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## Review Article

# Review on Transdermal Drug Delivery System

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Transdermal drug delivery systems are polymeric patches containing dissolved or dispersed drug that deliver therapeutic agent at a constant rate through skin. Transdermal delivery has made an important contribution to medical practice but has yet to fully achieve its potential as an alternative to oral delivery and hypodermic injections. The principle of TDDS is that they could provide sustained drug delivery (and hence constant drug concentration in plasma) over a prolonged period of time. TDDS can be designed to input drug at appropriate rate to maintain plasma-drug levels for therapeutic efficacy. Ultimately the success of all the transdermal system depends on the ability of the drug to permeate skin in sufficient quantities to achieve its desired therapeutic effect. This review article provides a detailed study of transdermal that is advantage, disadvantages, mechanism, factors affecting skin permeation and types. This article also focuses on the application and future approaches of transdermal drug delivery system.

**Key words:** Transdermal, skin, delivery system.

## 1. INTRODUCTION

Delivering medicine to the general circulation through the skin is seen as a desirable alternative to taking it by mouth or by oral route. Patients often forget to take their medicine and also they get tired of swallowing pills. Additionally bypassing the gastrointestinal tract would obviate the GI irritation that frequently occurs & avoid partial first pass inactivation by the liver. Further, steady absorption of drug over hours or days is usually preferable to blood level spikes and troughs produced by oral dosage forms.

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These advantages are offered by the currently marketed transdermal products. Transdermal drug delivery is defined as self-contained, discrete dosage forms which when applied to intact skin delivers the drug through the skin at controlled rate to the systemic circulation<sup>1</sup>. TDDS established itself as an integral part of novel drug delivery system. The transdermal patches uses a polymer membrane to control the rate at which the drug contained in the reservoir within the patch can pass through the skin and into the blood stream<sup>2</sup>.

FDA approved the first transdermal patches product in 1981. TDDS are currently available containing scopolamine (Hyoscine) for motion sickness, clonidine & nitroglycerine for cardiovascular disease, fentanyl for chronic pain, nicotine to aid smoking cessation, oestradiol (alone or in combination with levonorgestrel or norethisterone) for hormone replacement and testosterone for hypogonadism. There are several product in late stage development that will further expand TDD usage into new therapeutic area including Parkinson's disease, attention deficit and hyperactivity disorder and female sexual dysfunction. Over the last two decades more than 35 transdermal patches have been approved, generating sales of \$3.2 billion in 2002 to \$4.5 billion in 2008<sup>3</sup>. More recently such dosage forms have been developed and or modified in order to enhance the driving force of diffusion (thermodynamic activity) and or increase the permeability of skin. These approaches include permeability enhancer, prodrug, liposome and other vesicles.

Today four drug have been successfully incorporated into TDDS for clinical use (scopolamine, nitroglycerine, clonidine & estradiol) which established the dermal route for systemic drug delivery.

### **1.1 Transdermal Drug Delivery System<sup>4</sup>**

Today most of the drug are taken orally but, they are found not to be as effective as desired, So to improve such character TDDS was emerged. Drug delivery

through the skin to achieve a systemic effect of a drug is commonly known as transdermal drug delivery system. These are dosage forms which involves drug transport to viable epidermal and or dermal tissue of the skin for local therapeutic effect while a very major fraction of the drug is transported into systemic blood circulation. Currently TDDS is one of the most promising methods for drug application.

Transdermal drug delivery provide a leading edge over injectables and oral route by increasing patient compliances and avoiding first pass metabolism respectively. TDDS not only provides a controlled, constant administration of drug, but also allows continuous input of drug with short biological half life and eliminates pulsed entry into systemic circulation which often causes undesirable side effect.

