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"Transdermal Patches"

A Comprehensive Review of Permeation, Types, Advantages, Disadvantages, Design, Development and Application.

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ABSTRACT

The transdermal drug delivery system (TDDS) has established itself as an essential component of new drug delivery systems. The term "transdermal delivery system" refers to all topically given medication formulations that transport active ingredients into the body's circulation. Transdermal drug delivery systems are polymeric formulations that, when applied to the skin, deliver the drug at a predetermined mined rate throughout the dermis to produce systemic effects. Although transdermal dosing options are more expensive than traditional formulations, are gaining popularity due to their distinct advantages. Controlled absorption, more consistent plasma levels, increased bioavailability, minimized adverse effects, painless and uncomplicated application, and the option of discontinuing drug administration by simply removing the patch from skin is one of the potential benefits of transdermal medication administration. Development of controlled release transdermal dosage form is a complex process involving extensive efforts. This review article describes the methods of preparation of different types of transdermal patches, evaluation parameters and some available marketed products.

Key Word

Transdermal Drug Delivery System, Patches, Convenient, Skin, Evaluation of TDDS.

Introduction:

A group of physicochemical technologies that can regulate the distribution and release of pharmacologically active compounds are collectively referred to as drug delivery systems (DDS) into organs, tissues, and cells, so that these dynamic sub-Positions could have the best results. Stated differently DDS addresses the drug delivery systems and dosages to for. Among Transdermal drug delivery system (TDDS) representative-resents

a charming strategy. TDDS has emerged as one of the most extensively studied methods for delivering drugs without becoming invasive.

A medicated adhesive patch called a transdermal patch or skin patch is applied to the skin to provide a prescribed dosage of medication through the skin and into the blood.

The transdermal distribution increases patient compliance and prevents first-pass metabolism, it offers a significant advantage over injectables and oral methods. Correspondingly Transdermal application has competed with oral considered the most fruitful and inventive research aspect of medication distribution, since oral therapy entails achieving and preserving medication concentration in the body inside a range. That is therapeutically useful by introduction of a set dosage on a regular basis because wherein the body's medication concentration corresponds to a peak and trough pattern, increasing the likelihood significant side effects or treatment failure. Substantial quantity of medication is lost close to the intended organ and Monitoring therapy requires continuous attention in order to prevent taking too much. The oral route's limitations surmountable and advantageous.

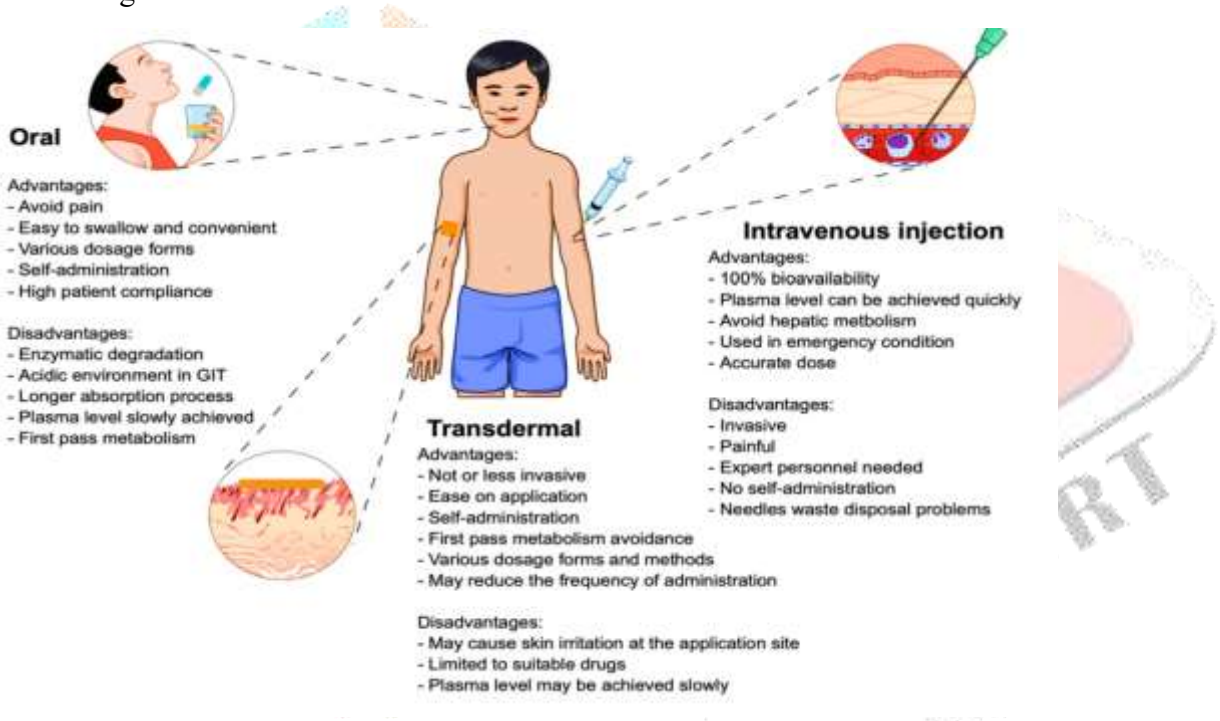


Fig 1: Comparison of three different route of drug administration.

The skin serves as the drug administration location for transdermal drug delivery systems via blood arteries. The medication is absorbed into the systemic circulation in the skin before moving throughout the body. Systems for transdermal medication administration have certain benefits. For patients, like requiring less intrusive techniques (some are completely noninvasive), avoiding first-pass metabolism, simplicity in administration and application, absence of knowledgeable staff and the possibility of lowering frequency of management. Furthermore, this technology has be employed to offer various types of medications, including hydrophilic and hydrophobic substances. The benefits listed above have attracted attention. From scientists studying pharmaceuticals to create and investigate transdermal medication delivery methods, especially in altering or penetrating the stratum corneum to improve medication.

