

## TRANSDERMAL PATCHES: A RECENT APPROCH TO NEW DRUG DELIVERY SYSTEM

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## ABSTRACT

Transdermal drug delivery system was introduced to overcome the difficulties of drug delivery through oral route. A transdermal patch is medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. Often, this promotes healing to an injured area of the body. An advantage of a transdermal drug delivery route over other types of medication delivery such as oral, topical, intravenous, intramuscular, etc. is that the patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive. The main disadvantage to transdermal delivery systems stems from the fact that the skin is a very effective barrier; as a result, only medications whose molecules are small enough to penetrate the skin can be delivered in this method. This review article describes the methods of preparation of different types of transdermal patches such as matrix patches, reservoir type, membrane matrix, drug-in-adhesive patches and micro reservoir patches. In addition, the various methods of evaluation of transdermal dosage form have also been reviewed.

**Keywords:** Transdermal Patch, Matrix Patches, Reservoir Type, Membrane Matrix, Drug-In-Adhesive Patches, Micro Reservoir Patches

## INTRODUCTION

A transdermal patch is used to deliver a specific dose of medication through the skin and into bloodstream. Transdermal patches products were first approved in 1981 by FDA. Transdermal delivery systems are currently available containing scopolamine (hyoscine) for motion sickness, clonidine and nitroglycerin for cardiovascular disease, fentanyl for chronic pain, nicotine to aid smoking cessation. Transdermal delivery provides controlled, constant administration of the drug, and allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into systemic circulation. TDDS offers many advantages over conventional injection and oral methods. It reduces the load that the oral route commonly places on the digestive tract and liver. It enhances patient compliance and minimizes harmful side effects of a drug caused from temporary overdose. It is convenient, especially notable in patches which require only once weekly application. Such a simple dosing regimen aids in patient adherence to drug therapy<sup>1</sup>.

The main components to a transdermal patch are:

- **Polymer matrix**- backbone of TDDS, which control the release of the drug. Polymer should be chemically non-reactive, should not decompose on storage, should be non toxic, cost should not be high. E.g.- cellulose derivatives, zein, gelatin, shellac, waxes, gums, Polybutadiene, hydriin rubber, polyisobutylene, silicon rubber, nitrile, acrylonitrile, neoprene, Polyvinyl alcohol, polyvinylchloride, polyethylene, polypropylene, polyacrylate, polyamide, polyurea, polyvinylpyrrolidone, polymethylmethacrylate.
- **Drug**- The transdermal route is an extremely attractive option for the drugs with appropriate pharmacology and physical chemistry. Transdermal patches offer much to drugs which undergo extensive first pass metabolism, drugs with narrow therapeutic window, or drugs with short half life. eg fenatyl, nitroglycerine etc.
- **Permeation enhancers**- increase permeability of stratum corneum so as to attain higher therapeutic levels of the drug. These are of three types-lipophilic solvent, surface active agents and two component systems. E.g. DMSO
- **Adhesive**- increase permeability of stratum corneum so as to attain higher therapeutic levels of the drug that increase permeability of stratum corneum so as to attain higher therapeutic levels of the drug.

- **Backing laminates**- should have low modulus or high flexibility. Eg-vinyl, polyethylene.
- **Release liner**- Protects the patch during storage. The liner is removed prior to use.
- Other excipients like plasticizers and solvents<sup>2</sup>.

## Drug Delivery Routes across Human Skin

Drug molecules can penetrate by three pathways:

1. Sweat ducts
2. Hair follicles
3. Sebaceous glands

Or

Directly across the stratum corneum.

The stratum corneum is the outermost layer of the epidermis, composed of large, flat, polyhedral, plate-like envelopes filled with keratin that is made up of dead cells that have migrated up from the stratum granulosum. This skin layer is composed mainly of dead cells that lack nuclei. As these dead cells slough off on the surface in the thin air-filled stratum disjunctum, they are continuously replaced by new cells from the stratum germinativum (basale). The stratum corneum consists of 10-15 layers of corneocytes and varies in thickness from approximately 10-15  $\mu\text{m}$  in the dry state to 40  $\mu\text{m}$  when they are hydrated. It is comprised mainly of a multi-layered "brick and mortar" like structure of keratin-rich corneocytes (bricks) in an intercellular matrix (mortar) that is composed of long chain ceramides, free fatty acids, triglycerides, cholesterol, cholesterol sulfate and sterol/wax esters. The intercellular lipid matrix is generated by keratinocytes in the mid to upper part of the stratum granulosum discharging their lamellar contents into the intercellular space. The initial layers of the stratum corneum rearrange to form broad intercellular lipid lamellae which then associate into lipid bilayers. As a result of the stratum corneum lipid composition, the lipid phase behavior is different from that of other biological membranes. Water is an essential component of the stratum corneum, which acts as a plasticizer to prevent cracking of the stratum corneum and is also involved in the generation of natural moisturizing factor which helps to maintain suppleness. To understand the physicochemical properties of the diffusing drug and vehicle influence across stratum corneum, it is essential to determine the predominant route of drug permeation within the stratum corneum. A molecule travelling via

the transcellular route partition into and diffuse through the keratinocyte, but in order to move to the next keratinocyte, the molecule must partition into and diffuse through the estimated 4-20 lipid lamellae between each keratinocyte. This series of partitioning

into and diffusing across multiple hydrophilic and hydrophobic domains is unfavorable for most drugs. Therefore the intercellular route is now considered to be the major pathway for permeation of most drugs across the stratum corneum.

