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Review Article

A Review on the Development of Transdermal Patches with Natural Polymers

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Abstract

Transdermal drug delivery system, also known as transdermal patches, represent an advanced pharmaceutical approach designed to deliver therapeutic agents across the skin surface and enters into systemic circulation. These systems overcome several limitations associated with conventional oral and parenteral dosage forms, such as hepatic first-pass metabolism, gastrointestinal degradation, poor patient compliance, and frequent dosing. In recent decades, transdermal patches have gained popularity due to their non-invasive nature, controlled and sustained release capabilities, and enhanced safety profiles. A typical transdermal patch consists of a drug-loaded matrix or reservoir, an adhesive layer for skin application, a backing membrane to prevent drug loss, and a rate controlling membrane in some formulations. Upon application, the drug permeates through the stratum corneum—the primary barrier of the skin—followed by diffusion into deeper epidermal and dermal layers before entering the systemic circulation. Various permeation enhancement techniques, including chemical enhancers, microneedles, iontophoresis, and microemulsions, are employed to improve drug penetration, particularly for molecules with poor skin permeability. Transdermal patches provide several clinical advantages, including maintenance of steady plasma drug concentrations, reduction in adverse effects, improved therapeutic efficacy, and enhanced patient adherence, especially for chronic therapy. Drugs with low molecular weight, adequate lipophilicity, and potency are considered ideal candidates for transdermal delivery. Currently approved patches include formulations of nicotine, fentanyl, clonidine, nitroglycerin, and hormonal therapies. Continuous research focuses on expanding the range of drugs suitable for transdermal administration through advanced materials, nanotechnology-based carriers, and physical enhancement approaches. Despite these advantages, TDDS also present challenges such as limited drug permeability across intact skin, potential for skin irritation, variability in absorption based on physiological and environmental factors, and complexity of manufacturing processes. Regulatory considerations and quality control parameters require careful evaluation of drug release kinetics, adhesive properties, safety and stability.

Keywords: Transdermal Patch; Polymer Matrix; Adhesives; Permeation Enhancers; Backing Membrane

Introduction

The oral route of administration is most common route of drug administration, because it is convenient and easy for patients. However, this route has several limitations, such as first pass metabolism and the degradation of drugs in the gastrointestinal tract due to enzymes, acidic pH, and other physiological factors. To overcome these drawbacks, scientists developed a Transdermal drug delivery system, which is considered a novel and effective

method of drug administration. Research and development in this field where significantly contributed to by scientists such as Banker (1990), Chien (1992), and Guy (1996). A Transdermal drug delivery system mainly contains drug induced adhesive patches that are applied directly to the skin. These patches are designed for controlled and therapeutic effective amount of drug through the skin into the bloodstream. Transdermal patches are manufactured in different sizes and may along with other supporting components. When the patch is placed on healthy and unbroken skin, the drug is gradually released and passes through the layers of the skin before reaching the systematic circulation. These patches usually contain a sufficient amount of drug to maintain drug release for a long duration, often for several hours or even days. The drug enters the bloodstream mainly through a diffusion process, allowing for controlled and sustained drug delivery [1].

Drugs can penetrate the skin through three main pathways-

- Hair follicle
- Sebaceous glands
- Sweat ducts

Advantages

- Constant Plasma Levels: Provides sustained, controlled drug release, avoiding the drawbacks associated with oral route of administration [4].
- Transdermal patches improves compliance: simplified dosage regimens (e.g., once -a-day or weekly) increase patient compliance.
- Avoid First pass drug metabolism: Bypasses GI and hepatic metabolism, which increases bioavailability and reduces digestive side effects.
- Non -Invasive: Easy to apply and remove, providing an alternative to needles.
- Immediate Termination: Medication can be stopped instantly by removing the patch.

