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A Review on Transdermal Patch

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HUMAN

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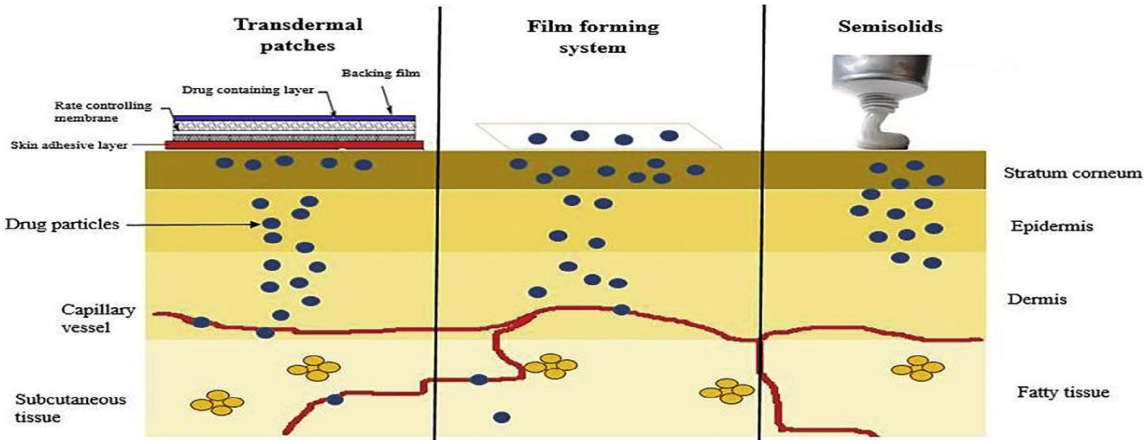
ABSTRACT

A self-contained, covert, medicated adhesive patch known as a transdermal patch offers a practical mode of delivery for a range of skin and body problems. Multiple drug administration has several disadvantages including inconvenient administration, the risk of overdose, lack of patient compliance, and drug plasma level fluctuations. Transdermal medication delivery has emerged as a creative means of achieving systemic drug absorption at a predefined rate over an extended period. Its primary benefits are reduced dose frequency, avoiding first-pass metabolism by entering directly into the systemic circulation, suitability for elderly patients who cannot take pharmaceuticals orally, and ability to be self-administered with fewer adverse effects. This review covers general aspects like drug absorption pathways through the skin, the kinetics of drug absorption, different factors affecting the transdermal permeability, various types of transdermal patches, their components, and evaluation parameters. Additionally, some marketed transdermal patches and therapeutic applications of transdermal drug delivery systems have been discussed. Moreover, the article includes various generations of advancements in the transdermal drug delivery system and its future aspect.

INTRODUCTION

The oral route is the most widely used drug delivery method; yet, it has several drawbacks, such as first pass metabolism and drug breakdown in the gastrointestinal tract as a result of pH and enzymes. A unique medication delivery mechanism was created by Chien (1992), Banker (1990), and Guy (1996) to get around these issues. Transdermal delivery systems, or transdermal patches, were used. Medicated adhesive patches are created in this technology, and when applied to the skin, they distribute a therapeutically effective dosage of medication. They come in various sizes and contain multiple ingredients. After application to intact skin, they penetrate skin barriers to release the active components into the bloodstream.



A transdermal patch with a high dosage of medication inside that is applied to the skin and left there for a long time to diffuse into the bloodstream.

Three routes exist for drugs to enter the skin: a) Through hair follicles.

b) Using sebaceous glands.

c). via the sweat duct(1,2)

Materials and method

Polymers like, polyvinyl chloride, polyvinylalcohol, polyurea, polyethylene, polyacrylate, polypropelene.and by using free film method.

Benefits

a) Drug metabolisms that are first pass are avoided.

b) Incompatibilities with the digestive system are avoided.

c) It is feasible to self-medicate.

d) The action's duration becomes longer and more predictable.