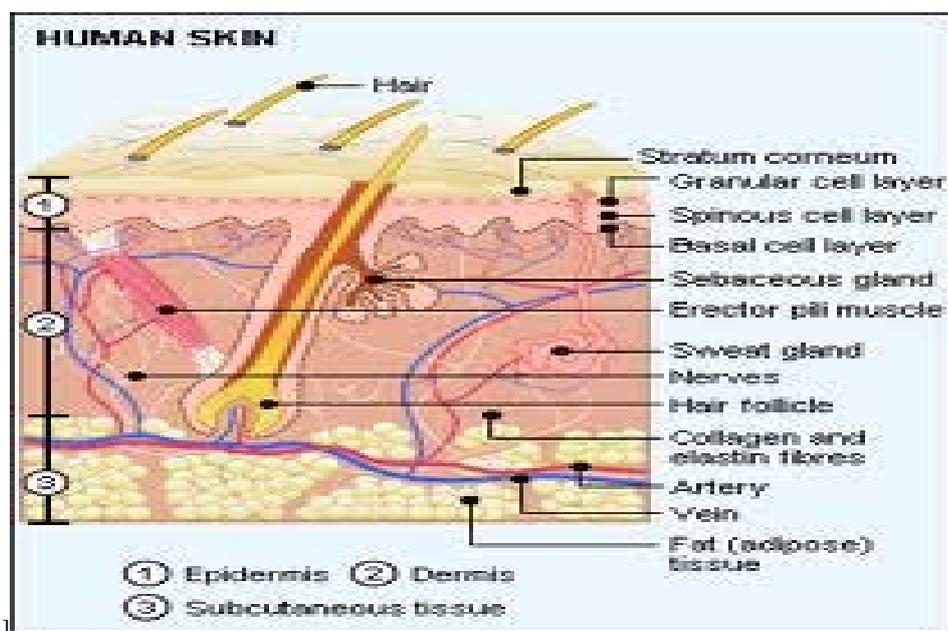


Fig. 1: Transverse section of skin showing routes of penetration 1. Through the sweat ducts; 2. Directly across the stratum corneum; 3. Via the hair follicles<sup>2</sup>

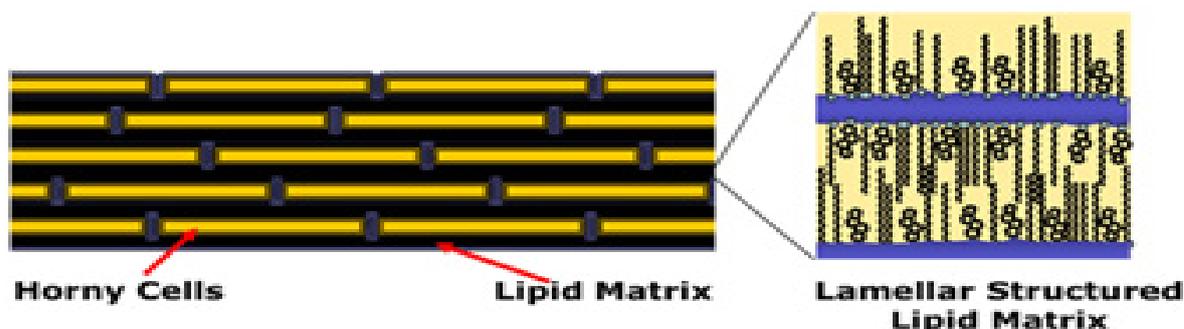


Fig. 2: Schematic structure of the stratum corneum according to the brick and mortar model<sup>3</sup>

#### Advantages

1. It is convenient method and requires only once weekly application. Such a simple dosing regimen can aid in patient adherence to drug therapy.
2. Transdermal drug delivery can be used as an alternative route of administration to accommodate patients who cannot tolerate oral dosage forms.
3. It is of great advantage in patients who are nauseated or unconscious.
4. Drugs that cause gastrointestinal upset can be good candidates for transdermal delivery because this method avoids direct effects on the stomach and intestine.
5. Drugs that are degraded by the enzymes and acids in the gastrointestinal system may also be good targets.
6. First pass metabolism, an additional limitation to oral drug delivery, can be avoided with transdermal administration.

7. Drugs that require relatively consistent plasma levels are very good candidates for transdermal drug delivery<sup>3</sup>.

#### Disadvantages

1. Possibility of local irritation at the site of application.
2. Erythema, itching, and local edema can be caused by the drug, the adhesive, or other excipients in the patch formulation.
3. May cause allergic reactions.
4. A molecular weight less than 500 Da is essential.
5. Sufficient aqueous and lipid solubility, a log P (octanol/water) between 1 and 3 is required for permeate to transverse SC and underlying aqueous layers.