Disadvantages

- Transdermal patches causes skin Irritation, Adhesive or the medication itself can cause allergic reactions, contact dermatitis, or irritation [4].
- **Limited Drug suitability:** Only low -dose, highly potent, and lipid-soluble drugs can be delivered efficiently through the skin barrier [5].
- **Variable Absorption:** Skin permiability varies depending on age, application site, and skin condition.
- Drug having hydrophilic character is less suitable as compare to drug with lipophyllic character because of their low permeability.
- **Slow Onset:** Not suitable for conditions requiring rapid therapeutic effects.

Properties of chitosan

- **Biological Activity**: It acts as an antibacterial, antifungal, antitumor, and anti -inflammatory agent, making it ideal for wound healing, drug delivery, and food preservation.
- **Chemical characteristics:** Chitosan has a high content of amino (-NH2) and hydroxyl (-OH) groups, which are highly reactive, allowing for chemical modification and crosslinking. It is generally insoluble at neutral or basic PH but dissolves in acidic media.
- **Physical Forms:** It can be processed into various physical forms, including membranes, gels, fibers, sponges, and nanoparticles [3].

Physiology of skin

Transdermal patches work by delivering drug content through the skin layers, primarily the outermost skin layer stratum corneum, which acts as the main barrier, using passive diffusion or enhanced permeation. Drugs move through the skin via intercellular lipid pathways, transcellular routes or appendageal routes, eventually reaching the dermis and entering blood capillaries for systemic distribution, bypassing digestion and first-pass metabolism. The skin's natural properties, like it's lipid-rich barrier and slightly acidic pH, limit drug entry, making effective drugs typically small, lipophilic molecules [1].

Key skin layer and their roles

- **Stratum corneum:** The primary barrier, rate limiting barrier for drug penetration. This layer composed of Corneocytes which are flattened and anucleated [2]
- **Epidermis:** It contains living keratinocytes and langerhans cells providing further barrier function [2].

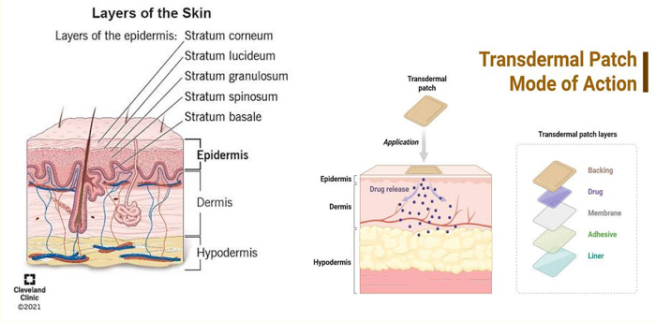

Figure 1

- **DERMIS:** It contains blood vessels (capillaries) where the drug enters the blood stream for distribution [2].

Drug penetration pathways

- **Intracellular:** Through the lipid matrix between skin cells.
- **Transcellular:** Directly through skin cells
- **Appendageal:** Via sweat ducts and hair follicles.

Mechanism

- The patch holds the drug, which moves out into the skin layers by diffusion, driven by the concentration gradient.
- Lipophilic (fat -soluble) drugs easily pass the stratum corneum; hydrophilic Once use polar routes.
- Once the dermis, drugs reach the capillaries and enter systemic circulation, avoiding the liver's first - pass metabolism.

Factors influencing efficacy:

- **Drug Properties:** Size and Lipophilicity.
- **Skin Factors:** Age, Condition, Skin Type and Location.
- **Patch Design:** Release Rate, Adhesive and Penetration Enhancers.

Transdermal patches basic components:

Transdermal patch is a drug induced adhesive patchwith several basic components designed to deliver a specific amount of drug through the skin followed by systemic circulation. in a controlled manner [4,5].

