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A Review on Transdermal Patch

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ABSTRACT
Transdermal drug delivery (TDDS) is one of the most promising methods for drug application. Increasing numbers of drugs are being added to the list of therapeutic agents that can be delivered to the systemic circulation via the skin. Transdermal patch products were first approved by the FDA in 1981. Transdermal delivery is the most common painless technique of administering drugs to systemic circulation, providing controlled, constant administration of the drug, allowing continuous input of drugs with short biological half-lives, and eliminating pulsed entry into the systemic circulation. A transdermal patch is one such drug delivery technique, it is used to deliver a specific dose of drug through the skin into the systemic circulation. This review article summarizes the advantages of transdermal patches over conventional drug administration methods, some common components used in polymer matrix type patches, types of transdermal patches, factors affecting transdermal bioavailability, methods of preparation of transdermal patches, methods of evaluation, recent advancement, and some marketed formulations of transdermal patches. Thus, transdermal patches reduce the load that the oral route commonly places on the digestive tract and liver. It enhances patient compliance and minimizes the harmful side effects of a drug caused by temporary overdose.

Keywords: TDDS, skin permeation, permeation enhancer, matrix, reservoir, In-vitro permeation study

I. INTRODUCTION

Nowadays, about 74% of medications are taken orally and are not as effective as expected. To upgrade similar characteristics, a transdermal medicine delivery system was created. Medicine delivery through the skin to achieve a systemic effect of a medicine is generally known as transdermal medicine delivery and differs from traditional topical medicine delivery**(Alam et al., 2013).**

Transdermal medicine delivery is defined as a one-contained, separate lozenge forms that, when applied to the skin, deliver the medicine through the skin at a controlled rate to the systemic circulation. The transdermal medicine delivery system(TDDS) established itself as an integral part of new medicine delivery systems**(Arunachalam et al., 2010).**

The number of transdermal devices that will reach the market is anticipated to rise significantly as more and more research is conducted in this area and as researchers' interest in this method of drug delivery grows. The transdermal route of drug administration is a novel and dependable way to deliver drugs continuously**(Sharma et al.,2022).**

The topical administration of therapeutic agents offers many advantages over conventional oral and invasive methods of drug delivery. Transdermal drug delivery systems (TDDS) are dosage forms that involve drug transport to viable epidermal and/or dermal tissues of the skin for local therapeutic effect, while a very large fraction of the drug is transported into the systemic blood circulation. Among the major benefits of transdermal drug delivery are the reduction of hepatic first-pass metabolism, the improvement of therapeutic efficiency, and the maintenance of a steady plasma level of the drug **(Shingade et al., 2012).**

The complete morphological, biophysical, and physicochemical characteristics of the human skin must be taken into account in order to transport medicinal substances through it for systemic effects. By improving patient compliance and eliminating first-pass metabolism, transdermal delivery offers a significant advantage over injectables and oral routes, respectively. Transdermal delivery prevents pulsed entry into the systemic circulation, which frequently results in unwanted side effects, and permits continuous input of medications with short biological half-lives in addition to providing controlled, continuous drug administration **(Mali et al., 2015).**

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These consist of stable medication plasma concentrations, no first-pass hepatic metabolism, great bioavailability, and non-invasive treatment. To increase bioavailability and expand the range of medications for which topical and transdermal distribution are feasible options, skin penetration augmentation techniques have been developed **(Arunachalam et al., 2010).**

In the 1970s, transdermal patches were created, and the FDA authorized the first one in 1979 to treat motion sickness. The first nitroglycerin patches were authorized in 1981, and today there are many patches for nitroglycerin, nicotine, fentanyl, clonidine, estradiol, oxybutinin, scopolamine, testosterone, and lidocaine**(Galgeand Pagire and 2022).**

Transdermal patches are designed to treat a variety of illnesses, and the transdermal drug delivery system (TDDS) is a commonly used drug delivery method **(Shivalingam et al., 2021).** Delivering medications into the systemic circulation through the skin at a predefined rate with little variation between and among patients is the primary goal of transdermal drug delivery systems**(Patel and Shah 2018).**

ADVANTAGES:

1) Salivary metabolism, intestinal metabolism, and hepatic first-pass metabolism are avoided.
2)Patients can self-administer these systems due to their ease of use.
3) In the event of an emergency, drug intake can be immediately stopped by taking off the patch at any time during treatment.
4) There is little difference between and within patients because practically all individuals have the same anatomical and biochemical makeup of skin.
5) Skin administration is an appropriate method for medications exhibiting stomach discomfort and poor absorption.
6) Drugs having short biological half-lives that would otherwise require frequent dosing can be continuously administered non-invasively.
7) Better patient compliance results from less frequent dosing.
8) It is possible to prevent therapeutic failures linked to dosage discrepancies with traditional remedies.
9) A consistent and ideal blood concentration time profile reduces adverse effects.
10) Parenteral therapy's risks, discomfort, and inconvenience are avoided. Compared to oral sustained drug delivery systems, the release lasts longer.
11) Transdermal devices are appropriate in situations where it is not desirable to maintain the medication concentration within the biophase.
12) A smaller daily dosage of medication is needed than with traditional treatments.
13) The period of activity is predictable and prolonged due to the way drugs are released **(Patel and Shah 2018, Alam et al., 2013).**

Disadvantages

1) One or more system components may cause contact dermatitis at the application site in certain individuals, requiring stopping the treatment.
2) Due to the skin's inherent limitations on drug entrance caused by its impermeability, only strong medications make good transdermal patch candidates.
3) Some medications are painful, such as the transdermal patch of scopolamine, which is applied behind the ear.
4) Long-term adhesion is challenging **(Mali et al., 2015).**
5) The likelihood of a localized bacterial population may rise due to the patch's longer residency period.
6) High dosages of drugs are not appropriate for the transdermal medication delivery technology.
7) The size of the patch, the type of skin, and the surrounding environment can all affect how well it adheres to the skin.
8) The release of the drug from the system may be significantly influenced by patch location, age, and individual variability.
9) Transdermal patches may cause severe skin allergic responses in certain patients.
10) A lot of medications with hydrophilic structures penetrate the skin too slowly to be effective. If a transdermal patch is damaged, the drug release may not be well controlled.
11) Because they are poorly soluble in fat and water, medications with a high melting point make poor candidates for a transdermal drug delivery system **(Ali et al., 2015).**

ANATOMY AND PHYSIOLOGY OF SKIN (Abhang et al., 2024; Ghosh et al., 2010).

There are three different but interdependent tissues that make up human skin: The cellular, stratified, vascular "epidermis" is the layer beneath the connective tissue's dermis, or hypodermis(fig-1)

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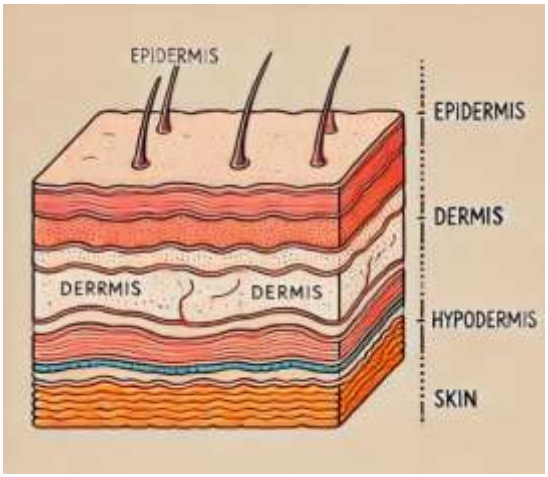

Fig-1(structure of skin)

EPIDERMIS:

The thickness of the multilayered epidermis varies depending on the size and number of cell layers. The eyelids have a thickness of 0.06 mm, while the palms and soles have a thickness of 0.8 mm. When completely hydrated, the outermost layer, sometimes referred to as the stratum corneum or horny layer, grows to several times its dry thickness of about 10 mm. Ten to twenty-five layers of dead, keratinized cells known as corneocytes make up this layer. Despite its flexibility, it is nevertheless largely impenetrable. As the main defense against drug penetration, the stratum corneum can be thought of as a wall-like structure, with keratinized cells acting as protein "bricks" linked together by lipid "mortar." This layer's lipids are arranged into several bilayers.

The lipid fraction has sufficient levels of amphiphilic compounds, like cholesterol and polar free fatty acids, which support the bilayer structure. The viable epidermis is located underneath the stratum corneum and ranges in thickness from 0.06 mm on the eyelids to 0.8 mm on the palms. This layer, which moves inward, is made up of the stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale, among other components. The basal layer compensates for the loss of dead horny cells from the skin's surface by continuously renewing the epidermis through mitosis. The outermost stratum corneum is created by the keratinization of the newly formed cells in the basal layer as they move outward and go through morphological and histochemical changes.

