

Transdermal Drug Delivery system

Pradip bhagwat kathole. Mr. V.G. Rokade, Mr.Hingane L.D.

Aditya pharmacy college beed

Date of Submission: 01-08-2021

Date of Acceptance: 18-08-2021

ABSTRACT:-

Drug delivery through the skin to achieve a systemic effect of a drug is commonly known as transdermal drug delivery and differs from traditional topical drug delivery.

The conventional oral dosage forms has significant drawbacks of poor bioavailability due to hepatic first pass metabolism and tendency to produce major fraction of drug is transported into the systemic blood circulation, leading to a need for high or frequent dosing, which can be both cost prohibitive and inconvenient.

To improve such characters transdermal drug delivery system (TDDS) was emerged which will improve the therapeutic efficacy and safety of drugs by more precise (i.e. site specific) placement within the body thereby reducing both the size and number of doses.

Today number of drugs is taken orally and is found not to be as effective as desired. To improve such characters transdermal drug delivery system was emerged.

This article provides an overview on introduction about the transdermal drug delivery system and types of Transdermal patches, use of polymer as a transdermal drug delivery system, methods of preparation, and its physicochemical methods of evaluation and the types of transdermal systems currently available in the market to focus on the recent innovations in Transdermal Drug Delivery Systems.

Which can be a platform for the research and development of pharmaceutical drug dosage form for Transdermal Drug Delivery.

I. INTRODUCTION:-

Transdermal drug delivery systems (TDDS), also known as "patches," are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin.

Transdermal drug delivery system has been in existence for a long time. In the past, the most commonly applied systems were topically applied creams and ointments for dermatological disorders.

The occurrence of systemic side-effects with some of these formulations is indicative of absorption through the skin.

A number of drugs have been applied to the skin for systemic treatment.

In a broad sense, the term transdermal delivery system includes all topically administered drug formulations intended to deliver the active ingredient into the general circulation.

Transdermal therapeutic systems have been designed to provide controlled continuous delivery of drugs via the skin to the 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.

Several important advantages of transdermal drug delivery are limitation of hepatic first pass metabolism, enhancement of therapeutic efficiency and maintenance of steady plasma level of the drug.

The first Transdermal system, Transderm -SCOP was approved by FDA in 1979 for the prevention of nausea and vomiting associated with travel, particularly by sea.

The evidence of percutaneous drug absorption may be found through measurable blood levels of the drug, detectable excretion of the drug and its metabolites in the urine and through the clinical response of the patient to the administered drug therapy.

Route of Penetration:-

In order to design a successful transdermal drug delivery system (TDDS), it is important to understand the structure, physiology and function of the skin. The skin is the largest organ and is primarily composed of three layers.

The skin is divided into epidermis, dermis, and subcutaneous layer or hypodermis. Each layer has its own function and own importance in maintaining the integrity of skin and thereby the whole body structure.

In the past, the most commonly applied systems were topically applied creams and ointments for dermatological disorders and these show local action but occurrence of systemic side-effects with some of these formulations is indicative of absorption through the skin this concept lead to the birth of TDDS.

In a broad sense, the term transdermal delivery system includes all topically administered drug formulations intended to deliver the active ingredient into the general circulation.

Transdermal therapeutic systems have been designed to provide controlled continuous delivery of drugs via the skin to the systemic circulation. Moreover, it over comes various side effects like painful delivery of the drugs and the first pass metabolism of the drug occurred by other means of drug delivery systems.

TDDS has been a great field of interest in recent times. Many drugs which can be injected directly into the blood stream via skin have been formulated by TDDS.

There are critically three ways in which a drug molecule can cross the intact SC: via skin appendages (shunt routes), through the intercellular lipid domains or by a transcellular route. Physiochemical properties of the molecule govern the flux of a particular drug to permeate by a combination of these routes.

There are three types of route of penetration:-

1. The appendageal route

2. Transcellular route

3. Intercellular route

1. The appendageal route:-

The transappendageal routes are also known as the shunt routes, and include permeation through the sweat glands and across the hair follicles with their associated sebaceous glands. Skin appendages provide a continuous channel directly across the SC barrier.

