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Review article on transdermal patches

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Abstract

A transdermal patch is a medicated adhesive patch that is placed on skin to deliver a specific dose of medication through the skin and into a systemic circulation often the promotes healing to an injured area of the body. An advantage of a transdermal drug delivery route over other types of medication Delivery such as oral topical intravenous intramuscular etc. is that the patch provides a controlled release of the medication into the patient usually through either the a porous membrane covering a reservoir of medication embedded in the adhesive transdermal drug delivery system is to deliver drugs Into systemic circulation through skin at predetermined rate with minimal inter and intra patient variations.**1**

Introduction

Transdermal drug delivery system is the desirable drug delivery system to control and sustain the drug release via skin control release drug system limits the release of drug and improve the efficiency of the drug which is relatively fast release system containing the same drug now a days many drugs are administrated orally but due to first pass metabolism Increase the increase the dose and decrease the effects of drug So transdermal drug delivery system is design to improve the efficiency and bioavailability of the drug and decrease the number of dosage **2** transdermal drug. The main objective of transdermal drug Delivery system is to deliver drugs into systemic circulation in to the skin through skin at predetermined rate with minimal inter and intra patient. Currently transdermal delivery is one of the most promising method for drug application. It reduces the load that the oral route commonly place on the digestive tract and liver.**3** It enhances the patient compliance and minimizes harmful side effects of a drug caused from temporarily overdose and is convenience in transdermal delivered drugs that requires only once weakly application. That will improve bioavailability, more uniform plasma levels longer duration of action resulting in a reduction dosing frequency, reduce side effects and improved therapy due to maintenance of plasma levels up to the end of dosing interval compared to a decline in a plasma level with conventional oral dosage forms. Transdermal delivery not only provides controlled constant administration of drugs but also allows continuous input of drugs with short biological half lives and eliminates pulsed entry into systemic circulation which often cause undesirable side effects several important advantages of transdermal drug delivery are limitation of hepatic first metabolism enhancement of therapeutic efficacy and maintenance of steady plasma level of drug. **4**The development of TDDS is a multidisciplinary activity that encompasses fundamental feasibility studies starting from the selection of drug molecule to the demonstration of sufficient drug flux in an ex vivo and in vivo model followed by fabrication of a drug delivery system that meets all the stringent needs that are specific to the drug molecule (Physicochemical stability factor) Optimum therapeutic outcomes require not only proper drug selection but also effective drug delivery system The human skin is a readily accessible surface for drug delivery.**5** Over the past three decades developing controlled drug delivery has become increasingly important in the pharmaceutical industries The pharmacological response both the desired therapeutic effect and the undesired adverse effect of a drug is dependent on the concentration of the drug at the site of action which in turns depend upon the dosage form and the extent of absorption of the drug at the site of action.6 Tablets and injections have been the traditional

way to take medication new options are becoming increasingly popular one highly successful alternative delivery method is the transdermal skin of an average adult body covers a surface of approximately 2m2 and receive about one third of body circulating through the body. The deliver a drug into the body through transdermal layer of skin it is necessary to understand about the skin. 7

