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A Review on Transdermal Patches.

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ABSTRACT:

In order to overcome the difficulties associated with administering medication, especially orally, the application of medication transdermal administration technique Was developed . Transdermal patches are an a sticky patch that has been medicated and put to the skin to provide a certain dosage delivering medicine transdermally into the bloodstream. It promotes the healing process when a body part is injured. By using a membrane that is permeable to cover a supply of medicine or by liquefying small layers of drugs imbedded within the glue with body heat a transdermal application allows for a managed delivery of medicine to the individual. One advantages of transdermal medicine delivery above alternative kinds of administration, like current, i.v., and i.m., or oral, is that the fix offers a regulated the drug's release.

Keywords: TDDS, Transdermal patches, Skin, Matrix, Reservoir, Systemic circulation, routes of penetration.

Introduction

Reducing adverse effects and achieving desired therapeutic benefits is the aim of pharmaceutical research[1]. Numerous methods of administration, including oral, sublingual, rectum, intramuscular, intravascular, subcutaneous, inhalation, and others, are created to accomplish this purpose.To cure a variety of diseases and ailments, the dose form is administered via the channel of administration given into the body. The various ways of administration have a substantial impact on the body's ability to absorb the active medicine. In the pharmacy, a drug's mode of administration refers to how it enters the body[2]. Despite being the most popular transport mode, oral medication has some disadvantages due to gastrointestinal Enzymes, pH, and other factors, such as first-pass metabolism and drug degradation. To solve these problems, Chien (1992), and Guy (1996), Banker (1990),it was a transdermal application or transdermal delivery device. Adhesive medication patches are placed to the epidermis in this manner to deliver therapeutically appropriate pharmaceutical doses[3]. They have numerous ingredients and come in a range of sizes. When applied to undamaged skin, they pierce skin barriers to release active chemicals into the systemic circulation. A transdermal patch designed to provide a high-dosage, long-lasting drug to the skin that diffuses into the bloodstream. There are three ways that medicines can enter the skin: a) via sebaceous glands (b) via hair follicles (C) through an air vent. Transdermal medicine transport devices apply to treat pain, angina pectoris, neurological diseases like Parkinson's disease, and quitting smoking, in addition to a range of skin conditions. [4]

The application of transdermal drugs to the skin

The biggest One of the body's organs is the skin. Though Yes, it is a masterpiece of architecture, the skin usually receives relatively little regard from its occupants. It weighs 4-5 kg, or 9–11 pounds, includes the entire body, and makes up around 7% of an average adult's total body weight. Its surface area is 1.2–2.2 m^2. The breadth of the skin scale from 1.5 to 4.0 mm. The In addition to being a metabolic organ with synthesizing, excretory, and absorptive functions, skin also serves as a sense organ. It serves as a barrier of defense against the outside world and regulates temperature significantly.[5]

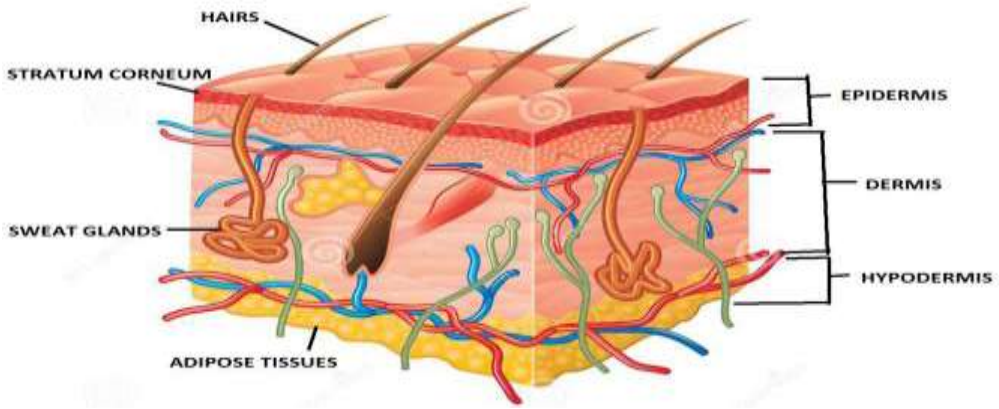


Fig no 1: Diagram of skin.

Functions of skin:

Another name for it is the integumentary system, which literally translates to "covering." The skin performs much more than just act as a big, opaque container for bodily fluids.

1. Because it maintains water and other valuable molecules in the body, it is critically necessary. It is also a miracle at preserving water out of the skin's structure.
2. It shields the whole body made of mechanical harm UV rays, chemical damage (from acid and base), and bumps and cuts, sunshine, and microorganisms. It also cushions and insulates the body's deeper organs.
3. Sensation: They skin has a large number of nerve endings and receptors that sense pain, pressure, temperature, and other stimuli.
4. Body temperature regulation: Sweat evaporating from the exterior of the skin return a higher-than-normal body temperature in reaction to high temperatures or vigorous exercise. Alterations in the blood supply to the skin further aid in controlling body condition.
5. Resistance : It transfers immunological data acquired when processing antigens to the relevant lymphatic tissue affector cells.
6. Excretion: Sweat, sebaceous secretions, and apocrine gland secretions are exocrine secretions that facilitate excretion. These excretory secretions are being used to identify specific blood disorders.[6]

Transdermal drug delivery system or (TDDS) :