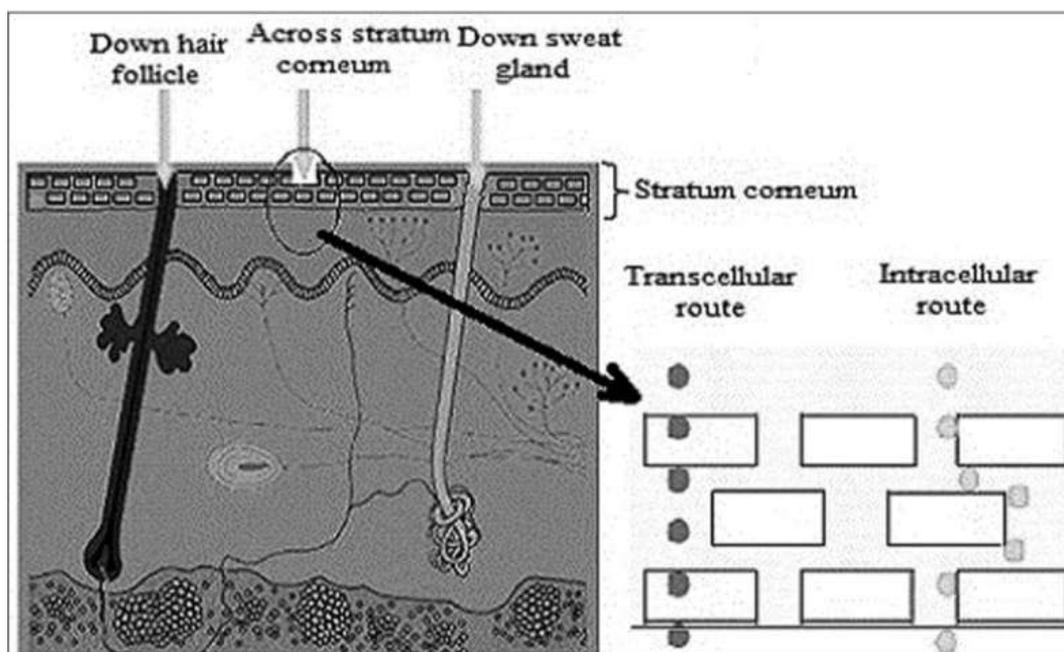
Recent studies have re-examined the long held assumption that the follicles occupy approximately 0.1% of the surface area of the human skin. Otberg et al. showed that the follicular number, opening diameter and follicular volume are important considerations in drug delivery through these appendages and, indeed, the forehead provides 13.7 mm²/cm² as the follicular infundibula, i.e. approximately 13.7% of the surface area of the forehead is available as follicles.

Interestingly, the same study also showed that the historically held view of the follicles providing approximately 0.1% of the SC appears to be valid for forearm skin.

2. Transcellular route:-

Drugs entering the skin via the transcellular route pass through the corneocytes. Corneocytes containing highly hydrated keratin provide an aqueous environment from which hydrophilic drugs can pass.

The transcellular pathway requires not only partitioning into and diffusion through the keratin bricks but also into and across the intercellular lipids.



3. Intercellular route:-

The intercellular route involves drug diffusion through the continuous lipid matrix.

This route is a significant obstacle for two reasons:-

(i) Recalling the “bricks and mortar” model of SC, the interdigitating nature of the corneocytes yields a tortuous pathway for intercellular drug permeation, which is in contrast to the relatively direct path of the transcellular route.

(ii) The intercellular domain is a region of alternating structured bilayers. Consequently, a drug must sequentially partition into and diffuse through repeated aqueous and lipid domains. This route is generally accepted as the most common path for small uncharged molecules penetrating the skin

Factors Affecting Transdermal Permeation:-

Physicochemical properties of the penetrate molecules-

Partition coefficient, pH conditions, Penetrate concentration.

Formulation factor:-

- Physical chemistry of transport.
- Vehicles and membrane used.
- Penetration enhancers used.
- Method of application.
- Device used.

Physiological factors:-

- Stratum corneum layer of the skin.
- Anatomic site of application on the body.
- Skin condition and disease. Age of the patient.
- Skin metabolism. Desquamation (peeling or flaking of the surface of skin).
- Skin irritation and sensitization.
- Race.

Skin condition:-

The intact skin itself acts as a barrier, but many agents like acids and alkali cross the barrier cells and penetrate through the skin. Many solvents open the complex dense structure of the horny layer: solvents like methanol and chloroform remove the lipid fraction, forming artificial shunts through which drug molecules can pass easily.