### ***Advantages of transdermal drug delivery system<sup>5</sup>***

Delivery via the transdermal route is an interesting option because transdermal route is convenient and safe. The positive features of delivering drug across skin to achieve systemic effect are

1. Avoidance of first pass metabolism.
2. Avoidance of gastrointestinal incompatibility.
3. Predictable and extended duration of activity.
4. Minimizing undesirable side effect.
5. Provides utilization of drug with short biological half life, narrow therapeutic window.
6. Avoiding the fluctuation in drug level.
7. Maintain plasma concentration of potent drug.
8. Termination of therapy is easy at any point of time.
9. Greater patient compliances due to elimination of multiple dosing profile.
10. Ability to deliver the drug more selectively to a specific site.
11. Provide suitability for self administration.
12. Enhance therapeutic efficacy.

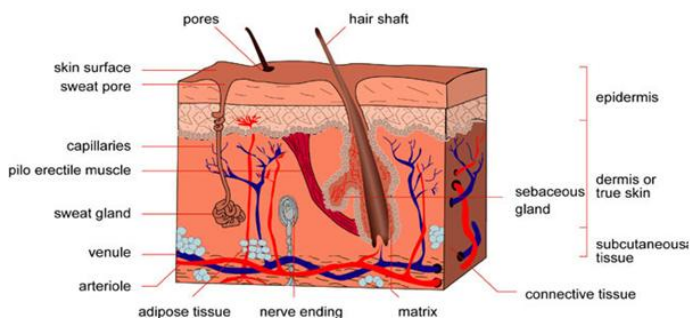
**Disadvantages of transdermal drug delivery system**

1. The drug must have some desirable physicochemical properties for penetration through stratum corneum and if the drug dose required for therapeutic value is more than 10 mg/day, the transdermal delivery will be very difficult.
2. Only relatively potent drugs are suitable candidates for TDDS because of the natural limits of drug entry imposed by the skin's impermeability.
3. Some patients develop contact dermatitis at the site of application for one or more of the system components, necessitating discontinuation.
4. Clinical need is another area that has to be examined carefully before a decision is made to develop a transdermal product.
5. The barrier function of the skin changes from one site to another on the same person, from person to person and with age.

**Skin as site for transdermal drug administration<sup>6</sup>**

The skin of an average adult body covers a surface area of approximately two square meters and receives about one-third of the blood circulating through the body. The skin is a multilayered organ composed of many histological layers. It is generally described in terms of three major tissue layers: the epidermis, the dermis, and the hypodermis (Fig 1). Microscopically, the epidermis is further divided into five anatomical layers with stratum corneum forming the outer most layer of the epidermis, exposing to the external environment. An average human skin surface is known to contain, on the average, 40-70 hair follicles and 200-250 sweat ducts on each square centimeter of skin area. These skin appendages, however, actually occupy, grossly, only 0.1% of the total human skin surface. Even though the foreign agents, especially the water-soluble ones, may be able to penetrate into the skin via these skin appendages at a rate which is faster than through the intact area of the stratum corneum, this trans-

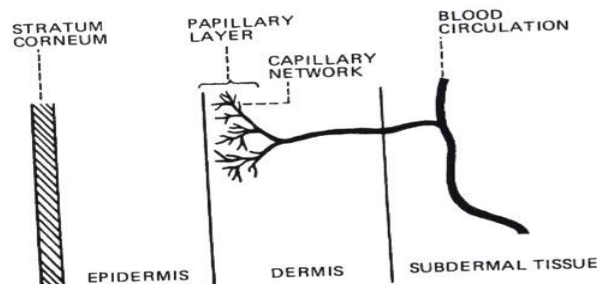
appendage route of percutaneous absorption has, at steady state, a very limited contribution to the overall kinetic profile of transdermal permeation. Therefore, the transdermal permeation of most neutral molecules can thus, be considered as a process of passive diffusion through the intact stratum corneum in the inter follicular region.



