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TRANSCENDING BARRIERS: INNOVATIONS IN TRANSDERMAL DRUG DELIVERY SYSTEM DESIGN AND THEIR EVALUATION

Rounak Bhattacharya*, Sudip Mukherjee, Rudrajit Saha, Somenath Mondal
Seacom Skills University, Bolpur, West Bengal-731236.

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ABSTRACT

Traditional needle injections have been replaced by a variety of non-intrusive administrations in recent times. Among these, a transdermal delivery system for drugs (TDDS) offers the most pleasant procedure due to its low rate of refusal, remarkable ease of administration, and exceptional patient amenities and attentiveness. The main benefits of TDDS are reduced side effects, enhanced bioavailability with regulated drug release, and bypass first-pass metabolism. The transdermal system for drug delivery, skin anatomy and physiology, formulation development, and a critical analysis of the particular benefits and drawbacks, preparation, assessment, and application methods, as well as future innovations and limitations for transdermal patch selection, are all succinctly summarised in this review article.

Corresponding author
Mr. Rounak Bhattacharya
Assistant Professor, Department: Pharmaceutics,
Institute: School of Pharmacy,
Seacom Skills University, Village- Kendradangal,
P.O- Sattore, P.S- Panrui, Dist- Birbhum,
State-West Bengal, Country- India, Pin- 731236.
rounak.sopssu@gmail.com

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INTRODUCTION

A collection of physical-chemical technologies collectively referred to as "drug delivery systems" (DDS) can maximize the effects of pharmacologically active chemicals by delivering and releasing them into cells, tissues, and organs. Concerning the delivery route, there are several alternative administration methods, such as oral, transdermal, mucosal, lung inhalation, and intravenous injection. One of the more promising ones is the transdermal drug delivery system (TDDS). One of the most popular methods for noninvasively drug delivery through the skin is TDDS. The delivery of various therapeutic medications has been greatly impacted by TDDS, especially when it comes to hormone therapy, pain management, and illnesses of the cardiovascular and central nervous systems. As TDDS does not submerge movement through the gastrointestinal tract, it does not cause loss during first-pass metabolism and does not interfere with the intestinal flora, pH, or enzymes when administering medications. Moreover, the strong persistence of the method is demonstrated by the ability to use TDDS to control medication release based on consumption limitations. Most importantly, TDDS is a silent administration technique that puts little strain or discomfort on the patient and makes it possible to give medications to kids and adults conveniently and safely.[1]

The transdermal patch, also known as a skin patch, regulates the speed at which the liquid medication that has been modified in the reservoir inside the patch can permeate the skin and enter the bloodstream using a unique membrane. For effective use in a skin patch, some medications need to be mixed with substances like alcohol that make them more soluble in the skin. Scopolamine (for motion discomfort), nicotine (for sporadic smoking), estrogens (for menopause and osteoporosis prevention postmenopausal), Nitro-glycerine (for angina), and lidocaine (for shingles pain, herpes zoster) are among the medications applied via skin patches. But a lot of other things, like insulin compounds, are too large to pass through the skin.

Using patches on the skin removes the need for syringe access to the blood vessels or pumps. After being developed in the 1970s, the very first transdermal patch was approved by the FDA in 1979 to treat motion sickness. Scopolamine was applied as a patch for three days. In 1981, the first nitro-glycerine patch was authorized. These days, patches for nitro-glycerine, oestradiol, oxybutynin, scopolamine, nicotine, clonidine, fentanyl, lidocaine, and testosterone are available. Hormone replacement and combination patches are also available for contraception. Depending on the medication, the patches last anywhere from one to seven days. Several significant advantages come with transdermal drug delivery, including better therapy as plasma levels are sustained till the end of the dosing period, a reduction in plasma levels with traditional oral dosage forms, increased bioavailability greater consistency in plasma levels, and an extended period of action that minimizes the requirement for frequently issued dosage, fewer adverse reactions.

