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Transdermal Drug Delivery System

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ABSTRACT

Various non-invasive administrations have recently emerged as an alternative to conventional needle injections. A transdermal drug delivery system (TDDS) represents the most attractive method among these because of its low rejection rate, excellent ease of administration, and superb convenience and persistence among patients. TDDS could be applicable in not only pharmaceuticals but also in the skin care industry, including cosmetics. Because this method mainly involves local administration, it can prevent local build-up in drug concentration and nonspecific delivery to tissues not targeted by the drug. However, the physicochemical properties of the skin translate to multiple obstacles and restrictions in transdermal delivery, with numerous investigations conducted to overcome these bottlenecks. In this review, we describe the different types of available TDDS methods, along with a critical discussion of the specific advantages and disadvantages, characterization methods, and potential of each method. Progress in research on these alternative methods has established the high efficiency inherent to TDDS, which is expected to find applications in a wide range of fields.

Keywords: Transdermal drug delivery, Skin, Active/passive method, Characterization

INTRODUCTION

A new drug delivery system's TDDS is a crucial component. Numerous compounds have been applied to human skin as cosmetics and healing agents since life first evolved on Earth. The skin was first employed as a delivery method for long-term medication in the tenth century. One of the most successful and dependable methods of drug administration is transdermal. One of the most effective and cutting-edge methods for delivering medications is transdermal.**[2]**

Compared to the previous two decades, innovation in the field of medication delivery is occurring significantly more quickly. enhanced patient compliance Effectiveness is a crucial component of modern drug delivery systems**.[3**]

The term "transdermal drug delivery system" refers to a method of delivering a medicine's active components through the skin. The most efficient route for a medication to be absorbed and enter the circulatory system is through the skin.[4] Many medications are administered orally these days, but the first-pass metabolism makes the dose higher and the effects of the drug weaker. Transdermal medication delivery systems are therefore created to decrease the number of dosages while increasing the effectiveness and bioavailability of the medicament**.[5]** Transdermal drug delivery is the term used to describe the process of delivering a drug through the skin to have a systemic impact. and is unique from conventional topical medication administration.**[6]**

TDDS OF Advantage and DisadvantageAdvantage [7]

- Transdermal medication provides a consistent infusion of the drug over an extended period, helping to prevent the negative side effects and therapeutic failure typically associated with sporadic dosage.
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- Patients who are unable to take oral dosage forms, such as patients who are vomiting, should consider an alternative route of administration
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- First-pass metabolism should be avoided since it skips the liver
  They can be self-administered and are non-invasive, therefore parenteral therapy is not necessary.

Disadvantage [8]

- Some patients get contact dermatitis from one or more system components at the application site,

requiringcessation.

- Because of the permeability of the skin and the inherent restrictions on drug entrance imposed by it, only strong medicines are appropriate candidates for transdermal patches.
- Some medications, like the transdermal scopolamine patch used behind the ear, are painful.
- Long-term adherence is challenging.

Limitations

- The limitations of TDDS can be partially solved by cutting-edge techniques like Iontophoresis, electroporation, and ultrasound.
- Limited to strong drugs and long lag times.
- Not suitable for a drug, which doesn't possess a favourable, o/w partition coefficient
- The stratum cornea is typically difficult to penetrate by heavy drug molecules (>500 Da)
- medications with a very low or high partition coefficient are unable to enter the bloodstream.
- reduced permeability of the skin
- Skin rash and allergy symptoms**.[9] [10]**

Types of Transdermal Drug Delivery System [11] [12]Single-layer drug-in-adhesive:-
The medication is also present in this system's sticky layer. In this kind of patch, the adhesive layer is also in charge of the drug release in addition to holding the other layers and the overall system to the skin. There is the lining of a temporary liner and a backing on the exterior of the adhesive layer.

multi-layer drug in adhesive:-
In that both sticky layers are in charge of the drug's release, it is identical to the single-layer method in that regard. However, the multilayer system differs in that it includes an additional layer of drug-inadhesive, typically separated by a membrane (though not always). A permanent backing and a temporary liner layer are also present around this patch Figure 1].