They seems to exist a painless method of delivering medication to the circulation throughout the body when applied to unbroken skin. Research and interest in the area of transdermal delivery have rapidly increased [5]. When applied to intact skin, a A discrete dose form that is self-contained is the transdermal medication delivery system that delivers the medication to the systemic circulation at a controlled pace via the skin [6]. Drug delivery systems applied topically (TDDS), sometimes Known as patches, these dosage forms are meant to distribute a medicinal effective quantity of medication into the patient's skin. An advantage over injectables and oral methods is transdermal administration.through preventing first pass metabolism and boosting patient compliance [7]. When Transdermal Scope was established in 1980, it included the drug Scopolamine to alleviate motion sickness. The transdermal device is a membrane-moderated system. The membrane in this technology is made of a microporous polypropylene sheet. The drug reservoir is created by dissolving the medication in a mixture of mineral oil and polyisobutylene. This research release is available for three days at a time. [8]

Transdermal medication delivery system type :

1. Adhesive System Drug with One Layer:

They kind of film has an clinging layer that includes the medication. Furthermore to securing the many layers and the system as a whole to the skin, the adhesive layer is responsible for releasing the medication. Both a temporary and permanent liner encircle the adhesive layer.

2. System of Reservoirs:

The medication is kept in this system's reservoir, which is encircled by a membrane that controls flow rate and a backing layer. Additionally, a membrane with a microporous rate allows the medication to be discharge command The medication may be distributed through a gel, suspension, solution, solid polymer matrix, or reservoir section.

The matrix system There are two types of this system:

a) Substance within the matrix framework :

The medication is first scattered in the polymer that sticks.The polymer adhesive with medication is next spread either solvent casting, or melting the glue over an impermeable backing layer in the case of hot-melt adhesives, therefore forming

B) System of Matrix Dispersion:

They technique disperses the medication consistently using a matrix of hydrophilic or lipophilic polymers. This also comprises polymer, in addition The medicine is secured to an occlusive base plate within a drug-resistant support layer compartment. They method distributes the sticky around the edge of the drug reservoir rather than apply.

Micro-Reservoir System:

It is uniformly dispersing Its Storage systems and matrix-dispersion are combined in this system. This technique produces millions of impermeable, microscopic drug reservoir spheres by suspending the medication in an aqueous solution of a lipophilic polymer that is soluble in water. [10,11,12]

Transdermal patch

An adhesive patch that has been medicated and placed to the skin to allow a prescribed dosage of medication to enter the bloodstream through the skin is called a transdermal patch. When medication input is no longer desired, this technology allows the drug therapy to be discontinued immediately. The technique makes it possible to reduce dosage frequency, which is particularly beneficial for a substance having a brief half-life in biology. The basic function of human skin affects transdermal medication delivery, hence posing restrictions. Many Drugs can be applied topically. As an example, the transdermal technique is presently utilized for scopolamine patches to prevent motion sickness and fentanyl patches to treat cancer pain or chronic pain syndromes.[13,14]

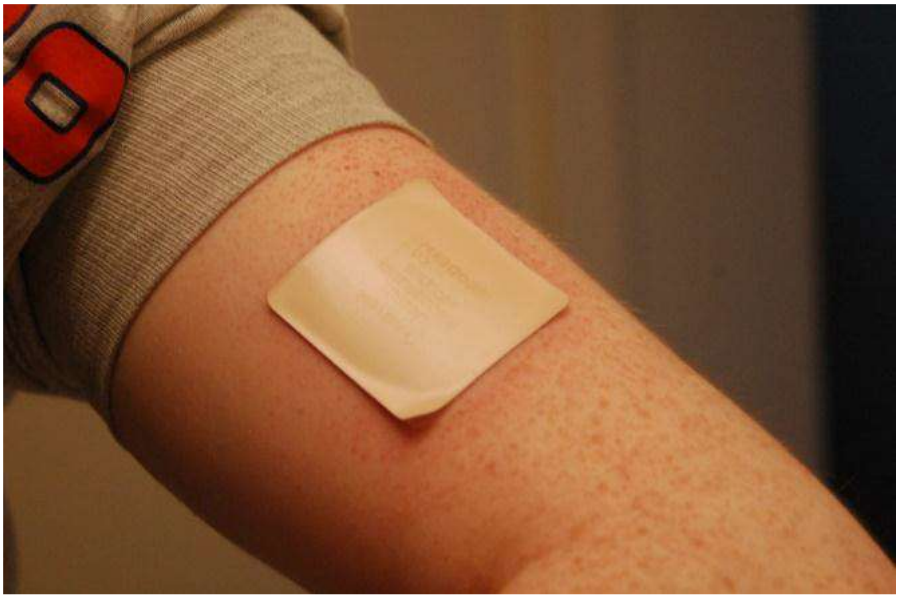
Advantages of transdermal patches

- Enhanced systemic bioavailability due to leaving out of the first hepatic metabolism.
- Give a continuous pharmacological infusion for an extended period of time.
- no disruption of the intestinal and stomach juices.
- Because the streamlined drug schedule is non-invasive, painless, and easy to use, it improves patient compliance and comfort.
- Action duration lengthens and becomes predictable.
- Handling and application ease.
- When patients are unconscious or sick, it is a huge benefit.
- steady medication penetration via the skin that maintains constant plasma levels while remaining non-invasive.
- Medication therapy is a quickly ceased by taking the application off of the skin's exterior.
- Transdermal distribution can be a useful option for medications that upset the stomach because it doesn't directly affect the stomach or intestines.
- By preventing both intra- and inter-individual variance, it can improve the effectiveness of treatment.
- Transdermal patches are easily removed from the skin in the event of poisoning.
- less frequent dosage because to the prolonged action.
- There have been transdermal patches helpful within creating fresh uses for currently available medicinal.
- For those who find it difficult to take their medication orally, this is an alternate method.[15,16]

Disadvantage of transdermal patches

- The use transdermal delivery could not be cost-effective.
- It is unable to produce high blood or plasma drug levels.

