limitations, studies show that patients often prefer patches for their comfort, simplicity, and ease of use, making them a valuable option in specific clinical scenarios [35-36].

4. Regulatory and Formulation Issues of Transdermal Patches

Transdermal patches, being advanced drug delivery systems, are required to satisfy strict regulatory and formulation requirements to provide their safety, efficacy, and reproducibility in clinical use—most notably in pain alleviation. They are defined as combination products, which include a pharmacologically active component and device-like delivery system [37]. Regulation is mostly performed by agencies like the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), etc., based on the acceptance criteria including safety of the drug, patch integrity, adhesion, kinetic release of the drug, and patient tolerability. Transdermal patches are generally approved through the New Drug Application (NDA) or Abbreviated New Drug Application (ANDA) process, where the innovators must submit detailed information such as *in vitro* skin permeation studies, pharmacokinetics, possible irritation, stability, and adhesion tests [38].

With regard to formulation, a transdermal patch has various layers: environmental protection backing layer, controlled release drug reservoir or matrix, adhesive layer (in the majority of cases also drug-containing), and release liner. Drug choice for transdermal delivery is highly selective, with preference for lipophilic molecules of low molecular weight, low-dose potency, and no irritation potential. Fentanyl, buprenorphine, lidocaine, diclofenac, and ketoprofen are some common analgesic drugs administered through this route. Permeation across the stratum corneum barrier needs to be supplied, and chemical penetration enhancers such as ethanol or new devices such as warm patches and microneedles are utilized [39].

Therapeutic dependability needs to be ensured using bioequivalence testing, usually carried out by *in vitro-in vivo* correlation (IVIVC) tests and comparison of pharmacokinetics with reference products. Patches are also monitored for uniformity of drug content, wear ability, adhesion, and integrity when exposed to several environmental conditions. Safety is a very crucial issue; typical side effects include skin irritation, allergy, or risk of overdose due to abuse—like exposure to ambient heat [40]. Used patches also have residual drug, so there should be good disposal process in order to prevent accidental pediatric exposure or contamination. Regulatory requirements of the future are evolving to suit the newer modalities like smart patches, iontophoretic systems, and AI-assisted feedback systems. These modalities are creating new requirements in drug-device-software integration, cyber security, and extended post-market surveillance. Therefore, the regulatory and formulation environment for transdermal patches is dynamic and holistic in placing on the market such systems that provide safe, patient-focused, and clinically effective solutions for pain relief [41].

5. Future Directions

The destiny of transdermal patches for pain management is fast changing, with the majority of innovation aimed at addressing existing shortcomings and expanding clinical uses. Conventional patches, admirably well-suited to deliver small, lipid-soluble drugs such as fentanyl, buprenorphine, and lidocaine, are plagued by retarded onset of action, drug loadability, and skin permeability variability [42]. To counter these problems, the next generation of transdermal systems is converging intelligent technology that acts based on physiological signals like temperature, pH, or inflammatory biomarkers. These "responsive" or "smart" patches are being designed to dispense drugs on-demand, varying delivery as per an individual patient's needs in real-time. This is especially useful in cases of chronic pain where the dosage changes with the progression of the day. Wearable electronics have made it possible to integrate biosensors into patch matrices that can detect patient vital signs or pain signals and interface with mobile health applications to modulate dosing, enhance compliance, and trigger alerts to caregivers or clinicians when treatment is needed [43].

Another innovative area uses microneedle-mediated delivery systems. These patches have extremely fine, minimally painful needles that penetrate the stratum corneum without causing pain, circumventing the major barrier of skin to provide hydrophilic drugs, peptides, and indeed biologics efficiently [44]. Microneedle patches also inherently provide speed-of-action analgesia and have potential for the delivery of high-molecular-weight drugs like monoclonal antibodies and neuropeptides, which are limited to parenteral administration presently. Biodegradable microneedles are also being investigated to reduce the risk of infection and patch removal. Meanwhile, formulation researchers are creating dual-drug patches that can co-deliver synergistic therapies—such as pairing an opioid with an NSAID or antiemetic—to offer integrated pain relief with reduced individual drug doses and side effects [45].

