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A REVIEW ARTICLE ON TRANSDERMAL PATCHES: A COMPREHENSIVE GUIDE

Satheeshkumar P.*, Dharineesh N., Dharmasimma B. and Dhinesh Britto C.

SSM College of Pharmacy, Jambai, Erode.
The Tamilnadu Dr. MGR Medical University Chennai.

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Corresponding Author: Satheeshkumar P.
SSM College of Pharmacy, Jambai, Erode, The Tamilnadu Dr. MGR Medical University Chennai.
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ABSTRACT

Transdermal drug delivery systems (TDDS) are non-invasive and provide an alternative route to the traditional method of drug administration. Drugs pass through the skin and into the bloodstream through these systems, which confer advantages such as continuous drug delivery, avoidance of first-pass metabolism, and bypassing the digestive system. History The history of TDDS begins as early as the early 20th century, and great developments have been made over the years, especially during the 1960s and 1970s. In 1979, the first FDA approved transdermal patch came out, and since then, different types of TDDS have emerged, such as single-layer drug-in-adhesive patches, multi-layer drug-in-adhesive patches, reservoir patches, matrix patches, and microneedle-based patches. TDDS designing and development are done in accordance with several factors, like drug selection, type of patch, and evaluation parameters. The evaluation parameters include thickness, weight uniformity, folding endurance, percentage moisture content, content uniformity test, moisture uptake, flatness, tensile strength, and skin permeation. In-vitro methods, such as diffusion cell permeation tests, are used to evaluate the release of drugs from TDDS. In-vivo studies, including animal models and human clinical trials, are also conducted to assess the performance of TDDS. The advantages of TDDS include continuous drug delivery, avoidance of first-pass metabolism, and bypassing the digestive system. Challenges associated with TDDS are skin irritation, inconsistent absorption, and limited dosing options. TDDS provides an alternative promising route for the administration of drugs in contrast to traditional methods of drug administration. Ongoing research and development are focused on improving the design, efficacy, and safety of these systems.

KEYWORDS: Transdermal drug delivery systems (TDDS), bloodstream, Transdermal patches.

INTRODUCTION

Transdermal drug delivery offers a non-invasive alternative to traditional drug administration methods by allowing drugs to pass through the skin and enter the bloodstream. This approach provides advantages such as continuous drug delivery, avoidance of first-pass metabolism, and bypassing the digestive system, which are not possible with oral or intravenous routes. Commonly used for conditions like smoking cessation, chronic pain, and hormone replacement therapy, transdermal patches can deliver drugs over extended periods, from hours to days. Examples of drugs delivered via patches include nicotine, fentanyl, estradiol, and scopolamine. Developed in 1985, the nitroglycerin patch was one of the first, and today, a variety of patches use rate-controlling membranes to ensure steady drug release. The choice of application site depends on the drug, with options such as the chest for nitroglycerin or the abdomen for estradiol.

Transdermal patches provide a convenient, effective way to manage treatment with minimal invasiveness.[1,2,3]

- Dose: Should be low (generally <20mg/day).
- Elimination Half-life of drug (hr.): ≤10.
- Molecular weight: < 500-400 Daltons.
- Partition Coefficient: Log P (Octanol- Water) should be in the range of 1 to 3.
- Skin permeability: >0.5 X 10-3 cm/hr.
- The drug should be non-irritating and non-Sensitizing.
- Drug with low oral bioavailability.
- Drug with low therapeutic index.

