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A BRIEF REVIEW ON TRANSDERMAL DRUG DELIVERY SYSTEM

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***Abstract*:** Transdermal drug delivery system (TDDS) is an integral part of advanced drug delivery systems. About 75% of drugs are taken orally and are found not to be as effective as desired. To improve such characters there is need to developed transdermal drug delivery system. This advancement in drug delivery offers many advantages over traditional methods. Uniform drug plasma concentration, improved bioavailability, Predetermined rate of drug release, reduction in toxic side effects, painless and easy application and simply removing the patch from the skin if any unwanted effects occur are some of the potential advantages of transdermal drug delivery. Transdermal drug delivery system (TDDS) are very effectively overcome the hepatic first pass metabolism and improve the steady plasma drug concentration. This article gives a brief overview over principles behind transdermal drug delivery, as well as the advantages and disadvantages of transdermal drug delivery systems and describes the factor affecting transdermal permeability of different types of transdermal patches, evaluation parameters.

Key words: Transdermal patch, Permeation, Percutaneous absorption

I. Introduction:

From the beginning of life on the earth the human being have been used the various substance on the skin for cosmetic or for the therapeutic purpose. Now we are growing in the twentieth century here we can used the skin as a route for drug delivery purpose. Now a day most of the drug available in the market are taken by oral route but not showing the that much effect as required. So that to improve the effect of drug and also for patient compliance we have to introduced the newer route for the delivery of drug that is transdermal patches or transdermal route. Today Transdermal drug delivery system is most consistent and applied technique amongst all techniques. The delivery of drug through skin is most challenging concept in the research work. Transdermal drug delivery system overcome the many disadvantages or limitation of conventional and parenteral dosage forms.

II. Percutaneous Absorption:

It is defined as penetration of substance into various layers of skin and permeation across the skin into systemic circulation.

The percutaneous absorption is a step wise process and can be divided into three steps:

1) Penetration is the entry of the substance into a particular layer.
2) Permeation is the penetration from one layer into another,and is different both functionally and structurally from the first layer.
3) Absorption is the uptake of a substance into systemic circulation.

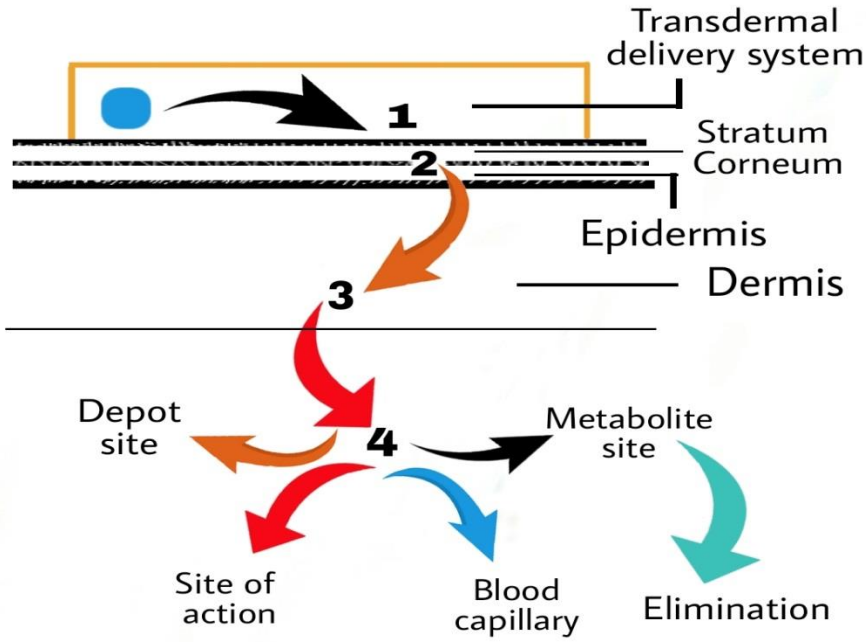

Figure 1 :Process of Transdermal Permeation

III. Factor affecting transdemal permeability:

1) Physicochemical properties of the penetrant molecule:

i) Partition coefficient :

Drug possessing both hydrophilic and lipophilic characteristic are favorably absorbed through the skin. The partition co-efficient of the drug molecule may be altered by chemical modification without affecting the pharmacological activity of the drug.

ii) pH condition:

Unchanged form of the drug has better penetrating capacity. Transport of ionization species from aqueous solutions shows strong pH dependence.

iii) Drug concentration:

Transdermal permeability depends on the concentration of penetrant molecule on the surface layer of skin.