TDDS Advantages:

1. They can avoid gastrointestinal pH-related issues with drug absorption in the gastrointestinal tract medication interactions with diet and enzymatic activity, alcohol and other medications taken orally.
2. They can serve as a replacement for oral drug when the route is inappropriate, as in the case of diarrhea and vomiting.
3. To prevent the first pass impact, such as with transdermal nitroglycerin. It is quickly broken down by the when consumed orally.
4. They avoid the inconvenience because they are non-invasive of intravenous treatment.
5. They offered prolonged treatment using a single application, enhancing adherence compared to dosage types that need to be taken more frequently delivery, such as Transdermal Clonidine Day.
6. The way that medications with a start half-life work is stretched through the medication reservoir in the medicinal delivery mechanism and its regulated.

TDDS'S Disadvantages:

1. Price is exorbitant.
2. Ionic medicines cannot be delivered by TDDS.
3. High drug levels cannot be achieved by TDDS in plasma or blood. Because of the skin's inherent limitations on drug entrance caused by its impervious only strong medications are appropriate candidates for transdermal patches.
4. Is unable to create TDDS for medications with big molecular sizes.
5. Pulsatile medication delivery is not possible with TDDs.

Skin Anatomy and Physiology:

The three different yet interdependent tissues that make up human skin are as follows:

A) The vascular, cellular, stratified epidermis,

B) Connective tissue's underlying dermis and

C) The hypodermis.

- **Epidermis:**

The thickness of the stratified epidermis varies, based on the size and quantity of cell layers of epidermis, with palm and sole thicknesses varying from 0.8 mm on the eyelids, down to 0.06 mm. The water permeability, diffusivity, and thickness of water via the skin's layer. It is composed of the outer strata. corneum and healthy skin layers.

a) Corneum stratum:

This is the skin's outermost layer, commonly known as layer of horniness. It has a thickness of about 10µm when dry, but expands to a thickness several times this amount when completely hydrated.

Ten to twenty-five layers of dead, corneocytes are keratinized cells. Although it is adaptable, comparatively impervious. Stratum corneum: this is the main obstacle to the drug's permeation. The horney layer's architecture can be represented as a wall-like construction. This model shows that the keratinized Cells are like "bricks" of

protein buried in lipid. "mortar" Lipids are organized into several bilayers. There is enough amphiphilic content in the fat component, including polar free fatty acids and cholesterol, so as to keep the bilayer structure.

b) A healthy epidermis

This is located below the corneum stratum and differs in thickness on the eyelids, ranging from 0.06mm to on the palms, 0.8 mm. Looking inward, it is made up of layers such are the stratum lucidum and stratum. The stratum spinosum, granulosum, and the stratum base. The basal layer's epidermis is continuously renewed by cell mitosis, which makes up for the loss of dead horney cells. skin surface cells. As the cells generated by the basal layer expands, they change both histologically and morphologically, moving through in order to create the outermost layer of layer of corneum.

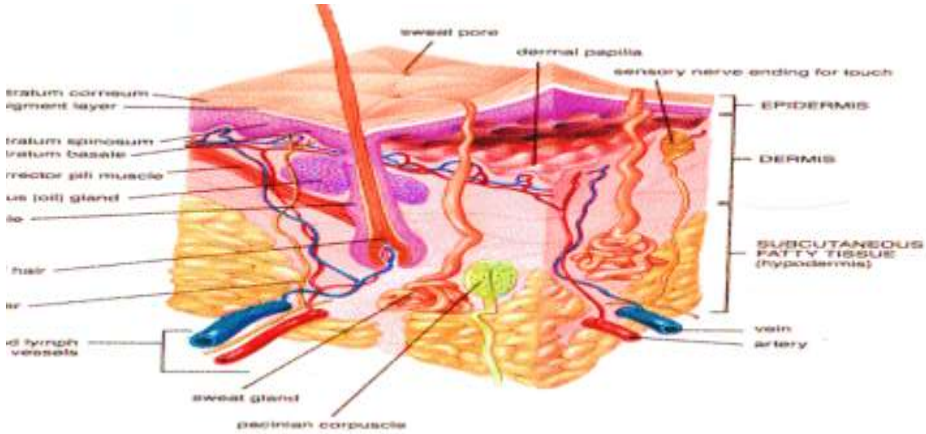
- **Skin Dermis:**

It is a layer that is 3 to 5 mm thick and is made up of a connective tissue matrix, which is blood-filled vessels, nerves, and lymph vessels. The skin blood supply is crucial for the control of body's warmth. Additionally, it offers nutrients and delivering oxygen to the skin and eliminating waste and pollutants goods. Capillaries extend 0.2 mm into the skin. Most people's surface and create sinking circumstances. molecules that cross the epidermal barrier. As a result, the blood supply maintains a permeant's dermal concentration extremely low, and the consequent concentration variations throughout the epidermis offer the necessary gradient of concentration for transdermal penetration.

- **The hypodermis:**

Subcutaneous fat, or the hypodermis, provides support for both the epidermis and dermis. It acts as a repository for fat. region. This layer facilitates temperature regulation. offers dietary assistance and mechanical support. defense. It contains the main blood vessels and nerves to the skin, maybe with sensory pressure organs. For transdermal administration, the medication must permeate beyond each of these three layers and extend into systemic circulation, whereas topical medications distribution only through the stratum cornea

Fig 2: Structure of skin.



Perimetral Entry Point:

Three crucial pathways exist for a medicinal molecule to traverse the intact SC via skin extensions (shunt pathways), either by a transcellular route or via the intercellular lipid domains path. Characteristics of the molecule's physiochemistry control the amount of a specific medicine that percolates through a mix of these paths. The passage via the appendages another name for the trans appendageal routes is the shunt pathways, such as permeability via the sweat glands additionally throughout the sebaceous glands that are connected to the hair follicles. Appendages of the skin offer a continuous conduit that crosses the SC divide. Current research has reexamined the long-held presumption that the hair follicles take up roughly 0.1% of the amount of skin on an individual. According to Otberg et al. that the follicular showed that the follicular number, opening diameter and follicular volume are important considerations in drug delivery through these appendages and indeed the forehead provides 13.7 mm2/cm2 as the follicular infundibula, i.e. approximately 13.7% of the surface area of the forehead is available as thirteen percent of the forehead's surface area might be used as follicles. Remarkably, the research also revealed that the demonstrated that the volume, opening diameter, and number of follicles are crucial factors to take into account while administering medication through. These limbs and in fact the forehead offer 13.7 mm2.