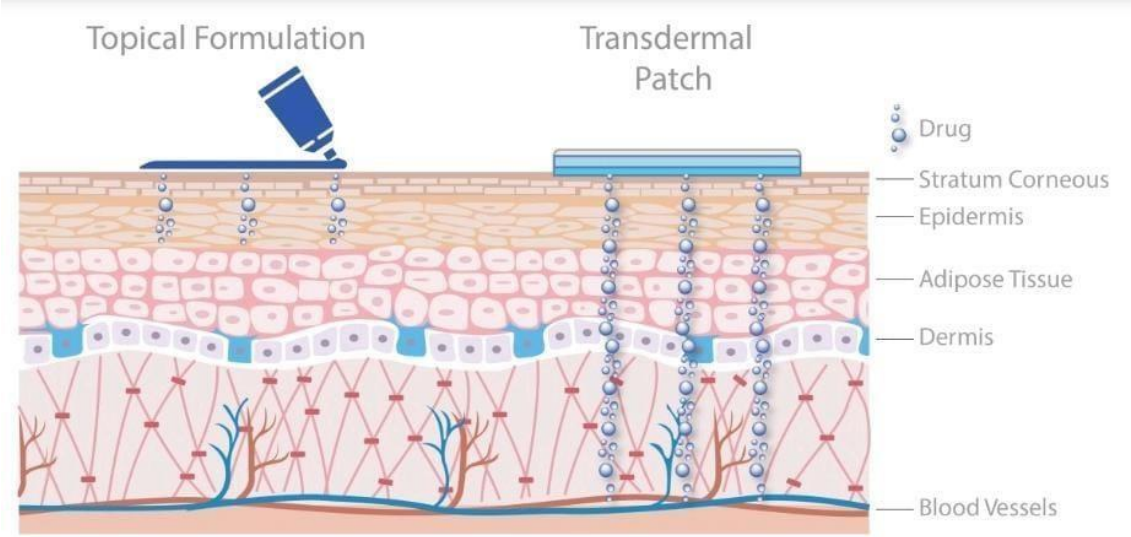

Figure 1: Transdermal patch on skin.

Advantages	Disadvantages
Continuous dosing, multiday treatment	Limited type of medication
Bypass the digestive system	Skin irritation
Avoid first-pass metabolism	Inconsistent absorption
Can be terminated anytime	Patch failure
Less invasive	Limited dosing option

History[18]

The History of Transdermal Patches

Transdermal patches represent a significant advancement in drug delivery systems, offering a noninvasive method of administering medications through the skin. The history of these patches dates back to the early 20th century, with gradual developments that have led to the modern patches used today.

Early 20th Century: Preliminary Uses

The concept of using topical products for medicinal purposes has existed for centuries. In the early 1900s, remedies like mustard plasters were used to treat chest congestion, while Belladonna Plasters served as transdermal analgesics for pain relief. These early uses paved the way for future innovations in transdermal drug delivery.[4-7]

1961: Early Experimentation

The scientific foundations of transdermal patch technology were laid in 1961, when researchers Sherman Kramer and Dale Wurster began experimenting with a diffusion cell that was used to study the skin's ability to absorb drugs. They tested the permeability of human skin to various substances, which helped to develop the concept of delivering drugs through the skin over extended periods.

1979: First FDA-Approved Transdermal Patch

A major milestone in transdermal patch history came in 1979, when the U.S. Food and Drug Administration (FDA) approved the first transdermal system for systemic drug delivery. The patch, which was used to deliver scopolamine, a medication to treat motion sickness, was designed to be worn for three days. This marked the beginning of the widespread acceptance and commercialization of transdermal patches.[8]

1984: Clonidine for Hypertension

In 1984, the FDA approved the use of clonidine patches for treating mild-to-moderate hypertension. This was another significant milestone, as it demonstrated the potential for transdermal patches to manage chronic conditions and provide consistent, controlled drug release over time.[9,10]

Nicotine Patches: A Blockbuster Success

The introduction of the nicotine patch in the 1990s was a game-changer in the field of smoking cessation. These patches, which provided a steady, controlled dose of nicotine to help manage withdrawal symptoms, became one of the most successful transdermal products ever. They marked the first transdermal "blockbuster" product and helped propel the popularity of transdermal drug delivery systems in the consumer market.[11-13]

Today: Diverse Applications and Advances[18]

Today, transdermal patches are widely used for a variety of medical conditions, offering benefits such as ease of use, continuous drug delivery, and reduced side effects. Some of the most common applications include:

Hormone replacement therapy: Estradiol patches are commonly used in female hormone replacement therapy for menopausal women.

Pain management: Fentanyl patches are used for chronic pain management, providing a continuous release of the powerful opioid.

Local anesthesia: Lidocaine patches are used for localized pain relief, particularly in conditions like postherpetic neuralgia.

Hormone replacement for men: Testosterone patches help treat hypogonadism in men, providing a steady release of the hormone to normalize testosterone levels.

Additionally, there are combination patches for contraception and hormone replacement, offering women a convenient and effective way to manage both their reproductive health and hormonal balance.

Notable Developments in Transdermal Technology

Other significant innovations in the field include:

Topical products with systemic effects: Some transdermal products are designed not only for localized treatment but also for systemic absorption, allowing for more convenient medication regimens.

Oestradiol patches: Used widely in female hormone replacement therapy, these patches provide a steady dose of estrogen, helping to alleviate menopausal symptoms.[14,15]

Fentanyl and Testosterone Patches: Beyond pain management and hormone therapy, fentanyl and testosterone patches represent an ongoing evolution in delivering potent drugs through the skin.[16,17]

Transdermal Patch Design[1]

The transport of a drug across the skin is influenced by several factors, including skin permeability, the area and duration of application, and the metabolic activity of the skin (i.e., firstpass metabolism). Each drug has unique properties that can impact its transdermal delivery. For effective absorption and penetration through the skin, the drug should ideally be non-ionic and relatively lipophilic, as these characteristics enhance the drug's ability to cross the skin's barrier. Additionally, molecules with a molecular weight greater than 500 Daltons generally struggle to penetrate the stratum corneum. Furthermore, for optimal transdermal delivery, the drug's therapeutic dose should typically be less than 10 mg per day to ensure adequate absorption without exceeding safe exposure limits.