Transdermal patches have shown promise in both alleviating the side effects associated with first-pass drug degradation and in generating new applications for existing treatments. Furthermore, patches can have unfavorable adverse reactions (oestradiol patches, for example, are utilized by more than a million patients annually and do not damage the liver like oral medications for the two primary subdivisions, therapeutic and cosmetic), weight loss patches, aroma patches, and non-medicated patch markets include those for dietary patches, warmth, and cold patches, alongside dermatological patches (which are in the sun exposure patch category).[2]

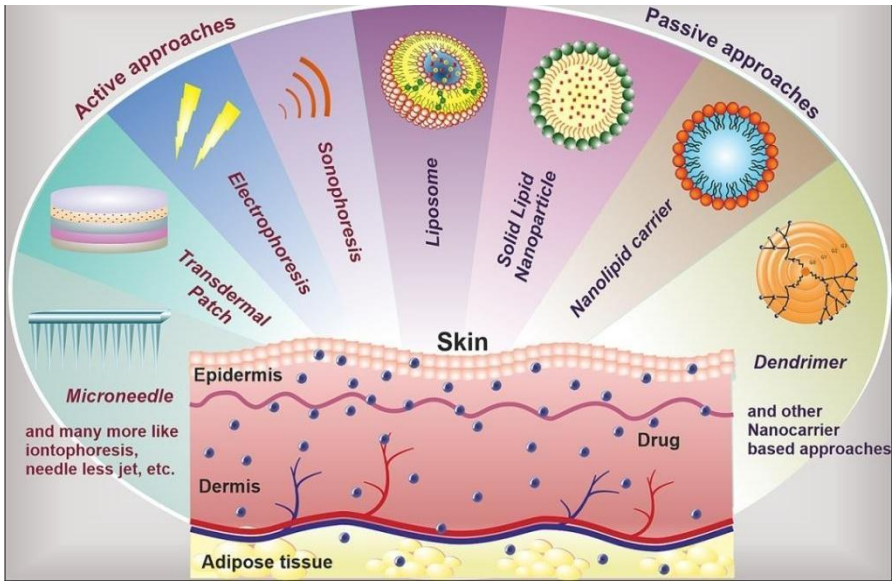


Fig 1: Different types of enhancers for recovering skin.

ANATOMY AND PHYSIOLOGY OF THE SKIN: -

The human skin is a complex organ with numerous histological layers. The body's most accessible organ is the skin. Its main duties include controlling body temperature, controlling the flow of water, and protecting essential internal organs from external influences. A typical adult's skin covers two square meters of surface area and takes in 1/3 of the blood that circulates throughout the body.

The following is a list of the three distinct yet connected tissues that comprise human skin:

- The laminated, vascular, cellular epidermis,
- Underlying dermis of connective tissues
- Hypodermis

A) Epidermis-

The keratinizing, scaly, stratified epidermis epithelium. The thickness of the multifaceted epidermis varies from 0.8 mm on the palms and soles to 0.06 millimeters on the eyelids, depending on the quantity and amount of cell layers in the epidermis. Ninety percent of epidermal cells are five-layered-grooming keratinocytes, which generate keratin protein. There are 8% melanocytes present. They create the brown, black, or yellow pigment known as melanin, which gives skin its color and blocks harmful UV rays. A Langerhans cell originates in the red bone marrow and travels to the epidermis, where it makes up a tiny portion of the cell layer. The smallest number of epidermal cells are Markel cells.

Five layers of epidermis-

- Stratum basales
- Spinosum
- Granulosum
- Lucidum
- Corneum

B) Dermis-

It is a 3 to 5 mm thick layer with a connective tissue matrix that includes nerves, lymph vessels, and blood vessels. The dermis, which makes up 90% of the inside and larger skin layer, is mainly composed of connective tissues and provides support for the skin's epidermis layer. The dermal-epidermal junction, which separates the dermis from the epidermis layer, acts as a physical barrier to keep large drug molecules and cells out. Nerve endings, blood vessels, and lymphatic vesicles are all integrated into the dermis. The reticular and papillary regions make up the dermis.

1. **Papillary region:-**

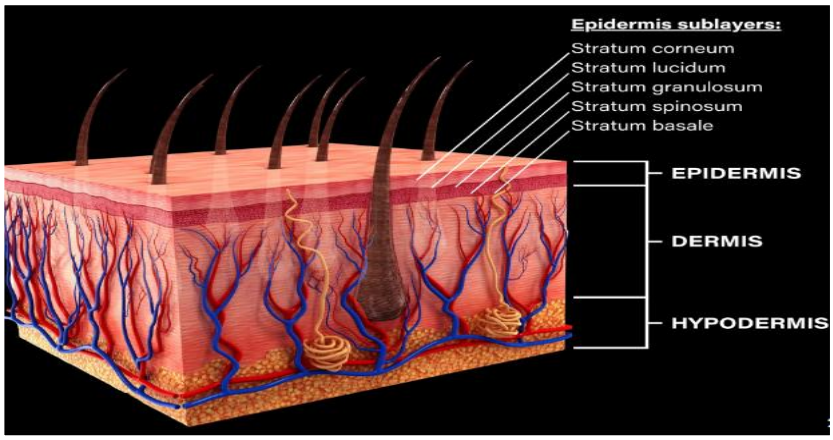
Constituting one-fifth of the overall layer thickness, it is comprised of areolar connective tissue, a network of fine elastic fibers.

