

Transdermal Patches a successful tool in Transdermal Drug Delivery System: An overview

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ABSTRACT

Transdermal drug delivery (TDD) is a non-invasive route of drug administration, although its applications are limited by low skin permeability. It is an attractive alternative technique over the conventional techniques for administration of systemic approaches. For both local and systemic effects skin is the major site of application. However, to penetrate the drug through skin, stratum corneum is the main barrier. So to evade the stratum corneum and to increase the flux through skin membrane, different approaches of penetration enhancement are used. Several new active rate controlled transdermal drug delivery system (TDDS) technologies have been found, developed and commercialized for the TDD. This review presents mainly the structure of skin, routes of penetration through skin, different approaches to enhance the penetration, transdermal patches to optimize the transdermal delivery system into an effective drug delivery system.

Keywords: Penetration enhancers, Transdermal, Transdermal Drug Delivery System (TDDS).

INTRODUCTION

Currently transdermal drug delivery is one of the most promising methods for drug application. Increasing numbers of drugs are being added to the list of therapeutic agents that can be delivered to the systemic circulation via skin. The transdermal route offers several advantages over conventional dosage forms such as tablets and injections, including avoidance of first-pass metabolism by the liver. Transdermal drug delivery systems are devices containing drug of defined surface area that delivers a pre-determined amount of drug to the surface of intact skin at a pre-predefined rate. This system overcomes the disadvantages associated with oral products [1]. So the aim of this article is to describe the structure, routes, criteria of selection, approaches etc.

Benefits of Patches over Other Dosage Forms [2-5]

- Eliminate first pass metabolism

- Provide steady delivery/ blood vessels
- Increase compliance/ convenience
- Reduce systemic drug interaction
- Can minimize abuse/ diversion
- Permit dose discontinuation via removal
- Provides product life cycle extension opportunities at lower cost with lower risks.
- Improved bioavailability
- Longer duration of action
- More uniform plasma levels

Limitations of TDDS

- Possibility of local irritation at the site of application
- Erythema, itching, and local edema can be caused by the drug, the adhesive, or other excipients in the patch formulation.

Structure of the skin barrier

Skin is the largest human organ of our body composed of several layers: the stratum corneum (uppermost layer), the viable epidermis, the dermis and the lower layers of adipose tissue (fig. 1). The stratum corneum consists of flat, roughly hexagonally shaped, partly overlapping cells, with a thickness of $0.3\mu\text{m}$ and a diameter of $30\mu\text{m}$. Just below the stratum corneum is the viable epidermis, which made of three layers: the stratum granulosum, spinosum and basale. It has a thickness of the cells ranging from $50\text{-}100\mu\text{m}$. Below the viable epidermis dermis is present. Dermis thickness is about $2000\text{-}3000\mu\text{m}$ and consists of a matrix of loose connective tissue composed of fibrous protein embedded in an amorphous ground substance [6,7]. For the past few decades, the transdermal route has been selected for delivery of certain drugs. However, its use is limited due to low permeability of the skin to many drugs [8].

