Quest Journals
Journal of Research in Pharmaceutical Science
Volume 10 ~ Issue 4 (2024) pp: 80-87
ISSN(Online) : 2347-2995
www.questjournals.org

Research Paper

A Review: Formulation and Evaluation of Transdermal Patches

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ABSTRACT:
A medical patch offering has been surgically medicated and attach on the skin epidermis to enable the recommendedamountof medications to cross the skin and enter into the bloodstream is called the transdermal patch.One innovative medicine delivery method that circumvents the challenges associated with traditional dose is the epidermal delivery system. Pharmaceutical preparations with one or more active components for the systemically circulations come in the form of transdermal patches and come in different sizes. The review provides important details regarding patches for the skin, including their benefits, drawbacks, mechanisms of action, types, and fundamental components as well as methods and evaluations and how to apply them. Transdermal patches are now a widely accessible form of medication.

KEYWORDS: *Transdermal; drug delivery; medical patch; Development and Technology.*

***R**eceived 18 Apr., 2024; **R**evised 28 Apr., 2024; **A**ccepted 30 Apr., 2024 © The author(s) 2024.*
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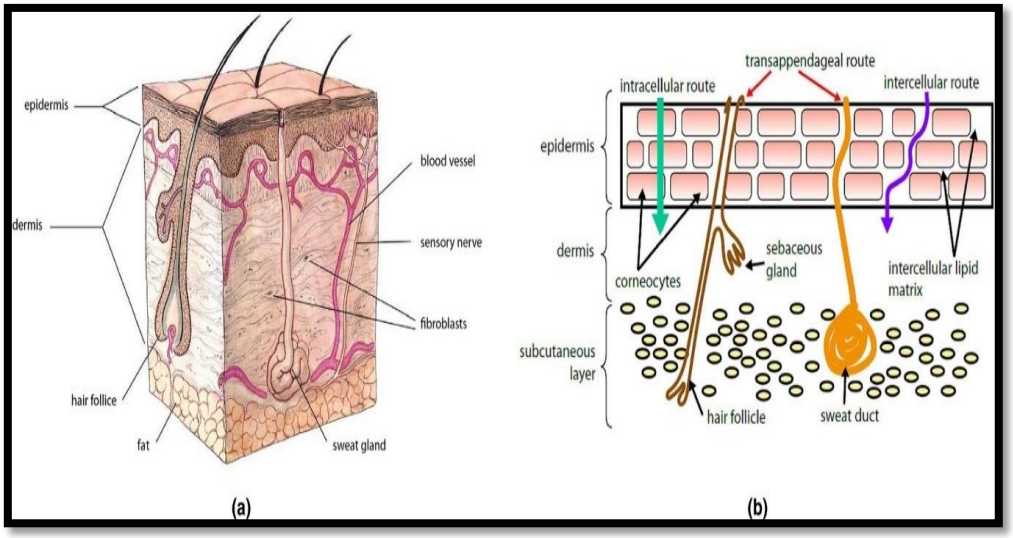
I. INTRODUCTION:

The skin, a layer of tissue which ranges in size from 1.5 to 2.0 m^3 on an adult, is the largest organ in the human body in terms of mass. Medications have been used topically to treat disorders of the skin, transdermally to treat illnesses of the system, and cosmetically since the beginning of human medical history. For instance, in ancient Egypt and Babylonian therapy (c. 3000 BC), the use of plant, animal, or mineral preparations in salves, lotions, liqueurs, and even patched was prevalent(Güngör, 2012). However, transdermal drugs were not commonly used until thelaterhalf of the 20th century. Transportation technologies at the time improved to enable precise and reliable delivery(Won Fen Wong, 2023 Apr 17).The chemical utilized in Transderm-Scop, the first transdermal drug delivery (TDD) system, was scopolamine.Itwas developed in 1980 for relieving motion sickness. The subcutaneous device is powered by a membrane-moderatedmechanism. A microporous polypropylene sheet acts as an obstruction in this technology(nna M. Wokovich, August 2006).

