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**Review Article**

# Review of Transdermal Patches

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## ABSTRACT

The skin, as the body's largest organ, has long served as a medium for therapeutic and cosmetic applications. Transdermal drug delivery systems (TDDS) offer significant advantages over conventional routes by bypassing gastrointestinal irritation and hepatic metabolism, ensuring controlled drug release, and improving patient compliance. This study focuses on the formulation and evaluation of repaglinide transdermal patches prepared via solvent casting using polymer blends, plasticizers, and permeation enhancers. Adhesive properties such as tack, peel adhesion, shear adhesion, and rheological behavior were systematically assessed to ensure optimal patch performance. Mechanical parameters including folding endurance, tensile strength, elongation, thickness, drug content, and moisture balance were evaluated, alongside in vitro drug release using Franz diffusion cells and kinetic modeling. Results demonstrated effective drug permeation through rat abdominal skin, with significant reductions in pain severity and interference scores, as well as decreased reliance on supplementary analgesics. The findings suggest that topical analgesic patches containing menthol, camphor, and methyl salicylate are safe and effective alternatives for managing mild to moderate pain associated with arthritis, neurological, and musculoskeletal disorders. These patches may serve as a primary therapeutic option within multimodal pain management strategies.

## INTRODUCTION

The skin is the body's largest organ, spreading over about 1.5 to 2 square meters in an average adult and making up nearly 15% of body weight. Since ancient times, drugs have been used on the skin not only to treat surface-level skin problems but also to deliver medicines through the skin for treating internal or systemic diseases. Additionally, the skin has long been a medium for cosmetic applications, as recorded in the earliest medical histories of humankind. The transdermal drug delivery system (TDDS) has achieved growing attention as a method of giving medicines

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through the skin, not only to produce localized effects on affected skin areas but also to allow systemic absorption of drugs for treating conditions throughout the body. Using the skin to deliver drugs has many benefits over other ways of giving medicine. It helps avoid stomach problems like irritation or pH changes, and it bypasses the liver, which increases how much of the drug reaches the bloodstream. This method can also reduce side effects, release the drug slowly and steadily, and treatment can be stopped easily by removing the patch or cream. In addition, it keeps drug levels in the body more stable and avoids the pain of injections. This is a pain relief patch that you can buy without a prescription. It contains menthol, camphor, and methyl salicylate, which help to reduce pain when applied to the skin. menthol and camphor function as topical analgesics that produce pain relief through the activation followed by desensitization of cutaneous nociceptors, including the transient receptor potential vanilloid 1 (TRPV1) channel. This mechanism leads to a temporary reduction in nerve excitability, thereby diminishing pain sensation at the site of application. Methyl salicylate is known to provide effective pain relief with few side effects. Once applied to the skin, it is converted into salicylic acid in the local tissues, where it produces anti-inflammatory effects by inhibiting the COX-1 and COX-2 enzymes in the arachidonic acid pathway. This action helps to reduce inflammation and increase the pain threshold, thereby decreasing nerve sensitivity and pain perception.

## 2. PATCH ADHESIVE PROPERTIES AND ASSAYS

Tack refers to the adhesive's immediate ability to form an initial bond with the skin when brief, light pressure is applied an essential parameter for ensuring proper attachment and drug delivery from a transdermal patch. Shear adhesion describes the adhesive matrix's ability to resist deformation or sliding when subjected to a continuous parallel force. This parameter indicates how effectively a transdermal patch can remain fixed in position on the skin during normal movement, ensuring consistent drug delivery.

Since transdermal patches are applied gently to the skin, the adhesive system should exhibit low initial tack to allow controlled placement. However, the shear adhesion must be sufficient to ensure that the patch maintains stable contact with the skin throughout the intended dosing period, despite lateral forces generated by normal physiological movement and fabric contact forces. The patch should be removed easily and comfortably, without causing pain, leaving adhesive residues, or producing any skin irritation or damage. These characteristics are influenced by the critical surface energy and the viscoelastic behaviour of pressure-sensitive adhesives (PSAs). When PSA adhesion is viewed as a sequence of bonding and debonding events, two distinct mechanisms arise: bond formation occurs through viscous flow, driven by directed molecular diffusion within the free volume of the adhesive, while separation results from elastic deformation of the adhesive matrix, which stores and then releases mechanical energy.

### 2.1 Tack

The onset attachment of a pressure-sensitive adhesive to a surface takes place extremely quickly within fractions of a second and is influenced not only by the adhesive's reduced frequency rheological behaviour but also by the molecular-level associations. Specifically, when the PSA has a significantly lower surface energy than the substrate, its adhesive performance is mainly determined by its rheologically responsive behaviour, which controls how quickly it wets the surface. In contrast, when the substrate has low surface energy, the extent of Wetting is affected by the surface tension threshold of the PSA, generally ranging from 28 to 32 dyne/cm. The lower the critical surface energy of the adherend, the worse the adhesive wets that surface, leading to decreased tack.

