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Transdermal Therapeutic System And The Impact Of Wearable Patches In Future Healthcare.

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ABSTRACT

For millennia, human societies have used substances on the skin for both cosmetic and medicinal purposes.Transdermal drug delivery allows drugs to enter the bloodstream through the skin, achieving systemic effects without causing fluctuations in drug plasma concentrations. Compared to traditional oral or invasive methods, topical administration of therapeutic agents offers numerous benefits. It also ensures controlled and prolonged release of medications. A novel form of transdermal drug delivery systems involves wearable patches applied to the skin surface for medication delivery. These patches are typically categorized as either passive or active based on their material properties, design principles, and inclusion of integrated devices.This review summarizes the advantages, skin pathways involved in transdermal drug delivery systems (TDDS), components of transdermal patches, and methods used for their preparation.

INTRODUCTION

Depending on the medicine and formulation, frequent and long-term dosage may be necessary for disease treatment and prevention. Currently, drugs are administered primarily through oral pills and parenteral injections. Oral dosing is commonly used due to its ease of administration, patient convenience, cost-effectiveness, and large-scale manufacturing. However, due to first-pass metabolism and low bioavailability, most drugs require high or multiple daily doses to maintain therapeutic levels. This approach is often associated with GI side effects and poor adherence due to the high pill burden, reducing the effectiveness of treatment regimens.A controlled drug delivery system is a dosage form that delivers multiple medications in a planned pattern over a set length of time, either systemically or to a specific organ. Controlled medication delivery aims to assure drug safety, efficacy, and patient compliance.This is accomplished through greater control over plasma drug levels and less frequent dosing. Transdermal therapy systems are self-contained dosage forms that administer drugs via unbroken skin at a controlled rate to the systemic circulation.[1]Over the years, numerous TDD formulations have been created to improve medication absorption, wearability, and patient compliance.TDD platforms are classified as either passive or active . Passive delivery is the spontaneous decay of drug reservoirs or diffusion-based drug release. Active delivery refers to medication release triggered by internal or external stimuli such as enzymes, pH, electrical, mechanical (ultrasound), or optical fields.In contrast to passive delivery, active delivery delivers medications to target sites with controlled spatial, temporal, and dose accuracy.The FDA approved the first TDD patch (Transderm Scop) in 1979 to treat motion sickness with scopolamine. Since then, many TDD patches have been licenced for vaccination, pain relief, and skin care.Wearability has recently gained popularity in the construction of TDD patches. The term “wearability” refers to the physical, psychological, and social elements that impact the comfort of wearing a patch. Innovative materials and designs enhance wearability and comfort.[2,3,4]TDS has the advantage of bypassing first-pass metabolism and GI adverse effects associated with oral dosage, allowing for continuous drug administration over an extended period of time. TDS has a significant benefit over injectables since it is a painless medication delivery method that may be administered by healthcare providers or end users with minimum training. TDS reduces changes in medication systemic exposure, improving therapeutic outcomes.[5]

However, this method of drug administration has several complications. Molecules bigger than 500 Daltons cannot pass through the epidermal barrier, making transdermal application problematic. Chemical and physical approaches have been developed to improve skin permeability, allowing for material penetration. Penetration enhancers include tape peeling, heat ablation, electroporation (EP), ultrasound, jet injection, and formulations including liposomes, transferosomes, and MN patches.This study covers the latest advancements in developing multifunctional biomaterials for transdermal immunotherapy and their potential uses in diverse disorders.[6]

Antigen-presenting cells of human skin

The human skin has three layers: the epidermis on the outside, the dermis in the middle, and the hypodermis at the bottom.The epidermal layer, composed of 90% keratinocytes, serves as the body's first line of defence against microbes and external influences.