The increasing need for combination therapy patches is reflected in the demand for multimodal pain management modalities, especially in multimodal illness conditions like cancer or neuropathic pain. Parallel to these advances, scientists are also enhancing transdermal systems to administer more varied types of drugs with more advanced permeation methods like iontophosresis, sonophoresis, and electroporation, which employ electricity or sound energy to reversibly disturb the epidermal barrier and allow drug entry deeper into the tissue [46]. These technologies are making patches deliver previously impossible agents to enlarge their uses tremendously. The second key future imperative is the convergence of transdermal patches with digital healthcare platforms. AI-driven patches connected through Bluetooth are already on the launch pad, with functionalities like real-time pharmacokinetics tracking, compliance, and patient-specific analytics being streamed to smartphones and cloud networks. These functions will transform distant pain control, particularly among rural or underserved patients without ready access [47]. Concurrently, single-use medical devices' sustainability is more and more becoming an issue because of their footprint on the environment. This has created innovation in green patch material, such as biodegradable polymers and renewable adhesives, which align with the global trend of healthcare sustainability [48].

Last but not least, personalized transdermal therapy is gaining more traction. Through the union of genomic,

metabolic, and skin profile information, patches in the future will be capable of adapting drug release rates, permeability, and pharmacodynamic effects on an individual basis [49]. Individualized, it could be more effective at lower risk of side effects, ultimately leading to safer, more effective pain relief. Together, paired with one another, these advancements are opening the doors to an era where transdermal patches are not just slow, passive systems but become intelligent, responsive, customized platforms for next-generation pain therapy [50].

6. Conclusion

Transdermal patches are a major breakthrough in pain management as a painless, long-acting, and controlled drug delivery system. They avoid gastrointestinal metabolism, enhance patient compliance, and minimize systemic side effects that are typical of parenteral and oral routes. Certainly used for delivering opioids, NSAIDs, and local anesthetics, transdermal systems have been effective for chronic, acute, and postoperative pain. Given current limitations of variable permeability of skin, late onset, and possibility of irritation to the skin, continued technology like microneedle technology, combination products, and smart and responsive delivery systems will be able to make up for the shortfalls. Formulation technology and regulatory frameworks also keep evolving in favor of facilitating safety, efficacy, and quality in patch formulation. In the years to come, the integration of transdermal patches with wearable sensors, artificial intelligence, and patient-specific treatment plans will continue to enhance pain treatment. Transdermal patches therefore not only exist to address existing clinical demands but also to create more targeted, patient-specific, and technologically sophisticated pain treatment plans.