2. **Reticular region:-**

It is composed of dense, asymmetric, and reactive tissue attached to the layer beneath the skin. Collagen, which is fibroblast and a few coerce elastic fibers are bundled together in this tissue.

C) Hypodermis-

The dermis and epidermis are supported by the hypodermis or subcutaneous fat tissue. It acts as a place to store fat. This layer offers mechanical protection, nutritional support, and easier temperature control. Principal blood vessels, nerves, and possibly sensory pressure organs are imported into the skin. The loose connective tissues that make up the hypodermis layer vary in thickness depending on the body's surface. [3]



FORMULATION DEVELOPMENT OF TDDS: -

1. Polymer matrix / Drug reservoir
2. Drug
3. Permeation enhancers
4. Pressure-sensitive adhesive (PSA)
5. Backing laminates
6. Release liner
7. Other excipients like plasticizers and solvents

1. Polymer matrix/Drug reservoir:-

The main component of TDDS is polymers, which control how the medication is released from the apparatus. Drug dispersion in a solid or liquid state artificial polymer base can be used to equip a polymer matrix. The polymers utilized in TDDS should be stable, compatible with the drug and other system components, and capable of releasing the drug effectively and safely throughout the device.

Different polymers are used for the preparation of TDDS. Some examples are the following: -

Table 1: (Several polymers which are used for TDDS): -

Natural Polymers	Synthetic Elastomers	Synthetic Polymers
Cellulose derivatives, Zein, Gelatine, Waxes, Proteins, Gums, Natural rubber, Starch.	Polybutadiene, Hydrin rubber, polysiloxane, silicone rubber, Nitrile, Acrylonitrile, Butyl rubber, Styrene butadiene, Neoprene, etc.	Polyethylene, Polypropylene, Polyacrylate, Polyamide, Polyvinylpyrrolidone, Polymethyl methacrylate, Epoxy, Polyurea, etc.

2. Selection of drugs:-

The physicochemical properties of the drug are what determine which drug is best for TDDS. Transdermal drug delivery is a highly suitable method for drugs with a broad first-pass metabolism.

- Narrow therapeutic window.
- Short half-life which causes non-compliance due to prevalent dosing.
- The dose should be lower (mg/day).
- Low molecular weight (less than 500 Daltons).
- Adequate solubility in oil and water (log P in the range of 1-3).
- Low melting point (less than 200°C).

3. Permeation enhancers:-

By interacting with the stratum corneum's structural elements, such as proteins or lipids, these compounds can increase the stratum corneum's permeability and achieve higher therapeutic drug levels. Through chemical qualification of the barrier functions, they increase permeability by changing the stratum corneum's protein and lipid packaging.

A few examples include sodium lauryl sulfate, sorbitol, cardamom, caraway, lemon, menthol, linoleic acid, and propylene glycol. Other examples include 2-pyrrolidone, isopropyl myristate, and laurocapram.

4. Pressure-sensitive adhesives:-

Pressure-sensitive glue helps the TDDS stick to the surface of the skin firmly (PSA). It should have a strong holding force, be techy firmly and permanently, and adhere only through finger pressure. It ought to be effortlessly extracted from its smooth outer layer without leaving any traces behind. Adhesives must conform to the skin, resulting in the lowest possible level of sensitivity or irritation, and have the ability to be detached without causing harm to the body or leaving residue behind. In addition, the drug and excipient must be dissolved in sufficient amounts to yield the desired pharmacological effect without sacrificing their adhesive and skin-acceptable properties.

5. Backing laminate:-

Good tensile strength and versatility are requirements for backing materials. Materials that are commonly used include polyolefins, polyester-based materials, and elastic materials in apparent pigmented, or metalized forms. Compared to less flexible materials like polyester, elastomeric materials—like low-density polyethylene—provide superior adhesion and correspond more easily to skin movement. Low water vapor transfer rates are also important for backing materials because they promote elevated skin hydration and, consequently, increased skin permeability.

