

Transdermal Drug Delivery System: A Tool for Novel Drug Delivery System

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Abstract

The human skin is a readily accessible surface for drug delivery. Skin of an average adult body covers a surface of approximately 2m² and receives about one-third of the blood circulating through the body. Over the past decades, developing controlled drug delivery has become increasingly important in the pharmaceutical industry. The human skin surface is known to contain, on an average, 10-70 hair follicles and 200-250 sweat ducts on every square centimeters of the skin area. It is one of the most readily accessible organs of the human body. There is considerable interest in the skin as a site of drug application both for local and systemic effect.

However, the skin, in particular the stratum corneum, poses a formidable barrier drug penetration there by limiting topical and Transdermal bioavailability. Skin penetration enhancement techniques have been developed to improve bioavailability and increase the range of drugs for which topical and Transdermal delivery systems (NDDS).

Keywords: NDDS, Transdermal, Importance

Introduction

Optimum therapeutic outcomes require not only proper drug selection but also effective drug delivery. The human skin is a readily accessible surface for drug delivery. Over the past three decades, developing controlled drug delivery has become increasingly important in the pharmaceutical industry. The pharmacological response, both the desired therapeutic effect and the undesired adverse effect, of a drug is dependent on the concentration of the drug at the site of action, which in turn depends upon the dosage form and the extent

of absorption of the drug at the site of action¹. One highly successful alternative delivery method is the transdermal.

Skin of an average adult body covers a surface of approximately 2m² and receives about one-third of the blood circulating through the body. To deliver a drug into the body through transdermal, a layer of skin, it is necessary to understand about the skin.

A) The stratified, vascular, cellular epidermis, B) Underlying dermis of connective tissues and C) Hypodermis.

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The multilayered epidermis varies in thickness, depending on cells size and number of cell layers of epidermis, ranging from 0.8 mm on palms and soles down to 0.06 mm on the eyelids. Table 1 gives thickness, water permeability and diffusivity of water through epidermis. a) Stratum corneum

This is the outermost layer of skin also called as horny layer. It is approximately 10 μ m thick when dry but swells to several times this thickness when fully hydrated. It contains 10 to 25 layers of dead, keratinized cells called corneocytes. It is flexible but relatively impermeable. The stratum corneum is the principal barrier for penetration of drug. The architecture of horny layer may be modeled as a wall-

like structure. In this model, the keratinized cells function as protein "bricks" bilayers. There is sufficient amphiphilic material in the lipid fraction, such as polar free fatty acids and cholesterol, to maintain a bilayer form.

b) Viable epidermis

This is situated beneath the stratum corneum and varies in thickness from 0.06 mm on the eyelids to 0.8 mm on the palms. Going inwards, it consists of various layers as stratum lucidum, stratum granulosum, stratum spinosum and the stratum basale. In the basal layer, mitosis of the cells constantly renews the epidermis and

this proliferation compensates the loss of dead horny cells from the skin surface. As the cells produce by the basal layer move outward, they alter morphologically. Dermis

Dermis is 3 to 5 mm thick layer and is composed of a matrix of connective tissue, which contains blood vessels, lymph vessels and nerves. The cutaneous blood supply has essential function in regulation of body temperature. It also provides nutrients and oxygen to the skin while removing toxins and waste products. Capillaries reach to within 0.2 mm of skin surface and provide in conditions for most molecules penetrating the skin barrier.

Hypodermis

The hypodermis or subcutaneous fat tissue supports the dermis and epidermis. It serves as a fat storage area.

This layer helps to regulate temperature, provides nutritional support and mechanical protection. T

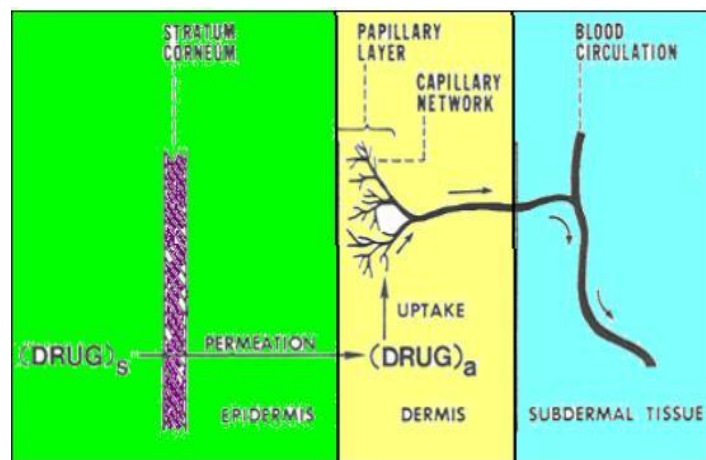
he transdermal drug delivery, drug has to penetrate through all these three layers and reach into systemic circulation while

of topical drug delivery only penetration through stratum corneum is desired.

Fundamentals of skin permeation

Until the last century the skin was supposed to be impermeable with exception to gases. However, in the current century the study indicated the permeability to lipids and drugs. Also it was recognized that various layers of skin are not equally permeable i.e. epidermis is less permeable than dermis. After a large controversy, all doubts about stratum corneum permeability were removed and drug is isotopic tracers.