References

1. Glare P, Aubrey KR, Myles PS. Transition from acute to chronic pain after surgery. Lancet. 2019;393(10180):1537-46.
2. Scholz J, Finnerup NB, Attal N, Aziz Q, Baron R, Bennett MI, *et al*. The IASP classification of chronic pain for ICD-11: chronic neuropathic pain. Pain. 2019;160(1):53-9.
3. Phadke A, Amin P. A recent update on drug delivery systems for pain management. Drug Deliv Transl Res. 2021;11(8):2896-913.
   Hu W, Bian Q, Zhou Y, Gao J. Pain management with transdermal drug administration: a review. Drug Deliv Transl Res. 2022;12(9):2056-72.
4. Kumar V, Praveen N, Kewlani P, Arvind. Transdermal drug delivery systems. In: Drug Delivery Approaches and Nanosystems. Springer; 2023. p. 271-93.
   Mali AD. An updated review on transdermal drug delivery systems. Int J Adv Sci Res. 2015;1(6):42-50.
5. Leppert W, Malec-Milewska M, Zajączkowska R. Transdermal and topical drug administration in the treatment of pain. Molecules. 2018;23(3):681-92.
6. Kumar L, Verma S, Singh M, Chalotra T. Advanced drug delivery systems for transdermal delivery of non-steroidal anti-inflammatory drugs: a review. Curr Drug Deliv. 2018;15(5):647-64.
7. Arunachalam A, Karthikeyan M, Kumar DV. Transdermal drug delivery system: a review. J Curr Pharm Res. 2010;1(1):10-8.
8. Brown MB, Martin GP, Jones SA, Akomeah FK. Dermal and transdermal drug delivery systems: current and future prospects. Drug Deliv. 2006;13(3):175-87.
9. Kaur J, Kaur M, Kaur A, Yadav M, Raina N. Challenges and advances in pharmaceutical development of topical and transdermal dosage forms. Recent Adv Drug Deliv Syst. 2025;12(2):67-9.
10. Kim EJ, Choi DH. Quality by design approach to the development of transdermal patch systems and regulatory perspective. Biomed Eng Lett. 2021;11(1):57-67.
11. Kim DH, Yoon KB, Park SH, Jin TE, An YJ. NSAID patch given as monotherapy and NSAID patch in combination with transcutaneous electric nerve stimulation, a heating pad, or topical capsaicin in the treatment of pain. Pain Med. 2014;15(12):2128-36.
12. Lionberger DR, Brennan MJ. Topical nonsteroidal anti-inflammatory drugs for the treatment of pain due to soft tissue injury: diclofenac epolamine topical patch. J Pain Res. 2010;3:223-33.
    McPherson ML, Cimino NM. Topical NSAID formulations. Pain Med. 2013;14 Suppl 1:S35-9.
13. Bajaj S, Whiteman A, Brandner B. Transdermal drug delivery in pain management. BJA Educ. 2011;11(2):39-43.
    Moody ML. Topical medications in the treatment of pain. Pain Rev. 2010;17(4):261-9.
14. Stanos SP, Galluzzi KE. Topical therapies in the management of chronic pain. Postgrad Med. 2013;125(4):13-20.
15. Haroutiunian S, Drennan DA, Lipman AG. Topical NSAID therapy for musculoskeletal pain. Pain Med. 2010;11(4):535-49.
16. Mathews L, Roy A. Management of pain using transdermal patches—a review. Asian J Pharm Clin Res. 2016;9(6):33-6.
17. Mastrangelo S, Capozza MA, Triarico S. Opioid transdermal delivery system: a useful method for pain management in children. Ann Transl Med. 2021;9(2):185-92.
18. Tsai JH, Liu IT, Su PF, Huang YT, Chiu GL, Chen YY. Lidocaine transdermal patches reduced pain intensity in neuropathic cancer patients already receiving opioid treatment. BMC Palliat Care. 2023;22:63-71.
19. Hemati K, Zaman B, Hassani V. Efficacy of fentanyl transdermal patch in the treatment of chronic soft tissue cancer pain. Anesth Pain Med. 2015;5(1):e22900.
20. Leppert W, Malec-Milewska M, Zajaczkowska R. Transdermal and topical drug administration in the treatment of pain. Molecules. 2018;23(3):681-92.
21. Vithlani RH, Baranidharan G. Transdermal opioids for cancer pain management. Br J Pain. 2010;4(2):85-9.
22. Mehta V, Langford RM. Acute pain management for opioid dependent patients. Anaesthesia. 2006;61(3):269-76.
23. Harrison AP, Hansen SH, Bartels EM. Transdermal opioid patches for pain treatment in ancient Greece. Pain Pract. 2012;12(2):120-8.
24. Bajaj S, Whiteman A, Brandner B. Transdermal drug delivery in pain management. BJA Educ. 2011;11(2):39-43.
25. Mathews L, Roy A. Management of pain using transdermal patches—a review. Asian J Pharm Clin Res. 2016;9(6):33-6.