6. Release Liner:-

Remove and release the barrier of the liner that encases the patch while it is being stored before applying it to the skin. Rather than being the dosage form, it is therefore considered to be a part of the main protective material for drug distribution. The liner is in direct contact with the route of the administration system; therefore, it has to follow stringent guidelines about water permeation, drug penetration, chemical inertness, and penetration enhancer.

7. Other excipients:-

To prepare drug reservoirs, a variety of solvents are used, including dichloromethane, acetone, methanol, and chloroform. Furthermore, plasticizers like triethyl citrate, polyethylene glycol, propylene glycol, and dibutyl phthalate are added to the transdermal patch to give it flexibility. [4]

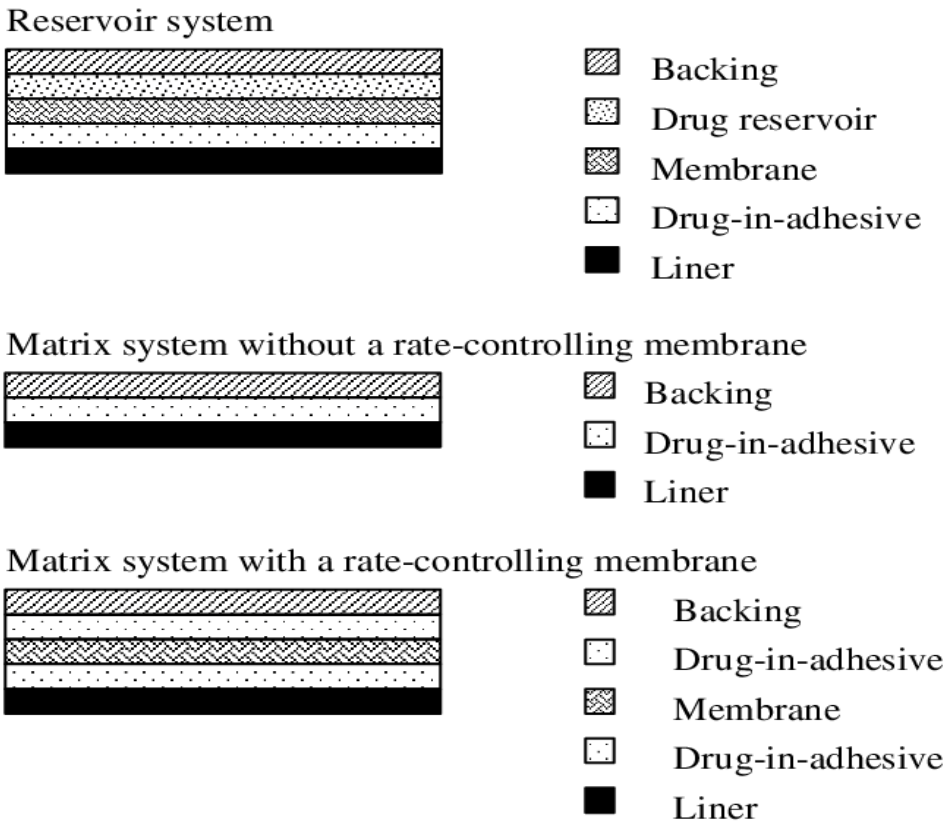


Fig 3:- Different parts of TDDS.

ADVANTAGES: -

• There is avoidance of intestinal metabolism, salivary metabolism, and hepatic first-pass metabolism.
• The ease of use allows patients to operate these devices on their own.
• In an emergency, drug input can be stopped right away during therapy by removing a patch at any time.
• There is little variation between and within patients because almost all humans have the same structural and biological makeup of their skin.
• Drugs that cause digestive problems, dissatisfaction, and absorption can be effectively administered through the skin.
• Drugs that would otherwise need frequent dosing but have a short biological half-life can be continuously infused without invasive procedures.
• Better patient compliance is a result of less frequent dosing.
• It is possible to avoid therapeutic failures associated with irregularities in dosage when using conventional therapies.
• A consistent and ideal blood level time profile leads to an increase in adverse effects.
• Parenteral therapy avoids the risks, discomfort, and inconvenience that come with it. Compared to oral sustained administration methods, the release is longer lasting.
• Transdermal applications are wonderful in this instance because it is not always desirable to maintain the amount of medication within the BioPhase.
• The amount of medication needed each day is less than with traditional therapies.
• The drug is released in a way that results in an extended period of activity.[5]