To create the medication's reservoirs, a solution of mineral oil and polyisobutylene is added to the medication.

With a focus on the hundreds of thousands of years that topical and transdermal distribution have evolved throughout, this article attempts to provide a thorough examination of theon the development and contemporary application of transdermal patches(Michael Horstmann3, n.d.).

Drug blood level–time profiles are typically used to assess the prospective efficacy and acceptability of this technique for systemic therapy. "Patching," another name for transdermal delivery systems to deliver drugs are forms of medicine intended to distribute a highly beneficial dosage of medication throughout an individual's skin(Won Fen Wong, 2023 Apr 17). The entire appearance, biological, and physiological aspects of skin must be taken into account when delivering a medicinal drug through the human skin for systemic effects.



(Figure no: 01)

Advantages of TDDS:

- The person receiving treatment can do it because of how simple it is to use.
- It can be Reduce systemic adverse reaction.
- In a critical situation, drug intake can be immediately stopped while treatments by removing the patch at any time.
- Drug showing Gastrointestinal Irritation.
- Transdermal patches are cost effective.
- Avoiding in drug fluctuation levels.
- Minimizing the undesirable side effects.
- Hematologic Avoiding salivary metabolic and the first pass of metabolism.

Disadvantages of TDDS:

• Drugadherenceto the skin may cause dosage spilling.
• Only long-term illnesses are appropriate for its use.
• Lag time varies depending on the drug option and can range from a few hrs to many days.
• It is unable to distribute medication in an intermittent manner.
• If the medicine or composition irritates the skin, it cannot develop.
• Tough to stick with for a long time.
• Because of the skin's inherent resistance to drug entrance, only highly strong drugs are appropriate prospects for transdermal patches to be applied.

2.HISTORY:

Drug	**Indication**	**Product Name**	**Duration of Action**
Scopolamine	Motion sickness	Transderm-scop	72h
Nitroglycerine	Angina pectoris	Minitrin, Nitro-dur	12-14h
Clonidine	Hypertension Tic disorder	Catapres-TTS	7days
Nicotine	Smoking Cessation	Habitrol Nicoderm	24-16h
Lidocaine/epinephrine	Treatment pain	Lidoderm Dermalid	Upto 3 times daily
Estradiol/norethidrone	Prevent Pregnency	Ortho Evra	7 days
Testosterone	Hypogonadism in males	Androderm	24h
Fentanyl	Moderate pain	Duragesics	72h
Estradiol/levonorgestrel	Postmentrual syndrome	Climara Pro	7 days
Granistron	Anti-emetic	Sancuso	Upto 7 days
Methylphenidate	ADHD	Daytrana	Upto 9 days

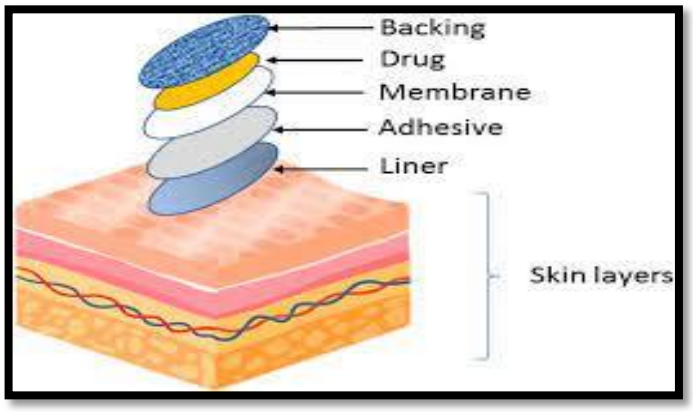
Rotogotine	Parkinsons disease	Neupro	24h
Rivastigmine	Alzeihmers disease	Exelon	24h
Selegiline	Depression	Emsam	24h
Oxybutynin	Bladder Hyperactivity	Oxytrol	3-4 days
Estrogen	Postmentrual syndrome	Fematrix	7 days
Donepezil	Alzheimers disease	Adlarity	7 days
EthinylEstradiol	Avoid pregnancy	Orthodox Evra	7 days