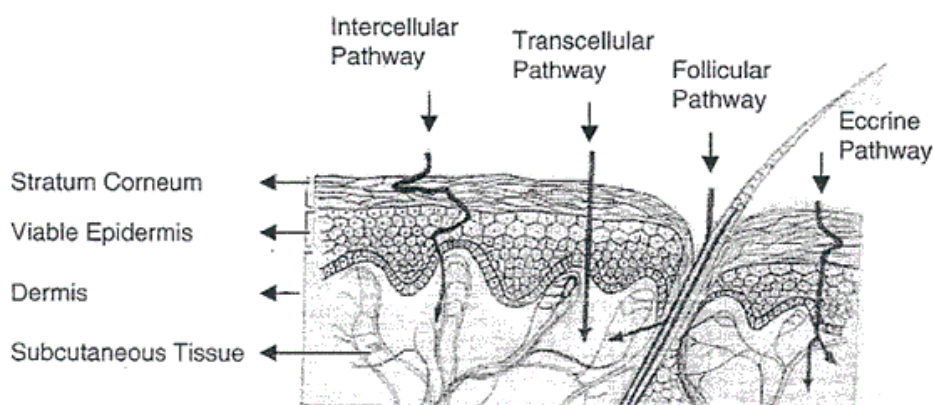


Fig.1: Anatomical and physiological structure of skin

Routes of Penetration

Transdermal drug delivery system is a most suitable system for a long-term treatment or for a multi dose treatment because different transdermal patches are prepared for a long period of time in a suitable dose proving treatment from a day to even up to seven days. To penetrate a molecule in the normal human intact skin there are two diffusion pathways: the appendageal and the transepidermal pathway. The appendageal route is for ions and large polar molecules and the transepidermal route is for the unionized molecules which can cross the intact layer. A molecule should have adequate lipophilicity and optimum molecular weight to penetrate in to the intact skin. Hydrophilic drugs partitioned preferentially via intracellular domains, whereas lipophilic permeants (octanol/water $\log K > 2$) partitioned the subcutaneous (SC) via intercellular route.

Most of the molecules traverse the stratum corneum by both routes. The transport of various drug molecules through the skin, promptly restricted by the barrier properties of epidermis. To avoid these difficulties in permeation through SC, carriers\vesicles can be used as penetration enhancers for circumventing the SC barrier [9-11].

Criteria for the selection of drugs in tdds

Various parameters to be considered during selection of drugs in TDDS are mentioned in table no. 1.

Laws for the Development of Transdermal Drug System

According to an “S-urve” profile it follows the general law of developing and evolving (the plot of a major index of the system performance versus time). All transdermal systems consist of four essential parts, a sub-system that transmits system energy to those locations where it is required for performance, a control system that monitors and controls system functioning, the part (or parts) that actually accomplish the main function of the system, and an energy source. These four essential parts are very necessary to complete a TDDS system to function at a high level. A most important aspect of the further development of transdermal drug delivery systems will be breakthroughs in how effectively energy is transmitted through out the systems. The relationship between transdermal drug delivery systems and other existing and new systems are defined by various laws. Next generation transdermal drug delivery systems will show improved degrees of coordination among certain system parts, and intentional dis-coordination among other system parts. The purpose of this coordination or dis-coordination by design is to achieve significant breakthroughs in overall system performance [12].

Table 1. Parameters affecting selection of drugs in TDDS

Parameters	Ideal limits
Aqueous solubility	>1 mg/ml
Lipophilicity	$10 < K_{o/w} < 1000$
Molecular weight	<500 Daltons
Melting point	<200 °C
pH of aqueous saturated solution	5-9
Dose deliverable	< 10 mg/day

Transdermal Patches [13-18]

A transdermal patch is also known by the name of skin patch which is used to deliver the specific amount of dose through skin and it directly goes into the blood stream (Fig. 2). An advantage of a transdermal drug delivery route over other types such as oral, topical, etc is that it provides a controlled release of the medicament in to the patient. A wide variety of drugs are delivered by transdermal patches. A new crystal reservoir technology has come out successfully with the advancement in TDDS which produce comparable smaller patches with a more controlled and sustained release. Success of a transdermal patch depends on a variety of biological physiological, biochemical, and biophysical factors including the following:

- Direct application on the body
- Composition, integrity & thickness of the stratum corneum
- Structure & size of the molecule which is an indicator of diffusivity
- Permeability of the membrane in the transdermal drug delivery system
- State of skin hydration pH and other physiochemical drug properties
- Drug metabolism/first pass metabolism
- Lipid solubility/lipophilicity

- Degree of partitioning of the drug and associated components
- Depot of drug in skin
- Alteration of drug flow in the skin by additives and body temperature
- Interactions between the molecules and among the molecules

Components of a Transdermal Patch [19, 20]

Transdermal patch may include the following components:

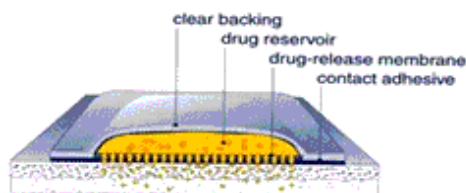


Fig. 2: transdermal patch

- **Liner** - It protect the patch when we stored for long period of time. Before use the transdermal patch liner is removed eg. Polyester film.
- **Drug** - Drug solution is in direct contact with release liner eg. Nicotine and estrogen.
- **Adhesive** - It adhere the components of the patch and the patch to the skin eg. acrylates, silicones.
- **Membrane** - Control the release of drug from the reservoir and multilayer patches.
- **Backing** -It is a process by which we can save the patch from outer environment. Ex: cellulose derivatives, poly vinyl alcohol, polypropylene silicon rubber.
- **Permeation enhancers** - Controlled amount of drug is released by the use of permeation enhancers eg. terpenes, pyrrolidones, alcohol, ethanol, surfactants like sodium lauryl sulfate, pluronic F127 etc.

Types of Transdermal Patches [21-29]

Single layer Drug-in-adhesive

In this type the adhesive layer contains the drug and it not only serves to adhere the various layers together but with the entire system to the skin but is also responsible for the releasing of the drug. To the outer side of adhesive layer there is lining of temporary liner and a backing (Fig. 3a).

Multi-layer Drug-in-Adhesive

It is similar to the single layer system in respect that both adhesive layers are also responsible for the releasing of the drug. The multilayer 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 surrounded by a temporary liner-layer and a permanent backing (Fig. 3b).

Reservoir System

In this system the drug reservoir is embedded between an impervious backing layer and a rate controlling membrane. The rate controlling membrane can be microporous or nonporous only which can release the drug. In the drug reservoir compartment, the drug can be in the form of a solution, suspension, gel or dispersed in a solid polymer matrix. Hypoallergenic adhesive polymer can be applied as outer surface polymeric membrane which is compatible with the drug. This patch is backed by the backing layer (fig. 3c). Zero order kinetics is followed by this system.

Micro reservoir system

In this type the drug delivery system is a combination of reservoir and matrix system. The drug reservoir is formed by suspending the drug in an aqueous solution of water soluble polymer and then dispersing the solution homogenously in a lipophilic polymer to form thousands of unreachible, microscopic spheres of drug reservoirs. This thermodynamically unstable dispersion is stabilized quickly by immediately cross linking the polymer in situ by using cross linking agents.

Vapour Patch

In this type of patch the adhesive layer serves to adhere the various layers together but also to release vapour. The vapour patches are new to the market and release essential oils for up to 6 h. Essential oils are release from this patch and they are used only in cases of decongestion mainly. Controller vapour patches are available in the market that improves the quality of sleep. Vapour patches that reduce the quantity of cigarettes that one smoke in a month are also available in the market.

Matrix system

- **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 adhesive) on an impervious backing layer. On top of the reservoir, unmediated adhesive polymer layers are applied for protection purpose (fig. 3d).

- **Matrix dispersion system**

In this type the drug is dispersed homogenously in a hydrophilic or lipophilic polymer matrix. This drug containing polymer disk is fixed on to 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 reservoir, it is spread along with the circumference to form a strip of adhesive rim.

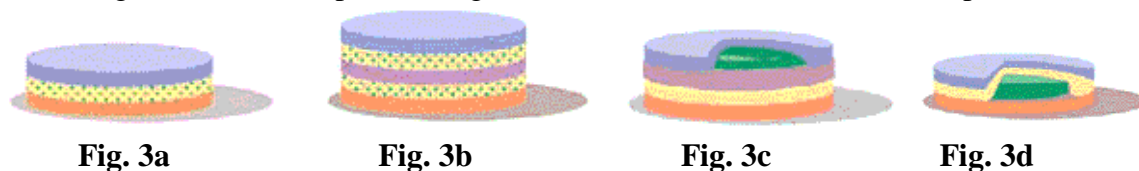


Fig. 3: Various types of transdermal patches

Various methods for preparation of TDDS**Asymmetric TPX membrane method**

A prototype patch can be fabricated by a heat sealable polyester film (type 1009, 3m) with a concave of 1cm diameter used as the backing membrane. Drug sample is dispensed into the concave membrane, covered by a TPX {poly (4-methyl-1-pentene)} asymmetric membrane, and sealed by an adhesive [30].