DISADVANTAGES: -

• There is a probability of skin irritation due to one or many of the formulation components.
• Binding of the drug to the skin may result in dose dumping.
• It can be used only for long-term conditions where drug therapy is preferred for a long period including hypertension, angina, and diabetes.
• The latency phase is variable and can differ from several hours to days for different drug candidates.
• Cutaneous metabolism will influence the therapeutic performance of the system. Transdermal therapy is attainable for certain potent drugs only.[5]

Methods of Preparation of TDDS: -

1. Polymer membrane permeation-controlled TDDS:-

The drug reservoir in this system is embedded between a rate-controlling membrane and an impermeable backing layer. Only the rate-regulating membrane—which may or may not be microporous—allows the drug to be released. The drug may be dispersed in a solid polymer matrix or in the form of a gel, solution, or suspension in the drug's storage compartment. A thin layer of hypoallergenic, drug-compatible binding agent polymer can be used on the polymeric membrane's exterior.

By adjusting the thickness of the rate-controlling membrane, penetrability coefficient, and polymer composition, the transdermal drug delivery system's drug release rate can be customized.

TransdermNitro (nitro-glycerine) is a once-daily medication for angina pectoris, and TransdermScop (scopolamine) provides three days of motion sickness protection.

2. Adhesive diffusion-controlled TDDS:-

The medication reservoir is created by first circulating the medication through an adhesive polymer, and then applying the treated polymer adhesive inside an inaccessible backing layer by solvent-casting the adhesive or, in the case of hot-melt adhesives, melting it. A non-medicated, constant-thickness adhesive polymer is then applied to the drug reservoir layer, creating an adhesive diffusion-controlled drug delivery system.

3. Matrix diffusion-controlled TDDS:-

Both hydrophilic and lipophilic polymer matrices can dispense the medication equally well. Next, in a compartment made of a backing layer impermeable to drugs, the drug-containing polymer disc is secured onto an occlusive foundation plate. To create an adhesive rim strip, the adhesive is not applied on the drug reservoir's face but rather around its circumference.

4. Micro reservoir controlled TDDS:-

Matrix-dispersion and reservoir technologies are combined to create this drug delivery system. A lipophilic polymer is used to uniformly disperse the drug suspension in an aqueous solution, creating thousands of microscopic, unreachable drug reservoirs. This process begins with dispersing the drug in the aqueous solution. Through in situ cross-linking of the polymer, the thermodynamically unsteady dispersion is rapidly stabilized. In this way, a medicated disc with an adhesive rim around it and a central position became the transdermal system therapeutic system.

Nitro-dur® System (Nitro-glycerine) for once-a-day treatment of angina pectoris.[4]

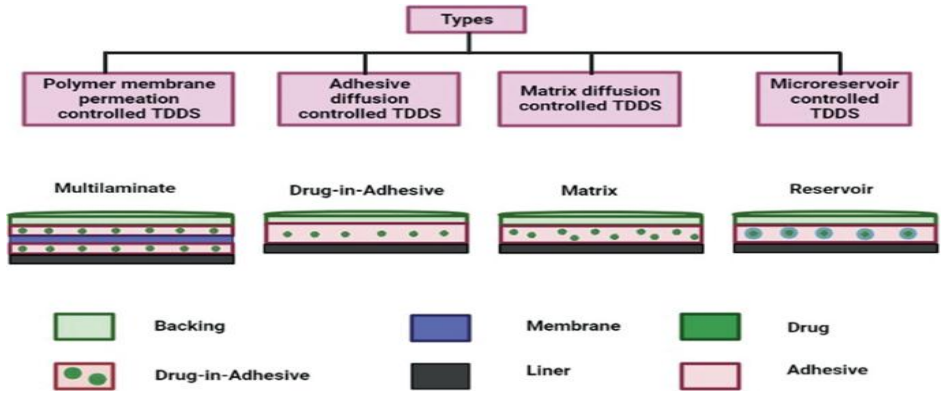


Fig 4: - Types of preparation for TDDS.

EVALUATION METHODS:-

The assessment techniques for transdermal dosage forms can be divided into three categories: in vitro, in vivo, and physicochemical evaluation. physical-chemical analysis.