#### Methods for Enhancing Transdermal Drug Delivery

Skin penetration can be enhanced by following methods:

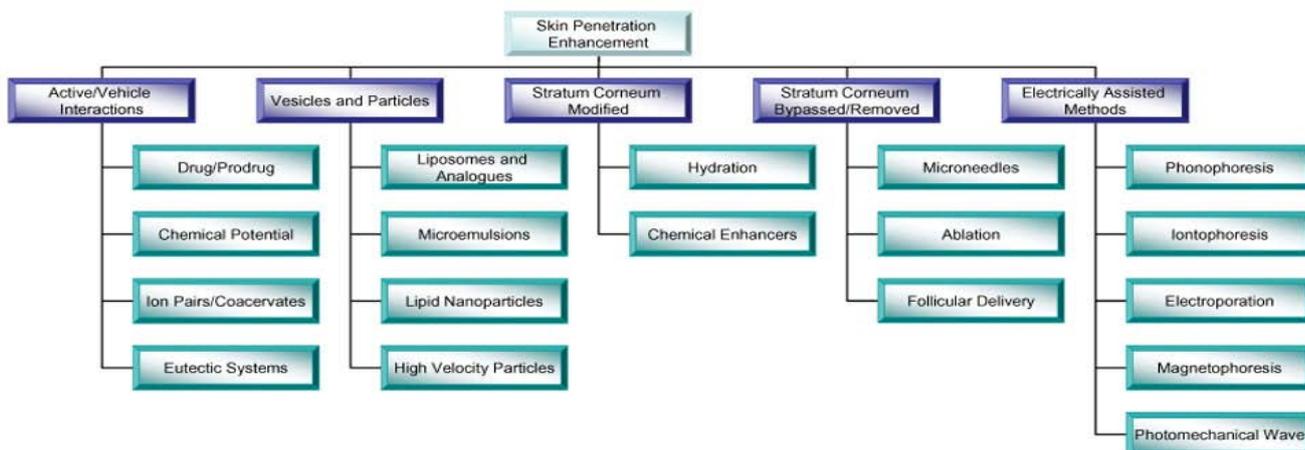


Fig. 3: Various methods used to enhance the Skin penetration <sup>4</sup>

1. **Drug/prodrug**-The prodrug approach has been used to enhance the dermal and transdermal delivery of drugs with unfavourable partition coefficients the prodrug design involves addition of a promoiety to increase partition coefficient and also solubility and transport of the parent drug in the stratum corneum. Upon reaching the viable epidermis, esterases release the parent drug by hydrolysis thereby optimising solubility in the aqueous epidermis. For example: The intrinsic poor permeability of the very polar 6-mercaptopurine was increased up to 240 times using S6-acyloxymethyl and 9-dialkylaminomethyl promoieties. The prodrug approach has also been investigated for increasing skin permeability of non-steroidal anti-inflammatory drugs, like naltrexone nalbuphine buprenorphin alpha-blocker and other drugs <sup>3,4</sup>.

2. **Eutectic system**-A eutectic system is a mixture of chemical compounds or elements that has a single chemical composition that solidifies at a lower temperature than any other composition. According to regular solution theory, the lower the melting point, the greater the solubility of a material in a given solvent, including skin lipids. The melting point of a drug delivery system can be lowered EMLA cream, a formulation consisting of a eutectic mixture of lignocaine and prilocaine applied under an occlusive film, provides effective local anesthesia for pain-free venepuncture and other procedures <sup>3,4</sup>.

3. **Liposomes and vehicles**- Liposome are colloidal particles formed as concentric bimolecular layers that are capable of encapsulating drugs. There are many examples of cosmetic products in which the

active ingredients are encapsulated in vesicles. These include humectants such as glycerol and urea, unscreening and tanning agents, enzymes, etc. Phosphatidylcholine from soybean or egg yolk is the most common composition although many other potential ingredients have been evaluated <sup>4</sup>. Cholesterol added to the composition tends to stabilize the structure thereby generating more rigid liposomes. The mechanism of enhanced drug uptake into the stratum corneum is unclear. It is possible that the liposomes either penetrate the stratum corneum to some extent then interact with the skin lipids to release their drug or that only their components enter the stratum corneum.

4. **Solid lipid Nanoparticles**- Solid lipid nanoparticles (SLN) have recently been investigated as carriers for enhanced skin delivery of sunscreens, vitamins A and E, triptolide and glucocorticoids. It is thought their enhanced skin penetration is primarily due to an increase in skin hydration caused by the occlusive film formed on the skin surface <sup>5</sup>.

5. **Iontophoresis**-This method involves permeation of a topically applied therapeutic agent by application of low level electric current either directly to skin or indirectly via dosage form. Parameters that effect design of a iontophoretic skin delivery system include electrode type, current intensity, pH of system. Increased drug permeation as a result of this methodology can be attributed to either one or a combination of the following mechanisms: Electro-repulsion (for charged solutes), electro-osmosis (for uncharged solutes) and electro-perturbation (for both charged and uncharged) <sup>6</sup>.

