INDO AMERICAN JOURNAL OF PHARMACEUTICAL RESEARCH

A REVIEW: RECENT AND NOVEL APPROACHES IN TRANSDERMAL DRUG DELIVERY SYSTEM

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ARTICLE INFO

Article history
Received 08/02/2023
Available online
28/02/2023

Keywords
Transdermal Patches,
Permeation Enhancers,
Reservoir,
Techniques,
Factors,
Marketed Products.

ABSTRACT

Today, about 74% of medications are taken orally, and many people do not find them as effective as they would like. To improve these properties, transdermal drug delivery systems have been developed. The deck system of the transition drug includes the production of pharmaceuticals on the skin to have a topical therapy effect, and the largest of the drug is transported by systematic circulation and quality. The modern administration of therapies offers a lot of advantages compared to the traditional methods of recovering oral and invasive drugs. In addition to transitional medicines, other than the drug, the first metabolism and therapeutic efficiency increases and maintains its normal condition.

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*Please cite this article in press as **Arati G. Lohar** et al. A Review: Recent and Novel Approaches in Transdermal Drug Delivery System. Indo American Journal of Pharmaceutical Research.2023:13(02).*

INTRODUCTION

Transdermal patches, often known as skin patches, use an unique membrane to regulate how quickly the pharmaceutical solution in the patch reservoir enters the bloodstream through the skin. Some drugs must be coupled with chemicals like alcohol to boost their capacity to enter the skin when applied to a skin patch. Scopolamine (for motion sickness), nicotine (to help you stop smoking), oestrogen (to prevent menopause and postmenopausal osteoporosis), nitroglycerin (for angina), and lidocaine (to treat shingles pain) are some of the drugs that can be applied as skin patches. However, many chemicals, including insulin molecules, are too big to penetrate through the epidermis. Using needles and pumps to access blood arteries is no longer necessary thanks to skin grafts. After being developed in the 1970s, In order to relieve motion sickness, the Food and Drug Administration approved the first transdermal patch in 1979. His 3-day patch was responsible for the scopolamine discharge. Since the 1981 approval of the nitroglycerin patch, numerous other medications have been licensed for patches, including nicotine, clonidine, fentanyl, lidocaine, scopolamine, and testosterone. Additionally, there are patches that act as both birth control and hormone replacement. Some of the main advantages of transdermal administration are improved absorption, more stable plasma levels, duration of action longer resulting in some doses, side effects decrease, and stability of plasma levels during treatment. Enhanced processing is one among them. Interval dosing in comparison to standard oral dose forms' lower plasma levels. By reducing the effects of the initial drug's deterioration, transdermal patches allow for the creation of new drug applications. Additionally, patches can lessen side effects. For instance, more than 1 million patients use the estradiol patch every year, and unlike the oral formulation, it does not harm the liver. [1,2,3,]

ADVANTAGES:

Transdermal delivery has the following benefits over other delivery methods:

1. Avoid first-time drug metabolism.
2. Reduce medication plasma concentration and negative effects.
3. Use medications with short half-lives and low therapeutic indices to lessen changes in plasma drug concentrations.
4. Drugs can be easily eliminated in the event of poisoning.
5. Lower drug dosages and boost patient compliance. [4]
6. The medicine is delivered steadily and long-term through the skin. Negative effects

DISADVANTAGES:

i) A few patients had contact dermatitis when one or more system components were applied, which made it necessary to stop using the product.
ii) Few drugs, like the transdermal patch of scopolamine applied backside the ear, slight irritate the skin.
iii) Prolonged sticking is difficult.[5,6,7]

LIMITATION:

a) Ionic medicines can't be delivered using TDDS.
b) High blood/plasma drug concentrations cannot be reached with TDDS.
c) Drugs with big molecules cannot be made with it.
d) Drugs cannot be administered impulsively with TDDS.
e) If the medication or formulation irritates the skin, TDDS cannot occur.[8]

TRANSDERMAL DRUG DELIVERY SYSTEMS GENERATION:

I st Generation of TDDS:

The initial iteration of the transdermal drug delivery method, which has produced the majority of transdermal patches used in clinical settings to date. First-generation transdermal patches have recently become increasingly common on the market because to significant improvements in patching technology and general acceptability. The depletion of medications with qualities appropriate for such systems will cause this growth to decline. Low-molecular-weight, lipophilic, and potent at low dosages are requirements for candidates for first-generation use. Their method of transdermal dispersion is frequently considered more appealing than oral because to poor oral bioavailability, a requirement or demand for much less frequent use or rapid delivery patterns, or for another reason.