Skin age:-

It is seen that the skin of adults and young ones is more permeable than that of the older ones. but there is no dramatic difference. Children show toxic effects because of the greater surface area per unit body weight. Thus, potent steroids, boric acid and hexachlorophene have produced severe side-effects.

Physicochemical factors:-

Hydration of skin:

Generally, when water saturates the skin,

it swells tissues, softens wrinkles on the skin and its permeability increases for the drug molecules that penetrate through the skin.

Temperature and pH of the skin:

The penetration rate varies if the temperature varies and the diffusion coefficient decreases as the temperature falls; however adequate clothing on the body prevents wide fluctuations in temperature and penetration rates.

According to pH, only unionized molecules pass readily across the lipid membrane, and weak acids and bases dissociate to different degrees according to their pH and pKa or pKb values. Thus, the concentration of unionized drug in applied phase will determine the effective membrane gradient, which is directly related to its pH.

Environmental factors:-

Sunlight:

Because of to sunlight, the walls of blood vessels become thinner, leading to bruising, with only minor trauma in the sun-exposed areas. Also, pigmentation, the most noticeable sun-induced pigment change, is a freckle or solar lentigo.[18]

Cold season:

The cold season often results in itchy and dry skin. The skin responds by increasing oil production to compensate for the weather's drying effects. A good moisturizer will help ease symptoms of dry skin. Also, drinking lots of water can keep your skin hydrated and looking radiant.

Air pollution:

Dust can clog pores and increase bacteria on the face and the surface of skin, both of which lead to acne or spots, which affects drug delivery through the skin. Invisible chemical pollutants in the air can interfere with the skin's natural protection system, breaking down the skin's natural oils that normally trap moisture in the skin and keep it supple.

Advantages of Transdermal Drug Delivery Systems:-

Delivery via the transdermal route is an interesting option because transdermal route is convenient and safe. The positive features of delivery drugs across the skin to achieve systemic effects are:

- Avoidance of first pass metabolism.
- Avoidance of gastro intestinal incompatibility.
- Predictable and extended duration of activity.
- Minimizing undesirable side effects.

- Provides utilization of drugs with short biological half lives, narrow therapeutic window.
- Enhance therapeutic efficacy.
- Drug administration stops with patch removal.
- Alternate route for patients who are unable to take oral medications.
- Improved patient compliance and comfort via non-invasive, painless and simple application.

Disadvantages Of Transdermal Drug Delivery Systems:-

- Only small, lipophilic drugs can be delivered currently through.
- Drug molecule must be potent because patch size limits amount.
- Drugs with very low or high partition coefficient fail to reach blood circulation.
- Easy elimination of drug delivery in case of toxicity.
- Drugs that are highly melting can be given by this route due to their low solubility both in water and fat.
- Erythema, itching, and local edema can be caused by the drug, the adhesive, or other excipients in the patch formulation.

Components Of Transdermal Drug Delivery System Drug:-

Drug is in direct contact with release liner. The selection of drug for TDDS is based on physicochemical properties of drug. Transdermal drug delivery system is much suitable for drug having

Physicochemical properties:-

- The drug should have some degree of solubility in both oil and water (ideally greater than 1mg/ml).
- The substance should have melting point less than 200°F.
- Hydrogen bonding groups should be less than 2.
- Low molecular weight (less than 500 Daltons).

Biological properties:-

- Drug should be very potent, i.e., It should be effective in few mg per day (ideally less than 25mg/day).
- Tolerance to drug must not develop under near zero order release profile of transdermal delivery.
- The drug should not get irreversibly bound in the subcutaneous tissue.
- The drug should not get extensively

metabolized in the skin.

- Narrow therapeutic window.

BASIC COMPONENTS TDDS:-

- **Polymer matrix/drug reservoir**
- **Membrane**
- **Drug**
- **Permeation enhancers**
- **Pressure-sensitive adhesives (PSA)**
- **Backing laminates**
- **Release liner**
- **Other excipients like plasticizers and solvents**

Polymer matrix/drug reservoir:-

Polymers are the backbone of TDDS, which control the release of the drug from the device. A polymer matrix can be prepared by dispersion of drug in a liquid or solid state synthetic polymer base.

Polymers used in TDDS should have biocompatibility and chemical compatibility with the drug and other components of the system, such as penetration enhancers and PSAs. Additionally, they should provide consistent and effective delivery of a drug throughout the product's intended shelf-life, and should be safe.

