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An Overview Of Transdermal Drug Delivery System

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ABSTRACT

Transdermal drug delivery system falls under the control drug delivery category aiming to administer drug through the skin a pre determine and controlled rate over extended period. Transdermal drug delivery system have several advantages such as reduced dose frequency, avoiding first pass metabolism by entering direct into systemic circulation, Suitability for elderly patient who cannot take pharmaceuticals orally and ability to be self administer with fever side effect. Multiple drug administration has several disadvantages include cannot achieve high drug level in blood, long time adherence is difficult. This review cover general aspects like drug absorption pathways through skin, different factor affecting transdermal permeability, various types of transdermal patches, components of transdermal patches, evaluation parameter. Additionally therapeutic application of transdermal drug delivery system, moreover, the articles includes various advancements in the transdermal drug delivery system.

KEYWORDS: Skin, Transdermal Patch, polymer matrix, Permeability.

INTRODUCTION:

The NDDS may involve a new dosage form e.g. from thrice a day dosage to once a day dosage form or developing a patch in place of injection. Throughout the past two decades, the Transdermal patch had become approved proven technology that offers a variety of significant clinical benefits over other dosage forms. Because Transdermal drug delivery offers controlled release of the drug into the patient, it enable a steady blood-level profile, resulting in reduced systemic side effects and, sometimes, improved efficacy over other dosage forms Transdermal drug delivery system was first introduced more than 20 years ago. The technology generated tremendous excitement and interest amongst major pharmaceutical companies in the 1980s and 90s. The first Transdermal patch “SCOPOLAMINE” was approved in 1979 prevents the nausea and vomiting associated with motion sickness. Two new recently approved transdermal patch products (contraceptive patch containing ethylene estradiol and nor-elgestromin and a patch to treat overactive bladder coating oxybutyanin).The future, regulated doses, reduced frequency of dosing, and increase patient compliance will make transdermal drug administration the preferable method. To quit smoking, nicotine patches for transdermal application were created twenty years ago. After that, various medications were developed as

transdermal patches, including Nitroglycerin for angina, estradiol for estrogen insufficiency, and fentanyl for pain.

ADVANTAGES

- Transdermal drug delivery enables the avoidance of gastrointestinal absorption with its associated pitfalls of enzymatic and pH associated deactivation.
- Avoidance of first pass metabolism.
- The lack of peaks in plasma concentration can reduce the risk of side effects, thus drugs that require relatively consistent plasma levels are very good candidate for transdermal drug delivery.
- Rapid notifications of medication in the event of emergency as well as the capacity to terminate drug effects rapidly via patch removal.
- Avoidance of gastro intestinal incompatibility.
- Avoiding in drug fluctuation drug level.
- Termination of therapy is easy at any point of time.
- Provide suitability for self administration and As a substitute for oral route.
- They are non invasive, avoiding the inconvenience of parenteral therapy.
- It is of great advantages in patient who are nauseated and unconscious.

DISADVANTAGES:

- Transdermal drug delivery system cannot deliver ionic drugs.
- It cannot achieve high drug level in blood.
- Only potent drug are suitable candidates for transdermal patch. because
- It cannot develop for drugs of large molecular size.
- It cannot develop if drug or formulation causes irritation to skin
- May causes allergic reaction and Long time adherence is difficult.
- Daily dose more than 10mg is not possible.
- Barrier function changes from person to person and within the same person.

ANATOMY OF SKIN

The largest organ: The skin is the largest organ of the human body which covers a surface area of approximately 2 sq.m. and receive about one third of the blood circulation through the body. It serve as a permeability barrier against the transdermal absorption of various chemical and biological agents. It is one of the most readily available organ of the body with a thickness of few millimeters (2.97-0.28 mm) which,

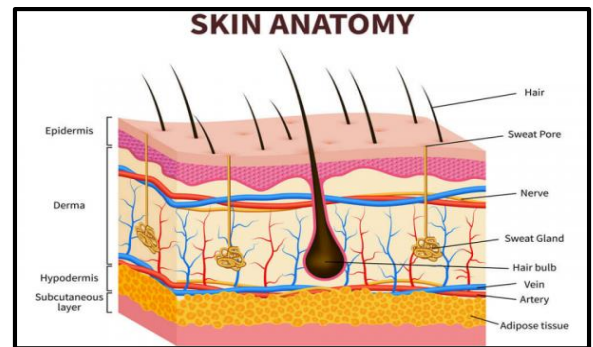
- Separates the underlying blood circulation network from the outside environment.
- Serve as a barrier against physical, chemical and microbiological attacks.
- Act as a thermostat in maintaining body temperature.
- Play role in regulation of blood pressure.
- Protect against the penetration of UV rays.
- Skin is a major factor in determining the various drug delivery aspects like permeation and absorption of drug cross the dermis. The diffusional. Resistance of the skin is greatly dependent on its anatomy and ultra structure.