II. TANSDERMAL PATCH:

A number of variables, encompassing the permeability of the skin, the application's duration and scope, and the skin's metabolic activity (i.e., first pass metabolism), influence how well a drug travels through the skin(Won Fen Wong, 2023 Apr 17). Because each medication is different, transdermal distribution may be impacted. The medication needs to be non-ionic and somewhat lipophilic in order to penetrate the epidermal obstacle and succeed sufficient diffusion and uptake(Michael Horstmann3, n.d.). It is more difficult for molecules bigger than 500 Daltons to get through the corneum layer, and the drug's therapeutic dose should preferably be below ten milligrams daily.

III. BASIC COMPONENTS OF TRANSDERMAL PATCH:

Transdermal patches are usually made up of multiple layers that work together to transfer the drug enters the circulatory system via the skin. A medicated patch's fundamental components are shown in Figure 1. According to the substance being used and the desired delivery schedule, the patch's Transdermal patches are usually made up of multiple layers that work together to inject the medication via the epidermis entering the circulatory system(Patel, 2009). A medicated patch's fundamental components are shown in Figure 1. The exact form and contents of the patches may vary according to the medication that's being provided and the desired rate of drug distribution.



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The supporting stratum, which the finest layer of the patch, shields the inner layers from the outside world. Typically, a flexible, waterproof substance like polyethylene or polypropylene is used to create this layer. The purpose of the adhesive layer is to adhere and maintain the patch's position on the skin. Usually, it is made of a strong, skin-friendly, hypoallergenic adhesive. Drugs that are absorbed through the skin are found in the drug layer. It is designed to release the medications gradually and at a steady pace(Prajapati, 2011). The rapid rate at which drugs are administered are freed from the protective layer is managed by the rate-controlling membrane. Drugs are able to flow through membranes because they are often composed of semi-permeable materials(Michael Horstmann3, n.d.).

The transdermal device's components consist of:

1.Matrix of polymer
2. A Drug
3. Enhancers of penetration
4.Other excipients

1. Matrix of polymer:
The medicine is released from the device under the control of the synthetic material. To be employed in a transdermal system, a polymer needs to meet the following requirements are applicable for the delivery. Transdermal devices may benefit from the following polymers(Won Fen Wong, 2023 Apr 17):

Table2:-Various types of polymers

Natural Polymers	Synthetic Polymers	Semisynthetic Polymers
Gelatin, waxes	Polybutadiene, Hydrin rubber	Polyethylene, Polypropylene
Cellulose derivatives	Polysiloxane, Silicone rubber	Polyacrylate, Polyamide
Natural rubber	Nitrile, Acrylonitrile	Polyvinylpyrrolidone
Starch	Butylrubber, Styrenebutadiene	Polymethyl methacrylate
Proteins, Gums	Neoprene	Epoxy, Polyurea

Ideal Properties of Polymers:
1.Should be NonToxic.
2.Should be Inexpensive.
3.Should be Stable.
4. Should be easily of manufactured.
5. There will be a significant concentration of therapeutic drugs added to it.

2.Drug:
An effective transdermal delivery route requires careful selection of the medication. A pharmaceutical for subcutaneous distribution should have a few key components, and the drug itself should be carefully chosen(Hai, 2008). The removal of the membrane is directly linked to the pharmaceutical solutions are as follows:

Physiological properties of drug:
- The medication needs to have a molecular weight. < 1000 Dalton.
- The ideal melting point is to be low.
- Both aqueous and a Lipophilicnatures should be favored by the medication.

Biological properties of drug:
- The medication must not cause a reaction of allergy.
- Drugs should have a brief half-life.
- The medication should be strong and have a daily dosage of around mg.
- Under the nearly zero order release profile of via transdermal, tolerance to drugs cannot develop.