I st generation approaches of TDDS:

The majority of transdermal patches available on the market for clinical usage belong to the first generation of techniques. The viable epidermis, which is 50 to 100 m in thickness and is vascular, is beneath this layer. A capillary bed for systemic drug absorption is present in the 1 to 2 nm thick dermis under the epidermis. Diffusion across the intercellular lipids is normally how drugs are transported across the stratum corneum. The improvement over the first generation method uses a liquid spray or gel applied topically to the skin. This formulation's lipophilic medication was absorbed into the stratum corneum and delivered gradually over a period of several hours to the living epidermis. E.g. testosterone gel.

II nd Generation of TDDS:

Improved transdermal permeability is required to increase the range of transdermal medications, and this is acknowledged by this generation.

The sophisticated techniques created in 2nd generation, like electrophoresis, traditional chemical activators, and non-driver ultrasound, have had difficulty striking a compromise between improving the ability to disperse throughout the entire cornea and safeguarding deeper tissues from harm. By boosting the administration of small molecules for local, dermatological, cosmetic, and some systemic purposes, this second generation delivery method enhances therapeutic practice. However, it has minimal effect on the distribution of macromolecules.

II nd generation approaches of TDDS:

Although the 2nd generation TDDS delivery system techniques have improved the penetration of small molecules for localized, cosmetic, dermatological, and certain systemic applications, they have had little effect on the delivery of macromolecules as well. In TDDS, this method makes considerable use of chemical enhancers. The perfect booster should be able to increase skin permeability by temporarily altering the stratum corneum's structure, provide an additional push for delivery into the skin, and guard against injury to deeper, vital tissues. Pharmaceutical boosters, iontophoresis, and non-cavitational ultrasonic techniques are frequently used in this therapy.[9,10,11,12,13,14,30]

A TECHNICAL SOPHISTICATION-BASED CLASSIFICATION OF TDDS:

A) A rate-based medication delivery system
B) Drug delivery system with activation modulation
C) Feedback-controlled medication delivery system
D) A medication delivery system based on carriers

A) A rate-based medication delivery system.

By regulating the molecular diffusion of drug molecules over the epidermal within barrier or near the delivery system, it entails designing drug delivery systems.

1. System for Controlled Drug Delivery through Polymer Membrane:-

In this approach, the medication is contained in a medicine tank. A semi-permeable polymeric membrane that controls release and has a particular permeability covers this membrane. Membrane permeation has the potential to lead to a number of advances, including drug delivery systems, controlled-release digestive devices, and microporous membrane-permeable controlled gastrointestinal drug delivery devices gel diffusion regulates.

2. The Diffusion Drug Delivery System of Polymer Matrix:

It is developed by dispersing drug particles in a (homogeneous) carrier matrix for speed control, i.e. Nitrous. It is designed to be applied to intact skin for 24 hours, delivering a consistent amount of transdermal nitro-glycerine.

3. Drug distribution system with a micro reservoir partition:

It is the high-energy dispersion of tiny drug suspension particles in a polymer, which is essentially water. Implants that are timed. Designed to deliver norgestomet usage under the skin.

B) Mechanism for administering drugs that modulates activation

In order to implement this kind of delivery system,

1-Physical means:-

- System for osmotically activating medication delivery
- Hydrodynamic pressure is used to regulate the drug delivery mechanism.
- Vapour pressure activates the drug delivery mechanism.
- A drug delivery mechanism that is mechanically actuated.
- A medication delivery system that uses magnets.
- A drug delivery system that is electrically actuated.
- A drug delivery device activated by ultrasound.
- A drug delivery mechanism that is activated by hydration.

2-Chemical means:-

• A medicine delivery mechanism that uses ions
• A medication delivery system initiated by hydrolysis.

3-Biochemical vehicle

Drug delivery system by Enzyme-activated.

C) Feedback-controlled medication delivery system

Agents that cause drug release help the drug molecules release from transdermal systems. Regulated in the body biochemically and by its concentration through feedback mechanisms.

- Drug delivery systems regulated by bioerosion.
- Bioresponsive drug delivery systems.