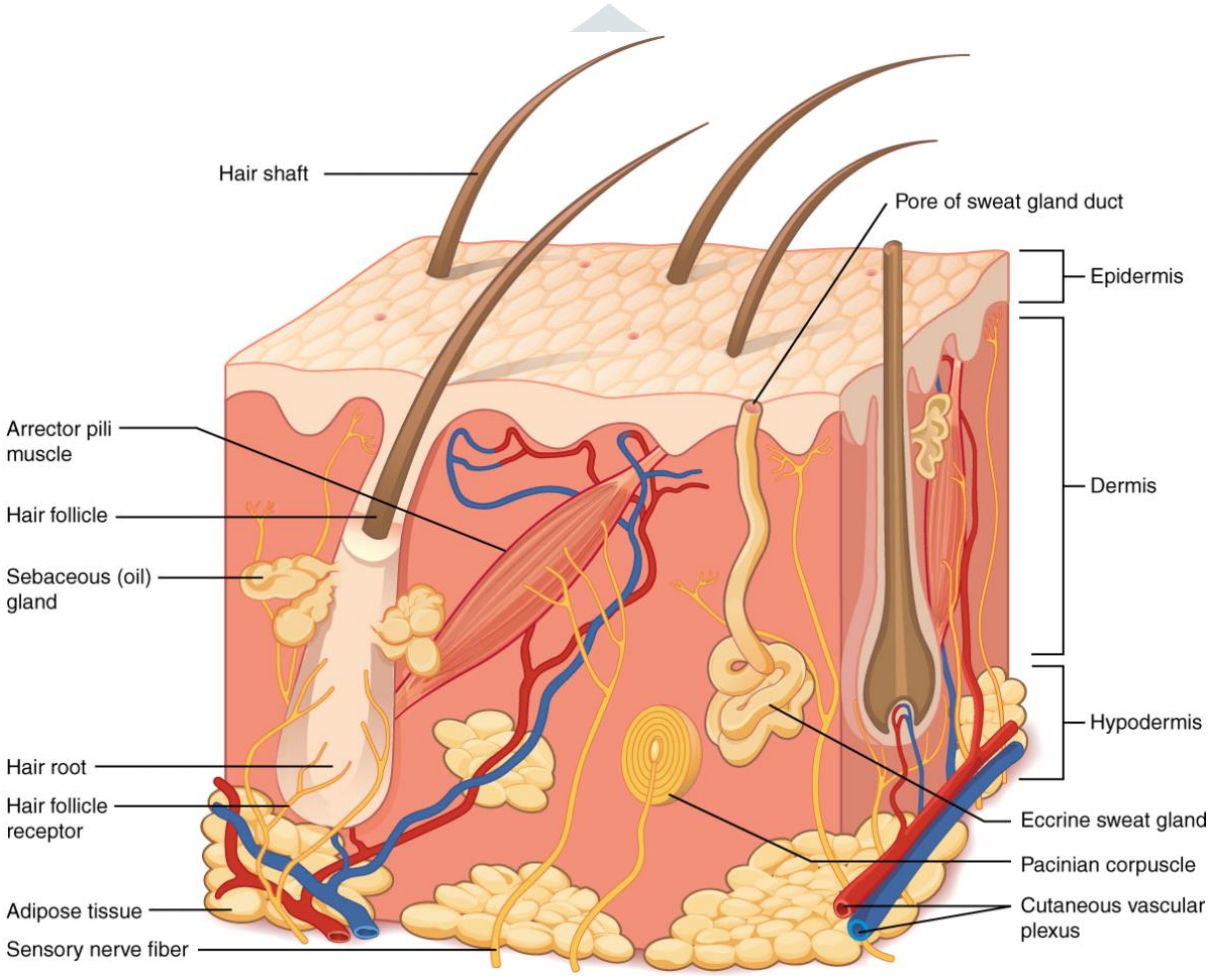
Anatomy and Physiology of skin

Human skin comprises of three distinct but mutually dependent tissue

A) The stratified vascular cellular epidermis.

B) Underlying dermis of connective tissue.

C) hypodermis.



Epidermis

The multi-layered epidermis varies in thickness depending on cell size and number of cell layers of epidermis ranging from 0.8 mm on palms down to 0.06 on the eyelids table 1 gives thickness water permeability and diffusivity of water through epidermis it consist outer stratum corneum and viable epidermis

a) stratum corneum

This is the outermost layer of skin also called bilayers. There is sufficient amphiphilic material in the lipid fraction such as polar free fatty acids and cholesterol to maintain a bilayer form.

b) Viable epidermis This is situated beneath the stratum corneum and varies in thickness from 0.06 mm on the eyelids to 0.8 mm on the palms Going inwards it consists of various layers as stratum lucidum stratum granulosum stratum spinosum and the stratum basal. In the basal layer mitosis of the call constantly renews the epidermis and this proliferation compensates the loss of dead horny cells from the skin surface As the cells produced by the basal layer move outward they alter morphologically and histochemical undergoing keratinization to form the outermost layer of stratum corneum.