2) Physiochemical properties of drug delivery system:

i) The affinity of the vehicle for the drug molecule:

Solubility in the vehicle will determine the release rate of drug. The mechanism of drug release depends on whether the drug is dissolved or suspended in the delivery system and on the interracial partition co-efficient.

ii) Composition of drug delivery system:

It may affect not only the rate of drug release but also the permeability of the stratum corneum by means of hydration.

iii) Enhancement of transdermal permeation:

Penetration enhancer caused the physicochemical or physiological change in stratum corneum and increase the penetration of drug through the skin.

3) Formulation characteristics:

i) Release rate of the drug:

It is influenced by affinity of the career of the drug in formulation, physicochemical properties of the drug.

ii) Ingredients of formulation:

Various excipient and polymers present in the formulation can effect either release or permeation of the drug alternating the physicochemical properties of drug for skin physiology.

iii) Presence of permeation enhancer:

They are used to increase the permeation of drug through the skin. This alter the integrity of skin (physicochemical and physiological modification) temporarily and open the skin pores for absorption.

4) Physiological and pathological condition of the skin:

i) Skin age:

Foetal and in infant skin appears to be more permeable than adults skin. It is assume that skin of young and elderly are more permeable. In premature infants stratum corneum is absent and children are more susceptible to toxic effect of drugs through the skin.

ii) Lipid Film:

The liquid film on the skin surface is formed by excretion of sebaceous gland and cell lipid like sebum and epidermal cell provide a protective film to protect and removal of natural moisturizing factor from the skin.

iii) Skin hydration:

Hydration of stratum corneum can enhance transdermal permeability.

iv) Skin temperature:

Increase skin temperature results in an increase in the rate of skin permeation.

v) Cutaneous drug metabolism:

Some of the drug reaches the general circulation in active form and some of this in inactive form or metabolic form, because of presence of metabolic enzyme present in the skin layer.

vi) Species differences:

Different species have different sizes in Anatomy like thickness of stratum corneum, the number of sweat glands and hair follicles.

vii) Pathological injury to the skin: Leads to increase in skin permeability.

viii) Blood Flow:

Changes in peripheral circulation do not affect transdermal absorption but an increase in blood flow increase the concentration gradient across the skin and reduce the total time of residence of the drug molecules in dermis continuously removing it.

ix) Pathology of skin:

Disease of the skin and any injury to the skin cause the rapturing of the lipid layer of the stratum corneum which alters the skin penetration of drug.

x) Regional Site of skin:

The skin difference in Anatomical feature such as thickness of stratum corneum, number of hair follicles and number of sweat glands per unit surface area.

xi) Skin flora and enzymes:

Various metabolism enzymes and metabolism microbes are present in the skin which metabolized the drug passing through the skin.

IV. Skin Membrane:

The skin covers the whole outer surface of the body. It is largest organ in the body making up 12-15% of body weight and which surface area of 1-2m². Skin varies from person to person and varies in appearance with age Gender and race. Generally skin of men is thicker than the women. There are three main layers ;

1) Epidermis

2) Dermis

3) Hypodermis

1) The Epidermis:

The epidermis is thinnest outermost layer of the skin and varies in thickness in different parts of our body(between 0.04 and 1.5 mm thick).Even though it is thin the epidermis has five sublayer or strata

- Stratum corneum
- Stratum lucidum
- Stratum granulosum
- Stratum spinosum
- Stratum geminativum

2) The dermis:

The dermis is much thicker than epidermis and is strong and flexible. It consists of connective tissue, nerves, sebaceous (oil) glands, hair follicles, sweat glands and lymphatic vessels. It gives the thick structure to protect the body against stress and strain.
The dermis consists of two layers:

- Papillion layer
- Reticular region

3) The hypodermis or subcutaneous layer:

This layer provides the connection between the skin the underlying muscle and bones, as well as supplying the skin with nerves and blood vessels. It also contains about 50% of our body fat, which protects, cushion and insulates the body, as well as providing fuel.

4) Other components of skin

- Pores
- Hair
- Sebaceous glands
- Sweat glands

V) Transdermal Patches:

Transdermal patches are the in dependable and different dosage form from the other conventional preparations, when we applied the transdermal patches on the skin it can release the drug through the skin at controlled rate in the blood circulation[15]. The transdermal route of administration is reflected as one of the potential route for the local and systemic delivery of drugs.