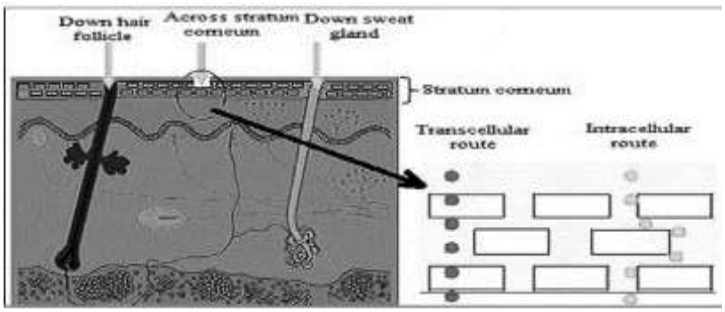


Fig 3: Drug penetration path across skin.

Transcellular pathway:

Substances that reach the skin through the transcellular pathway go through the corneocytes. Corneocytes that are rich in hydrated keratin creates a moist environment that shields certain medicines are hydrophilic and can pass. The route that crosses cells demands not just diffusion through and dividing within the keratin blocks as well as through and into the lipids that separate cells.

- **Intercellular pathway**

Drug diffusion via the intercellular pathway is a component of the lipid matrix that is continuous. This path presents a serious challenge due to two factors:

1. Thinking back to the "bricks and mortar" parading in SC, the corneocytes' interdigitating structure produces a twisted route for medication penetration between cells, which contrasted with the transcellular pathway's comparatively direct course path.
2. Alternating cells make up the intercellular domain bilayers with structure. As such, a medication needs to be taken in turn.

Factors influencing transdermal permeability.

- **Physicochemical characteristics of penetrant molecules.**

A. Partition Coefficient:

A lipid/water partition coefficient of 1 or higher typically necessary for optimal transdermal permeability. Chemical modification may occur without influencing the pharmacological activity of the medication.

B. Temperature and pH:

Can significantly impact medication permeability. The diffusion coefficient decreases with decreasing temperature.

Weak acids and weak bases separate depending on pH and pKa or pKb values. Proportion of Unionized drug determines

the drug concentration in skin.

Therefore, temperature and pH are crucial considerations. Affecting drug penetration.

C. Skin Hydration:

When exposed to water, the skin's permeability increases substantially.

Hydration plays a crucial role in enhancing skin permeability. Humectants are commonly used during transdermal

delivery

D. Concentration of Drug

The flux of drugs is proportional to the concentration gradient across the barrier, with a higher gradient indicating a

higher concentration. The concentration of medication will be higher across the barrier.

E. Molecular shape and size

Drug absorption is inversely proportional to molecular weight, with smaller molecules penetrating faster than larger

ones. Because of partition coefficient dominance, the impact of molecular size is not known.

- **Biological Factors influencing TDDS**

A. **Skin Condition:**

Although skin acts as a natural barrier, certain chemicals, such as acids and alkalis, can permeate and damage skin tissues. Methanol and chloroform are solvents. renowned for removing the skin's lipid fraction. They can cause microscopic openings or shunts in the skin, possibly allowing other chemicals to penetrate more easily. These consequence emphasize the necessity of understanding how different agents interact with the skin's barrier qualities, especially in circumstances such as chemical exposure or transdermal medication. delivery.

B. Skin aging:

Younger skin tends to be more porous. Toxins are more easily absorbed through children fragile skin. So, skin aging is one of the factors affecting drug penetration in TDDS.

C. Blood supply:

Transdermal absorption may be impacted by modifications to peripheral circulation.

D. Regional skin site:

Skin type and thickness stratum corneum and appendage density differ from site to site. These elements have a big impact infiltration.

E. Skin metabolism:

Steroids are metabolized via skin hormones, some medications, and chemical carcinogens. Thus, skin metabolism impacts a drug's effectiveness. penetrated the epidermis.

- **Transdermal Patches**

Transdermal patches are adhesive patches that are put to the skin and deliver medication directly into the circulation. They are intended to give a controlled release of the medicine over a set time period, providing for consistent therapeutic benefits without the need for frequent doses. Common applications include pain management, hormone replacement therapy, and smoking cessation. Patches are sometimes more convenient than oral drugs and can increase patient compliance.

- **An Ideal Patches:**

1. Transdermal patches are painless and intrusive, as they transport drugs straight into the body.
2. Topical patches are an effective way to deliver drugs that are not easily absorbed through the mouth due to stomach acid.
3. There is substantial hepatic deterioration of the intestines.
4. Topical patches provide for consistent and controlled drug administration over time.
5. Topical patches have less undesirable side effects.
6. Topical patches are easy to use.
7. Topical patches provide an alternative for those who are unable or unable to take oral medications or supplements.

8. Topical patches are inexpensive.
9. Topical patches are most popular among users.
10. Rejection of first pass metabolism.
11. Rejection of gastro-intestinal incompatibility.
12. Ensures consistent and sustained activity.

➢ **Transdermal drug delivery systems consist of:**

1. Polymer matrices.
2. The drug
3. Permeation enhancers.
4. Different excipients.

- **Polymer Matrix**

The polymer controls the drug's release from the device.

Possible polymers for transdermal devices include:

1) **Natural polymers:** Examples include cellulose compounds, zein, gelatin, shellac, waxes, proteins, gums and derivatives, natural rubber, and starch.
2) **Synthetic elastomers:** Examples include polybutadiene hydrin, rubber, polysiloxane, and silicone. rubber, nitrile, acrylonitrile, butyl rubber, styrenebutadieine, Neoprene, etc.
3) **Synthetic polymers**: Examples include polyvinyl alcohol, polyvinyl chloride, and polyethylene. Polypropylene, polyacrylate, polyamide, polyurea.

- **Ideal qualities for a polymer utilized in transdermal systems include molecular weight and chemical functionality.**

a. The polymer should have a particular.
b. The medicine diffuses adequately and is released through it.
c. Polymer should be stable.
d. Polymer should be nontoxic.
e. The polymer should be easy to manufactured.
f. The polymer should be affordable.
g. The polymer and its degradation product must be neither poisonous nor unfriendly to the host.