- **Backing layer**: It is the outermost layer of the transdermal patch.it provides structural support, makes the patch visible for compliance monitoring, and protects the medication and adhesive from the outside environment and water [10].
- **Drug containing reservoir/matrix**: This layer holds the active pharmaceutical ingredient (API), it is either in solution, suspension, gel form or dispersed in a polymer matrix.
- **Adhesive layer**: The adhesive layer has two main functions: it adheres the various layers of the patch together, and it ensures the patch stays securely on the skin to allow for drug transfer. In some designs, this layer itself contains the drug.
- **Release linear**: This is protective layer that covers the adhesive and drug reservoir during storage. It is removed by the user immediately before the application of patch [10].
- **Rate-controlling membrane**: Found the reservoir and some multi -layer patches, this semi - permeable membrane controls the rate at which the drug is released from the reservoir into the skin, ensuring a consistent dose over time.
- **Permeation enhancers** (excipients): These chemical substances (e.g. alcohol, propylene glycol, oleic acid) are often included the formulation to temporarily increase the skin permeability, allowing the drug through more easily.
- **Other excipients**: Plastisizer (e.g.: glycerin, polyethylene glycol) is added to the polymer matrix to provide flexibility and prevent the patch from becoming brittle. solvents are used during the manufacturing process.
- **Mechanism of action of Chitosan:** Chitosan is a product of natural polysaccharide chitin, and it has multiple physiological functions such as enhancing immunity, reducing blood fat, inhibiting bacterial growth and resisting cancer [3].
    - Chitosan contains acetamido, amino and OH groups in the molecule.
    - Chitosan is a product of N- deacetylation of chitin, it is Polycationic in nature. It interacts with negative charge on the protein to form protein encapsulation.

- Chitosan also has chelating property, its derivatives can chelate heavy metal ions and are metal ion trapping agents.
- Chitosan can be modified, coupled and activated for providing biological applications

- **Bioadhesion:** Due to its cationic nature, chitosan adheres to the negatively charged mucosal membranes or skin, increasing the contact time between the patch and the skin.
- **Penetration Enhancement:** Chitosan has penetration enhancing property through opening tight junctions. It acts on the tight junctions of the granular layer, promoting drug transport.
- **Modifying skin structure:** It alters the structure of stratum corneum proteins and affects intercellular lipids, reducing barrier resistance.
- **Increasing hydration:** It enhances the water content of the stratum corneum, promoting diffusion.
- **Controlled Drug Release:** The polymeric matrix of chitosan (often used with polymers like HPMC) regulates the diffusion of the drug, enabling sustained release over time.
- **Drug Delivery Formats:** Chitosan is used in various patch types, including:
- **Films:** For topical or Transdermal delivery, providing good adhesion.
- **Microneedles:** Used for the transdermal delivery of larger molecules or vaccines, sometimes in a core/shell structure for rapid or long-term release.

Changing the stratum corneum protein structure

Primarily keratin is a key mechanism in transdermal patch technology to enhance drug delivery. The stratum corneum of skin described as a bricks and mortar structure consists of keratin filled corneocytes surrounded by lipid bilayers. Transdermal systems use both chemical and physical methods to temporarily alter these proteins, increasing skin permeability for drugs that would otherwise not pass through [3].

Methods for modifying stratum corneum protein structure:

- **Chemical Penetration Enhancers:** These agents, such as dimethyl sulphoxide, urea, and various surfactants, act by interacting with the keratin filaments inside the corneocytes.
- **Confirmational Changes:** Chemical Penetration Enhancers cause confirmational changes in the protein structure, reducing the binding forces between protein molecules, which increases the intracellular diffusion coefficient.
- **Solvent Swelling:** Certain agents cause the keratin to swell, increasing content of water in stratum corneum, which further reduces the barrier resistance.
- **Solubilization:** Specific enhancers can solubilize, the skin components, facilitating the movements of molecules.
- **Physical Enhancement Methods:** Electroporation: Application of high voltage (60-1000V) pulses causes temporary reorganization of the stratum corneum structure and creates aqueous pathways.
- **Thermal Ablation/Radio frequency:** These techniques heat the stratum corneum surface to 100°C several hundred degrees Celsius for milliseconds, creating micro craters or micropores (10-50). These causes rapid dehydration and localized degradation of keratin, allowing for the passage of larger molecules like insulin.
- **Microneedles:** These pierce the stratum corneum, directly creating pathways through the corneocytes, bypassing the traditional tortuous diffusion route.