- Since skin is impermeable, only strong API can be injected with this method due to drug entrance barriers.
- It is difficult for drugs with big molecular sizes to be absorbed.
- Ionic medications create problems.
- Delivering a high dose More than 10 milligrams daily can be difficult.
- Medications with high or extremely low partition coefficients are unable to go into the bloodstream.[17,18]



Transdermal device type

Adhesive patches with drugs:

This type of dose format acts as a depot for medicine replacement and is made of polymer with sticky properties. On the other hand, backing laminate is positioned above polymeric liner, which serves in order to assist prescription drugs depot.

Transdermal vapor patches:

They're made of polymer sticky layers qualities that have release of vapor characteristics, allowing fumes to be released after being seen. These films typically include flammable oils. non-invasive additionally painless, to prevent gastrointestinal (GI).

Membrane moderated transdermal reservoir patches:

The drug release rate in these kinds of systems regulates the the publication of the pharmaceuticals via a permeable polymeric cell membrane. Typically, a transdermal prescription drugs delivery device with membrane moderation has a drug reservoir with an impermeable layer of plastic or metal serving as a backing membrane, and embedded in porous polymer.[19,20]

Formation of transdermal patch

1. **DRUG**:

A drug has to possess favorable physicochemical characteristics.A drug should be strong, non-irritating, have a low melting point, a short half-life, a low molecular weight (up to 1000 Dalton), and an affinity for both lipophilic and hydrophilic substances.[21]

Sr no.	Measurement	Effects
1.	Quantity	Must be small
2.	Duration of half a life in hours	10 or lower is the ideal number**.**
3.	Molecular mass	It ought to be lower than 500.
4.	Dividend per unit	Log P (water and octanol in the -1 to 3)
5.	The permeability coefficient of skin	Not to exceed 0.5 x 10^-3 cm/h

6.	Cutaneous response	It ought not to irritate
7.	Bioavailability of oral	Must be tiny
8.	Index of therapeutics	Must be small
9.	Focus	Moment
10.	pH of saturation solubility in water	5 to 9
11.	Quantity delivered	Less than 20 mg daily

2. **Supporting layer :** It allows printing, shields the patch that was taken from the outside world, and offers assistance.

3. **Polymer:** The primary component within the system that establishes and regulates the loading of drugs, drug release rate, and appropriate patch adherence to the skin is made of polymer.

Polymer controls the medication's release from the device.

Organic polymers	**Artificial polymers**	**Artificial polymers**
Waxes, Gelatin, and Zein,, Natural Rubber, Gummis, Zein derivatives, and glucose	For example, nitrile, acrylonitrile, silicone rubber, polybutadiene, Hydrine rubber, polysiloxane, butyl rubber, styrene butadiene, Neoprene, etc.	Polypropylene and Polyethylene, Epoxy, Polyurea, Polyvinylpyrrolidone, Polyamide, Polyacrylate, and so forth.

1. **Permeation Enhancers:**

Agents known as penetration enhancers or promoters can transfer the absorption of medications from drug delivery systems onto the skin without having any direct therapeutic effects.

The flux, of medicines across the skin can be stated as.

J equals D Xdc/dx

Where C is the concentration of the diffusing species, X is the spatial coordinate, and D is the diffusion coefficient, which depends on the size, shape, and flexibility of the diffusing molecule as well as the membrane resistance.

Even if the answer for J with different membrane heterogeneities and boundary conditions can be highly complex, the following equation can be used to determine the basic ideas of flux enhancement. At first, the concentration gradient is thermodynamic.[22,23]

2. **Backing Laminate:**

It is a supportive material that resists permeability-inducing agents and drugs alike. They should be chemically compatible with the medication, adhesive, enhancer, and other excipients. Ex: Polyester, vinyl, and polyethylene films.[24]

Other excipient

Adhesives:

far, pressure-sensitive adhesive has been used to complete the transdermal device's skin attachment. The pressure Thus -sensitive adhesive can be applied to the device's face or inside its back, expanding outwards from there.

Release Liner:

Release liner stops contamination and drug loss during storage by preventing migration of the drug into the sticky layer. As a result, it is thought of as a component of the best packing material as opposed to the drug's dose form. The composition of the release liner comprises a base layer composed of either non- enclose material (fabric (paper) or occlusive material (vinyl chloride, polyethylene), as well as a layer of coating composed either Teflon or silicon. Additional components utilized for the TDDS release liner consist of metalized laminate and polyester foil.[25]

Surfactants :

It is suggested that these substances improve the transport of hydrophilic medicines along polar pathways. A surfactant's ability to alter penetration depends on its length of the hydrocarbon chain and head group. Since certain substances irritate the skin, it is necessary to strike a harmony between irritation and improvement of penetration. Anionic surfactants have a significant ability to permeate and engage in skin interaction. These polymers can

cause significant alterations once they've entered the skin. It is said that cationic surfactants cause more irritation than anionic surfactants, and as skin penetration enhancers, they are no longer extensively researched. The nonionic surfactant class, out of the three basic classes, is well-studied and has a reputation for having the least irritability.[26]

PREPARATION OF TRANSDERMAL PATCHEs

i. Mercury substrate method:

Plasticizer and polymer solution are added to the medication to dissolve it. After agitating for ten to fifteen minutes to create a uniform dispersion, it is poured into a mercury surface that has been leveled and covered with an inverted funnel to prevent solvent evaporation (Wiechers 1992).In a 2006 study, Rathore et al. investigated the fabrication of terbutaline sulfate transdermal matrix patches utilizing ethyl cellulose and cellulose acetate polymer. Solvent casting was used to create the transdermal terbutaline sulphate patches using a mercury substrate. Several polymeric transdermal patches containing terbutaline sulfate were made for the current study. Studies were conducted to determine how permeability enhancers affected the drug's permeability through cellulose acetate and ethyl cellulose patches. The polymeric blends demonstrated good film-forming qualities, and the casting technique. [27,28]

ii. Asymmetric TPX Membrane Method:

This finding was made in 1994 by Berner and John. Prototype patches can be made with this method by utilizing heat sealable polyester film (type 1009, 3m) with a backing membrane that is concave and has a diameter of 1 cm. The medication is spread across a concave membrane after being coated with an asymmetric TPX [poly (4-methyl-1-pentene)] membrane and sealed with an adhesive.Either the wet or the dry inversion process is used to make them. In this, TPX is dissolved at 60 °C in a mixture of solvent (cyclohexane) and non-solvent additives to create a polymer solution. The polymer solution is kept at 40°C for 24 hours before being cast onto a glass plate. Following 30 seconds of evaporation of the casting film at 50°C, the glass plate needs to be a steady 25°C temperature. After soaking for 10 minutes, the membrane can be removed and left to air dry in a 50°C circulation oven for 12 hours.[29]

iii. "EVAC membranes" method:

Rate control membranes such as 1% carbopol reservoir gel, polyethylene (PE), and ethylene vinyl acetate copolymer (EVAC) membranes can be utilized to set up the goal transdermal treatment system. Propylene glycol is utilized if the medication is not soluble in water for the getting the gel ready. Propylene glycol is used to dissolve the drug; carbopol resin is then added to the mixture and neutralized using a 5% w/w sodium hydroxide solution. The medication (in gel form) is applied to a backing layer sheet that covers the designated area. To create a leak-proof device, a rate-regulating membrane will be placed over the gel and the borders will be sealed with heat. Friend et al. (1991) investigated the irritability of transdermal levonorgestrel delivery systems .[30]

iv. Teflon Circular Mould Method:

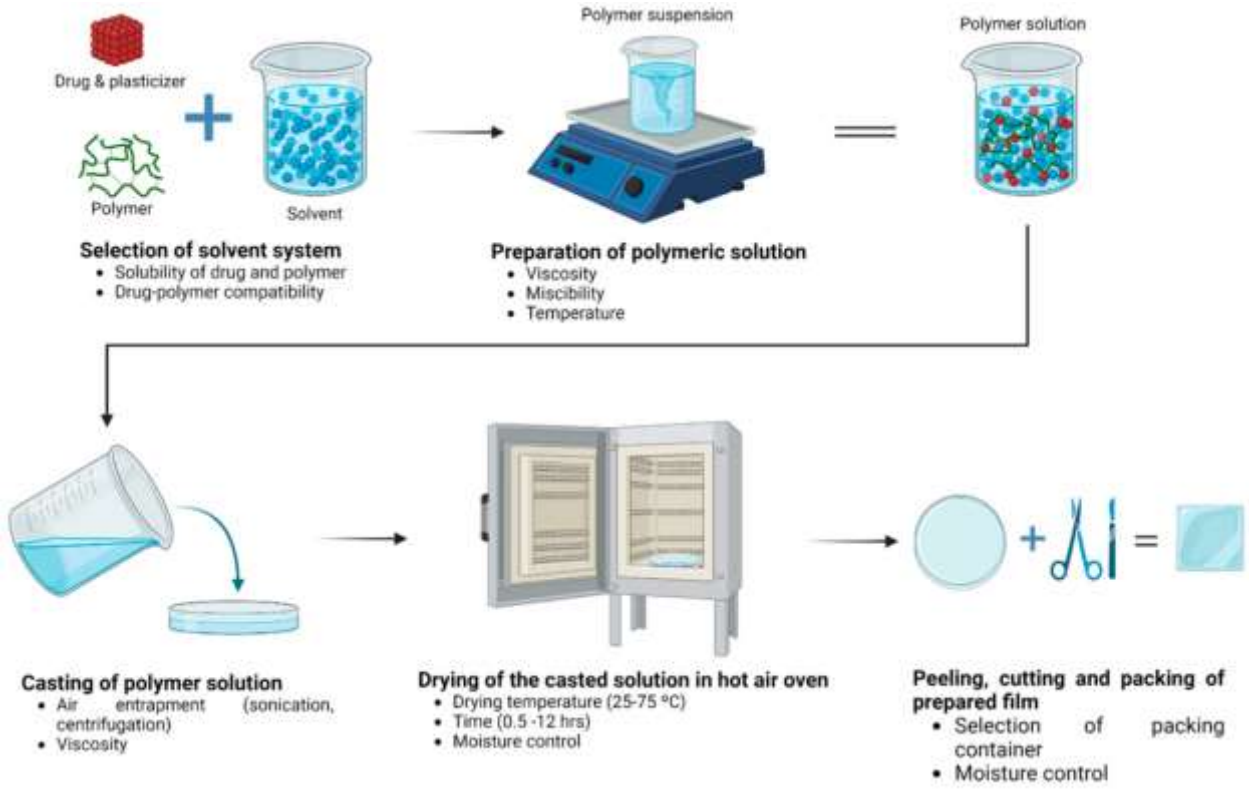
It was discovered by Baker and Heller in 1989. Polymeric solutions in different ratios are used as an organic solvent. Next, the solution is divided into two halves. One component is filled with the specified dosage of medication, while the other is filled with varying concentrations of enhancers. The two sections are then mixed together. Next, a plasticizer (such di-nbutylphthalate) is added to the drug polymer solution. Before the material is poured into a Teflon mold shaped like a circle, it must be well mixed for 12 hours. The molds need to be placed on a level platform and covered with an inverted funnel in order to control solvent vaporization in a laminar flow hood model with an air speed of 0.5 m/s. A day is twenty-four .[31,32]

v. Free film method:

Casting on a mercury surface creates a free film of cellulose acetate. Chloroform, an organic solvent, is used to produce a polymer solution (e.g., 2% w/w). The polymer solution is mixed with the plasticizer at the desired concentration (for example, 40% w/w ofweight of polymers). A glass ring that is put over the mercury surface in a glass petri dish is filled with a small volume (5 ml) of polymer solution. Covering the petri dish with an inverted funnel regulates the solvent's rate of evaporation. When the solvent has completely evaporated, the mercury surface is examined to determine the film formation. In a desiccator, the dried film is removed and kept between the wax paper sheets until needed.[33]

vi. solvent casting method:

Transdermal patches were made via the solvent casting procedure. In addition to polyethylene glycol 400 acting as a plasticizer, oleic acid and propylene glycol were employed to improve permeability. We then assessed the mechanical and physicochemical properties of the newly developed patches**.**



vii. By Using IPM Membranes method:

Using a magnetic stirrer, the medication is dissolved in a solution of water and propylene glycol that contains carbomer 940 polymers, and the combination is agitated for 12 hours. Triethanolamine is to be added to the dispersion in order to neutralize it and make it viscous. If the drug has a very low solubility in aqueous solution, solution gel can be obtained by using buffer pH 7.4. The gel that has developed can be integrated into the IPM membrane.[34]

viii. Glass Substrate method:

After allowing the polymeric solutions to expand, the necessary quantity of plasticizer and medication solution are added, and everything is mixed for ten minutes. In order to remove any trapped air, it is further put alone for a time before being poured into a dry, clean Anumbra Petri plate. To control the solvent evaporation rate, place a glass funnel upside-down over the Petri plate. The dry films are removed and kept in a desiccator overnight.[35]

ix. Solvent evaporation method : In solvent evaporation, a polymer is emulsified in an aqueous phase and then dispersed in a volatile solvent, such as ethyl acetate, dichloromethane, or chloroform. The solvent is then continuously stirred, heated to a high temperature, or evaporated using a vacuum**.**

Evaluation of transdermal patch :

1. **Drug content determination**: After breaking the transdermal patch, it is dissolved in solvent to evaluate the drug content. A particular analytical technique is then used to measure the amount of drug present in the filtrate.[36]
2. **Weight Uniformity :** Before testing, the created patches must be dried for four hours at 60°C. A particular patch section needs to be divided into several sections and weighed using a digital balance. From the individual weights, the average weight and standard deviation values must be determined[37]
3. **Patch Thickness :** The goal of this patch is to keep transdermal compositions consistent. It is ascertained by using a micrometer to measure the patch's thickness three times.[38]
4. **Folding Endurance** : Assessing the folding durability of films that are frequently folded under harsh conditions entails figuring out their folding capacity. The film is folded at the same spot repeatedly until it breaks to assess the folding endurance. The quantity of The folding endurance value () is the number of times the films could be folded in the same direction without breaking.[39]
5. **Moisture Content :** The transdermal patch's moisture loss after being stored in a desiccator can be used to compute this value. Weighed and stored in desiccators, the patch Calcium chloride for 24 hours, after which the ultimate The transdermal patch's weight is established. It is stated as a percentage:% (Initial Mass - Final Mass) / Initial Moisture Content mass times 100 [40]

6. **Moisture Uptake** : The weighing films must be stored in desiccators with saturated potassium chloride solutions that allow you to maintain a RH of 84% for 24 hours at room temperature. The films must be reweighed after 24 hours in order to calculate the percentage of moisture uptake using the formula below. [Final Weight-Initial Weight/Initial Weight] × 100 = percent moisture uptake. [41, 42]

7. **Flatness:** A transdermal patch should not tighten over time and have a smooth surface. The study of flatness can be used to illustrate this. Two strips are cut from each side of the patches and one from the center to determine the flatness of the patches. Every strip's length is measured and the % constriction is used to measure the variance in length. One hundred percent flatness is equal to zero percent constriction.[43]

8. **Tensile Strength:** The film's tensile strength was ascertained using a typical strength testing The upper is moveable and the lower is fixed. A 4-by-1-centimeter test film is placed between these cell grips, and pressure is exerted gradually until the film breaks. (30) The dial reading in kg is immediately used to determine the film's tensile power. This is how tensile strength is expressed. Tensile strength is equal to cross sectional area / tensile load at break.

9. **Water vapour transmission studies (WVT):** One gram of calcium chloride is placed into previously dried, empty vials with similar diameters to estimate WVT. Using an adhesive such as silicon adhesive grease, the polymer films are adhered to the brim and then Let it sit for five minutes. The vials are weighed precisely and put in a humidity chamber with a 68% relative humidity. Subsequently, the vials undergo repeated weighing for a period of seven days, with an increase in weight being interpreted as a quantitative indicator of the amount of moisture transferred via the patch.[44]

10. **Stability Studies:** The patch is kept at 40 ± 0.5 °C and 75 ± 5% relative humidity to ensure stability. Drug analysis is performed on samples throughout storage at intervals of 0, 30, 60, 90, and 180 days.material to provide insight into the stability of the product.[45]

11. **Swellability:** To measure this transdermal patch property, place a known weight in a Petri plate filled with 50 mL of pH 7.4 phosphate buffer. The sample absorbs over the course of around 30 minutes.