- **Drug**

The drug solution makes direct contact with the release liner.

Physiochemical Properties: -

a) The drug's molecular weight should be less than 1,000 Daltons.
b) The medication must have affinity for both lipophilic and hydrophilic phases.
c) The drug's melting point should be low.

Biological properties:

a) The medicine should be strong, requiring a daily dose of a few milligrams.

b) Ensure the medicine has a short half-life (t½).

c)The medicine must not cause allergic reactions.

d)Tolerance to the drug cannot develop under the Transdermal release profile nearly zero-order patches.

- **Enhancers**

These chemicals increase skin permeability by changing the skin's barrier to penetrants.

Formulation		Ratio of drug flux with enhancer to drug flux without enhancer
Drug	Enhancer system	
Progesterone	EVA 40	1.00
Progesterone	GML/EP/EVA 40	5.67
Progesterone	Polysiloxane	1.00
Progesterone	GML/EP/PVP/Polysiloxane	1.70
Buspirone	EVA 40	1.00
Buspirone	GML/EVA 40	0.19
Buspirone	GML/EP/EVA 40	10.03
Buspirone	GML/EP/PVP/Polysiloxane	3.53
Buspirone	EP/EVA 40	1.28
Buspirone	Polysiloxane	1.00
Estradiol	EVA 40	1.00
Estradiol	GML/EP/EVA 40	2.11
Estradiol	Polysiloxane	1.00
Estradiol	GML/EP/PVP/Polysiloxane	1.38
Oxybutynin base	Polysiloxane	1.00
Oxybutynin base	GML/EP/PVP/Polysiloxane	1.46

EVA 40: Ethylene vinyl acetate; GML: Glycerol monolaurate; EP: Ethyl palmitate; PVP: Poly vinyl pyrrolidone

Table no 1: The Enhancement of drug in presence of Enhancers.

1. Solvents

These chemicals improve penetration by eating the polar route and/or fluidizing lipids. Examples include aqueous alcohols (methanol and ethanol) and alkyl methyl sulfoxides.

Dimethyl sulfoxide, alkyl homologs of methyl sulfoxide, acetamide and dimethyl formamide, pyrrolidones2 pyrrolidone, N. The solvents used include propylene glycol, glycerol, silicone fluids, and isopropyl palmitate. Other ingredients include methyl, 2-purrolidone, laurocapram (azone).

2. Surfactants

These chemicals are proposed to boost the polar route. Transport, particularly for hydrophilic medicines. The capability of a surfactant

To change penetration is a function of the polar head group and hydrocarbon chain length.

3. Anionic surfactants

Examples include dioctyl sulphosuccinate, sodium lauryl sulfate, Decodecylmethyl sulphoxide, etc.

4. Nonionic surfactants

Pluronic F127, F68, and so on. Bile salts, such as sodium MS taurocholate, sodium deoxycholate, and sodium Tauro glycocholate.

5. Binary system

These systems open up both the heterogeneous multilaminate and continuous paths. Examples are propylene glycol-oleic acid and 1,4-butane diol-linoleic acid.

6. Miscellaneous chemicals

These include urea, a hydrating and keratolytic agent; N, N-dimethyl-m-toluamide; calcium thioglycolate; and anticholinergic drugs. Some possible permeability enhancers were recently described. However, there is limited evidence of their usefulness. They include Eucalyptol, di-o-methyl-ß-cyclodextrin, and soybean casein.

Other Excipients

1. **Adhesives:**

The fastening of all transdermal devices to the skin has so far been done by using a pressure sensitive adhesive which can be positioned on the face of the device or in the back of the device and extending peripherally.

PSAs are materials that cling to a substrate, in this example skin, with modest pressure and leave no residue when removed. Interatomic and intermolecular attractive forces arise at interfaces when intimate contact is formed. To attain this level of touch, the material must be able to bend with slight pressure, hence the term "pressure sensitive." Adhesion involves a liquid-like flow, resulting in when pressure is applied to the skin floor, it wets the floor, and the adhesive units remain in that state until the pressure is removed. The PSA wets and distributes onto the skin, yet its surface energy is substantially lower than that of pores and skin

2. **Release Liner**

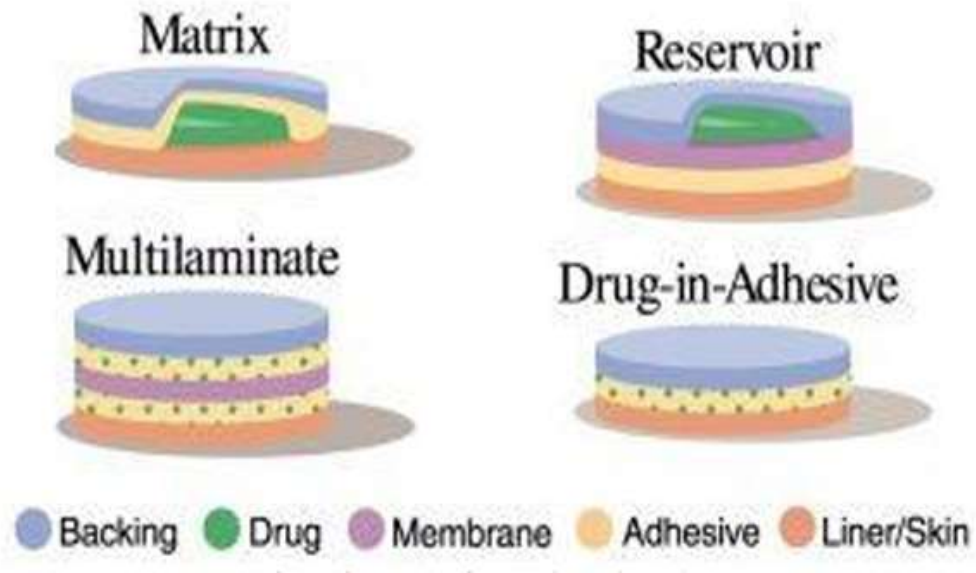
A release liner is a protective layer that is removed before applying a transdermal patch to the skin. This layer is part of the primary packing (38). The liner must be inert to the dosage form's components due to its close contact. System and penetration characteristics (41). Fluoropolymers, fluor olefin-based polymers, linear fluor acrylates are widely employed to make a release liner, such as BIO PSA. High Tack 7-4301, BIO PSA Medium Tack 7-4201.