Tight junction acting in granular layer

These are in the stratum granulosum of the epidermis act as a crucial secondary. “inside out” barrier that restricts the paracellular passage of water, ions, and small molecules. While the top most layer, Stratum corneum acts as the primary barrier, the tight junctions in the immediately underlying granular layer provide an additional, dynamic barrier that regulates skin hydration and acts as a gateway for transdermal drug delivery [3].

- **Permeability Barrier:** The tight junctions, specifically the claudin proteins form a barrier that limits the penetration of hydrophilic drugs.
- **Target for Enhancers:** Many modern transdermal delivery systems aim to temporarily modulate or “open” these junctions to increase the delivery of large molecules or hydrophilic drugs.

Modulation mechanisms

- **Chitosan and Derivatives:** These can cause reversible redistribution of claudin proteins, loosening the junction and allowing improved penetration of large, hydrophilic drugs.
- **Peptide Modulators:** Short peptides are used to open tight junctions by inducing phosphorylation of the protein.
- **Microneedles:** These devices mechanically breach both the layers, providing a direct pathway for drug transport.
- **Chemical Enhancers:** Agents such as sodium caprate can reduce the electrical resistance of the tissue, indicating a loosening of the tight junctions barrier.

Interaction with intercellular lipids

The lipid contents included in skin are, cholesterol, ceramides and free fatty acids. Lipid-based nanocarriers, of skin incorporated into patches, are particularly effective because of their similarity to endogenous skin lipids, facilitating a high degree of biocompatability and interaction. These vesicles interact with skin lipids, increasing drug partition and merging with epidermal layers to deliver drugs into deeper tissues [3].

- **Ethosomes:** Containing high concentrations of ethanol (20-50%w/w), these carriers fluidize the intracellular lipids and increase the deformability of the vesicles for deeper penetration.
- **Transferosomes:** These are ultra-flexible vesicles designed to squeeze through the narrow intercellular gaps by using edge activators to alter their shape.
- **Lipid Solid Nanoparticles and Nanostructured Lipid Carriers**: These interact with the skin by creating an occlusive moisturizing film that improves the penetration of encapsulated drugs.

Increasing the stratum corneum water content

Increasing the content of water on stratum corneum is primary method for enhancing the efficacy of transdermal patches.

Hydration swells the stratum corneum, increases the permeability of both hydrophilic and lipophilic compounds, and disrupts the orderly lipid structure [3].

Occlusive patch design (Physical Hydration)

- **Occlusion Mechanism:** Using impermeable or low permeability backing materials prevents the evaporation of wate from the skin, causing moisture to accumulate.
- **Result:** This process can boost stratum corneum hydration from a normal 15-20% upto 50% or more, with effects lasting throughout the 24hour application period.
- **Patch Type Comparison:** Film-backed patches show significantly higher hydration levels compared to breathable, woven polyester patches.

Chemical Enhancers and Formulation Factors Humectants and Glycols: Propylene glycol is frequently used as a co-solvent that accumulates in the hydrophilic regions of lipid layers, promoting hydration and altering drug solubility.

- **Lipid- Based Nano-Formulations:** Vesicles such as liposomes, ethosomes, and niosomes can interact with the stratum corneum, delivering water directly to the skin surface and increasing hydration.
- **Alcohols and Terpenes:** While often acting as solvent carriers, ethanol and certain terpenes can distrupt the lipid arrangement, promoting water uptake in the intercellular spaces.
- **Water-Saturated Matrices:** Directly incorporating water into hydrogel- based patches ensures high moisture delivery, which is especially effective for hydrophilic drug compounds.