The following criteria should be preferred in selecting the polymer to be used in the transdermal system:-

- (i) Molecular weight, glass transition temperature and chemical functionality of the polymer should be such that the specific drug diffuses properly and gets released through it.
- (ii) The polymer should be stable, nonreactive with the drug, easily manufactured and fabricated into the desired product, and should be inexpensive.
- (iii) The polymer and its degradation products must be nontoxic or nonantagonistic to the host.
- (iv) The mechanical properties of the polymer should not deteriorate excessively when large amounts of active ingredients are incorporated into it.

Membrane:-

A membrane may be sealed to the backing to form a pocket to enclose the drug-containing matrix or used as a single layer in the patch construction. The diffusion properties of the membrane are used to control availability of the drug and/or excipients to the skin.

For example, ethylene vinyl acetate, silicone rubber, polyurethane, etc. are used as rate-controlling membrane.

Drug:-

For successfully developing a TDDS, the drug should be chosen with great care. Transdermal patches offer many advantages to drugs that undergo extensive first-pass metabolism, drugs with narrow therapeutic window or drugs with a short half-life, which cause noncompliance due to frequent dosing.

Some of the desirable properties of a drug and factors to be considered for transdermal delivery

There are some examples of drugs that are suitable for TDDS, like Nicardipine hydrochloride, Captopril, Atenolol, Metoprolol tartarate, Clonidine, Indapamide, Propranolol hydrochloride, Carvedilol, Verapamil hydrochloride and Nifedipine, etc.

Permeation enhancers:-

One long-standing approach for improving TDD uses penetration enhancers (also called sorption promoters or accelerants), which increase the permeability of the SC so as to attain higher therapeutic levels of the drug candidate.

Penetration enhancers interact with structural components of the SC thus modifying the barrier functions, leading to increased permeability. Three pathways are suggested for drug penetration through the skin: polar, nonpolar and polar/nonpolar. The enhancers act by altering one of these pathways.

The key to altering the polar pathway is to cause protein conformational change or solvent swelling. The key to altering the nonpolar pathway is to alter the rigidity of the lipid structure and fluidize the crystalline pathway (this substantially increases diffusion).

The fatty acid enhancers increase the fluidity of the lipid portion of the SC. Some enhancers (binary vehicles) act on both polar and nonpolar pathways by altering the multilaminar pathway for penetrants.

The methods employed for modifying the barrier properties of the SC to enhance drug penetration (and absorption) through the skin can be categorized as two enhancers:-

(a) Chemical Enhancers:-

(b) Physical Enhancers.

a) Chemical enhancers:-

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

- Increasing (and optimizing) the

thermodynamic activity of the drug when functioning as a co-solvent.

- Increasing the partition coefficient of the drug to promote its release from the vehicle into the skin.
- Conditioning the SC to promote drug diffusion.
- Promoting penetration and establishing drug reservoir in the SC. Some of the more desirable properties for penetration enhancers acting within the skin have been given as:
 - They should be nontoxic, nonirritating and nonallergenic
 - They should ideally work rapidly, and the activity and duration of the effect should be both predictable and reproducible
 - They should have no pharmacological activity within the body, i.e. should not bind to receptor sites
 - The penetration enhancers should work unidirectionally, i.e. should allow therapeutic agents into the body while preventing the loss of endogenous material from the body
 - When removed from the skin, barrier properties should return both rapidly and fully
 - The penetration enhancers should be appropriate for formulation into diverse topical preparations and, thus, should be compatible with both excipients and drugs
 - They should be cosmetically acceptable with an appropriate skin "feel" Some of the most widely studied permeation enhancers are sulphoxide (DMSO), fatty acids (oleic acid), alcohol (methanol), glycol (propylene glycol) and surfactant (anionic surfactant), azone (lauracapan), etc.

Physical enhancers:-

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

PSAs:-

PSAs are the material that adhere to a substrate, in this case skin, by application of light force and leave no residue when removed. They form interatomic and intermolecular attractive forces at the interface, provided that the intimate contact is formed.

To obtain this degree of contact, the material must be able to deform under slight pressure, giving rise to the term "pressure sensitive." Adhesion involves a liquid-like flow,

resulting in wetting of the skin surface upon the application of pressure, and, when the pressure is removed, the adhesive sets in that state. A PSA wets and spreads onto the skin when its surface energy is less than that of the skin.