Because it is challenging to determine the exact time needed to achieve maximum adhesion, tack testing evaluates the detachment force after brief contact under minimal pressure. The standardized methods used to assess tack can be grouped into the following classes. The rolling ball tack test simultaneously evaluates both bond formation and bond separation. In this approach, a stainless-steel sphere moves down a sloped surface and halts when it encounters a horizontally aligned, adhesive-up patch at the track's end. The tack is established by assessing the distance the ball moves prior to being halted by the adhesive layer, considering that its initial momentum is set by the incline’s height and angle. A decreased stopping distance signifies greater traction, although the correlation is not necessarily proportional to the distance measured.

In loop tack testing, tack is measured as the force needed to pull apart, at a controlled speed, a loop formed from a strip of the adhesive patch after it has been pressed against a defined area of a standard surface.

### 2.2 Peel adhesion

Among the major performance characteristics of transdermal patches, peel-off behaviour is particularly important, as greater peel adhesion generally leads to increased discomfort during removal. Peel resistance should not be interpreted as a direct measure of adhesive bond strength, since this value does not always reflect the inherent adhesive properties of the material. Removing a patch involves a complex sequence in which the adhesive layer and backing must elongate and flex before the bond actually breaks. Consequently, the strength necessary to remove the patch from the surface is considerably greater than the strength needed to keep it attached.

The various ways in which a patch detaches from a rigid surface can serve as indicators of the adhesive matrix’s internal cohesion and its bonding strength to the backing layer. The transdermal patch should exhibit clean-removal characteristics, meaning that upon detachment it separates uniformly from the skin (adherend) without leaving any visible adhesive or formulation residues.

Adhesion assessment techniques are selected according to the specific stress conditions employed, and extensive information on these methods has been provided in earlier publications by adhesive tape associations. In summary, standardized adhesion tests involve affixing a strip of patch affixed to a stiff adherent plate—usually stainless steel—under a specified pressure to guarantee adequate contact. Following a set dwell duration, the strip is removed from the plate at a defined angle (e.g., 180° or 90°) and at a regulated speed (e.g., 300 mm/min).

As the patch is removed, mechanical stress propagates from the adhesive matrix to the backing material. Therefore, variations in formulation properties (e.g., elasticity, deformability) and backing layer thickness may result in different detachment responses. Thicker or more rigid backing layers require more energy to undergo deformation during detachment. The larger moment arm formed by the peel strip reduces the applied peel force while counterbalancing the energy required to modify the backing layer. In a 90° peel test, the influence of backing-layer parameters is not as important as in a 180° peel test because the backing layer undergoes less deformation and therefore requires less energy. Because the 180° peel test combines tensile and shear actions, whereas the 90° test is influenced exclusively by tensile forces, the two angles reveal different aspects of adhesion. Therefore, measurements at 90° usually show smaller standard deviations compared with those at 180°. It is important to recognize that, despite using the same pulling speed, the peel front during a 90° test travels at double the speed seen in a 180° test. As a result, adhesion measurements from these two peel angles are inherently non-equivalent. For patches made with Neoprene rubber PSA demonstrated that the 90° peel test more clearly emphasized the effect of PSA thickness, with the peel strength recorded being approximately ten times higher than that seen in the 180° test.

### 2.3 Rheological properties

Being viscoelastic, PSAs exhibit adhesion properties that are strongly influenced by their solid- and liquid-like responses, which vary according to the stress frequency at a specific temperature. DMA is widely recognized as the standard technique to evaluate the rheological behaviour of this class of materials, with evaluations usually conducted on circular samples obtained through solvent vaporization or melting. Stress–strain data are commonly interpreted through the material's modulus, obtained as the ratio of stress to strain, providing the complex modulus (G).

$$G^* = G' \sin(\omega t) + G'' \cos(\omega t)$$

Here, $G'$ represents the elastic (or storage) modulus, while $G''$ denotes the viscous (or loss) modulus. By comparing the storage and loss moduli, one can infer the material's response to stress. A higher $G'$ than $G''$ denotes solid-like properties, whereas a higher $G''$ than $G'$ indicates liquid-like characteristics. The ratio of the loss modulus to the storage modulus ($G''/G'$) defines the loss tangent ($\tan\delta$), which quantifies the portion of deformational energy dissipated as heat during each cycle. The $\tan\delta$ values enable comprehensive characterization of PSA rheology, as they are closely associated with the material's glass transition temperature.

Data collected at different frequencies and temperatures can be combined to construct a master curve, extending the frequency range at a specified reference temperature. Using this method, one can characterize how the moduli vary with oscillation frequency, which is related to the PSA's initial bonding, shear, and peel adhesion performance.