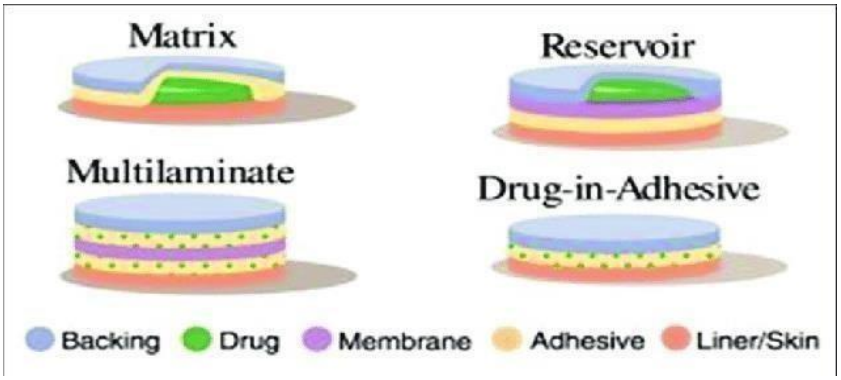


Figure 1: Representative designs of transdermal drug delivery system

Reservoir:-
The medication reservoir is retained in this system sandwiched between a backing layer and a membrane that regulates the flow rate. And the medicine is released through a membrane with a microporous rate control. The drug may be disseminated in a solid polymer matrix or as a solution, suspension, or gel in the reservoir compartment**.**

Matrix:-
A] Drug-in-Adhesive System: To create a drug reservoir, the drug is dispersed in an adhesive polymer, and the medicated polymer adhesive is then disseminated by solvent casting or, in the case of hot-melt adhesives, by meltingthe adhesive on top of an impervious backing layer.

B] Matrix-Dispersion System: In this system, a hydrophilic or lipophilic polymer matrix evenly disperses the medication. And in a compartment made from a drugimpermeable backing layer, this containing polymer and drug are attached on to an occlusive base plate. In this approach, the adhesive is applied around the perimeter rather than directly to the face of the drug reservoir to create an adhesive rim.

Penetration Through Skin:-
Passive skin dispersion of the compounds occurs during percutaneous absorption. The appendageal route and the epidermal route are two diffusional pathways that molecules can use to pass through normally undamaged skin

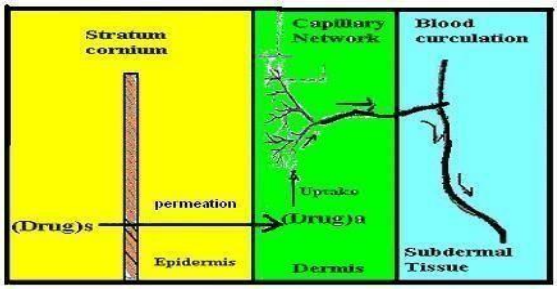
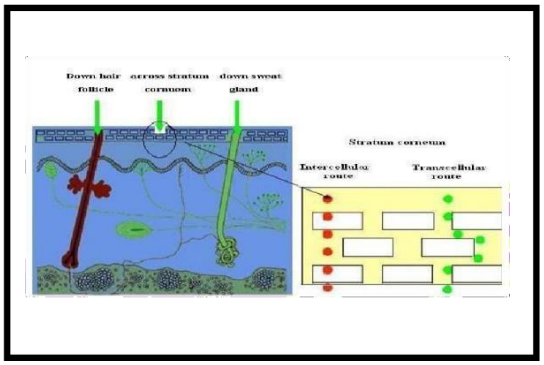


Figure 2: Multilayer skin model demonstrating the transdermal medication delivery sequence

There are three key routes that a medicinal molecule can enter the intact stratum corneum: through skin appendages (shunt paths), intercellular lipid domains, or a transcellular pathway.



(Figure 3). Transport occurs by sweat glands and hair follicles with accompanying sebaceous glands along theappendageal route

These paths are referred to as "shunt" routes because they avoid penetrating the stratum corneum. Due to its tiny Size roughly 0.1% of the total skin area this pathway is regarded as being of minor significance.**[13]**

A medicinal molecule can penetrate the intact stratum corneum in three important ways: by skin appendages (shunt pathways), intercellular lipid domains, or a transcellular route

Epidermal rout [14]Transcellular
This method for drug delivery comes from corneocytes, which have highly hydrated keratin and so create a hydrophilic pathway. Lipids encircling corneocytes connect these cells. Therefore, medication needs to go through several partitioning and diffusion processes. It is the pathway that different types of medications employ the most frequently. Drugs administered via the transcellular route pass through the cytoplasm of the cells' matrix. Hydrophilic medicines are appropriate for this approach. The stratum corneum's corneocytes allow the medication to flow through. The highly hydrated keratin offers a water-based route for hydrophilic medications. The medicine must pass through several partitioning and diffusion processes in order to enter the cell matrix.