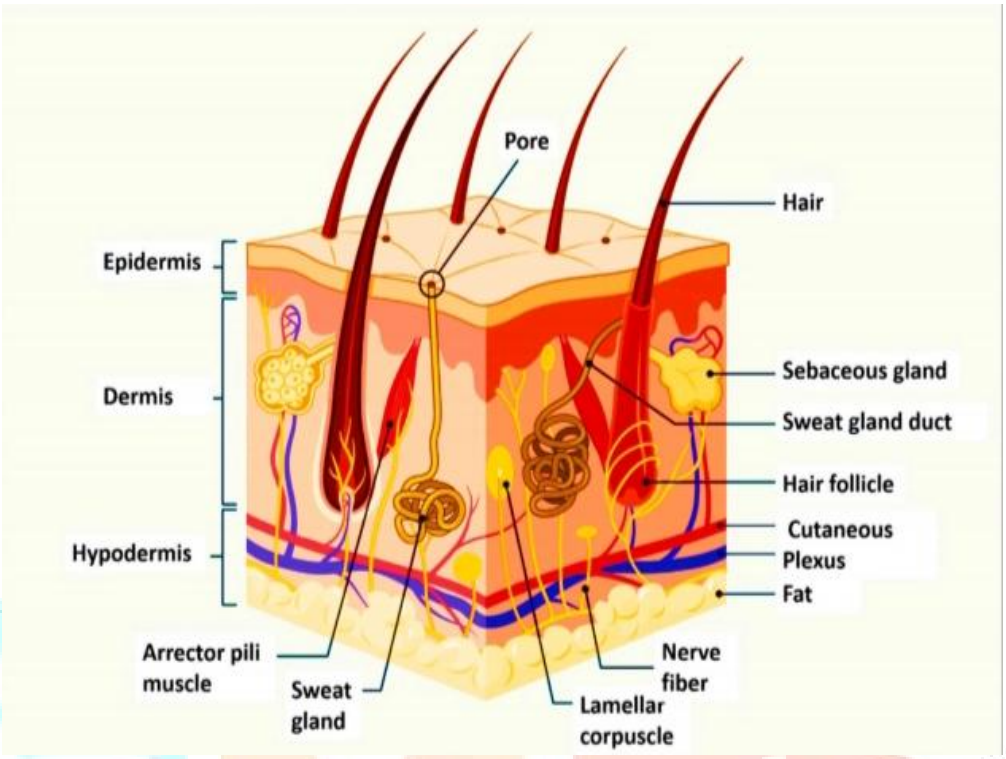

Fig.no.1(The skin is composed of three main layers: the epidermis, the dermis, and the hypodermis. Each of these layers contains various sub-layers and components.)[8]

The epidermis is a layer without blood vessels, primarily consisting of keratinocytes, Merkel cells, and Langerhans cells. The dermis includes a dense network of capillaries that connect with the body's circulation system, serving as the primary route for drug absorption. The hypodermis is the deepest layer of the skin, comprising vascularized, loose areolar connective tissue, and adipose tissue.[9]

Keratinocytes have the ability to eliminate microorganisms using innate immune factors. When pattern recognition receptors (PRRs) detect microorganisms, keratinocytes release substances like β-defensin and ribonuclease, which can effectively eliminate these pathogens. Additionally, keratinocytes secrete various cytokines, both pro-inflammatory (such as IL-1b, TNF-α, IL-18, IL-6) and anti-inflammatory (like TGF-β and IL-10), to activate the innate immune response.Moreover, chemokines released by keratinocytes play a significant role in recruiting T-cells, monocytes, and neutrophils, which are crucial for defence [10,11]. Langerhans cells (LC), a type of macrophage located in the epidermis, capture antigens and present them to T-cells in lymph nodes.[9] Langerhans cells are important in modulating the immune response by inducing T regulatory cells.The dermis is a loose tissue containing blood and lymphatic vessels, which support a dynamic immune response [13]. Immune cells involved in dermal defense include dendritic cells (DCs), mast cells, innate lymphoid cells, and alpha and beta TCR lymphocytes. Gamma and delta TCR lymphocytes are also present in the dermis and contribute to wound healing [14]. Mast cells recognize pathogen antigens via toll-like receptors (TLR), triggering the release of TNF-α and CCL3 chemokines that recruit T lymphocytes, monocytes, and neutrophils to the infection site [15]. DCs are crucial for capturing and transporting antigens to local lymph nodes, where they present them to T-cells.[7]

SKIN PATHWAYS FOR TRANSDERMAL DRUG DELIVERY SYSTEMS:[16]

When drugs are applied to the skin, they can penetrate into and through it via different pathways. These include penetration through the stratum corneum (transepidermal) or through the skin appendages (transappendageal) .When penetrating through the stratum corneum, drugs can take two main routes: passing through the corneocytes and lipid lamellae (transcellular route) or following a winding path along the lipid lamellae.It is widely acknowledged that the primary pathway for penetration through the stratum corneum is through the intercellular route. This is primarily due to the dense, interconnected cornified envelope that covers the keratinocytes. However, transcellular transport may still occur, especially for small hydrophilic molecules like water, although it is not the predominant route.The appendage route, also known as the shunt route, involves either the duct of the eccrine sweat glands or the follicular duct. The content of eccrine sweat glands is predominantly hydrophilic, whereas the follicular duct contains lipophilic substances, primarily due to the sebum discharged into its opening. It is widely accepted that passive skin permeation primarily occurs through the intact stratum corneum, largely due to its extensive surface area.