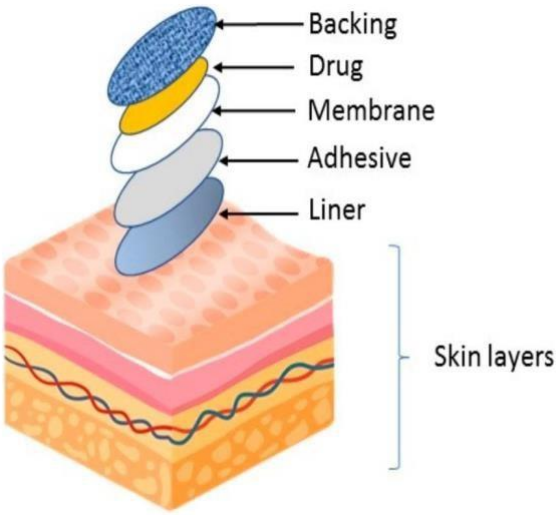

Figure 2: Basic components of transdermal patch.

Types of Transdermal Patches[27-32]

1. Single-layer Drug-in-Adhesive Patch

In this system, the adhesive layer is the key functional component. It not only adheres the patch to the skin but also serves as the drug reservoir, releasing the active ingredient over time. The drug is embedded within the adhesive itself. This patch is typically backed by a protective layer and a temporary liner that is removed before application. The primary advantage of this system is its simplicity and ease of use, but its release rate is typically more difficult to control due to the drug being directly in the adhesive.

2. Multi-layer Drug-in-Adhesive Patch

The multi-layer drug-in-adhesive patch builds upon the single-layer system by adding additional layers, each serving distinct functions. One adhesive layer provides immediate drug release, while another is designed for controlled release over a longer duration. In some designs, the drug-inadhesive layers are separated by a membrane, although this is not always the case. The patch also includes a temporary liner and a permanent backing layer. This system allows for a more controlled and sustained release of the drug, making it ideal for prolonged treatments or for drugs that require gradual administration.

3. Reservoir Patch

In contrast to the drug-in-adhesive systems, the reservoir patch has a separate drug compartment that holds a solution or suspension of the drug. The drug layer is contained within a liquid reservoir and is separated from the skin by an adhesive layer. This system typically provides a zero-order release, meaning that the drug is released at a constant rate over time, offering precise control over drug delivery. The reservoir system is advantageous for drugs that require steady, controlled release, but the system may be more complex and costlier to manufacture.

4. Matrix Patch

The matrix system features a semisolid matrix layer containing a drug solution or suspension. This matrix is typically surrounded by an adhesive layer that partially overlays the drug matrix, forming a monolithic device. In this configuration, the drug release depends on the rate at which the drug diffuses through the matrix and the adhesive layer. Unlike the reservoir system, there is no separate drug compartment, and the drug release is governed by the matrix's composition and the diffusion properties of the drug. This system offers a balance between simplicity and controlled release, with applications ranging from pain management to hormone therapy.

5. Vapour Patch

Vapour patches are a newer category in transdermal drug delivery systems. Instead of delivering solid or liquid drugs, vapour patches release volatile compounds such as essential oils into the air. The adhesive layer in this system not only adheres the patch to the skin but also facilitates the release of vapour. Vapour patches are used for a variety of purposes, such as decongestion, relaxation, and improving sleep quality. Some vapour patches even claim to help reduce smoking frequency by releasing compounds that help curb cravings. These patches typically provide vapour release for up to six hours and are marketed as an alternative to traditional medicinal products, offering a non-invasive way to address specific health concerns.