SKIN

The skin is commonly categorised as into the three primary layers

- The outermost layer known as epidermis.
- The middle layer, referred as dermis.
- The innermost layer, called the hypodermis

Here is a brief overview of each layer:



Epidermis:

The epidermis constitutes the skin's outermost layer. It provides a waterproof barrier and contains no blood vessels. The cells in the epidermis include keratinocytes, which produce the protein keratin and help make the skin tough and protective. The epidermis includes melanocytes responsible for skin colour, and Langerhans cells, integral components of the immune system. The epidermis has several sub-layers, including:

1. Stratum corneum
2. Stratum granulosum.
3. Stratum spinosum
4. Stratum basale

STRATUM CORNEUM:

The stratum corneum, sometimes referred to as the horny layer, is the skin's outermost layer. It is around 10mm thick. The stratum corneum layer is the main inhibitor of drug entry.

DERMIS:

The dermis is located beneath the epidermis, which is 3 to 5 mm thick, and it is thicker than the epidermis. The dermis is an essential component of controlling body temperature and is the cutaneous blood supply. The dermis is responsible for providing nutrients to the epidermis. It comprises diverse structures, such as:-

- ◆ blood vessels
- ◆ hair follicles
- ◆ Sweat glands
- ◆ Sebaceous gland
- ◆ Nerve ending
- ◆ Collagen and elastin fibers

HYPODERMIS: It is the deepest layer of skin, consisting of adipocytes (fat cells) and connective tissue. It serves as a place to store fat. When medicines are applied to skin like cream or patches, they have to go through this layer to get into our bloodstream.

MECHANISM OF PERCUTANEOUS ABSORPTION:

Percutaneous absorption involves the passive diffusion of a substance through the skin. The mechanism of permeation can involve passages through the epidermis itself (Transepidermal absorption) or diffusion through shunts. The transepidermal pathway is principally responsible for diffusion across the skin. The stratum corneum is the barrier layer of the skin; permeation involves partitioning into the stratum corneum and permeation via the intracellular lipid route.

FICK'S FIRST LAW OF DIFFUSION:

It can be state that movement of drug molecule from the region of higher concentration to the region of lower concentration until its equilibrium.

$$J = D \frac{dc}{dx}$$

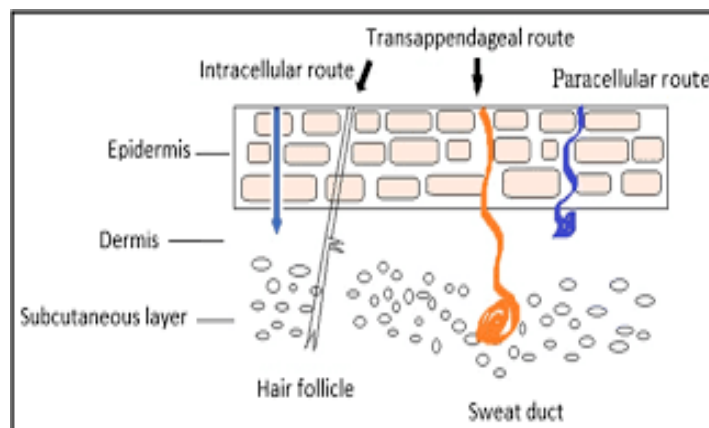
Where,

J = the mass flux

D = diffusion coefficient

C = concentration of the diffusing species,

X = Spatial coordinate.



PATHWAYS OF PERMEATION

The following are the three main drug absorption

- 1) TRANS-FOLLICULAR PATHWAY
- 2) TRANS-CELLULAR PATHWAY
- 3) INTER – CELLULAR PATHWAY

1. TRANSFOLLICULAR PATHWAY-

Tran follicular channel offers a broad area for drug diffusion and is the quickest mechanism for a medication to enter the systemic circulation. The skin has a large number of pores, sweat glands, oil glands, hair follicles, and ducts that allow them to open to the skins surface. Drug transport through these ducts is continuous across the stratum corneum, although it is impacted by several variables, including gland secretion the kind and volume of secretion. However, the Trans appendageal pathway contributes less because it only takes up 0.1% of the skins surface.

2. TRANS-CELLULAR PATHWAY

Through this system, drug is administered from corneocytes, which have a hydrophilic pathway and contain hydrated keratin. Lipids that surrounds and connect corneocytes. A drug therefore, needs several partitioning and diffusion processes. It is the route that many different kinds of medication most frequently take. The trans-cellular method allows the medicine to pass through the cytoplasm (matrix) of the cells. Hydrophilic medicine is suited for this approach. The highly hydrated keratin provides an aqueous route for hydrophilic drugs.

