DESIGN, DEVELOPMENT AND EVALUATION METHODS FOR PREPARATION OF TRANSDERMAL PATCHES

Ragini Verma*1, Prof. Dr. S.K. Prajapati1, Prashant Kumar Singh1 and Pankaj Kumar Singh2

1Department of Pharmaceutics, Bundelkhand University, Jhansi, (U.P.), INDIA.
2Department of Pharmaceutics, Hygia Institute of Pharmaceutical Education & Research, Lucknow, (U.P.), INDIA.

ABSTRACT

In recent years, a variety of pharmaceutical research has been conducted to develop new dosage forms. Among the dosage forms developed to facilitate simplicity of medication, Transdermal drug delivery system is one of the most widely employed for commercial products. As our society is becoming increasingly aged, the development of Transdermal patches have been formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and traveling and may not have access to water. Such formulations provide an opportunity for product line extension in the many elderly persons will have difficulties in taking oral dosage forms (viz., solutions, suspensions, tablets, and capsules). To improve characters of transdermal drug delivery system (TDDS) was emerged, which will improve the therapeutic efficacy and safety of drugs by specific sites within the body, thereby reducing both the size and number of doses. This review article describes all information related to TDDS such as advantage, active ingredients, factors affecting TDDS, markets products, mechanism of action, types, method of preparation and methods of evaluations.

KEYWORDS: Transdermal Drug Delivery System (TDDS), Partition coefficient, Reservoir, etc.

1 INTRODUCTION

Transdermal drug delivery system is defined as the topically administered medications in the form of patches which when applied to the skin deliver the drug, through the skin at a
predetermined and controlled rate. Transdermal patches are delivered the drug through the skin in controlled and predetermined manner in order to increase the therapeutic efficacy of drug and reduced side effect of drug. Controlled drug release can be achieved by transdermal drug delivery systems (TDDS) which can deliver the drug via the skin portal to systemic circulation at a predetermined rate over a prolonged period of time. For effective Transdermal drug delivery system, the drug are easily able to penetrate the skin and easily reach the target site. TDDS increase the patient compliance and reduces the load as compared to oral route. FDA approved the first Transdermal system Transderm SCOP in 1979. FDA approved this for the prevention of nausea and vomiting associated with ravel, particularly by sea. Transdermal therapeutic systems are also defined as a self contained, discrete dosage forms which, when applied to the intact skin, deliver the drug, through the skin at control rate to the systemic circulation. Transdermal formulation maintain drug concentration within the therapeutic window for prolong period of time ensuring that drug levels neither fall below the minimum effective concentration nor exceed the maximum effective concentration. \[1\]

Now a days about 74% of drugs are taken orally and are found not to be as valuable as most wanted. To advance such characters transdermal drug delivery system was emerged. With the creation of current time of pharmaceutical dosage forms, transdermal drug delivery system (TDDS) recognized itself as an important part of novel drug delivery systems. Transdermal dosage forms, still a costly alternative to conventional formulations, are becoming popular because of their exclusive advantages. Improved bioavailability, Controlled absorption, extra uniform plasma levels, painless and reduced side effects easy application and flexibility of terminating drug administration by simply removing the patch to the skin are some of the potential advantages of transdermal drug delivery. Oral Conventional dosage forms like tablets and capsules are most widely used drug delivery system but both dosage forms face problem of gastric drug/enzyme instability first pass metabolism. Oral route has many further problems like unpleasant taste, odour and color. Numerous additional problems are arising during taking pills; hence problems are being faced during treatment. Sometimes Patients become non-compliant. TDDS patches drugs are used by continuous release so they show their effect for exact duration and Transdermal patch is non-irritating and noninvasive technique. It is attractive alternative techniques over conservative techniques for systemic administration of drug. Drug delivery through the skin to achieve a systemic effect of a drug is commonly known as transdermal drug delivery and differs from usual topical drug delivery. With the purpose of deliver therapeutic agents through the human skin for systemic
effects, the comprehensive morphological, biophysical and physicochemical properties of the skin are to be considered. Delivery of drug via transdermal provides the most important edge over oral and injectables routes by avoiding first pass metabolism and increasing patient compliance respectively. During the last decade transdermal drug delivery system has gained a lot of interest as it offers many advantages over the conventional dosage forms and oral controlled release delivery systems especially less frequency of administration, avoidance of hepatic first pass effect, reduction in gastrointestinal side effect and improves patient compliance. Transdermal drug delivery systems are defined as self-contained, discrete dosage forms which, when applied to intact skin, deliver the drug, through the skin, at a controlled rate to systemic circulation. Transdermal delivery not only provides controlled, constant administration of the drug, but also allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into systemic circulation, which often causes undesirable side effects. Thus various forms of Novel drug delivery system such as Transdermal drug delivery systems, Controlled release systems, Transmucosal delivery systems etc. emerged.