Asymmetric TPX membrane preparation

These are fabricated by using the dry/wet inversion process. TPX is dissolved in a mixture of solvent (cyclohexane) and non-solvent additives at 60 °C to form a polymer solution. The polymer solution is kept at 40 °C for 24 h and cast on a glass plate to a pre-determined thickness with a gardener knife. After that the casting film is evaporated at 50 °C for 30 sec, and then the glass plate is to be immersed immediately in coagulation bath at temperature 25 °C. After 10 minutes of immersion, the membrane can be removed, air dry in a circulation oven at 50 °C for 12 h.

Circular teflon mould method

Solutions containing polymers in various ratios are used in an organic solvent. Calculated amount of drug is dissolved in half the quantity of same organic solvent. Enhancers in different concentrations are dissolved in the other half of the organic solvent and then added. Di-N-butyl-phthalate is added as a plasticizer into drug polymer solution. The total contents are to be stirred for 12 h and then poured into a circular teflon mould. The moulds are placed on a levelled surface and covered with an inverted funnel to control solvent vaporization in a laminar flow hood model with speed of air 1/2 m /sec. The solvent is allowed to evaporate for 24 h. Before evaluation the dried films are to be stored for another 24 h at 25 ± 0.5 °C in a desiccators containing silica gel before to eliminate aging effects. These types of films are to be evaluated within one week of their preparation [31].

Mercury substrate method

In this method drug is dissolved in polymer solution along with plasticizer. The above solution is to be stirred for 10-15 min to produce a homogeneous dispersion and poured in to a levelled mercury surface. Then the solution is covered with inverted funnel to control solvent evaporation [32].

By using IPM membrane

In this method drug is dispersed in a mixture of water and propylene glycol containing carbomer-940 polymer and stirred for 12 h in magnetic stirrer. The dispersion is to be neutralized and made viscous by the addition of tri-ethanolamine. Buffer pH 7 can be used in order to obtain solution gel, if the drug solubility in aqueous solution is very poor. The formed gel will be incorporated in the IPM membrane [33].

By using EVAC membranes method

In order to prepare the target transdermal therapeutic system, 1% carbopol reservoir gel, polyethylene (PE), ethylene vinyl acetate copolymer (EVAC) membranes can be used as rate control membranes. If the drug is not soluble in water, propylene glycol is used for the preparation of gel. Drug is dissolved in propylene glycol; carbopol resin will be added to the above solution and neutralized by using 5% w/w sodium hydroxide solution. The drug (in gel form) is placed on a sheet of backing layer covering the specified area. A rate controlling membrane will be placed over the gel and the edges will be sealed by heat to obtain a leak proof device [34].

Aluminium backed adhesive film method

Transdermal drug delivery system may produce unstable matrices if the loading dose is greater than 10 mg. For preparation of aluminium backed film, chloroform is the choice of solvent, because most of the drugs as well as adhesives are soluble in chloroform. The drug is dissolved in chloroform and adhesive material will be added to the drug solution and dissolved. Former is lined with aluminium foil and the ends off with tightly fitting cork blocks [35].

