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A Review Article on Transdermal Patches

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ABSTRACT

Transdermal Drug Delivery System was presented to overcome the problems and issues of Drug Delivery especially through the oral route. The drug delivery system by Transdermal route offers the advantage of being relatively painless administration.

Transdermal Drug Delivery (TDD) :-

TDD is a painless method of delivering drugs systemically by applying a drug formulation onto an intact and healthy skin.

Initially the drug penetrates through the Stratum Corneum and then through the deeper dermis and epidermis it passes through without any accumulation of drug in the dermal layer. TDD was first used in **1981** to prevent the Nausea and Vomiting associated with Motion Sickness. It encourages healing to an injured area of the body. TDD is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream.

Over the other types of Delivery System such as oral, topical , i.v., i.m., etc. the TDD route provides an advantage that it provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or thin layers of the medicaments embedded in the adhesive melt through the body heat. A steady blood level profile enabled by the TDD which results in the reduced systemic side effects and, sometimes the efficacy over the other dosage forms will be improved by TDD.

The review article presents the overall introduction of TDD patches and main objective of TDD system is to deliver drugs into systemic circulation through sik at predetermined rate with minimal inter and intra patient variation.

Keywords :- Transdermal Delivery , Patches.

INTRODUCTION

- Transdermal Drug Delivery System (TDDS) are the medicaments which are administered topically in the form of patches. These patches at a predetermined and controlled rate will be delivered for a systemic effects. Oral route is the most popular route of drug delivery system but it has some disadvantages including first pass metabolism , drug degradation , etc in Gastrointestinal Track due to enzymes, pH, etc.

So, to prevent this problem and to overcome it, NDDS was developed in **1990** , Gay in **1996.** It was TDD system or Transdermal patches. A transdermal drug delivery device, which may be of an passive design or active design. It is a device which provides an alternative route for administering medication. In this system medicated patches which are adhesive in nature are prepared to deliver therapeutically effective amount of drug across the skin when placed on to the skin.

Transdermal patches works symply. Through the diffusion process, the drug enters the bloodstream directly through the skin, and this drug which is to be applied in a relatively high dose to inside of the patches , which are to be worn on the skin for an extended period of time. Through the diffusion process, the drug will keep diffusion into the blood from patches for a longer period of time because, there is a high concentration on the patches and low concentration in the blood. This will assist you to continue constant concentration of drug in blood flow.

Following are the three pathways, through which the drug can penetrate through the skin :-

1. Through the Sebaceous Gland
2. Through the Sweat ducts
3. Through the hair follicles.

Following are the basic components if TDD System :-

- Polymer matrix or Drug reservoir
- The drug
- Permeation enhancers
- Pressure Sensitive Adhesive (PSA)
- Backing Laminate
- Release Liner
- Other Excipients
- **Polymer matrix or Drug reservoir :-**

Polymer matrix is presented by dispersing the drug in liquid or solid state synthetic polymer base. This polymer controls the release of drug from patches or device. Polymer is an integral and foremost important component of TDDS.

It should have biocompatible and chemical compatibility with the drug and other components of the system such as penetration enhancers. The mechanism of drug release depends upon the physiochemical properties of the drug and polymer used in the manufacture of the device. Additionally they should provide consistent and effective delivery of a drug throughout the product's intended shelf life and should have a safe status.

1) Polymer should pass the incorporation of a large amount of drug
2) It must be stable
3) Must not decompose in the presence of drug
4) Other Excipients used in the formulation and a high humidity conditions or body temperature should not affect to it
5) Polymers and it's degradation products must be non-toxic

Polymers used in TDDS are classified as :-

1. Natural Polymer :-

Natural Rubber , Gums and their derivatives , Cellulose Derivatives , Waxes , Start , Shellac , Gelatin , Zein , Proteins Chitason.

2. Synthetic Polymer :-

Polyethylene , Polyvinylalcohol , Polypropylene , Polymethylmethacrylate , Epoxy , Polyvinylpyrrolidone , Polyurea , polyacrylate , etc.

3. Synthetic Elastomers :-

Acrylonitrile , Butyl Rubber , Neoprene , Polybutadiene , Silicon Rubber , Hydrin Rubber , Styrenbutadieine , Polysiloxane , Polyisobutylene.

2. The Drug :-

The drug substance should be choosen in such way that, because , it is the most important descision in succesful development of a Transdermal product.

Following are the some of ideal properties of drug and thare are some factors to be consider during preparation of Transdermal patches as follows :-

a. Ideal properties of Drug :-

Sr. No.	Parameters	Properties
1	Oral Bioavailability	Low
2	Molecular weight	Less than 600 da
3	Skin permeability coefficient	>0.5*10-3 cm/hr
4	Dose	Must be less in weight (less than 20 mg/day)
5	Skin reaction	Non-sensitizing , Non-irritating
6	Half life	Less than 10 hour

b. Factors affecting :-

Pharmacokinetic	Biological	Physicochemical
Therapeutic plasma concentration	Skin metabolism	Polarity
Bioavailabile factor	Skin toxicity	Melting point

Half life	**Allergic reaction**	**Crystalinity**
Total body clearance	**Site of application**	**Molecular weight**
Volume of distribution		**Solubility**

3. Penetration enhancers :-

Penetration enhancers are the compounds which promotes skin permeability especially Stratum Corneum so as to attain therapeutic levels of drug candidate. They alter the skin as a barrier to the flux of a desired penetrant.