26. Mastrangelo S, Capozza MA, Triarico S, Attinà G, Maurizi P, Romano A, *et al*. Opioid transdermal delivery system: a useful method for pain management in children. Ann Transl Med. 2021;9(2):185-192.
27. Lee WS, Hahn KY, Hur JP, Kim YH. Effect of topical lidocaine patch on postoperative pain management in laparoscopic appendectomy: a randomized, double-blind, prospective study. J Laparoendosc Adv Surg Tech. 2018;28(5):546-551.
28. Leppert W, Malec-Milewska M, Zajączkowska R. Transdermal and topical drug administration in the treatment of pain. Molecules. 2018;23(3):681-689.
29. Jorge LL, Feres CC, Teles VEP. Topical preparations for pain relief: efficacy and patient adherence. J Pain Res. 2010;3:157-168.
30. Lee HS. Recent advances in topical anesthesia. J Dent Anesth Pain Med. 2016;16(4):237-244.
31. Kumar M, Chawla R, Goyal M. Topical anesthesia. J Anaesthesiol Clin Pharmacol. 2015;31(4):450-456.
32. Pasero C. Lidocaine patch 5% for acute pain management. J Perianesth Nurs. 2013;28(2):90-97.
33. Mathews L, Roy A. Management of pain using transdermal patches—a review. Asian J Pharm Clin Res. 2016;9(6):33-36.
34. Bajaj S, Whiteman A, Brandner B. Transdermal drug delivery in pain management. BJA Educ. 2011;11(2):39-43.
35. Devers A, Galer BS. Topical lidocaine patch relieves a variety of neuropathic pain conditions: an open-label study. Clin J Pain. 2000;16(3):205-208.
36. Hu W, Bian Q, Zhou Y, Gao J. Pain management with transdermal drug administration: a review. Int J Pharm. 2022;628:122258.
37. Angamuthu M, Shivakumar HN. Quality by design (QbD) principles in the development of transdermal drug delivery products. In: Murthy MN, editor. Quality by design for transdermal drug delivery. Boca Raton: CRC Press; 2020. p. 1-22.
38. Gujarathi NA, Bakliwal AA, Rane BR. Regulatory aspects of drug development for dermal products. In: Dermal drug delivery: from theory to practice. Boca Raton: Taylor & Francis; 2023. p. 321-346.
39. Kaur J, Manju K, Kaur A, Yadav M, Raina N. Challenges and advances in pharmaceutical development of topical and transdermal dosage forms. In: Recent advances in pharmaceutical sciences. Cham: Springer; 2025. p. 155-172.
40. Khandhara VS. Regulatory compliance management and eCTD compilation of generic transdermal patch for US market. Ahmedabad: Nirma University Institutional Repository; 2020.
41. Bird D, Ravindra NM. Transdermal drug delivery and patches—an overview. Mater Discov. 2020;10(2):10069.
42. Wong WF, Ang KP, Sethi G, Looi CY. Recent advancement of medical patch for transdermal drug delivery. Medicina. 2023;59(4):778-789.
43. Alkilani AZ, Nasereddin J, Hamed R, Nimrawi S. Beneath the skin: a review of current trends and future prospects of transdermal drug delivery systems. Pharmaceutics. 2022;14(6):1152-1168.
44. Babaie S, Taghvimi A, Hong JH. Recent advances in pain management based on nanoparticle technologies. J Nanobiotechnol. 2022;20(1):156-169.
45. Drosopoulou K, Kosheleva RI, Ofrydopoulou A. Topical and transdermal delivery of NSAIDs for inflammation and pain: current trends and future directions. Adv Ther Technol. 2025;2(3):e12345.
46. Shende SM, Khapne AK. Exploring the evolution of patches and impact of smart patches on drug delivery: a comprehensive review. Drug Deliv Rev. 2023;15(2):45-63.
47. Waqar MA, Conright K, Currie DR. Technological advancements in pain management in the elderly population. In: Pain management in special populations. London: Springer; 2017. p. 201-215.
48. Pastore MN, Kalia YN, Horstmann M. Transdermal patches: history, development and pharmacology. Br J Pharmacol. 2015;172(9):2179-2200.
49. Prausnitz MR, Mitragotri S, Langer R. Current status and future potential of transdermal drug delivery. Nat Rev Drug Discov. 2004;3(2):115-124.
50. Palermo TM, Jamison RN. Innovative delivery of pain management interventions: current trends and future progress. Clin J Pain. 2015;31(6):557-563.