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RECENT TRENDS IN MODIFIED TRANSDERMAL PATCHES

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ABSTRACT

Transdermal drug delivery has emerged as a promising alternative to oral and injectable routes, offering non-invasive, convenient, and controlled drug administration. Modified transdermal patches enhance traditional systems by incorporating technologies such as microneedles, iontophoresis, nano-carriers, and smart responsive materials. These innovations improve drug permeation, bioavailability, and therapeutic efficiency while minimizing systemic side effects. Recent trends focus on delivering a wider range of drugs, including hormones, peptides, proteins, vaccines, and small molecules. Microneedle-based patches allow painless administration of macromolecules previously unsuitable for transdermal delivery. Nanotechnology integration improves solubility, stability, and controlled release of drugs. Smart patches with sensors enable real-time monitoring and personalized drug release for chronic diseases like diabetes and cardiovascular disorders. Current research emphasizes customization, patient adherence, and long-term therapy effectiveness. Transdermal systems now target neurological, psychiatric, dermatological, and immunotherapeutic applications. Clinical studies demonstrate improved pharmacokinetics. Advanced fabrication techniques, including 3D printing.

Keywords: Transdermal drug delivery, Microneedle patches, Nanotechnology-based carriers, Smart responsive patches, Controlled drug release, Personalized medicine.

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INTRODUCTION

Drug delivery systems play a crucial role in determining the therapeutic effectiveness, safety, and patient compliance of pharmaceutical products. Conventional drug administration routes such as oral, parenteral, and topical routes have been widely used for decades; however, they are often associated with limitations including poor bioavailability, frequent dosing, systemic side effects, and reduced patient adherence. These challenges have driven continuous research toward the development of advanced drug delivery systems that can provide controlled, targeted, and patient-friendly therapeutic outcomes. Among these, transdermal drug delivery systems (TDDS) have emerged as an important alternative route of drug administration [1].

Transdermal drug delivery refers to the administration of therapeutic agents through the skin into the systemic circulation. The skin, being the major advantage of transdermal drug delivery systems lies in their ability to bypass hepatic first-pass metabolism, which significantly improves drug bioavailability. Additionally, transdermal patches maintain relatively constant plasma drug concentrations, minimizing peak-and-trough fluctuations commonly observed with oral dosage forms. This leads to enhanced therapeutic efficacy and reduced side effects. Furthermore, transdermal systems improve patient compliance due to ease of administration, reduced dosing frequency, and painless delivery. These benefits make TDDS particularly suitable for chronic conditions requiring long-term therapy [2].



Fig No: 1. Transdermal Patch

Despite these advantages, conventional transdermal patches face significant limitations. The primary barrier to transdermal drug delivery is the stratum corneum, the outermost layer of the skin, which is highly resistant to the penetration of most drugs. Only drugs with specific physicochemical properties—such as low molecular weight, adequate lipophilicity, and high potency—can effectively permeate through intact skin. As a result, traditional transdermal patches are limited to a small group of drugs, restricting their wider clinical application. Additionally, skin irritation, allergic reactions, limited drug loading capacity, and interindividual variability in skin permeability pose further challenges. To overcome these limitations, significant advancements have been made in the design and development of modified transdermal patches. Modified transdermal systems aim to enhance drug permeation, expand the range of deliverable molecules, and improve therapeutic outcomes through innovative technologies and materials. These systems incorporate chemical, physical, and mechanical strategies to modify skin permeability and optimize drug transport across the skin barrier [3, 4].

Another major development in modified transdermal drug delivery is the application of nanotechnology-based carriers. Nanocarriers such as liposomes, niosomes, transferosomes, ethosomes, invasomes, polymeric nanoparticles, and nanoemulsions have demonstrated significant potential in enhancing skin penetration. These carriers improve drug solubility, protect labile drugs from degradation, and facilitate controlled release. Transferosomes and ethosomes, particular, exhibit high deformability, allowing them to penetrate deeper skin layers more effectively than conventional vesicular systems. The integration of nanocarriers into transdermal patches represents a promising strategy for delivering both lipophilic and hydrophilic drugs. In a microneedle-based transdermal patches represent a revolutionary advancement in modified TDDS.