D) A medication delivery system based on carriers

System for carrying colloidal particles:

These include nanoparticles, hydrogels, liposomes, niosomes, polymer complexes, microspheres, nanoerythrosomes, transphesosomes, dendrimers, and aquasomes[4]

VARIOUS TYPES OF TRANSDERMAL PATCH:

1. Single layer drug-in adhesive

The sticky layer of this system also contains a medication. The adhesive layer in this kind of patch aids in the drug's release and secures the system's numerous layers to the skin. An interim liner and backing encircle the adhesive layer.

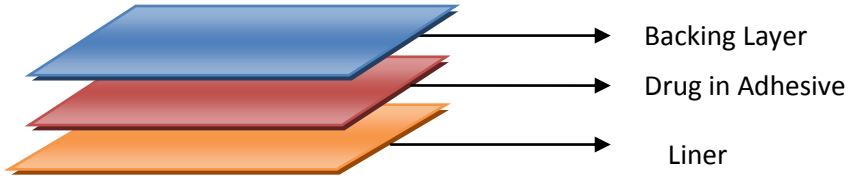


Figure 1: Single-layer Drug-in-Adhesive.

2. Multi-layer drug-in adhesive

In that both layers are involved in drug release, multi-layer drug-containing adhesive patches resemble monolayer systems. Multilayer systems, however, are distinct because they include an additional layer of drug adhesive, typically separated by a membrane (but not in all cases).

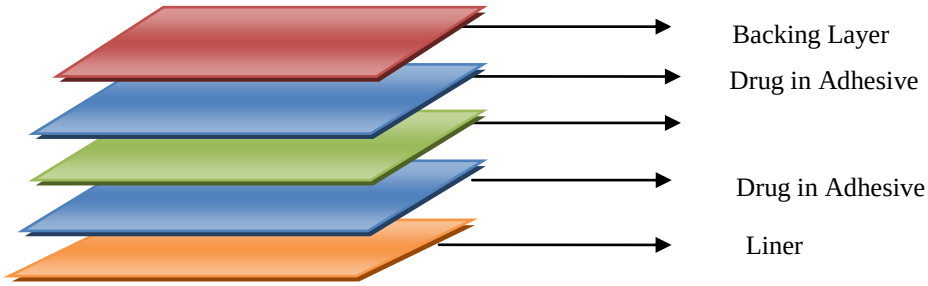


Figure 2: Multi-layer Drug-in-Adhesive.

3. Reservoir

Transdermal reservoir systems, in contrast to monolayer and multilayer drug-in-glue systems, contain distinct drug layers. A drug layer is an adhesive layer-separated liquid chamber containing a drug solution. The backing-layer also supports this patch. The emission rate in this kind of system is zero order.

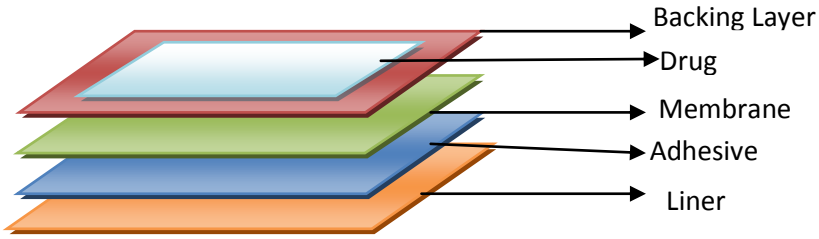


Figure 3: Reservoir Transdermal System.

4. Matrix

Drug layers in semi-solid matrixes that are part of matrix systems typically contain drug solutions or suspensions. This patch has a pharmacological layer that partially overlaps the adhesive layer.

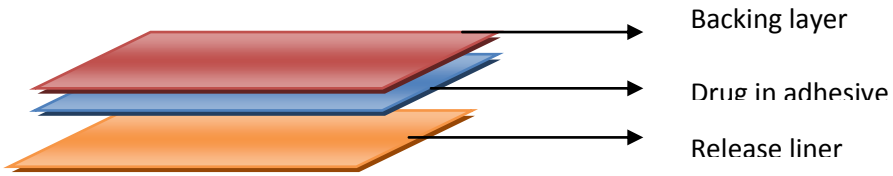


Figure 4: Matrix System.