Release principles of TDD [16]

Passive delivery

Passive delivery refers to the natural breakdown or dissolution of drug reservoirs or the gradual diffusion of drugs from these reservoirs into the skin. The effectiveness of passive delivery depends on factors such as the formulation's properties (like hydrophobicity, charge, molecular weight, and crystallinity), the dosage of active compounds, and the condition of the skin. For instance, cationic chitosan binds more strongly to protein agents compared to anionic sodium alginate, resulting in a slower release of drugs. Hyaluronic acid (HA) is expected to degrade more quickly in the body compared to polyesters or silk fibroin, which would lead to a faster release of the enclosed drugs.The degradation of transdermal drug delivery systems (TDDs) can also be influenced by factors such as skin thickness, pH levels, temperature variations, and the presence of surface microbes. For instance, microparticles loaded with hydrocortisone (using a polymer sensitive to pH that dissolves at pH 6) did not release drugs when exposed to the normal pH range of intact skin (around 5.0 to 5.5). However, drug release could be activated when applied to atopic dermatitis-affected skin, where the pH is higher.

Active delivery

Active delivery systems respond to stimuli such as electricity, ultrasound, and light. In particular, electrically assisted delivery methods, like iontophoresis and electroporation, utilize these stimuli. Iontophoresis employs a gentle, continuous electrical current across the skin, enabling ionized or charged particles to traverse the natural skin barrier. Additionally, uncharged and weakly charged molecules can move along with the solvent flow created by the selective movement of mobile cations.Unlike iontophoresis, electroporation involves applying brief (<ms), high-voltage pulses (> 100 V) to induce temporary pores in the skin. In both methods, the effectiveness of delivery can be regulated by adjusting pulse characteristics (such as waveform, duration, and amplitude) as well as considering drug attributes like oil-water partition coefficient (logP), pKa, and solubility.Ultrasound exhibits excellent directional control and can penetrate human tissue effectively. When ultrasound induces cavitation, it causes microbubbles to form, oscillate, and collapse, which disrupts the lipid bilayers of the stratum corneum (SC). This oscillation of microbubbles and the resulting acoustic streaming greatly enhance the passive diffusion of dissolved molecules or nanoparticles in solutions with low viscosity.

BASIC COMPONENETS OF TRANSDERMAL [18,29,30]

DRUG DELIVERY SYSTEMS:

The components of Transdermal device include

Polymer matrix

Drug

Permeation enhancers

Other excipients

Polymer Matrix:

The polymer regulates the drug's release from the device.

Natural Polymers: Cellulose derivatives,Zein, Gelatin, Waxes,Proteins, Gums,Natural rubber,Starch.

Synthetic elastomers:Polybutadiene, Hydrin rubber,Polysiloxane, silicone rubber,Nitrile, Acrylonitrile,Butylrubber, Styrenebutadiene, Neoprene etc.

Synthetic polymers: Polyethylene, Polypropylene,Polyacrylate, Polyamide,Polyvinylpyrrolidone,Polymethyl methacrylate,Epoxy, Polyurea, etc.

Drug

To create a successful transdermal drug delivery system, careful selection of the drug is crucial. Certain desirable characteristics include:

- The drug's molecular weight should be below around 1000 Daltons.
- The drug should exhibit affinity for both lipophilic and hydrophilic phases. Extreme partitioning characteristics are not favourable for effective skin delivery.
- The drug should have a low melting point.
- Tolerance to the drug should not develop with the nearly constant rate of release characteristic of transdermal delivery.

Permeation Enhancers:

Permeation enhancers or promoters are substances that lack therapeutic properties but facilitate the absorption of drugs from delivery systems into the skin.Permeation enhancers are believed to influence one or multiple skin layers to improve penetration. Numerous compounds have been studied for their potential to increase the permeability of the stratum corneum.

Other Excipients:

Adhesives:

Transdermal devices are typically secured to the skin using pressure-sensitive adhesive, which can be applied on the front or back of the device and extend around its edges.

Adhesive systems must meet the following criteria:

- They should not cause skin irritation, sensitization, or disrupt the normal skin flora.
- They should adhere firmly to the skin throughout the dosing period, remaining unaffected by activities such as bathing or exercise.
- They should be easy to remove.
- leave no residue on the skin that cannot be washed off.
- Maintain excellent contact with the skin at both macroscopic and microscopic levels.

Backing Membrane

Backing membranes are flexible and effectively adhere to the drug reservoir, preventing drug leakage from the top of the dosage form. They are impermeable and provide protection to the product when applied to the skin. Examples include metallic plastic laminates, plastic backings with absorbent pads, and occlusive base plates made of materials like aluminium foil.