Microneedles are microscopic needles that painlessly pierce the stratum corneum to create transient microchannels, allowing drugs to bypass the skin barrier without reaching nerve endings. Microneedle patches can deliver a wide range of therapeutic agents, including vaccines, peptides, proteins, insulin, and nucleic acids. They combine the advantages of transdermal delivery with the effectiveness of injectable routes while eliminating pain and needle-related risks. The development of dissolving, coated, hollow, and biodegradable microneedles has further expanded their clinical applicability [5].

Recent years have also witnessed the emergence of smart and wearable transdermal patches. These systems integrate sensors, microprocessors, and feedback mechanisms to monitor physiological parameters such as glucose levels, temperature, or drug concentration in real time. Smart patches can adjust drug release based on patient-specific needs, enabling personalized therapy. Such innovations are particularly valuable in managing chronic diseases like diabetes, cardiovascular disorders, and neurological conditions.

Advancements in polymer science and materials engineering have further contributed to the evolution of modified transdermal patches. The development of biocompatible, biodegradable, and stimuli-responsive polymers has enabled the design of patches that respond to changes in pH, temperature, or external stimuli. These materials enhance drug stability, improve adhesion, and allow controlled and targeted drug release. Additionally, the application of 3D printing technology has enabled precise fabrication of customized transdermal patches with tailored drug loading and release profiles.

MODELS

1. Introduction to Modeling in Transdermal Patch Research

Models in transdermal drug delivery serve as essential tools for understanding, predicting, and optimizing drug transport across the skin barrier. Because the skin's stratum corneum offers a significant barrier to drug permeation, researchers increasingly rely on mathematical, mechanistic, and simulation models to evaluate how formulation properties, patch design, and biological variables affect delivery efficiency. These models reduce experimental workload, enable *in silico* optimization, and guide design of novel modified patches such as microneedle-based and nanocarrier-enhanced systems [6].

2. Mechanistic Modeling of Transdermal Transport

Mechanistic models incorporate the physics and biology of skin structure and drug transport processes. A key class of such models reconstructs the skin's layered architecture and computes how drugs diffuse through each layer based on diffusion coefficients, partitioning, and boundary conditions [7].

3. Compartmental and Multi-Layer Models

A common framework in transdermal modeling uses compartmental or multi-layer representations of the skin. These treat the epidermis, dermis, and systemic compartment as interconnected domains, each with distinct transport parameters. Such models are particularly helpful for linking in vitro experiments with in vivo expectations, enabling prediction of systemic drug levels from patch design variables.

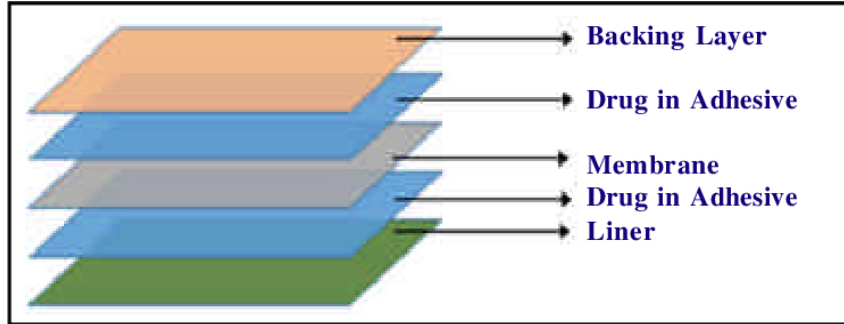


Fig No: 2. Multi Layer model

4. Iontophoretic and Electro-Transport Models

Some advanced models simulate active enhancement methods, such as iontophoresis, which uses an electrical gradient to drive charged drug molecules across the skin. These models couple electromigration, electroosmosis, and diffusion, often based on the Nernst-Planck and Laplace equations, to predict flux under different electrical conditions. Although originating from earlier foundational work, such models remain relevant to modern electrically enhanced transdermal patches and are being adapted for new compounds. These models couple electromigration, electroosmosis, and diffusion, often based on the Nernst-Planck and Laplace equations, to predict flux under different electrical conditions [8].