3. **Backing laminates.**

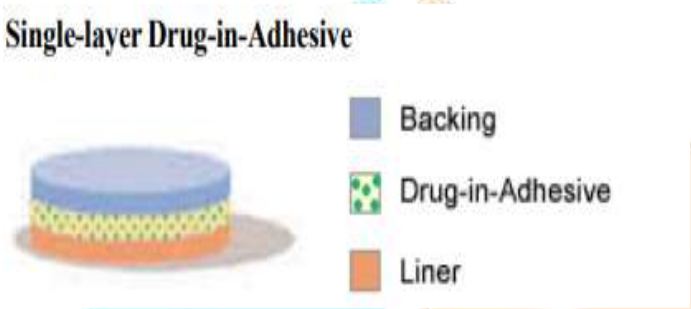
Backings are chosen for their look, flexibility, and occlusion needs. When developing a backing layer, it's crucial to consider the material's chemical resistance. Excipient compatibility must also be examined. Due to the prolonged interaction between

The backing layer Excipients may also cause additives to seep out of the backing layer or induce diffusion of excipients, drugs, or Improves penetration through the layer.

Transdermal Patch Types:



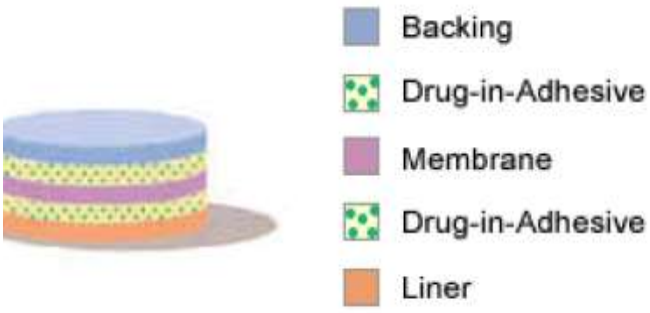
a) Adhesive single-layer medication



This kind has the medication embedded in the sticky layer. The layer of glue not only helps to keep the different layers together, but also accountable for the drug's skin-contact release. The layer of glue is encircled by a backing and a temporary liner.

(1) **Adhesive drug with many layers**

This kind is comparable to the single layer as well, except it has a instantaneous drug release layer and a regulated layer release in addition to the coating of glue. The layer of sticky material is accountable for the drug's release. Additionally, this patch features a both a transient liner layer and a long-term backing.



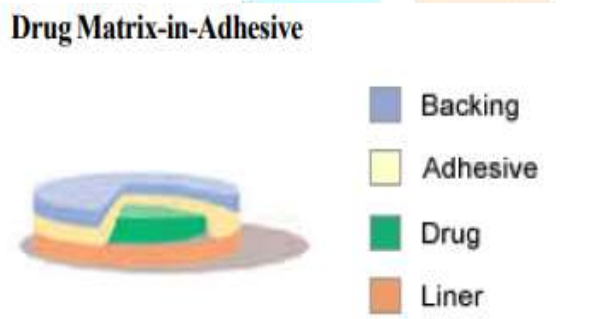
a) A vapour patches:

The adhesive layer in this kind of patch has two functions: it releases vapour and holds the different layers together. The vapor patches are recently available on the market and are frequently utilized to release crucial oils for clearing congestion. Numerous further varieties of vapor patches are also are on the market that are intended to enhance the quality of sleep and lessens the environment for cigarette smoking.

b) The reservoir structure:

The medication reservoir in this device is sandwiched between an a rate-controlling membrane and an impermeable backing layer. Only the rate-controlling membrane—which may or may not be microporous—allows the medication to release. Within the medication reservoir section, the medication can be distributed in the form of a gel, suspension, solution, or a strong matrix of polymers. The hypoallergenic polymer adhesive can be utilized as a polymeric membrane on the exterior that is compatible with medication.

c)The matrix system



i. Drug-in-adhesive system: In this kind, the drug is dispersed in an adhesive polymer to form the drug reservoir, and then using solvent casting to disperse the medicated sticky polymer or melting on an impermeable backing (hot-melt adhesives, for example) stratum. Unmediated sticky polymer films atop the reservoir are used with the intention of protecting.

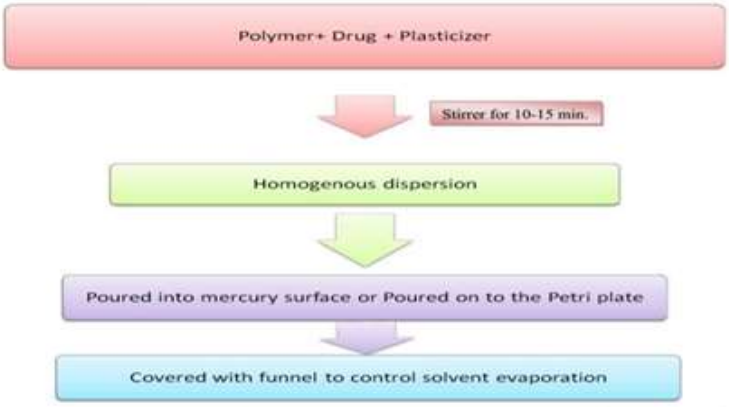
ii. Matrix-dispersion system:

This kind distributes the medication uniformly in a polymer matrix that is lipophilic or hydrophilic. This polymer disk holding medication is attached to an occlusive baseplate in a compartment made of a backing layer impenetrable to drugs. Rather than utilizing the adhesive on the medication reservoir's face, it is dispersed around the perimeter to create an adhesive rim strip.

d)Micro reservoir system:

This kind of drug delivery system combines a matrix-dispersion technology with a reservoir. The drug reservoirs created initially by suspending the medication in a water-soluble aqueous solution polymer, followed by evenly distributing the mixture in a lipophilic polymer to create hundreds of tiny, inaccessible drug reservoir spheres. As soon as possible, the thermodynamically unstable dispersion is stabilized by cross-linking the by employing cross-linking agents to polymer in situ.