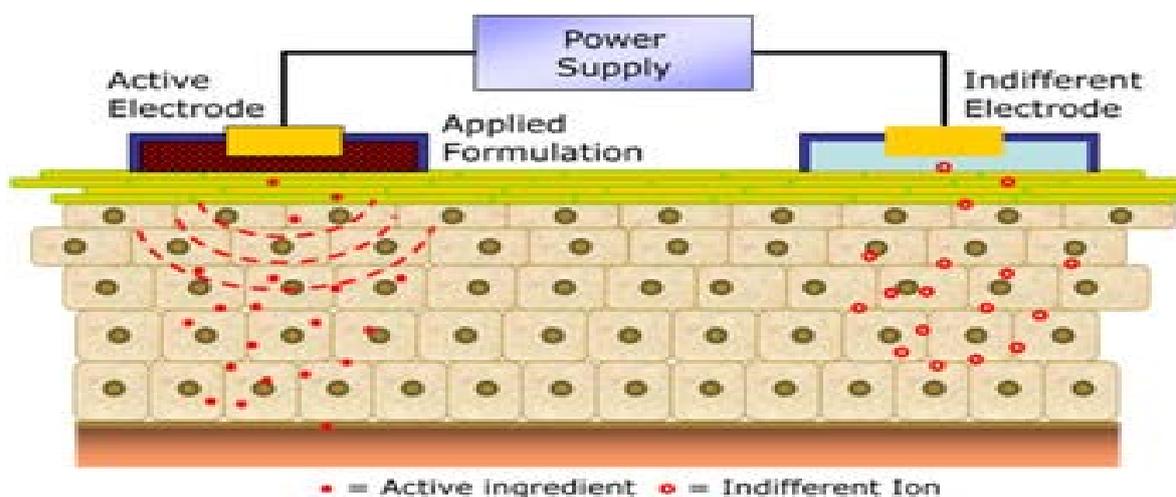


Fig. 4: Basic principle of Iontophoresis <sup>6</sup>

6. **Electroporation**-It involves the application of high voltage pulses to the skin that has been suggested to induce the formation of transient pores. High voltages (100 V) and short treatment durations (milliseconds) are most frequently employed. The technology has been successfully used to enhance the skin permeability of molecules with differing lipophilicity and size (i.e. small molecules, proteins, peptides and oligonucleotides) including biopharmaceuticals with molecular weights greater than 7kDa <sup>6</sup>.

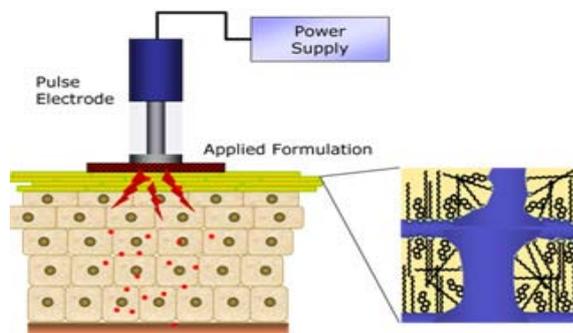


Fig. 5: Basic principle of electroporation <sup>7</sup>

7. **Ultrasound (sonophoresis and phonophoresis)**- This technique involves the use of ultrasonic energy to enhance the transdermal delivery of solutes either simultaneously or via pre-treatment. It uses low frequency ultrasound (55 kHz) for an average duration of 15 seconds to enhance skin permeability <sup>7</sup>.

8. **Laser radiation and photomechanical waves**- Lasers are frequently used for treatment of dermatological conditions like acne and to confer facial rejuvenation. This method involves direct and controlled exposure of a laser to the skin that results in the ablation

of the stratum corneum without significantly damaging the underlying epidermis <sup>8</sup>.

9. **Radio frequency**- It involves the exposure of skin to high frequency alternating current resulting in formation of heat induced micro channels in the membrane. The rate of drug delivery is controlled by number and depth of micro channels formed by device. Treatment duration takes less than a second <sup>9</sup>.

10. **Magnetophoresis**- It involves application of magnetic field that acts as an external driving force to enhance the diffusion of a diamagnetic solute across the skin. Skin exposure to a magnetic field might also induce structural alterations that could contribute to an increase in permeability <sup>9</sup>.

11. **Microneedle based devices**-The first ever patents for drug delivery for percutaneous administration of drug was based on this method. These microneedles of length 50-110 micrometre will penetrate SC and epidermis to deliver drug.

12. **Skin Abrasion**- The abrasion technique involves the direct removal or disruption of the upper layers of the skin. These devices are based on techniques employed by dermatologists for superficial skin resurfacing which are used in the treatment of acne, scars, hyperpigmentation and other skin blemishes.

13. **Needle-less Injection**- Transdermal delivery is achieved by firing the liquid or solid particles at supersonic speeds through the outer layers of the skin using a suitable energy source. The mechanism involves forcing compressed gas (helium) through the nozzle, with the resultant drug particles entrained within the jet flow reportedly traveling at sufficient velocity for skin penetration. This method avoids issues of safety, pain and fear <sup>10</sup>.

14. **Application of pressure**- The application of modest pressure i.e. 25kPa provides a potentially non-invasive and simplest method of skin permeability of molecules such as caffeine.