5. Microneedle Patch Models

A major trend in modified transdermal systems is the proliferation of microneedle-based patches. These models focus on how needle geometry (length, radius, spacing), drug loading, and dissolution rates influence local and systemic drug profiles. For example, a published model exploring dissolvable microneedle patches found that needle height, base radius, and drug loading fraction are key determinants of systemic pharmacokinetics, enabling optimization of design for therapeutic targets.

Microneedle models often include drug release kinetics coupled with mechanical interactions of the needles with skin tissue, accounting for dissolution dynamics and creation of microchannels. These models support both rapid release designs (e.g., pain or emergency drugs) and sustained release systems (e.g., hormone delivery), demonstrating the versatility of modeling in advanced patch design [9].

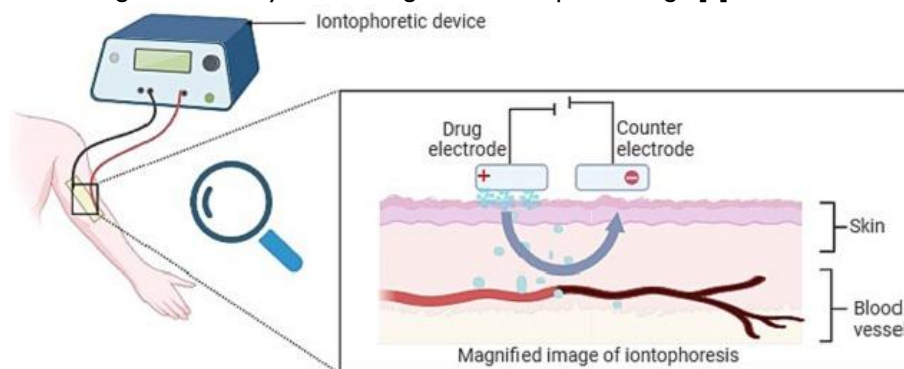


Fig No: 3. Iontophoretic and electro transport models

6. Computational Simulations and Numerical Methods

Modern transdermal research increasingly uses computational simulations-such as finite element analysis (FEA), finite volume methods (FVM), and lattice-Boltzmann techniques-to solve coupled transport equations over complex geometries. These simulations allow visualization of spatial concentration gradients and prediction of patch performance under realistic boundary conditions. These simulations allow visualization of spatial concentration gradients and prediction of patch performance under realistic boundary conditions.

Such tools are essential when evaluating nanocarrier distributions, non-linear diffusion, and anisotropic properties of skin tissues [10].

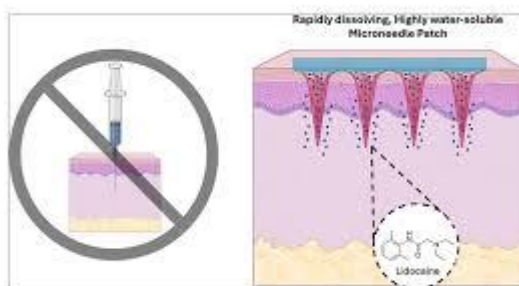


Fig No:4. Microneedle patch model

7. Model Validation and Integration with Experiments

Validated models often integrate with in vitro and in vivo data. For instance, models developed in microfluidic skin-on-a-chip systems match simulated drug penetration profiles with experimental measurements, confirming their utility in predictive optimization. These simulations allow visualization of spatial concentration gradients and prediction of patch performance under realistic boundary conditions. Such tools are essential when evaluating nanocarrier distributions, non-linear diffusion, and anisotropic properties of skin tissues. This synergy reduces reliance on extensive animal studies while accelerating formulation screening and patch customization for different therapeutic agents.

8. Emerging Hybrid and Smart Models

As patches become "smart"-for example, responsive insulin patches that modulate release based on glucose levels-models now include feedback control algorithms and real-time physiological inputs. These hybrid models combine biochemical sensing, release kinetics, and systemic response predictions to inform next-generation adaptive patch designs. These simulations allow visualization of spatial concentration gradients and prediction of patch performance under realistic boundary conditions [11].