A. Stratum corneum as skin permeation barrier
The average human skin contains 40-70 hair follicles and 200-250 sweat ducts per square centimeter. Especially water-soluble substances pass faster through the ducts, still the ducts don't contribute much for skin permeation.



Therefore most neutral molecules. Regional variation in water permeability of stratum corneum is shown in Table 1 and permeation of drug molecules through skin is shown in Figure 2.

2. Series of steps in sequence:

3. Sorption of a penetrant molecule on surface layer of stratum corneum.

4. Diffusion through it and viable epidermis and finally reach to dermis and then

5. The molecule is taken up into the microcirculation for systemic distribution.

Figure 2: A multilayer skin model showing sequence of Transdermal permeation of drug for systemic delivery B- Intracellular versus transcellular diffusion

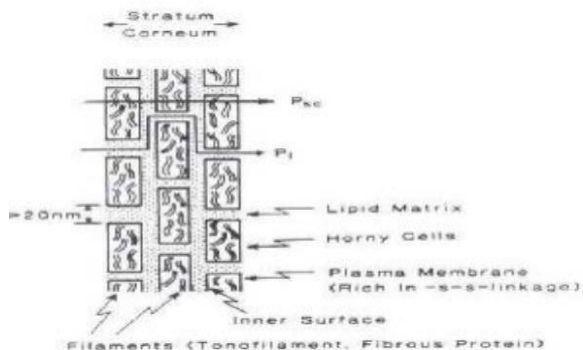


Table 1: Regional variation in water permeability of stratum corneum

Figure 3: The microstructure of stratum corneum

Intracellular regions in stratum corneum are filled with lipid rich amorphous material. In dry stratum

Sr. No.	Skin region	Thickness (μm)	Permeation rate (mg/cm ² /hr)	Diffusivity (cm ² /sec × 10 ¹⁰)
1	Abdomen	15.0	0.34	6.0
2	Volar forearm	16.0	0.31	5.9
3	Back	10.5	0.29	3.5
4	Forehead	13.0	0.85	12.9
5	Scrotum	5.0	1.70	7.4
6	Back of hand	49.0	0.56	32.3
7	Palm	400.0	1.14	535.0
8	Plantar	600.0	3.90	930.0

mcorneum intracellular volume may be 5% to 1% in fully hydrated stratum corneum. C. Permeation pathways 7-9 Percutaneous absorption

involves passive diffusion of the substance through the skin. A molecule may use two diffusion routes to penetrate normal intact skin, the appendageal route and the epidermal route.

1. Appendageal route: Appendageal route comprises transport via sweat glands and hair follicles with their associated sebaceous glands. These routes circumvent penetration through the stratum corneum and are therefore known as "shunt" routes.

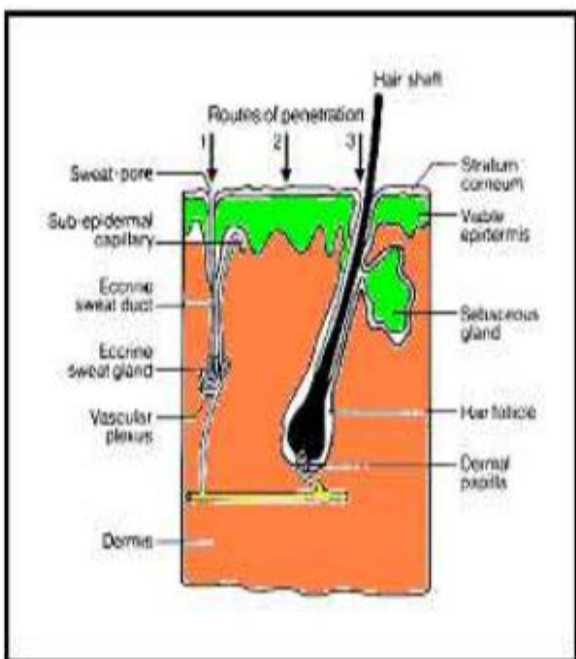


Figure 4: Routes for drug permeation For drugs, which mainly cross-intact horny layer, two potential micro routes of entry exist, the transcellular (intracellular) and intercellular pathways

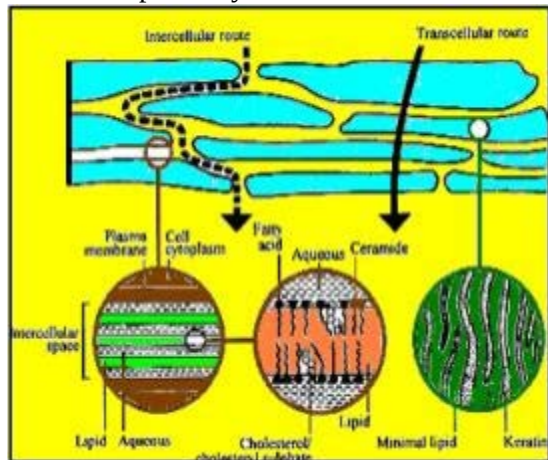


Figure 5: Epidermal routes for drug permeation
i) Transcellular: Transcellular pathway means transport of molecules across epithelial
1. Epidermal route: cellular membrane. These include passive transport of small molecules, active transport of ionic and polar compounds and endocytosis and transcytosis of macromolecules.
ii) Paracellular: Paracellular pathway means transport of molecules around or between the cells. Tight

junctions or similar situation exist between cells.