**Fig 1: Cross section of skin**

**Mechanism of transdermal permeation**

For a systemically-active drug to reach a target tissue, it has to possess some physico-chemical properties which facilitate the absorption of the drug through the skin and also the uptake of the drug by the capillary network in the dermal papillary layer (Fig2)



**Fig 2: Simplified model of the human skin for mechanistic analysis of Skin Permeation.**

The rate of permeation,  $dQ/dt$ , across various layers of skin tissues can be expressed as.

$$dQ/dt = P_s(C_d - C_r) \dots\dots\dots (1)$$

Where,  $C_d$  and  $C_r$  are respectively, the concentrations of skin penetrate in the donor phase (stratum corneum) and the receptor phase (systemic circulation); and  $P_s$  is the overall permeability coefficient of the skin and is defined by

$$P_s = K_s D_{ss} / H_s \dots\dots\dots(2)$$

Where,

$K_s$  = Partition coefficient of the penetrant

$D_{ss}$  = Apparent diffusivity of penetrant

$H_s$  = Thickness of skin

A constant rate of drug permeation achieved, if  $C_d > C_r$ , then the equation (1) may be reduced to

$$dQ/dt = P_s \cdot C_d \dots\dots\dots(3)$$

And the rate of skin permeation ( $dQ/dt$ ) becomes a constant, if the  $C_d$  value remains fairly constant throughout the course of skin permeation. To maintain the  $C_d$  at a constant value, it is critical to make the drug to be released at a rate ( $R_r$ ) which is always greater than the rate of skin uptake ( $R_a$ ), i.e.,  $R_r \gg R_a$

By doing so, the drug concentration on the skin surface ( $C_d$ ) is maintained at a level which is always greater than the equilibrium (or saturation) solubility of the drug in the stratum corneum ( $C_s^e$ ), i.e.,  $C_d \gg C_s^e$ ; and a maximum rate of skin permeation ( $(dQ/dt)_m$ ), as expressed by equation (4), is thus reached:

$$(dQ/dt)_m = P_s C_s^e \dots\dots\dots(4)$$

Apparently, the magnitude of  $(dQ/dt)_m$  is determined by the skin permeability coefficient ( $P_s$ ) of the drug and its equilibrium solubility in the stratum corneum ( $C_s^e$ ).

## 1.2 Factors affecting transdermal permeation<sup>7</sup>

### *Physicochemical properties of the penetrant molecules*

#### *A. 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.

#### *B. pH conditions*

- Applications of solutions whose pH values are very high or very low can be destructive to the drug.

- 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.

#### *C. 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.

### *Physicochemical properties of the drug delivery system<sup>8</sup>*

#### *A. 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

#### *B. Composition of the drug delivery systems*

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.

### **1.3 Basic components of transdermal patch<sup>9</sup>**

1. Polymer matrix / Drug reservoir
2. Drug
3. Permeation enhancers
4. Pressure sensitive adhesive (PSA)
5. Backing laminates

6. Release liner and other excipients like plasticizers and solvents

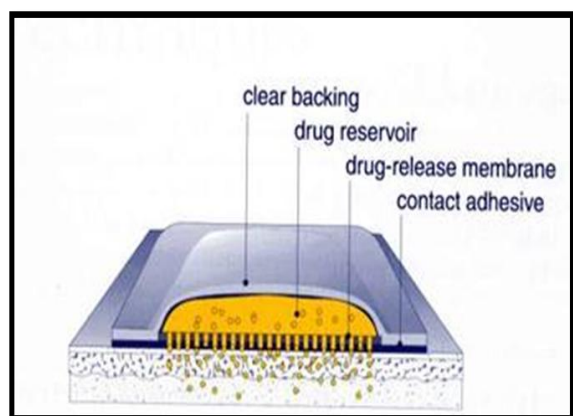


Fig 3: Components of transdermal patches

### Polymers<sup>10</sup>

Polymers are the important parameter of TDDS, which control the release of the drug from the device. Polymer matrix can be prepared by dispersion of drug in liquid or solid state synthetic polymer base. Companies involved in the field of transdermal delivery concentrate on a few selective polymeric systems. For example, Alza Corporation mainly concentrates on ethylene vinyl acetate (EVA) copolymers or microporous polypropylene and Searle Pharmacia concentrates on silicon rubber. The polymers utilized for TDDS can be classified as,

**Natural Polymers:** e.g. cellulose derivatives, zein, gelatin, shellac, waxes, gums

**Synthetic Elastomers:** e.g. polybutadiene, hydriin rubber, polyisobutylene, silicon acrylonitrile, neoprene, butylrubber etc.