Dermis Dermis is 3 to 5 mm thick layer and is composed of a matrix of connective tissue which contains blood vessels lymph vessels and nerves the cutaneous blood supply has supply has essential function in regulation of body temperature It also provides nutrients and oxygen to the skin while removing toxins and waste products capillaries reach to within 0.2 mm of skin surface and provides sink condition for most molecules penetrating the skin barrier The blood supply thus keeps the dermal concentration of a permanent very low and the resulting concentration difference across the epidermis provides the essential concentration gradient for transdermal permeation.

Hypodermis

The hypodermis or subcutaneous fat tissue supports the dermis and epidermis. It serves as a fat storage area This layer helps to regulate temperature provides nutritional support and mechanic al protection It carries principal blood vessels and nerves to skin and may contain sensory pressure organs for transdermal drug delivery drug has to penetrate through all these three layers and reach into systemic circulation while in case of topical drug delivery only penetration through stratum corneum is desired.

Fundamental of skin permeation

Until the last century the skin was supposed to be impermeable with exception to gasses However in the current century the study indicated the permeability to lipid soluble drugs also it was recognised that various layer are not equally permeable i.e. epidermis is less permeable than dermis after a log controversy all doubts about stratum corneum permeability were removed and using isotopic tracers it was suggested that stratum corneum greatly hamper permeation.

A. stratum corneum as skin permeation barrier The average human skin contains 40-70 hair follicle and 200-250 sweat ducts per square cm especially water soluble substances pass faster through these ducts still these ducts don't contribute much for skin permeation therefore most neutral molecule pass through stratum corneum through passive diffusion.

1.Sorption of a penetrant molecule on surface layer of stratum corneum.

2.Diffusion through it and viable epidermis and finally reaches to dermis and finally reaches to dermis and then.

3.The molecule is taken up into the microcirculation for distribution.

Types of transdermal patches

Reservoir system In this transdermal system the drug reservoir is embedded between an impervious backing layer and a rate controlling microporous and nonporous membrane the drug release only through the rate controlling membrane in the drug reservoir compartment the drug can be in the form of a solution suspension or gel or may be dispersed in a solid polymer matrix hypoallergenic adhesive polymer can be applied as a continuous layer between the membrane and release liner or in a concentric configuration around the membrane

Matrix system

drug in adhesive system

In this type the drug reservoir is formed by dispersing the drug in an adhesive polymer and then spreading the medicated adhesive polymer by solvent casting or melting (in the case of hot melt adhesive) on an impervious backing layer on the top face of the reservoir unmedicated adhesive polymer layers are applied for protection purpose.

Limitations for selection of TDDS

All types of drug cannot be administered through this route the drug must have some desirable physicochemical properties

Not suitable for drug that require high plasma levels.

Not suitable for drugs that produce skin irritation and contact dermatitis.

Not suitable for drug that undergo metabolism during the passage through the skin

Not suitable for drugs with high molecular weight.

The transdermal route can not be employed for a large number of drugs as the skin is a very efficient barrier for penetration of drugs only with low dose can be administered.

Evaluation of transdermal films

Interaction studies

Excipients are integral components of almost of all pharmaceutical dosage forms The stability of a formulation among other factors depend on the compatibility of drug with the excipient must be compatible with one another to produce the product that is stable thus it is mandatory to detect any possible physical or chemical interaction as it can affect the bioavailability and stability of the drug.

Thickness of the patches

The thickness of the drug loaded patch is measured in different points by using a digital micrometre and determines the average thickness and standard deviation for the same to ensure the thickness of the prepared patches.

Weight uniformity

the prepared patches are to be dried at 60°C for 4 hr before testing A specified area of patch is to be cut in different parts of the patch and weighed in a digital balance.

Folding endurance

A strip of the specific area is to be cut evenly and repeatedly folded at the same place till it breaks.

Percentage moisture content

The prepared films are to be weighed individually and are to be kept in a desiccator containing fused calcium chloride at room temperature

Percentage moisture content = (Final weight – Initial weight / initial weight) x 100

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