1. Physiochemical evaluation:-

1.a. Interaction studies:-

Stable product production requires good compatibility between the medication and the excipients. Drug stability and bioavailability are impacted by interactions between the drug and excipients. Compatibility studies are essential in the formulation development process when the additives are novel and haven't previously been utilized in compositions with the active ingredient. The methods of thermal evaluation, infrared spectroscopy using the Fourier transform (FTIR), ultraviolet (UV), and chromatography are used to extract interaction studies by comparing their physicochemical characteristics, such as method, point of melting, waveform figures, and absorption maximum.

1. b. Thickness of the patch:-

To ensure the prepared patch's thickness, the mean, and standard deviation are determined by measuring the depth or hardness of the drug at various points along the patch using a digital micrometer.

1. c. Weight uniformity:-

Testing must wait four hours for the prepared patches to dry at 60°C. A designated patch area must be divided into several sections and weighed using a digital balance. The individual weights must be used to compute the median weight and average deflection values. [6]

1.d. Folding Endurance:-

The assessment of folding endurance entails ascertaining the folding strength of films that are frequently folded under excessively demanding circumstances. Folding endurance is measured by folding the film repeatedly at the same location until it breaks. The folding endurance value of a film is the number of times it might be folded at the same spot without breaking. [7]

1.e. Polari scope Examination:-

The purpose of this test is to use a Polari scope to look at the drug crystals in the patch. The piece's specific surface area must be maintained on the component slide to detect whether or not the drug exists in the patch's crystalline or amorphous form by looking for drug crystals.. [8]

1. f. Percentage moisture content:-

After being individually weighed, the prepared patches must be kept at room temperature in a desiccator with fused calcium chloride. The films must be reweighed after 24 hours, and the following formula should be used to control the percentage moisture content:

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

1. g. Percentage moisture uptake:-

The prepared patches are to be weighed severally and kept in a desiccator containing a saturated solution of potassium chloride to maintain 84% Rhesus factor (RH). After 24 h, the films are to be reweighed and the percentage moisture uptake is controlled by the formula.

Percentage moisture uptake (%) = (Final weight - Initial weight / initial weight) × 100

1. h. Water vapor permeability (WVP) evaluation:-

Water vapor permeability can be regulated by a natural air circulation oven. The WVP can be determined by the following formula:

WVP = W/A

Where WVP is expressed in g/m^{2}per 24 h, W is the amount of vapor permeated through the patch demonstrated in g/24 h, A is the surface area of the exposure samples expressed in m^2.[6]

1. i. Swell ability:-

The patches of 3.14 cm² were weighed and put in a Petri dish containing 10 ml of double distilled water and were assumed to assimilate. The increase in weight of the patch was destined at predefined time intervals until a constant weight was observed. The degree of swelling (S) was calculated using the formula,

S (%) = Wt – Wo /Wo × 100

Where S is percent swelling, Wt is the weight of the patch at time t and Wo is the weight of the patch at time zero.[8]

1. j. Drug content determination:-

A precisely measured portion of the film (roughly 100 mg) dissolves in 100 milliliters of suitable solvent (the drug is soluble in this solvent), and the mixture is then continuously shaken in a shaker incubator for a full day. After that, the entire mixture is sonicated. A suitable dilution is used to assess the drug in solution spectrophotometrically following sonication and filtration. [7]

1. k. Content uniformity test:-

A total of ten (10) areas were chosen, with each patch's content scrutinized. Transdermal patches are considered to pass the content uniformity test if nine out of ten contain content that is between 85 and 115% of the value given, and one contains content that is at least 75 to 125% of the value given. However, 20 more patches are screened for drug content if three of the patches have content between 75 and 125%. Transdermal patches pass the test if the range of these 20 patches is between 85 and 115%.

1. l. Flatness test:-

Three longitudinal sections were extracted from every film, one from the middle, one from the left, and one from the right. Every strip was measured for length, and the length variation resulting from variations in flatness was calculated by taking percentage constriction into account, where 0% constriction was the same as 100% flatness.

Constriction (%) = I1 - I2 × 100 I1

Where, I1 = initial length of each strip. I2 = final length of each strip.

1.m. Percentage elongation break test:-

The percentage elongation break was resolved by noting the length just before the breakpoint and adjudged from the formula:

Elongation percentages = L1 - L2 / L2 × 100

Where L1 = final length of each strip; L2 = initial length of each strip.[6]

1. n. Tensile strength:-

A controlled pulley system was utilized to ascertain the tensile strength. It had two clamps: a stationary one and a movable one. A 2-by-2-cm2 patch strip was cut and positioned in between two clams. Weight was gradually increased on the pan to strengthen the pulling force until the patch broke. Tensile strength (kg/cm2) was defined as the force necessary to break film. The following equation determined the tensile strength.