**Synthetic Polymers:** e.g. polyvinyl alcohol, polyvinylchloride, polyethylene, polyacrylate, polyamide, polyurea, polyvinylpyrrolidone etc.

The following criteria should be satisfied for a polymer to be used in transdermal system.

1. Molecular weight and chemical functionality of the polymer should be such that specific drug diffuses properly and get released through it.

2. The polymer should be stable, non reactive, easily manufactured and fabricated into the desired product.
3. The polymer and its degradation product must be non-toxic to the host.

### Drug<sup>11</sup>

For successfully developing a TDDS, the drug should be chosen with great care. The following are some of the desirable properties of a drug for transdermal delivery.

### Physicochemical properties

1. The drug should have a molecular weight less than approximately 1000 Dalton.
2. The drug should have affinity for both lipophilic and hydrophilic phases.
3. The drug should have low melting point.

### Biological properties

1. The drug should be potent with a daily dose of the order of a few mg/day.
2. The half life should be short.
3. The drug must not induce a cutaneous irritant or allergic response.
4. Drug which degrade in the GI tract are suitable for transdermal delivery.
5. Drugs which have to be administered for a long period of time can be formulated for transdermal system.

### Permeation enhancers<sup>12</sup>

To increase the permeability of stratum corneum so as to attain higher therapeutic levels of the drug penetration enhancer interact with structural component of stratum corneum i.e protein and lipids. The enhancement of absorption of oil soluble drugs is apparently due to partial leaching of the epidermal lipids by chemical enhancers, resulting in the improvement of skin condition for wetting and transepithelial and transfollicular penetration.

Permeation enhancer is classified into two- chemical and physical enhancer.

1. **Chemical enhancer:** Chemicals that promote the penetration of topically applied drugs are commonly referred to as accelerants, absorption promoters, or penetration enhancers.

#### **Classification of chemical enhancer**

1. Terpenes : e.g. menthol, carvone etc.
2. Pyrrolidones : e.g. N-methyl-2-pyrrolidone, azone etc.
3. Fatty acids : e.g. oleic acid, lauric acid etc.
4. Sulfoxides : e.g. dimethyl sulfoxide.
5. Alcohols : e.g. ethanol, octyl alcohol etc.
6. Miscellaneous enhancer : e.g. phospholipid, cyclodextrin, amino derivative etc.

#### **2. Physical enhancers**

The iontophoresis and ultra sound (also known as phonophoresis or sonophoresis) techniques are examples of physical means of enhancement that have been used for enhancing percutaneous penetration (and absorption) of various therapeutic agents.

#### **Adhesives**

The pressure sensitive adhesive maintains an intimate contact between patch and the skin surface. E.g. polyacrylates, polyisobutylene and silicon based adhesive. Adhesive system should fulfill the following criteria

1. Should not irritate or sensitize the skin.
2. Should adhere to the skin aggressively during the dosing interval without its position being disturbed by activities such as bathing, exercise e.t.c.
3. Should be easily removed

4. Should not leave an unwashable residue on the skin.
5. Should have excellent contact with skin.

#### **Backing laminate**

The primary function is to provide a good bond to the drug reservoir, prevent drug from leaving the dosage forms through the top. It is impermeable substance that protect the product during use on the skin. eg metallic plastic laminate, occlusive base plate (aluminium foil), adhesive foam pad (flexible polyurethane) etc.

#### **Release liner**

During storage release liner prevents the loss of the drug that has migrated into adhesive layer. It is therefore regarded as a part of primary packaging material. E.g paper fabric, polyethylene, polyvinylchloride etc.