5. Steam Plaster

In this type of patch, in addition to holding the various layers together, the adhesive layer also functions to release the vapour. Steam patches, which are new brand on the market, release essential oils for up to six hours. Common use for steam patches includes decongesting and releasing essential oils. You may also get vape patches, which will enable you to smoke fewer cigarettes each month. [8]

COMPONENTS OF TRANSDERMAL PATHCHES

1 Polymer Matrix

Drug release from the device is regulated by the polymer. Transdermal patch polymers should adhere to the following standards:

a) The polymer's molecular weight and chemical functionality must be such that the particular medicine will diffuse and be released properly.
b) Stability of the polymer;
c) The polymer must be non-toxic;
d) It must be simple to make; and
e) The polymer must be reasonably priced.
f) The polymer need not be harmful to the host or produce hostile degradation products;
g) It contains a lot of active components.

1.Polymer types include:

a) Organic polymers
Proteins, Gelatine, shellac, gum, waxes, and starches are examples of cellulose derivatives.
b) Artificial Elastomers:
Acrylonitrile, Neoprene, Nitrile, Silicone Rubber, and Hydrin Rubber.
c) Artificial polymers
Epoxy, polyethylene, polypropylene, polyamiode, polyurea, and polyvinyl alcohol are examples of polyvinyl substances.

2. Drugs:-

Chemicals that come into direct contact with the release liner.
1. Physicochemical Characteristics.
a) The drug's molecular weight should be fewer than 1000 Daltons.
b) The medication needs to be equally attracted to the lipophilic and hydrophilic phases.
c) The medication needs to have a low melting point.
2. Biological characteristics:
a) The medication must be effective at doses of only a few milligrams per day.
b) The medication should have a brief half-life (t1/2)
c) The medication must not produce an adverse reaction**.**
d) No drug resistance should develop due to the transdermal patch's nearly zero-order release profile.

3. Penetration Enhancers:-

Drug flow across the skin J. can be written in As.
J = Ddc/dx ,
Where, J = river
D = diffusion coefficient
C = concentration of scattering spectrum
X = spatial coordinate

a) Solvents: -

These substances could make the polar route more permeable, increasing penetration. Methanol, ethanol, dimethylacetamide, propylene glycol, and glycerol are all hydroalcoholic substances.

b) Surfactant:

The polar head group and the length of the hydrocarbon chain affect a surfactant's capacity to change penetration.
Sodium lauryl sulphate diacetyl sulfosuccinate is an anionic surfactant. Pluronic F127 and Pluronic F68 are non-ionic surfactants.
• Sodium taurocholate and sodium deoxycholate, which are bile salts.

c) Additional substances:

Among these are urea, a keratolytic and moisturizing agent. Anticholinergics, calcium thioglycolate, and N, N-dimethyl-m-toluamide. Recently, a number of possible permeability enhancers have been described; however there is a lack of information on their effectiveness contains casein.

d) Improved Penetration.

Urea, calcium thioglycolate.

4. Other Excipients: -

Adhesive: -

i) Must not be overly provocative;
ii) Must be simple to remove;
iii) Must not leave a residue on the skin that cannot be washed off;
iv) Must make good contact with the skin;
v) Must be physically and chemically compatible with medications;
vi) Must not interfere with drug permeability;

Linear: - Protects patches during storage. Remove linear before use.
Back: - Protect the patch from the external environment. [5]

SEVERAL TECHNIQUES FOR TDDS PREPARETION:

Method using an asymmetric TPX membrane:

The support membrane for a prototype patch can be created from a polyester material that can be heat sealed and contains depressions that are 1 cm in diameter. A TPX poly (4-methyl-1-pentene) asymmetric membrane should be placed over the concave membrane once the drug sample has been placed inside of it.

Process for Molding Teflon Rounds:

Using an organic solvent and a mix of polymers in different ratios. After being dissolved in half of the same organic solvent, the dosage of drug is present. Before being applied, different amounts of the enhancer are dissolved in the remaining organic solvent. The drug-polymer solution also contains di-N-butyl phthalate as a plasticizer. Pour the entire slurry into a circular Teflon mould after spinning it for 12 hours. Use a laminar flow hood model with an air velocity of 0.5 m/s, an inverted funnel to cover the mould, and a laminar flow hood model to manage solvent evaporation (allowed evaporating for 24 hours). To counteract the effects of ageing, dry films are kept for a further 24 hours at 25 0.5°C in a desiccators containing silica gel prior to examination.