Techniques for Active Hydration Iontophoresis: This technique used low - voltage electrical current to drive charged molecules and electro- osmotic water flow into the skin.

- **Microneedles:** These create microchannels that bypass the main skin barrier, allowing for direct hydration of deeper tissue layers.

Techniques involved in transdermal patches drug delivery system

- **Polymer Membrane Permeation Controlled TDDS**: Polymer membrane permeation controller system are reservoir type patches. The drug reservoir is sandwiched between a drug impermeable metallic plastic layer and a rate controlling polymeric membrane involve in release of drug molecules.

This membrane can be microporous and nonporous polymeric membrane. A thin layer of drug is present on the outer surface of polymeric membrane [6,7].

- **Polymer Matrix Diffusion Controlled TDDS**: Polymer matrix diffusion controlled drug delivery system technique includes mixing of drug with rate controlling polymer. This matrix is called as matrix system. The polymers used in the matrix controlled the rate of drug. It is also as Monolithic system this technique involves dispersion of drug and Non-biodegradable polymer matrix, which controls the release rate, pressure -sensitive adhesives such as Silicone polyacrylates and Polyisobutylene [6,7].
- **Drug reservoir Gradient Controlled TDDS:** Drug reservoir gradient controlled Transdermal drug delivery system forms advanced patches they are designed to provide constant, zero-order drug release by varying the drug gradient with the reservoir along with the diffusion patch. This patches Overcome the declining release rate of traditional matrix by providing high drug concentration, the skin distal layer and lower concentrations near the skin. This technique involving increasing concentration gradient which compensate for the increase in diffusion distance over time. The deposition system of nitroglycerin is a primary example [6,7].
- **Micro-Reservoir Dissolution Controlled TDDS:** Micro Reservoir dissolution controlled TDDS is considered as hybrid of both the reservoir and matrix dispersion delivery system. These are advanced patches that combine reservoir and matrix characteristics. The preparation of micro Reservoir type controlled patches preparation includes creating a "micro Reservoir" system by forming dispersing drug loaded microscopic sphere within a pressure sensitive adhesive polymer. It includes suspending the solid drug form in the aqueous solution of water miscible drug solubilizer followed by homogeneous dispersion of drug suspension with controlled aqueous solubility in lipophyllic polymer. Unlike traditional reservoir patches, micro Reservoir patches ruptured and only a small portion of the drug leaks which prevents sudden drug dispensing [6,7].

Preparation of transdermal patches

- Asymmetric TPX membrane method
- Mercury Substrate Method
- Circular Teflon Mould Method
- Glass Substrate Method
- IPM membrane method
- Proliposomes Formation method
- Free Film Formation method

Asymmetric TPX membrane method

The asymmetric TPX membrane method is a technique for fabricating reservoir type transdermal patches, which is designed for the controlled drug release. This method includes the drug loaded reservoir, which is in gel or solution form further converted by an asymmetric membrane of poly(4-methy-1-pentene). The preparation of transdermal patch through this technique involves, presence of concave membrane covered with TPX asymmetric membrane here the drug is dispersed and sealed by an adhesive. Prepartion involves either dry or wet inversion process, Polymer is dissolved in both solvent and nonsolvent additives at 60 degrees to form a polymer solution. Polymer solution is kept at 40 degrees for 24hrs and cast on the glass plate. At 50 degrees for 30sec the casting film is evaporated followed by immersion in coagulation bath for 10minutes then the membrane is removed followed by air dry [9].

Mercury substrate method

The mercury substrate method is a solvent casting technique used to prepare matrix type transdermal patches by spreading a polymer drug plasticizer solution onto a liquid mercury surface, and placing a inverted funnel for solvent evaporation [8,9].