#### **Other excipients**

Solvents such as chloroform, methanol, acetone are used to prepare drug reservoir. In addition plasticizers such as castor oil, propylene glycol etc are added to provide plasticity to the patch.

### **2. TYPES OF TRANSDERMAL PATCHES<sup>13,14,15</sup>**

#### **Single Layer Drug -In- Adhesive**

The Single-layer Drug-in-Adhesive system is characterized by the inclusion of the drug directly within the skin-contacting adhesive. In this transdermal system design, the adhesive not only serves to affix the system to the skin, but also serves as the formulation foundation, containing the drug and all the excipients under a single backing film.

#### **Multi Layer Drug In Adhesive**

The Matrix system design is characterized by the inclusion of a semisolid matrix containing a drug solution or suspension which is in direct contact with the release liner. The component responsible for skin adhesion is incorporated in an overlay and forms a concentric configuration around the semisolid matrix.

#### **Drug Reservoir-in-Adhesive**

The Reservoir transdermal system design is characterized by the inclusion of a liquid compartment containing a drug solution or suspension separated from the release liner by a semi-permeable membrane and adhesive. The adhesive component of the product responsible for skin adhesion can either be incorporated as a continuous layer between the membrane and the release liner or in a concentric configuration around the membrane.

### ***Drug Matrix-in-Adhesive***

The Matrix system design is characterized by the inclusion of a semisolid matrix containing a drug solution or suspension which is in direct contact with the release liner. The component responsible for skin adhesion is incorporated in an overlay and forms a concentric configuration around the semisolid matrix.

### **2.1 Approches used in development of TDDS**

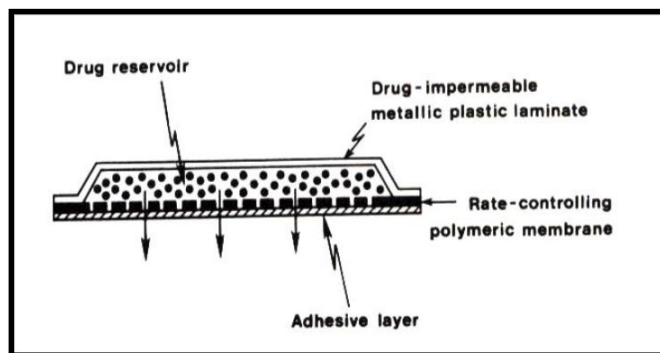
Several technologies have been successfully developed to provide a rate control over the release and the transdermal permeation of drugs. These technologies can be classified into four approaches as follows:

1. Membrane permeation – controlled systems
2. Adhesive dispersion – type systems.
3. Matrix diffusion – controlled systems.
4. Micro reservoir type or micro sealed dissolution controlled systems.

### ***Membrane permeation – controlled systems***

In this type of system, drug reservoir is encapsulated in a shallow compartment moulded from a drug-impermeable metallic plastic laminate and a rate controlling polymeric membrane which may be micro porous or non-porous as shown in fig.4. The drug molecules are permitted to release only through the rate – controlling polymeric membrane. In the drug reservoir compartment, the drug solids are either dispersed homogenously in a solid polymer matrix (e.g. Polyisobutylene adhesive) or suspended in an

unbleachable, viscous liquid medium (e.g. Silicon fluids) to form a paste like suspension.



**Fig 4: Membrane permeation controlled system**

The rate of drug release from this type of system can be tailored by varying the polymer composition, permeability coefficient and thickness of the rate limiting membrane and adhesive. The constant release rate of the drug is the major advantage of membrane permeation controlled system. However, a rare risk also exists when an accidental breakage of the rate controlling membrane can result in dose dumping or rapid release of entire drug content. Examples of this system are Transderm-nitro, Transderm-scop, Catapres and Estraderm etc.