Preparation of TDDS by using proliposomes

The proliposomes are prepared by carrier method using film deposition technique. From the earlier reference drug and lecithin in the ratio of 1:2 can be used as an optimized ratio. The proliposomes are prepared by taking 5mg of mannitol powder in a 100ml round bottom flask which is kept at 60-70 °C temperature and the flask is rotated at 80-90 rpm and dried the mannitol at vacuum for 30 min. After drying, the temperature of the water bath is adjusted to 20-30 °C. Drug and lecithin are dissolved in a suitable organic solvent mixture. Aliquot of 0.5 ml of the organic solution is introduced into the round bottomed flask at 37 °C containing mannitol,

after complete drying second aliquots (0.5ml) of the solution is to be added. After the last loading, the flask containing proliposomes are connected in a lyophilizer and subsequently drug loaded mannitol powders (proliposomes) are placed in desiccators over night and then sieved through 100 mesh. The collected powder is transferred in to a glass bottle and stored at the freeze temperature until characterization [36].

By using free film method

Free film of cellulose acetate is prepared by casting on mercury surface. A polymer solution 2% w/w is prepared by using chloroform. Plasticizers are incorporated at a concentration of 40% w/w of polymer weight. Five ml of polymer solution was poured in a glass ring which is placed over the mercury surface in a glass petri dish. The rate of evaporation of the solvent is controlled by placing an inverted funnel over the petri dish. The film formation is noted by observing the mercury surface after complete evaporation of the solvent. The dry film will be separated out and stored between the sheets of wax paper in desiccators until use. Free films of different thickness can be prepared by changing the volume of the polymer solution [37].

Physiochemical basis of transdermal drug delivery

Drug lipophilicity

Stratum corneum barrier is lipophilic, with the intercellular lipid lamellae forming a conduit through which drugs must diffuse in order to reach the underlying vascular infrastructure and to ultimately access the systemic circulation. For this reason lipophilic molecules are better accepted. Ideally a drug must possess both lipoidal and aqueous solubility.

Drug mobility

After the drug has partitioned into the membrane, it must be sufficiently mobile to diffuse across the SC. Diffusion within biological membranes does not obey the familiar stokes Einstein equation, which describe this process for spherical particles in a continuous fluid medium [38]. Non-stokesian diffusion has been explained in terms of the free volume theory, where diffusion occurs by the dynamic exchange of molecules with regions of free volume or holes within the membrane. Unlike stokesian diffusion shows an extremely sensitive dependence on molecular size as indicated by equation [39];

$$D_m = D_0 \times \exp(-\beta.MV)$$

Where D_m is the permeant diffusivity within the membrane, D_0 is the membrane diffusivity of a hypothetical molecule of zero molecular volume, and MV is the molecular volume of the permeant. Solute diffusivity decreases exponentially as molecular volume increases, imposing a size restriction on favourable transport across the skin, which can be usefully predicted from mathematical models incorporating this size dependence [40-41].

Optimizing passive drug diffusion

The influence of these physiochemical criteria on transdermal bioavailability can be readily appreciated from the following Fickian relationship, which describes the passive permeation of a solute across the SC, a 'rate-limiting membrane' [42]. It also serves as a useful device to identify mechanisms by which transdermal bioavailability can be optimized. In its simplest form, at steady - state, when the amount of drug entering the membrane is equal to the amount leaving the membrane, the flux (j_{ss}), is given by equation

$$J_{ss} = \frac{(D.K_{SC}/veh)/h}{h} \cdot C_{veh} = K_p \cdot C_{veh}$$

Where J_{SS} is the steady-state flux ($\text{mg cm}^{-2} \text{hr}^{-1}$) across a membrane of thickness, h cm; $K_{sc/veh}$ is the drug's SC-vehicle partition coefficient; D is the drug diffusivity ($\text{cm}^2\text{hr}^{-1}$) in the SC; C_{veh} is the drug concentration (mg cm^{-3}) in the vehicle, and K_p is the formulation dependent permeability coefficient of the drug.

Evaluation Parameters

Interaction studies

The integral part of almost all pharmaceutical dosage forms are the excipients. The stability of a formulation amongst other factors depends on the compatibility of the drug with the excipients. The drug and excipients must be compatible to produce a stable product, and thus it is mandatory to detect any possible physical and chemical interaction as it can affect the bioavailability and stability of the drug. Interaction studies are commonly carried out in thermal analysis, FT-IR, UV and chromatographic techniques by comparing their physiochemical characters such as assay, melting endotherms, characteristic wave numbers, and absorption maxima etc. [5, 43].