Mercury Substrate Method:

This process involves in a polymer solution dissolving the drug together with a plasticizer. The aforementioned solution is poured over a flat surface of mercury and stirred for 10 minutes to generate a homogenous dispersion in order to prevent solvent evaporation.

The "IPM Membrane" Approach: Using a magnetic stirrer, the drug is stirred for 12 hours while being dissolved in a solution of water and propylene glycol that contains Carbomer 940 polymer. Triethanolamine is intended to make the dispersion viscous and neutralize the dispersion. If the medication has a very low solubility in aqueous solution, a dissolving gel can be made using a buffer with a pH of 7.4.

The "EVAC Membrane" Approach:

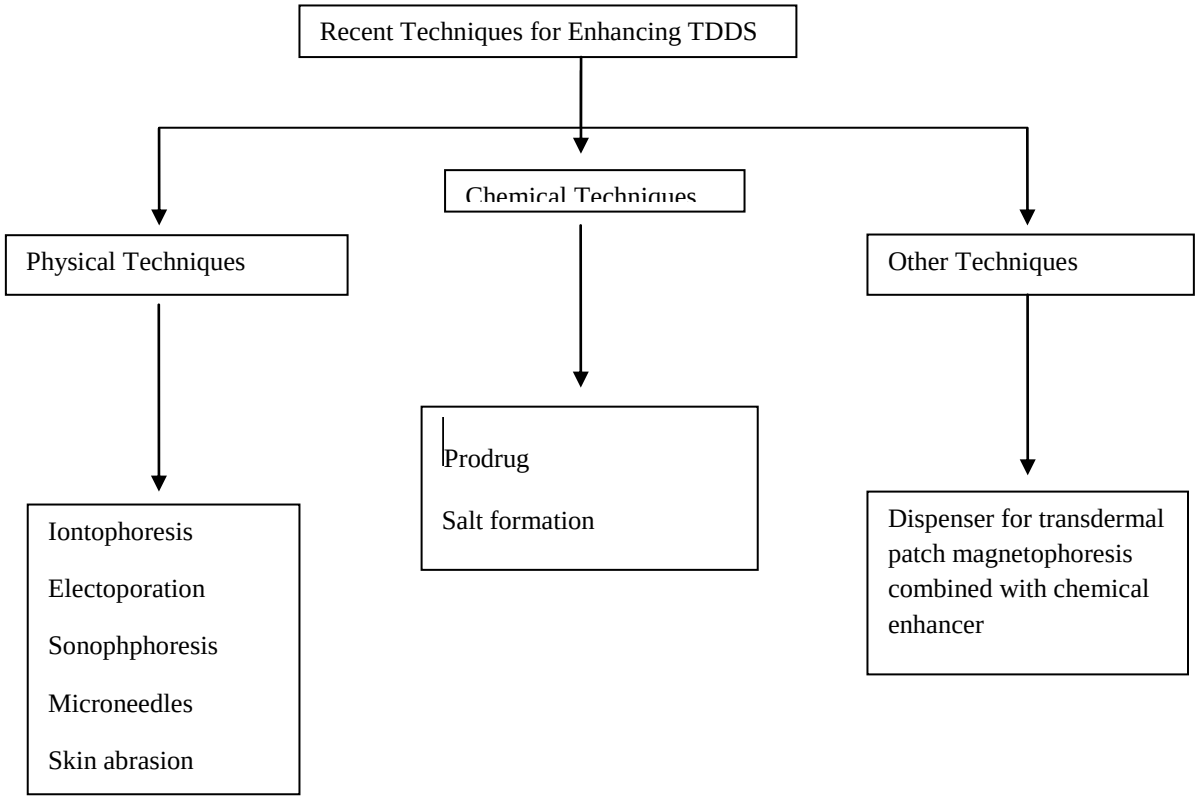
A membrane composed of Carbopol reservoir gel 1%, polyethylene (PE), and ethylene vinyl acetate copolymer (EVAC) serves as a rate-controlling membrane to construct a transdermal therapeutic targeting device. I can control it. Make a gel out of propylene glycol if the drug is not soluble in water. Propylene glycol should be used to dissolve the preparation. To the aforementioned solution, add 5% water or waste and carbopol resin. Use NaOH solution to neutralize. The drug in gel form is applied to the specified areas on a baking sheet. A rate-controlling membrane is placed over the gel, and the boundaries are heated to form a leak-proof device.