1.1 TRANSDERMAL PATCH

A transdermal patch is defined as adhesive medicated patch that is placed on to the above skin to deliver an exact dose of drug through the skin into the bloodstream with a predetermined rate of release to reach in the body. Today the most common transdermal system present in the market mainly based on semi permeable membranes which were called as patches. Transdermal drug delivery systems (TDDS), also known as “Transdermal patches” or “Skin patches” are dosage forms designed to deliver a therapeutically effective amount of drug across a patient’s skin and in the bloodstream.

1.2 MAIN INGREDIENTS USED FOR THE PREPARATION OF TRANSDERMAL DRUG DELIVERY SYSTEM

1. Liners- It provides the protection of patches during storage and the liner should be removed previous to use.

2. Adhesive- It served to adhere the components of the patch together along with adhering the patch to skin.

3. Membrane- Its controls the drug releases from the multi layer patches. It’s also known as the permeation enhancer.

4. Drug- Drug reservoir is direct contact with release liner.
5. **Backing** - protects the patches from outer environment.

![Fig. 1.1 Different layers of transdermal patches](image)

1.3 ADVANTAGES OF TRANSDERMAL DRUG DELIVERY SYSTEM\textsuperscript{10,14}

- Improved bioavailability and longer duration of action resulting in a reduction in dosing Frequency.
- Steady permeation of drug across the skin, allowing consistent serum drug level; often a goal of therapy.
- Reduced side effects and in addition, if toxicity develops from a drug administered transdermally, the effects could be moderated by removing the patch.
- Transdermal patches have been useful in developing new applications for existing therapeutics and for reducing first-pass drug degradation effects.
- Topical patches are a painless, noninvasive way to deliver substances directly into body.
- This is an effective route to deliver drugs that are broken down by the stomach acids, not well-absorbed from the gut, or extensively degraded by the liver.
- Transdermal patches are alternative to oral route for people who cannot, or prefer not to take medications or supplements orally. It is of great advantage in patients who are nauseated or unconscious.
- Topical patches are cost-effective, convenient, especially notable parameter in some patches is that it requires only once weekly application. Such a simple dosing regimen can aid in patient adherence to drug therapy.
1.4 DISADVANTAGES OF TRANSDERMAL DRUG DELIVERY SYSTEM\textsuperscript{10,14}

- Many drugs especially those with hydrophilic structures permeating the skin too slowly, may not achieve therapeutic level.
- The drug, the adhesive or other excipients in the patch formulation can cause erythema, itching, and local edema.
- The barrier function of the skin changes from one site to another on the same person, from person to person and also with age.
- TDDS cannot deliver ionic drugs.
- TDDS cannot achieve high drug levels in blood/plasma.
- TDDS cannot be developed for drugs of large molecular size.
- TDDS cannot deliver drugs in a pulsatile fashion.
- TDDS cannot be developed if drug or formulation causes irritation to skin.

1.5 LIMITATION OF TRANSDERMAL DRUG DELIVERY SYSTEM\textsuperscript{10,14}

- Limitation of TDDS can be overcome to some extent by novel approaches such as Iontophoresis, electroporation and ultrasound.
- Transdermal drug delivery system has limited skin permeability.
- Restricted to potent drug and Significant lag time.
- A molecular weight less than 500 Dalton (Cannot use for large molecules) is essential to ensure ease of diffusion across the SC, since solute diffusivity is inversely related to its size.
- Pre systemic metabolism the presence of enzymes in the skin such as peptidases might metabolise drug in inactive form and reduce efficacy of drug.
- Skin irritation and sensitization; referred to as Achilles heel of dermal and transdermal delivery.
- Transdermal delivery is neither practical nor affordable when required to deliver large doses of drugs through skin.
- Drug of drug formulation may cause irritation or sensitization.
- Not practical, when the drug is extensively metabolized in the skin and when molecular size is great enough to prevent the molecules from diffusing through the skin.
- Not suitable for a drug, which doesn’t possess a favourable, o/w partition coefficient.
• 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.
• Only relatively potent drugs are suitable candidates for Transdermal drug delivery system because of the natural limits of drug entry imposed by the skin is impermeability.
• Some patients develop contact dermatitis at the site of application for one or more of the system components, necessitating discontinuation.
• Clinical need is another area that has to be examined carefully before a decision is made to develop a transdermal product.