Unwanted side effects are reduced (e, f, g). The plasma concentration of the drug is maintained. Reduced dosage amounts lead to better patient compliance.
h) By eliminating drug-related issues such as decreased absorption, GI discomfort, and breakdown owing to hepatic first-pass metabolism, the therapeutic efficacy of many medications is boosted.(3,4)

Negative aspects

The possibility of allergic reactions, such as itching, rashes, local edema, etc., at the application site.

b. Drugs with larger molecular sizes (over 1000) have more difficulty being absorbed.

c. A person's skin's ability to act as a barrier differs depending on the location.

d. Due to their lower permeability, drugs with hydrophilic character are less suited than those with lipophilic character [16]. 14, 15].

The transdermal medication delivery system's ideal characteristics.

The recommended shelf life is up to 2.5 years.

2. The patch should not be larger than 40 cm.

3. Frequency of dose Every day or every week

4. Visual Appeal Must be either white or transparent.

5. Features of packaging It should be simple to remove the release liner from.

6. Skin response It ought not to irritate.

7. Properties of Release Pharmacokinetic and pharmacodynamic characteristics ought to be constant across time.

8. Properties of packaging It should be simple to remove the release liner. (5)

Components of transdermal patches

The following are examples of natural polymers: a) cellulose derivatives; b) synthetic polymers: polyvinyl alcohol, polyvinyl chloride, polyethylene, polypropylene; c) waxes, gums, shellac, zein, gelatin, and natural rubber, among others. elements that make up the transdermal patch.

1. Pressure-sensitive adhesive (PSA),

2. polymer matrix/drug reservoir, active ingredient (drug),

3. penetration enhancers

4. backing laminates are the fundamental parts of a transdermal patch.
5. as well as additional excipients such as solvents and plasticizers.(6)

1. Polymer matrix: The foundation of a transdermal medication delivery system is polymers. Transdermal delivery systems are made of multilayered polymeric laminates, where a drug reservoir or drug-polymer matrix is positioned between two polymeric layers: an inner polymeric layer that serves as a rate-controlling membrane and/or adhesive, and an outer polymeric layer that is impervious to drugs and prevents drug loss through the backing surface. In order to fabricate transdermal delivery systems that effectively meet the various criteria, careful consideration must be given to the selection and design of polymers.

(1) Natural polymers include chitosan, waxes, gums, zein, gelatin, shellac, and derivatives of cellulose.

(2) Synthetic elastomers: butyl rubber, nitrile, acrylonitrile, silicon rubber, hybrid rubber, polyisobutylene, and so forth

(3) Synthetic polymers, such as polyethylene, polypropylene, polyvinyl alcohol, polyvinyl chloride, polyacrylate, polyurea, and polymethylmethacrylate.(7,8)

2. Drug: Having the appropriate physicochemical and pharmacokinetic qualities is the most crucial requirement for TDDS. Drugs with a limited therapeutic window, high first-pass metabolism, or short half-lives that result in non-compliance from repeated dosage can all benefit greatly from transdermal patches.

3. Permeation enhancers: By interacting with the structural elements of the stratum corneum, such as proteins or lipids, permeation enhancers raise the permeability of the stratum corneum and achieve higher therapeutic levels of the drug. The improvement in skin conditions for wetting as well as trans-epidermal and trans-follicular permeation appears to be caused by the partial leaching of the epidermal lipids by the chemical enhancers, which also improves the absorption of oil-soluble medicines. The improved transdermal penetration of water-soluble agents may be due to the miscibility and solution characteristics of the enhancers utilized.(9)

4. Pressure-sensitive adhesive (PSA): This type of adhesive keeps the patch and the skin's surface in close contact. It should be aggressively and persistently sticky, attach with only finger pressure, and exert a strong gripping force. These adhesives include silicon-based

World Journal of Pharmacy and Pharmaceutical Sciences adhesives, polyacrylates, and polyisobutylene. Many considerations, such as the medicine composition and patch design, go into choosing an adhesive. PSA must not change medication release and must be consistent with biology and physicochemistry. The device's face or back, with the PSA extending peripherally, are two possible placements for it.

