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A Basic Overview on Transdermal Drug Delivery System

Bachhav Rishikesh Shankar[1], Kale Suvarna Bhausaheb[2]

[1]Department of Pharmacology,
[2]Department of Pharmaceutical Quality Assurance,
[1,2]KCT'S R.G. Sapkal College of Pharmacy, Anjaneri, Nashik, Maharashtra, India

ABSTRACT

Transdermal drug delivery system(TDDS) are topically administered medication. Transdermal drug delivery is the system in which the delivery of one or more active ingredient of the drug to the system circulation after passing through the skin. The Transdermal drug delivery system has been one of the most innovative and sophisticated approches of drug deliveries. Transdermal drug delivery system has attracted considerable attention because of its many potential advantages, improve bioavailability, controlled absorption, flexibility of the terminating drug administration by simply removing patch to the body skin are many more potential advantages of Transdermal drug delivery, like better patient compliance, hepatic first-pass metabolism and particularly for drugs with short half-lives, reduction in systemic side effects, and sustained delivery of drug to provide steady plasma profiles, and improve therapeutic efficacy.

KEYWORDS: *TDDS, Transdermal Patches, Anatomy and Physiology, Basic Components of TDDS, Types and Application of TDDS*

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INTRODUCTION:

Any drug delivery system is aim to provide a therapeutically effective amount of active ingredient of drug to proper site in the skin and then maintained or controlled desired drug concentration. Drug are administered by various type of routes such as oral, ocular, topical, transdermal, intramuscular, intravaginal, rectal, parentral, nasal etc.[1] Among all of them, oral route is most common and popular but this route of administration have some drawback like 1st pass metabolism, enzymes, drug degradation in GIT tract due to PH etc. TDDS is also known as "patches" or skin patch. TDDS is defined as the self–contained discreate dosage forms of patches which when applied to the skin deliver the drug, throught the skin portal to systemic circulation at a predetermined and controlled rate over prolonged period of time in order to increase the therapeutic efficacy and reduced side effect of drug.[2]

In 1965 stoughton 1st conceived of the percutaneous absorption of drug substance. In 1979 FDA 1st approved the transdermal system (patches) i.e. Transderm –scop for the treatment or prevention of nausea and vomiting.[3]

ADVANTAGES OF TDDS:

- Self administration.
- Improved patient compaliance.
- Avoidance 1st pass metabolism.
- It reduces systemic drug interaction.
- It is long duration of action.[4-9]
- They are non-invasive, avoiding the inconvenience of parentral therapy.
- They can avoide GIT drug absorption difficulties covered by GIT P^H, drink, enzymatic activity, drug interaction with food and other orally administration drug.[10]
- Avoidance of GIT incompatibility.
- Enhance therapeutic efficacy.
- End of therapy is easy at any point of time.

DISADVANTAGES OF TDDS:

- The drug must have some desirable physicochemical properties for penetration throught stratum corneum and if the drug dose required for therapeutic value is more than 10mg/day, the transdermal delivery will be very difficult.
- Some patient develop contact dermatitis at the site of application from one or more of the system components, necessitating discontinuation.[11]
- Many drugs especially with hydrophilic drugs cannot pass permeates the skin to slowly may not achieve therapeutic level.
- Many problems such as like itching, edema, erythema etc. May be seen due to patches.
- Tdds is not compatible with ionic drugs
- It is not use in acute condition, only used in chronic conditions.
- High drug level in blood cannot be attained.[12]
- The main disadvantages is that high cost, local irritation, no rapid, variation in barrier function (age, site) etc.[13-17]

IDEAL PROPERTIES OF TRANSDERMAL DRUG DELIVERY SYSTEM

TABLE 1: SHOWING IDEAL PROPERTIES OF TRANSDERMAL DRUG DELIVRY SYSTEM.[18]

S. No	Properties	Comments
1.	Shelf life	Up to 2 yrs
2.	Particle size	<40cm2
3.	Dose frequency	Once in a day or once in a week
4.	Aesthetic appeal	Clear or white colour
5.	Packaging	Easy removal of release liner and min.no.of steps required to apply
6.	Skin reaction	Non irritating and non sensitizing
7.	Release	Consistent pharmacokinetic and pharmacodynamic profile over time