After the initial adhesion, the PSA/skin bond can be built by stronger interactions (e.g., hydrogen bonding), which will depend on skin characteristics and other parameters.

Widely used PSA polymers in TDDS are polyisobutylene-based adhesives, acrylics and silicone-based PSAs, hydrocarbon resin, etc.

The PSA can be located around the edge of the TDDS or be laminated as a continuous adhesive layer on the TDDS surface.

The PSA should be compatible with the drug and excipients, as their presence can modify the mechanical characteristics of the PSA and the drug delivery rate.

Backing laminates:-

Backings are chosen for appearance, flexibility and need for occlusion; hence, while designing a backing layer, the consideration of chemical resistance of the material is most important. Excipient compatibility should also be considered because the prolonged contact between the backing layer and the excipients may cause the additives to leach out of the backing layer or may lead to diffusion of excipients, drug or penetration enhancer through the layer.

The most comfortable backing will be the one that exhibits lowest modulus or high flexibility, good oxygen transmission and a high moisture vapor transmission rate.

Examples of backing materials are vinyl, polyethylene, polyester films, aluminum and polyolefin films.

Release liner:-

During storage, the patch is covered by a protective liner that is removed and discarded before the application of the patch to the skin. Because the liner is in intimate contact with the TDDS, the liner should be chemically inert.

Typically, a release liner is composed of a base layer that may be nonocclusive (e.g. paper fabric) or occlusive (e.g. polyethylene, polyvinyl chloride) and a release coating layer made up of silicon or Teflon. Other materials used for TDDS release liner are polyester foil and metalized laminates.

Other excipients like plasticizers and solvents:-

Various solvents such as chloroform,

methanol, acetone, isopropanol and dichloromethane are used to prepare drug reservoir. In addition, plasticizers such as dibutylphthalate, triethyl citrate, polyethylene glycol and propylene glycol are added to provide plasticity to the transdermal patch.

TYPES OF TRANSDERMAL PATCHES:-

Most commercially available transdermal patches are categorized into the following three types:-

Reservoir system:

In this transdermal system, the drug reservoir is embedded between an impervious backing layer and a rate-controlling microporous or non-porous membrane. The drug releases only through the rate-controlling membrane. In the drug reservoir compartment, the drug can be in the form of a solution, suspension or gel, or may be dispersed in a solid polymer matrix.

Hypoallergenic adhesive polymer can be applied as a continuous layer between the membrane and the release liner or in a concentric configuration around the membrane.

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 adhesives) on an impervious backing layer. On the top face of the reservoir, unmedicated adhesive polymer layers are applied for protection purpose.

Matrix-dispersion system:

The drug is dispersed homogeneously in a hydrophilic or lipophilic polymer matrix. This drug-containing polymer disk is then fixed onto 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 the circumference to form a strip of adhesive rim.

Microreservoir systems:

This TDDS is a combination of a reservoir and a matrix-dispersion system. The drug reservoir is formed by first suspending the drug in an aqueous solution of water-soluble polymer and then dispersing the solution homogeneously in a lipophilic polymer to form thousands of unleachable, microscopic spheres of drug

reservoirs.

The thermodynamically unstable dispersion is stabilized quickly by immediately cross-linking the polymer in situ.

EVALUATION OF TRANSDERMAL FILMS:-

Interaction studies:

Excipients are integral components of almost all pharmaceutical dosage forms. The stability of a formulation among other factors depends on the compatibility of the drug with the excipients. The drug and the excipients must be compatible with one another to produce a product that is stable; thus, it is mandatory to detect any possible physical or chemical interaction as it can affect the bioavailability and stability of the drug.

If the excipients are new and have not been used in formulations containing the active substance, the compatibility studies play an important role in formulation development. Interaction studies are commonly carried out in thermal analysis, Fourier Transform Infrared spectroscopy, UV and chromatographic techniques by comparing their physicochemical characters, such as assay, melting endotherms, characteristic wave numbers, absorption maxima, etc.

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.