5. Backing laminate: The backing laminate's main job is to offer support. Because prolonged contact between the backing layer and the excipients may cause additives to leak out or may result in the diffusion of excipients, medication, or permeation enhancers through the layer, the backing layer should be chemically robust and compatible with the excipients. Their moisture vapor transmission rate ought to be minimal. They need to be as elastic, flexible, and tensile strong as possible.(10)

6. Release liner: The release liner stops contamination and the loss of medication that has migrated from the single-layer drug in adhesive into the adhesive layer during storage. As a result, it is thought of as a component of the main packing material as opposed to the drug's dose form. The release liner is comprised of two layers: a silicon or Teflon-based release coating layer and a base layer that can be either occlusive or non-occlusive. Additional materials utilized for the TDDS release liner consisting of metalized laminate and polyester foil.(11)

7. Additional additives: Drug reservoirs are made using a variety of solvents, including dichloromethane, methanol, acetone, isopropanol, and chloroform. To provide the transdermal patch7 additional flexibility, plasticizers including polyethylene glycol, propylene glycol, dibutyl phthalate, and triethyl citrate added. (11)

Patch types and techniques:

1.Single-layerdrugadhesive

The adhesive layer in this kind of patch is in charge of both drug release and adhering the system's several layers to the skin. A temporary liner and backing surround the adhesive layer.

2.Adhesive Drug with Multiple Layers

Because the medication release from this kind of patch is facilitated by both sticky layers, it resembles a single-layer patch. But in this arrangement, there's an additional layer that needs

to stick to the medication; often, a membrane separates them, but not always. There are both permanent and temporary liner layers in this patch.

2. The reservoir The medication is released through the micropore rate-controlled membrane in this system after a drug reservoir is placed between the support layer and the rate-control membrane. In the reservoir compartment, the medicine may be distributed in a solid polymer matrix or take the form of a gel, suspension, solution, or dispersion.

3.Matrix

The adhesive and backing material, which serves as the formulation's outer layer, are the two primary components of the matrix system. Medications are combined with other ingredients, like polymers and enhancers, to create an adhesive solution. The solvent is then removed to create a matrix film. Next, the backing film is joined to the matrix film using adhesive. The most widely utilized transdermal patch on the market is the matrix-type patch. This matrix approach has the advantage that the patch will provide a thin and elegant preparation, making it easy to use and facilitating a quick, simple, and affordable production process.

The Techniques for TDDS Preparation

a) The asymmetric TPX membrane technique.
b) Using a round Teflon mould.
c) using a mercury substrate.
d) Using the "IPM membranes" approach.
e) By applying the "EVAC membranes" technique.
f) Using proteasomes to prepare TDDS.
g) Using the free film technique

1.The Asymmetric TPX Membrane Method was developed in 1994 by Berner and John. Using heat sealable polyester film (type 1009, 3m) with a 1cm diameter concave as the backing membrane, a prototype patch can be made using this procedure. The drug was distributed on a concave membrane, sealed with an adhesive, and coated with an asymmetric TPX [poly (4-methyl-1-pentene)] membrane.

a) Preparation: The dry or wet inversion procedure is used to prepare them. In order to create a polymer solution, TPX is dissolved in a mixture of solvent (cyclohexane) and non-solvent additives at 60°C. After 24 hours at 40°C, the polymer solution is cast onto a glass

plate. After 30 seconds of evaporation at 50°C, the glass plate must be promptly submerged in a coagulation bath with a temperature maintained at 25°C. The membrane can be taken off and let to air dry 0in circulation after ten minutes of immersion.

b) The circular Teflon mold method was identified in 1989 by Baker and Heller. As an organic solvent, polymeric solutions in different ratios are employed. The answer is then split into two sections. A certain amount of the medicine is dissolved in one part, and enhancers in varying concentrations are dissolved in another part. The two portions are then combined. Subsequently, the drug-polymer solution is mixed with plasticizer (such as Di-N butylphthalate). After mixing the entire mixture for 12 hours, pour it into a circular Teflon mould. In a laminar flow hood model with an air speed of 0.5 m/s, the moulds must be levelled and covered with an inverted funnel to manage solvent vaporisation. It permits the solvent to evaporate. For twenty-four hours, the solvent is left to evaporate. Subsequently, a desiccator containing silica gel is to be used to preserve the dried film for a further 24 hours at 25±0.5°C before examination in order to prevent the effects of ageing.