DERMIS:

The dermis, which is between 3 and 5 mm thick, is composed of a network of connective tissue that contains nerves, lymph vessels, and blood vessels. One of the most important functions of the skin's blood supply is to keep the body temperature stable. In addition, it removes waste and impurities from the skin while providing it with vital nutrients and oxygen. Most chemicals that get through the skin barrier can be removed more easily because to the environment created by capillaries, which extend to a distance of around 0.2 mm from the skin's surface. A concentration differential across the epidermis is essential for transdermal absorption, and the blood circulation keeps the permeate's concentration in the dermal layer low.

HYPODERMIS:

The hypodermis, also called subcutaneous fat tissue, supports the dermis and epidermis, stores excess fat, helps regulate body temperature, provides nutritional support, and provides mechanical protection. It also carries vital blood vessels and nerves to the skin and may contain sensory pressure organs. In transdermal drug delivery, the drug must penetrate all three layers of the skin and enter the bloodstream; in topical drug delivery, only the stratum corneum, the outermost layer, must go through, and the drug must remain in the skin layers.

TRANSDERMAL PATCH:

Transdermal patches and medicated plasters (patches) are well-known prolonged-release dosage forms. Although satisfactory skin adhesion is strictly related to the safety and effectiveness of the therapeutic treatment, regulatory agencies are still receiving a lot of reports of in vivo "adhesion-lacking" these days. The adhesive properties of a patch should be described taking into account i) the ability to form a bond with the surface of another material on brief contact and under light pressure (tack); ii) the adhesive's resistance to flow (shear adhesion); and iii) the force needed to peel a patch away from a surface (peel adhesion) **(Cilurzo et al.,2012).**

Basic component of TDDS (SAROHA et al., 2011; Aggarwal, 2009)

- Polymer matrix/Drug reservoir
- Drug
- Permeation enhancers
- Pressure-sensitive adhesive PSA
- Backing laminates
- Release linear (fig-2)
- Other excipients like plasticizers and solvents

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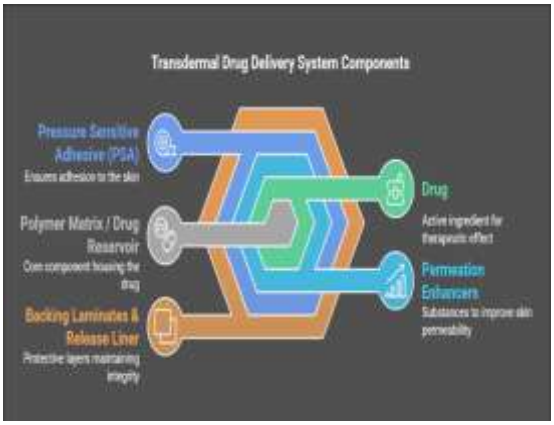

Fig-2(component of TDDS)

Polymer matrix:

Transdermal medication delivery systems are based on polymers. Transdermal delivery systems are made as multilayered polymeric laminates with a drug reservoir or drug–polymer matrix positioned between two polymeric layers: an inner polymeric layer that acts as an adhesive and/or rate-controlling membrane and an outer impervious backing layer that stops drug loss through the backing surface.

When attempting to satisfy the many requirements for the creation of efficient transdermal delivery systems, polymer selection and design must be taken into account. The design of a polymer matrix is the primary challenge, which is followed by optimization of the drug-loaded matrix with respect to its physicochemical properties, adhesion-cohesion balance, compatibility, and stability with skin and other system components, and release properties.

The polymers utilized for TDDS can be classifie d as

Natural polymers include things like chitosan, zein, gelatin, shellac, gums, waxes, cellulose derivatives, and natural rubber. Polybutadiene, hydrin rubber, polyisobutylene, silicon rubber, nitrile, acrylonitrile, neoprene, butyl rubber, and other synthetic elastomers are examples.

Polyvinyl alcohol, polyvinyl chloride, polyethylene, polypropylene, polyacrylate, polyamide, polyurea, polyvinylpyrrolidone, and polymethylmethacrylate are examples of synthetic polymers. As matrix formers for TDDS, polymers such as hydroxypropylmethylcellulose, ethyl cellulose, polyvinylpyrrolidone, eudragits, and cross-linked polyethylene glycol are employed. As rate-controlling membranes, other polymers such as silicon rubber, polyurethane, and EVA are employed.