Thickness of the patch

The thickness of the drug loaded patch is measured in different points by using a digital micrometer and determines the average thickness and standard deviation for the same to ensure the thickness of the prepared patch [44].

Weight uniformity

The prepared patches are dried at 60°C for 4h before testing. A specified area of patch is cut in different parts and weigh in digital balance. The average weight and standard deviation values are to be calculated from the individual weights [44].

Folding endurance

A strip of specific dimensions are cut evenly and repeatedly folded at the same place till it broke. Without breaking, the number of times the film could be folded at the same place and it gave the value of the folding endurance [44].

Percentage moisture content

The prepared films are weighed individually and kept in desiccators containing fused calcium chloride at room temperature for 24 h. After 24 h the films are reweighed and determine the percentage moisture content from the below mentioned formula [44].

$$\text{Percentage moisture content} = [\text{initial weight} - \text{final weight}/\text{final weight}] \times 100$$

Percentage moisture uptake

The weighed films are to be kept in desiccators at room temperature for 24 h containing saturated solution of potassium chloride in order to maintain 84% RH. After 24 h the films are to be reweighed and determine the percentage moisture uptake from the below mentioned formula [44].

$$\text{Percentage moisture uptake} = [\text{final weight} - \text{initial weight}/\text{initial weight}] \times 100$$

Water vapour permeability (WVP) evaluation

Water vapour permeability can be determined with foam dressing method. The WVP can be determined by the following formula

$$\text{WVP} = \text{W}/\text{A}$$

Where WVP is expressed in gm/m² per 24 h.

W is the amount of vapour permeated through the patch expressed in gm/24 h and A is the surface area of the exposure samples expressed in m².

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 the drug content is analysed with the suitable method (UV or HPLC technique). Each value should represent average of three different samples [45].

Uniformity of dosage unit test

An accurately weighed portion of the patch is to be cut into small pieces and transferred to a specific volume volumetric flask, dissolved in a suitable solvent and sonicate for complete extraction of drug from the patch and made up to the mark with same. The resulting solution was allowed to settle for about an hour, and the supernatant was suitably diluted to give the desired concentration with suitable solvent. The solution was filtered using 0.2µm membrane filter and analyzed by suitable analytical technique (UV or HPLC) and the drug content per piece will be calculated [46].

Polariscope examination

This test is to be performed to examine the drug crystals from patch by polariscope. A specific surface area of the piece is to be kept on the object slide and observe for the drugs crystals to distinguish whether the drug is present as crystalline form or amorphous form in the patch [47].

Shear adhesion test

This test is performed for the measurement of the cohesive strength of an adhesive polymer. It can be influenced by the molecular weight, the degree of crosslinking 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 from the plate. The longer the time take for removal, greater is the shear strength [46].

Peel adhesion test

In this test, 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 to remove the tape is measured [46].

Thumb tack test

The thumb is simply pressed on the adhesive and the related tack property is detected and it is a qualitative test [46].

Flatness test

Three longitudinal strips are cut from each film at different portion like one from the centre, other one from the left side, and one from the right side. The length of each strip was measured

and the variation in length because of non-uniformity in flatness was measured by determining percent constriction, with zero constriction equivalents to 100% flatness [47].

Percentage elongation break test

The percentage elongation break is determined by noting the length just before the break point, the percentage elongation can be determined from the below mentioned formula [47]

$$\text{Elongation percentage} = \frac{L_1 - L_2}{L_2} \times 100$$

Where, L_1 is the final length of each strip and L_2 is the initial length of each strip.

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 [48].

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. to break the bond between adhesive and substrate. The peel force required which is measured and recorded as tack value, and expresses in ounces or grams per inch width [49].