There are several ways to prepare the TDDS:



Asymmetric TPX membrane technique, including:

Heat sealable polyester can be used to create a prototype patch. Film having a 1 cm diameter concave will be utilized as the membrane at the back. A sample of the drug is poured into concave membrane, which is shielded by TPX poly- asymmetric membrane (methyl-1-pentene), and sealed through an adhesive.

Teflon mold technique in a circle:

Polymer solutions in different ratios are employed in an organic solvent. Determined quantity of medication dissolves in half the amount of the same natural soluble. Boosters within distinct Concentrations dissolve in the opposite half of the natural solvent and continued after that. Di-N To drugs, butyl phthalate is added as a plasticizer. polymer mixture. The entirety of the material must be 12 hours of stirring, followed by a circular pour Teflon mold. The molds are set up on a level surface. surface and placed an inverted funnel on top of it to regulate the vaporization of solvents in a laminar flow hood model at a speed of 1/2 m/sec. For twenty-four hours, the solvent is left to evaporate. Prior to assessment for a further twenty-four hours, the dried films must be kept at 25±0.5 ℃ in a silica gel-filled desiccator prior to reverse the symptoms of aging. These kinds of Films must be assessed within a week following release getting ready.

Mercury substrate method:

In this technique, the medication and plasticizer are dissolved in a polymer solution Stir the aforementioned mixture for ten to fifteen minutes. generate a uniform dispersion and add to a Mercury surface was flattened and covered with an inverted funnel. to regulate evaporation of a solvent

Using the "IPM membranes" approach:

This approach involves dispersing the medication in a solution of water and propylene glycol that contains carbomer. 940 polymer and swirled in a magnetic field for 12 hours stirring agent. It is necessary to neutralize and make the dispersion made viscous with the use of triethanolamine. Reserve To create solution gel, pH 7.4 can be utilized. If a medication is highly soluble in an aqueous solution, bad. The gel that has developed will be added to the IPM membrane.

"EVAC membranes" method:

Polyethylene (PE), ethylene vinyl acetate, and 1% Carbopol reservoir gel are needed to prepare the target transdermal therapeutic system. membranes made of EVAC copolymer can be utilized as rate regulate membranes. Should the medication not dissolve in water, The gel is prepared using propylene glycol. Drug is dissolved in Carbopol resin and propylene glycol. will be mixed with the a forementioned mixture and neutralized by utilizing a sodium hydroxide solution 5% w/w. The medication (in gel form) is applied to a backing layer sheet that covers the designated area. A rate-limiting over the gel, a membrane is applied, and the edges are sealed with heat to create a leak-proof apparatus.

Proliposome preparation:

of TDDS with the use of the carrier approach is used to prepare the proliposomes. employing the film deposition method. From the previous reference medication and lecithin in a 1:2 ratio can be employed as an ideal proportion. Proliposomes are what made by consuming 5 mg of powdered mannitol in a 100 ml round-bottom flask maintained between 60 and 70 °C, and the flask rotates between 80 and 90 rpm and vacuum-dried the mannitol for thirty minutes. Following drying, the water bath's temperature is set between 20 and 30 °C. Lecithin and drugs are dissolved in an appropriate blend of organic solvent.

A half-milliliter aliquot of the organic solution is filled the flask with a circular bottom at 37 °C. including mannitol following thorough drying It is necessary to add the second aliquot (0.5 ml) of the solution. Following the final loading, the flask holding. A lyophilized is used to link proliposomes, and subsequently, powdered mannitol with medication loading Overnight, (proliposomes) are kept in desiccators. Then after that, sieved using 100 mesh. The gathered the powder is placed inside a glass bottle and kept there. up till characterization, at the freezing temperature.

The free film method:

It involves casting cellulose acetate onto a surface containing mercury. It is necessary to create a 2% w/w polymer solution using chloroform. Plasticizers must be added gradually. 40% weight/weight concentration of the polymer. Five milliliters A glass ring containing a solution of polymer was filled with is put in a glass petri dish with the mercury surface facing upward. The solvent's rate of evaporation is regulated by putting the petri dish on top of an inverted funnel. The movie formation is detected through surface observation of Mercury. once the solvent has fully evaporated. The parched film shall be kept separate and in between the sheets of Store wax paper in a desiccator until needed. Free movies of Various thicknesses can be produced.

Condition in which Transdermal patches are used:

Because transdermal patches may administer medication through the skin, they are employed for a variety of medical ailments. Typical circumstances include the following:

1. Severe Pain: Fentanyl patches are used to treat chronic pain.
2. Hormone Replacement Therapy: Menopausal symptoms are treated with estrogen patches.
3. Nicotine addiction: Using nicotine patches to stop smoking can be helpful.
4. Cardiovascular Conditions: Angina is treated with nitroglycerin patches.
5. Motion Sickness: To avoid nausea, apply scopolamine patches.
   Buprenorphine patches are used in the treatment of opioid addiction.
6. Migraine: Medication for migraine relief can be applied with specific patches.
7. Depression and anxiety: Certain patches provide anxiolytics or antidepressants.

How to apply patches on skin surface:

When applying the transdermal patch, use caution. It is important to clean the area of skin completely before placing the patch. The patch shouldn't be cut because

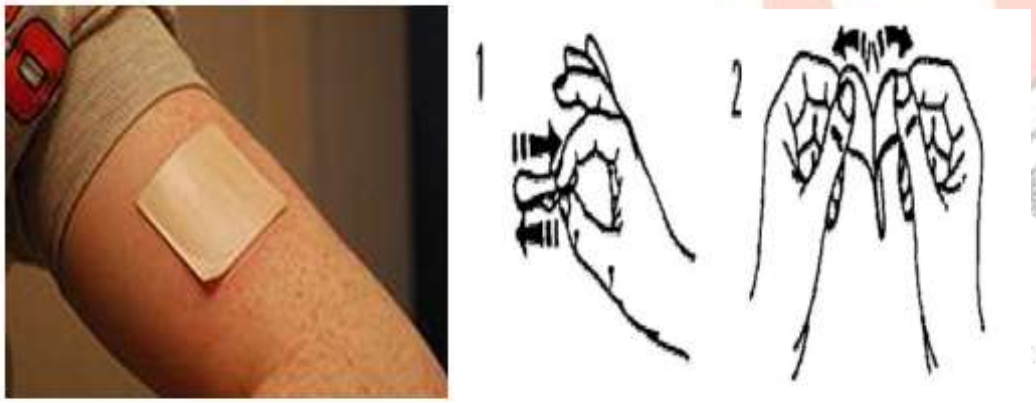


Fig 4: Instructions to apply transdermal patches

doing so will ruin the medication delivery system. Before applying a fresh patch, make sure you remove the previous one from the website. Patch. It's important to use caution when applying or taking off the patch is necessary because anyone handling it could absorb it. The administration site should receive a precise application of the fix. To prevent skin irritation, it's crucial to utilize a fresh application site each day.