Release Liner:

During storage, the release liner serves to prevent drug loss that may have moved into the adhesive layer and protects against contamination. It is considered a component of the primary packaging material rather than part of the drug delivery system. The release liner consists of a base layer, which can be non-occlusive (such as paper or fabric), or occlusive (like polyethylene or polyvinylchloride), along with a release coating layer composed of silicone or Teflon.

TECHNOLOGIES FOR DEVELOPING TRANSDERMAL DRUG DELIVERY SYSTEMS:[29,30]

Several methods have been effectively created to manage the speed at which drugs are released and permeate through the skin. These methods can be categorized into four fundamental approaches.

A)Polymer membrane permeation-controlled TDD Systems:

In this system, the drug reservoir is positioned between a drug-impermeable laminate made of metallic plastic and a polymeric membrane that controls the rate of drug release. The drug molecules are allowed to exit exclusively through this polymeric membrane, which can be either microporous or nonporous. Examples include ethylene-vinyl acetate copolymer, which allows drug permeation. A thin layer of hypoallergenic pressure-sensitive adhesive polymer, such as silicone adhesive, may be applied on the external surface of the polymeric membrane to ensure close contact between the TDD system and the skin.

Ex: Transderm-Nitro system, Transderm-Scop system, The Captures the Estraderm system, and the Duragesic system.

B)Polymer matrix Diffusion-Controlled TDD Systems:

In this method, the drug reservoir consists of drug solids evenly distributed within a hydrophilic or lipophilic polymer matrix. This medicated polymer is then shaped into discs of specific surface area and controlled thickness. These discs, containing the drug reservoir, are placed onto an occlusive base plate within a compartment made from a drug-impermeable plastic backing. An adhesive polymer is applied around the edge of the patch, creating a strip of adhesive that surrounds the medicated disc. Examples of systems utilizing this approach include the Nitro-Dur system.

C)Drug Reservoir Gradient-Controlled TDD Systems:

To address non-zero drug release profiles, the polymer matrix drug dispersion type TDD system can be adjusted by varying the drug loading level incrementally. This creates a gradient of drug reservoir across the multilayer adhesive, facilitating controlled drug diffusion. An example of this approach is seen in the Deponit system.

D)Microreservoir Dissolution-Controlled TDD Systems:

This delivery system can be seen as a blend of reservoir and matrix dispersion types. It begins by mixing drug solids with a water-miscible solubilizer like polyethylene glycol, forming a drug suspension. This suspension is then evenly dispersed in a lipophilic polymer using high shear force, creating numerous tiny drug reservoirs that cannot be washed out. To stabilize this unstable dispersion, the polymer chains are cross-linked immediately in place, resulting in a medicated polymer disc with consistent surface area and thickness. An example is the Nitrodisc system.

PREPARATION OF TRANSDERMAL PATCHES[17]

Transdermal drug delivery patches can be prepared by Various methods

A)Mercury Substrate Method:[17,20,21]

In this technique, a specific quantity of drug is dissolved in a predetermined volume of polymer solution with a plasticizer. The mixture is stirred until a uniform dispersion forms and left to stand until air bubbles are completely removed. It is then poured into a glass ring positioned on a mercury surface within a glass petri dish. The rate of solvent evaporation is regulated by placing an inverted funnel over the petri dish. After drying, the films are stored in a desiccator.

B)Glass Substrate Method:[24]

The process involves first allowing polymeric solutions to swell, then adding the necessary amount of plasticizer and drug solution, followed by stirring for 10 minutes. After setting aside to remove any trapped air, the mixture is poured into a clean, dry petriplate. A glass funnel is inverted over the petriplate to regulate the rate of solvent evaporation. The dried films are removed the next day and stored in a desiccator.

C)Circular Teflon Mould Method:[23]

Polymer solutions in different ratios are prepared using an organic solvent. A calculated amount of drug is dissolved in half the quantity of the same organic solvent. Plasticizer is added to this drug-polymer solution. The entire mixture is stirred and then poured into a circular Teflon mold. A glass funnel is placed upside down on the Teflon mold to control the rate of solvent evaporation. The solvent is allowed to evaporate for 24 hours. The dried films are then stored in a desiccator.

D)By Using IPM Membranes Method:[25,26]

In this approach, the drug is dispersed in a blend of water and propylene glycol containing carbomer 940 polymers, and stirred for 12 hours using a magnetic stirrer. The dispersion is then made viscous and neutralized by adding triethanolamine. If the drug has low solubility in aqueous solutions, a buffer at pH 7.4 can be used to achieve a solution gel. This gel will be integrated into the IPM membrane.