Weight uniformity:

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

Folding endurance:

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

Percentage moisture content:

The prepared films are to be weighed individually and are to be kept in a desiccator containing fused calcium chloride at room temperature for 24 h. After 24 h, the films are to be reweighed to determine the percentage moisture content from the

below-mentioned formula:

Percentage moisture content = [Initial weight - Final weight / Final weight] × 100

Percentage moisture uptake:

The weighed films are to be kept in a desiccator at room temperature for 24 h, which contains a saturated solution of potassium chloride in order to maintain 84% RH. After 24 h, the films are to be reweighed to determine the percentage moisture uptake from the below-mentioned formula:

Percentage moisture uptake = [Final weight - Initial weight / initial weight] × 100

Water vapor permeability evaluation:

WVP can be determined with the foam dressing method, wherein the air-forced oven is replaced by a natural air circulation oven. The WVP can be determined by the following formula:

WVP = W / A

Where, WVP = is expressed in gm/m²per 24 h,

W= is the amount of vapor permeated through the patch, expressed in gm/24 h,

A= is the surface area of the exposure samples, expressed in m.

Drug content:

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

Uniformity of the dosage unit test:

An accurately weighed portion of the patch is to be cut into small pieces and transferred to a specific volume using a volumetric flask, dissolved in a suitable solvent and sonicate for complete extraction of the drug from the patch and made up to the mark with the same. The resulting solution was allowed to settle for about 1 h and the supernatant was suitably diluted to give the desired concentration with the suitable solvent.

The solution was filtered using a 0.2-μm membrane, filtered and analyzed by a suitable analytical technique (UV or HPLC), and the drug content per piece was to be calculated.

Polariscope examination:

This test is to be performed to examine the

drug crystals from the patch by a polariscope. A specific surface area of the piece is to be kept on the object slide and observed for the drug crystals to distinguish whether the drug is present as a crystalline form or an amorphous form in the patch.

Shear adhesion test:

This test is to be performed for measurement of the cohesive strength of an adhesive polymer. It can be influenced by the molecular weight, the degree of cross-linking and the composition of the polymer and the type and amount of tackifier added. An adhesive-coated tape is applied onto a stainless steel plate; a specified weight is hung from the tape to affect it, pulling in a direction parallel to the plate. Shear adhesion strength is determined by measuring the time it takes to pull the tape off the plate. The longer the time taken for removal, greater is the shear strength.

Thumb tack test:

It is a qualitative test applied for tack property determination of the adhesive. The thumb is simply pressed on the adhesive and the relative tack property is detected.[6]

Flatness test:

Three longitudinal strips are to be cut from each film at different portions, like one from the center, one from the left side and another from the right side. The length of each strip was measured and the variation in length because of nonuniformity in flatness was measured by determining the percent constriction, with 0% constriction equivalent to 100% flatness.

Percentage elongation break test:

The percentage elongation break is to be determined by noting the length just before the break point. The percentage elongation can be determined from the below-mentioned formula:

Elongation percentage = (L1 - L2) / L2 × 100

Where, L1 = is the final length of each strip

L2 = 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, a stainless steel ball of 7/16 inches in diameter is released on an inclined track so that it rolls down and comes in contact with the horizontal, upward facing

adhesive. The distance the ball travels along the adhesive provides the measurement of tack, which is expressed in Inches.

Quick stick (peel-tack) test:

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

Probe tack test:

In this test, the tip of a clean probe with a defined surface roughness is brought into contact with the adhesive. And, when a bond is formed between the probe and the adhesive, the subsequent removal of the probe mechanically breaks it.

The force required to pull the probe away from the adhesive at a fixed rate is recorded as tack, and it is expressed in grams.

II. CONCLUSION:-

TDDS is a newer approach in the area of dosage forms for many injected and orally delivered drugs having appropriate physicochemical and pharmacological properties. The TDD ensures that a pharmacologically active substance arrives at a relevant in vivo location with minimal side-effects. Because of the several advantages of the TDDS, many new researches are going on to incorporate newer drugs in the system. Various devices that help in increasing the rate of absorption and penetration of the drug are also being studied. TDDSs are heavily based on polymers, penetration enhancers, backing laminates, plasticizers, liners to ensure good adhesion and controlled release of drug to systemic circulation via skin over a period of several hours or days. Transdermal patches can be divided into various systems, like reservoir system, matrix system and microreservoir system. After preparation of transdermal patches, consistent methodologies are adopted to test the various parameters. Because of the recent advances in technology and the incorporation of the drug to the site of action without rupturing the skin membrane, the transdermal route is becoming the most widely accepted route of drug administration. This drug delivery overcomes the challenges associated with current popular drug delivery; thus, it shows a promising future. According to the duration of therapy, various drugs are commercially available in the form of transdermal patches.