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. It is mechanically break by the subsequent removal of the probe. The force required to pull the probe away from the adhesive at fixed rate is recorded as tack and it is expressed in grams [48].

***In vitro* drug release studies**

The paddle over disc method (USP apparatus V) can be employed for assessment of the release of the drug from the prepared patches. Dry films of known thickness is to be cut into definite shape, weighed, and fixed over a glass plate with an adhesive. The glass plate was then placed in a 500 ml of the dissolution medium or phosphate buffer (pH 7.4), and the apparatus was equilibrated to 37±0.5 °C. The paddle was then set at a distance of 2.5 cm from the glass plate and operated at a speed of 50 rpm. Samples can be withdrawn at appropriate time intervals up to 24 h and analyzed by UV spectrophotometer or HPLC method. The experiment is to be performed in triplicate and the mean value can be calculated [46].

***In vitro* skin permeation studies**

Diffusion cell is used to carry out the permeation study on full thickness abdominal skin of male Wistar rats weighing 200-250g. Hair from the abdominal region is to be removed carefully by using an electric clipper; the dermal side of the skin was 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 was placed on a magnetic stirrer with a small magnetic needle for uniform distribution of the diffusant. The temperature of the cell was maintained at 32±0.5 °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 (mg cm^{-2}) vs. time in hours and permeability coefficients were deduced by dividing the flux by the initial drug load (mg cm^{-2}) [42].

Skin irritation study

Healthy rabbits are used to perform skin irritation and sensitization testing. The dorsal surface (50 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 h and the skin is observed and classified into five grades on the basis of the severity of skin injury [42].

Stability studies

Stability studies are conducted according to the ICH guidelines by storing the TDDS samples at $40 \pm 0.5 \text{ }^\circ\text{C}$ and $75 \pm 5\%$ RH for 6 months. The samples were withdrawn at 0, 30th, 60th, 90th and 120th day and analyse suitably for the drug content [38].

List of some transdermal marketed products

Table 2. Some transdermal products [8]

Product name	Manufacturer	Drug	Uses
Alora	TheraTech/Proctol and Gamble	Estradiol	Postmenstrual syndrome
Climaderm	Ethical Holdings/Wyeth-Ayerest		
Climara	3M Pharmaceuticals/Berlex Labs		
Estraderm	Alza/Norvatis		
FemPatch	Parke-Davis		
Minitran	3M Pharmaceuticals	Nitroglycerin	Angina pectoris
Deponit	Schwarz-Pharma		
Nitrodisc	Roberts Pharmaceuticals		
Nitro-dur	Key Pharmaceuticals		
Duragesic	Alza/Janssen Pharmaceutica	Fentanyl	Moderate/severe pain
CombiPatch	Noven , Inc./Aventis	Estradiol/Norethindrone	Hormone replacement therapy
Habitraol	Novartis	Nicotine	Smoking cessation
Nicoderm	Alza/GlaxoSmithKline		
Prostep	Elan Corp./Lederle Labs		
Fematrix	Ethical Holdings/Solvay Healthcare Ltd.	Estrogen	Postmenstrual syndrome
Ortho-Evra	Ortho-McNeil Pharmaceuticals	Norelgestromin/Estradiol	Birth control
Nuvelle TS	Ethical Holdings/Schering	Estrogen/Progesterone	Hormone replacement therapy

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 estradiol for estrogen deficiency, 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 are limited to the refinements of the materials to be used. The reason is the only a limited number of drugs fit the molecular weight, and potency requirements for transdermal absorption. Various patches are available from more than ten years, and they have a proven history [8].

CONCLUSION

Number and complexity of transdermal delivery system will increase in the near future. With the help of various enhancement techniques we can increase the permeability of low permeable drugs. To optimize this drug delivery system, greater understanding of the different mechanisms of biological interactions, and polymer are required. The future of transdermal rate controlled drug delivery is expected to grow day by day, and biomedical application of TDDS is expected to increase along with the successful development of new approaches. TDDS would be a realistic practical application as the next generation of drug delivery system.

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