

Transdermal Drug Delivery System – A New Approach for Drug Delivery

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Abstract: Transdermal drug delivery system provides a means to sustain drug release as well as reduce the intensity of action and thus reduces the side effects associated with its oral therapy. Transdermal drugs are self contained, discrete doses form. It delivers the drug through intact skin at a controlled rate into the systemic circulation. Delivery rate is controlled by the skin or membrane in the delivery system. A sophisticated complex drug delivery system difficult to formulate. It requires specialized manufacturing process / equipment. Formulated to meet the specific biopharmaceuticals and functional characteristics. The materials of construction, configuration and combination of the drug with a proper cosolvent, excipient, penetration enhancer and the membranes are carefully selected and matched to optimize properties and drug delivery requirements. Transdermal drug offers controlled release of drug into the patient. It enables a steady blood level profile, resulting in reduced systemic side effects and sometimes, and improved efficacy over other dosage form. The main objective of transdermal drug delivery system is to deliver drugs into systemic circulation through skin at predetermined rate with minimal inter and intra patient variation.

Index Terms: Transdermal patch, transdermal drug delivery system, controlled release, TDDS, systemic circulation, polymer.

INTRODUCTION:

The FDA approved the first transdermal patch of scopolamine for motion sickness in 1979, and the second patch of nitroglycerine in 1981. Several patches for transdermal delivery are now available on the market, including clonidine, nicotine, hormones, testosterone, and fentanyl. Technology innovation continues to grow at the fastest rate, making the field of innovation research and product development productive and dynamic. Transdermal drug technology experts are still looking for novel ways to deliver larger molecules in therapeutic quantities in a safe and effective manner, in order to overcome the challenges of the oral route. The transdermal delivery system refers to the method of delivering the drug's active ingredients via the skin. The absorption of the drug and its entry into the circulatory system occurs through the skin, which is an effective medium. The objective of any drug delivery system is to provide an effective therapeutic amount of drug to the desired site of action in the body to accomplish promptly and sustain the desired drug concentration throughout the dose duration. For decade, oral route has been most common drug delivery form and about 74 % of drugs are taken orally but still is found not as effective as anticipated. Even though oral administration has notable advantage of easy administration, it also carries significant drawback - namely poor bioavailability due to hepatic metabolism (first pass metabolism) and the inclination of yield rapid blood level spikes (both high and low) . To overcome these hurdles, there was a burning need for understanding/ development of new drug delivery system. Which can improve the therapeutic efficacy and safety of drugs by more precise spatial and temporal placement within the body there by reducing both the size and number of doses and also increasing its effectiveness with optimum dose concentration to achieve these goals and improve such characters transdermal drug delivery system was emerged.

❖ DEFINITION:

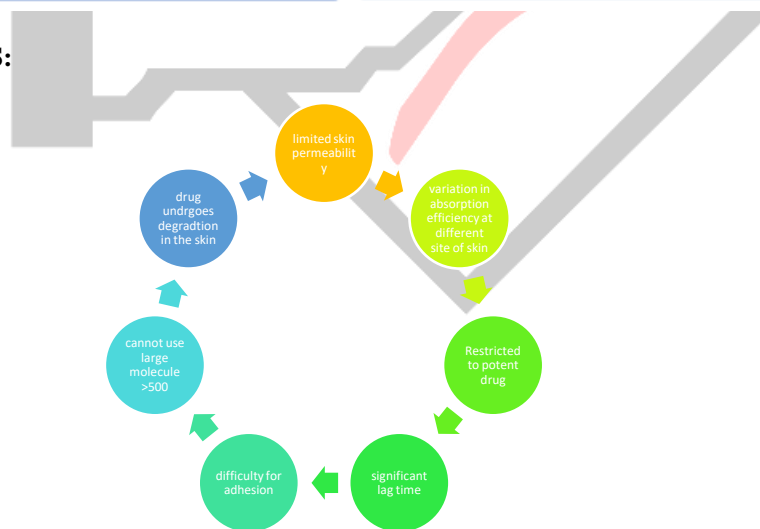
Transdermal drug delivery system can be defined as the topically administered medications in self – contained; discreet dosage forms of patches which when applied to the skin deliver the drugs through the skin portal to systemic circulation at predetermined and controlled rate over a prolonged period of time in order to increase the therapeutic efficacy and reduced side effects of drug. TDDS maintains drug concentration within the therapeutic window for prolonged period of time ensuring that drug level neither fall below the minimum effective concentration nor exceed the maximum effective concentration[1].