Method for Adhesive Aluminum-Coated Film:

Transdermal drug delivery devices may exhibit matrix instability at loading dosages greater than 10 mg. The use of sticky film with an aluminium layer is suitable. Chloroform is the chosen solvent for the production of medicines and adhesives because the bulk of these products are soluble in it. After the chemical has been dissolved in chloroform, add glue and then dissolve it. The interior of the specifically made aluminium former is lined with aluminium foil, and the borders are sealed with a form-fitting cork block.

Free Film Method: -

A layer of free cellulose acetate is produced while casting onto a mercury surface. Use chloroform to create a 2 weight percent polymer solution. Plasticizers must be added at a rate equal to 40% of the polymer's weight. Polymer solution 5 ml was added into a glass ring and placed on the mercury surface of a glass petri plate. The Petri dish is placed over an upside-down funnel to gauge the rate of solvent evaporation. Examining the mercury surface to see if a layer has developed after the solvent has entirely evaporated. When not in use, divide the dry film and put it between wax paper sheets in desiccators.Free films of different thicknesses can be produced by varying the polymer solution's volume wax paper.[5]



Flow chart no.1: Recent Techniques for Enhancing TDDS.

FACTORS AFFECTING TDDS:

Biological factor:

Skin diseases:

The stratum corneum's complex and dense structure is dissolved by several solvents, but many active chemicals, such as acids and alkalis, penetrate the skin by penetrating the barrier cells that operate as the skin's natural barrier. Methanol and other solvents that dissolve away the lipid portion, like chloroform, produce an artificial shunt through which drug molecules can flow with ease.

Skin age:

The difference between the skin of adults and teenagers and that of the elderly is not very noticeable. Due to their higher surface area per unit of body weight, children demonstrate hazardous consequences. Boric acid, hexachlorophene, and powerful steroids all have negative side effects.

Regional Headquarters:

The density of the appendages, stratum corneum texture, and skin thickness varies from place to place. These elements significantly impact penetration.

Skin Metabolisms:

The skin processes various substances including chemical carcinogens, steroids, hormones, and some medications. Therefore, skin metabolism affects how well skin-penetrating drugs work.

Physico-Chemical Factors:

1. Skin Moisture:

The permeability of the skin is significantly increased by contact with water. The most crucial element to improve skin penetration is hydration. Humectants are therefore administered transdermally.

2. Temperature and pH:

Drug penetration is increased tenfold when the temperature changes. Weak acids and bases separate based on pH and pKa, pKb values. The non-ionized drug level determines the drug concentration in the skin. As a result, the penetration of medications is significantly influenced by temperature and pH.

3. Diffusion Coefficients:

The drug's diffusion coefficient determines how well it penetrates the body. The features of the drug, the diffusion medium, and their interactions all affect a drug's diffusion coefficient at constant temperature.

4 .Active Substance Concentrations:

The flow increases when the drug concentration crosses the barrier in direct proportion to the gradient in concentration across the barrier.

5. Partition Coefficients:

For good efficacy, an ideal partition coefficient (K) is necessary. The lipid portion of the skin is still too thick for high K medicines to exit. Drugs with low K even do not penetrate 10.6 Molecular Size and Shape: Smaller molecules penetrate more quickly than larger molecules.

Environmental Factors:

1. Sunlight:

Sun exposure causes the walls of blood vessels to thin, resulting in a less traumatic bruise in the sun-exposed areas. The most noticeable sun-induced pigmentation changes are freckles or lentigines.

2. Cold weather:

It frequently causes dry, itchy skin. To counteract the dehydration brought on by the weather, the skin produces more sebum. An effective moisturizer can ease the signs of dry skin.

3. Air pollution:

A buildup of microorganisms on the surface of your skin and face can lead to acne and pimples when dust clogs pores. This affects how the medication is administered via the skin. This can impair the skin's natural defense mechanism.

4. Effect of heat on transdermal patch:

High heat causes drugs applied through the skin to be absorbed. Patients should keep hot water bottles and hot water bags away from the patch location to prevent infection. Drug distribution through the skin can be increased even with a higher body temperature. In this situation, the patch needs to be taken off right away. When not in use, transdermal patches are kept in their original package and kept in a cold, dry location.[15, 16, 17, 18, 19, 20, 21]

EVALUATION FOR TRANSDERMAL PATCHES:

- Physicochemical characterization
- In vitro release studies:
- In vivo release studies:

1. Physico-Chemical Characterization:

Thickness:

A moving dial gauge, screw gauge,microscope or micrometer is use to measure the thickness of the percutaneous film at different points on the film.