REFERENCES:

- [1]. Tiwary AK, Sapra B, Jain S. Innovation in transdermal drug delivery: Formulation and techniques. *Recent Pat Drug Deliv Formul* 2007;1:23-36.
- [2]. Chong S, Fung HL, In: Hadgraft J, Guy RH, editors. *Transdermal drug delivery. development issues and research initiatives*. New York: Marcel Dekker; 1989. p. 135-54.
- [3]. Singh A, Singh MP, Alam G, Patel R, Vishvakarma D, Datt N. Expanding opportunities for transdermal delivery systems: An overview. *J Pharm Res* 2011;4:1417-20.
- [4]. Ansel HC, Allen LV and Popovich NG. *Pharmaceutical dosage forms and drug delivery system*. 7th ed. New York: Lipponcott Williams and Wilkins; 2002.
- [5]. Patel RP, Baria AH. Formulation and evaluation consideration of transdermal drug delivery system. *Int J Pharm Res* 2011;3:1-9.
- [6]. Kumar JA, Pullakandam N, Prabu SL, Gopal V. Transdermal drug delivery system: An overview. *Int J Pharm Sci Rev Res* 2010;3:49-54.
- [7]. Jain NK. *Advances in controlled and novel drug delivery*. 1st ed. New Delhi: CBS Publishers and Distributors; 2001. p. 108-10.
- [8]. Soni M, Kumar S, Gupta GD. Transdermal drug delivery: A novel approach to skin permeation. *J Pharm Res* 2009;2:1184-90.
- [9]. Naik A, Kalia YN, Guy RH. Transdermal drug delivery: Overcoming the skin's barrier function. *Pharm Sci Technol Today* 2009;3:318-26.
- [10]. Chandrashekhar NS, Shobha R. Physicochemical and pharmacokinetic parameters in drug selection and loading for transdermal drug delivery. *Indian J Pharm Sci* 2008;70:94-5.
- [11]. Merkle HP. Transdermal delivery systems. *Methods Find Exp Clin Pharmacol* 1989;11:135-53.
- [12]. Brown L and Langer R. Transdermal delivery of drugs. *Annu Rev Med* 1988;39:221-9.
- [13]. Arunachalam A, Karthikeyan M, Kumar DV, Prathap M, Sethuram S, Kumar AS. Transdermal drug delivery system: A review. *Curr Pharma Res* 2010;1:70-81.
- [14]. Flynn GL. *Percutaneous Absorption*. 3rd ed. New York: Marcel Dekker; 1985.



- [15]. Hadgraft J. Skin Deep. Eur J Pharm Biopharm 2004;58:291-9.
- [16]. Singh MC, Naik AS, Sawant SD. Transdermal drug delivery systems with major emphasis on Transdermal Patches: A review. J Pharm Res 2010;3:2537-43.
- [17]. Aulton ME. Aulton's Pharmaceutics The design and manufacture of medicine. 3rd ed. Churchill Livingstone: Elsevier; 2007. p. 567-8.
- [18]. Jain NK. Controlled and Novel Drug Delivery. New Delhi: CBS Publishers and Distributors; 2002. p. 107.
- [19]. Kumar TS, Selvam RP, Singh AK. Transdermal drug delivery systems for antihypertensive drugs. Int J Pharm Biomed Res 2010;1:1-8.
- [20]. Chien YW. Novel drug delivery systems, Drugs and the Pharmaceutical Sciences, Vol. 50. New York: Marcel Dekker; 1992. p. 797.
- [21]. Sugibayashi K, Morimoto Y. Polymers for transdermal drug delivery systems. J Control Release 1994;29:177-85.
- [22]. Hadgraft J, Guy RH. Transdermal Drug Delivery. 2nd ed. New York: Marcel Dekker; 1989.
- [23]. Keleb E, Sharma RK, Mosa EB, Aljahwi A. Transdermal drug delivery system and evaluation. Int J Adv Pharm Sci 2010;1:201-11.
- [24]. Spencer TS, Smith SE, Conjeevaram S. Adhesive interactions between polymers and skin in transdermal delivery systems. Polym Mater: Sci Eng 1990;63:337-9.
- [25]. Minghetti P, Cilurzo F, Tosi L, Casiraghi A, Montanari L. Design of a new water-soluble pressure-sensitive adhesive for patch preparation. AAPS Pharm Sci Tech 2003;4:9.