ADVANTAGES:

DISADVANTAGES:



❖ **LIMITATIONS:**



❖ **IDEAL PROPERTIES OF TDDS:**

Table 1: Ideal properties of TDDS

Self life	Should be up to 2.5 years
Patch size	Should be less than 40 cm ²
Dose frequency	Once a daily once a week.
Appearance	Should be clear or white color
Packaging properties	Should be easily removable of release liner
Skin reaction	Should be non-irritating
Release properties	Should have consistent pharmacokinetic and pharmacodynamic profiles over time

❖ **IDEAL PROPERTIES OF DRUG FOR TDDS:**

Table 2: Ideal properties of drug for TDDS

1	Dose	Should be low
2	Molecular weight	should be 10 or less
3	Partition coefficient	Log p between 1 and 3
4	Skin permeability coefficient	Should be less than 0.5×10^{-3} cm / hr
5	Skin reaction	should be non-irritating
6	Oral bioavailability	should be low
7	Therapeutic index	should be low
8	Concentration	minute
9	PH of saturated aqueous solubility	5 - 9
10	Dose deliverable	< 10 mg / day

❖ **PATCH COMPONENT:**

Sr. No	Components	Function
1	Backing	Protects the patch from the outer environment, is impermeable to the transdermal patch components and provides the patch with it flexibility. It is made of elastomers (polyolefin oils, polyester, polyethylene. Polyvinyliden chloride and polyurethane) and is preferably non breathable (by adding aluminium foil)

2	Membrane	controls the release of the drug. It is made of natural or Synthetic polymer or synthetic elastomers, and its thickness ranges from about 2 mm to 7mm
3	Adhesive	It binds the components of the patch together and the patch to the skin. It is composed of silicone, rubber, polyvinyl acetate or polyisobutylene. depending on the skin adhesion properties desired. It may contain permeation enhancers (solvents, surfactants or miscellaneous chemicals) to promote skin permeability by altering its structure
4	Liner	The release liner has to be removed before the application of transdermal system, and it prevents the loss of the drug that has migrated into the adhesive layer during storage. It also helps to prevent contamination. It is composed of a base layer, which may be no occlusive or occlusive, and a release coating layer made of silicon or Teflon. Other materials include polyesters, foil. Mylar and metallized laminates.
5	Drug	drug solution in direct contact with release liner
6	Rate controlling membrane	Rate controlling membranes in transdermal devices govern drug release from the dosage form. Membranes made from natural polymeric material such as chitosan show great promise for use as rate controlling membranes. Recently composite poly-2-hydroxyethyl methacrylate (PHEMA) membranes have been evaluated as rate controlling barriers for transdermal application.
7	Penetration enhancer	These are the compounds, which promote skin permeability by altering the as a barrier to the flux of a desired penetrant and are considered as an integral part of most transdermal formulations. To achieve and maintain therapeutic concentration of drug in the blood, the resistance of skin to diffusion of drugs has to be reduced in order to allow drug molecules to cross skin and to maintain therapeutic levels in blood. They can modify the skin's barrier to penetration either by interacting with the formulation that applied or with the skin itself. The penetration enhancer should be pharmacologically inert , non toxic. Non allergenic, non-irritating and ability to act specifically, reversibly and for predictable duration. It should not cause loss of body fluids, electrolytes or other endogeneous materials.
8	Polymer matrix	Polymer is an integral and foremost important component of transdermal drug delivery systems. Different classes of polymeric materials have been used to achieve rate controlled drug delivery The mechanism of drug release depends upon the physicochemical properties of the drug and polymer used in the manufacture of the device.

❖ **TYPES:**

1. Single-layer Drug-in-Adhesive

The adhesive layer of this system also contains the drug. In this type of patch the adhesive layer not only serves to adhere the various layers together, along with the entire system to the skin, but is also responsible for the releasing of the drug. The adhesive layer is surrounded by a temporary liner and a backing [2].

2. Multi-layer Drug-in-Adhesive

The multi-layer drug-in adhesive patch is similar to the single-layer system in that both adhesive layers are also responsible for the releasing of the drug. The multi-layer system is different however that it adds another layer of drug-in-adhesive, usually separated by a membrane (but not in all cases). This patch also has a temporary liner-layer and a permanent backing[2].