ANATOMY AND PHYSIOLOGY OF SKIN

Human skin comprises of three but mutually dependent tissues:

- Epidermis
- Dermis
- Hypodermis and subcutaneous layer

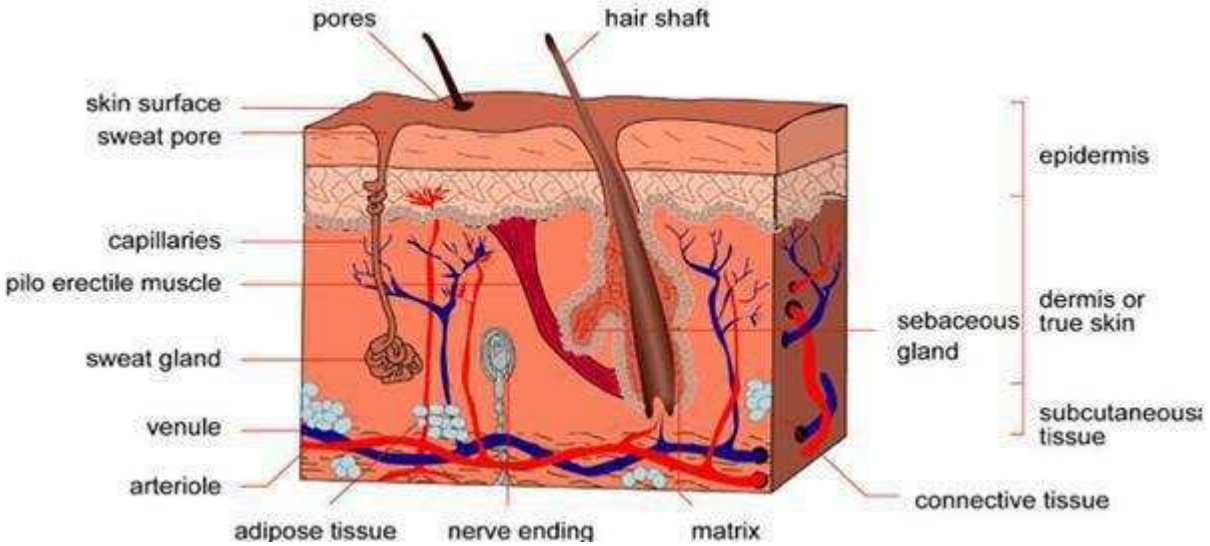

Figure 1: Cross sectional view of various epidermal layers, dermis and the subcutaneous.

EPIDERMIS

- Epidermis outer layer of the skin is made of stratified squamous epithelial cell.
- Epidermis is a thickest area in the palms and soles[19].
- Epidermis shows two main parts: 1) stratum corneum 2) stratum germinativum.
- Stratum corneum forms the outer layer 10-15 micrometer thick which consist of many layers of compacted, flattend, dehydrated keratinized cells in stratified layer.

- Keratin contains cells called as corneosites[20, 21].
- Stratum corneum layer forms permeability obstacle for outer environment.
- Water content of stratum corneum is around 20%.
- The moisture required stratum corneum is around 10% (w/w) to maintained flexibility and softness[22].
- It consist of cermides and neutral lipids such as sterols free fatty acids and triglyceride.
- The stratum corneum is responsible for the barrier function of the skin and behaves as a primary to the precutaneous absorption[23].
- It is made up of three layers in thicker parts stratum granulosum, stratum lucidum, stratum spinousum **figure.1.**
- Removal of this layers results in increased skin permeability and water loss[24].

DERMIS

- Dermis is composed of a regular network of robust collagen fiber and fairly uniform thickness with regularly spaced cross-straiations.
- This network or the gel structure is liable for the flexible properties of the skin.
- It is supplied by blood to convery nutrients, remove waste and regulate body temperature.
- Drug is well absorbed by this route.
- Upper portion of the dermis is formed into ridges containing lymphatics and nerve endings.

HYPODERMIS OR SUBCUTANEOUS LAYER

- This is a sheet of the fat containing areolar tissue, known as the superficial fascia, attaching the dermis to the underlaying structures[20].

BASIC COMPONENTS OF TDDS

1. Polymer matrix or matrices
2. Drug
3. Permeation enhancers
4. Adhesive
5. Liners
6. Backing
7. Plasticizer

1. POLYMER MATRIX OR MATRICES

The polymer controls the drug loading, rate of drug release. The selection criteria should be satisfied for a to be used in transdermal patches as following.