Intercellular rout
Intercellular path As the name suggests, the medication diffuses across the continuous lipid matrix present between the cells in the intercellular channel. The convoluted shape of corneocytes is what gives this route its barrier properties, and the drug must pass through the alternating lipid and aqueous domain by partitioning into the lipid bilayer and diffusing to the inner side. This pathway is best suited for uncharged lipophilic medicines because water must travel 50 times farther along it.

trans follicular route
The trans follicular route is the quickest route for a drug to take in order to get to the systemic circulation, which offers a huge surface area for drug dispersion. Numerous sweat glands, oil glands, hair follicles, and pores are present on the skin, with their ducts leading to the skin's outer surface. Drugs can be transported through these ducts, which provide a continuous path across the stratum corneum, but they are affected by a number of variables, including glandular secretion, the nature, and the volume of that secretion, among others. However, the trans appendageal pathway only accounts for 0.1% of the total skin surface and hence makes a small contribution.

Components of TDDS • POLYMER MATRIX /RESERVOIR

The foundation of TDDS is polymers, which control how quickly a drug leaves the body. Medication can be dispersed in an artificial polymer base that is liquid or solid to create a polymer matrix. The polymers used in TDDS are chemically and biologically compatible with the medication as well as other system additives including penetration enhancers and PSAs. They must also be secure and safe, and they must deliver a drug consistently and effectively for the duration of the product's stated shelf life. **[15]**

Baking layer

It protects the patch from the outer environment. Drugs and penetration boosters shouldn't be able to pass through the backing layer. It does the function of holding the entire system and protects the drug reservoir from the atmosphere. The commonly used backing materials are polyesters, aluminized polyethylene terephthalate, and siliconized polyethylene terephthalate.

Useful considerations while applying transdermal patch:-

- The area of skin where the patch will be put must be thoroughly cleaned. The patch must not be cut because doing so compromises its ability to distribute drugs.
- Care should be given when applying or removing the patch because anyone handling the patch can absorb the medicine from the patch. Before applying a new patch, the old patch should be removed from the location.
- The patch needs to be applied precisely to the administration site**.[16]**

Linear:

Release linear reduces contamination and drug loss during storage by stopping it from migrating into the sticky layer. The linear should, however, adhere to strict specifications regarding chemical inertness and permeability to the medication, penetration enhancer, and water because it is in close contact with the deliverysystem. **[17]**

MATERIAL AND METHODS

Modern techniques of transdermal drug delivery system Iontophoresis: -

- It entails applying a little amount of current (a few mill amperes) to the skin in a specific area while keeping the electrode in touch with the formulation that needs to be applied
- Iontophoretic delivery of lidocaine is regarded as a wonderful strategy for the rapid onset of anesthesia, and pilocarpine delivery can be used as an example to induce perspiration in the diagnosis of cystic fibrosis.
- Dexamethasone, iodine, chlorine, acetic acid, and hyaluronidase are other examples. **[18]**

Iontophoresis is a process that uses a low electrical current to push a charged medication molecule through the skin (Pathak et al2006). An anode (+) in a reservoir containing the positively-charged medication in a solution and a cathode (-) in a negatively-charged salt solution make up a conventional iontophoresis device. The electrodes generate a small electrical current when voltage is supplied, which repels positively charged medication molecules through the skin and into the bloodstream. The system's advantage is that medications are delivered under control and can be turned on and off as needed. Irritation and pain put a limit on the system, which lowers the drug's dose. Currently, it is used to give lidocaine quickly as a local anesthetic**. [19]**

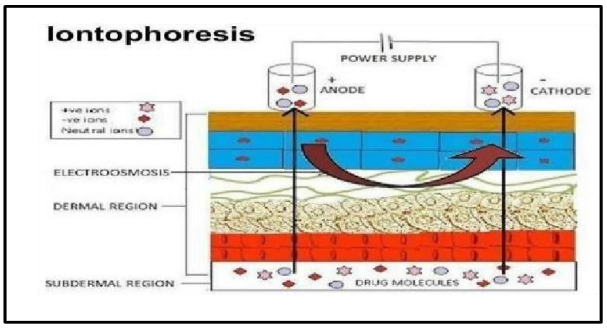


Figure: Iontophoresis

Figure 4: Iontophoresis

Electroporation :

- Electroporation is the process of applying high-voltage pulses to the skin to cause disruption. The most often used parameters are high voltages (100 V) and short treatment times (milliseconds).
- It is hypothesized that the development of temporary pores during the electro part is what causes the increase

in skin permeability.