E)Aluminium Backed Adhesive Film Method: [27]

In transdermal drug delivery systems, unstable matrices can result if the dose exceeds 10 mg. The aluminum-backed adhesive film method is suitable for this purpose. To prepare it, chloroform is chosen as the solvent because most drugs and adhesive materials dissolve well in chloroform. The drug is dissolved in chloroform, and then the adhesive material is added to the drug solution and dissolved as well. A specially designed aluminum mold is lined with aluminum foil, and the ends are sealed tightly with cork blocks.

F)Asymmetric TPX Membrane Method:[29]

A prototype patch is created using a heat-sealable polyester film (type 1009, 3M) with a concave area of 1 cm in diameter as the backing membrane. The drug sample is placed into the concave membrane, covered with an asymmetric membrane made of TPX (poly(4-methyl-1-pentene)), and sealed using an adhesive.

G)By Using EVAC Membranes Method:[25,26]

To create the targeted transdermal therapeutic system, a reservoir gel containing 1% carbopol can be used along with polyethylene (PE) and ethylene vinyl acetate copolymer (EVAC) membranes for controlling drug release rates. If the drug is not water-soluble, it is dissolved in propylene glycol to prepare the gel. The drug is mixed with propylene glycol, then carbopol resin is added and neutralized using a 5% w/w sodium hydroxide solution. The drug-containing gel is applied onto a backing layer covering a specific area. A rate-controlling membrane is placed over the gel and sealed around the edges with heat to create a secure device.

Wearable patch for passive delivery[16]

- **Hydrogel patch:**

Hydrogels enable convenient modification of chemical, physical, and biological characteristics. In transdermal delivery, the semi-solid nature of hydrogels is advantageous for loading and releasing drugs. Simultaneously, transdermal drug delivery is non-invasive yet effective, allowing for easy self-administration and potential bypassing of initial liver metabolism.The hybrid hydrogel utilizes arginine-based poly(ester amide) (Arg-PEA) as a carrier. Arg-PEA is positively charged, capable of absorbing protein drugs, exhibiting good biocompatibility, and forming a hydrogel scaffold with polyethylene glycol diacrylamide (PEG-DA) through UV photocrosslinking.

Hydrogel patches are categorized as either adhesive hydrogel patches or stimulus-responsive hydrogel patches.

Adhesive hydrogel patch:A strong bond between the hydrogel patch and skin prevents contaminants such as bacteria from entering and ensures consistent drug release into the skin. Pressure-sensitive adhesive hydrogel adheres to the skin upon application pressure and cleanly peels off without leaving residue.

Stimulus-responsive hydrogel patch:A hydrogel patch that responds to stimuli such as pH, temperature, or light alters its chemical or physical characteristics. This change affects how drugs are released from the patch.

- **Microneedle patch:**MNs are tiny needles, often tens to hundreds of micrometers in size, designed to mechanically puncture the outer layers of the skin to enhance drug absorption. Despite their small size relative to the skin area, MNs typically have limited capacity for holding drugs. One solution to address this limitation is the "poke and patch" method.TMAP (touch-MN array patch) utilized PMMA (polymethyl methacrylate)microneedles and a sponge containing insulin. Applying pressure to the tape caused the microneedles to pierce through both the sponge and the skin. Insulin from the sponge only diffused through the microneedle-created micro-holes into the skin when pressure was applied. The rate of insulin release could be regulated by adjusting the pressure and frequency of application.

Wearable patch for active delivery

- **Electricity-stimulated patch**

A wearable patch with integrated electronics enables precise regulation of drug delivery using electrical signals. The microprogrammed control unit (MCU) ensures accurate management of drug administration. For instance, Xu et al. Developed a software-controlled wearable device designed to diagnose and treat wound infections while promoting wound healing .An NFC antenna was incorporated into a flexible printed circuit to control the drug-infused adhesive patch and biosensing components. Utilizing a near-field coil, the device could be operated and powered remotely. The sensing module monitored infection site parameters such as temperature, pH levels, and uric acid levels. Hydrogel materials were also found suitable for constructing electrically stimulated wearable devices.Apart from wireless charging, self-powering serves as an alternative approach, addressing issues such as the bulky power component and limited capacity that could otherwise impact the performance of wearable electronics.The benefits of self-powered technology, where motion generates electrical power for active delivery, have the potential to facilitate the downsizing of wearable devices.