The principal pathway taken by a permeant is decided mainly by the partition coefficient ($\log K$). Hydrophilic drugs partition preferentially into the intracellular domains, whereas lipophilic permeants traverse the stratum corneum via the intercellular route.

Properties that influence transdermal drug delivery¹⁰⁻¹¹

The effective transdermal drug delivery can be formulated by considering three factors as drug, Skin and the vehicles. So the factors affecting can be divided into two classes as biological factors and physicochemical factors.

A. Biological factors

i) Skin condition: Acids and alkalis, many solvents like chloroform, methanol damage the

skin cells and promote penetration. Diseases state of patient alter the skin conditions. The intact skin is better barrier but the above mentioned conditions affect penetration.

ii) Skin age: The young skin is more permeable than older. Children are more sensitive

for skin absorption of toxins. Thus, skin age is one of the factors affecting penetration of drug in TDDS.

iii) Blood supply: Changes in peripheral circulation can affect transdermal absorption.

iv) Regional skin site: Thickness of skin, nature of stratum corneum and density of appendages vary with site.

These factors significantly affect penetration.

v) Skin metabolism: Skin metabolizes steroids, hormones, chemical carcinogens and some drugs. So skin metabolism determines efficacy of drug permeated through the skin.

vi) Species differences: The skin thickness, density of appendages and keratinization of skin varies from species to species, so it affects the penetration.

B. Physicochemical factors

i) Skin hydration: In contact with water the permeability of skin increases significantly. Hydration is most important factor in increasing the permeation of skin. So use of humectant is done in transdermal delivery.

ii) Temperature and pH: The permeation of drug increases tenfold with temperature variation.

The diffusion coefficient decreases as temperature falls.

Weak acids and weak bases dissociate depending on the pH and pK_a or pK_b values. The proportion of unionized drug determines the drug concentration in skin.

iii) Diffusion coefficient: Penetration of drug depends on diffusion coefficient of drug. At a constant temperature the diffusion coefficient of drug depends on properties of drug, diffusion medium and interaction between them.

iv) Drug concentration: The flux is proportional to the concentration gradient across the barrier and concentration gradient will be higher if the concentration of drug will be more across the barrier.

v) Partition coefficient: The optimal partition coefficient (K) is required for good action. Drugs with high K are not ready to leave the lipid portion of skin. Also, drugs with low K will not be permeated.

vi) Molecular size and shape: Drug absorption is inversely related to molecular weight, small molecules penetrate faster than large ones. Ideal molecular properties for transdermal drug delivery¹²

From the above considerations we can conclude with some observations that can termed as ideal molecular properties for drug penetration. They are as follows.

! Adequate solubility in lipid and water is necessary for better penetration of drug (1mg/ml).

! Optimum partition coefficient is required for good therapeutic action.

! Low melting point of drug is desired ($<200^{\circ}\text{C}$).

! The H_o of the saturated solutions should be in between 5 to 9.

Design of transdermal delivery system¹⁰

The basic components of any transdermal delivery system include the drug dissolved or dispersed in an inert polymer matrix that provides support and platform for drug release. There are two basic

designs of the patch system that dictate drug release characteristics and patch behavior:

i) Matrix or Monolithic: The inert polymer matrix binds with the drug and controls its release from the device.

ii) Reservoir or Membrane: The polymer matrix does not control drug release. Instead, a rate-controlling membrane present between the drug matrix and the adhesive layer provides the rate-limiting barrier for drug release from the device. Technologies for developing transdermal drug delivery systems^{4,6,11}

The technologies can be classified in four basic approaches:

A) Polymer membrane partition-controlled TDDS systems In this type of systems, the drug reservoir is sandwiched between a drug-impermeable backing laminate and a rate-controlling polymeric membrane.

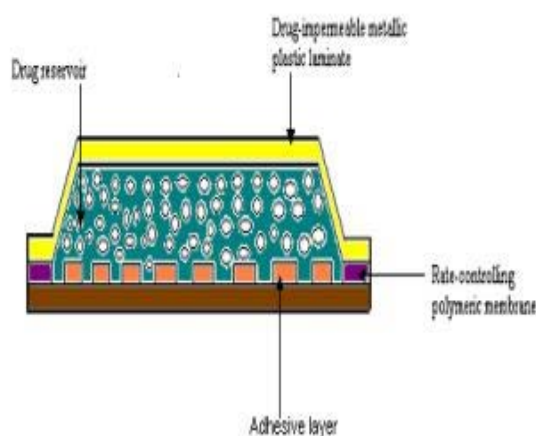


Figure 6: Cross-sectional view of polymer membrane permeation-controlled TDDS systems

The drug is allowed to permeate only through the rate-controlling membrane. The drug solids are homogeneously dispersed in a solid polymer matrix, suspended in an unleachable, viscous liquid medium.