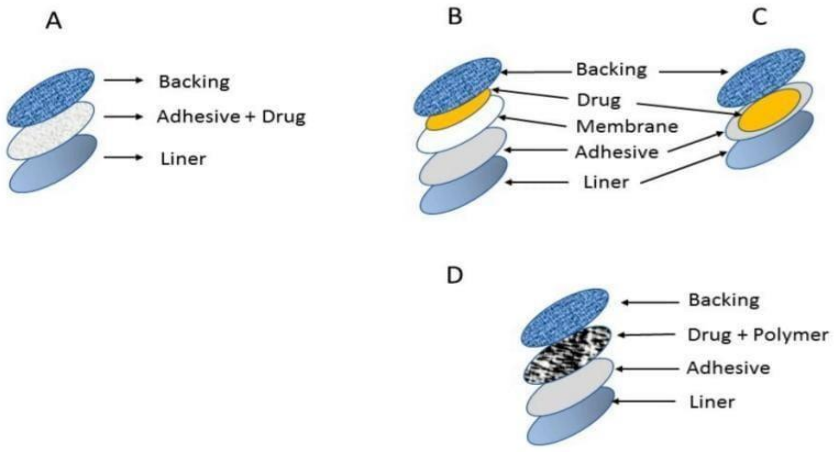

Figure 3: A) Single layer drug in adhensive patch B) Reservoir Patch C) Matrix Patch D) Multilayer Drug-in-Adhesive Patch.

Microneedle-Based Patches

There are many types of microneedles with distinctive features and characteristics, as outlined in. Broadly, four major categories of microneedle-based patches have been developed: solid, hollow, dissolving, and coated microneedle. The type of microneedle selected will be based on the specific application or requirements of the user. Solid Microneedles: These are the most elementary forms of microneedles, comprising solid

1. Needles that puncture the skin and form small pores. Solid microneedles are mainly used for drug delivery and cosmetic applications.
2. Hollow Microneedles: These microneedles have a hollow core where fluids or drugs can be delivered into the skin. Hollow microneedles are typically used for transdermal drug delivery and sampling of interstitial fluid.
3. Coated Microneedles: These microneedles have a coating that degrades upon penetration.Etration of the skin, permitting the drug or other agent to be released. Coated Microneedles are mostly used for drug delivery in transdermal applications.
4. Dissolving Microneedles: In this type of microneedle, dissolvable material is used to produce the drug or other substance delivery into the skin; it's a controlled release, and therefore, the most common usage is vaccines as well as other drug applications.

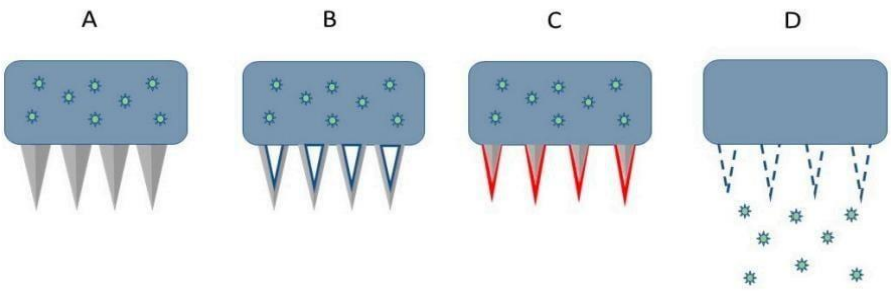

Figure 4: Microneedle based patch: A) Solid; B) Hollow; C) Coated; D) Dissolving.

Methods for Enhancing Transdermal Drug Delivery[19-26]

Skin penetration can be enhanced by following methods:

1. **Prodrug Approach:** A prodrug is designed to improve a drug's skin permeability. By adding a promoiety that enhances partition coefficient and solubility, the prodrug can pass through the skin, where esterases release the

active drug. This method has been effective for drugs like 6-mercaptopurine and non-steroidal anti-inflammatory drugs (NSAIDs).

