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A Review On Topical and Transdermal Delivery System

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ABSTRACT:
Topical drug delivery systems have been shown to overcome difficulties in drug delivery, especially orally. A topical patch is a drug-containing adhesive patch that is attached to the skin and a specific dose of drug can be delivered to the blood through the skin. It promotes the healing of an injured area of the body. Transdermal drug deliveryhas made an important contribution to medical practice, but it has yet to fully achieve its potential as an alternative to the oral delivery and hypodermic injections.The transdermal patch may essentially can provide a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive. An advantage of thistypes of delivery systems to avoid first pass metabolism. The disadvantage of the topical delivery system is the skin a very effective barrier, so only drugs with small molecules that can easily penetrate the skin can be delivered by this method.

KEY WORDS: Topical drug delivery, Transdermal drug delivery, Skin permeation, Systemic circulation, Kinetics.

I. INTRODUCTION:

Transdermal:

Topical formulations containing drugs showing systemic action are called transdermal delivery systems (TDS) or transdermal systems .Transdermal delivery may be defined as the delivery of a drug through 'intact' skin so that it reaches the systemic circulation in sufficient quantity to be beneficial after administration of a therapeutic dose[1].

Advantages:

Avoidance of First pass metabolism of drugs, Self administration is possible, Topical are a painless, Prolonged duration of action.

Disadvantages:

Possibility of local irritation at the site of application, It can be uncomfortable to wear, Slower onset than oral preparation[2].

Basic Components of Transdermal Drug Delivery Systems-

1. Polymer matrix or matrices.
2. The drug.
3. Permeation enhancers.
4. Other excipients.

1. **Polymer Matrix:** The Polymer controls the release of the drug from the device. Possible useful polymers for Transdermal,

a.Natural Polymers: e.g., cellulose derivatives, Zein, Gelatin, Shellac, Waxes, Proteins, Gums and their derivatives, Natural rubber, Starch etc.
b. Synthetic Elastomers: e.g., polybutadieine, Hydrin rubber, Polysiloxane, Silicone rubber, Nitrile Acrylonitrile, Butyl rubber, Styrenebutadieine rubber, Neoprene etc.
c. Synthetic Polymers: e.g., polyvinyl alcohol, Polyvinyl chloride, Polyethylene, Polypropylene, Polyacrylate, Polyamide, Polyurea, Polyvinyl pyrrolidone, Polymethylmethacrylate ,Epoxy etc.

2. **Drug:** For successfully developing a transdermal drug delivery system, the drug should be chosen with greatcare. The following are some of the desirable properties of a drug for transdermal delivery.
3. **Permeation Enhancers:** These are compounds which promote skin permeability by altering the skin as a barrier to the flux of a desired penetrant.
4. **Other Excipients:** Adhesives: The fastening of all transdermal devices to the skin has so far been done by using a pressure sensitive adhesive which can be positioned on the face

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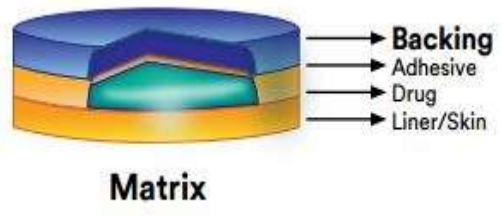
of the device and in the back of the device and extending peripherally.

- Should not irritateor sensitize the skin.
- Permeation of drug should not be affected.
- The delivery of simple or blended permeation enhancers should not be affected[3].



Topical:

Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders like acne or the cutaneous manisfestations of a general disease like psoriasis with the intent of containing the pharmacological or other effect of the drug to the surface of the skin or within the skin[3].It capable of enhancing the efficacy, tolerability, and cosmetic acceptability of topical formulations.

Advantages:

It may ease of delivery, a cooperative patient, increased compliance as well as the avoidance of first-pass metabolism.

Disadvantages:

The lack of or reduced rates of absorption and cosmetic considerations. New drug delivery technology and penetration enhancers may help to obviate some of these objections. There are important issues to consider as you contemplate development of a topical dermatological product. You may already have experience with oral or parenteral products, but there are challenges and issues which are unique to development of topical formulations[4].