3. INTER-CELLULAR PATHWAY

The continuous lipid matrix that is present between the cells serves as the conduit through which medicine diffuse in this channel. The barrier nature of this pathway is due to the tortuous structure created by corneocytes, and the medication must diffuse to the inner side and partition into the lipid layer to pass through the alternating lipid and aqueous domain. It is preferred mostly for unchanged lipophilic medicines because it has been shown that water flows 50 times more quickly by this route.

FACTOR AFFECTING TRANSDERMAL PERMIABILITY:**1. Physicochemical properties of drug**

A. Partition coefficient and solubility: Water and lipid soluble drug are absorbed through the skin .If the vehicle is changed by the lipid / water partition coefficient of drug molecule may also alter. A drug molecule partition coefficient can be changed by chemical modification without affecting its pharmacological activity.

B. Drug concentration: Transdermal permeability across mammalian skin is a passive diffusion process that depends on the concentration of penetrant molecule on the skin surface.

C. PH Condition: The rate of absorption of acidic and basic drugs are affected by PH, whereas the unchanged form of drug exhibit of better penetrating capacity. Transport of ionisable species from aqueous solution is strongly dependent on PH.

2. Formulation characteristics:

A. Release rate of drug: Solubility of drug in the vehicle determines the release rate.

B. Ingredients in formulation: It affects both the rate of drug release and the permeability of stratum corneum by mixing the skin lipids.

C. Presence of permeation enhancers: Permeation enhancer interacts with structural component of the stratum corneum layer, and modifies barrier function thereby leading to increase permeability.

3. Skin physiology and pathology:

A. Hydration of skin: Transdermal permeability increases by hydration of stratum corneum although; the degree of penetration enhancement varies from drug to drug.

B. Skin temperature: Increase in skin temperature enhances the skin permeation rate.

C. Skin age: The permeability of foetal and infant skin is more than that of mature adult skin therefore, Percutaneous absorption of topical steroids is rapid in children than in adults but water permeation is same in both.

D. Blood flow: Changes in peripheral circulation can affect Transdermal absorption.

BASIC COMPONENTS OF TDDS:

The basic component of transdermal drug delivery system is:

- Drug
- Polymer matrix / Drug reservoir
- Membrane. .
- Permeation enhancers.
- Pressure -sensitive adhesive.
- Baking laminates.
- Release liner.
- Other excipients like plasticizers and solvents

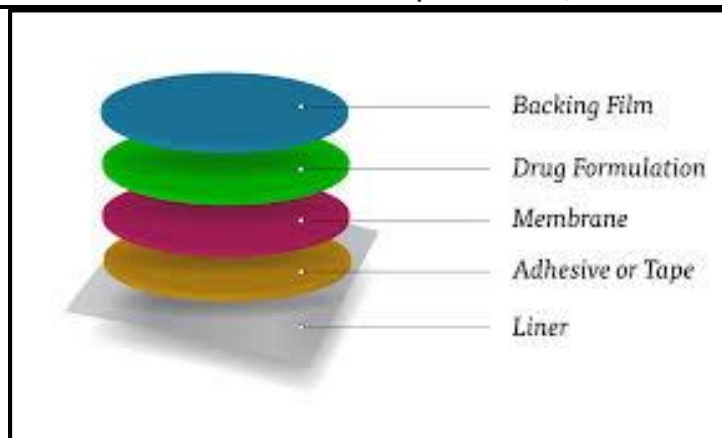


Fig. Basic component of TDDS

DRUG:

For successfully developing a TDDS, the drug should be chosen with great care. Transdermal patches offer many advantages to drugs that undergo extensive first-pass metabolism, drugs with a narrow therapeutic window, or drugs with short half-life, which cause noncompliance due to frequent dosing. The skin penetration is also affected by the structure of the drug. Skin irritation and clinical need are the other parameters that should be considered before a drug is chosen.

POLYMER MATRIX \ DRUG RESERVOIR:

Polymers are the backbone of TDDS, which controls the release of the drug from the device. A polymer matrix can be prepared by dispersion of drug in a liquid or solid-state synthetic polymer base. Polymer used in TDDS, should have biocompatibility and chemical compatibility with drug and other components of the system, such as penetration enhancers and pressure-sensitive adhesives. Additionally, they should provide consistent and effective delivery of a drug throughout the product's intended self life is should be safe.

MEMBRANE:

A membrane may be sealed to the backing to form a pocket to enclose the drug containing matrix or used as a single layer in the patches construction. The diffusion properties of the membrane are used to control the availability of the drug and/or excipients to the skin.