- **Ultrasound-stimulated patch**

The ultrasound-responsive patch includes components sensitive to either low-frequency (<100 kHz) or high-frequency ultrasound (>100 kHz and MHz range). Since the 1990s, ultrasound has been demonstrated to enhance the penetration of substances into cells and tissues primarily through thermal and non-thermal mechanisms. Thermal effects arise from the absorption of acoustic energy in tissues, while non-thermal effects are produced by ultrasound pressure, acoustic streaming, microjets, and cavitation.In wearable patches, ultrasound fields can be generated by separate removal devices or integrated components, facilitating the controlled release of drugs from reservoirs.The advanced use of focused ultrasound allowed for precise control over the penetration area. Additionally, the system monitored skin penetration through ultrasonic imaging, ensuring the release rate was carefully managed to prevent skin damage. In vaccine delivery, the device offered different penetration patterns with aligned micro holes, allowing for adjustable vaccine dosages by modifying these patterns.

- **Light-stimulated patch**

The light-responsive system gains advantages from precise management of light intensity and coverage, ensuring accurate dosage. NIR light is favoured due to its ability to penetrate deeply into skin tissue with minimal tissue damage.

Transdermal immunotherapy [31]

Immunotherapy approaches aim to improve the immune system of the recipient and vary in how they work. They are typically categorized as passive (adoptive) or active immunotherapies based on their ability to trigger memory immune responses. Active immunotherapy directly stimulates an immune response, leading to immune memory and a sustained reaction. These responses can be nonspecific, involving general immune system activation through cell signaling molecules, or specific, which involves generating immune responses targeted against particular antigens.Administering antibodies directly does not activate the immune system or induce immune memory formation. This approach is termed passive immunotherapy.

The physicochemical characteristics of therapeutic agents play a crucial role in transdermal immunotherapy. The route of administration significantly influences the bioavailability of these agents. Transdermal delivery offers a convenient, non-invasive, and painless method for administering medications.It is an effective method for systemic delivery as it avoids the digestive system and shields drugs from initial metabolism in the liver.

Moreover, it enables direct access to the immune system, allowing immunotherapeutic agents like proteins, peptides, and cancer vaccines to reach their target cells without undergoing degradation by enzymes found in the gastrointestinal tract and systemic circulation.The dissolution of the topically applied drug is essential for its diffusion, as most drugs traverse the skin through passive diffusion. Drug transport can occur through intercellular, transcellular, and/or appendage pathways such as hair follicles and sweat glands.

GENERAL CLINICAL CONSIDERATIONS IN THE USE OF TDDS:[17]

Patients should be advised to rotate the application site regularly to allow the skin to restore its natural permeability and prevent irritation.

- The transdermal drug delivery system (TDDS) should be applied to clean, dry skin that is generally free from hair and not oily, inflamed, irritated, or broken. Moist or wet skin can expedite the permeation time of the drug.

- The presence of oily skin can reduce the patch's ability to adhere. If hair is present at the application site, it should be trimmed carefully, avoiding wet shaving or the use of depilatory agents, as they can remove the outer layer of skin (stratum corneum) and impact the rate and amount of drug absorption.
- Avoid applying skin lotion at the site of application, as lotions can change the skin's hydration level and modify the drug's partition coefficient.
- Patients should refrain from physically manipulating the TDDS, as this can compromise the system's integrity.
- Remove the protective backing carefully without touching it with your fingertips. Press the TDDS firmly against the skin using the heel of your hand for approximately 10 seconds.
- Place the TDDS on a location where it will not be rubbed off by clothing or movement. It should remain on during showering, bathing, or swimming.
- A TDDS should be worn for the entire duration specified in the product's instructions before removing and replacing it with a new system.
- After applying a TDDS, the patient or caregiver should wash their hands. Avoid rubbing the eyes or touching the mouth while handling the system.
- If the patient experiences sensitivity or cannot tolerate a TDDS, or if excessive skin irritation occurs, they should seek reassessment.
- To prevent skin irritation, it's crucial to apply the transdermal patch to a different site each day.
- After removal, a used TDDS should be folded with the adhesive layer together to prevent reuse. Dispose of the used patch safely, ensuring it is out of reach of children and pets.

LIMITATIONS FOR SELECTION OF TDDS:[17]

Not all drugs can be administered via transdermal delivery due to specific PhysicoChemical properties they must possess. Drugs requiring high plasma levels, causing skin irritation or contact dermatitis, having high molecular weight, or undergoing metabolism through the skin are unsuitable for this route. The skin's efficient barrier limits the number of drugs that can be administered transdermally to those requiring low doses.