3.Permeation Enhancers:
These substances improve the capacity of the skin to act as an obstacle against the flow of substances that are intended to permeate, hence increasing the skin's permeation and penetrability(Won Fen Wong, 2023 Apr 17).Enhancing agents interact with proteins or lipids, two structural elements of the outermost layer of the stratum, to improve penetration and achieve greater therapeutic levels of the medicine(Kumar, 2013). The improving of skin problems for wetness and for chemical enhancer-mediated fractional leaching of the epidermis lipids is thought to be the cause of the boost in the absorption of soluble in oil medicines.

The ideal characteristics of penetration enhancers:
- Must not result in bodily fluid loss,electrolyte or other native materials.
- It should be Nontoxic,Nonallergic, Nonirritating.
- It should be Odourless, Colourless and Economical.
- The ability to work for a set amount of time with consistency.
- It should possespharmacological inertness.
- **Solutions:** By enlarging the polar routes in the dermis, these chemicals may enhance permeability.
- Lipids becomes more fluid.

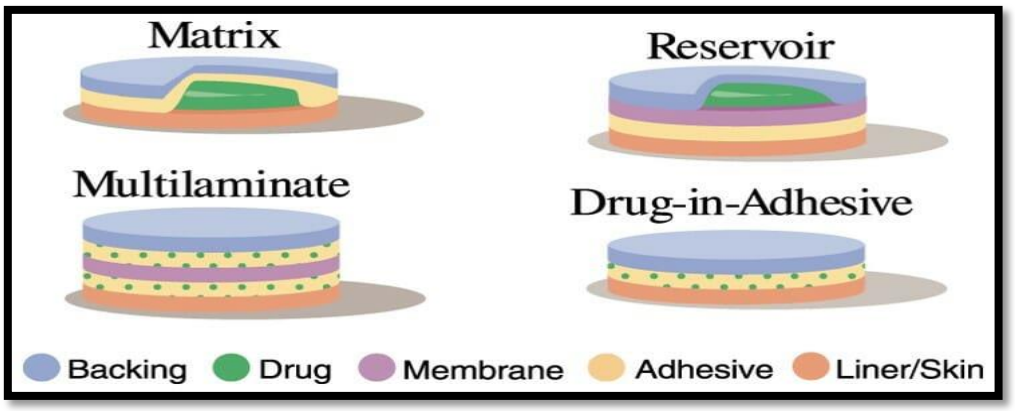
- Examples include pyrrolidones-2-pyrrolidone, laurocapram (Azone), Alkyl homology of methyl sulfoxide, dimethyl acetamide, and dimethyl formamide, such as propylene glycol glycerin silicon fluids, and isopropyl palmate, and ethyl dimethyl sulfur dioxide, including the presence of dimethyl sulfoxide.
- **Surfactants:** It has been suggested that these substances improve the transport of hydrophilic medicines down polar pathways.
- A surfactant's capacity to modify penetration is determined by its hydrocarbon chain length and head group(Güngör, 2012). Since these substances irritate the skin, it is necessary to strike a balance between irritation and penetration enhancement.
- Sodium taurocholate, Sodium deoxycholate, and Salt tauroglycocholate are the The bile Salts in them.

4.Additional Ingredients:

- **Adhesives:**Thus far, adhesives that are pressure-sensitive have been used to adhere transdermal devices to the skin. Either the device's front or its back, with the adhesive that responds to pressure extended superficially, can be used for this purpose(Vishwakarma, 2012).
- **Backing Membrane:**This kind of barrier is flexible, provides a firm grip on the drug a reservoir, prevents the drug from leaking out the top of the dosing form, and permits engraving.Products like sticky foam pad (flexible polyurethane) with occlusive base plate (aluminum foil disc), plastic supporting with absorbency pad and occlusive base panel a (aluminum foil), and metal-based plastic lamination are impermeable and protect the contents from causing skin damage when in use(Pastore, 2015).
- **Release Liner:** Release liner stops contamination and drug loss during storage by moving into the adhesive layer. As a result, it is thought of as a component of the main packing material as opposed to the drug's dose form. The base layer of the release liner can be either occlusive (polyethylene, polyvinyl chloride) or non-occlusive (paper cloth)(Kriplani, 2018).