Drug

The drug's appropriate physicochemical and pharmacokinetic characteristics are the most crucial requirements for TDDS. Drugs that have a limited therapeutic window, a lengthy first-pass metabolism, or a short half-life that results in non-compliance from frequent dosing can benefit greatly from transdermal patches(Table 1). For instance, medications such as methylphenidate for attention deficit hyperactivity disorder, selegiline for depression, rotigotine for Parkinson's disease, and rivastigmine for Alzheimer's and Parkinson's dementia have recently been approved as TDDS.

Table 1:Ideal properties of drug for TDDS (Dhiman et al.,2011, Keleb et al.,2010, Williams and Barry, 2004)

S.No.	Parameter	Properties
1	Dose	Should be low
2	Half-life in hr	It should be 10 or less
3	Molecular weight	It should be less than 500
4	Partition coefficient	Log P (octanol-water) between –1 and 3
5	Skin permeability coefficient	Should be less than 0.5 x10-3cm/hr
6	Skin reaction	Should be non-irritating
7	Oral bioavailability	Should be low
8	Therapeutic index	Should be low
9	Concentration	Minute
10	pH of saturated aqueous solubility	5-9
11	Dose deliverable	<10mg/day

Permeation enhancers:

To increase stratum corneum permeability in order to achieve greater therapeutic levels, drug penetration enhancers interact with stratum corneum structural components such as proteins and lipids. The increase in oil-soluble medication

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absorption appears to be owing to chemical enhancers partially leaching epidermal lipids, resulting in improved skin conditions for wetting as well as trans epidermal and trans follicular penetration. The miscibility and solution qualities of the enhancers utilized could explain why water-soluble medicines permeate the skin more effectively(Table 2). Pharmaceutical experts have worked hard on transdermal permeation experiments with various enhancers for a variety of drug moieties.

Table 2: Permeation enhancer classification (Alam et al.,2013)

Permeation enhancers	**Examples**
Terpenes (essential oils)	Nerodilol, Menthol, Cineol, Limonene, Carvone.
Pyrrolidones	N- methyl- 2- pyrrolidone (NMP), Azone.
Fatty acids and esters	Oleic acid, Linoleic acid, Lauric acid, Capric acid.
Sulfoxides and similar compound	Dimethyl sulfoxide(DMSO), Dimethyl formamide.
Alcohols, Glycols and Glycerides	Ethanol, Propylene glycol, and Octyl alcohol.
Miscellaneous enhancers	Phospholipids, Cyclodextrins, Aminoacid derivatives, Enzymes.

Pressure-sensitive adhesive

The PSA patch maintains close contact with the skin's surface. It should adhere with only finger pressure, be aggressively and persistently sticky, and have a strong holding force. Adhesives based on polyacrylates, polyisobutylene, and silicon are some examples. Avariety of factors influence adhesive choices, including patch design and medication formulation. PSA should be physicochemically and physiologically compatible while not interfering with medication release. The PSA can be placed on the device's front (as in a reservoir system) or on its back and extending peripherally (as in a matrix system).

Backing laminate

The main purpose of the backing laminate is to give support. The backing layer should be chemically robust and compatible with the excipients because prolonged contact between the backing layer and the excipients may cause the additives to leak out or allow excipients, drugs, or permeation enhancers to diffuse through the layer. They should have low moisture vapor transmission rates. They must have maximum elasticity, flexibility, and tensile strength. Backing materials include an aluminum vapor-coated layer, a plastic film (polyethylene, polyvinyl chloride, or polyester), and a heat seal layer.

Release liner

During storage, the release liner prevents drug loss and contamination from the adhesive layer. It is thus considered a component of the principal packaging material rather than a component of the dosage form used to deliver the medicine. The release liner consists of a non-occlusive base layer (paper fabric) or an occlusive layer (polyethylene and polyvinyl chloride) and a silicon or teflon coating. Polyester foil and metalized laminate are also utilized to make TDDS release liners.