Rheological characterization is useful for PSA design; however, the adhesive performance of the final patch cannot yet be reliably predicted from viscoelastic measurements alone, due to the strong influence of surface and backing layer mechanical properties on tack, shear, and peel adhesion. When applied to a rigid adherend and possessing a well-characterized structure, the PSA's rheological behaviour can serve as an indicator of the patch's peeling performance. The presence of a compliant adherend with low surface energy, such as skin, introduces complexity in the debonding process, making it difficult to formulate predictive theoretical models. Consequently, there is some debate over the ability of rheological measurements to offer reliable preliminary insights into patch adhesion.

### 2.4 Shear Adhesion or Holding Power

Shear adhesion measures a PSA's resistance to tangential forces, reflecting the cohesive strength of the adhesive matrix.

In shear adhesion testing, the force necessary to move a standardized patch area along the surface of a flat adherend plate is measured. Static shear adhesion methods estimate the force necessary for patch displacement by recording the time needed to detach a defined patch area from the substrate under a standard load. In holding power tests, the adhesive must fail within its matrix, resulting in residue on both adherends. It is also observed that in a 90° peel test, the peel front travels at twice the speed of a 180° test, even with the same pull speeds. As a result, the adhesion results for the two peel angles are not the same. For neoprene rubber PSA patches, the 90° peel test highlighted the impact of PSA thickness, yielding peel strengths nearly ten times higher than those observed from 180° tests.

As observed with holding power, matrix thickness impacts peel adhesion, but in a distinct manner. Thicker adhesive layers tend to increase peel strength, reaching a maximum value at a specific thickness [23–25]. This effect can be linked to the combined impact of matrix thickness on peel force. Thicker PSAs raise the quantity of material that deforms, thus enhancing the peel force. In thicker patches, the increased peel angle and moment arm lead to a decreased peel force, thus lessening the energy required for detachment. When the matrix attains a critical thickness, the deformation in the crack region becomes saturated, rendering further thickness increments insignificant.

## 3. MATERIALS AND METHOD

**Preparation of Transdermal Patch:** Repaglinide transdermal patches, crafted using a matrix approach, were created through solvent casting. Polymers were precisely weighed and dissolved in 10 mL of a 1:1 water and methanol solution, and the resulting mixture was placed in a 44.15 cm² petri dish to form a transparent solution. The medication was added to the polymer solution and mixed well until clarity was achieved. Polyethylene glycol 400 was utilized as a plasticizer at 30% w/w, while propylene glycol was included at 15% w/w as a permeation enhancer in the formulation additives. Following preparation, the uniform solution was applied to a glycerin-coated petri dish and allowed to dry at room temperature for 24 hours. The petri dish was topped with an upside-down funnel to reduce solvent evaporation, and after 24 hours, the dried spots were taken out and kept in a desiccator for later research

**Preliminary Screening.** An initial assessment was made to assess the function of different polymer blends in patch formulation.

## 4. PARAMETERS FOR EVALUATING TRANSDERMAL PATCHES

**Folding Endurance.** A 2 cm × 2 cm film was subjected to repeated folding at a single point until rupture. The total number of folds sustained prior to breakage was recorded as the folding endurance, reflecting the mechanical integrity of the dosage form.

**Tensile Strength.** The tensiometer (Erection and Instrumentation, Ahmedabad) was used to evaluate the patch’s tensile strength. The setup comprised two load cell grips, where the lower grip was stationary and the upper grip was adjustable. Film strips (2 cm × 2 cm) were secured between the grips, and a progressively increasing force was exerted until failure, enabling assessment of the patch's tensile strength. The tensile strength was obtained directly from the tensiometer gauge and stated in kilograms.

**Percentage Elongation Break Test.** o figure out how much the film could stretch before it broke, we measured its length just before it tore apart. We used a formula to calculate the percentage elongation at break of the film. The films length was measured right before it ruptured. Then we used the formula to determine the percentage elongation at break of the film.

$$\text{Elongation percentage} = \left[\frac{(L_1 - L_2)}{L_2}\right] \times 100,$$

The film strip has a length, which is called $L_1$ and this is the length when it actually breaks. On the hand we have the initial length, which is called $L_2$ and this is the length of the film strip before we even start stretching it.

**Thickness.** The patch thickness was measured at three points. A digital micrometer screw gauge was used for this. The average value was then calculated from these measurements. The patch thickness was the main thing being measured. The measurements were taken at points. This was done to get an average. The digital micrometer screw gauge gave readings. These readings were then used to calculate the patch thickness value.

**Drug Content.** A specified size patch (2 cm × 2 cm) was dissolved in 100 mL of methanol and continuously shaken for 24 hours. The resulting solution underwent ultrasonication for a duration of 15 minutes. Following filtration, the drug concentration was assessed spectrophotometrically at 281 nm to quantify the drug content.