5.Different Transdermal Delivery Types:

Transdermal patches generally fall into four categories: drug-in adhesive,reservoirs, matrix, and micro-reservoir system(Saroha, 2015)as illustrated in Figure 3. The most widely used covers fall into one of two categories: networks or reservoirs.



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Single-layer Drug-in-Adhesive System:

The medication is contained in this kind of patch's sticky layers. Along with holding the system to the skin and holding the different layers together, the sticky layers release the medication. The covering and temporary linear elements around the adhesive surfaces(Pastore, 2015).

Reservoir System:

Between the outer layer and the rate-controlling layer in these systems is where the drug reservoir is located. Drug release via layer with microporous rate-controlling capabilities. In the reservoir, the drug may be distributed in a solid polymer matrix or in the form of a gel, a suspension, solution, or dispersion(Saroha, 2015).

Network of Matrix construction:

a) Adhesive-in-Drug System: medication reservoirs by distributing the medication within a sticky polymeric material, followed by using a solvent to disseminate the medicated polymer adhesive.

b) Matrix-Dispersion method: This approach distributes the drug uniformly using a hydrophilic or lipophilic polymer framework. Instead of applying the glue to the medication reservoir's surface to produce an adhesive rim strip, this approach distributes it throughout the circle(Kumar, 2013).

c) Micro-Reservoir System: Matrix-dispersion and reservoir technologies are combined in this system. By putting the medication in a liquid form of a polymer that dissolves in water and uniformly dispersing the mixture in a lipophilic polymer, it creates millions of unleachable, microscopic spheres of drug reservoirs(Cilurzo, 2012).

6.METHODS OF PREPARATION OF TDDS:

Mercury Substrate Method:

I. The medication dissolves in a pre-made polymeric solution.
II. Polymer added and the medication needs to be agitated for a while.
III. Keep until air bubbles removed and filled a transparent plate with.
IV. Applied to the petri dish cover over the mercury and rate of evaporation is controlled.
V. The materials need to be kept dry in an dehydrator.

Glass Substrate Method:

I. For expanding, the mixture of polymers is retained.
II. The necessary amount of polymeric and plasticizer After adding the mixture, stir for ten minutes.
III. And then poured intoAumbrapetriplate.
IV. By rotating the transparent funnel, the rate of solvent evaporation can be adjusted.
V. Desiccants are used to store removed films.

Circular Teflon Mould Method:

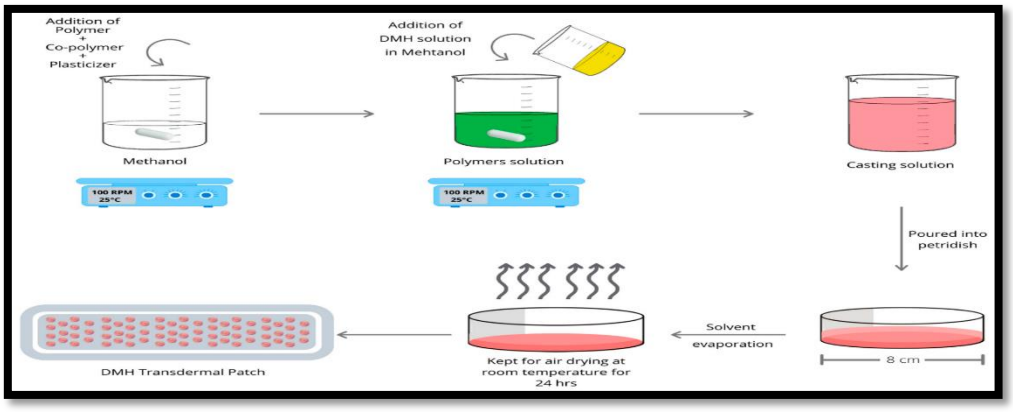
I. Solvents made from organic materials employ mixtures that have proportions of polymers in them(Prajapati, 2011).
II. A specified dose of medication dissolves in the solvent.
III. Plasticizers added to the polymers solution films are kept in desiccators after being put onto an elongated Teflon Mold(Michael Horstmann3, n.d.).