- Chemical and molecular weight functionality of the polymer should be such that the specific drug diffuses properly and gets released throught it.
- The polymer should be stable.
- The polymer should be nontoxic.
- The polymer should be easily of manufactured.
- The polymer should be inexpensive.
- The polymer and its degration product must be non toxic or non-antagonistic to the host.
- Big amounts of the active agent are incorporated into it.

Types of polymer

A. Natural polymers: Gelatin, shellac, waxes, chitosan, natural rubber, cellulose derivatives.
B. Synthetic polymers: PVA, PVC, polypropylene, polyacrylate, polyurea, polyamide, polypropylene.
C. Synthetic elastomers: Polybutadiene, silicon rubber**,** hydrine rubber, nitril, acrylonitril, neoprene.

2. DRUG :

The selection drug should have some desirable physiochemical and biological properties favorable for drug transport across the skin.

Physiochemical properties:

A. The drug should have low mole. Weight (up to 1000 Daltons).

B. The drug should have affinity for hydrophilic and lipophilic phases.

C. The drug should have a low melting point (less than 200 deg c).

Biological properties:

A. The drug should be potent with a daily dose of a few mg/day in order.

B. The half life (t½) of the drug should be short.

C. The drug must not produce allergic response.

D. Toleration to the drug must not develop under the near zero-order release profile of skin patches.

3. PERMEATION ENHANCER:

These are compounds which promote skin permeability by altering the skin as a obstacle to the flux of a desired penetrant.

The flux J, can be given by - $J = D\, dc/dx$

J = The Flux
D = diffusion coefficient
C = Concentration of the diffusing species

Permeation enhance are hypothesized to affect one or more of these layers to achieve skin penetration enhancement. A big number of compounds have been investigated for their ability to increaces stratum corneum permeability. These may be conveniently be classified under the following headings.

A. Solvent: These compound enhance permeability possibly by swelling the polar pathway.
e.g. propylene glycol and Glycerol, water alcohols-methanol and ethanol, Dimethyl acetamide.

B. Surfactant: The ability of a surfactant to alter penetration is a function of both the hydrocarbon chain length and polar head group.

- **Anionic surfactant :** SLS, Decodecyl methyl sulfonamide, Diacetyl sulphosuccinate.
- **Nonionic surfactant:** pluronic F68, pluronic F127.
- **Bile salt :** sodium deoxycholate, sodium taurocholate.

C. Binary system: These systems apparently open up the heterogenous multilaminate pathway as well as the continous pathways.
e.g. Propylene glycol-oleic acid and 1,4-butanediol- linoleic acid.

D. Miscellaneous chemicals: These include urea, a hydrating and keratolytics agent;

4. ADHESIVE:

Adhesive maintains the patch in continuous contact with the skin the selection criteria for patch include adhesive properties e.g. polyisobutadine, polyacrylate.

- It should not be irritant.
- It should be easily removed.
- It should be removable from the smooth surface without leaving a residue.
- It should have excellent contact with the smooth surface.
- Physical and chemical compatibility with the drug.
- Permeation of drug should not effected[25,26].

5. Liner: Protect the patch from outside environment during storage. The linear is removed prior to use **e.g.** PVC

6. Backing: It protect the polymeric drug reservoir from the external environment[27].

7. Plasticizers: plasticizer provides flexibility and improves the brittleness of the polymer.
e. g. PEG, PG, phthalic acid ester[28].

TRANSDERMAL PATCH:

Transdermal drug delivery system are tropically administered medicaments. TDDS is defined as medicated adhesive patch which when applied to the skin to delivery the drug throught the skin at a predetermined and controlled rate release to reach into the bloodstream. Today the most common transdermal system present in the market mainly based on semipermiable membranes which were called as patches. TDDS patch shows different component as following **figure. 2[29-32].**

