IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, January 2024

Review on Transdermal Drug Delivery System

Sonali Ankush Ugale, Dr. Shekhar S. Pandav, Dr.Gajanan S. Sanap
Late Bhagirathi Yashwantrao Pathrikar College of Pharmacy, Pathri, Chhatraptai Sambhajinagar, India

Abstract: *A transdermal drug is an adhesive patch with a prescription that is applied to the skin in order to penetrate the epidermis and enter the bloodstream. This frequently encourages the body's wounded area to mend. A benefit of a topical medicationThe advantage of this delivery method over oral, topical, intravenous, intramuscular, etc. medication delivery is that the patch allows for a controlled release of medication into the patient. This is typically achieved by either a porous membrane covering a medication reservoir or by body heat melting thin layers of medication embedded in the adhesive. Transdermal medication delivery allows for a consistent blood level profile, which minimizes systemic side effects, regulated drug release into the patient.*

Keywords: transdermal drug

I. INTRODUCTION

Transdermal drug delivery system (TDDS) is the system under the category of control drug delivery system. Main aim of the this system is to deliver the drop through the skin in a pre- determined and controlled rate[1]. Tdds are connecting device of define surface area that deliver a predetermined amount of drug to the surface of intact skin at a programmed rate to reach the systemic circulation. Transdermal delivery provides a over injectables and oral routes by the increasing patient compliance and avoiding first pass metabolism. Transdermal road has weed with oral treatment asthe most successful innovative research area in drug delivery. Treatment involves attainment and maintenance of drug concentration in the body within a therapeutic early effective range by introduction of a fixed dose at a regular intervals. That's why the drug concentration in the body follows a peak and through profile. There is a greater chance of adverse effect or therapeutic failure. Large amount of drug is lost in the victim ATI of the target organ and close a tension isrequired to monitor therapy to the avoid overdosing. The limitation of the oral route can be overcome and benefits of the intravenous drug infusion such as the bypass hepatic first pass hepatic elimination to maintain constant prolong and therapeutic effective drug levels in the body can be closely duplicated. Without its potential hazards by transdermal drug administration through intact skin[2]

II. ANATOMY AND PHYSIOLOGY OF SKIN

Skin is the largest organ of human body which covers around 2sq. area and receives about one third of the blood circulation through the body[3]. It act as permeability barrier against the transdermal absorption of various chemical and biological agents. - Acts as a thermostat in maintaining body temperature. - Plays role in regulation of blood pressure. - Protects against the penetration of UV rays. - Separates the underlying blood circulation network from the outside environment - Skin is majorfactorin determining the various drug delivery aspectslike permeation and absorption of drug across the dermis.

Four layers of skin - Epidermis - Dermis - Hypodermis - Percutaneous absorption

1 – EPIDERMIS

Epidermis having 150 micro m thickness arises from an active epithelial basal cell population. It is the skin outermost layer and differentiation process results in migration of the sales from the basal layer towards the skin surface thats why the epidermis has no blood vessels , the nutrients and waste product diffuses across the dermal dermal junction to maintain its strength epidermis is a multi layered it varies in thickness, depending on the cellsize and number of cell layers of epidermis ranging from 0.8 mm on palms and soles down to 0.0 MM on the eyelids

2. Dermis

Dermis is 3 to 5 mm thick layer and is composed of a matrix of connective tissue, which contains a blood vessels lymph vessels nerves. vessels the cutaneous blood supply has essential function in regulation of body temperature. It is also

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provides nutrients and oxygen to the skin while removing toxins and waste products. capillaries reach to within 0.2 mm of skin surface and provide sink conditions for most molecules penetrating the skin barrier. The blood supply the keeps the dermal concentration of permeate very low and resulting concentration difference across the epidermis provides essential concentration gradient for transdermal permeation. It comprises of a dense network of connective tissue having bundle of collagen fibres grade with elastic tissue in a superficial lavels. Dermis contain fine plexuses of blood vessels, lymphatic, nerves, hair follicles, sweat gland, and subcutaneous gland.

3. Hypodermis (subcutaneous)

This layer helps to regulate temperature, provides nutritional support and mechanically protection. It carries a principal blood vessels and nerves to skin and may contain sensory pressure organs[4]. The hypothermia are subcutaneous fat tissue supports the dermis and epidermis. For the transdermal drug delivery, drug has to penetrate through the these three layers and reach into systemic circulation wily in case of topical drug delivery only penetration through strategy corneum is essential and then retention of drug in skin layers is desired.