Weight uniformity:

By weighing 10 randomly chosen areas individually and figuring out the average weight, you can examine weight variations. The average weight should not be greatly deviated from by an individual's weight.

Determination of drug content:

After the drug has been precisely solubilize in 100 ml of a suitable solvent in which it is soluble, the solution is then aggressively agitated in a shaking incubator for 24 hours. The entire solution is then sonicated after that. After sonication and subsequent filtrate, the drug in solution is appropriately diluted and analyzed spectrophotometrically.

Content Consistency Test:

The contents of each of the ten patches are chosen and determined. A transdermal patch is considered to be effective if, out of ten patches, nine have contents that range from 85% to 115% of the specified value and one has contents that range from 75% to 125% of the claimed value. The volume uniformity test is successful. Test the effectiveness of 20 further patches, nevertheless, if the content of the first three patches is between 75% and 125%. The transdermal patch passes the test if the range of these 20 patches is between 85% and 115%.

Moisture content:

Weigh each of the produced films and dehydrate them with calcium chloride in desiccators for 24 hours at room temperature. The film is weighted again after some time has passed till it reaches a constant weight. The moisture content is calculated using the formula below: Moisture content = Starting Weigh - End Weight x 100.

Hygroscopicity:

For 24 hours, balanced films are kept at room temperature indesiccators. Once at constant weight, they are removed and placed indesiccators with saturated potassium chloride solution at 84% relative humidity. This is how moisture absorption is determined: Final weight less beginning weight multiplied by 100 is the moisture absorption rate.

Flatness:

Transdermal patches must not shrink over time and have a smooth surface. With a flatness survey, this can be confirmed. Cut three strips—two from each side and one from the patch's center—to test the flatness. By measuring the length of each strip and calculating the neck down percentage, you can calculate the length change. 100 percent flatness is equivalent to zero necking. I1 - I2 X 100 = % neck down I2 = each strip's final length I1 = the first strip's length

Folding durability:

Film's ability to bend under situations of high flexure is determined by its flexural durability rating. By folding the film in the same spot repeatedly until it breaks, fold durability is assessed. The amount of times the film is folded without folding at the same spot is known as the folding resistance.

Sticky properties:

It is polymers' capacity to stick to surfaces despite low contact pressure. The molecular weight, composition, and inclusion of adhesive resin in the polymer all affect the polymer's stickiness.

Thumb error check:

A measurement of adhesion is the amount of force needed to pry the thumb free from the

Probe adhesion test:

Stickiness is measured as the amount of force needed to remove a probe from an adhesive at a constant speed.

2. In vitro release studies:

Disc Stirrer:

The procedure is the same as the USP Dissolution Wing, with the exception that the transdermal system is fastened to a plate or cell that is situated at 32 5 ° C at the bottom of the medium container USP modified

Basket cylinder:

The process is comparable to the USP basket-type solubilizer, but instead of being submerged in the medium at a temperature of 32 5 °C, the system is mounted to the top of a hollow cylinder.

Alternating dish:

This technique uses carrier-attached patches that oscillate in small media volumes, making the device effective for drug delivery systems that require low drug concentrations. The pallet extraction cell approach is an additional option.

In vitro permeability studies:

The amount of medication released from the transdermal macromolecular membranes has a significant impact on the amount of medication that is available for systemic absorption. Drugs that reach the skin's surface are subsequently transported to the skin's microcirculation via entering through the epidermis' cells and between its cells through the appendages. A transdermal patch composed of skin rat or a synthetic membrane is frequently positioned between in both receptor and the compartment in a longitudinally diffusing cell like the Franz Diffusion cell to conduct permeability investigations. Diffusion Keshary-Chien cells. The lipophilic side of the membrane, which is in contact with the receiving fluid on the diffuse cell's hydrophilic side, is exposed to the transdermal system. The receiver chamber is continually triggered at a steady pace and kept at a set temperature (about 32.5°C for skin). Every time a sample was obtained, the amount of buffer was altered by an equal amount. After properly diluting the samples, the absorbance was calculated spectrophotometrically. Then, it is determined how much medicine was impregnated per square centimeter at each interval. Variables that can affect medication release include system design, patch size, skin area, skin thickness, and temperature, among others. In order to analyze permeation, the skin must be prepared, attached to the permeable cell, and experimental conditions like temperature, agitation, immersion, and sample removal at different time intervals must be established. Each other, evaluate the sample, and determine the flow, i.e., the rate of drug impregnation cm2 per second.