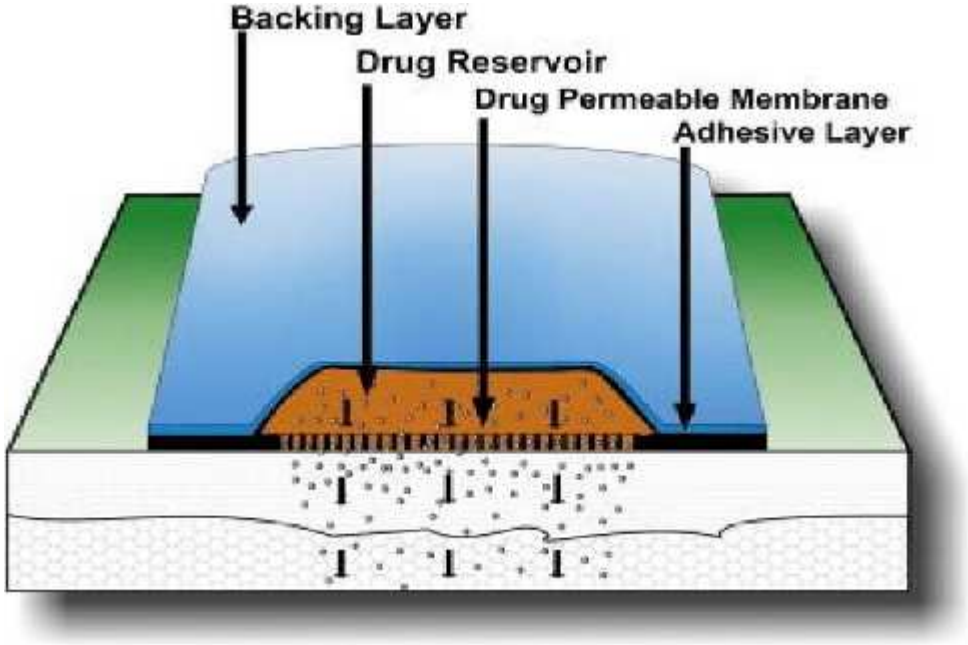

Figure 2: Transdermal patch showing its different components.

Figure 3: Transdermal patch (skin patch)

TYPES OF TRANSDERMAL PATCHES

1. Single-layer drug in-adhesive.
2. Multi-layer drug in-adhesive.
3. Drug reservoir-in-adhesive.
4. Drug matrix-in-adhesive.

➢ **SINGLE-LAYER DRUG IN-ADHESIVE**

In this system drug is dispersed in the adhesive layer of the skin patch. In this type of patches the adhesive layer serves to adhere the various layer together and also responsible for the releasing of the drug. The adhesive layer is surrounded by a temporary backing and a liner.

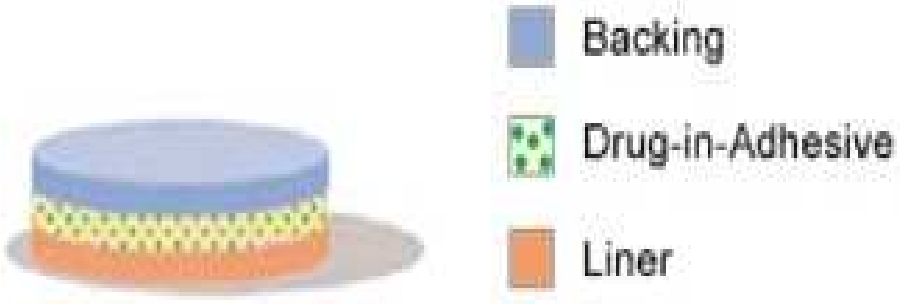

Figure 4: Single-layer drug in-adhesive

➢ **MULTI-LAYER DRUG IN-ADHESIVE**

In this system drug is dispersed in the adhesive layers of the patch same as in single layer drug in adhesive. But the only difference is that it contains multiple layers of drug in-adhesive separated by a membrane. This patch also has a temporary liner-layer permanent backing**.**