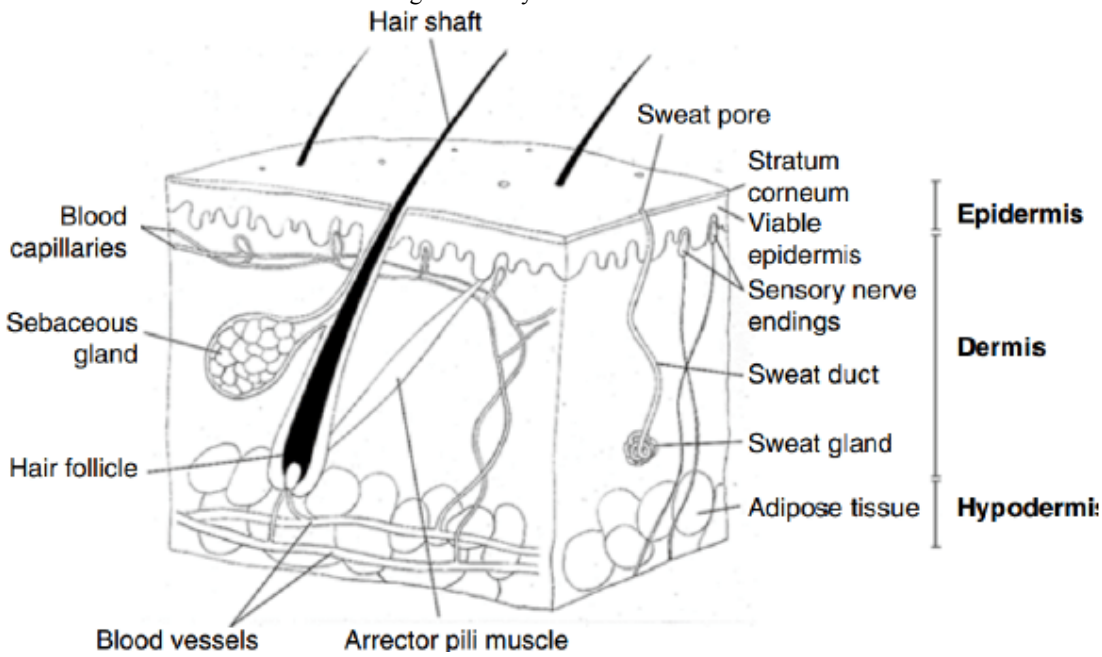

Fig.no 1

Pathways of drug absorption through the skin

In the process of percutaneous permission a drug molecule may pass through the epidermis itself or get diffuse through shunts, particularly those offered by the relative Lee widely distributed hair follicles and eccrine glands in the initial transient diffusion stage drug molecules may penetrate the skin along the hair follicles are sweet ducts and then absorbed through the pellicular epithelium and sebaceous glands. When a steady state has been reach the diffusion through the intact stratum corneum becomes the primary pathway for transdermal pera) Transfollicularroute Trans follicularis route is the shortest pathway that drug has to follow to reach the systemic circulation that provides a large area for diffusion of drugs b) Transcellular route The drug delivery through this route passes from corneocytes which has highly hydrated keratin creating a hydrophilic pathway the drug passesthrough the cornea sites of stratum corneum. c) Intercellular route In intercellular pathway the - 0.1 % area of the total skins these route seems to be most important for the ions and large polar molecules which hardly permeate through the stratum corneum.-

Barrier functions of the skin

The top layer ofskin is most important function in maintaining the effectiveness of the barrier here the individual sale overall I each other and tightly packed preventing bacteria from entry and maintaining the water holding properties of

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skin. It is mainly consists of the keratinized dead cell and water content is also less as compared to the other skin components lipids are secreted by the cells from the base layer of the screen to the top. This lipid molecules join up and form a tough connective network in effect acting as the mortar between the bricks of a wall.

Fundamentals of skin permeation

It is mainly based on passive diffusion skin isthe most intensive and readily accessible organ of the body as only a fraction of mm of tissue separates its surface from the underlying capillary network. The release of the therapeutic agent from a formulation applied to the skin surface and its transport to the systemic circulation is a multistep process, which includes

Diffusion of drug from drug to rate controlling membrane. b. These illusion within a release from the formulation. c. Absorption by stratum corneum and penetration through viable epidermis d. A pic of drug by capillary network in the dermal papillary layer. e. Effect on the target organs. f. Partitioning into the skins outermost layer the stratum corneum. g. Diffusion through the stratum corneum principle via alpidic inter cellular pathways.