PERMEATION ENHANCERS:

One long-standing approach for improving TDDS uses permeation enhancer (also called as penetration enhancers sorption promoters or accelerants), which increase the permeability of the stratum corneum , to attain higher therapeutic levels of the drug candidate penetration enhancer interact with structural components of the stratum corneum thus modifying the barrier function , leading to increased permeability . **EXAMPLE:** Solvents like Ethanol, DMF, DMSO, and surfactants like sodium lauryl sulfate, pluronic F127, Pluronic F68.

PRESSURE-SENSITIVE ADHESIVES:

A pressure sensitive adhesive (PSA) is a material that help's in maintaining an intimate contact between transdermal system and skin surface. The PSA should be physicochemical and biologically compatible and should not alter drug release .The selection of adhesive based on the numerous factors, including patch design and drug formulation.

EXAMPLE: Polyacrylates, Polyisobutylene, Silicon based adhesive.

BACKING LAMINATES:

It supports and protects the transdermal patches from the external environment. To prevent drug loss, the backing membrane must be elastic, flexible, and impermeable to drug diffusion. It must be compatible with polymer, excipients and drug. It is made up of aluminium foil, polyethylene, polyester, polyvinyl-chloride, heat-sealed layer, polyurethane, and contain adhesive foam pad.

RELEASE LINER: The release liner, which is a part of primary packaging, guards against drug loss from the polymer matrix and external environment contamination of the patch during storage and shipping. At the time of use, it is peeled off.

EXAMPLE: 1) Occlusive- polyethylene or polyvinyl-chloride.

2) Non-occlusive {paper fabric} - polyester foil and metallic foil

OTHER EXCIPIENTS LIKE PLASTICIZERS AND SOLVENTS:

The plasticizer increases the flexibility and brittleness of the polymer. EX: - Dibutyl-phthalate, Polyethylene glycol, and propylene glycol are added to provide plasticity to the transdermal patch. Various solvent such as chloroform, methanol, acetone, and iso-propanol are used to prepare drug reservoir.

PERMEATION ENHANCER:

Penetration enhancer is the compounds that promote or provide skin permeability by altering the skin as a barrier to the flux of desired penetrant.

It is also known as sorption, promoters and accelerants.

There are three pathway of drug penetration through the skin polar, non polar and polar/non polar.

The polar pathway can be altered by causing protein conformational changes are by solvent swelling. The non polar pathway can be altering by altering the rigidity of lipid structure and by fluidizing the crystalline pathway, which in turn increases diffusion. Some enhancers are binary vehicle act on both polar and non polar pathways by altering the multi laminate pathway for penetrant.

Ideal properties of permeation enhancer

1. It should be pharmacologically inert, inexpensive and osmotically acceptable.
2. It should be non toxic, none irritating, non allergenic.
3. It should have a rapid onset of action and predictable and suitable duration of action.
4. It should have reversible effect on the barrier property of stratum corneum.
5. It should be chemically and physically compatible with the TDDS.
6. It should be non damaging to viable cell
7. The transdermal permeation permeation can be achieved by physical enhancers and chemical enhancers.

1. CHEMICAL ENHANCERS:

Chemicals added to formulations which interact with the skin components (keratin, lipids) and increase drug transport across skin.

Chemical enhancers will function in one or more ways from given possibilities

- **LIPID ACTION:** Enhancers act by disrupting intracellular lipid structures are by extractive lipid component of stratum corneum and make it more permeable to drug.
- **PROTEIN MODIFICATION:** Ionic surface active molecules interact with dense intracellular keratin structure of corneocytes, and make it more permeable to drug.
- **PARTITIONING PROMOTIONS:** Solvents enter into stratum corneum and modify the partitioning of drug molecule into stratum corneum.

EXAMPLE OF CHEMICAL ENHANCERS:

1. **SULPHOXIDES AND SIMILAR CHEMICALS:** diethyl sulphoxide (DMSO) is effective penetration enhancers that promote permeation by reducing skin resistance of drug molecule by promotion drug partitioning from the dosage form.
2. **AZONES:** Azones enhances the skin transport of wide variety of drug including steroids, antibiotics and antiviral agents.
3. **PYROLIDINES:** Pyrollidine able to promote between penetration of hydrophilic drug (e.g. mannitol and progesterone).
4. **FATTY ACIDS:** Interact and modify stratum corneum lipid.(e.g. oleic acid).

2. PHYSICAL ENHANCERS:

The following methods such as Electroporation, Iontophoresis, Ultrasound, Thermophoresis, Micro-needle based device, and Needleless injection are used to enhance the skin permeability.