Tensile strength = F/a x b (l+L/l)

Where F= force required to break; a=width of the film; b= thickness of the film; L= length of film; L=elongation of film at the breaking point.

1. o. Peel adhesion test:-

In this test, the force required to take out an adhesive coating from a substrate is referred to as peel adhesion. A single tape is applied to a stainless-steel plate or a backing membrane of choice and then the tape is plucked from the substrate at a 180° angle, and the required to pull tape is measured.

1. p. Thumbtack test:

This test is applied for tack property determination of adhesive. The thumb is easily pressed on the adhesive and the relative tack property is detected. [5]

1. q. Probe Tack test:-

In this test, an adhesive is brought into contact with the pointed end of a clean probe with a predetermined surface roughness. The test is completed when the adhesive and probe form a bond. It is mechanically broken by the probe's subsequent withdrawal. Tack is the unit of measurement for the force required to remove the probe from the binding agent at a constant rate. It is measured in grams. [8]

1. r. Flux and Permeability coefficient:-

By using linear regression analysis to calculate the slope of the plot of the addition of meclizine HCl permeated per cm2 of skin at constant status against time, the flux (mg centimeters-2 hr-1) of meclizine in HCl was determined. The following formula was used to calculate the drug's constant-state permeability coefficient (Kp) through the rat epidermis.

Kp= J/C

Where J= flux C= concentration meclizine HCl patch. [5]

1.s. Stability studies:-

The TDDS samples were stored for six months at 40 ± 0.5°C and 75 ± 5% relative humidity by the guidelines set forth by the International Symposium on Harmonisation (ICH) for stability studies. Samples were taken out at0,30,60,90, and 180 days, and the drug material was properly analyzed. [6]

2. In vitro evaluation of TDDS:-

2. a. In vitro drug release studies:-

To evaluate the drug's release from the prepared patches, use the paddle technique over the disc technique (USP apparatus V). Dry films with a predetermined thickness were weighed, shaped, and adjusted using an adhesive over a glass plate. After that, the apparatus was stabilized at 32 ± 0.5°C and the glass plate was placed in 500 ml of the phosphate buffer with a pH of 7.4 or dissolution medium. After that, the paddle was moved at a speed of 50 revolutions per minute and positioned 2.5 centimeters away from the glass plate. Samples (5 ml portions) can be removed at the appropriate time interval for up to 24 hours to be examined using an HPLC or UV spectrophotometer. The mean value was computed after the experiment was run in triplicate.

2. b. In vitro skin permeation studies:-

Diffusion cells can be used on the thick gastrointestinal skin of Wistar rats with males weighing 200–250 g to complete an in vitro permeability study. The experiment involved carefully removing hair from the abdominal area using an electric clipper, cleaning the outermost side of the skin with distilled water to eliminate any blood vessels or attaching tissues, balancing the skin for an hour in phosphate buffer or dissolving medium (pH 7.4), and distributing the diffusant evenly on a magnetic stirrer using a small magnetic needle.

With the use of a thermostatically controlled heater, the temperature of the cell was confirmed to be 32 ± 0.5°C. Through the outermost layer dealing upwards into the donor compartment, the separated piece of rat skin was securely fastened between the diffusion cell's compartments. At regular intervals, a predetermined volume of sample was removed coming from the cell receptor compartment and replaced with an equivalent volume of fresh medium. Samples were passed through a filtering medium and either HPLC or spectrophotometry were used to interpret the results.

Flux was determined directly as the slope of the curve between the steady-state values of the amount of drug permeated (mg cm^2) versus time in hours, and permeability coefficients were deduced by dividing the flux by the initial drug load (mg cm^2).