Circular teflon mould method

Circular Teflon mould method is used for the preparation of the uniform transdermal patches by film casting technique. This technique mainly includes circular mould made of polytetrafluoroethylene (PTFE). In 1989 Baker and Heller discovered this technique. The polymeric solution in various different concentrations are used as solvent for dissolving the contents. The organic solution is divided into two equal halves dissolving different contents followed by mixing both the solutions and addition of the other excipients, the formed solution is continuously mixed until the uniform mixture is obtained. The total content is poured into a circular Teflon mould by placing inverted funnel on top. Followed by storing in the desiccator [8].

IPM membranes method

Isopropyl Myristate method for transdermal patches involves formation of drug loaded viscous gel using Carbomer 940, propylene glycol and water which is then incorporated into a rate controlling IPM membrane. In a mixture of water, propylene glycol and Carbomer 940 the drug is dispersed followed by continuous 12 hours. Followed by neutralizing the mixture by adding Triethanolamine, incorporating the solution gel into a IPM membrane [8,9].

Proliposomes formation method

These are the novel, advanced, and carrier mediated method for preparation of the transdermal formulations. Proliposomes prepared by using carrier method through film deposition technique, Preparation of transdermal patches using proliposomes includes 2 step process, where the first step involves in the formation of the free flowing dry proliposomes, proliposomes are drug loaded lipid carriers using solvent evaporation or carrier method. Followed by incorporating the proliposomes into a polymer matrix to form a transdermal patch, the technique involved is solvent casting. Carrier preparation includes placing in a RBF by maintaining temperature at 60°-70° and rotate with 80-90rpm, while drying under the vaccum for 30 minutes. Followed by lipid and the drug are dissolved in organic solvent mixture, Using aliquots the drug lipid solution is heated. Addition of other excipients and formation of transdermal patch by pouring the mixture on the mercury surface or Teflon mould [8].

Film forming method

Film Forming method of transdermal patch preparation includes solvent casting technique, This technique includes dissolving polymer, drug and plasticizer in a solvent and pouring in glass ring, That is placed on the mercury surface in a glass petridish and allowing the solvent to evaporate by placing a inverted funnel on top of it. The dry film gets separated after the complete solvent evaporation.

Evaluation of transdermal patches

Physicochemical evaluation

Thickness of the patch

Transdermal patches typically have a thickness within the range of 0.1 mm to 1.2mm (often averaging around), ensuring they are thin enough for comfort while maintaining structural integrity and drug delivery efficiency. Patch thickness directly impacts drug loading, release rates, and user comfort, with higher polymer content generally increasing the thickness [8].

Weight uniformity

Weight uniformity in transdermal patches is a critical quality control parameter ensuring consistent drug dosage, thickness, and therapeutic efficacy, typically verified by weighing multiple patches or similar samples on a weighing balance to calculate the average weight and standard deviation. Low standard deviation indicates high-quality, reproducible, and uniform matrix formulation [7,8].

Folding endurance

Folding endurance in transdermal patches measures flexibility and structural integrity by counting the number of times a patch can be folded at the same location without cracking. A higher value (>200) indicates good flexibility, allowing the patch to withstand skin movement without breaking, typically measured by repeated manual folding [7].

Percentage moisture content

Percentage moisture uptake in transdermal patches typically ranges from 2%, depending on the polymers used (e.g., PVA, HPMC, Eudragit) and hydrophilic components. Low moisture uptake is preferred to ensure stability, prevent brittleness, and avoid microbial growth, with values often optimized around 5-15% for optimal adhesion and drug realese [11].

Percentage moisture uptake

The ideal moisture content in transdermal patches is generally kept low, typically ranging from 2% to 10% w/w. Maintaining this range is critical, as excessive moisture leads to microbial growth and patch deterioration, while extremely low levels result in brittle, high-risk patches [11,12].

Water vapour permeability evaluation

Water vapour permeability (WVP) in transdermal patches is crucial for stability and adhesive performance, typically evaluated using the “cup test” (ASTM standards) or specialized, modified TEWL (trans epidermal water loss) sensors. The test measures the rate at which moisture passes through the patch into a controlled environment (often 63 - 84% relative humidity), affecting how the patch behaves on skin [11].