For a clear drug solution. The rate-controlling membrane can be either a microporous or a nonporous polymeric membrane, e.g. ethylene-vinyl acetate copolymer, with specific drug permeability. On the external surface of the polymeric membrane is a thin layer of drug-compatible, hypoallergenic pressure-sensitive adhesive polymer, e.g. silicone adhesive may be applied to provide intimate contact of TDDS with the skin surface.

Varying the composition of drug reservoir formulation, the permeability coefficient

efficient and thickness of rate controlling membrane can alter the drug release rate.

e.g. Some FDA approved systems – Transdermal Nitroglycerin patch, Transdermal Scopolamine patch, Catapres-TTS system for hypertension.

The intrinsic rate of drug release from this type of TDDS system is defined by

$$\frac{dQ}{dt} = \left[\frac{K_m / r K_a / m D_a D_m}{K_m / r D_m h_a + K_a / m D_a h_m} \right] C_R$$

K_m / r the partition coefficient for the interfacial partitioning of drug from the reservoir to the membrane.

K_a / m the partition coefficient for the interfacial partitioning of drug from membrane to adhesive.

D_a diffusion coefficient in rate controlling membrane.

D_m diffusion coefficient in adhesive layer.

h thickness of rate controlling membrane.

h_m thickness of adhesive layer.

B) Polymer matrix diffusion-

controlled TDDS systems In this system, the drug reservoir is formed by homogeneously dispersing the drug solids in a hydrophilic or lipophilic polymer matrix and then the medicated polymer formed is molded into medicated disks with defined surface area and thickness. This drug reservoir containing polymer disk is then mounted on occlusive base plate in a compartment fabricated from drug-impermeable plastic backing.

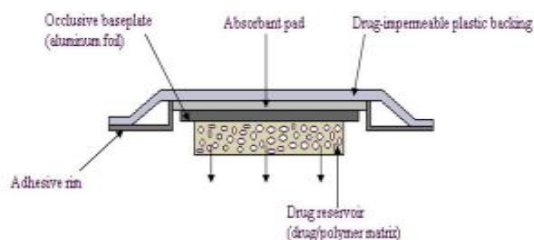


Figure 7: Cross-sectional view of polymer matrix diffusion-controlled TDDS systems.

The rate of release from polymer matrix drug dispersion-type is

$$\frac{dQ}{dt} = \left[\frac{L_d C_p D_p}{2t} \right]^{1/2}$$

where,

L_d is drug loading dose initially dispersed in polymer matrix.

C_p is solubility of drug in polymer matrix.

D_p diffusivity of drug in polymer matrix.

t is time elapsed since drug dissolved in polymer matrix and diffused out. When t is small, $\frac{dQ}{dt}$ is approximately equal to C_R .

Alternatively, the polymer matrix drug dispersion-type TDDS can be fabricated by directly dispersing drug in a pressure-sensitive adhesive polymer e.g. polyacrylate and then coating the drug-dispersed adhesive polymer by solvent casting or hot melt onto a flat sheet of drug-impermeable backing laminate to form a single layer of drug reservoir, this yields a thin patch. e.g. Minitrans system, Nitro-Dur II system for angina pectoris.

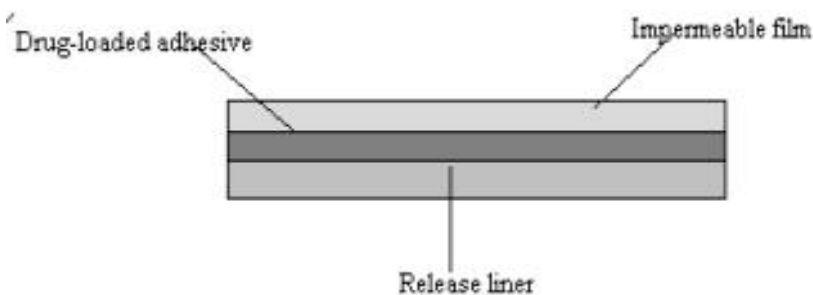


Figure 8: Cross-sectional view of an adhesive polymer drug dispersion-type TDDS systems showing various major structural components.

C) Drug reservoir gradient-controlled TDDS systems Polymer matrix drug dispersion-type TDDS can be modified to have the drug load in a level varied in an incremental manner, forming a gradient of drug reservoir along the diffusion path across the multilaminar adhesive layers. The drug release

from this type of drug reservoir controlled TDDS can be expressed by:

$$\frac{dQ}{dt} = \frac{K F a / r}{h a(t)}$$

Ld(ha)

In this system, the thickness of diffusional path through which drug molecules diffuse increases with time i.e. $L_d(ha)$. The drug loading level in the multilaminated adhesive layer is designed to increase proportionally i.e. $L_d(ha)$ so as to compensate a time dependent increase in diffusional path as

a result of drug depletion due to release.