12. **skin irritation study** : Sensitization and irritation of the skin Healthy bunnies (average weight 1.2 to 1.5 kg) can be checked out. The rabbit's dorsal surface (50 cm2) should be well cleaned. The hair should be removed from the clean surface by shaving, and the surface can then be cleaned using rectified spirit and representative formulations applied to the skin. After a day, the patch is taken off. and depending on the degree of skin damage, the skin must be examined and graded into five categories.[46]

In-vitro drug release studies

The drug release from the produced patches can be evaluated using the paddle over disc method (USP equipment V). Dry films of a known thickness must be precisely shaped, weighed, and adhered to a glass plate using an adhesive. After the apparatus was equilibrated to 32±0.5°C, the glass plate was submerged in 500 milliliters of the phosphate buffer (pH 7.4) or dissolving medium.

At a speed of 50 revolutions per minute, the paddle was then adjusted to be 2.5 cm away from the glass plate. Samples (5 ml aliquots) can be taken out at appropriate intervals for up to 24 hours, and high-performance liquid chromatography (HPLC) or a UV spectrophotometer can be used for analysis. It is necessary to carry out the test.[47]

***Ex vivo* Permeation Studies**

The Franz diffusion cell is used, and the donor and acceptor compartments are divided by animal biological membranes such as the skin of a rat or pig's ear, which typically has phosphate buffer pH 7.4 in acceptor compartment with suitable magnetic stirrin supply and ambient temperature controlled at 37 ± 0.5°C.[48]

A. **Animal models:** Small-scale animal research are chosen over human studies because they don't take as much time or money. The most often utilized animal species in transdermal drug delivery system evaluations are hairless rat, dog, rhesus, and mouse, rabbit, guinea pig, monkey, etc. The current body of research indicates that, in both in vitro and in vivo settings, hairless animals are favored over hairy animals.[49]

B. **Human models** : After the patch is applied to human volunteers, the last phase of a transdermal device's development entails gathering pharmacokinetic and pharmacodynamic data. Clinical trials are carried out to evaluate transdermal systems, such as the effectiveness, associated risk, adverse reactions, and patient adherence. Phase-II clinical trials evaluate the short-term safety and primary efficacy in patients, while phase-II clinical trials primarily assess safety in volunteers. Phase-III studies demonstrate the safety and efficacy in a sizable patient population, while phase-IV studies are conducted for marketed patches as part of post-marketing surveillance to identify adverse medication reactions. Even though they need a lot of money, human studies are the most effective way to evaluate a drug's effectiveness.[50,51]

Marketed Products:

BRAND NAME	ACTIVE INGREDIENTS	INDICATION	MANUFACTURER
NICODERM	nicotine	Giving up smoking	GlaxoSmithKline

TESTODERM	Testimonials	Low testosterone levels	Mountain View, Alza
LIDODERM	Lido cane	Pain from post-herpetic neuralgia	Endo Pharmaceuticals
HYTROTROL	oxybutynin	bladder hyperactivity	Watson Pharmaceutical
EMSAN	Selegiline	severe depression	Squibb Bristol-Myers
TRANSDERMSCOP	scopolamine	shaky motion	Consumer Health Novartis
TRANSDERMNITRO	nitroglycerin	Pectorile angina	Novartis
TATS-CATAPRESS	Clonidine	High blood pressure	Ingelheim Boehringer
ESTRADERM	Estradiol	symptoms of menopause	Novartis

Adverse events :

- The FDA declared in 2005 that it was looking into reports of fatalities and other severe side effects associated with opiate overdose in patients taking Duragesic, a transdermal patch containing fentanyl, for pain relief. Later, in June 2005, the Duragesic product label was revised to include safety information.[52]
- The makers of the Daytrana ADHD patch, Shire and Noven Pharmaceuticals, announced a voluntary recall of multiple lots of the patch in 2007 because of issues releasing the patch from its protective release liner. Since then, there have been no reports of any further issues with the patch or its protective packaging.[53]
- A manufacturing flaw that allowed the gel containing the drug to leak out of its pouch too quickly led to a recall of the fentanyl patch in 2008 by two manufacturers: Sandoz and ALZA Pharmaceuticals, a division of large medical manufacturer Johnson & Johnson. This could have resulted in an overdose or even death.[54]
- Transdermal medication patches with metallic backings have the potential to cause burns during MRI scans, according to a 2009 public health advice issued by the FDA. It is recommended that patients take off any medicated patches before having an MRI and replace them with fresh ones when the scan is finished.[55]

Conclusion:

Drug delivery via TDD devices has proven to be painless, efficient, non-toxic, and patient-compliant. The creation of a reliable method for NSAID transdermal delivery could boost local soft tissue and joint concentrations, as well as lessens the adverse effects of oral administration. A range of NSAID medications can be used to treat different types of skin conditions, however not all NSAIDs can be administered in this way due to their physicochemical characteristics, which are crucial for transdermal drug delivery. Consequently, in the case of NSAIDs, it is necessary to investigate the possibilities of this administration method.[56,57]

Reference:

1. Namdeo A; Garud N; Guard A. *Int. J. Drug Delivery*, **2012**, 4,470-476.
2. Verma P; Thakur AS; Deshmukh K; Dr.Jha AK; Verma S. *Int. J. Pharm. Study & Res*., **2010**, 1, 54-59
3. Vandana Yadav, Sipia Altaf Bhai M, Mamatha Y, Prashant VV (2012) Transdermal Drug Delivery System: A Technical Writeup. Journal of Pharmaceutical & Scientific innovation .
4. P K Gaur, S Mishra, S Purohit, K Dave (2009) Transdermal Drug Delivery System: AReview. Asian Journal of Pharmaceutical and Clinical Research 14-20.
5. Mzrieb EN. Human anatomy and physiology. 6thedition, India, Dorling Kindersley Pvt.Ltd, **2006**; 152-15
6. Freedberg IM, Eisen AZ, Wolf K, Austen KF, Goldsmith LA, Katz SI. Fitzpatrick's dermatology in general
7. medicine, 6thedition, Vol-1, Mc Graw-Hill Medical publishing division, **2003**; 58-85
8. Pastore MN, Kalia YN, Horstmann M, Roberts MS. Transdermal patches: History, development and pharmacology. British Journal of Pharmacology. 2015. 2015 May;172(9):2179-2209
9. Reddy YK; Reddy DM; Kumar MA. *Indian J. Res. Pharm. Biotechnol*., **2014**, 1094-110
10. Shingade GM; Quazi1 A**;** Sabale PM; Grampurohit ND; Gadhave MV; Jadhav SL; Gaikwad DD. *J. dru delivery Ther*. **2012**, 66-75.
11. Chowdary K.P.R and Naidu R.A.S, Transdermal Drug Delivery, A Review of Current Status, Indian Drugs, 1995; 32: 414- 422 .

12. Saurabh Pandey, Ashutosh Badola, Ganesh Kumar Bhatt, Preeti Kothiyal (2013) An Overview on Transdermal Drug Delivery System. International Journal of Pharmaceutical and Chemical sciences 2(3).
13. P K Gaur, S Mishra, S Purohit, K Dave (2009) Transdermal Drug Delivery System: AReview. Asian Journal of Pharmaceutical and Clinical Research 2(1): 14-20.
14. Dhiman S; Thakur GS; Rehni AK. *Int. J. Pharm. Pharm. Sci.*, **2011**, 3(5), 26-34
15. Shingade GM; Quazi1 A**;** Sabale PM; Grampurohit ND; Gadhave MV; Jadhav SL; Gaikwad DD. *J. drugdelivery Ther*. **2012**, 2(1), 66-75
16. Dhiman S; Thakur GS; Rehni AK. *Int. J. Pharm. Pharm. Sci.*, **2011**, 3(5), 26-34.
17. Sun L, Cun D, Yuan B, Cui H, Xi H, Mu L, et al. Formulation and in vitro/in vivo correlation of a drug-in-adhesive transdermal patch containing azasetron. Journal of Pharmaceutical Sciences. 2012 Dec;101(12):4540-4548.
18. Raghuraman V, Pandey VP. Approaches And Significance Of Transdermal Drug Delivery Systems: A Review. International Journal Of Pharmaceutical Sciences And Research. 2014 Feb;5(2):340–345.
19. Sandhu P; Bilandi A; Kataria S; Middha A. *Int. J. Res. Pharm. Chem.* **2011**, 1(40), 1139-1151.
20. Sugibayashi K; Morimoto Y. *J. controlled Release*, **1994**, 29, 177-185.
21. Arora A; Prausnitz MR; Mitragotri S. *Int. J. Pharm*., **2008**, 364, 227-236
22. Hemangi J, Patel, Jitendra S, Patel, Keyur D, Patel, Transdermal Patch for Ketotifen Fumarate as Asthmatic Drug, IJPR, 2009; l(1): 1297-1304
23. Shalu Rani, Kamal Saroha, Navneet Syan, Transdermal Patches a successful tool in Transdermal Drug Delivery System: An overview, Der Pharmacia Sinica, 2011; 2(5): 17-29.
24. K Ezhumalai, P Ilavarasan, R Murali Mugundhan, U Sathiyaraj, AN Rajalakshmi (2011) Transdermal Patches in Novel Drug Delivery System. International Journal of Pharmacy & Technology 3(2): 2402- 2419.
25. Chowdary K.PR and Naidu R.A.S, Preparation and Evaluation of Cellulose Acetate Films as Rate Controlling Membranes for Transdermal use, Indian Drugs, 1991; 29(7): 312-315.
26. Azhar Ahmed, Nirmal Karki, Rita Charde, Manoj Charde, Bhushan Gandhare, Transdermal Drug Delivery Systems, An overview, International Journal of Biomedical and Advance Research, 2011; 02(01): 38-56.
27. Jeans CW, Heard CM, A therapeutic dose of primaquine can be delivered across excise human skin from simple transdermal patches, Int J Pharm, 1999,189(1),1-6.
28. Xi H, Yang Y, Zhao D, et al. Transdermal patches for site-specific delivery of anastrozole: In vitro and local tissue disposition evaluation, Int J Pharm, 2010,391(1-2),73-78
29. Willams AC, Barry BW, Penetration Enhancers, Adv Drug Del Rev, 2004, 56, 603-618.
30. Tsai JC, Guy RH, Thornfeldt CR, Gao WN, Feingold KR, Elias PM, MetabolicApproaches to Enhance Transdermal drug delivery, J Pharm Sci, 1998, 85,643-648
31. Nikhil Sharma, Bharat Parashar, Shalini Sharma, Uday Mahajan (2012) Blooming Pharma Industry with Transdermal Drug Delivery System. Indo Global Journal of Pharmaceutical Sciences 2(3): 262-278.
32. Nikhil Sharma, Bharat Parashar, Shalini Sharma, Uday Mahajan (2012) Blooming Pharma Industry with Transdermal Drug Delivery System. Indo Global Journal of Pharmaceutical Sciences 2(3): 262-278 .
33. Kalantaridou SN, Calis KA, Mazer NA, Godoy H, Nelson LM, A pilot study of an investigational testosterone transdermal patch system in young women with premature ovarian failure, J Clin Endocrinol Metab, 2005,90(12),6549-52.
34. Dhiman Sonia (2011) Transdermal Patches: A Recent Approch To New Drug Delivery System. International Journal of Pharmacy and Pharm 3(5).
35. Levin G, Gershonowitz A, Sacks H, Stern M, Sherman A, Rudaev S, Zivin I, Phillip M,Transdermal delivery of human growth hormone through RF-microchannels, PharmRes, 2005,22(4),550-5.
36. Priya JK, Kumar PP, Begum SKS. Formulation and evaluation of clopidogrel bisulphate transdermal patches using vegetable oils as permeation enhancer. International Journal Of Pharmaceutical Sciences And Research. 2014 Feb;5(2):473–482.
37. Mutalik, N, Udupa, Glibenclamide Transdermal Patches, Physicochemical, Pharmacodynamic and Pharmacokinetic Evaluations, Journal of Pharmaceutical Sciences, 2004; 93(6): 1557-1594.