1. ELECTROPORATION:

The use of electro permeabilization a method of enhancing diffusion across the biological barriers back as far as 100 years. It applies high voltage pulses across the skin for a fraction of seconds. The increase in skin permeability is suggested for cancer chemotherapy, delivery of peptides, protein, polysaccharides, oligosaccharides, and genes.

2. IONTOPHORESIS:

It is a non-invasive and painless method of delivering drugs. Iontophoresis enhance and control the drug penetration through the skin by applying low-density current at a physiologically acceptable level.

3. ULTRASOUND:

It is also known as Phonophoresis\ Sonophoresis. Enhance the migration of molecules by ultrasonic energy, but, the main problem with this method is some foreign particles a bacteria's also may penetrate with the drug molecule.

4. THERMOPHORESIS:

A range of homeostatic controls maintain the skin temperature at 32 C. In the recent years, use of thermoregulation for improving the delivery profile of topical medicaments has been increased. It has shown a 2to3 fold increases in flux every 7-8 C rise in temperature of skin surface.

5. MICRONEEDLE- BASED DEVICES:

One of the first patents was filed for a drug delivery device on micro needle method for percutaneous drug administration. These micro needles (50-110mm long) penetrate the stratum corneum and epidermis to deliver drug from reservoirs.

6. NEEDLE-LESS-INJECTION:

This is a pain-free method of administering drugs to the skin. Needle-less injection avoids the issue of safety, pain, and fear related to use of hypodermic needles

7. MAGNETOPHORESIS:

This method involves the application of a magnetic field that acts as an external driving force to enhance the diffusion of a diamagnetic solute across the skin. Skin exposure to a magnetic field might also induce structural alterations that could contribute to an increase in permeability.

FORMULATION OR PREPARATION OF TDDS:

Formulation approaches used in development of TDDS are:

1. MEMBRANE PERMEATION CONTROLLED SYSTEMS: In this system the drug reservoir is embedded between an impervious backing layer and a rate controlling membrane. The drug releases only through the rate controlling membrane, which can be micro porous or non- porous. In drug reservoir compartment, the drug can be in the form of a solution, suspension, or gel or dispersed in solid polymer matrix.

2. ADHESIVE DIFFUSION CONTROLLED TDDS: The drug reservoir formed by dispersing the drug in an adhesive polymer and then spreading medicated polymer adhesive by solvent casting are by melting the adhesive (in case of hot melt adhesives) onto an impervious backing layer. The drug reservoir layer is then covered by. Non-medicated rate controlling adhesive polymer of constant thickness to produce an adhesive diffusion controlling drug delivery system. EXAMPLE - Deponit (Nitroglycerine)

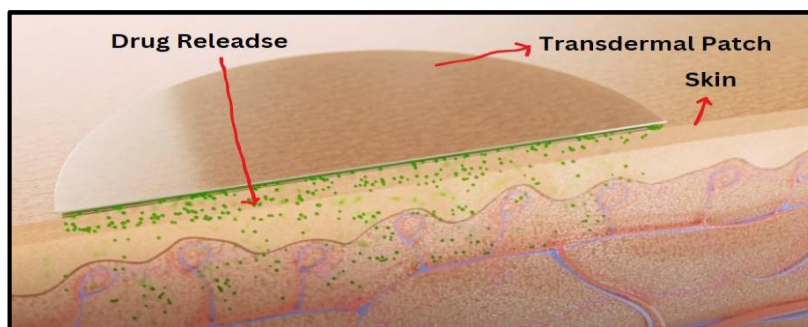
3. MATRIX DIFFUSION CONTROLLED TDDS: The drug is dispersed homogeneously in a hydrophilic or lipophilic polymer matrix. This drug containing polymer disk then is fixed onto an occlusive base plate in a compartment fabricated from a drug-impermeable backing layer. Instead of applying the adhesive on the face of the drug reservoir, It is spread along the circumference to form a strip of adhesive rim. EXAMPLE- Nitro Dur (Nitroglycerine)

4. MICRORESERVOIR CONTROLLED TDDS: This drug delivery system is a combination of reservoir and matrix dispersion system. The drug reservoir is formed by first suspending the drug in an aqueous solution of water soluble polymer and then dispersing the solution homogeneously in a lipophilic polymer to form thousands of unreachable, microscopic spheres of drug reservoir.