Transdermal patches deliver the medicament through the skin in a controlled and predetermined manner in order to increase the therapeutic efficacy of drug and reduced side effect of drug. It delivers the drug via skin portal to systemic circulation at a predetermined rate over a prolonged period with a specific amount of dose. Success of a transdermal patch depends on a variety of biological, physiological, biochemical and biophysical factors. It depends on the composition, integrity and thickness of the stratum corneum. The structure and size of the molecule are acts as indicators of diffusivity. It depends on the permeability of the membrane in the transdermal drug delivery system, state of skin hydration pH and other physiochemical drug properties. Lipophillicity of the drug, degree of partitioning of the drug and associated components are also essential. Presently this method of drug delivery has the most potential than other routes of administration because it avoids problems like gastric irritation, metabolic variation and due to the presence of food certain food-drug interactions may happen. This delivery system is also useful for unconscious patients. It has certain limitations like slow penetration rates, lack of dosage flexibility and use of low dosage drugs are restricted. Its main advantage is that it avoids first-pass metabolism.

❖ Advantages:

1. Avoids hepatic first pass metabolism.
2. Maintains constant drug levels for longer period of time.
3. Enhance bioavailability.
4. Decrease the dosing frequency.
5. Decrease unwanted effects.
6. Decrease gastrointestinal side effects.
7. It is very easy to remove in case of toxic effects is observed.
8. Should have good patient compliance.

❖ Disadvantages:

1. The cost of the formulation is high.
2. This drug delivery system is not suitable for ionic drugs.
3. Formulation cannot achieve high drug plasma levels.
4. Transdermal delivery is not suitable for drugs of large molecular size.
5. This formulation is not suitable, if drug or formulation causes irritation to skin.

❖ Types Of Transdermal Patches:

1) **Single-layer drug in-adhesive:** In this system drug and excipients in inclusive with skin adhesive which serve as formulation Foundation as a single breaking layer. The rate of release of drug through diffusion phenomenon.
2) **Multi-layer drug in-adhesive:** In this system drug and excipients incorporated with adhesive but both layer of adhesive separated by single-layer membrane. The release of drug occurred through diffusion phenomenon.
3) **Drug reservoir-in-adhesive:** In the Reserve system, inclusion of liquid compartment containing drugs solution/suspension between breaking layer and semipermeable membrane followed by a adhesive layer and release liner.
4) **Drug matrix in-adhesive:** This system design by inclusion of semisolid matrix having drug in solution or suspension from which is in direct contact with the release liner.

VI) Evaluation of Transdermal Patches:

1)Physicochemical evaluation: -

a) Physical appearance:

Transdermal patches were visually inspected for color, flexibility, homogeneity and smoothness.

b) Thickness:

The thickness of transdermal film is determined by digital microscope , dial gauge, screw gauge or micrometer at different points of the same patch .

c) **Uniformity of weight**:

Weight variation is studied by individually weighing 10 randomly selected patches and calculate the average weight of the patches.

d) **Drug content determination**:

An correctly weighed section of patche (about 100 mg) is dissolved in 100 mL of suitable solvent in which drug is soluble and then the solution is shaken continuously for 24 h in shaker incubator. Then the whole solution is sonicated. After sonication and following filtration, drug in solution is estimated spectrophotometrically by appropriate dilution.

e) **Moisture content**:

The films are weighed individually and place in a desiccators containing calcium chloride at room temperature for 24 h. The films are removed weighed again after a specified interval till they show a constant weight.

f) Folding Endurance:

The evaluation of folding endurance of the transdermal patches was done to determine the folding capacity of the film subjected to frequent extreme condition of folding. A strip of specific area 2.5 cm^2 was cut evenly and repeatedly folded at the same place till it breaks. The number of times the patches folded at same place without breaking was noted as its folding endurance value.

2) *In vitro* drug release studies:

The *in vitro* permeation of the drug from the patches was studied using modified Franz diffusion cell.It consists of 2 compartments, the donor compartment and the receptor compartment. The donar compartment was in contact with the ambient conditions of the atmosphere and was in contact with a solution in the receptor compartment, which is pH 7.4 buffer and was stirred by magnetic bead and driven by a magnetic stirrer at temperature 32°C. The samples were withdrawn at the specified time intervals upto 8 hours and equivalent volume of solution was replaced into receptor compartment after each withdrawal. And the percentage drug release can be calculated.

Conclusion:

Transdermal drug delivery system is useful for topical and local action of the drug. The drugs which shows hepatic first pass effect and unstable in GI conditions are the suitable candidate for TDDS. Transdermal drug delivery system may be ideal for many injected as well as orally given drugs, but many drugs cannot penetrate the skin membrane effectively because of low permeability of skin barrier.

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