Conclusion

Transdermal drug delivery offers a painless and convenient method for administering regular doses of various medications, potentially enhancing drug absorption with minimal complications and side effects. It is also cost-effective and user-friendly.These devices are categorized into passive and active systems based on material properties, design principles, and integrated components. Passive systems include hydrogel patches and MN patches, while active systems respond to stimuli such as light, electric fields, ultrasound, and others.These wearable transdermal drug delivery (TDD) devices are used in treating diabetes, skin diseases, birth control, wound healing, and more. Despite exciting advancements, there are significant opportunities for enhancing TDD technology, such as evaluating side effects, efficacy, and safety to optimize delivery systems.The development of transdermal delivery for psychotropic medications has made it possible to personalize therapy for patients by adjusting treatment duration, reducing first-pass metabolism and the risk of drug interactions, and lowering the chance of gastrointestinal irritation. Maintaining steady-state absorption through the skin offers more consistent drug exposure during dosing, eliminating the variability of plasma drug peaks and troughs. This reduction in peaks and troughs improves medication effectiveness and reduces the occurrence of side effects.Long-acting patches need less frequent administration, potentially reducing disruptions to daily routines and enhancing patient adherence. Despite the numerous benefits of transdermal drug delivery, there are drawbacks to consider. Patches can lead to localized skin irritation, typically have a slower onset of action compared to oral or injectable forms, and may detach due to inadequate skin adhesion.Upcoming advancements in delivery technologies have the potential to increase the variety and extend the clinical application of psychotropic drugs. This would enable clinicians to address challenges such as the low bioavailability of oral medications, the discomfort and inconvenience of injections, and the limited options for controlled-release formulations.Exciting new concepts in transdermal drug delivery systems (TDS) are emerging, driven by the exchange of knowledge and collaboration across diverse fields such as material science, engineering, and pharmaceutical formulations. These efforts aim to integrate these technologies into advanced, long-acting, and cost-effective transdermal delivery products. Despite facing specific challenges, dedicated initiatives are actively addressing these obstacles to fully harness the potential of long-acting transdermal drug delivery in the near future.

Despite its promising benefits, transdermal delivery can lead to skin issues such as contact dermatitis, rashes, erythema, or local irritation due to ingredients in the patch like excipients, adhesives, or drugs. Additionally, the skin varies in its barrier function from person to person, with age, and even across different sites on the same individual.Therefore, selected biomaterials must exhibit good biocompatibility and compatibility with immunotherapeutic agents such as antigens, chemical agents, cells, and adjuvants.Combining transdermal immunotherapy with personalized medicine and conducting comprehensive animal and clinical trials can address the variability in skin barrier function. Overall, research indicates that transdermal immunotherapy holds significant promise for advancing cancer and infection treatments, representing a next-generation approach with transformative potential in clinical practice.

References

1) Panner Selvam R, Anoop Kumar Singh, Sivakumar T. Transdermal drug delivery systems for antihypertensive drugs –A review. IJPBR. 2010;1(1):1-8.

2)Kakkar A, Gupta PA. Gelatin Based Transdermal Therapeutic System. Indian Drugs. 1991;29(7):308-315.

3)Bagherifard S, Tamayol A, Mostafalu P, Akbari M, Comotto M, Annabi N, et al. Dermal patch with integrated flexible heater for on Demand drug delivery. Adv Healthc Mater. 2016;5:175-84.

4)Amjadi M, Sheykhansari S, Nelson BJ, Sitti M. Recent advances in Wearable transdermal delivery systems. Adv Mater. 2018;30:1704530.

5)Kamei, Kanamori T, Yamamoto Y, Edirippulige S. The use of wearable Devices in chronic disease management to enhance adherence and improve Telehealth outcomes: a systematic review and meta-analysis. J Telemed Telecare. 2022;28:342-359

6)Mohammad Dahri,Nima Beheshtizadeh ,Nasrin Seyedpour ,Amin Nakhostin-Ansari,Faezeh Aghajani, Simin Seyedpour ,Moein Masjedi, Fatemeh Farjadian, Reza Maleki , Khosro Adibkia Biomaterial-based delivery platforms for transdermal immunotherapy Int J Pharm. 2023;612:121237.

7)Maheswary T, Nurul AA, Fauzi MB. The insights of microbes' roles in Wound healing: a comprehensive review. Pharmaceutics 2021;13:981.

8)R. Dehez, Scar Massage and Treatment, in: G. Mespli´E (Ed.), Hand and Wrist Therapy: Clinical Examination and Advanced Rehabilitation Tools, Springer International Publishing, Cham, 2022, pp. 81–98.

9) N. Kumar, A. Vyas, S.K. Agnihotri, N. Chattopadhyay, M. Sachdev, Small Secretory proteins of immune cells can modulate gynecological cancers, Semin. Cancer Biol. (2022).

10)W.R. Heath, F.R. Carbone, The skin-resident and migratory immune system in Steady state and memory: innate lymphocytes, dendritic cells and T cells, Nat. Immunol. 14 (10) (2013) 978–985.