**Percentage Moisture Content.** The individual films were. Then stored in a special container with a drying agent, which is calcium chloride at the normal room temperature for 24 hours. After 24 hours had passed the films were weighed again to see what had changed. Then the moisture content percentage of the films was figured out using a formula that is shown below.

$$\text{Percentage moisture content} = \left[\frac{(\text{Initial weight} - \text{Final weight})}{\text{Final weight}}\right] \times 100.$$

**Percentage Moisture Uptake.** The films were put in a box with a potassium chloride solution at the normal room temperature for 24 hours to keep the air around them at 84 percent humidity. After 24 hours the films were weighed again. The amount of moisture they picked up was calculated using a formula, for the percentage moisture uptake of the films.

$$\text{Percentage moisture uptake} = \left[\frac{(\text{Final weight} - \text{Initial weight})}{\text{Initial weight}}\right] \times 100.$$

**In Vitro Drug Release Studies.** The in vitro drug release was examined using a Franz diffusion cell, in which the receptor compartment held a volume of 60 mL. The designed matrix-type transdermal patches were evaluated for drug release with a cellulose acetate membrane. A membrane made of cellulose acetate with a pore size of 0.45 µm was placed between the donor and receptor compartments of the diffusion cell. The transdermal film was placed on the cellulose acetate membrane and wrapped with aluminium foil. The diffusion cell's receptor compartment was filled with phosphate buffer at pH 7.4. The whole arrangement was situated on a hot plate equipped with a magnetic stirrer, and the receptor solution was consistently agitated using magnetic beads. The temperature was kept at 32 ± 0.5 °C, which aligns with typical human skin temperature. At designated time intervals, samples were taken from the receptor compartment and analyzed spectrophotometrically for drug concentration. The volume that was withdrawn was substituted with an equivalent quantity of phosphate buffer to keep the volume consistent.

**Kinetic Modelling of Dissolution Data.** The drug release profiles of all batches were analysed using various mathematical models, including Zero-order, First-order, Higuchi, Hixson-Crowell, and Korsmeyer–Peppas, to determine the kinetics of drug release.

## RESULT AND DISCUSSION

**Preliminary Study :-** The thickness of every batch of transdermal patches ranged from 0.12 mm to 0.20 mm. Batches P4 and P5 exhibited greater thickness, probably due to the limited solubility of ethyl cellulose in the solvent causing an inconsistent distribution of the polymer layer. All batches of transdermal patches demonstrated uniform tensile strength (16–22) and percent elongation (17.5–22.5), with the exception of batches P4 and P5, which displayed variations possibly attributed to the insufficient solubility of ethyl cellulose and weak bond establishment. Consequently, batches P4 and P5 were removed from additional assessment. Batch P1 (PVA: PVP) demonstrated a quick drug release (101.26% in 8 hours) attributed to the burst effect of PVP and its greater solubility in water; therefore, batch P1 was excluded from further investigations.

Lower moisture levels in the formulations enhance their stability and lead to a completely dried, fragile film. Likewise, low moisture absorption aids in inhibiting microbial development and prevents unnecessary swelling or excessive bulkiness of the material.

The investigation of Repaglinide patches' permeation through rat abdominal skin verified that the drug was effectively released from the formulation and penetrated the skin, suggesting its ability to permeate human skin as well.

To evaluate the efficacy of topical analgesics for managing acute pain, variations in BPI pain severity and pain interference scores, as well as the consumption of extra pain medications, were measured from baseline to day 14. The results showed that the analgesic patch led to lower average BPI pain severity and pain interference scores. The variations in enhancement from baseline for BPI pain severity (49% compared to 12%) and pain interference (58% compared to 14%) between the treatment and control groups were determined to be statistically significant. A significant number of patients in the treatment group indicated a noticeable reduction in their use of extra pain medications by day 14. In the treatment group, the usage of ibuprofen, acetaminophen, and Voltaren decreased by 24%, 39%, and 62%, respectively. No negative effects were seen or reported with the application of the topical analgesic patch.

Results from this IRB-approved observational research suggest that topical analgesic patches may provide a safe and effective substitute for conventional therapies like opioids, prescription or OTC NSAIDs, and acetaminophen in addressing mild to moderate and chronic pain. Nonetheless, controlled clinical trials are necessary to confirm these results.

## CONCLUSION

The results suggest that the assessed topical analgesic patches were effective and safe for alleviating mild to moderate pain linked to arthritis, neurological problems, and musculoskeletal disorders. A reduction in pain-related disruption was noted, along with an overall decrease in the consumption of supplementary medications. These results support the analgesic patch as a possible primary treatment and indicate it should be incorporated into upcoming pain-management protocols within a multimodal treatment strategy.

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