Other excipients

Drug reservoirs are prepared using a variety of solvents, including chloroform, methanol, acetone, isopropanol, and dichloromethane. Plasticizers such as dibutyl phthalate, triethyl citrate, polyethylene glycol, and propylene glycol are also used to provide the transdermal patch flexibility**.**

TYPE OF TRANSDERMAL PATCH

Single-layer Drug-in-Adhesive: This system's adhesive layer also contains the drug. In this sort of patch, the adhesive layer not only holds the numerous layers together and the entire system to the skin, but it is also responsible for medication release. A temporary liner and backing are used to enclose the adhesive layer(Fig. 3) **(Ghulaxe and Verma 2015; Patel et al. 2012).**

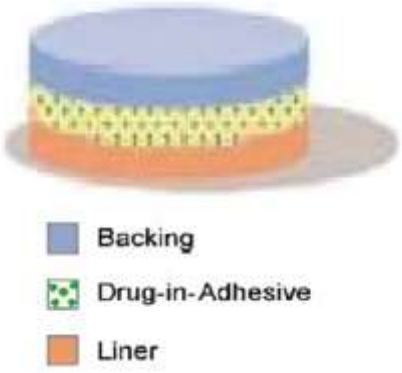

Fig-3(Single-layer Drug-in-Adhesive)

International Journal of Pharmaceutical Research and Applications
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The multilayer drug in adhesive: Patches are similar to single-layer systems in that both sticky layers are responsible for medication release. One layer is for immediate medication release, while the other is for controlled drug release from the reservoir. The multi-layer system differs in that it includes an additional layer of drug-in-adhesive, which is often separated by a membrane. This patch also has a temporary liner layer and a permanent backing(fig-4)**(Ghulaxe and Verma 2015, Patel et al. 2012).**

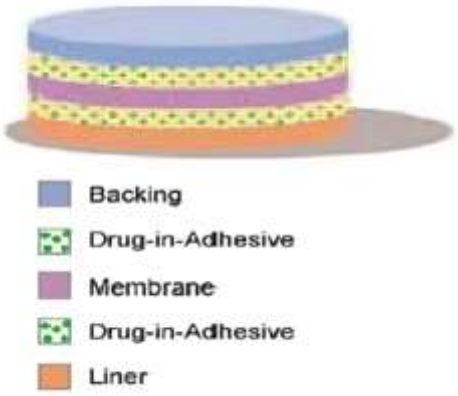

Fig-4(Multilayer drug in adhesive)

Reservoir: In contrast to single- and multi-layer drug-inadhesive systems, reservoir transdermal systems have a separate drug layer. The sticky layer separates the drug layer, which is a liquid compartment containing a drug solution or suspension. The backing layer also provides support to this patch. The release rate in this system is zero order (fig-5)**(Ghulaxeand Verma 2015; Patel et al. 2012).**

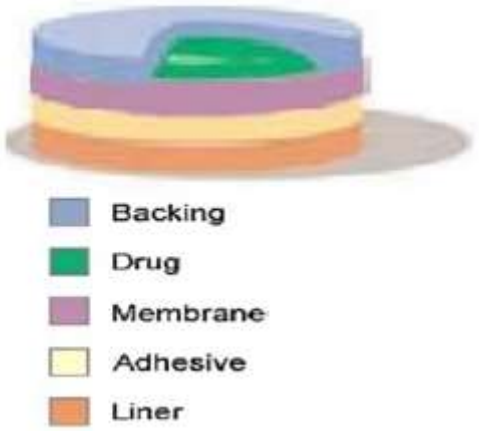

Fig-5(Reservoir)

Matrix: The Matrix system includes a drug layer made of a semisolid matrix that contains a drug suspension or solution. The adhesive layer in this patch partially covers the medication layer(fig-6)**(Mali et al., 2015; Bharadwaj et al., 2012).**

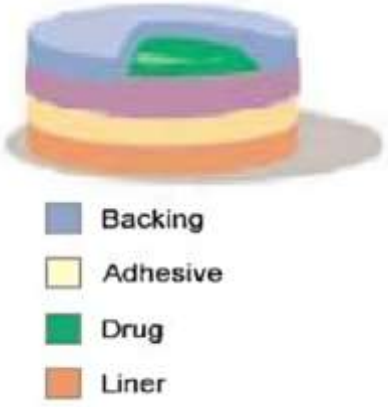

Fig-6(Reservoir)

Vapour Patch: In this particular kind of patch, the adhesive layer not only adheres the several layers together but also releases vapour. The vapor patches are new to the market and provide essential oils for up to 6 hours. The vapor patches produce essential oils and are mostly utilized for decongestion. Other vapour patches available on the market are controller vapour patches, which increase sleep quality. Vapour patches that lower the number of cigarettes smoked each month are also available **(Ghulaxe and Verma, 2015; Patel et al., 2012).**

METHOD OF PREPRATION OF TRANSDERMAL PATCH

Asymmetric TPX Membrane method:

A prototype patch may be created for this, using a heat-sealable polyester material with a 1cm diameter concave serving as the backing membrane. The drug sample is dispensed into the concave membrane, covered by a TPX {poly(4-methyl-1-pentene)} asymmetric membrane, and sealed with an adhesive.