11)F.O. Nestle, P. Di Meglio, J.-Z. Qin, B.J. Nickoloff, Skin immune sentinels in Health and disease, Nat. Rev. Immunol. 9 (10) (2009) 679–691.

12)H.C. West, C.L. Bennett, Redefining the role of langerhans cells as immune Regulators within the skin, Front. Immunol. 8 (2018) 1941.

13)C.R. Black, V. Goriainov, D. Gibbs, J. Kanczler, R.S. Tare, R.O. Oreffo, Bone tissue Engineering, Curr. Mol. Biol. Rep. 1 (3) (2015) 132–140.

14)R. Yu, H. Zhang, B. Guo, Conductive biomaterials as bioactive wound dressing for Wound healing and skin tissue engineering, Nano-Micro Lett. 14 (1) (2022) 1–46.

15)L. Sun, W. Liu, Zhang L-j. The role of toll-like receptors in skin host defense, Psoriasis, and atopic dermatitis, J. Immunol. Res. 2019 (2019).

16)Jiahui He,Yuyue Zhanga,y, Xinge Yua,b, Chenjie Xu a review on Wearable patches for transdermal drug delivery,Acta Pharmaceutica Sinica B 2023;13(6):2298e2309

17)D. Prabhakar1, J. Sreekanth2, K.N. Jayaveera TRANSDERMAL DRUG DELIVERY PATCHES: A REVIEW Journal of Drug Delivery & Therapeutics; 2013, 3(4), 213-221

18)Jain N. K, Controlled and Novel Drug Delivery, 1997, 100-115.

19)Nikhil Sharma, Geta Agarwal, Rana A.C, A Review Transdermal Drug Delivery System a tool for Novel Drug Delivery System, IJDDR, 2011, 3 (3), 70.

20)Mohamed Aqil, Yasmin Sultana and Asgar Ali, Matrix Type Transdermal Drug Delivery Systems of Metoprolol Tartrate, Invitro Characterization, Acta Pharm, 2003,53, 119-125.

21)Basubramanian V, Iyer and Ravindra C, Vasavada, Evaluation Of Lanolin alcohol flims and Kinetics of Triamcinolone Acetonide Release, Journal of Pharmaceutical Sciences, 1979, 68(6),119-125.

22)Sharma Teja, Rawal Gaurav, Transdermal Therapeutic Systems, An overview, International Journal of Pharmaceutical & Biological Archives, 2011, 2(6),1581-1587.

23)Wiechers J, Use of Chemical Penetration Enhancers in Transdermal Drug Delivery-Possibilities and Difficulties, Acta Pharm, 1992, 4, 123.

24)Manvi F.V, Dandagi P.M, Gadad A.P, Mastiholimat V.S and Jagdeesh T, Formulation of Transdermal Drug Delivery System Of Ketotifen Fumarate, IJPS, 2003, 65(3), 239-243.

25)Shalu Rani, Kamal Saroha, Navneet Syan, Transdermal Patches A successful tool in Transdermal Drug Delivery System: An Overview, Der Pharmacia Sinica, 2011, 2 (5),17-29

26)Azhar Ahmed, Nirmal Karki, Rita Charde, Manoj Charde, Bhushan Gandhare, Transdermal Drug Delivery Systems, An Overview, International Journal of Biomedical and Advance Research, 2011, 02(01),38-56.

27)Parthasarathy G, Bhaskar reddy K and Prasanth V.V, Formulation and Characterization of Transdermal Patches of Naproxen with various polymers, International Journal of Comprehensive Pharmacy , 2011, 6 (07), 1-3.

28)Shalu Rani, Kamal Saroha, Navneet Syan, Pooja Mathur, Transdermal Patches A Successful Tool In Transdermal Drug Delivery System: An overview, Der Pharmacia Sinica, 2011, 2 (5), 17-29.

29)Swarnlata Sonl and Vinod K, Dixit, Transdermal Penetration Enhancers, Categorization, Indian Drugs, 1992, 29(11), 465-471.

30)Tanu Bhargava, Current trends in NDDS with special reference To NSAIDS, International Journal of Pharma and Bio Sciences, 2011, 2, 92-114

31)Mohammad Dahri,Nima Beheshtizadeh, Nasrin Seyedpour,Amin Nakhostin-Ansari ,Faezeh Aghajani ,Simin Seyedpour,Moein Masjedi,Fatemeh Farjadian,Reza Maleki, Khosro Adibkia A,Biomaterial-based delivery platforms for transdermal immunotherapy ,Biomedicine & Pharmacotherapy 165 (2023) 115048