3. Reservoir

Unlike the Single-layer and Multi-layer Drug-in adhesive systems the reservoir transdermal system has a separate drug layer. The drug layer is a liquid compartment containing a drug solution or suspension separated by the adhesive layer. This patch is also backed by the backing layer. In this type of system the rate of release is zero order[2].

4. Matrix

The Matrix system has a drug layer of a semisolid matrix containing a drug solution or suspension. The adhesive layer in this patch surrounds the drug layer partially overlaying it.[2]

5. Vapour Patch

In this type of patch the adhesive layer not only serves to adhere the various layers together but also to release vapour. The vapour patches are new on the market and they release essential oils for up to 6 hours. The vapour patches release essential oils and are used in cases of decongestion mainly. Other vapour patches on the market are controller vapour patches that improve the quality of sleep. Vapour patches that reduce the quantity of cigarettes that one smokes in a month are also available on the market.[2]

❖ **FACTORS AFFECTING TRANSDERMAL PERMEATION:**1. **Physicochemical properties of the penetration molecules**

- Partition coefficient - A lipid water partition coefficient of 1 or greater is generally required for optimal transdermal permeability. It may be altered by chemical modification without affecting the pharmacological activity of the drug
- Ph conditions - Applications of solutions whose pH values are very high or very low can be destructive to the skin. With moderate pH values, the flux of ionizable drugs can be affected by changes in pH that alter the ratio of charged and uncharged species and their transdermal permeability
- Penetrant concentration - Assuming membrane related transport, increasing concentration of dissolved drug causes a proportional increase in flux At concentration higher than the solubility, excess solid drug functions as a reservoir and helps maintain a constant drug constitution for a prolonged period of time[10].

2. **Physicochemical properties of the drug delivery system**

- Release characteristics -
 - Solubility of the drug in the vehicle determines the release rate The mechanism of drug release depends on the following factors Whether the drug molecules are dissolved or suspended in the delivery Systems.
 - The interfacial partition coefficient of the drug from the delivery system to the skin tissue.
 - pH of the vehicle
- Composition of the drug delivery system -

The composition of the drug delivery systems e.g.. boundary layers, thickness. polymers, vehicles not only affects the rate of drug release. but also the permeability of the stratum corneum by means of hydration, making with skin lipids, or other sorption promoting effects e.g. benzocaine permeation decreases with PEG of low molecular weight.
- Enhancement of transdermal permeation -

Majority of drugs will not penetrate skin at rates sufficiently high for therapeutic efficacy. In order to allow clinically useful transdermal permeation of most drugs, the penetration can be improved by the addition of a permeation promoter into the drug delivery systems [10].

3. Biological factors -

- Skin condition: Acids and alkalis, many solvents like e chloroform, methanol damage the skin cells and it promotes penetration. Diseased state of patient alters the skin conditions. The intact skin is better barrier but the above mentioned conditions affect penetration.
- Skin age: The young skin is more permeable than older. Children's are more sensitive for skin absorption of toxins. Thus, skin age is one of the factors affecting - penetration of drug in TDDS.
- Blood flow: Changes in peripheral circulation can affect transdermal absorption. Regional skin sites Thickness of skin, nature of stratum corneum and density of appendages vary site to site. These factors affect significantly penetration. Skin metabolism Skin metabolizes steroids, hormones, chemical carcinogens and some drugs. So skin metabolism determines efficacy of drug permeated through the skin.
- Species differences - The skin thickness, density of appendages and keratinization of skin vary species to species, so affects the penetration. [10].

❖ CARE TAKEN WHILE APPLYING TRANSDERMAL PATCH

The part of the skin should be properly cleaned before application of patch. Cutting the patch destroys the drug delivery system therefore patch should not be cut. It should be made sure that the old patch is removed from the site before applying a new patch. Care should be taken while applying or removing the patch because anyone handling the patch can absorb the drug from the patch. The patch should be applied accurately to the site of administration [4].

CONCLUSION:

This article provides valuable information regarding the transdermal drug delivery systems and its evaluation process details as a ready reference for the research scientist who are involved in TDDS. The foregoing shows that TDDS have great potentials. Being able to use for both hydrophobic and hydrophilic active substance into promising deliverable drugs. To optimize this drug delivery system. Greater understanding of the different mechanisms of biological interactions, and polymer are required. TDDS a realistic practical application as the next generation of drug delivery system.

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