1.6 Factors affecting transdermal drug delivery. [3,11,12]
Two major factors affect the bioavailability of the drug via transdermal routes:

1.6.1 Physicochemical factors

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

Temperature and pH
The permeation of drug increase ten folds with temperature variation. The diffusion coefficient decreases as temperature falls. Weak acids and weak bases dissociate depending on the pH and pKa or pKb values. The proportion of unionized drug determines the drug concentration in skin. Thus, temperature and pH are important factors affecting drug penetration.

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

Drug concentration
The flux is proportional to the concentration gradient across the barrier and concentration gradient will be higher if the concentration of drug will be more across the barrier.
Partition coefficient
The optimal partition coefficient (K) is required for good action. Drugs with high K are not ready to leave the lipid portion of skin. Also, drugs with low K will not be permeated.

Molecular size and shape
Drug absorption is inversely related to molecular weight, small molecules penetrate faster than large ones.

1.6.2 Biological factors
Skin condition
Acids and alkalis, many solvents like chloroform, methanol damage the skin cells and promote penetration. Diseased state of patient alters the skin conditions. The intact skin is better barrier but the above mentioned conditions affect penetration.

Skin age
The young skin is more permeable than older. Children’s are more sensitive for skin absorption of toxins. Thus, skin age is one of the factor affecting penetration of drug in TDDS.

Blood flow
Changes in peripheral circulation can affect transdermal absorption.

Regional skin sites
Thickness of skin, nature of stratum corneum and density of appendages vary site to site. These factors affect significantly penetration.

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

Species differences
The skin thickness, density of appendages and keratinization of skin vary species to species, so affects the penetration.
1.7 Mechanism of Action of Transdermal Patch.\[^7\]

The application of the transdermal patch and the flow of the active drug constituent from the patch to the circulatory system via skin occur through various methods.

1.7.1 Iontophoresis

Iontophoresis passes a few milliamperes of current to a few square centimeters of skin through the electrode placed in contact with the formulation, which facilitates drug delivery across the barrier. Mainly used of pilocarpine delivery to induce sweating as part of cystic fibrosis diagnostic test. Iontophoretic delivery of lidocaine appears to be a promising approach for rapid onset of anesthesia.

1.7.2 Electroporation

Electroporation is a method of application of short, high-voltage electrical pulses to the skin. After electroporation, the permeability of the skin for diffusion of drugs is increased by 4 orders of magnitude. The electrical pulses are believed to form transient aqueous pores in the stratum corneum, through which drug transport occurs. It is safe and the electrical pulses can be administered painlessly using closely spaced electrodes to constrain the electric field within the nerve-free stratum corneum.

1.7.3 Application by ultrasound

Application of ultrasound, particularly low frequency ultrasound, has been shown to enhance transdermal transport of various drugs including macromolecules. It is also known as sonophoresis. Katz et al. reported on the use of low-frequency sonophoresis for topical delivery of EMLA cream.

1.7.4 Use of microscopic projection

Transdermal patches with microscopic projections called microneedles were used to facilitate transdermal drug transport. Needles ranging from approximately 10-100 μm in length are arranged in arrays. When pressed into the skin, the arrays make microscopic punctures that are large enough to deliver macromolecules, but small enough that the patient does not feel the penetration or pain. The drug is surface coated on the microneedles to aid in rapid absorption. They are used in development of cutaneous vaccines for tetanus and influenza. Various other methods are also used for the application of the transdermal patches like thermal poration, magnetophoresis, and photomechanical waves. However, these methods are in their early stage of development and required further detail studying.
1.8 **Types of Transdermal Patch**.\(^{[4,8,16]}\)

1.8.1 **Single-layer Drug-in-Adhesive**

The adhesive layer of this system also 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.

![Fig. 1.2 Single-layer Drug-in-Adhesive](image)

1.8.2 **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. 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. 1.3 Multi-layer Drug-in-Adhesive](image)
1.8.3 Reservoir

Unlike the Single-layer and Multi-layer Drug-inadhesive 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.