Ideal properties of Penetration enhancers that must meet are :-

1. Non-toxic , Non-irritating , and non-allergic
2. It should be cosmetically acceptable with as appropriate skin feel
3. Should not bind to receptor site ie. Not showing any pharmacological activity i.e.means it should have pharmacological inertness property
4. Should be a good solvent for drugs
5. Rapid onset of action
6. Readily incorporated into Delivery System
7. Should not cause loss of body fluids
8. Physically and chemically compatible with drugs and other pharmacological Excipients with which it is used
9. Economical, odourless, and colourless

4. Pressure Sensitive Adhesive (PSA) :-

Pressure Sensitive Adhesive (PSA) is one of the most critical components used in a Transdermal Drug Delivery System (TDDS). It helps to enhance the adhere property of Transdermal patch to the skin surface.

But most importantly it acts as a matrix for the drug and other excipients. It can easily remove from the smooth surface without leaving a residue on it.

- Polyacrylates
- Silicon based adhesive
- Polyisobutylene

5. Backing Laminate :-

Backing Laminate or backing membrane are flexible and providing a good bond to the drug reservoir. It is a supportive material which is permeable to the drugs and also enhances the permeation. It prevents drug from leaving dosage form through the top. It is impermeable substance and it protects the product during use on to the skin. They should be chemically compatible with the drug, enhancer, adhesive and other excipients

Ex :- Vinyl, Polyethylene and polyester films

6. Release Liner :-

This is the primary packaging material. The liner must be removed before the application of Transdermal patch on to the skin.

Ex :- Polyethylene-foil pouch.

Release Liner can be film based, paper based, Polycoated based, or even have unique substrate, such as metallized papers or films as their base.

It is composed of a base layer which may be of :-

i. Non-Occlusive (eg:- Paper fabric)

ii. Occlusive (eg:- Polyethylene)

Some are often coated with Silicon, in which allows whatever the liner is carrying to release when the time is right.

7. Other Excipients :-

Other Excipients like plasticisers and Solvents are used :-

- Plasticisers :- Triethylcitrate , propylene Glycol , Dibutylpthalate , Polyethylene Glycol.
- Solvents :- Isopropanol , Dichloromethane , Acetone , Chloroform , Methanol.

Methods of Preparation Of TDDS :-

1) Assymetric TPX membrane method
2) Preparation of TDDS by using proliposomes
3) By using "IPM Membrane" method
4) Circular Teflon mould method
5) By using free film method
6) Mercury substrate method
7) By using "EVAC Membrane" method

Advantages Of Transdermal Drug Delivery System :-

Delivery through the TDDS route is an very interesting option. Because TDDS route is a very convenient and safe and effective route. Transdermal patches offers many advantages like:-

- It avoiding the fluctuations in Drug levels
- It avoiding the Gastrointestinal incompatibility
- Self medication is possible
- No. Of doses can be reduced
- Increase in patient's compliance
- Conclusion and Ending of therapy is easy at any point of time
- Enhances and improve the therapeutic efficacy
- Ability to deliver drug more selectivity to a specific site
- Problems associated with drugs like lower absorption , Gastrointestinal-Irritation , decomposition due to hepatic first pass metabolism
- Duration Of Action gets extended
- Duration Of Action can be predictable
- Minimization of undesirable side effects
- Inter and intra patient variation
- Drugs with short biological half lives , narrow therapeutic window can be utilised
- First pass metabolism can be avoided
- Pharmacological and Physiological response can be improved
- Elimination of multiple dosing profile
- Drug can be delivere and transported more selectively and perticularly to a specific site
- Convenient and Pain-free selfmedication
- Constant Drug Concentration can be maintained
- Toxicity can be reduced
- Systemic side effects can be avoided
- Smooth drug delivery
- Avoids accidental overdose

Disadvantages Of Transdermal Drug Delivery System (TDDS) :-

1) Possible skin irritation and sensitisation

2) No. Of drugs can pass through the skin due to its low permeability
3) Imperfect skin adhesion
4) Discomfort from adhesion
5) Cost and selectivity for specific Physicochemical drug properties
6) Very few drugs can be delivered at a variable rate using this route
7) Greater molecular size of drug (above 1000) creates difficulty and problems in absorption
8) Drugs having Hydrophilic properties are less suitable as comparing to Lipophilic drugs because of their low permeability
9) Barrier function of skin varies from site to site on some or different person
10) Chances of Local edema and rashes
11) Cannot adminster drugs that require High blood levels
12) Not suitable for a drug, which doesn't possess a favouble , O/W partition coefficient
13) Neither practical nor affordable when necessary and required to deliver large amount doses of drugs through skin