TRANSDERMAL PATCHES:

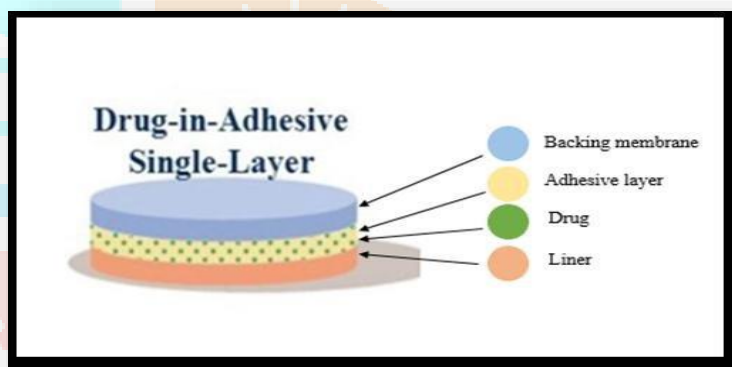
1. The first Transdermal patch "SCOPOLAMINE" was approved in 1979 prevents the nausea and vomiting associated with motion sickness.
2. The FDA has approved, till 2003, more than transdermal patch product, spanning 13 molecules.
3. The US Transdermal market approached 1.2 billion in 2001. it was based on 11 drug molecules : fentanyl , nitroglycerin, estradiol , ethinylestradiol , nor-ethindrone acetate , testosterone ,clonidine ,nicotine ,lidocaine,prilocaine,and scopolamine.
4. Two new recently approved transdermal patch produce (contraceptive patch containing ethylene estradiol and nor-elgestromin and a patch to treat overactive bladder coating oxybutynin)

Transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin into the bloodstream.

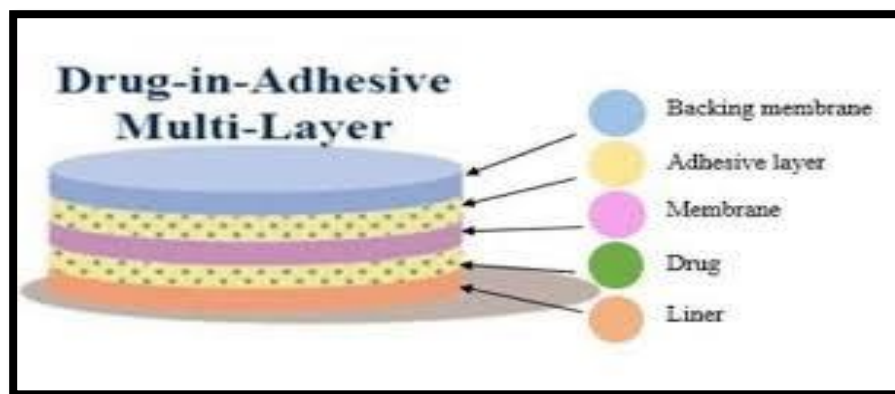


TYPES OF PATCHES:

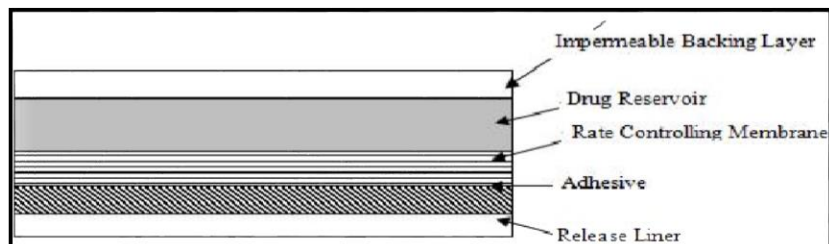
1. **SINGLE LAYER-IN-ADHESIVE PATCHES:** A single layer of polymer with adhesive properties is used as a reservoir for drug dispersion. An impermeable backing laminate is placed beneath the single layer. The drug is deposited in and adheres to the single polymer layer, and is released from the backing laminate layer that supports the drug reservoir. The transdermal product Day-trana is an example of single layer drug-in-adhesive transdermal patch containing methylphenidate



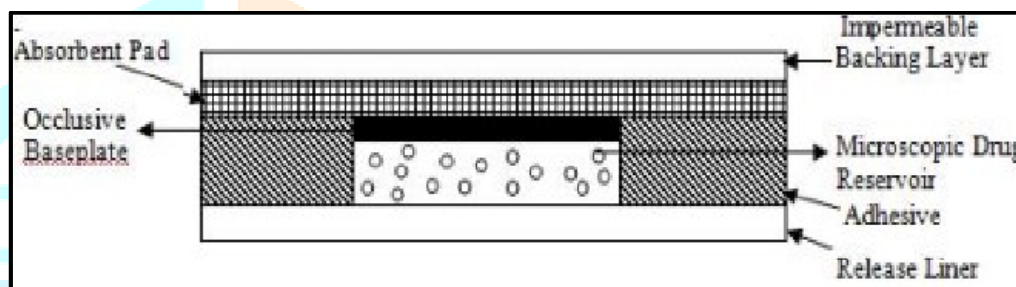
2. **MULTILAYER-IN-ADHESIVE PATCHES:** Multi-layer transdermal patches consist of a drug reservoir layer and an adhesive layer where drug release is controlled over a period of time (24-25). A temporary protective layer and a permanent backing laminate are included in a multilayer systems. Multilayer patches are used to deliver pain medication, drug that encourages smoking cessation, and hormone therapy; drug delivery can be prolonged for up to seven days.