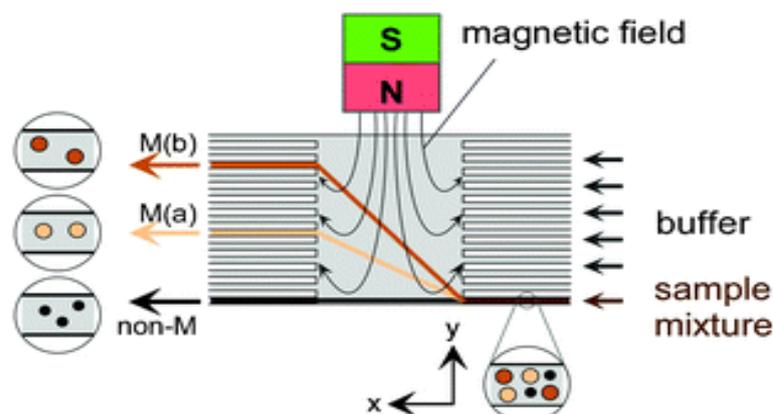


Fig. 6: Technique of magnetophoresis <sup>9</sup>

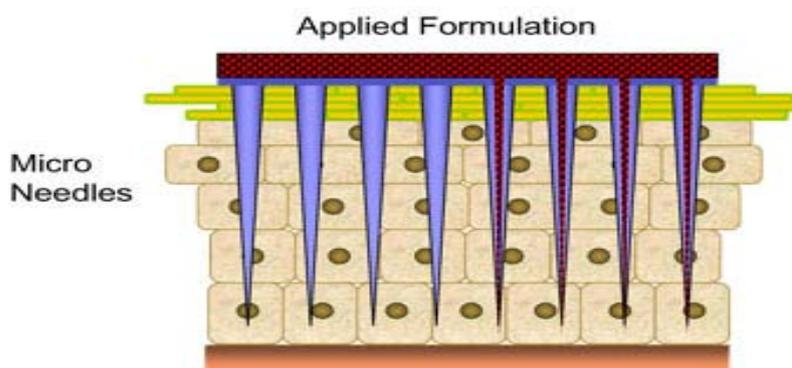


Fig. 7: Basic design of micro needle delivery devices <sup>10</sup>

**Table 1: Ideal properties of transdermal drug delivery system<sup>11</sup>**

S. No.	Properties	Range
1.	Shelf life	Should be up to 2.5 years
2.	Patch size	Should be less than 40 cm <sup>2</sup>
3.	Dose frequency	Once a daily - once a week
4.	Appearance	Should be clear or white color
5.	Packaging properties	Should be easily removable of release liner
6.	Skin reaction	Should be non-irritating
7.	Release Properties	Should have consistent pharmacokinetic and pharmacodynamic profiles over time
8.	Packaging properties	Should be easily removable of release liner

**Table 2: Ideal properties of drug for TDDS<sup>11,12</sup>**

S. No.	Parameter	Properties
1.	Dose	Should be low
2.	Half life in hr	Should be 10 or less
3.	Molecular weight	Should be less than 500
4.	Partition coefficient	Log P ( octanol-water) between -1 and 3
5.	Skin permeability coefficient	Should be less than 0.5 x10 <sup>-3</sup> cm/hr
6.	Skin reaction	Should be non-irritating
7.	Oral bioavailability	Should be low
8.	Therapeutic index	Should be low
9.	Concentration	Minute
10.	pH of saturated aqueous solubility	5-9
11.	Dose deliverable	<10mg/day

**Types of Transdermal Patches**

**A. Single-layer Drug-in-Adhesive**

The adhesive layer of this system 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.

**B. 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. One of the layers is for immediate release of the drug and other layer is for control release of drug from the reservoir. The multi-layer system is different however that it adds another layer of drug-in-adhesive, usually separated by a membrane

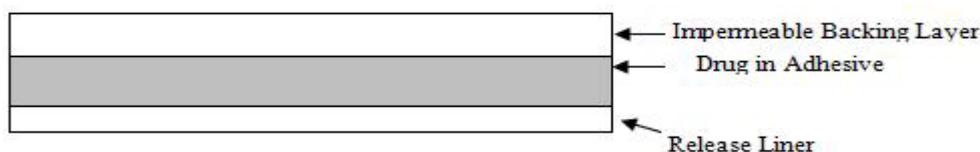
(but not in all cases). This patch also has a temporary liner-layer and a permanent backing. (Fig 8)

**C. Reservoir**

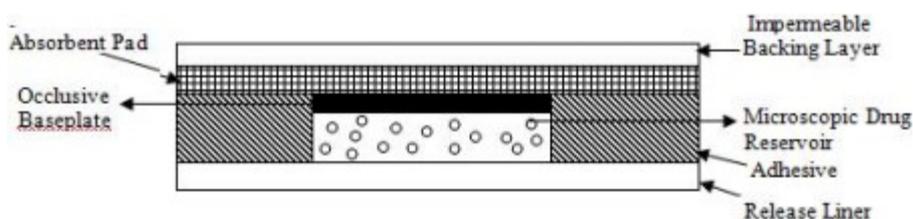
Unlike the Single-layer and Multi-layer Drug-in-adhesive systems the reservoir transdermal system has a separate drug layer. The drug layer is a liquid compartment containing a drug solution or suspension separated by the adhesive layer. This patch is also backed by the backing layer. In this type of system the rate of release is zero order<sup>8</sup>. (Fig 9)

**D. Matrix**

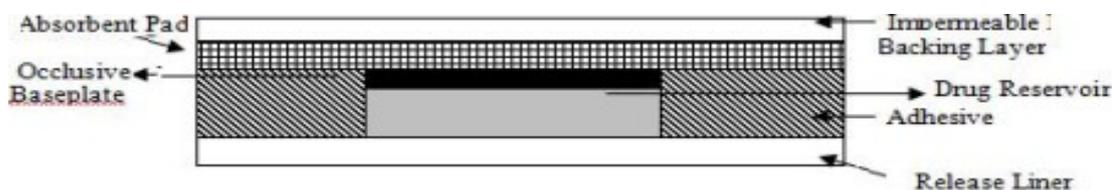
The Matrix system has a drug layer of a semisolid matrix containing a drug solution or suspension. The adhesive layer in this patch surrounds the drug layer partially overlaying it. Also known as a monolithic device. (Fig 10)



**Fig. 8: Design of drug in adhesive type transdermal patch<sup>8</sup>**



**Fig. 9: Design of reservoir type transdermal patch<sup>8</sup>**



**Fig. 10: Design of matrix type transdermal patch<sup>12</sup>**

## E. 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 is 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 <sup>12</sup>.