Formula: WVP=W/A

Drug content [7]

Transdermal patches are pharmaceutical systems delivering drugs through the layers of skin into the Systemic Circulation at a controlled rate, with API loads ranging from under 1 mg to over 80 mg depending on the drug and application duration. Common examples include 7-21 mg of nicotine, 0.288-2.4 mg/day of fentanyl, and 0.025-0.1 mg/day of estradiol. They ensure sustained, uniform release for up to 7 days, avoiding hepatic first -pass metabolism.

Content uniformity test

Content uniformity tests for Transdermal patches ensure that each patch contains the labelled amount of drug, crucial for consistent dosing. The procedure generally involves selecting 10-30 patches, dissolving each, and measuring drug content (typically 85-115% of lable claim)via spectrophotometry (e.g., 264 nm) or HPLC.

Uniformity of dosage unit test

This Evaluation test for transdermal patches ensure that each patch contains the specified amount of API uniformly distributed, typically verified using content uniformity, often via HPLC, to meet USap <905> standards. Ten patches are analysed, requiring on Acceptance Value (AV) of 15.0 to pass, with specific procedures involving extracting the drug from cut pieces of the patch.

Moisture content

The moisture content of Transdermal patches typically ranges between 2%abd and 10%, which is critical for maintaining stability, flexibility, and drug release rates. A low moisture content is generally desirable to reduce brittleness, prevent bacterial growth, and stable optimal Range: The percentage of moisture content is usually kept within 2-10% to prevent the patch from becoming too brittle (too low) or too soft/susceptible to microbial growth (too high). Impact Of Polymers: The use of hydrophilic polymers like hydroxypropyl methyl cellulose (HPMC) in formulations increases moisture content and uptake, whereas hydrophobic polymers like Eudragit (e.g., Eudragit RS 100) decrease it. Moisture Uptake: Studies show moisture Uptake (absorption) can range from roughly 2.9% to 15.56%, Influencing the patch's flexibility and adhesion. Evaluation Method: Moisture content is often tested by calculating the difference in weight before and after storage in a desiccant (often containing silica gel) [8].

Fourier transformation-infrared Spectroscopy (FT-IR)

Fourier Transform Infrared Spectroscopy (FTIR) is a critical analytical technique used in Transdermal patch development to ensure drug-polymer compatibility, characterize functional groups, and confirm the stability of active ingredients within the matrix. It enables rapid, non-destructive analysis using techniques like Attenuated Total Reflectance(ATR) to verify that no unwanted chemical interactions occurred during formulation. Compatibility Studies: FTIR (often with KBr pellet or ATR methods) is used to check for changes in spectra when drugs are mixed with polymers, ensuring no degradation or unintended reactions occur. Molecular Interaction Analysis: It helps determine the intermolecular hydrogen bonding or interactions between drugs and excitements, which affects drug release rates. Stability Monitoring: It monitors changes in the drug over time, such as in the drug over time, such as in the case of oxidation or, and investigates causes for patch failure, such as in the case of oxidation or, and investigates causes for patch failure, such as the effect of sweating. Penetration Enhancement Studies: FTIR is used to analyze changes in the stratum corneum (skin) lipid and protein structure when treated with penetration enhancers contained in the patch [12].

Differential scanning colorimetry (DSC)

Differential Scanning Calorimetry in transdermal patches evaluates drug- excipient compatibility, crystallinity, and stability by measuring heat flow during thermal transitions. It detects drug crystallization, which can inhibit release, and assesses polymer-drug interactions. Key Applications include ensuring consistent drug release and monitoring long-term stability via thermograms. Drug excipient compatibility: Identifies interactions between the drug and formulation components by observing shifts or disappearance of endothermic melting peaks. Crystallinity and Amorphous State Detection: Determines if the drug is dissolved or crystalline within the polymer matrix, which is critical for drug release rates. Stability Testing: Compares thermograms before and after storage to monitor changes in thermal behaviour, indicating physical aging or degradation. Glass Transition Temperature Determination: Identifies the polymer, helping to determine its rubbery or glassy state at room temperature, which affects drug diffusion [12].