2. **Eutectic System:** Eutectic mixtures, which are combinations of chemicals that solidify at lower temperatures, can be used to lower the melting point of drugs, enhancing their solubility in skin lipids. EMLA cream (a mixture of lignocaine and prilocaine) is an example that provides effective local anesthesia.
3. **Liposomes and Vehicles:** Liposomes are spherical vesicles capable of encapsulating drugs and delivering them to the skin. They can enhance skin delivery for cosmetic and therapeutic products, often using phosphatidylcholine.
4. **Solid Lipid Nanoparticles (SLNs):** SLNs are lipid-based carriers that can improve the delivery of sunscreens, vitamins, and glucocorticoids. Their ability to form an occlusive film on the skin increases hydration and drug penetration.
5. **Iontophoreskin:** This technique uses low electric currents to facilitate drug permeation through the skin. It works by using electro-repulsion, electro-osmosis, or electroperturbation to drive drugs across the skin.
6. **Electroporation:** High-voltage pulses are used to create temporary pores in the skin, enhancing drug penetration. This method is effective for molecules of various sizes, including proteins and peptides.
7. **Ultrasound (Sonophoresis and Phonophoresis):** Low-frequency ultrasound enhances skin permeability either as a pre-treatment or simultaneously with drug delivery. This technique works by increasing the skin's permeability temporarily.
8. **Laser Radiation and Photomechanical Waves:** Lasers can ablate the stratum corneum, allowing for deeper penetration of drugs without significantly damaging the underlying epidermis. It is commonly used in dermatological treatments.
9. **Radio Frequency:** Exposure to high-frequency alternating currents generates heat that forms microchannels in the skin, which facilitates drug delivery. The microchannels' number and depth are controlled to regulate drug penetration.
10. **Magnetophoresis:** A magnetic field is applied to enhance the diffusion of diamagnetic drugs across the skin. It may also induce structural changes in the skin, further aiding in drug penetration.
11. **Microneedle Devices:** Microneedles, which are small (50–110 micrometers) and capable of piercing the stratum corneum and epidermis, enable drugs to be delivered directly into the skin. This approach avoids the need for syringes or traditional injections.
12. **Skin Abrasion:** Skin abrasion techniques physically remove or disrupt the upper layers of the skin, creating an entry point for drugs. This method is commonly used for skin resurfacing treatments.
13. **Needle-less Injection:** This method uses high-pressure jets to force liquid or solid drug particles through the skin without using needles. The jet stream, often created with compressed gas, allows for painless, needle-free drug delivery.
14. **Application of Pressure:** Applying modest pressure to the skin (e.g., 25 kPa) can improve drug penetration. This simple, non-invasive method is effective for small molecules like caffeine.

Evaluation Parameters

1. Thickness of the patch[34-36]

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.

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.

3. Folding endurance[38,40]

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.

4. Percentage Moisture content[46]

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.

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

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.

6. Moisture Uptake[46]

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.

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

7. Flatness[37,38]

The ideal transdermal patch should possess a Smooth surface and should not fold or constrict with the progress of time. The flatness of a Patchcan be studied by performing the Following test: three longitudinal strips are cut From each patch i.e. the patch is cut from the Center, left side and right side of the patch thus Covering almost the entire part of patch Surface. The length of each strip should be Measured and minimum deviation is preferred. The variation in length is measured by Determining percent constriction.

$$\text{Constriction (\%)} = \frac{l1\text{-}l2}{l2} \times 100$$

8. Tensile strength[58]

Tensile strength instrument or tensiometer can be used for this purpose. Tensile strength is the maximum stress applied to a point at which the specimen breaks. Tensile strength helps understand themechanical properties of the polymeric patches. The instrument consists of two load cell groups, the lower one is fixed and the upper one is movable. The strips (dimension- 2*2 cm) are fixed between these two groups. Force is gradually applied till the film breaks and the break force recorded is expressed in kg. Also elongation can be measured with the help of pointer mounted on the assembly.

$$T.S.= \frac{\text{tensile force}}{a \text{ X } bX(1+\Delta L/l)}$$

Where, a- width of strip.

b- Thickness of strip. l- Length of strip.

ΔL- Elongation of patch at break point.

9. Swellability[37,41]

This test is to check the swellability of the patch due to presence of polymer. This test requires petri plates and double distilled water, to see how much the patch would swell upon contact with water. The patches of 3.14 cm² are weighed and placed in a petri plates containing 10 ml of double distilled water and are allowed to imbibe for specified time. Increase in weight of the patch is then determined at specific time intervals until a constant weight is observed.

The degree of swelling (% S) is calculated using the formula. $S(\%) = \frac{W_t - W_0}{W0} X\ 100$

10. Surface pH[37,42]

Surface pH of the patches is described by Bottenberg et al. The patches are kept in 0.5 ml double distilled water and thus allowed to swell for 1hour. The surface pH is known by bringing a combined glass electrode near the surface of the patch and allowing it to equilibrate for 1 minute.

11. Peel Adhesion test[33,39,43-45]

The force required to remove an adhesive coating form a test substrate gives peel adhesion factor. Molecular weight of adhesive polymer, the type and amount of additives are the variables that determine the peel adhesion properties. A single tape is applied to a stainless steel plate or a backing membrane of choice and then the tape is pulled from the substrate at a 180º angle and the force required for tape removed is measured. This gives Peel adhesion rate.

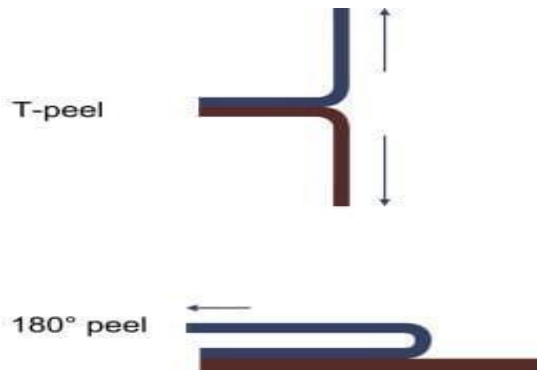

Figure 5: Peel adhesion test.