Factors affecting transdermal drug delivery system

Physicochemical properties of drug

1. Partition coefficient
2. Molecular size
3. Solubility or melting point
4. Ionization 5. Diffusion coefficient

1. Partition coefficient

Drug possessing both water and lipid solubility are several e absorbed through the skin. Transdermal permeability coefficient shows a linear dependence on partition coefficient. A liquid water partition of one or greater is generally required for optimal transdermal permeability.

2. Molecular size

Molecularsize of drug isinversely proportional to transdermal flux the ideal molecular size of drug molecule for transdermal delivery is greater than 400

3. Solubility or melting

point Most organic solutes have high melting point and low solubility at normal temperature and pressure. Lipophilic drugs permits faster than hydrophilic substances, but it should also have aqueous solubility as needed in most of topical formulations.

4. Ionization

Unionized drug permits the skin as according to pH partition hypothesis.

5. Diffusion

Coefficient Penetration of drug depends on diffusion coefficient of drug. At a constant temperature the diffusion coefficient of drug mainly depends on properties of drug. Diffusion medium and their interaction.

A physiological and pathological condition of skin

a. Presence of hair follicles: absorption israpid where more hair follicle presence example scalp
b. Thickness of stratum corneum: absorption is low frothe m region as foot and palm
c. Trauma: cut, inflammation: rashes, mild burn where stratum corneum is destroyed promote drug absorption.
d. Hydration ofskin: Soaking skin in H2O, plastic film dressing promote hydration of skin and drug absorption increase.
e. Age: aged skin more prone to allergy and irritant effect, of topically contacted drug infant particularly concerned.

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f. Grooming: The frequency and vigor with which one bath and type of soap that is used also contributes variability in drug absorption.
g. Chronic use of certain drug: long term use of keratolytics like salicylic acid results in increase drug penetration.
h. Skin temperature: Increase temperature increase absorption

Classification of TDD

1) Drug in reservoir (membrane type)
2) Drug in matrix (monolithic type)
3) Drug in adhesive (matrix
4) Drug in microreservoir(reservoir in adhesive matrix)

In the first case reservoir is separate from skin wire rate controlling membrane designs in which a u is remote from the drug delivery and area of the system can also be developed it is possible to combine the name type of 50 by placing a membrane over Matrix along with a membrane Matrix device to deliver an initial bolus dose.

Drug in reservoir

In membrane a delivery rate controlling membrane is present between the drug reservoir and skin microporous membrane or dense polymeric membrane can also be used ethylene vinyl acetate copolymer silicon high density polyethylene poly is are the example of materials that can be used as rate controlling membranes and ideal membrane should be permeable to the drop and enhancer and should also retain other formulation excipients. The drug reservoir can be composed of various material ranging from simple formulation to complex formulations

Drug matrix

The drug is uniformly dispersed in a polymeric matrix through which it diffuses to the skin surface the matrix is composed of silicone elastomers, poly urethane, polyvinyl alcohol, can be considered as a drug reservoirthe steps involved in drug delivery process from this system are. 1- The drug molecule dissociated from the crystal lattice 2- The drug molecule undergo solubilization for partitioning in the polymer matrix 3- The drug molecule diffuses through the Matrix to the skin surface Drug can be released from a polymeric matrix under zero order kinetics, if the drug is maintained at a saturation level in the fluid phase of the matrix and if it diffusion rate in a matrix is much greater than its diffusion rate in the skin

Drug in adhesive matrix

These are the simplest system in which the drug and in formulated in an address mixture that is coated into a backing member and to produce and adhesive tap However this systems have a few limitation.. 1- They may undergo chemical interaction which may interfere with a average performance result in a breakdown of activespecies are form New chemical entities 2- physicochemical characteristics of a drug and address system may provide different release rate for hydrophilic and hydrophobic drugs.