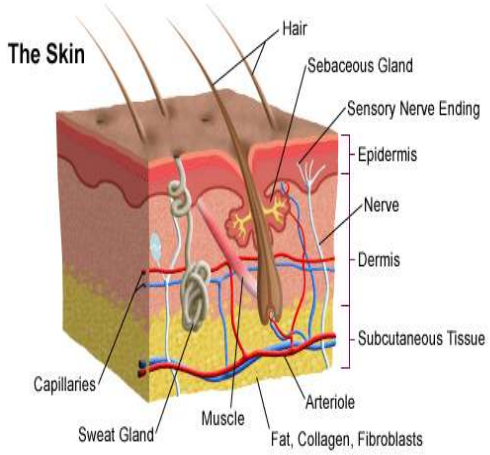
Active methods for enhancing transdermal delivery to skin:

The skin in order to enhance permeation of drug molecules. Recent progress in these technologies has occurred as a result of advances in two methods such as Active and Passive methods. In Active enhancement methods as electrically assisted method, mechanical method and other physical method. In Passive enhancement methods as drug and vesicle interactions, stratum corneum modification , optimisation of formulation vesicle.

Active methods for enhancing topical delivery to skin:

These active methods are applied by producing external energy to act as a driving force and or act to reduce the barrier nature of the skin in order to enhance permeation of drug molecules in to the skin. Recent progress in these technologies has occurred as a result of advances in precision engineering (bioengineering), computing, chemical engineering and material science, and this all results in creation of devices for skin delivery of drug to achieve the desired therapeutic effect[5].

Structure of skin:



The skin is the largest organ of the body, according for about 15% of the total adult body weight. The skin is composed of three layers: the epidermis ,the dermis and subcutaneous tissue. The outer most level, the epidermis consists of a specific cencellation of cells known as keratinocytes ,Which function to synthesize keratin. The middle layer dermis , the dermis, is fundamentally made up of the fibrillar structural protein known as collagen. The dermis lies on the subcutaneous tissue , or panniculus, Which contains small lobes of fat cells known as lipocytes[6].

NOVEL TOPICAL DRUG DELIVERY SYSTEMS:

Following are the advances in the topical drug delivery systems:

1. Aerosol foams,
2. Liposomes,

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3. Nanoemulsion,
4. Polymers,
5. Dendrimer,
6. Microsponges,
7. Emulsifier free formulations,
8. Fullerenes,
9. Dynamic foams,
10. Solid lipid nanoparticles,
11. Ethosomes,
12. Microneedles,
13. Skin abrasion[7].

Principle of Transdermal permeation:

Earlier skin was considered as an impermeable protective barrier , but later investigations were carried out which proved the utility of skin as a route for systemic administration . Skin is the most intensive and readily accessible organ of the body as only a fractions of millimeter of tissue separates its surface from the underlying capillary network. The various steps involved in transport of drug from patch to systemic circulations are as follows ;

1.Diffusion of drug from drug reservoir to the rate controlling membrane.
2.Diffusion of the drug from rate limiting membrane to stratum corneum.
3.Sorption by stratum corneum and penetration through viable epidermis.
4.Effect on target organ.
5.Uptake of drug by capillary network in the dermal capillary layer[8].

Kinetics of Transdermal Permeation:

Knowledge of skin permeation kinetics is vital to the successful development of transdermal therapeutic systems. Transdermal permeation of a drug involves the following steps:

1. Sorption by stratum corneum.
2. Penetration of drug through epidermis.
3. Uptake of the drug by the capillary network in the dermal papillary layer[9].