The following rotation is advised:

Day 1: Upper right arm

Day 3: Left upper chest.

Day 2: upper chest right

Day 4: Left upper arm; then, carry over from Day

Therapeutic agent	TDDS	Design
Clonidine	Catapres-TTS (Boehringer Ingelheim	Four layer patch
Estradiol	Estraderm(Novartis)	Four layer patch
Estradiol	Vivelle(Novartis)	Three layer system
Estradiol	Climara (Novartis)	Three layer system
Fentanyl	Duragesic (Janssen)	Four layer system
Nicotine	Prosstep (Lederie)	Multistep round patch
Testosterone	Testoderm (Alza)	Three layer patch
Nicotine	Habitrol (Novartis Consumer)	Multilayer round patch
Nicotine	Nicoderm CQ (Smithkline Beecham Consumer)	Multilayer rectangular patch
Nicotine	Nicotrol (McNell Consumer)	Multilayer rectangular patch

Table no 2: Examples of Marketed TDDS.

Parameters for Evaluation

1. **The patch's thickness**

The drug-loaded patch's thickness is expressed in various points by utilizing the average thickness and a digital micrometer. The standard deviation is calculated to guarantee that the ready-made patch. Transdermal film thickness is established via dial gauge, screw gauge, or micrometer for a moving microscope at several scenes in the movie

2. **Uniformity of weight**

The created patches must be dried for four hours at 60°C. prior to testing. A designated patch area needs to be cut in various patch sections and digitally weighted equilibrium. The standard deviation and average weight Values must be computed using each weight separately.

3. **Capacity to fold**

An area-specific strip is to be cut uniformly, then folded in the same spot repeatedly until it breaks. How many times the movie might be being folded in the same spot without cracking, reveals the worth of the folding

4. **Moisture Content**

Each film was weighed separately and stored in a desiccator that held 10 grams of calcium. chloride for 24 hours at 37 ^{0}C as a desiccant. The Once more, each film was weighed separately and once more until it displayed a steady weight. The ultimate weight was recorded in the event that their further variation in the weight of each movie. The moisture content % was computed as the difference between the starting and ultimate weight in relation to ultimate weight

5. **Drug content**

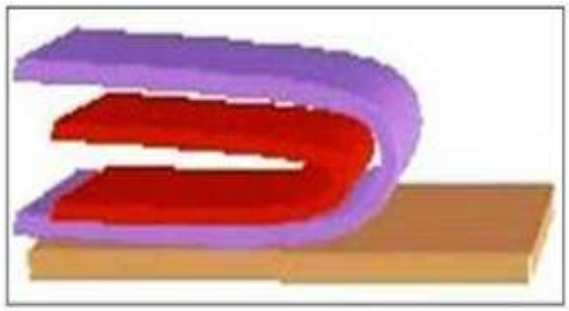
The patch should be dissolved in a precise volume of solvent. The solution will be filtered via a filter. medium and evaluate the drug contained with the appropriate method (UV).

Alternatively, you can use HPLC. Each number is the average of three different Samples

6. **Skin irritation.**

Skin irritation tests were conducted on healthy male rabbits weighing 2-3.5 kg. USP adhesive tape was utilized as a control patch. The transdermal films measured 6.1544 cm2. Used as test samples. A study was undertaken. on rabbits' unabraded skin; the control patch. was placed on the rabbit's left dorsal surface The test formulations were placed on the same side of the right dorsal surface of the rabbits. The patches were removed after 24 hours. Using an alcohol swab, the skin was inspected for any erythema or oedema.

7. **Peel Adhesion Test.**



Peel adhesion refers to the force required to remove an adhesive coating from a substrate during testing. The Molecular Weight of the sticky polymer, the type and amount of additives are Variables that influenced peel adhesion qualities. A single. Tape is put on a backing membrane or a stainless-steel plate choice The tape is peeled from the substrate at a 180º angle. The force required to remove the tape is measured at one.

8. **Water Vapour Permeability (WVP) Evaluation.**

Water vapour permeability is determined by a Natural air circulation oven. WVP can be determined.

Shaila et al. (2006) used the following formula:

WVP == W/A.

Where, WVP is represented in g/m2 per day, and W is the amount of vapor permeated through the patch. given in g/24 hours, A is the surface area of the Exposure samples expressed in square meters.

9. **Flatness test**

Three longitudinal strips were cut from each film at different portion like one from the center, other one from the left side, and another one from the right side. The length of each strip was measured, and the variation in length because of non-uniformity in flatness was measured by determining percentage constriction, with 0% constriction equivalent to 100% flatness (Lec et al., 1991).

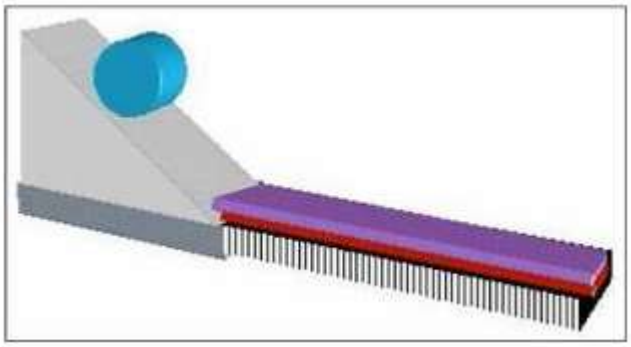
Constriction (%) = I1 - I2 × 100 I1 Where, I1 = initial length of each strip.

I2 = final length of each strip.