![Reservoir system](image)

**Fig. 1.4 Reservoir system**

1.8.4 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.

![Matrix system](image)

**Fig. 1.5 Matrix system**

1.8.5 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 vapours patches release essential oils and are 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.

1.9 METHOD OF PREPARATION

One or more of the following process can be used to manufacture the fast dissolving films-

- Solvent casting
- Semisolid casting
- Hot melt extrusion
- Rolling methods

1.9.1 Solvent Casting Method

Fast dissolving buccal films are preferably formulated using the solvent casting method, whereby the water soluble ingredients are dissolved to form a clear viscous solution and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted into the Petri plate and dried.

![Solvent casting method](image)

Fig. 1.6 Solvent casting method

1.9.2 Semisolid Casting

In this method, solution of water soluble film forming polymer is mixed to solution of acid insoluble polymer to form homogenous viscous solution (e.g. cellulose acetate phthalate and cellulose acetate butyrate). After sonication, it is coated on non-treated casting film. On drying the thickness of the film should be about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4.
1.9.3 Hot Melt Extrusion
In this method the polymers which have low molecular weight and low viscosity are preferred. Drug is mixed with the carrier in the solid form so that granular material is formed. These granules are then dried and then introduced into the extruder. The speed of the screw should be around 15rpm so that the granules reside inside the extruder for about 3-4min. The processing temperatures should be 80°C (zone1), 115°C (zone 2), 100°C (zone 3), and 65°C (zone 4). The extrudate (T= 65°C) then pressed into a cylindrical calendar to obtain a film.

![Fig. 1.7 Hot melt extrusion](image1)

1.9.4 Rolling Method
In rolling method, a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cutted in to desired shapes and sizes. Other ingredients including active agent are dissolved in small portion of aqueous solvent using high shear processor. Water soluble hydrocolloids dissolved in water to form homogenous viscous solution.

![Fig. 1.8 Three roll coating unit](image2)
1.9.5 Solid Dispersion Extrusion

The term solid dispersions refer to the dispersion of one or more active ingredients in an inert carrier in a solid state in the presence of amorphous hydrophilic polymers. Drug is dissolved in a suitable liquid solvent. Then solution is incorporated into the melt of PEG, obtainable below 70°C. Finally the solid dispersions are shaped into the films by means of dies.

1.10 Marketed products

Now a days various drugs are available in the market in the form of transdermal patches. Some of them are listed below-