Asymmetric TPX membrane preparation:

The dry/wet inversion method is used to make them. To create a polymer solution, TPX is dissolved at 60°C in a solution of solvent (cyclohexane) and nonsolvent additives. A gardner knife is used to cast the polymer solution onto a glass plate to the desired thickness after it has been maintained at 40°C for 24 hours. Following a 30-second evaporation of the casting film at 50°C, the glass plate must be promptly submerged in a

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coagulation bath with the temperature kept at 25°C. The membrane can be removed after 10 minutes of soaking and allowed to air dry for 12 hours at 50°C in a circulation oven **(Rao and Kiran 2013).**

Teflon mold technique in a circle:

In an organic solvent, polymer solutions are used in various ratios. Half as much of the same naturally soluble substance dissolves as the prescribed amount of medication. Boosters in different concentrations dissolve in the natural solvent's opposing half and then proceed. Di-N. Butyl phthalate is used as a plasticizer in medications. Blend of polymers. After 12 hours of stirring, the entire mixture must be poured into a circular Teflon mold. On a level surface, the molds are positioned. Surface, using an inverted funnel to control the solvent vaporization rate at 1/2 m/sec in a laminar flow hood model. After 24 hours, the solvent is allowed to evaporate. The dried films must be stored at 25±0.5 °C in a desiccator packed with silica gel for a further twenty-four hours before being assessed in order to reverse the signs of aging. Within a week of their release, these films need to be evaluated in preparation.

Using the "IPM membranes" approach:

Using this method, the drug is dissolved in a water and propylene glycol solution that contains carbomer. Stirring agent, 940 polymer, spun in a magnetic field for 12 hours. Triethanolamine is required to neutralize and thicken the dispersion. Keep in mind that Solution gel can be made with a pH of 7.4. If a drug dissolves easily in water, that's a bad thing. The gel will be incorporated into the IPM membrane.

"EVAC membranes" method

To prepare the target transdermal treatment system, 1% Carbopol reservoir gel, ethylene vinyl acetate, and polyethylene (PE) are required. EVAC copolymer membranes can be used as rate-regulating membranes. Propylene glycol is used to make the gel in case the drug does not dissolve in water. Propylene glycol and carbopol resin are used to dissolve the drug. Will be combined with the previously described combination and neutralized using a 5% w/w sodium hydroxide solution. A backing layer sheet covering the specified area is covered with the drug (in gel form). To build a leak-proof device, a membrane is applied, a rate-limiting layer is placed over the gel, and the edges are heated to seal **(Pratiksha GorakshaKatore, 2024).**

Proliposome preparation:

The proliposomes are prepared using the film deposition method and TDDS with the carrier strategy. A 1:2 ratio between the drug and lecithin can be used as the optimal ratio, according to the preceding reference. In order to create proliposomes, 5 mg of powdered mannitol is consumed in a 100 ml round-bottom flask that is kept between 60 and 70 °C. The flask rotates between 80 and 90 rpm, and the mannitol is vacuum-dried for 30 minutes. The temperature of the water bath is adjusted to between 20 and 30 °C after drying. Drugs and lecithin are dissolved in a suitable mixture of organic solvents. The flask with a round bottom is filled with a half-milliliter aliquot of the organic solution at 37 °C. After careful drying,the second aliquot (0.5 ml) of the solution must be added. The flask is holding after the last loading. Proliposomes are linked with a lyophilized substance, and then powdered mannitol with drug loading is added. Proliposomes are stored in desiccators overnight. Then, a 100 mesh sieve was used. After being collected, the powder is stored in a glass bottle. At the freezing temperature till characterization**(Pratiksha GorakshaKatore, 2024).**

Mercury Substrate Method:

This process dissolves the medication and plasticizer in a polymeric solution. After stirring for ten to fifteen minutes to create a uniform dispersion, it is placed onto a leveled mercury surface and covered with an inverted funnel to regulate the evaporation of the solvent **(Mane et al.,2024).**