APPLICATIONS:

Applications of Modified Transdermal Patches

Transdermal patches have evolved significantly from simple drug-inadhesive systems to advanced, controlled delivery platforms. Modified patches incorporate technologies such as microneedles, iontophoresis, nanoformulations, and smart responsive systems to expand their utility beyond conventional uses. These innovations have enabled transdermal delivery of a wider range of therapeutic agents, improved pharmacokinetics, enhanced patient compliance, and broadened clinical applications. The following section discusses the major applications across therapeutic areas, highlighting recent trends, clinical relevance, and future potential [12].

1. Pain Management

Chronic and acute pain conditions represent one of the most prominent application areas for modified transdermal patches. Traditional patches delivered analgesics such as fentanyl or lidocaine to manage moderate to severe pain, particularly in cancer patients or for post-operative care. However, newer designs have significantly improved localized delivery and reduced systemic side effects.

2. Hormonal and Endocrine Therapies

Hormone replacement therapies (HRT), contraceptives, and endocrine disorder treatments benefit substantially from transdermal delivery due to improved steady-state plasma levels and reduced first-pass metabolism.

Transdermal Hormone Replacement

Modified patches for estrogen and testosterone replacement have become mainstream for managing menopause symptoms and hypogonadism. Their ability to provide consistent hormone levels reduces the peaks and troughs commonly associated with oral therapy, lowering the risk of side effects such as nausea or hepatic stress.

Contraceptive Patches

Contraceptive transdermal

patches deliver combination hormones (ethinylestradiol and progestin) with weekly dosing. Recent trends include adhesive improvements to extend wear time even under conditions like exercise or water exposure.

3. Cardio vascular Diseases

Hormonal and Endocrine Therapies

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Contraceptive Patches

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4. Vaccination and Immunotherapy

Transdermal patches are gaining attention as needle-free alternatives for vaccination, offering benefits especially in mass immunization campaigns.

Microneedle Vaccine Patches

Microneedle patches for vaccines allow antigen delivery to antigen-presenting cells in the skin, often eliciting strong immune responses with lower doses compared to intramuscular injections. This is particularly valuable in pandemic responses where dose-sparing is crucial. Examples under clinical evaluation include influenza, measles, and COVID-19 antigen patches.

5. Diabetes Management

Transdermal delivery in diabetes has historically been limited due to the challenge of delivering large molecules like insulin. However, recent modifications have begun to overcome these barriers.

Dissolvable microneedles loaded with insulin offer a painless, self-administered alternative to subcutaneous injections. These patches can be engineered for glucose-responsive release, where insulin is released more rapidly when glucose levels rise, mimicking physiological insulin dynamics.

Continuous Glucose Monitoring Integration

Emerging systems integrate continuous glucose monitoring sensors with drug-release patches. These "closed-loop" smart patches automatically adjust drug delivery based on real-time glucose readings. While still largely in research stages, they hold promise for enhancing glycemic control and reducing patient burden.

6. Neurological and Psychiatric Conditions

Modified transdermal patches support the controlled delivery of drugs for neurological disorders.

Parkinson's Disease

Transdermal delivery of dopaminergic agents (such as rotigotine) provides continuous stimulation of dopamine receptors, decreasing motor fluctuations seen with oral therapy. Newer formulations aim to improve patch adhesion and reduce skin irritation to enhance long-term use.

7. Dermatological and Cosmetic

Beyond systemic therapies, modified transdermal patches are widely used in dermatology and aesthetics. By delivering drugs directly into systemic circulation or targeting localized tissues, modified transdermal patches reduce gastrointestinal irritation and systemic adverse effects [13].

ADVANTAGES

1. Improved Patient Compliance

One of the most important advantages of modified transdermal patches is enhanced patient compliance. These systems are non-invasive, painless, and easy to use, making them highly acceptable for pediatric, geriatric, and chronic disease patients. Reduced dosing frequency (once daily or weekly) minimizes missed doses compared to oral medications that require multiple daily administrations.