Utilising the EVAC Membranes Technique:

I. polyethylene, acetate, and ethylene vinyl acetate copolymer (EVAC) membranes in this 1% Carbopol reservoirs gels.
II. The gel is prepared using propylene glycol as the solvent.
III. The drug is dissolved in the mixture, carbapol polymer added, and the solution is neutralized with five percent W/W sodium hydroxide.

Unbalanced TPX Laminate Technique:

I. It is made of heat-sealable polymer that has a 1 cm curvature.
II. The medication material is distributed into a conical barrier that is TPX-covered.



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7.ASSESSMENT STUDY FOR TRANSDERMAL PATCH:

Drug Content: The patch has to be dispersed in a particular amount of a suggested solution. over a predetermined region. Next, using an appropriate technology (UV or HPLCtechnique), the solution must be filtered through a filter media in order to determine the drug content. The average of three samples is shown by each number(Won Fen Wong, 2023 Apr 17).

Weight Uniformity: Four hours must pass at 60°C for the prepared patches to dry before testing. To weigh in a digital balance, a certain patch area needs to be cut in several sections. Each weight must be divided into its average weight and standard deviation(Kharia, 2020).
Thickness of the Patch: To guarantee the thickness of the prepared patch, a computerized micrometers is used to determine the drug-loaded patch's thickness at several locations. Next, the mean width and variance are calculated for the same(Bhatia, 2012).
Flatness test: Entails slicing every sheet into three longitudinally pieces at several locations, including the center, the left edge, and correct side.
Moisture Loss: Each produced film must be weighed separately and stored at 40°C in a desiccant that has calcium chloride within. This equation must be used to reweigh the films after a 24-hour period in order to determine the proportion of humidity loss(Kharia, 2020).Start weight - End weight / Total weight] x 100 = 43.0% Moisture Loss(Kriplani, 2018).
Study on Skin Irritation: Wholesome bunnies with In general, between 1.2 and 1.5 kilograms can be used to test for skin irritation and sensitization. The rabbit's dorsal surface (50 cm2) needs to be cleansed. The hair ought to be shaved off of the spotless area., and the surface area can then be washed with rectified spirit and representative formulas applied to the skin(Cilurzo, 2012).
Swellability: The 3.14 cm2 areas were weighed, then they were put in a petri dish with 10 ml of double-distilled water and allowed to digest. The patch's value rose at prearranged periods until a consistent mass was observed.The following formula was used to determine the swelling degree (S)(Michael Horstmann3, n.d.):
$S\ (\%) = Wt - Wo\ /\ Wo \times 100.$
In-vivo studies: Experimental animals and Human participants are two ways to carry out the in-vivo assessment TDDS. In-vivo evaluations are the true representation of the medication's effectiveness. They allow for the full exploration of factors that are not possible to account for in in-vitro investigations(Vishwakarma, 2012).
Stability Studies: For the purpose of conducting durability tests, the TDDS materials were removed at 0, 30, 60, 90, and 180 days after being stored for six months at 40±0.5°C and 75±5% RH, in accordance with ICH recommendations.

8.RECENT ADVANCEMENT IN TRANSDERMAL DELIVERY:

1. Amino administration by patch technologies
2. Pain-free diabetic monitoring using patches.
3. Pain relief.
4. Molecular absorptionenhancement Technology.
5. Transdermal patch of Oxybutynin used in overactive bladder.
6. Modelling and Stimulation.
7. Smart Patches.
8. Three-Dimension (3D) Patches
9. Transdermal Patch for vaccination.
10. Transdermal Patch for insulin delivery.

IV. CONCLUSION:

Thin , flexible , transparent and smooth film were obtained with Polyvinylpyrrolidine , Methyl cellulose and HPMC polymers using plasticizer which is Dibutyl phthalate. All these formulations were found to be stable at room temperature and it is easy for the pharmacodynamic and pharmacokinetic evaluations.Other than disadvantages the system of TDDS offers more capable for improving and delivering drug into the skin for the relief.

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