Drug in microreservoir

This dress is a combination of reservoir and matrix dispersion system. For preparing the reservoir in this system. The drug is suspended into aqua solution of water-soluble polymer and then resultant solution is a homogeneously dispered in lipophilic polymer to form numerous unleachable, microscopic spheres of drug reserve the thermodynamically unstable dispersion is stabilized by immediately cross linking the polymer

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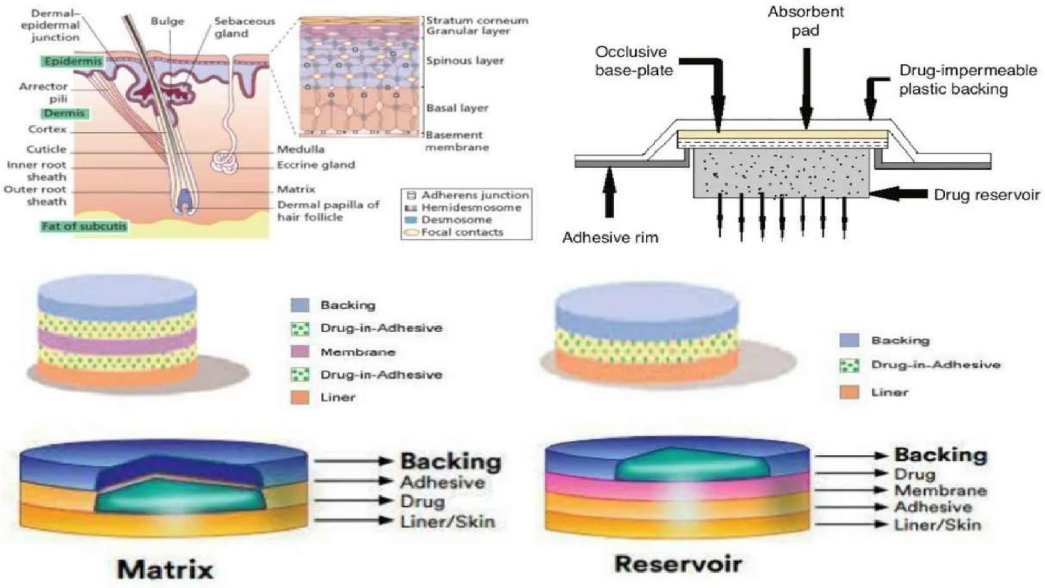

Fig.no 2

- Membrane-controlled transdermal systems are designed to contain a drug reservoir, or pouch, usually in liquid or gel form; a rate-controlling membrane; and backing, adhesive, and protecting layers .

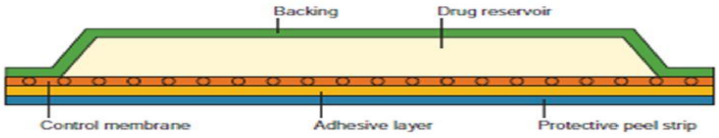

Fig.no 3

Advantages of TDDS

1) No interference with gastric and intestinal fluids in suitable for drugsthat can be destroyed by gastric and intestinal fluids.
2) Maintains stable or constant and controlled blood levels for a longer period of time
3) Reduce side effectsecondary to gastrointestinal intolerance and fluctuations of drug levels.
4) Limiting hepatic first pass metabolism hence lower dose of medication can obtain a desired plasma level compared with oral formulations.
5) Transdermal medication delivers a study in fusion of drug over a prolonged period of time.
6) The simplified medication regimens leadsto improved patient compliance and reduce the side effects inter and intra patient variability
7) Comparable characteristics with intravenous infusion
8) Potentially reduce the risk of drug overdose
9) Easier to titrate to achieve optimal therapeutic doses

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10) Suitable for patient experience nausea and vomiting
11) Patient and career satisfaction because of age of use of tolerance ability
12) Avoidance of unpleasant and inconvenient painful parenteral administration

Disadvantages of TDDS

1) Only potent drugs are suitable candidates for transdermal patch because of the natural limits of the drug entry imposed by the skins impermeability .
2) Doses of only 5 mg are less can be administered in a day. Limit of the dose .
3) The drug, adhesive or excipients in the patch formulation may cause rashes local irritation erythema for contact dermatitis.
4) The barrier function of the skin changes from one side to another one the same person from person to person and with age.
5) Only drugs with a lipophilic character can effectively cross the stratum corneum and hence the drug must have some desirable physicochemical properties for penetration .drug with a hydrophilic structure will not be able to reach the systemic circulation unless modified to some suitable form.
6) Transdermal Drug delivery system cannot achieve high drug levels in blood or plasma
7) The pat may be uncomfortable to where as a user may not adhere to all types of skin.
8) Patch may fall of unnotice.

III. CONCLUSION TDDS

a newer approach in the area of dosage forms for many injected and Orally delivered drugs having appropriate physiochemical and pharmacological properties. The TDDS ensures that a pharmacologically active substance arrives at a relevant in vivo location with minimal side- effects. Because of the several advantages of the TDDS, many new researches are going on to incorporate newer drugs in the system.

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