2. Avoidance of First-Pass Metabolism

Transdermal patches bypass hepatic first-pass metabolism, which is a major limitation of oral drug delivery. This leads to improved bioavailability of drugs that are extensively metabolized in the liver, such as hormones, cardiovascular drugs, and certain analgesics. As a result, lower drug doses are required to achieve therapeutic effects, reducing systemic toxicity.

3. Enhanced Skin Permeation

Recent technologies such as microneedles, chemical permeation enhancers, ultrasound (sonophoresis), and electrical methods (iontophoresis) significantly improve drug penetration across the stratum corneum. These modifications enable the delivery of drugs with poor skin permeability, including macromolecules, peptides, and vaccines, which were previously unsuitable for transdermal administration.

4. Reduced Systemic Side Effects

By delivering drugs directly into systemic circulation or targeting localized tissues, modified transdermal patches reduce gastrointestinal irritation and systemic adverse effects commonly associated with oral and injectable therapies. Stable drug levels also help prevent toxicity caused by high plasma peaks.

PRESENT SCENARIO

Present Scenario of Modified Transdermal Patches

1. At present, modified transdermal patches are gaining wide acceptance in pharmaceutical and clinical practice due to their non-invasive nature and improved patient compliance. They are increasingly preferred for long-term therapy in chronic diseases where sustained and controlled drug delivery is required.
2. Commercially available transdermal patches such as those containing nitroglycerin, fentanyl, nicotine, rivastigmine, and hormonal drugs indicate the successful application of this drug delivery system. These products demonstrate the ability of transdermal patches to maintain steady plasma drug levels and reduce dosing frequency.
3. Nanotechnology-based modified patches represent another important trend. Incorporation of nanoparticles such as liposomes, nanoemulsions, and polymeric carriers improves drug solubility, stability, and skin permeation. This approach enhances therapeutic efficacy while minimizing systemic side effects.
4. Smart and wearable transdermal patches are emerging as an innovative approach in modern healthcare. These patches integrate sensors and electronic components to monitor physiological parameters and regulate drug release in real time, particularly useful in conditions such as diabetes and cardiovascular disorders.
5. The present scenario also shows increasing use of transdermal patches in neurological and psychiatric disorders. Drugs used in Parkinson's disease, Alzheimer's disease, and depression are now being formulated into modified patches to provide continuous drug delivery and reduce fluctuations in plasma drug concentration.
6. In vaccination and immunotherapy, modified transdermal patches, especially microneedle patches, are under active research and clinical trials. These patches offer needle-free immunization, improved patient acceptance, and potential dose-sparing effects.
7. Advances in manufacturing technologies such as microfabrication and 3D printing are supporting the development of customized transdermal patches. These techniques allow precise control over drug dose, release rate, and patch design, contributing to personalized medicine.
8. Despite technological progress, challenges such as skin irritation, variability in skin permeability among individuals, high manufacturing costs, and complex regulatory approval processes continue to limit widespread commercialization of advanced transdermal patches.
9. At present, modified transdermal patches are gaining wide acceptance in pharmaceutical and clinical practice due to their non-invasive nature and improved patient compliance [14].

CONCLUSION

Modified transdermal drug delivery systems represent a significant advancement in pharmaceutical technology, offering controlled, non-invasive, and patient-friendly drug administration. By overcoming limitations of conventional methods, these systems enhance bioavailability, reduce side effects, and improve therapeutic outcomes. Innovations such as microneedles, nanocarriers, and smart wearable patches have expanded their applicability across various diseases, including chronic and complex conditions. Modeling and simulation further support optimized design and performance. Despite challenges like skin permeability and cost, continuous research and technological progress are driving their clinical acceptance, making modified transdermal patches a promising future approach for safe, effective, and personalized drug delivery.

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CONFLICT OF INTEREST

Not declared

INFORMED CONSENT AND ETHICAL STATEMENT

Not Applicable

AUTHOR CONTRIBUTIONS

All Authors Are Contributed Equally

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