3. **RESERVOIR TYPE:** Unlike the Single-layer and Multi-layer Drug-in adhesive systems the reservoir transdermal system has a separate drug layer. The drug layer is a liquid compartment containing a drug solution or suspension separated by the adhesive layer. This patch is also backed by the backing layer. In this type of system the rate of release is zero order.



4. MICRORESERVOIR TRANSDERMAL PATCHES: Micro-reservoir transdermal patches combine matrix dispersion with a drug reservoir. The reservoir is prepared by suspending the drug in an aqueous solution of hydrophilic polymer, then homogeneously dispersing the drug suspension on a lipophilic polymer. Dispersion is carried out with a high shear mechanical force, which results in the formation of thousands of microscopic, unreachable spheres. The drug release profile follows a zero order rate of kinetic drug release maintaining a constant or level in the plasma. Cross-linking polymeric agents are usually added, since the drug dispersion needs to be thermodynamically stable.



ADVANTAGES OF PATCHES:

1. Topical patches are a painless, non invasive way to deliver substances directly into the body.
2. Topical patches are cost effective.
3. Topical patches over a controlled, steady delivery of medication over long periods of time.
4. Dose delivery unaffected by vomiting and diarrhea.
5. Avoid the first-pass hepatic metabolism and
6. Enzymatic degradation by the gastro intestinal-tract.
7. Less frequent dosing improve the patient compliance.
8. Drug administration stop with patch remove.

DISADVANTAGES OF PATCHES:

1. Transdermal drug delivery system can deliver ionic drugs.
2. Drug molecule must be potent.
3. Adhesion may be varying with patch type and environmental condition.
4. Only small lipophilic drug can deliver to the skin.

EVALUATION PARAMETER`S OF TRANSDERMAL PATCHE`S:

A.PHYSICOCHEMICAL EVALUATION: Transdermal patches can be physicochemical evaluated in terms of this parameter:

- 1. THICKNESS:** The thickness of transdermal patches is measured using a travelling microscopic, dial gauge, screw gauge or micrometer at different points of the film.
- 2. UNIFORMITY OF WEIGHT:** Weight variation is studied by individually weighing 10 randomly selected patches and calculating the average weight. The individual weight should not deviate significantly from the average weight.

3. DRUG CONTENT DETERMINATION: An accurately weighed portion of film (about 100 mg) is dissolved in 100ml of suitable solvent in which drug is soluble and then the solution is shaking continuously for 24 hr in shaker incubator. Then the solution is sonicated. After sonicated and subsequent filtration, drug in solution is estimated spectrophotometrically by appropriate dilution.

4. CONTENT UNIFORMITY TEST: 10 patches are selected and content is determined for individual patches. If 9 out of 10 patches have content between 85% to 115% of the specified value and one has content not less than 75% to 125% of the specified value, then transdermal patches pass the test of content uniformity. But if 3 patches have content in the range of 75% to 125%. Then additional 20 patches are tested for drug content. If these 20 patches have range from 85% to 115%, those transdermal patches pass the test.

5. MOISTURE CONTENT: The prepared film is weighed individually. and kept in a desiccators containing calcium chloride at room temperature for 24h . The films are weighed again after a specified interval until they show a constant weight. The percent moisture content is calculated using following formula.

$$\% \text{Moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

6. MOISTURE UPTAKE: Weighed films are kept in a desiccators at room temperature for 24h. These are then taken out and exposed to 84% relative humidity using saturated solution of Potassium chloride in a desiccators until a constant weight is achieved. % moisture uptake is calculated as given below.

$$\% \text{moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

7. FLATNESS: A transdermal patch should possess a smooth surface and should not constrict with time. This can be demonstrated with flatness study. For flatness study. For flatness determination, one strip is cut from the centre and two from each side of patches. The length of each strip is measured by determining percent constriction. Zero percent constriction is equivalent to 100 percent flatness.

$$\% \text{ constriction} = \frac{11 - 12}{11} \times 100$$

12=Final length of each strip.

11=Initial length of each strip

8. FOLDING ENDURANCE: Evaluation of folding endurance involves determining the folding capacity of the films subjected to frequent extreme conditions of folding. Folding endurance is determined by repeatedly folding the film at the same place until it break. The number of times the films could be folded at the same place without breaking is folding endurance value.