This permeation can be possible only if the drug possesses certain physiochemical properties. The rate of permeation across the skin is given by:

$$dQ/dt = Ps (Cd - Cr) \quad \text{.....1}$$

Where Cd and Cr are the concentration of the skin penetrant in the donor compartment i.e. on the surface of stratum corneum and in the receptor compartment i.e. body respectively. Ps is the overall permeability coefficient the skin tissue to the penetrant. This permeability coefficient is given by the relationship:

$$Ps = Dss\ Ks/\ hs \quad \text{..... 2}$$

Where Ks is the partition coefficient for the interfacial partitioning of the penetrant molecule from a solution medium or a transdermal therapeutic system on to the stratum corneum, Dss is the apparent diffusivity for the steady state diffusion of the penetrant molecule through a thickness of skin tissues and hs is the overall thickness of skin tissues. As Ks, Dss and hs are constant thickness of skin tissues. As Ks, Dss and hs are constant for a skin penetrant can be considered to be constant. From equation (1) it is clear that a constant rate of drug permeation can be obtained only when Cd >> Cr i.e. the drug concentration at the surface of the stratum corneum Cd is consistently and substantially greater than the drug concentration in the body Cr. The equation becomes:

$$dQ/dt = Ps\ Cd \quad \text{..... 3}$$

The rate of skin permeation is constant provided the magnitude of Cd remains fairly constant throughout the course of skin permeation. For keeping Cd constant the drug should be released from the device at a rate Rr i.e. either constant or greater than the rate of skin uptake Ra i.e. Rr >> Ra. Since Rr >> Ra , the drug concentration on the skin surface Cd is maintained at a level equal to or greater than the equilibrium solubility of drug in the stratum corneum Cs .i.e. Cd>>Cs. Therefore a maximum rate of skin permeation is obtained and is given by the equation:

$$(dQ/dt)m = Ps\ Cs. \quad \text{..... 4}$$

From the above equation it can be seen that the maximum rate of skin permeation depends upon the skin permeability coefficient Ps and is equilibrium solubility in the stratum corneum Cs. Thus skin permeation appears to be stratum corneum Limited[10].

Kinetics of Topical permeation:

TDDDSs are designed in order to effectively deliver a therapeutic modality at the site of action; however, formulations offer distinct drug release and permeation patterns depending on the composition and or cross-linking network. For

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instance, ointments due to the presence of lipid-soluble bases acquiesce lipidic nature and thus favour delivery of lipophilic molecules. In contrast, aqueous nature of gels promotes encapsulation of hydrophilic molecules. Hence, mechanism of drug release and permeation of molecules from the matrices are usually different owing to dissimilar compositions. This consequently displays diverse therapeutic behaviors of different semisolid dosage forms. Hence, permeation kinetic should be monitored carefully to predict the therapeutic efficacy of customized TDDDs.

To understand the concept behind the release kinetics and structuring the method of data analysis and interpretation,integration of drug delivery science and mathematical functions is performed to yield equations that can accurately predict the release kinetic and ultimately the therapeutic efficacy. Zero-order, first-order, Higuchi, Hixson-Crowell, Peppas, and Korsmeyer-Peppas [Figure 2] equations are being employed to calculate the release kinetic of drug permeated from topical dermal dosage forms[11]]

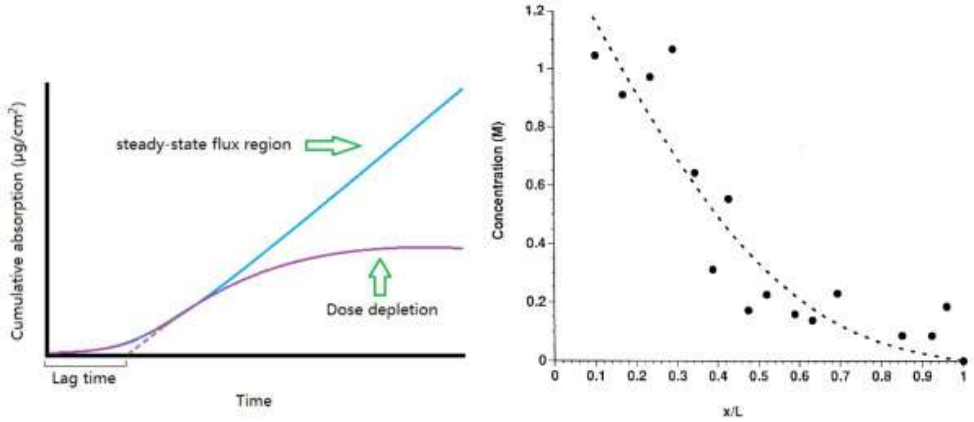

Figure:2 kinetics of topical permeation.

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