3. In vivo evaluation:-

3.a. Skin irritation study: -

Testing for skin sensitivity and irritation can be done on healthy rabbits weighing between 1.2 and 1.5 kg on average. The rabbit's posterior exterior (50 cm2) needs to be cleaned, the hair on the clean dorsal surface needs to be removed by shaving, and neutral spirit should be used to clean the surface while the delegate formulations are applied to the skin. After 24 hours, the dressing is to be removed, the skin examined, and the degree of skin damage is to be graded into 5 categories. [6]

APPLICATION

• Medications called Duragesic (biologically fentanyl) and Bu Trans (biologically buprenorphine) are used to provide quick relief from acute pain.
• Nicotine patches, which help smokers quit by releasing the medication in steady-state dosages.
• Nitro-glycerine patches are used to treat angina in place of sublingual pills.
• Postmenopausal osteoporosis and menopausal symptoms are treated with estrogen-containing patches.
• Selegiline, an MAOI, in transdermal form, was the initial TDDS drug for an antidepressant.
• TDDS form of the antihypertensive medication clonidine is used.
• An attention deficit hyperactivity disorder, or AD transdermal delivery system. (9)

RECENT TECHNIQUES FOR ENHANCING TDDS: -

A) Structure-based enhancement techniques

1. Transdermal Patches
2. Microfabricated Microneedles
3. Macro flux
4. Metered-Dose Transdermal Spray (Mdts)

B) Electrically-Based Enhancement Techniques

1. Iontophoresis
2. Ultrasound
3. Photomechanical Waves
4. Electroporation
5. Electro-Osmosis

C) Velocity-Based Enhancement Techniques

1. Needle-Free Injections
2. Powder ject Device

D) Other Enhancement Techniques

1. Transferosomes
2. Medicated Tattoos
3. Skin Corrasion
4. Controlled Heat Aided Drug Delivery (CHADD) System
5. Laser Radiation [3]

Future Technologies and Approaches: -

1. Caloric Portion has been used to extract glucose from human subjects' intestinal fluid and administer common medications by creating sedimentary pathways across the stratum corneum through pulsed heat.
2. These days, there is more focus on pneumatic injectors, which is making it possible to design more advanced devices for the regulated, needleless administration of drug solutions into inner tissue and over the skin.
3. A micro-infusion pump housed in a large skin-attached patch is used to deliver drug solution at controlled rates through a small needle that is inserted a few millimeters into the skin. This method has been used to deliver morphine to humans.
4. Theories concerning the mixtures of chemicals and iontophoresis, chemicals and electroporation, chemicals and ultrasound, iontophoresis and ultrasound, electroporation and iontophoresis, and electroporation and ultrasound have been proposed during the last ten years.
5. Trans Pharma focuses on developing products that, thanks to our technology, will outperform currently available treatments. These advantages might include, among other things, improving efficacy with prolonged-release patch formulations or addressing safety and compliance issues with medication patches.
6. Dermatology and cosmetics are two areas where local drug delivery via topical application may find use for the Via Derm system. In addition to facilitating boosted immunizations, the Via Derm system offers a painless, secure, and efficient replacement for the current through muscle or subcutaneous vaccination techniques.
7. Currently, Altea Therapeutics is developing a transdermal patch for clinical use that will fill a significant gap in the market.
8. Voiding "off" times and offering a superior therapeutic choice for Parkinson's disease management. [7]

LIMITATIONS FOR SELECTION OF TDDS: -

- This method cannot be used to regulate all drug types; the drug needs to have some desirable physicochemical qualities.
- Inaccessible for medications requiring elevated plasma concentrations.
- Unfavorable for medications that cause contact dermatitis and skin irritation.
- Incompatible with medications having a large molecular weight.
- Ineffective for medications that are metabolized while passing through the skin.
- Since the skin acts as a highly effective barrier against drug penetration, many medications cannot be administered via the transdermal route. The only way to cure it is by using a minimal dose..[8]

CONCLUSION

As a contemporary solution for dosage forms, TDDS offers a wide range of injectable and oral drugs with suitable physicochemical and pharmacological characteristics. A clinically effective drug is delivered to a pertinent in vivo site with the least amount of side effects possible thanks to the TDDS. A lot of new research is being done to incorporate the newest medications into the system because of the TDDS's many benefits. Additionally, under investigation are several devices that facilitate faster drug penetration and absorption rates. TDDSs are made up primarily of polymer compounds, penetration enhancements, backing laminates, plasticizers, and liners. They ensure that the drug adheres well to the skin and releases gradually over several hours or days into the systemic circulation. Several systems can be used with transdermal patches, including matrix, reservoir, and micro reservoir systems. Consistent approaches are acknowledged for testing the different parameters following transdermal patch preparation. The transdermal form of drug administration is becoming the most commonly assumed method due to the advancements in technology that allow drugs to be incorporated into the location where they work without breaking the skin membrane. This medication delivery indicates a bright future since it solves the problems with today's prevalent drug delivery system. Several medications are commercially available as transdermal patches, depending on the length of the treatment plan.

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