### ***Adhesive Dispersion – Type Systems***

This is a simplified form of the membrane-permeation controlled system. As shown in fig.5, the drug reservoir is formulated by directly dispersing the drug in an adhesive polymer e.g. Poly (isobutylene) or poly (acrylate) adhesive and then spreading the medicated adhesive, by solvent casting or hot melt, on to a flat sheet of drug impermeable metallic plastic backing to form a thin drug reservoir layer. On the top of the drug reservoir layer, thin layers of non-medicated, rate-controlling adhesive polymer of a specific permeability and constant thickness are applied to produce an adhesive diffusion – controlled delivery system.

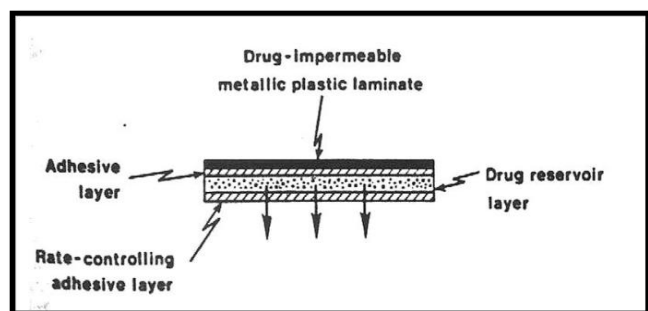


Fig 5: Adhesive dispersion type system

Eg of this system: isosorbite trinitrate, nitroglycerine.

### Matrix Diffusion- Controlled Systems

In this approach, the drug reservoir is formed by homogeneously dispersing the drug solids in a hydrophilic or lipophilic polymer matrix. The resultant medicated polymer is then molded into a medicated disc with a defined surface area and controlled thickness. Drug reservoir containing polymer disc is then pasted onto an occlusive base plate in a compartment fabricated from a drug-impermeable plastic backing membrane (fig.6). e.g. Nitro-Dur: Delivers nitroglycerin for the treatment of angina pectoris.

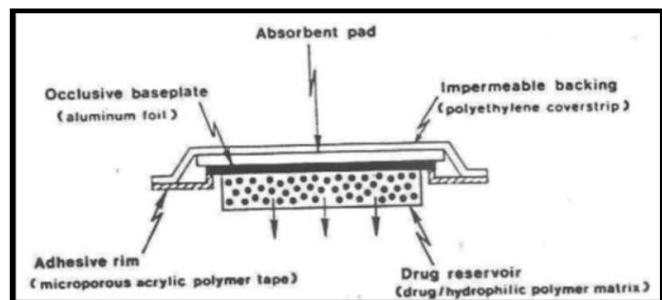


Fig 6: Matrix diffusion controlled system

### Micro reservoir type or Micro sealed Dissolution

The micro reservoir type drug delivery system can be considered a combination of the reservoir and matrix diffusion type drug delivery systems. The drug reservoir is formed by first suspending the drug solids in the aqueous solution of water soluble liquid polymer (e.g. Polyethylene glycol) and then dispersing the drug suspension homogeneously in lipophilic polymer viz.

silicone elastomers by high energy dispersion technique to form several discrete, unleachable microspheres of drug reservoirs. This transdermal therapeutic system is then produced by positioning the medicated disc at the centre and surrounding it with an adhesive rim (fig. 7). E.g. nitroglycerine.