### Evaluation Parameters

#### 1. Thickness of the patch

The thickness of the drug loaded patch is measured in different points by using a digital micrometer and the average thickness and standard deviation is determined to ensure the thickness of the prepared patch. The thickness of transdermal film is determined by traveling microscope dial gauge, screw gauge or micrometer at different points of the film <sup>11,13</sup>.

#### 2. Weight uniformity

The prepared patches are dried at 60°C for 4hrs before testing. A specified area of patch is to be cut in different parts of the patch and weigh in digital balance. The average weight and standard deviation values are to be calculated from the individual weights <sup>13</sup>.

#### 3. Folding endurance

A strip of specific area is to be cut evenly and repeatedly folded at the same place till it breaks. The number of times the film could be folded at the same place without breaking gives the value of the folding endurance <sup>14</sup>.

#### 4. Percentage Moisture content

The prepared films are to be weighed individually and to be kept in a desiccators containing fused calcium chloride at room temperature for 24 hrs. After 24 hrs the films are to be reweighed and determine the percentage moisture content from the below mentioned formula <sup>2,13</sup>.

$$\% \text{ Moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

#### 5. Content uniformity test

10 patches are selected and content is determined for individual patches. If 9 out of 10 patches have content between 85% to 115% of the specified value and one has content not less than 75% to 125% of the specified value, then transdermal patches pass the test of content uniformity. But if 3 patches have content in the range of 75% to 125%, then additional 20 patches are tested for drug content. If these 20 patches have range from 85% to 115%, then the transdermal patches pass the test <sup>11,2</sup>.

#### 6. Moisture Uptake

Weighed films are kept in desiccators at room temperature for 24 h. These are then taken out and exposed to 84% relative humidity using saturated solution of Potassium chloride in desiccators until a constant weight is achieved. % moisture uptake is calculated as given below <sup>11,13</sup>.

$$\% \text{ moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

#### 7. Drug content

A specified area of patch is to be dissolved in a suitable solvent in specific volume. Then the solution is to be filtered through a filter medium and analyze the drug contain with the suitable method (UV or HPLC technique). Each value represents average of three different samples <sup>11,14</sup>.

#### 8. Shear Adhesion test

This test is to be performed for the measurement of the cohesive strength of an adhesive polymer. It can be influenced by the

molecular weight, the degree of cross linking and the composition of polymer, type and the amount of tackifier added. An adhesive coated tape is applied onto a stainless steel plate; a specified weight is hung from the tape, to affect it pulling in a direction parallel to the plate. Shear adhesion strength is determined by measuring the time it takes to pull the tape off the plate. The longer the time take for removal, greater is the shear strength <sup>15</sup>.

#### 9. Peel Adhesion test

In this test, the force required to remove an adhesive coating from a test substrate is referred to as peel adhesion. Molecular weight of adhesive polymer, the type and amount of additives are the variables that determined the peel adhesion properties. A single tape is applied to a stainless steel plate or a backing membrane of choice and then tape is pulled from the substrate at a 180° angle, and the force required for tape removed is measured <sup>15</sup>.

#### 10. Water vapor transmission studies (WVT)

For the determination of WVT, weigh one gram of calcium chloride and place it in previously dried empty vials having equal diameter. The polymer films are pasted over the brim with the help of adhesive like silicon adhesive grease and the adhesive was allowed to set for 5 minutes. Then, the vials are accurately weighed and placed in humidity chamber maintained at 68 % RH. The vials are again weighed at the end of every 1<sup>st</sup> day, 2<sup>nd</sup> day, 3<sup>rd</sup> day up to 7 consecutive days and an increase in weight was considered as a quantitative measure of moisture transmitted through the patch. In other reported method, desiccators were used to place vials, in which 200 mL of saturated sodium bromide and saturated potassium chloride solution were placed. The desiccators were tightly closed and humidity inside the desiccators was measured by using hygrometer. The weighed vials were then placed in desiccators and procedure was repeated.

$$WVT = W / ST$$

W is the increase in weight in 24 h; S is area of film exposed (cm<sup>2</sup>); T is exposure time <sup>16</sup>.

#### 11. Rolling ball tack test

This test measures the softness of a polymer that relates to tack. In this test, stainless steel ball of 7/16 inches in diameter is released on an inclined track so that it rolls down and comes into contact with horizontal, upward facing adhesive. The distance the ball travels along the adhesive provides the measurement of tack, which is expressed in inch <sup>17</sup>.

#### 12. Quick Stick (peel-tack) test

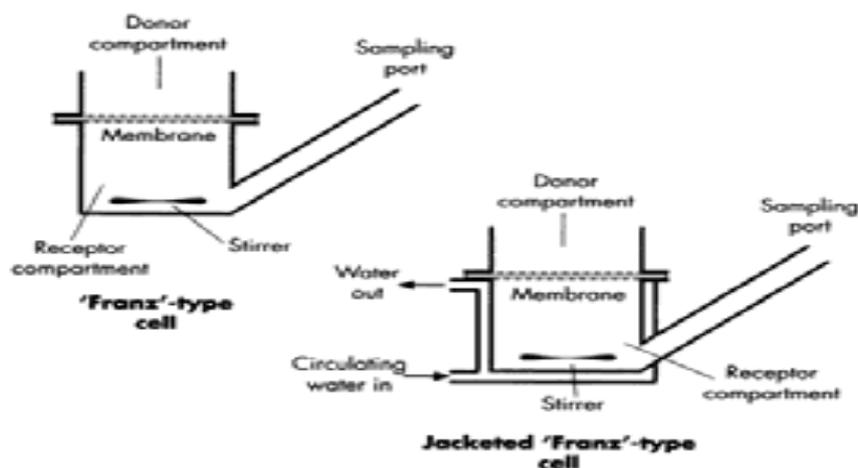
In this test, the tape is pulled away from the substrate at 90°C at a speed of 12 inches/min. The peel force required breaking the bond between adhesive and substrate is measured and recorded as tack value, which is expressed in ounces or grams per inch width <sup>17</sup>.