Factors Affecting On Transdermal Patches :-

There are a variety of factors that are affecting on the Action Of Transdermal patches, these are given below :-

1. Biological Factors
2. Formulation Factors
3. Physicochemical Factors

A. Biological Factors :-

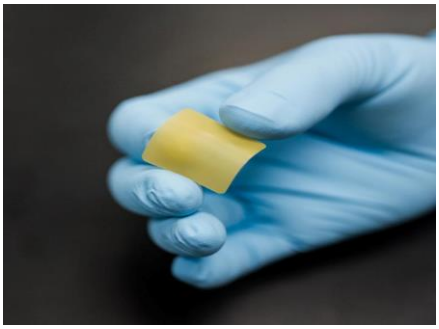
1. pH of the skin
2. Hydration condition of the skin
3. Site of application
4. Sex and race
5. Age of candidate
6. Pathological condition of the skin
7. Lipid films over the skin

B. Formulation Factors :-

1. Permeation enhancers
2. Release Characteristics of Patch or Drug
3. pH of vehicles

C. Physicochemical Factors :-

1. Molecular Size and shape of drug molecules
2. Stability and Half life of Patch or Drug inside of patch
3. Partition coefficient
4. Drug Concentration



Evaluation Test for TDDS :-

1. Physical appearance of the Transdermal Patch :-

All the Transdermal patches are photographically examined for flexibility, color and smoothness.

2. Weight Uniformity :-

This test makes sure the consistency of the created patch. From the whole patch Three small-scaled portable pieces were cut randomly. Each having area of about 4 Cm' square (2*2cm) and seperately weighed. The standard diversionance from the mean value will be detailed.

3. Moisture content :-

The prepared or already made films are weighed separately and kept in the descicator containing silica gel and calcium chloride at normal room temperature for 24 hours. After 24 hours the films are again reweighed and the percentage of moisture content is calculated and determined using formula mentioned below :-

Percentage moisture content :- (Initial weight - final weight) × 100

4. Folding Endurance / Tolerancy :-

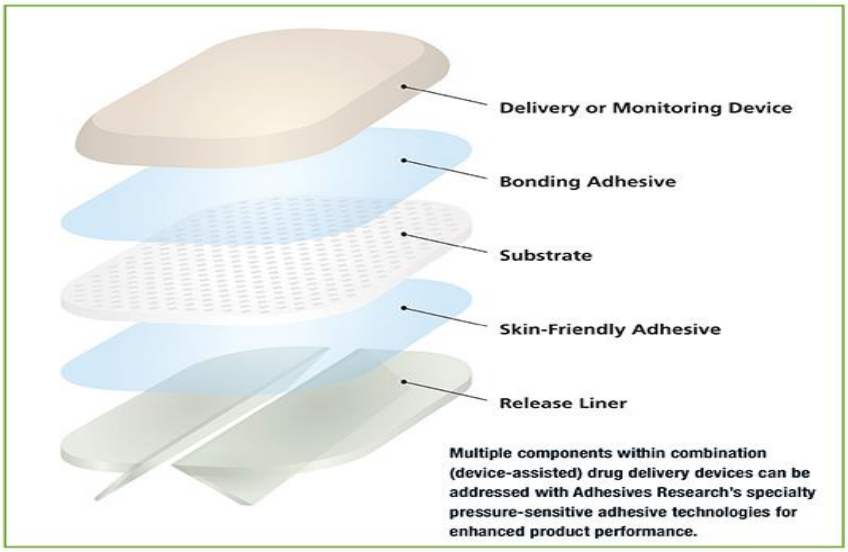
The folding Endurance Or Tolerancy will be calculating by cutting a perticular area of Transdermal Patch strip having uniform size (2×2 cm) and repeatedly folded at the same place till the patch breaks. The number of times, the patch will be folded at the same place without breaking will give the value of folding Endurance Or Tolerancy.

5. Flatness :-

A Transdermal patche will be cut into three longitudinal strips from left side, right side and the centre. The length of each strip was determined and measured. The flatness of Transdermal Patch will be determined by using equation :-

Construction (%) = (L1-L2) ×100

Where, L1= initial length of the strip and L2 = final length of the strip



Conclusion :-

The use of Transdermal patch is the most convenient way to deliver a specific amount of drug to a specific site. They have both the advantages and very few drawbacks also of using Transdermal patches. Transdermal patches through transdermal drug delivery system provide a specific, predetermined medication that is absorbed by our skin and there by into our bloodstream. Therefore transdermal patches offers a non-invasive and painless method of drug delivery with a benefit of providing a consistent therapeutic dosage over a predetermined time period. Otherwise it has also very few drawbacks including skin dermatitis, sometimes an accidental and excess drug release and there ineffectiveness for those drugs that require a high level of drugs in the blood. And sometimes difficulty in delivering hydrophilic drugs dto natural barriers of skin.

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