10. **Percentage elongation break test**

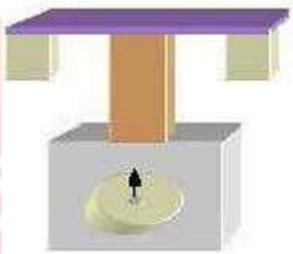
The percentage elongation break was determined by noting the length just before the break point and determined from the formula (Lech et al., 1991). Elongation percentages = L1 - L2 / L2 × 100 Where L1 = final length of each strip; L2 = initial length of each strip.

11. Rolling ball tack test



This test measures the softness of a polymer that relates to talk. In this test, stainless steel ball of 7/16 inches in diameter is released on an inclined track so that it rolls down and comes into contact with horizontal, upward facing adhesive. The distance the ball travels along the adhesive provides the measurement of tack, which is expressed in inch.

12. Probe Tack test



In this test, the tip of a clean probe with a defined surface roughness is brought into contact with adhesive, and when a bond is formed between probe and adhesive. The subsequent removal of the probe mechanically breaks it. The force required to pull the probe away from the adhesive at fixed rate is recorded as tack and it is expressed in grams.

13. **Drug release in vitro studies.**

The paddle over disc method (USP apparatus V) is used to assess the drug release from prepared patches. Dry Films of known thickness have to be cut into definite shapes and weighed. and attached to a glass plate with adhesive. A glass plate is then Place in 500 mL of the dissolving medium or phosphate buffer. (pH 7.4) and the equipment is equilibrated to 32±0.5°C. The paddle is then placed at a distance of 2.5 cm from the glass plate and operated. At a speed of 50 rpm. Samples (5-mL aliquots) can be drawn at appropriate time intervals up to 24 hours and tested by UV. spectrophotometer, or HPLC.

14. **In vitro skin permeation studies.**

To conduct an in vitro permeation investigation, use diffusion cells on male Wistar rats' thick abdomen skin. weighing 200 to 250 grams. Hair from the abdominal area is the dermis layer was carefully removed with an electric clipper. The side of the skin was thoroughly washed with distilled Water to remove any clinging tissues or blood vessels. Equilibrated for an hour in the dissolving medium or before beginning the experiment, prepare a phosphate buffer at pH 7.4. It was placed on a magnetic stirrer with a tiny Magnetic needle for even distribution of the diffusant. The temperature of the cell was kept at 32 ± 0.5°C. Using a thermostat-controlled heater.

15. **Stability studies**.

To conduct stability studies, follow ICH guidelines and store TDDS samples at 40±0.5°C and 75±5% RH for 6 months. months. Samples are withdrawn after 0, 30, 60, 90, and 180 days. and assess appropriately for the drug content

Recent enhancements to TDDS technology.

1. **Microfabricated microneedles**:

These are devices that Are hybrids of the hypodermic needle and Transdermal patch through the use of microscopic needles capable of delivering the medication Effectively (as a hypodermic needle). Their Small size gives the potential benefits of transporting big molecules through the stratum corneum without causing severe pain to the sufferer Several varieties of microneedles have been studied, including in-plane and out-of-plane, hollow, solid, microporous, dissolving, and swelling.

2. **Macro flux:**

These devices are around 8cm in size and have 300 micro projections per cm2, each with a length of 1 micron. Projection less than 200 μm. There have been three types of Macro flux. It is designed. They include: Dry-coated Macro flux system is utilized for a short period. delivery consists of micro projection array covered with A medication was bonded to an elastic polymer adhesive backing. D-TRANS Macro flux system (also for short) duration administration that includes a micro projection. array coupled with a medication reservoir. The E-TRANS Macro flux system is for on-demand. delivery using a micro projection array coupled has an electric transportation system.

3. **Iontophoresis**

The procedure involves delivering a little amount of electricity (few milliamperes) through the skin to a specific location while the electrode stays in place. Contact with the formulation that will be delivered. Pilocarpine administration can be considered an example to induce Sweat in the diagnosis of cystic fibrosis and Iontophoretic The administration of lidocaine is seen to be a good strategy. for the quick onset of anesthesia.

4. **Ultrasound**

This procedure involves combining the pharmacological substance with a coupling agent (often with gel, cream, or ointment). This causes the mechanism to transfer ultrasonic energy. The skin. This entails rupturing the lipids in stratum cornea, which permits the medication to penetrate via the biological barrier.

Future Perspectives:

TDDS technology is generally recognized as a tool for mass dissemination. This makes it the favored medication injection. Modality for transdermal administration across skin types. while blocking first-pass metabolism and other sensi. Activities linked with varied alternative drug administration routes. Various devices including TDDSs can contain medications. be injected into the bloodstream via the skin. Drugs are normally given consistently and safely through TDDS are safe and stable against biochemical modifications. cations until they reach their intended tissue. TDDS is non. intrusive, nonallergenic, with a fixed duration and dose Delivery mechanism that provides for uniform dispersion. of medications at approved and regulated dosage Therefore, the TDDS is growing rapidly in the pharmaceutical field. Ten years ago, the nicotine patch revolutionized smoking cessation. Patients were previously treated with nitroglycerin for angina and clonidine for hypertension. Scopolamine for motion sickness, and estradiol for Estrogen insufficiency is treated entirely with patches. At that at the time, biotech medicines were still in development. Over the previous ten years, the number of medications Formulated in the patches has barely increased, and there has been little change in the composition Patchwork systems. Modifications have been primarily Limited to material enhancements. The rationale is that only a small number of medications fit the molecular weight and potency requirements for Transdermal absorption.

Conclusion:

Transdermal medication delivery is a modern technology that extends beyond sticky patches. Due to recent Advances in technology and the inclusion of the medicine into the site of action without disrupting the skin membrane. This page provides essential information on transdermal drug delivery systems and its review procedure, making it a useful reference for the research scientists participating in TDDS. The following demonstrates that TDDS have considerable potential. having the ability to use both hydrophobic and hydrophilic active substance into promising Deliverable medications. To maximize the medication delivery. system, improved comprehension of the various Mechanisms of biological interactions with polymers Are essential. TDDS is a realistic and practical use as the next generation of pharmaceutical delivery system.

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