#### 13. Probe Tack test

In this test, the tip of a clean probe with a defined surface roughness is brought into contact with adhesive, and when a bond is formed between probe and adhesive. The subsequent removal of the probe mechanically breaks it. The force required to pull the probe away from the adhesive at fixed rate is recorded as tack and it is expressed in grams <sup>17</sup>.

#### 14. In vitro drug release studies

The paddle over disc method (USP apparatus V) is employed for assessment of the release of the drug from the prepared patches. Dry films of known thickness are to be cut into definite shape, weighed, and fixed over a glass plate with an adhesive. The glass plate is then placed in a 500-mL of the dissolution medium or phosphate buffer (pH 7.4), and the apparatus is equilibrated to 32± 0.5°C. The paddle is then set at a distance of 2.5 cm from the glass plate and operated at a speed of 50 rpm. Samples (5- mL aliquots) can be withdrawn at appropriate time intervals up to 24 h and analyzed by UV spectrophotometer or HPLC. The experiment is to be performed in triplicate and the mean value can be calculated <sup>18</sup>.

Fig. 11: Diffusion cell for in vitro experiments <sup>18,19</sup>

### 15. In vitro skin permeation studies

An in vitro permeation study can be carried out by using diffusion cell. Full thickness abdominal skin of male Westar rats weighing 200 to 250g. Hair from the abdominal region is to be removed carefully by using a electric clipper; the dermal side of the skin is thoroughly cleaned with distilled water to remove any adhering tissues or blood vessels, equilibrated for an hour in dissolution medium or phosphate buffer pH 7.4 before starting the experiment and is placed on a magnetic stirrer with a small magnetic needle for uniform distribution of the diffusant. The temperature of the cell is maintained at  $32 \pm 0.5^\circ\text{C}$  using a thermostatically controlled heater. The isolated rat skin piece is to be mounted between the compartments of the diffusion cell, with the epidermis facing upward into the donor compartment. Sample volume of definite volume is to be removed from the receptor compartment at regular intervals, and an equal volume of fresh medium is to be replaced. Samples are to be filtered through filtering medium and can be analyzed spectrophotometrically or HPLC. Flux can be determined directly

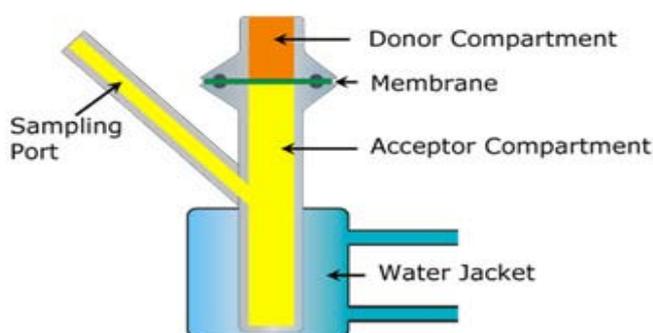
as the slope of the curve between the steady-state values of the amount of drug permeated ( $\text{mg cm}^{-2}$ ) vs. time in hours and permeability coefficients were deduced by dividing the flux by the initial drug load ( $\text{mg cm}^{-2}$ ) <sup>18,19,20</sup>.

### 16. Skin Irritation study

Skin irritation and sensitization testing can be performed on healthy rabbits (average weight 1.2 to 1.5 kg). The dorsal surface ( $50\text{cm}^2$ ) of the rabbit is to be cleaned and remove the hair from the clean dorsal surface by shaving and clean the surface by using rectified spirit and the representative formulations can be applied over the skin. The patch is to be removed after 24 hr and the skin is to be observed and classified into 5 grades on the basis of the severity of skin injury <sup>15</sup>.

### 17. Stability studies

Stability studies are to be conducted according to the ICH guidelines by storing the TDDS samples at  $40 \pm 0.5^\circ\text{C}$  and  $75 \pm 5\%$  RH for 6 months. The samples are withdrawn at 0, 30, 60, 90 and 180 days and analyze suitably for the drug content <sup>18</sup>.

Fig. 12: Tran's diffusion cell <sup>18,15</sup>Table 3: Physicochemical properties of drugs <sup>17</sup>

Drug	Molecular weight	Log k o/w	Clearance(l/h)	T <sub>1/2</sub> (hr.)	Oral bioavailability	Efficacious blood level (mg/ml)
Scopolamine	303	1.24	67.2	2.9	27	0.04
Clonidine	230	0.83	13	6-20	95	0.2-2.0
Nitroglycerine	227	2.05	966	0.04	<1	1.2-11.0
Estradiol	272	2.49	615-790	0.05	-	0.04-0.06
Fentanyl	337	2.93	27-75	3-12	32	1
Nicotine	162	-	77.7	2	30	10-30
Testosterone	288	3.31	-	-	<1	10-100