12. Rolling ball tack test[33,39,43-45]

In this, 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 the horizontal, upward facing adhesive. The distance the ball travels along the adhesive provides the measurement of tack, expressed in inch.

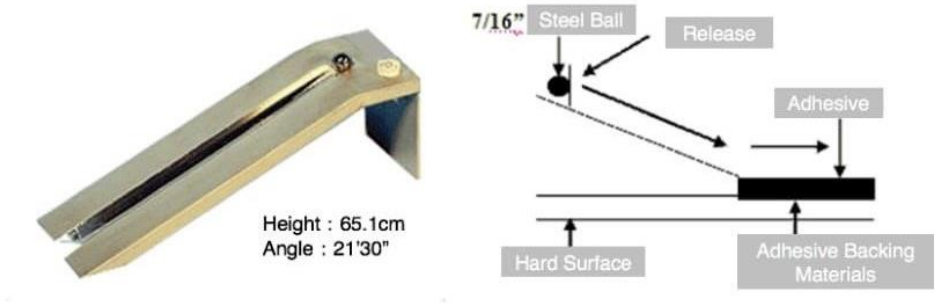

Figure 6: Rolling ball tack test.

13. Probe Tack test[33,39,43-45]

The Force required to pull a probe away from an adhesive at a fixed rate is recorded as tack. 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.

Skin permeation In -Vitro Method

Diffusion Cell permeation test[33,48,45,49]

Permeation test involves various skin tissues, whole skin, epidermis or dermis in a specialized cell also known as "diffusion cell" (Fig) 27. Skin or tissue is mounted sandwiched between the donor and the receptor compartment. Drug formulation is placed in the donor compartment. It is in contact with tissue on one side and the tissue is in contact with the receptor solution. The temperature is controlled in the whole process. The sampling time points are fixed and the receptor solution is assayed for the drug 6, 28, 29. Since the skin membrane is used between the compartments, it is essential to find out if a drug is immobilized or if it is going through the skin, if so then at what rate. The Franz cell can also be modified by using it directly for drug dissolution wherein, the skin membrane is replaced by the transdermal membrane.

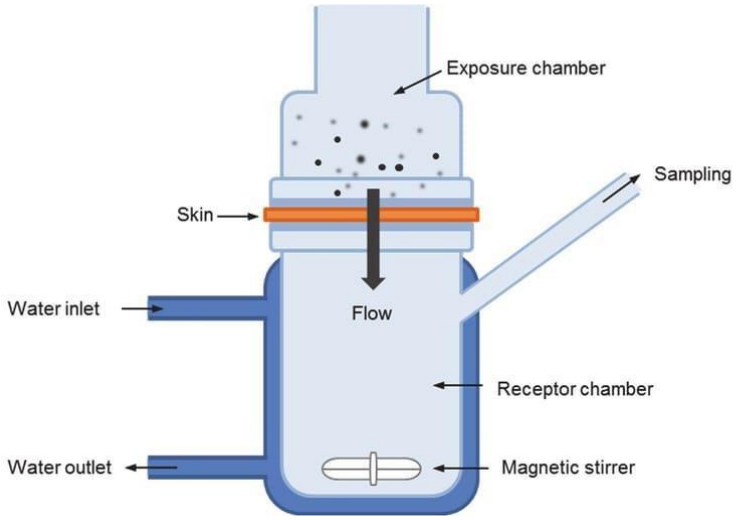

Figure 7: Diffusion Cell permeation test.

The various factors affecting the testing performance[47]

- System Design
- Effect of Temperature
- Effect of Stirring
- Drug Solubility

1) System design

The primary concernis that method must be ableTo put up the basic system size and type. The arrangement should be planned such that it too must be able to fit the system's theoretical release pattern. In case the system is to provide burst release or loading dose, the time intervals of sampling should be set to specifically, in order to capture the part of release pattern in addition to the controlled-release rate portion.

2) Temperature influence

Temperature affects the rate of drug diffusion through the polymer and the rate control membranes. The targeted temperature is usually set at 32/35oC to mimic the temperature of the surface on the skin. The temperature will be regulated during the test, within ±0.3oC in order to obtain the accurate measurement of the rate. For the above stated reasons, the temperature effect will play a critical role for: controlled portion rather than the burst portion. Stirrer Donor Compartment Sample Port Receptor Compartment Skin mounted between donor and receptor compartment.