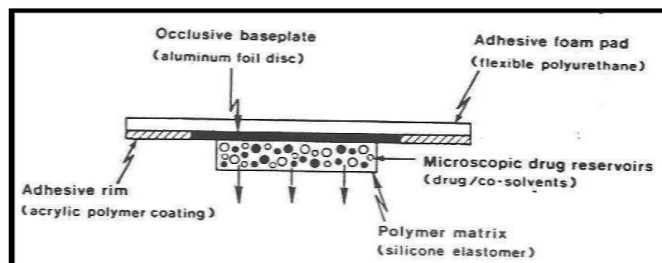


Fig 7: Micro reservoir type controlled system

### Applications of Transdermal Patches<sup>16</sup>

1. The highest selling transdermal patch in the United States is the nicotine patch, which releases nicotine in controlled doses to help with cessation of tobacco smoking.
2. Two opioid medications used to provide round-the-clock relief for severe pain are often prescribed in patch form: Fentanyl (marketed as Duragesic) and Buprenorphine (marketed as BuTrans).
3. Estrogen patches are sometimes prescribed to treat menopausal symptoms as well as post-menopausal osteoporosis. Other transdermal patches for hormone delivery include the contraceptive patch (marketed as Ortho Evra or Evra).
4. Nitroglycerin patches are sometimes prescribed for the treatment of angina pectoris.
5. The anti-hypertensive drug Clonidine is available in transdermal patch form.
6. Transdermal form of the MAOI selegiline, became the first transdermal delivery agent for an antidepressant.<sup>17</sup>



## 2.2 Recent Advances in Transdermal delivery system

Latest research done in field of transdermal patches are stated below:

### *Patch technology for protein delivery*<sup>18</sup>

Transdermal delivery of large protein is a novel and exciting delivery method. transpharma uses its unique printed patch technology for transdermal delivery of protein thereby complementing its via Derm delivery technology. It is postulated that the highly water soluble proteins are dissolved by the interstitial fluid that is secreted from the skin through the RF-MicroChannels, forming a highly concentrated protein solution in situ. The delivery of the dissolved molecules is then carried out, via the RF-Micro Channels, into the viable tissues of the skin, diffusing across a steep concentration gradient.

### *Testosterone transdermal patch system in young women with spontaneous premature ovarian failure*<sup>19</sup>

In premenopausal women, the daily testosterone production is approximately 300 µg, of which approximately half is derived from the ovaries and half from the adrenal glands. Young women with spontaneous premature ovarian failure (sPOF) may have lower androgen levels, compared with normal ovulatory women. Testosterone transdermal patch (TTP) was designed to deliver the normal ovarian production rate of testosterone.

### *Transdermal patch of oxybutynin used in overactive bladder*<sup>20</sup>

The product is a transdermal patch containing Oxybutynin HCl and is approved in US under the brand name of Oxytrol and in Europe under the brand name of Kentera. OXYTROL is a thin, flexible and clear patch that is applied to the abdomen, hip or buttock twice weekly and provides continuous and consistent delivery of oxybutynin over a three to four day interval. OXYTROL offers over active bladder(

OAB) patient's continuous effective bladder control with some of the side effects, such as dry mouth and constipation encountered with an oral formulation.

### *Nanotechnology gaining hold*<sup>21</sup>

Another enhancer that is gaining advancement is microneedles. This technology combines the advantage of a needle and the transdermal patch. The devices are dime-sized pieces of polymer with hundreds of hollow microneedles between 100 and 1,000 micrometers long. These small needles penetrate the top layers of skin and allow the drug to pass through with ease. This technology can be combined with an electronically controlled micropump that delivers the drug at specific times or upon demand. Alza is using a slightly different variation on the use of needles. The company has developed the patented Macroflux transdermal technology that uses microprojections to create superficial pathways through the dead skin barrier.

### *Pain relief*<sup>22</sup>

Pain relief routinely benefits from transdermal patch technology. Most of the readers are aware of the Duragesic patch. One is Lidoderm, a lidocaine percent patch, which is used for post herpetic neuralgia. Other exciting advancements in pain control include the E-Trans fentanyl HCl patch. This credit card-size patch is an active delivery device that has a self-contained battery that delivers pulses of fentanyl HCl, a strong narcotic. This mimics the use of intravenous self-controlled analgesic systems that are very expensive.