Aluminum-Backed Adhesive Film Method:

If the loading dose is more than 10 mg, the transdermal drug delivery system may result in unstable matrices. The sticky film technique with an aluminum backing is appropriate. Since most medications and adhesives dissolve in chloroform, it is the solvent of choice for making the. After the medicine has been dissolved in chloroform, sticky material is added and dissolved in the drug solution. Aluminum foil is used to line a specially constructed aluminum former, and precisely fitted cork blocks are used to blank off the ends **(Rao and Kiran 2013).**

Solvent casting method

The solvent casting process is used to prepare transdermal patches. Methanol was used as the solvent to dissolve a PVP solution containing

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EC, HPMC, and carbopol. The necessary amounts of plasticizer and penetration enhancer were added, and the solution was made and thoroughly agitated. To create a uniform mixture, the precisely weighed medication was combined with the previously mentioned combination and thoroughly mixed. The solution was retained for stabilization and total elimination of air bubbles following adequate mixing. The aforementioned liquid was then poured into a glass mold that had been lightly sprayed with glycerine to stop the patch from sticking to the mold. A glass funnel was inverted over the glass mold to regulate the rate of evaporation. The mold was left to dry for twenty-four hours at room temperature. The films were carefully taken out of the mold and placed in a desiccator after they had dried for 24 hours **(Geethalakshmi et al., 2021).**

Evaluation parameter of the transdermal patch
Thickness

A screw gauge with the lowest count was used to measure the thickness of the manufactured transdermal films at five different locations, and an SD was used to compute the average **(Cherukur et al., 2017; Pandit et al., 2009).**

Folding endurance

In order to identify the type of plasticizer, the folding endurance of the patches is crucial. The prepared patches were continuously folded in the same spot until a break or fracture showed up. The value for folding durability was obtained by folding the patches in the same location **(Latif et al.,2022;Ullah et al.,2021).**

Weight uniformity

Before testing, the created patches are dried for four hours at 60°C. A predetermined patch area must be divided into various sections and weighed using a digital scale. The individual weights must be used to compute the average weight and standard deviation values **(Dhiman et al., 2011;Rhaghuramet al.,2003).**

Percentage Moisture Content (Prajapati et al.,2011; Keleb et al.,2010)

After being individually weighed, the produced films were stored for 24 hours at room temperature in a desiccator filled with fused calcium chloride. The films were reweighed after 24 hours, and the percentage moisture content was calculated using the procedure below:

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

Percentage moisture uptake

To maintain 84% relative humidity, the weighted films were stored in a desiccator with a saturated potassium chloride solution at room temperature for 24 hours. The films were reweighed after 24 hours, and the % moisture uptake was calculated using the formula below:

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

Drug content

A tiny area (1 cm2) of polymeric film can be fully dissolved in an appropriate solvent with a certain volume to identify it. The medication is freely soluble in the solvent that is used. The chosen region is weighed before being dissolved in the solvent. After being continually shaken for 24 hours in a shaker incubator, the entire contents are sonicated and filtered. The proper analytical technique is used to evaluate the drug in **solution (Alam et al., 2013; Costa et al., 1997).**

Drug uniformity test:

Ten patches are chosen, and the content of each patch is established. In the event that nine of the ten patches contain between 85% and 115% of the prescribed value, and one patch has at least 75% to 125% of the given value, transdermal patches are considered to have passed the content uniformity test. However, if three patches show content between 75 and 152 percent, then another 20 patches are tested for drug content. If the range of these patches is between 85% and 115%, the transdermal patches are considered successful.

Flatness

A transdermal patch should not tighten over time and should have a smooth surface. The flatness research can be used to illustrate this. To determine the flatness of the patches, two strips are cut from each side and one from the center. The length of every strip is measured, and the percentage of constriction is used to calculate the variance in length. Complete flatness is equal to zero percent restriction.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 3 May–June 2025, pp: 518-529 www.ijprajournal.com ISSN: 2456-4494

Take properties

The polymer's capacity to stick to a substrate with minimal contact pressure is what it is. The molecular weight, content, and application of tackifying resins in the polymer all affect tack.

Thumbtack test

A measure of tack is the amount of force needed to extract the thumb from the glue.

Rolling ball test

The stainless steel ball's travel distance along an upward-facing adhesive is measured in this test. The ball's range increases with the adhesive's tackiness.