Table 1.1 List of transdermal patch approved by USFDA

<table>
<thead>
<tr>
<th>Approval year</th>
<th>Drug</th>
<th>Indication</th>
<th>Product name</th>
<th>Marketing company</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>Scopolamine</td>
<td>Motion sickness</td>
<td>Transderm-scop®</td>
<td>Novartis consumer health</td>
</tr>
<tr>
<td>1981</td>
<td>Nitroglycerin</td>
<td>Angina pectoris</td>
<td>Transderm-nitro®</td>
<td>Novartis</td>
</tr>
<tr>
<td>1984</td>
<td>Clonidine</td>
<td>Hypertension</td>
<td>Catapres TTS®</td>
<td>Boehringer Ingelheim</td>
</tr>
<tr>
<td>1986</td>
<td>Estradiol</td>
<td>Menopausal symptoms</td>
<td>Estraderm®</td>
<td>Novartis</td>
</tr>
<tr>
<td>1990</td>
<td>Fentanyl</td>
<td>Chronic pain</td>
<td>Duragesic®</td>
<td>Janssen pharmaeutica</td>
</tr>
<tr>
<td>1991</td>
<td>Nicotine</td>
<td>Smoking cessation</td>
<td>Nicoderm®, Habitrol®, proStep®</td>
<td>GSK, Novartis, Elan</td>
</tr>
<tr>
<td>1993</td>
<td>Testosterone</td>
<td>Testosterone deficiency</td>
<td>Testoderm®</td>
<td>Alza</td>
</tr>
<tr>
<td>1995</td>
<td>Lidocaine/epinephrine (iontophoresis)</td>
<td>Local dermal analgesic</td>
<td>Iontocaine®</td>
<td>lomed</td>
</tr>
<tr>
<td>1998</td>
<td>Estradiol / norethidrone</td>
<td>Menopausal symptoms</td>
<td>CombiPatch®</td>
<td>Novartis</td>
</tr>
<tr>
<td>1999</td>
<td>Lidocaine</td>
<td>Post-herpetic neuralgia pain</td>
<td>Lidoderm®</td>
<td>Endo</td>
</tr>
<tr>
<td>2001</td>
<td>Estradiol / norelgestromin</td>
<td>Contraception</td>
<td>Ortho Evra®</td>
<td>Ortho-McNeil</td>
</tr>
<tr>
<td>2003</td>
<td>Estradiol / levonorgestrol</td>
<td>Menopausal symptoms</td>
<td>Clima Pro®</td>
<td>Bayer healthcare</td>
</tr>
<tr>
<td>2003</td>
<td>Oxybutynin</td>
<td>Overactive bladder</td>
<td>Oxyto®</td>
<td>Watson pharma</td>
</tr>
<tr>
<td>2004</td>
<td>Lidocaine (ultrasound)</td>
<td>Local dermal anesthesia</td>
<td>Sonoprep®</td>
<td>Echo therapeutics</td>
</tr>
<tr>
<td>2005</td>
<td>Lidocaine / tetracaine</td>
<td>Local dermal analgesia</td>
<td>Synera®</td>
<td>Endo pharmaceuticals</td>
</tr>
<tr>
<td>2006</td>
<td>Methylphenidate</td>
<td>Attention deficit hyperactivity disorder</td>
<td>Daytrana®</td>
<td>Shire</td>
</tr>
<tr>
<td>2006</td>
<td>Selegiline</td>
<td>Major depressive disorder</td>
<td>Emsam®</td>
<td>Bristol-Myers squibb</td>
</tr>
<tr>
<td>2007</td>
<td>Rotigotine</td>
<td>Parkinson’s disease</td>
<td>Neupro®</td>
<td>Schwarz pharma</td>
</tr>
<tr>
<td>2007</td>
<td>Rivastigmine</td>
<td>Dementia</td>
<td>Exelon®</td>
<td>Novartis</td>
</tr>
<tr>
<td>2013</td>
<td>Sumatriptan</td>
<td>Migraine</td>
<td>Zecuity®</td>
<td>NuPathé Inc.</td>
</tr>
</tbody>
</table>
2 Evaluation methods\textsuperscript{[5,6,9,13,14,15]}

Interaction Studies
To produce stable product the drug & excipient must be compatible with each other. Drug-excipient interaction will affect the stability & bioavailability of the final formulation. When excipients are new, firstly used with the active substance in the formulation in that condition compatibility or interaction study is very much important. Interaction studies are carried out by Thermal analysis, Fourier transform infrared spectroscopy (FTIR), ultra violet (UV) and chromatographic techniques by comparing their physicochemical properties like assay, melting point, wave numbers, and absorption maxima.

Thickness of the patch-
At different points the thickness of the patch is measured by using digital mirometer & determine average thickness & standard deviation of the same.

Weight of uniformity
Before testing the patch is dried at 60 c for 4 hrs. Cut that patch in different parts & weighed in digital balance. Take average weight & calculate standard deviation from individual weight.

Folding endurance
A strip is cut with specific area. Fold that strip repeatedly at specific point till it get break. The number of times strip film get break gives the value of folding endurance.

Percentage moisture content
Patch or film is weighed first then it is kept in desicator containing calcium chloride at room temperature. Taken it out after 24hrs again reweighed & percentage moisture content is calculated by following formula-

\[
\text{Percentage moisture content (\%)} = \left(\frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}}\right) \times 100
\]

Percentage moisture uptake
Patch is weighed individually then it is kept in desicator containing saturated solution of potassium chloride in order to maintain 84% Rhesus factor (RF) then film is reweighed & percentage moisture uptake is calculated by using following formula-

\[
\text{Percentage moisture uptake (\%)} = \left(\frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}}\right) \times 100
\]
**Water vapour permeability (WVP) evaluation**
The WVP can be determined by the following formula:

\[
WVP = \frac{W}{A}
\]

Where, WVP is expressed in g/m² per 24 h, W is the amount of vapour permeated through the patch expressed in g/24 h, A is the surface area of the exposure samples expressed in m².

**Drug content**
Take the patch with specific area dissolve it in specific volume of solvent. Solution is then filtered and the drug content analyzed with the suitable method (UV or HPLC technique). Then take the average of three different samples.

**Uniformity of dosage unit test**
Take ten patches and content 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.

**Polaroscope evaluation**
This examination determines whether drug is present as amorphous or crystalline form in the final formulation by using polaroscope. Patch with specific surface area is kept on the object slide & observed for drug crystals.