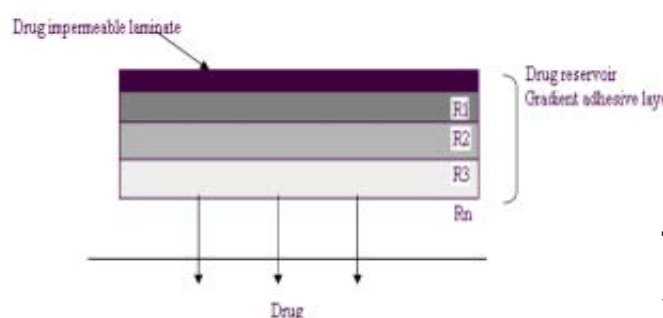


Figure 9: Cross-sectional view of a drug reservoir gradient-controlled TDDS system.

D. Microreservoir dissolution-controlled TDDS systems

A hybrid of reservoir and matrix dispersion type drug delivery systems, which contains drug reservoir formed by first suspending the drug solids in an aqueous solution of water-miscible drug solubilizer e.g. propylene glycol, the homogeneous dispersion in the drug suspension with controlled aqueous solubility in a lipophilic polymer by high shear mechanical force to form thousands of unleachable microscopic drug reservoirs.

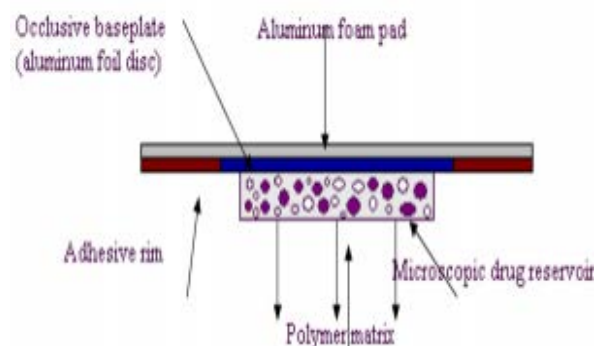


Figure 10: Cross-sectional view of Microreservoir dissolution-controlled TDDS systems. This thermodynamically unstable system is quickly stabilized by immediately cross-linking the polymer chains in situ, which produces a medicated polymer disk with a constant surface area and a fixed thickness. The medicated disk is mounted at the center of an adhesive pad. eg. Nitro disk system for angina pectoris. The rate of drug release from this system is defined by:

$$\frac{dQ}{dt} = \frac{D_p D_s A K_p}{D_p h_d + D_s h_p A K_p} \left(\frac{F A_b D_s S_l (1-B)}{B S_p h_l} \left[\frac{l}{K_l} - \frac{l}{K_w} \right] \right)$$

Components of TDDS

The main components of a transdermal patch are:

i. Release Liner

Protects the patch during storage. The liner is removed prior to use.

ii. Drug reservoir

The most important part of TDDS is drug reservoir. It consists of drug particles dissolved or dispersed in the matrix. To make the drug soluble, solvents and cosolvents are used. The effect of solvent and cosolvents should be considered while doing selection.

iii. Adhesive

Serves to adhere the components of the patch together along with adhering the patch to the skin. The adhesive must possess sufficient adhesion properties so that the TDDS should remain in place for a long time. Pressure sensitive adhesives are commonly used for transdermal patch to hold the skin. Commonly used adhesives are silicone adhesives, polyisobutylene adhesives and polyacrylate based adhesives.

iv. Membrane

Membrane controls the release of the drug from the reservoir and multi-layer patches. It may or may not contain rate-controlling membrane. It should be flexible enough not to split or crack on bending or stretching. So membrane

controlling membranes are polyethylene sheets, ethylene vinyl acetate copolymer and cellulose acetate.
v. Backing
Protects the patch from the outer environment. The backing layers should be impermeable to drug and penetration enhance. Its serves

a function of holding the entire stem and protects drug reservoir from atmosphere. The commonly used backing materials are polyesters, aluminumized polyethylene terephthalate and siliconized polyethylene terephthalate.

General clinical considerations in the use of TDDS^{7,13}

The patients should be advised of the following general guidelines. The patients should be advised of the importance of using the recommended site and rotating locations within the site. Rotating location is important to allow the skin to regain its normal permeability and to prevent skin irritation.

1. TDDS should be applied to clean, dry skin relatively free of hair and not oily, inflamed, irritated, broken. Wet or moist skin can accelerate drug permeation time. Oily skin can impair the adhesion of patch. If hair is present at the site, it should be carefully cut, not wet shaved nor should a depilatory agent be used.

2. Use of skin lotions should be avoided at the application site, because lotions affect the hydration of skin and can alter partition coefficient of drug.

3. Patients should not physically alter TDDS, since this destroys integrity of the system.

4. The protecting backings should be removed with care not to touch fingertips. The TDDS should be pressed firmly against skin with the heel of hand for about 10 seconds.

5. ATDDS should be placed at a site that will not be subject to being rubbed off by clothing or movement. TDDS should be left on when showering, bathing or swimming.