- The method has been utilized effectively to increase the skin permeability of molecules with various lipophilicity and size properties (i.e., small molecules, proteins, Peptides, oligonucleotides).
- Examples are the Gene Pulse and BT Press Electroporation Buffers. **[20]**

Successful applications of the technology include accelerating the permeability of molecules with varying lipophilicity and size. (i.e., proteins, oligonucleotides, and tiny molecules), as well as biopharmaceuticals with molecular weights larger than 7 Kad. Electrical factors such as waveform (exponential decay or square wave), voltage (50-1500 V), duration (a few s to ms), and the space between pulses are used to describe electrical pulses (a few seconds to a minute). Depending on the needs of the experiment and the intended use of the electroporation technique in medicine, these electrical parameters can be optimized. According to research by Mori, two crucial elements in electroporation are the electric field and the voltage's temporal profile (or AUCof voltage against time). increase the effectiveness of electroporation, and that the effectiveness can be optimized by the electrodes' shapes in addition to electroporation's application settings **[21]**

Ultrasounds:

- In these methods, the medicinal material is combined with a coupling agent (often a gel, cream, or ointment) to facilitate the transmission of ultrasonic energy from the system to the skin.
- The lipids in the stratum cornea must be ruptured in order for the medication to get across a biological barrier.

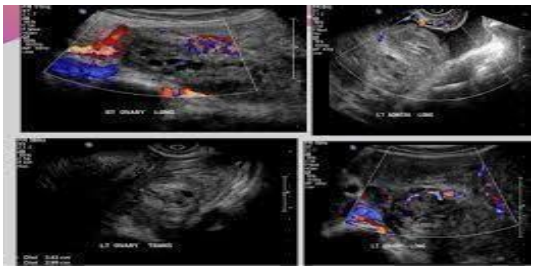


Figure 5 : ultrasound

The major medicinal ingredient is combined with a coupling agent (often a cream or gelor ointment), which results in the transfer of ultrasonic energy from the system to the skin. This procedure breaks down the lipids in SC, allowing the medication to pass over a biological barrier. **[22]**

Microporation:

Microporation is the process of increasing skin permeability by piercing only the stratum cornea using tiny needles that are applied to the skin. • Micro needles have a height of 10 to 200 m and a width of 10 to 50

m. Since microneedles do not activate the patient's nerves, they do not cause pain or suffering. Typically, they are hollow metal needles with medication fillings or solid silicon projections covered in drugs. **[23] [24]**

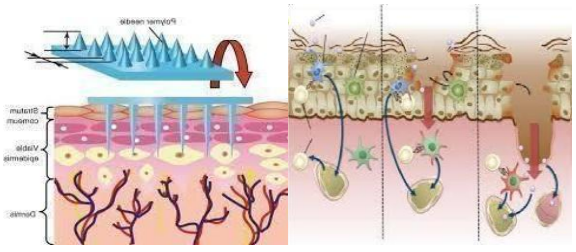


Figure 6 : microporation

Skin abrasion:

- In this approach, the top layers of the skin are directly removed or disturbed, making it more easier for medications to penetrate the skin when applied topically.
- there are also certain devices that cure acne, scars, hyperpigmentation, and other skin imperfections by using procedures doctors utilise for superficial skin resurfacing (such as microdermabrasion).
- Examples include Ranisilver spray, Povidone Iodine, and ACERIN Protect liquid. **[21][22]**

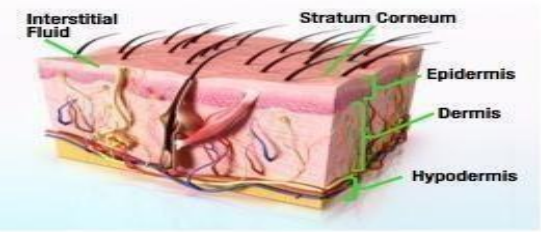


Figure 7 : Skin Abrasion

CONCLUSION

Transdermal drug delivery offers compelling opportunities to address the low bioavailability of many oral drugs; the pain and inconvenience of injections; and the limited controlled release options of both. Third generation physical enhancers (such as ultrasound, thermal ablation, and micro needles) could enable transdermal delivery of macromolecules and vaccines. Second generation chemical enhancers and iontophoresis are expanding delivery capabilities for small molecules, building on the successes of first generation transdermal patches. The field has reached a new level of capabilities that position transdermal drug delivery for an increasingly significant influence on medicine as a result of all these scientific and technological advancements that allow targeted disruption of stratum cornea while safeguarding deeper tissues. There have been a tonne of studies conducted on TDDS. Recent research has focused on changing the chemistry of the medication and reservoir as well as the delivery module to introduce newer pharmaceuticals using this system. It is also being researched how different devices can boost the drug's penetration and rate of absorption. However, the application of TDDS has been restricted because of a number of drawbacks, including the inability to deliver big drug molecules, the inability to administer high doses, the drug's slower rate of absorption, skin irritation, etc. However, the usage of TDDS is currently expanding quickly because to the ongoing, regular innovation of new devices and new medications that can be suppliedvia this system.

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