**Shear adhesion test**
This test determines cohesive strength of adhesive polymer. Factors affecting are type & composition of polymers, its molecular weight, the degree of cross linking & 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 direction parallel to the plate. Shear adhesion test is determined by measuring the time it takes to pull the tape off the plate. The longer the time takes for removal, greater is the shear strength.
Peel adhesion test
Here peel adhesion is the force required to remove an adhesive coating from a substrate. A single tape is applied to a stainless steel plate then tape is pulled from the substrate at a 180° angle, and the required to pull the tape is measured.

Thumb tack test
This test determines the tack property of adhesive. Thumb is pressed on adhesive & tack property is determined.

Flatness test
Three longitudinal strips are cut from different portions of the films. The length of the each strip is measured and the variation in length because of non-uniformity in flatness is measured by determining percentage constriction, with 0% constriction equivalent to 100% flatness.

Percentage elongation break test
Percentage elongation can be determine by using following formula:
Elongation percentage = \( \frac{L_1 - L_2}{L_2} \times 100 \)
Where \( L_1 \) is the final length of each strip & \( L_2 \) is the initial length of each strip.

Rolling ball tack test
This test determines the softness of the polymer that relates the talk. Here the stainless steel ball of size 7/16 inches in diameter is released on an inclined track so that it rolls down & comes in contact with horizontal, upward facing adhesive. Distance travelled by ball along adhesive track gives the measurement of tack expressed in inch.

Quick stick (peel tack) test
Here the tape is pulled away from the substrate at 90°C at a speed of 12 inches/min. The peel force required to break the bond between adhesive and substrate is measured and recorded as tack value, which is expressed in ounces or gms per inch width.

Probe tack test
Here the probe with specific surface kept in contact with adhesive so as to form bond between them. Then probe is remove so that it mechanically break it. The force required to pull the probe is the tack measured in terms of grams.
In vitro drug release studies
For the assessment of the release of the drug from the patches the paddle over disc method (USP apparatus V) can be used. Here the film with defined thickness, shape taken, weigh it, fixed over glass plate attached with adhesive. It is kept in 500ml phosphate buffer (pH7.4) as dissolution media & set the apparatus at 32±0.5°C. Keep the paddle at a distance 2.5cm from the glass plate & operated at a speed of 50rpm. 5ml of sample can withdraw at specific time interval for 24hrs & analysed by UV or HPLC. Perform the experiment in triplicate.

In vitro skin permeation studies
By using diffusion cell in vitro skin permeation study is carried out. Here use of male wistar rat weighing 200-250gm. Take the abdominal skin of rat by removing the hairs from abdominal region by using electric clipper. Then dermal side of the skin is washed with distilled water to remove adhesive tissues then it is kept in dissolution media or phosphate buffer pH 7.4 for 1hr. before starting the experiment & was placed on magnetic stirrer with small magnetic needle for uniform distribution of diffusant. The temperature of cell was maintained at 32±0.5°C using thermostatically controlled heater. Rat skin is placed between the compartment of diffusion cell with epidermis facing in upward into donar compartment. Specific amount of volume is withdraw from receptor compartment at specific time interval & equal volume of fresh sample is add. Withdraw sample is filtered & analysed by UV or by using HPLC. Flux can be determine by plotting the slop between steady state values of the amount of drug permeated mg cm$^2$ vs. time in hours & permeability coefficient were deduced by dividing the flux by initial drug load mg cm$^2$.

Skin irritation test
This study is performed on healthy rabbits (average weight 1.2-1.5kg). Remove the dorsal surface of rabbit by shaving & clean by using spirit. Formulation applied on skin surface & remove after 24hrs & skin is to be observed & classified in to 5 grades on the basis of severity of skin injury.

Stability studies
Stability studies were done as per ICH guidelines where TDDS samples are stored at 40 ± 0.5°C and 75 ± 5% RH for 6 months. The samples were withdrawn at 0, 30, 60, 90 and 180 days and analyzed suitably for the drug content.
3 CONCLUSION
The use of transdermal drug delivery devices has experienced a remarkable increase. This interest in transdermal products can be attributed to many advantages offered by this unique route of administration by increase bioavailability and avoid fast pass metabolism. Although, the transdermal patches have become a proven technology that offers variety of significant clinical benefits over other dosage forms, the systems still offer many challenges in evaluation and testing area of transdermal patches.

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