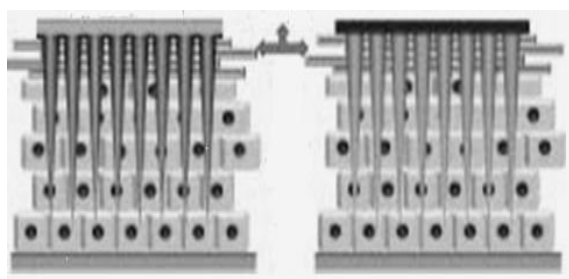
### *Molecular absorption enhancement technology*<sup>23</sup>

Considerable research has been done on absorption enhancers, compounds that promote the passage of drugs through the stratum corneum. Terpene derivatives as well as certain phenols seem to improve transdermal absorption. For example Limonene, menthone, and eugenol were found to enhance

transdermal absorption of tamoxifen. Phloretin, a polyphenol, enhanced the absorption of lignocaine.

### **Microfabricated microneedle<sup>24</sup>**

These are the devices which are having the features of both the hypodermic needle and transdermal patch that can deliver the drug that transports the drug effectively across the membrane. The system consists of a drug reservoir and some projections (microneedles as shown in fig. 8) extending from the reservoir, these help in penetrating the stratum corneum and epidermis to deliver the drug.



**Fig 8: Delivery site for microneedle technology. (a) Hollow microneedles with applied formulation; (b) Solid microneedles**

Microneedles are tiny and very sleek devices that are manufactured by the silicon etching technology and micro-mechanical system manufacturing (MEMS) technique, which do not penetrate deep enough into the skin to reach up to the nerve endings and thus there is no pain sensation during the microneedles insertion into the skin. There are number of delivery approaches that have been employed to use the microneedles for TDDS. These include-

**Poke with patch approach-** Involves piercing into the skin followed by application of the drug patch at the site of treatment.

**Coat and poke approach-** Needles coated with the drug are inserted into the skin and release of medicament is then occurs by dissolution.

**Biodegradable microneedles-** Involves encapsulation of the drug within the biodegradable, polymeric microneedles, which is then inserted into the skin.

**Hollow microneedles-** Involves injecting the drug through the needle with a hollow bore.

### **Future Technologies and Approaches<sup>25</sup>**

- Thermal Poration is the formation of aqueous pathways across stratum corneum by the application of pulsed heat, this approach has been used to deliver conventional drugs .
- Jet injectors are receiving increased attention now days, which is opening doors for improved device design for controlled, needle free injection of drug solutions across the skin and into deeper tissue.
- Small needle is inserted a few millimeters into skin and drug solution is flowed through the needle into the skin at controlled rates using a micro-infusion pump that is contained within a large patch affixed to skin, morphine has been delivered to humans using this approach.
- During the past decade several theories have been put forward in addressing the combinations of chemicals and iontophoresis; chemicals and electroporation; chemicals and ultrasound; iontophoresis and ultrasound; electroporation and iontophoresis; and electroporation and ultrasound.
- TransPharma is focused on products for which our technology will provide clear benefits over existing therapies. Such benefits could include improving safety and compliance through the use of a drug patch or enhancing efficacy with the use of sustained release patch formulations, among others.
- The ViaDerm system may be applied to the delivery of local medications for topical applications in the fields of dermatology and cosmetics. The ViaDerm system may also allow enhanced immunizations, providing a nonpainful, safe and effective alternative to current intramuscular or subcutaneous vaccination methods.
- Altea Therapeutics is currently in clinical development of a transdermal patch designed to

address a major unmet need by preventing 'off' periods and provide an improved therapeutic option for managing Parkinson's disease.

### 3. CONCLUSION

Transdermal drug delivery systems represent a beneficial innovation for drug delivery, particularly in patients who cannot swallow or remember to take their medications. Clinicians and other allied health professionals should understand the appropriate administration techniques for transdermal systems to ensure optimal patient outcomes and to ensure the safety of all who encounter patients who use TDDS. Future developments of TDDSs will likely focus on the increased control of therapeutic regimens and the continuing expansion of drugs available for use. Transdermal dosage forms may provide clinicians an opportunity to offer more therapeutic options to their patients to optimize their care.

### 4. ACKNOWLEDGEMENT

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### **Conflict of Interest Statement**

There are no conflicts of interest.