6. ATDDS should be worn for full period as stated in the product's instructions followed by removal and replacement with fresh system.

7. The patient or caregiver should clean the hands after applying a TDDS. Patients should not rub eye or touch the mouth during handling of the system.

8. If the patient exhibits sensitivity or

intolerance to a TDDS or if undue skin irritation results, the patients should seek reevaluation.

9. Upon removal, used TDDS should be folded in such a way with the adhesive layer together so that it cannot be reused. The used patch should be discarded in a safe manner from children and pets.



Figure 11: Use of transdermal patch. It is important to use a different application site every day to avoid skin irritation.

Suggested rotation is:

Day 1 – Upper right arm
Day 2 – upper right chest
Day 3 – Upper left chest
Day 4 – Upper left arm,

then repeat from Day 1.

Table 2: Examples of marketed transdermal drug delivery system⁴

Sr. No. Therapeutic agent TDDS Design			
1	Clonidine	Catapres-TTS (Boehringer Ingelheim)	Four-layer patch
2	Estradiol	Estraderm (Novartis)	Four-layer patch
3	Estradiol	Vivelle (Novartis)	Three-layer system
4	Estradiol	Climara (Novartis)	Three-layer system
5	Fentanyl	Duragesic (Janssen)	Four-layer patch
6	Nicotine	Prosstep (Lederle)	Multilayer round patch
7	Testosterone	Testoderm (Alza)	Three-layer patch
8	Nicotine	Habitrol (Novartis Consumer)	Multilayer round patch

9	Nicotine	Nicoderm CQ (Smithkline Beecham Consumer)	Multilayer rectangular patch
10	Nicotine	Nicotrol (McNeil Consumer)	Multilayer rectangular patch

Transdermal patches⁹ Both topical and transdermal products are intended for external application. However, topical dermatological products are intended for local action whereas transdermal drug delivery system is used for systemic drug delivery.

Transdermal system delivers medications through the skin directly into the bloodstream. The transdermal route of drug delivery is becoming popular because a large number of drugs can be delivered by this route to treat various diseases. Currently, transdermal patches are used in several therapeutic areas like pain management, smoking cessation, treatment of heart disease, hormone replacement and management of motion sickness.

TYPES OF TRANSDERMAL PATCHES: 18-22

a) Single layer drug in adhesive: In this type the adhesive layer contains the drug. The adhesive layer not only serves to adhere the various layers together and also responsible for the releasing the drug to the skin. The adhesive layer is surrounded by a temporary liner and a backing.

b) Multi-layer drug in adhesive: This type is also similar to the single layer but it contains an immediate drug release layer and other layer will be a controlled release along with the adhesive layer. The adhesive layer is responsible for temporary liner-layer and a permanent backing.

c) Vapour patch: In this type of patch the role of adhesive layer not only serves to adhere the various layers together but also serves market, commonly used for releasing of essential oils in decongestion. Various other types of vapour patches are also available in the market which are used to improve the quality of sleep and reduce the cigarette smoking conditions.

d) Reservoir system: In this system the drug reservoir is embedded between an impervious backing layer and a rate controlling membrane.

The drug releases only through the rate controlling membrane, which can be microporous or nonporous. In the drug reservoir compartment, the drug can be in the form of a solution, suspension, gel or dispersed in a solid can be applied as outer surface polymeric membrane which is compatible with drug.

e) Matrix system:

i. Drug-in-adhesive system:

In this type the drug reservoir is formed by dispersing the drug in an adhesive polymer and then spreading the medicated adhesive polymer by solvent casting or melting (in the case of hot-melt adhesives) on an impervious backing layer. On top of the reservoir, unmediated adhesive polymer layers are applied for protection purpose.

ii. Matrix-dispersions system:

In this type the drug is dispersed homogeneously in a hydrophilic or lipophilic polymer matrix. This drug containing polymer disk is fixed onto an occlusive base plate in a compartment fabricated from a drug impermeable backing layer. Instead of applying the

adhesive on the face of the drug.

f) Microreservoir system:

In this type the drug delivery system is a combination of reservoir and matrix-dispersions system. The drug reservoir is formed by first suspending the drug in an aqueous solution or water soluble polymer and then dispersing the solution homogeneously in a lipophilic polymer to form thousands of unreachably small microscopic spheres of drug reservoirs.