9. TENSILE STRENGTH: To determine tensile strength. Polymeric films are sandwiched separately by corked linear iron plates. One end of the films is kept fixed with the help of an iron screen and other end is connected to a freely movable thread over a pulley. The weights are added gradually to the pan attached with the hanging end of the thread. A pointer on the thread is used to measure the elongation of the film the weight just sufficient to break the film is noted.

10. TACK PROPERTIES: It is the ability of the polymer to adhere to substrate with little contact pressure. Tack is dependent on molecular weight and composition of polymer as well as on the use of tackifying resins in polymer.

11. THUMB TACK TEST: The force required to remove thumb from adhesive is a measure of tack.

12. ROLLING BALL TEST: This test involves measurement of the distance that stainless steel ball travels along an upward facing adhesive. The less tacky the adhesive, the further the ball will travel.

13. QUICK STICK (PEEL TACK) TEST: The peel force required breaking the bond between an adhesive and substrate is measured by pulling the tape away from the substance at 90 at the speed of 12 inch/min.

14. PROBE TACK TEST: Force required to pull a probe away from an-adhesive at a fixed rate is recorded as tack.

Conclusion :

Transdermal drug delivery system represents a beneficial innovation for drug delivery, particularly in patient who cannot swallow or remember to take their medication. Due to the recent advances in technology and incorporation of the drug to the site of action without rupturing the skin membrane transdermal route is becoming the most widely accepted route of drug administration. TDDS have great potentials being able to use for both hydrophobic and hydrophilic active substance into promising deliverable drugs. To drug delivery system great understanding of the different mechanism of biological interaction, and polymer are required, TDDS is a realistic practical application as the next generation of drug delivery system.

REFERENCE

- Ahmed A, Karki N, Charde R, Charde M, Ganghare B. Transdermal Drug Delivery System an Overview. Int J Biomed Adv Res 2011; 2:38-56.
- Bathe R, Kapoor R. Transdermal drug delivery system: formulation, development and evaluation-An overview. Int. J Biomedical and Advance Res 2015; 6(01):1-10
- .Brahmankar.D.M, Jaiswal.S.B, Biopharmaceutics and pharmacokinetics A Teatise. Vallabh Prakashan, Delhi 1995, 335- 371.
- Jain NK, Controlled and novel drug delivery. 1st Ed., CBS Publisher and Distributors, New Delhi. 2001:100-129
- Ellen JW, "Three Generation: The Past, Present and Future of Transdermal Drug Delivery Systems" FreeCE. Pharmaceutical Education Cosutants, 2011; 1-22.
- Ghosh S, Das S, Singh A, Gupta S. Applicability Of Natural Polymer And Natural Permeation Enhancer In Transdermal Drug Delivery System: A Detailed Review. Int J Innov Pharm Sci Res. 2021; 9(8):1– 24.
- Gaikwad AK. Transdermal drug delivery system: Formulation aspects and evaluation. Comprehensive J Pharm Sci. 2013; 1(1):1-10.
- Hwang I, Kim HN, Seong M, Lee S, Kang M, Yi H, et al. Multifunctional Smart Skin Adhesive Patches for Advanced Health Care. Adv Health Mater. 2018;7(15):1800275. doi:10.1002/adhm.201800275.
- Jalwal P, Jangra A, Dhaiya L, Sangwan Y, Saroha R. A review on transdermal patches. Pharm Res. J. 2010; 3:139- 149
- Marwah, H.; Garg, T.; Goyal, A.K.; Rath, G. Permeation enhancer strategies in transdermal drug delivery. Drug Deliv. **2016**, 23, 564–578. [] [[CrossRef](#)]
- Mali AD, Bathe R, Patil M. An updated review on transdermal drug delivery systems. Int. J advances Sci. Res. 2015; 1(06): 244-254.
- Neupane R, Boddu SH, Abou-Dahech MS, Bachu RD, Terrero D, Babu RJ, Tiwari AK, "Transdermal delivery of chemotherapeutics: Strategies, requirements, and opportunities" Pharmaceutics, 2021; 13(7):960. <https://doi.org/10.3390/pharmaceutics13070960>
- Tanwar H, Sachdeva R, "Transdermal drug delivery system: A review" International journal of pharmaceutical sciences and research, 2016; 7(6):2274.
- Verma S, Ojha A, Transdermal Drug Delivery System: A Review. International Journal of Medical Sciences and Pharma Research, 2018; 4(1):1-9. <https://doi.org/10.22270/ijmspr.v4i1.21>
- Wong, W.F.; Ang, K.P.; Sethi, G.; Looi, C.Y. Recent Advancement of Medical Patch for Transdermal Drug Delivery. Medicina **2023**, 59, 778. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
- Yadav B, Sharma B, Saroha K. Transdermal patches: a discrete dosage form. Int. J Current Pharm Res. 2011;3(3):98-108