X-Ray powder diffraction

The physical state of the drug is determined such as both either crystalline or amorphous form. The crystallinity of the pure drug and the formulation is evaluated [12].

In-vitro studies

Skin irritation test

Based on higher drug permeation, formulation. The animals are examined at 24 and 72 h after application of the patch, Here the animals such as rabbits are used. The rabbits are shaved and the kind of the animal is exposed to the formulated transdermal patch. Further after the few hours the possibility of either Erythema and oedema are seen. If the drug show any kind of skin effect then the formulation should be discontinued [11,12].

S. no	Drug	Excipients	Disease	Remark
1	Asiaticoside	Polyvinyl Alcohol, Ethyl cellulose, Hydroxy propyl methyl cellulose (HPMC), Propylene glycol, PEG-400, Glycerin , Adhesive polymer, Baking Membrane	Wound Healing, Keloids, Skin ulcers, Hypertrophic scars.	Enhances collagen Synthesis And Promotes Skin Regeneration, Suitable For Sustained release through skin.
2	Camptothecin	Ethyl cellulose, HPMC, PEG-400, Propylene glycol, PVA baking membrane.	Skin cancer, melanoma.	Provides sustained release, avoids rapid systemic toxicity.
3	Bufalin	Eudragit RS100, PVP K30, Dibutyl pthalate, isopropy myristate.	Solid tumours/anti tumors	Improves skin permeability and patch flexibility.
4	Podophyllotoxin	Polyvinyl alcohol, Ethyl cellulose, oleic acid, propylene glycol.	Parkinson's disease, CNS disorder.	Provides sustained release and avoids first pass metabolism.
5	Harmaline	Ethyl cellulose, HPMC, PEG-400, Propylene glycol, PVA baking membrane.	Parkinson's disease, CNS disorder.	Provides sustained release and avoids first pass metabolism.
6	Ferulic acid	Carbopol 934, HPMC< ethanol, glycerin.	Anti- inflammatory, skin disorders.	Improves adhesion and controlled drug delivery.
7	Psoralen	Eudragit RS 100,PVP K30, dibutyl phthalate, isopropyl myristate.	Psoriasis	Enhances skin permeability and patch flexibility.
8	Paclitaxel	Polyvinyl alcohol, ethyl cellulose, oleic acid, propylene glycol	Anti-cancer, localized therapy.	Oleic acid acts as penetration enhancer.
9	Baicalin	Carbopol 934, HPMC, glycerin, ethanol.	Wound healing.	Improves adhesion and controlled drug delivery.
10	Menthol	Polyvinyl alcohol, ethyl cellulose, oleic acid, propylene glycol	Local analgesic therapy.	Oleic acid acts as penetration enhancer.

Table

Conclusion

Transdermal drug delivery system has emerged as a significant alternative for conventional drug administration routes, offering sustained and controlled drug release while improving patient compliance and therapeutic efficacy. By bypassing hepatic metabolism and by maintaining the steady plasma drug concentrations, TDDS minimize systemic side effects and dosing variability. Advances in polymer science, adhesive technologies, and skin permeation enhancement strategies—including chemical enhancers, iontophoresis, microneedles, and nanocarrier-based

systems—have substantially broadened the range of drugs suitable for transdermal delivery system. The integration of nanotechnology, smart patches, and personalized medicine approaches further highlights the future potential of TDDS. Overall, transdermal drug delivery systems represent a promising and continuously evolving platform, with expanding clinical applications and significant scope for future pharmaceutical development.

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