Advances in transdermal patch technology

i) Adhesives: For transdermal patches to provide consistent and continuous drug delivery through the skin, they must adhere well. There are several adhesives in regular use in transdermal systems including silicones and polyisobutylenes. Newer adhesives, including acrylates, have recently become available. Acrylates are known as pressure-sensitive adhesives and they are preferred because they have selective adhesive properties once in contact with the skin. Pressure-sensitive adhesives can also be removed with ease and they are compatible

with skin and various drug molecules. The polymeric nature of a crylate prevents the patches from undergoing physical breakdown.

i) Penetration Enhancers:

substances will not diffuse into the skin at sufficient rates to obtain therapeutic concentrations. Substances that reduce the skin's ability to perform its barrier function are collectively known as penetration enhancers. These substances make the skin more permeable and they allow drug molecules to cross the skin at a faster rate. With regard to both safety and efficacy, water is the optimum permeation enhancer. By increasing the hydration of the stratum corneum, the barrier function of the skin can be reduced. Alcohol is commonly considered as a solvent in transdermal patches; it actually serves as an effective penetration enhancer. Some penetration enhancers remove lipids from the skin.²³⁻²⁵

EVALUATION PARAMETERS:²⁶

1. Interactions studies
2. Thickness of the patch
3. Weight uniformity
4. Folding endurance
5. Percentage Moisture content
6. Percentage Moisture uptake
7. Water vapour permeability (WVP) evaluation
8. Drug content
9. Uniformity of dosage unit test
10. Polariscopes examination
11. Shear Adhesion test
12. Peel Adhesion test
13. Thumb tack test
14. Flatness test
15. Percentage Elongation break test
16. Rolling ball tack test
17. Quick Stick (peel-tack) test
18. Probe Tack test
19. In vitro drug release studies
20. In vitro skin permeation studies
21. Skin Irritation study
22. Stability studies

Animal Models to Study Transdermal Absorption¹⁵⁻¹⁷

Ex vivo penetration and permeation are routinely performed to study percutaneous absorption and transdermal permeation characteristics of drugs and other chemicals. These ex vivo studies

allow the determination of drug concentration in the skin (penetration) and rate of transfer across the skin (permeation). Ex vivo experiments are easy to perform and the simplicity of methodology allows flexibility in adapting the model in addressing different

aspects involved in preliminary or feasibility studies in the development of skin/transdermal drug delivery systems.

Human skin is difficult to obtain and uniformity is difficult to maintain, since most of human skin comes

from cadavers whose sex, age and genetic history are uncontrolled. Whereas,

animal skin is easy to obtain and is more uniform.

Humans and animals have wide differences in the number of appendages, openings, per unit area thickness of skin, structure and porosity of skin, and the sex factors clearly affect the percutaneous absorption of drugs. Only the progress in in vitro methodology with an appropriate

animal model can resolve these limitations. It would be as simple as mathematics to predict the skin permeability in humans from animal experiments. If there is a constant ratio between skin permeability in human

to animal, independent of the drug under study. If correlation can be established for drugs with different physicochemical properties, experiments using appropriate animal skin will be more reliable in the developmental stage of skin/transdermal drug delivery systems. It appears that hairless guinea pig and Brattleboro rat are good animal models for skin/transdermal drug delivery systems, whereas snake appears not to be a good model to evaluate permeation of drugs across skin (unpublished data). In review in the studies comparing transdermal absorption of

drugs between animals and humans, care must be taken to ascertain the influences of methodology and model might have on the data, and utmost care must be taken to avoid any misinterpretation or wrong conclusions. According to the literature available, no consensus is available regarding animal models which truly reflect human skin.

Transdermal drug delivery systems have following advantages over conventional drug delivery.

Advantages 27-29

1. They can avoid gastrointestinal drug absorption difficulties caused by gastrointestinal pH, enzymatic activity and drug interactions with food, drink and other orally administered drugs.
2. They can substitute for oral administration of medication when that route is unsuitable, as in case of vomiting and diarrhea.
3. They avoid the first-pass metabolism and avoid drug deactivation by liver enzymes.
4. They are non-invasive so avoiding the inconvenience of parenteral therapy.
5. They provide extended therapy with a single application, improving compliance over other dosage forms, requiring more frequent dose administration.
6. Drug therapy may be terminated rapidly by removal of Transdermal drug delivery systems from the surface of the skin.
7. They are easily and rapidly identified in emergencies (e.g. unresponsive, unconscious or comatose patient) because of their physical presence, features and identifying markings.
8. They can be used for drugs with narrow therapeutic window.

Transdermal drug delivery systems have following disadvantages

Disadvantages

1. The limitations of transdermal drug delivery are mainly associated with barrier function of skin, so it is limited to potent drug molecules.
2. Skin irritation or contact dermatitis due to drug, excipients and enhancers is another limitation.

Future of Transdermal Therapy

Ten years ago, the nicotine patch had revolutionized smoking cessation; patients were being treated with nitroglycerin for angina, clonidine for hypertension, scopolamine for motion sickness and triamterene for glaucoma, all through patches. At that time, biotech medicinal was still being developed. During the past decade, the number of drugs formulated in the patches has hardly increased, and there has been little change in the composition

of the patch systems. Modifications have been mostly limited to refinements of the materials used. Conclusion

Successful transdermal drug application requires numerous considerations. Bearing in mind that the basic functions of the skin are protection and containment, it would seem exceptionally difficult to target the skin for drug delivery. However, with our greater understanding of the structure and function of the skin, and how to alter these properties, more and more new drug products are being developed for transdermal delivery. The properties of the drug, the characteristics of the transdermal device, selection of in-vivo model and the status of patient's skin are all important for a safe and effective drug delivery. The transdermal drug delivery system could be one of the best novel drug delivery systems.