3) Effect of Stirring

Diffusion dependent controlled release of the system is directly relative to Apparent concentration' at the system-receptor solution interface. Poor stirring leads to building up of the concentration gradient at the interface, leading to reduced diffusional drug flow. Too high stirring rates will be useless.

4) Drug Solubility

Release of the drug from donor to receptor compartment is directly influenced by the drug in the receptor solution in general and at the system solution interface in particular. The drug release is influenced by "percent saturation" (also termed activity) in the system and the receptor solution. The concentration (concentration Gradient) is the driving force for diffusion. The release mechanism are best predicted when we can limit drug concentration in the solution to less than 10% saturation (sink condition). For hydrophobic drug/ drug with low solubility, their solubility can be improved by adding a surfactant or organic solvent to receptor compartment. However, it may cause to increase the release rate or modify diffusion coefficients of the drug in the membranes. Therefore, the easiest way to limit saturation effects is to use larger volumes or shorter collection intervals to maintain sink condition.

In-Vitro Dissolution Methods[47-57]

The USP 30 has three official apparatuses (5, 6 and 7). The whole system for dissolution study needs to have a larger receptor solution volumes that can meet saturation-limit requirements. Therefore, diffusion cells are not the apparatus of choice. Collection format is a characteristic feature. It is either cumulative, flow through or interval. In the cumulative collection format we collect the released drug in a single container. For example apparatus 5 and 6. Apparatus 5 is referred to as “paddle over disk” and 6 utilizes a spinning cylinder to stir the system. Drug concentration increases in vessel in a cumulative manner. Apparatus 6 uses the same system as apparatus 1, except the basket is

replaced with the “cylinder stirring element”. The transdermal is attached to the circumference of the cylinder with the help of a water-permeable occlusive Cuprophan. Cuprophan is inert porous cellulose material.

Flow through/interval systems (USP apparatus 7) have small “cell volumes” and controlled flow of receptor solution is used through cell to collect the drug. Drug solution can either be measured in flowing solution or from a well-stirred collection vessel. The main advantage of this format is that the fresh receptor solution in constantly in the contact with donor solution. Interval collection involves collecting the drug released in a series of receptor solutions, each indexed at particular intervals, USP apparatus 7.

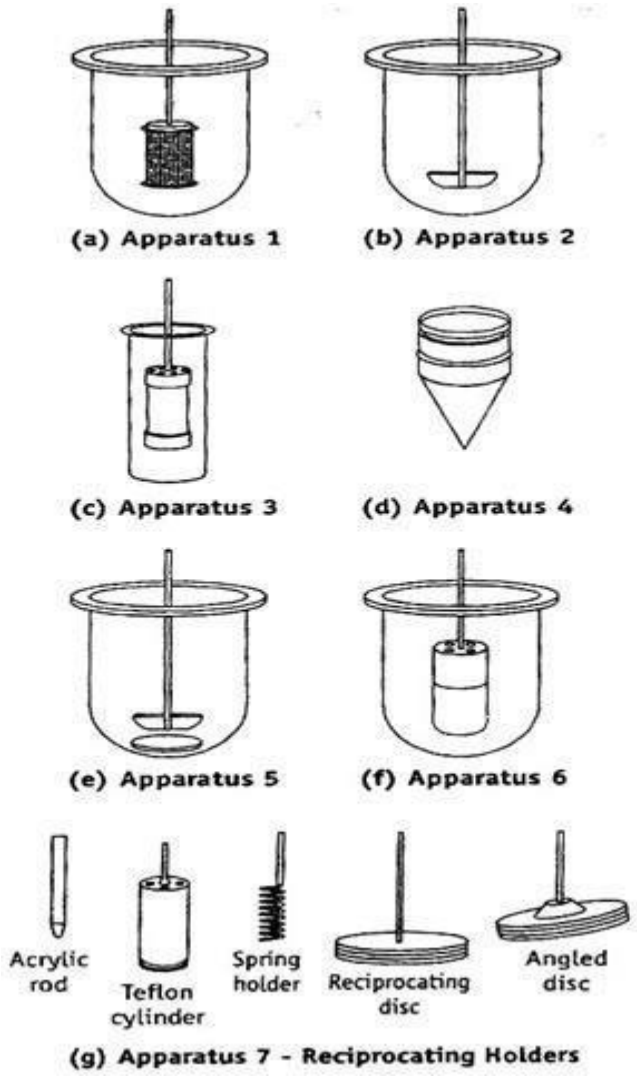

Figure 8: In-Vitro Dissolution Methods.