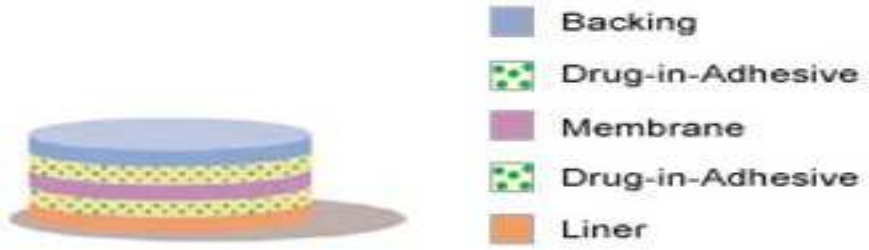

Figure 5: Multi-Layer Drug In-Adhesive

➢ **DRUG RESERVOIR-IN-ADHESIVE**

Reservoir transdermal system has a sepreate drug layer enclosed in a rate controlling microporous or nonporous membrane and an impermeable backing laminate. The drug layer is a liquid mix compartment containing a drug suspension or solution sepreated by the backing layer. The release rate of the drug is determined by the permeability diffusion, abrasion rate and thickness of the membrane. In this type of system the rate of drug release is zero order.

Figure 6: Drug reservoir in-adhesive

➢ **DRUG MATRIX-IN-ADHESIVE**

In this approach, the reservoir is prepared by homogenously dispersing drug particles in a lipophilic or hydrophilic polymer matrix. The adhesive layer in drug matrix patch surrounds the drug layer partially overlaying it. It also has occlusive base plate, absorbent pad and backing laminate on the back[33-35].

Figure 7: Drug matrix-in-adhesive

APPLICATION OF TRANSDERMAL PATCHES

- Nitroglycerine patches are also used in the treatment of angina pectoris.
- Transdermal patches of nicotine, which releases nicotine in controlled doses is used in treatment of tobacco smoking cessation.
- Clonidine is antihypertensive drug and ketoprofen, the non-steroidal anti-inflamatory drug are also available in the form of transdermal patches.
- Transdermal delivery agent for the attention deficit hyperactivity disorder (ADHD), Antiemetic, contraceptive.
- Transdermal forms of the MAOI selegilline, became the 1st transdermal delivery agent for an antidepressant[36-38].
- Estrogen patches are sometimes prescribed to treat menopausal symptoms as well as post-menopausal osteoporosis[39].
- TDDS marketed product list as following **Table. 2[40].**

TABLE 2: TDDS MARKETED PRODUCTS

Product Name	Drug	Manufacturer	Indication
Alora	Estradiol	TheraTech/ Proctol and Gamble	Postmenstrual Syndrome
Androderm	Testosterone	TheraTech/GlaxoSmithKline	Hypogonadism in Males
Catapres –TTS	Clonidine	Alza/ Boehinger Ingelheim	Hypertension
Climaderm	Estradiol	Ethical Holdings/ Wyeth –Ayerest	Postmenstrual Syndrome
Climara	Estradiol	3M Pharmaceuticals/ Berlex Labs	Postmenstrual syndrome
CombiPatch	Estradiol/ Nore thindrone	Noven, Inc./ Aventis	Hormone replacement therapy
Deponit	Nitroglycerin	Schwarz –Pharma	Angina pectoris
Duragesic	Fentanyl	Alza/ Janssen Pharmaceutical	Moderate/ severe pain
Estraderm	Estradiol	Alza/ Norvatis	Postmenstrual Syndrome
Fematrix	Estrogen	Ethical Holdings/ Solvay Healthcare Ltd.	Postmenstrual Syndrome
FemPatch	Estradiol	Parke-Davis	Postmenstrual Syndrome
Habitraol	Nicotine	Novartis	Smoking Cessation
Minitran	Nitroglycerin	3M Pharmaceuticals	Angina pectoris
Nicoderm	Nicotine	Alza/ GlaxoSmithKline	Smoking Cessation
Nitrodisc	Nitroglycerin	Roberts Pharmaceuticals	Angina pectoris
Nicotrol	Nicotine	Cygnus Inc./ McNeil Consumer Products, Ltd.	Smoking cessation

CONCLUSION

Transdermal drug delivery system have been used as safe and effective drug delivery devices since 1981. The purpose of this article was to give precious and basic information about the transdermal drug delivery system. Transdermal medication provides safe, convenient and self-administration, pain free for patient. Many more drugs have been formulated in TDDS form, such as hypertention, chronic pain, dermal analgesic, heart diseases, first pass metabolism. TDDS is used particulary in that patient who cannot swallow or remember to take their medications. Many more disadvantages like large drug molecules cannot be delivered, more costly, skin irritation, rate of absorption or the drug is less etc. TDDS is a realistic or usefull practical application as the next generation of drug delivery system.

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