Quick stick peel tack test

The tape is pulled away from the substrate at a pace of 12 inches per minute at 90 degrees to determine the peel force needed to break the binding between an adhesive and substrate.

Probe tack test. Tack is the amount of force needed to remove a probe from an adhesive at a set rate **(Saroha et al., 2011; Aggarwal, 2009).**

In vitro drug release study

The drug release from the produced patches can be evaluated using the paddle over disc method (USP equipment V). Dry films of a given thickness must be cut into precise shapes, weighed, and adhered to a glass plate. After that, the apparatus was equilibrated to 32±0.5 °C, and the glass plate was submerged in 500 mL of the phosphate buffer or dissolving media (pH 7.4). After that, the paddle was positioned 2.5 cm away from the glass plate and ran at 50 rpm. 5-mL aliquots of samples can be taken out at suitable intervals for up to 24 hours and subjected to HPLC or UV spectrophotometer analysis.

It is possible to determine the mean value by conducting the experiment in triplicate **(Shingade et al., 2012; Singh et al., 1993).**

In vitro, a skin permeation study

This investigation was conducted using a Franz diffusion cell. Between the donor compartment and the receptor compartment, the rat or goat's abdominal skin was securely attached. The receptor compartment had a 7.4 pH phosphate buffer and held 20 milliliters. The skin was repaired with the patch. This apparatus was fixed to a stirrer. A magnetic stirrer (32±0.5 C) was used to agitate the receptor compartment that contained the phosphate buffer solution. The samples were removed at various times, and a spectrophotometer was used to determine the drug content. Every time a sample was removed, the same volume of buffer solution was added. The cumulative amount of drug penetration and time were represented on a graph**(Mounika et al., 2014)**.

Stability study

The purpose of the stability studies is to find out how temperature and relative humidity affect the amount of medication in various formulations. According to ICH recommendations, stability studies are conducted on the transdermal **formulations (Mali et al., 2015).**

Marketed formulation of TDDS (Patel and Shah 2018, Arti K 2013)

APPROVAL YEAR	DRUG	INDICATION	PRODUCT NAME	MARKETING COMPANY
1991	Nicotine	Smoking cessation	Nicoderm®, Habitrol®, proStep®	GSK, Novartis, Elan
1993	Testosterone	Testosterone deficiency	Testoderm®	Alza
2001	Estradiol /norelgestromin	Contraception	OrthoEvra®	Ortho-McNell
2005	Lidocaine/tetra Caine	Local dermal analgesia	Synera®	Endo pharmaceuticals
2006	Methylphenidate	Attention deficit hyperactivity disorder	Daytrana®	Shire
2007	Rotigotine	Parkinson's disease	Neupro®	Schwarz pharma
2013	Sumatriptan	Migraine	Zecuity®	Nupathes Inc.

Future paespect

TDDS technology is widely acknowledged as a mass dissemination method. Because of this, it is the preferred drug for injection. Method for administering transdermal medication to all skin types. By inhibiting other senses and first-pass metabolism. Actions connected to a variety of other drug delivery methods. TDDSs are among the several devices that can be used to inject drugs into the

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bloodstream through the skin. Typically, TDDS is used to administer drugs in a constant, safe manner that is stable against biochemical changes until the drugs reach the target region. Non-intrusive and non-allergic, TDDS has a set time and dosage. A delivery system that ensures consistent dispersion of drugs at a dosage that has been authorized and regulated. The TDDS is expanding quickly in the pharmaceutical industry as a result. The nicotine patch transformed quitting smoking ten years ago. In the past, nitroglycerin was used to treat angina in patients, and clonidine was used for hypertension. Patches are the only way to treat motion sickness with scopolamine and estrogen deficiency with estradiol. Biotech medications were still being developed at the time. The makeup of Patchwork systems has not changed much over the past decade, and the number of drugs developed in the patches has hardly increased. The majority of the changes have been restricted to material improvements. The reasoning behind this is that very few drugs meet the molecular weight and potency standards needed for transdermal absorption**.**

II. CONCLUSION:

For research scientists working on transdermal drug delivery systems, this article offers useful information about these systems and the specifics of their review procedure. The aforementioned demonstrates the immense potential of TDDS, which can be used to create promising deliverable pharmaceuticals with both hydrophobic and hydrophilic active substances. More knowledge of the various biological interaction processes and polymers is needed to optimize this drug delivery technology. TDDS is a viable, real-world use case for the next drug delivery technology.

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The authors have no conflictsof interest.

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