In – vitro permeation study

After release from the polymeric films, drug reaches at skin surface is then passed to the dermal microcirculation by permeation through cells of epidermis and/or between the cells of epidermis through skin appendages. Usually permeation studies are performed by placing the fabricated transdermal patch with rat skin or synthetic membrane in between receptor and donor compartment in a vertical diffusion cell such as Franz diffusion cell or Keshary-Chien diffusion cell. The transdermal system is applied to the hydrophilic side of the membrane and then mounted in the diffusion cell with lipophillic side in contact with receptor fluid. The receiver compartment is maintained at specific

temperature (usually 32±5°C for skin) and is continuously stirred at a constant rate. The samples are withdrawn at different time intervals and equal amount of buffer is replaced each time. The samples are diluted appropriately and estimated by suitable analytical method. The amount of drug permeated per square centimetre at each time interval is calculated. Many variables including design of system, patch size, surface area of skin, thickness of skin and temperature may affect the in-vitro properties of drug. Thus, the permeation studies involves preparation of skin, mounting of skin on permeation cell, setting of experimental conditions like temperature, stirring, sink conditions, withdrawing samples at different time intervals, sample analysis and calculation of flux (i.e., drug permeated per unit area per unit time).

In-vivo Studies[59-61]

In-vivo evaluations are the actual presentation of the drug performance. The variables which cannot be accounted for during in-vitro studies can be completely researched during in vivo studies. In-vivo evaluation of TDDS may be carried out using either animal models or human volunteers or both.

A. Animal models[62-64]

Significant time and resources are needed to conduct human studies, so animal studies are preferred at small scale. The most common animal species used for evaluating transdermal drug delivery systems are mouse, hairless rat, hairless dog, hairless rhesus monkey, rabbit, guinea pig etc. Based on the experiments conducted so far it is concluded that hairless animals are preferred over hairy animals in both in-vitro and in-vivo experiments Rhesus monkey is one of the most reliable models for in Vivo evaluation of transdermal drug delivery.

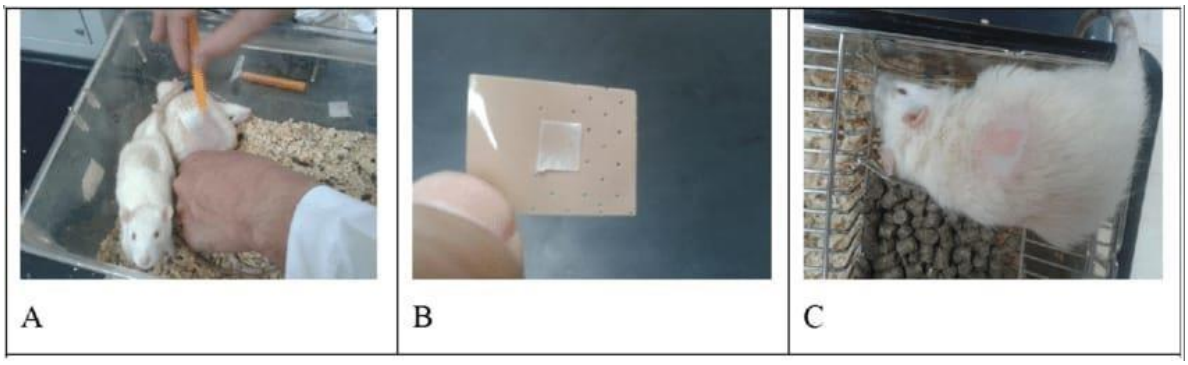

Figure 9: Transdermal Patch used in animal model.

B. Human models[65]

The last stage of the development of a transdermal device is to collect pharmacokinetic and pharmacodynamic data after application of the patch to human volunteers. Clinical trials are carried out to analyze the transdermal systems containing the efficacy, risk related, side effects, and compliance of the patient. Phase-I clinical trials are conducted to determine mainly safety in volunteers and phase-II clinical trials determine short term safety and mainly effectiveness in patients. Phase-III trials indicate the safety and effectiveness in large number of patient population and phase-IV trials at post marketing surveillance are done for marketed patches to detect adverse drug reactions. Though human studies require considerable resources but they are the best to assess the performance of the drug.

Figure 10: Transdermal patch used in human.

CONCLUSION

A Transdermal drug delivery system provides a painless, hassle-free and very effective non invasive system of managing diseases. Continuous delivery of drug without coming in contact with the gastrointestinal tract and circumventing the first-pass effect make them highly desirable routes over conventional oral and IV administration routes.

Evaluation of TDDS relates to both in vivo as well as in vitro studies. In vitro studies include diffusion cell permeation tests and dissolution methods, which give valuable information about the release and permeation of the drug. In vivo studies are done by determining the safety, efficacy, and pharmacokinetics using animal models and human volunteers in the case of TDDS.

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