Horizontal Permeation System:

It has been routinely used to assess how well drugs penetrate the skin. Each cell had a modest membrane area and solution volume (3.5 ml) that were separated into receiving and giving compartments (0.64 cm2). A matching pair of star magnets that rotate at 600 rpm continuously stirs them. The thermostatic water flowing through the water jacket enclosing the two compartments regulates the system.

Franz Diffusion Cell:

The donor compartment and the receiver compartment are the two compartments that make up a cell. The capacity and effective area of the receiving compartment are 5–12 ml and 1–5 cm2, respectively. A magnetic rod was used to stir the diffusion buffer constantly at a speed of 600rpm. By flowing thermostatically controlled water through the water jacket enclosing the reception chamber, the temperature of the majority of solutions is kept constant.

3. In vivo studies:

Reviews conducted in vivo provide an accurate picture of a drug's effectiveness. In vivo studies allow researchers to fully study the range of factors that are unavailable for consideration in in vitro research. Evaluation of TDDS in vivo can be accomplished utilizing human volunteer animal models.

Animal models:

Animal research isfavored on a small scale because conducting human studies requires a lot of time and resources. Rats, hairless rats, hairless dogs, hairless monkeys, rabbits, guinea pigs, etc. are the most typical animals used to test transdermal drug delivery systems. Numerous studies have shown that hairless animals perform better in in-vitro and in-vivo study than hairy animals. One of the most trustworthy models for testing human percutaneous medication administration in vivo is the rush monkey.

Human models:

In the last phase of development, the transdermal patch was applied to volunteers and pharmacodynamic and pharmacokinetic data were collected. Clinical trials were conducted to evaluate effectiveness as well as related dangers, adverse reactions, better patient, and other factors. Stage I clinical studies mainly centre on evaluating the safety on volunteers, whereas second phase clinical studies mostly concentrated on evaluating the quick safety and effectiveness in patients. Fourth Phase trials were conducted for commercially accessible patch in post-marketing surveillance to identify adverse medication reactions, even if phase III trials showed efficacy and safety in a large number of patients. Regardless of the fact that they necessitate a lot of money, studies in humans are the most effective for determining a drug's effectiveness. [7, 22, 23]

Table no .1 :Marketed products of TDDS [24, 25, 26, 27, 28, 29]

Sr no.	Drugs	Types of TDDS	Type Of Disease Treat
1	Estradiol	Membrane	Postmenstrual syndrome
2	Scopolamine	Matrix	Motion sickness
3	Testosterone	Reservoir	Hypogonadism
4	Rivastigmine	Microreservoir	Alzheimer’s Disease
5	Fentanyl	Reservoir	oral mucositis pain Convulsions, dry mouth
6	Lidocaine	Sonophoresis	Local dermal anaesthesia and local dermal analgesia

FUTURE PROSPECTIVE OF TDDS:-

Transdermal delivery devices have undergone three phases of development. Many of the patches we use today were developed by the first generation of systems by carefully choosing drugs that could reach the skin at therapeutic rates with little to no improvement. By allowing for greater skin permeability and providing the requisite propellants for transdermal dispersion, the second generation increased small molecule delivery. Small molecule drugs, macromolecules and other compounds will all be able to be administered transdermally thanks to the third generation. 1st transdermal patch designs feature a reservoir that holds the medication, which is covered on one side with an adhesive layer that makes contact with the skin and another with an impermeable backing membrane. In some designs, liquid chemical enhancers can be used if the reservoir is made of a liquid or gel and contains dissolved drugs.

CONCLUSION

This review provides useful information about transdermal drug delivery systems and its analysis methodology as a prepared resource for those involved in TDDS research. The information above demonstrates that TDDS possesses admirable potentials, with the capacity to use both hydrophilic and hydrophobic active substances to create viable deliverable medications. To optimize this medicine delivery technique, a deeper comprehension of the various biological interactions and chemical component mechanisms is required. TDDS is probably going to be used in the next generation of medication delivery systems.

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