**Table 4: Marketed Products of Transdermal Drug Delivery System** <sup>11, 17, 18</sup>

S. No	Product	Active drug	Type of transdermal patch	Purpose
1.	Estraderm	Estradiol	Membrane	Postmenstrual syndrome
2.	Duragesic	Fentanyl	Reservoir	Pain relief patch
3.	Transderm-Scop	(Scopolamine)		Motion sickness
4.	Alora	Estradiol	Matrix	Postmenstrual Syndrome
5.	Climara	Estradiol	Matrix	Postmenstrual Syndrome
6.	Androderm	Testosterone	Membrane	Hypogonadism in males
7.	Captopress TTS	Clonidine	Membrane	Hypertension
8.	Combipatch	Estradiol	Matrix	Postmenstrual Syndrome
9.	Esclim	Estradiol	Matrix	Hormone replacement therapy
10.	Deponit	Nitroglycerine	Drug in adhesive	Angina Pectoris
11.	FemPatch	Estradio	Matrix	Postmenstrual syndrome
12.	Lidoderm	Lidocaine	Drug in adhesive	Anesthetic
13.	Ortho Evra	Estradiol	Drug in adhesive	Postmenstrual Syndrome
14.	Testoderm TTS	Testosterone	Reservoir	Hypogonadism in males
15.	Habitraol	Nicotine	Drug in adhesive	Smoking Cessation
16.	Prostep	Nicotine	Reservoir	Smoking Cessation
17.	Nicotrol	Nicotine	Drug in adhesive	Smoking Cessation
18.	Vivelle	Estradiol	Reservoir	Postmenstrual syndrome
19.	Matrifen <sup>R</sup>	Fentanyl	Reservoir	Pain relief patch
20.	NuPatch 100	Diclofenac diethylamine	Drug in adhesive	Anti Inflammatory
21.	Nicoderm CQ	Nicotine	Drug in adhesive	Smoking Cessation
22.	Vivelle-Dot	Estradiol	Reservoir	Postmenstrual syndrome
23.	Minitran	Nitroglycerine	Drug in adhesive	Angina Pectoris
24.	Nitrodisc	Nitroglycerine	Micro reservoir	Angina Pectoris
25.	Nitroderm	Nitroglycerine	Matrix	Angina Pectoris
26.	TransdermNitro	Nitroglycerine	Reservoir	Angina Pectoris
27.	Oxytrol <sup>R</sup>	oxybutynin	Matrix	Overactive bladder
28.	Nouvelle TS	Estradiol	Drug in adhesive	Hormone replacement therapy
29.	Fematrix	Estrogen	Matrix	Postmenstrual syndrome
30.	Climaderm	Estradiol	Matrix	Postmenstrual syndrome

### Future of Transdermal Drug Delivery System

Future novel formulation approaches and technologies include liposomes, niosomes and micro emulsion. Aim of this strategy is to improve delivery of drug that has low inherent solubility in most of classical formulation excipients. A wide range of potential drugs for delivery like steroids, antifungal, antibacterial, interferon, methotrexate, local anesthetics are formulated. The market for transdermal devices has been estimated to increase in future and has recently experienced annual growth of at rate of 25%. This figure will rise in future as novel devices emerge and list of marketed transdermal drug increases. Transdermal delivery of analgesics is likely to continue to increase in popularity as there are further improvements in design. Research is being performed to increase safety and efficacy. To improve practical matters such as the experience for the wearer of the patch, and also to provide more precise drug delivery associated with increased duration of action. Other potential improvements include improved transdermal technology that utilizes mechanical energy to increase drug flux across the skin either by altering the skin barrier or increasing the energy of the drug molecules. After the successful design of patches using iontophoresis, various modes of 'active' transdermal technologies are being investigated for different drugs. These include electroporation (short electrical pulses of high voltage to create transient aqueous pores in the skin), sonophoresis (uses low-frequency ultrasonic energy to disrupt the stratum corneum), and thermal energy (uses heat to make the skin more permeable and to increase the energy of drug molecules). Magnetic energy, magnetophoresis, has been investigated as a means to increase drug flux across the skin. The transdermal patch may be an underutilized tool for management of acute and chronic pain. With improved delivery and a wider range of analgesics, we expect the popularity and applicability of this modality to deliver drugs to increase. In current scenario, transdermal route of drug delivery system in comparison with oral treatment as the most successful innovative research area in new drug delivery system, with around 40% of the drug delivery candidate products under clinical trails related to transdermal or dermal system. The transdermal drug delivery systems (TDDS) have been designed as an alternative, safest and

easy route for systemic drug delivery. The systemic drug administration though skin holds several advantages such as maintenance constant drug level in blood plasma, less number of side effects, and improvement of bio availability by circumvention of hepatic first pass metabolism and increase patient compliance with respect to drug regime used for treatment. In recent times, skin considered as a safest port for drug administration, to provide continuous drug release into systemic circulation.

### CONCLUSION

Transdermal drug delivery systems have been used as safe and effective drug delivery devices since 1981. A lot of progress has been done in the field of Transdermal Patches. Due to large advantages of the Transdermal Drug Delivery System, this system interests a lot of researchers. Many new researches are going on in the present day to incorporate newer drugs via this system. Transdermal dosage forms may provide clinicians an opportunity to offer more therapeutic options to their patients to optimize their care. In recent years the use of a number of biophysical techniques has aided in our understanding of the nature of the stratum corneum barrier and the way in which chemicals interact with and influence this structure. A better understanding of the interaction of enhancers with the stratum corneum and the development of structure activity relationships for enhancers will aid in the design of enhancers with optimal characteristics and minimal toxicity. This article provides valuable information regarding the transdermal drug delivery systems and its evaluation process in details.

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