38. Mohammadpoor SA, Akbari S, Sadrjahani M, Nourpanah P. Fabrication of electrospun ibuprofen-loaded poly(vinyl alcohol)/ hyper-branched poly(ethylenimine) fibers and their release behaviors. Journal of biomaterials science-polymer edition. 2020 Jan;31(2):261–275.

39. Costa P, Ferreria DC, Morgado R, Sousa Lobo JM, Design and evaluation of alorazepam transdermal delivery system, Drug Dev Ind Pharm, 1997,23,939-944.

40. Priyanka Arora, Biswajit Mukherjee, Design Development Physicochemical and in-vitro Evaluation of Transdermal Patches Containing Diclofenac Diethylammonium Salt, Journal of Pharmaceutical Sciences, 2002; 91(9): 2076-2089.

41. Koteshwar K.B, Udupa N and Vasantha Kumar, Design and Evaluation of Captopril Transdermal Preparations, Indian Drugs, 15(29): 680-685

42. Baker W and Heller J, Material Selection for Transdermal Delivery Syste Transdermal Drug Delivery: Developmental Issues and Research Initiatives, J. Hadgraft and Eds. Marcel Dekker, Inc., New York 1989;293-311.

43. Yuveraj Singh Tanwar, Chetan Singh Chauhan, Anshu Sharma, Development and Evaluation of Carvidilol Transdermal Patches, Acta Pharm, 2007; 57: 151–159.

44. Katz NP, Gammaitoni AR, Davis MW, Dworkin RH, Lidocaine patch 5% reduces painintensity and interference with quality of life in patients with postherpetic neuralgia: an effectiveness trial, Pain Med, 2002,3(4),324-32.

45. Prabu SL, Shirwaikar AA, Shirwaikar A, Kumar A, Jacob A. Design and Evaluation of Matrix Diffusion Controlled Transdermal Patches of Diltiazem Hydrochloride. ARS Pharmaceutica. 2008;49(3):211–217

46. Pravin Gavali, Atul, Gaikwad, Radhika P.R, Sivakumar T, Design and Development of Hydroxypropyl Methylcellulose based polymeric film of Enalapril Maleate, International Journal Of Pharmtech Research, 2010; 2(1): 274-282.

47. Koteshwar K.B, Udupa N and Vasantha Kumar, Design and Evaluation of Captopril Transdermal Preparations, Indian Drugs, 15(29): 680-685.

48. Zanela da Silva Marques T, Santos-Oliveira R, De Siqueira LB de O, Da Silva Cardoso V, De Freitas ZMF, Da Silva Ascenção Barros RDC, et al. Development and characterization of a nanoemulsion containing propranolol for topical delivery. International Journal of Nanomedicine. 2018 May 14;13: 2827-2837.

49. Walker M, Dugard PH, Scott RC, In vitro percutaneous absorption studies: a comparison of human and laboratory species, Hum Toxicol, 1983,2,561–562.

50. Wester RC, Maibach HI, Percutaneous absorption: Neonate compared with adult, In:Hunt MKD, ed, Environmental factors in human growth and development, Cold Spring Harbor, New York, Cold Spring Harbor Press 1982, 3-15

51. Walker M, Dugard PH, Scott RC, In vitro percutaneous absorption studies: a comparison of human and laboratory species, Hum Toxicol, 1983,2,561–562.

52. FDA ALERT (07/2005): Narcotic Overdose and Death". Food and Drug Administration. 2005-07-15. Archived from the original on 2007-02-20. Retrieved 2007-02-24.

53. Megget, Katrina (2007-09-05). "ADHD Transdermal Patches Withdrawn". Retrieved 2010-09-28.

54. Silverman, Ed (2008-02-12). "J&J and Sandoz Recall Fentanyl Patches". Retrieved 2010-09-28.

55. "FDA Public Health Advisory: Risk of Burns during MRI Scans from Transdermal Drug Patches with Metallic Backings". Food and Drug Administration. Archived from the original on March 7, 2009. Retrieved March 9, 2009 .

56. Jones P, Lamdin R, Dalziel SR. Oral non-steroidal anti-inflammatorydrugs versus other oral analgesic agents for acute soft tissue injury.Cochrane Database Syst Rev 2020;8:CD007789.

57. Gyöngyösi A, Verner V, Bereczki I, Kiss-Szikszai A, Zilinyi R,Tósaki A, et al. Basic pharmacological characterization of EV-34, a New H2S-releasing ibuprofen derivative. Molecules 2021;26:599