c) Mercury Substrate Method: This technique dissolves the medication and plasticizer in a polymeric solution. After agitating for ten to fifteen minutes to achieve a uniform dispersion, the mixture is poured onto a leveled mercury surface and covered with an inverted funnel to regulate the evaporation of the solvent. Using the "IPM Membranes" Method: The medication is distributed and shaken in a magnetic stirrer for 12 hours in a mixture of water and polymer (propylene glycol containing Carbomer 940 polymer) Triethanolamine is to be added to the dispersion to neutralise it and make it viscous. Buffer pH 7.4 is used to create solution gel in cases where the drug's solubility in aqueous solution is extremely low. The IPM membrane will incorporate the gel that has produced.

d) Employing the "EVAC Membranes" Approach: Polyethylene (PE), ethylene vinyl acetate copolymer (EVAC) membrane, and 1% carbopol reservoir gel are required as rate control membranes for the manufacture of TDS. For the manufacture of gels, utilise propylene glycol if the medication is insoluble in water. Propylene glycol is used to dissolve the drug. Carbopol resin is then added to the mixture and neutralized with 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 edges will be heated to seal.

e) Proliposome-Based TDDS Preparation: Proliposomes are made via the film deposition process with a carrier approach. The ideal drug-to-lecithin ratio, as determined by earlier sources, is 0.1:2.0. 5 mg of mannitol powder is used to manufacture proliosomes in a 100 ml round-bottom flask. The flask is then held at a temperature between 60 and 70 °C, spun at 80 to 90 rpm, and vacuum-dried for 30 minutes. The water bath's temperature is changed to between 20 and 30°C after drying. A 0.5 ml aliquot of the organic solution is added to the round-bottomed flask at 37°C after the drug and lecithin have been dissolved in an appropriate organic solvent mixture. After the solution has completely dried, another 0.5 ml aliquot of the solution is to be added. Following the final loading, the proliposome-containing flask is attached to a lyophilizer. The drug-loaded mannitol powders (proliposomes) are then left in a desiccator for the entire night before being sieved through a 100 mesh screen. After being gathered, the powder is put into a glass bottle and kept at freezing temperature until it is characterized.

f) Using the Free Film Method: In this method, free film made of cellulose acetate is first made by casting it onto a surface covered in mercury. Chloroform is also used to prepare a 2% w/w polymer solution. At a concentration of 40% w/w of polymer weight, plasticizers have to be applied. Next, a glass ring with 5 ml of the polymer solution is poured into it and set over the mercury surface in a glass Petri dish. By covering the petridish with an inverted funnel, the solvent's rate of evaporation can be regulated. Upon full solvent evaporation, the mercury surface is observed to detect the creation of a layer. After being separated, the dry film will be kept in a desiccator in between the wax paper sheets until it is needed. By virtue of this. (12,13)

CHARACTERIZATION OF TRANSDERMAL PATCHES

(A) Health assessment

(i) Uniform drug content

It is ascertained by taking a certain quantity of patches and fully dissolving them in a particular medium. A membrane filter is used to filter the resultant solution. The samples are then examined using a UV spectrophotometer or HPLC.

(ii) Determining the surface pH: A pH meter is used to record the pH after a certain number of patches are kept in contact with distilled water and any excess water is evaporated.

(iii) Holding endurance: This is determined by using a sharp blade to cut the patch to a precise size. A short strip of the patch was repeatedly followed at the same location until it broke to determine the folding durability. The value of folding endurance was determined by counting how many times the patch could be folded in the same direction without breaking.

(iv) Patch thickness: A micrometer screw gauge is used to measure the transdermal patches' thickness. (iv) The patch's weight A certain quantity of patches for every formulation are weighed separately on a digital balance, and the standard deviation is computed.(13,14)

CONCLUSION-

Method of drug delivery. Many drugs, including hormonal therapy, a wide range of analgesics, and drugs for heart disease, have been developed in Transdermal drug delivery systems form to avoid Gastrointestinal tract effects and first-pass metabolism. Transdermal drug delivery systems are gaining popularity and attracting the attention of researchers, there will be the formulation of many new drugs in a transdermal form. While designing a transdermal drug delivery sys Transdermal drug delivery is the most secure and effective, it should be kept in mind that the formulation may not alter the physiology of the skin. A better understanding of the physiology and anatomy of skin would help us to improve the future advancement of transdermal patches. However, a thorough understanding of the interactions of various polymers and skin components is required to design and optimize transdermal delivery.

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