References

1. Kelebe E, Sharma RK, Mosa EB, Aljahwi AZ. Transdermal Drug Delivery System- Design and Evaluation. International Journal of Advances in Pharmaceutical Sciences 2010; 1:201-211.
2. Tortora GS, Grabowski SK. Principles of Anatomy and Physiology, 11th edition, 2000, pp 140-194.
3. Schofield OMV, Rees JL. Skin disease, In Hunter J editor, Textbook of medicine and practice of medicine, 19th edition, Churchill Livingstone, 2002, pp 1049-1055.
4. Vyas SP, Khar RK. Controlled Drug Delivery: Concepts and Advances, first edition, Vallabh Prakashan, 2002, pp 411-447.
5. Images [Internet] URL: <http://Google.com/images>.
6. Chein YW. Transdermal Drug Delivery, In: Swarbrick J editor, Novel Drug Delivery Systems, second edition, New York: Marcel Dekker, 2005, 50, pp 301-380.
7. Barry B. Transdermal Drug Delivery, In: Aulton M.E., editor, Pharmaceutics: The Science of Dosage Form Design, Churchill Livingstone Ltd., 2002, pp 499-533.
8. Barry BW. Dermatological Formulations: New York, Marcel Dekker, 1983, 18, pp 95-120.
9. Bodae HE, DeHenn FH. Drug Permeation Enhancement: Theory and Application, In: Hsieh DS editor, Drugs and Pharmaceutical Sciences, New York: Marcel Dekker, 1994, 62, pp 59-90.
10. Ortho Evra, simple, convenient way to get the medicine you need, [Internet] URL: <http://www.orthoevra.com>.

11. Zhou Y, Wu XY. Fine elemental analysis of diffusion and drug release from complex matrix system, *J Control Rel* 1997; 49:277–288.
12. Misra AN. Transdermal Drug Delivery, In: Jain N.K., editor, *Controlled and Novel Drug Delivery*, first edition, CBS publication, 1997, pp 100–129.
13. Chad RW. Development and Selection of Components for Transdermal Drug Delivery Systems, [Internate].
14. Mehtra R. Topical and transdermal drug delivery: What a pharmacist needs to know, *Inet CE* 221-146-04-054-H01. [Internate]
15. Bronaugh RL, Stewart RF, Congdon ER. Methods for in vitro percutaneous absorption studies II. Animal models for human skin. *Toxicol Appl Pharmacol* 1982; 62:481–8.
16. Wester RC, Noonan PK. Relevance of animal models for percutaneous absorption. *Int J Pharm* 1980; 7:99–110.
17. Lin RY, Hsu CW, Chein YW. A method to predict the transdermal permeability of amino acids and dipeptides through porcine skin. *J Cont Rel*. 1996; 38: 229–34.
18. Williams AC, Barry BW. “Penetration Enhancers,” *Adv. Drug Del. Rev* 2004; 56:603–618.
19. Pellet M, Raghavan S.L, Hadgraft J and Davis A.F. “The application of supersaturated systems to percutaneous drug delivery” In: Guy R. Hand Dekker, Inc., New York 2003, pp. 305–326.
20. Brown MB, Jones SA. Hyaluronic acid: a unique topical vehicle for localized drug delivery of drugs to the skin. *J EDV* 2000; 19:308–318.
21. Tsai JC, Guy RH, Thomfeldt CR, Gao WN, Feingold KR, Elias PM. “Metabolic Approaches to Enhance Transdermal drug delivery”. *Jour. pharm. Sci.* 1998; 85:643–648.
22. Berner B, John VA. Pharmacokinetic characterization of transdermal delivery systems. *Jour. Clinical pharmacokinetics* 1994; 26(2):121–34.
23. Finnin BC, Morgan TM, Transdermal Penetration: Application, Limitation and Potential, *J Pharm Sci* 1999; 88:955–958.
24. Dosage and Design of Transdermal Patch, [Internate], URL: <http://www.nitto.com/rd/technical/2000/pdf/15nakano.qxd.pdf>.
25. Robinson JR, Yang X. Absorption enhancers, In: Boylan J., Swarbrick J., editors, *Encyclopedia of Pharmaceutical Technology*, New York: Marcel Dekker, 1999, 18, 1–20.
26. Kumar JA, Pullakandam N, Prabu SL, Gopal V. Transdermal drug delivery system: an overview. *International Journal of Pharmaceutical Sciences Review and Research*. 2010; 3(2): 49–54.
27. Delivery Times, You can’t Tech an old patch new trick or can you, an Alza Technologies publication, volume-I, Issue III, [Internate], URL: <http://www.Alza.com>.
28. Wilkosz MF. Transdermal Drug Delivery, Part I: CURRENT STATUS U.S. Pharmacist, 2003, 28, [Internate] URL: <http://USPharmacist.htm>.
29. Allen LV, Popovich NG, Ansel HC. *Pharmaceutical dosage forms and drug delivery systems*, seventh edition, Lippincott Williams and Wilkins, 2002, 263–278.

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