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Transdermal Drug Delivery System

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INTRODUCTION:

In recent years Interest in developing new drug delivery systems systems for existing drug molecules renewed. The development of a new delivery System not only for existing drug molecules improves the performance of the drug in terms of Efficiency and safety, but also improves the patient Adherence and overall therapeutic benefit for a Significant scope.

Transdermal Drug Delivery system (TDDS) are defined as stand-alone, discrete dosage forms, also known as "Patches" 2, 3 when patches are applied to the undamaged part skin, administering the drug through the skin to a controlled rate to systemic circulation. TDDS are dosage forms for the administration of a therapeutically effective amount of drug via a patient's skin 10Several important benefits of transdermal medication Birth are hepatic first pass limitations Metabolism, increased therapeutic efficacy and maintain a constant plasma level of the drug. TDDS developments are multidisciplinary Activity that includes basic feasibility Studies starting with the selection of the drug molecule prove a sufficient flow of active substance in an example vivo and in vivo model followed by the production of a Medication delivery system that meets all stringent requirements

Drug Molecule-Specific Needs (physicochemicals, stability factors), the patient (Comfort and aesthetics), the manufacturer (scaling and manufacturability) and most significant savings .The first transdermal system, Transderm SCOP was approved by the FDA for prevention in 1979. Travel-related nausea and vomiting. Most transdermal patches are designed to be released the drug at a zero order rate for a Periods of several hours to several days follow Apply to the skin. It is special beneficial for the prophylactic treatment of chronic diseases Conditions. The Evidence of Percutaneous Medicine Absorption can be found by measurable blood Drug level, detectable drug excretion and its metabolites in urine and by patient's clinical response to the administered dose pharmacotherapy.

Transdermal route and drug delivery prospects Skin::

The largest organ:

The skin is the largest organ of the human bodycovering an area of about 2 m² and receives about a third of the blood circulation throughout the body. 5It serves as Transdermal permeability barrier Absorption of various chemicals and biological officers. It is one of the most available Organs of the body with a thickness of a few millimeters (2.97 0.28 mm), the Disconnects the underlying blood circulation external environment network.

Serves as a barrier against chemical and microbiological attacks Acts as a thermostat in maintaining the body Temperature. Plays a role in blood regulation To print. Protects against the penetration of UV rays. The skin is an important factor in determining the various aspects of drug delivery, such as Permeation and absorption of the drug on the dermis. The diffusion resistance of The skin is highly dependent on its anatomy and ultrastructure.

Skin anatomy:

The structure of the human skin candivided into four main layers:

- 1 The epidermis
- The vital epidermis
- A non-viable epidermis (Stratum corneum)□4 The overlying dermis
- The internal subcutaneous fat layer(hypodermis)

The epidermis:

The epidermis is constantly renewed, stratified squamous epithelium covering the whole external surface of the body and mainly composed of two parts: the living or viable cells of the Squamous layer (viable epidermis) and the dead Commonly known as stratum corneumcells as stratum corneum

. The viable epidermis is additionally classified into four **different** layers as shown

1. shiny layer
2. grainy layer
3. Thorny layer
4. Basal layer

stratum corneum:

This is the outermost layer of the skin, also called ash stratum corneum. It isthe speed limiting barrier that: limits the inbound and outbound movement of chemical substances. The barrier character of the the stratum corneum critically depends on its constituents:
75-80% protein, 5-15% lipid and 5-10% dry weight ondansetron material.
The stratum corneum is about 10 mm thick when it is dry, but it swells several times when it is full hydrated. It is flexible but relatively impenetrable. The architecture of the stratum corneum can be modeled as a wall-like structure with protein bricks and lipid mortar. It is made up of keratinized skin cells (corneocytes) connected by desmosomes (protein-rich appendages of the cell membrane). Corneocytes are embedded in a lipid matrix which plays an important role in determining permeability of the substance through the skin.

Viable Epidermis:

It is located under the stratum corneum and varies in thickness up to 0.06 mm on the eyelids 0.8 mm on the palms. Facing inwards, it consists of different layers like stratum lucidum, stratum Granulosum, stratum spinosum and stratum basic. In the basal layer mitosis of cells constantly renews the epidermis and this
Growth compensates for loss of dead horns skin surface cells. How cells produced as the basal layer moves outward, they change morphologically and histochemically Keratinization to form the outermost layer of Stratum corneum.14 shown in

dermis:

The dermis is the layer of skin just below the skin The epidermis, which is a layer 3 to 5 mm thick and is composed of a connective tissue matrix that contains blood vessels, lymphatic vessels and nerves. Cutaneous vascularization has an essential function in the regulation of body temperature. It also offers nutrients and oxygen to the skin during its elimination toxins and waste. The capillaries reach less than 0.2 mm from the surface of the skin and allow sinking Conditions for most molecules that enter the skin Fence. The blood supply thus stops the dermal Very low permeate concentration, and the resulting concentration difference on the The epidermis provides the essential driving force for transdermal permeation. Regarding transdermal Drug Delivery, this layer is often seen as essentially gelled water, thus providing a minimal barrier to delivery of most polar drugs, although the skin barrier can be important in the delivery of highly lipophilic molecules.

Hypodermis:

Supports the hypodermis or subcutaneous fatty tissue the dermis and epidermis. It serves as a storage of fat Surface. This layer helps regulate the temperature, provides nutritional and mechanical support

Precaution absorption-

It transports major blood vessels and nerves to the skin and may contain sensory pressure Organs. For transdermal drug delivery, the drug should be used penetrate and reach the three layers systemic **cycle.**

Percutaneous grip:

Prior to this, a locally applied drug may not work either locally or systemically it must infiltrate stratum corneum. Percutaneous absorption is defined as the penetration of substances into different Skin layers and penetration through the skin systemic circulation.11 Percutaneous absorption of Drug molecules are of particular importance transdermal drug delivery system because the drug must be ingested in sufficient quantities and in appropriate amounts uniform, systemic, therapeutic levels throughoutthe period of use. in the usually as soon as the drug molecule crosses the layer Corneal barrier, passage into the deeper layers of the skin and systemic absorption occurs relatively rapidly and easy.
The release of a therapeutic agent from a formulation applied to the surface of the skin and the transport to the systemic circulation is multi-stage process

which includes:

- Dissolution on site and release of art formulation
- Division in the outermost skin layer, the Stratum corneum (SC)
- Dissemination through the CS

Intercellular lipid pathway.

1) Separation of the SC in the aqueous medium viable epidermis, diffusion through viable epidermis5)Epidermis and upper dermis

Routes of drug penetration through skin:

micrograph in the papillary dermis (capillary system) andin the microcirculation.3 ways of drug penetration through the skin:
In percutaneous permeation,a drug The molecule can cross the epidermis itself or can get diffuse through shunts, especially this one provide relatively widespread hair Follicles and eccrine glands as shown . In the initial stage of transient diffusion, drug molecules can penetrate the skin along the hair follicles or Sweat ducts then absorbed by the follicular epithelium and sebaceous glands. When a steady state is reached, diffusion occurs through the intact stratum corneum Main route of transdermal permeation

Barrier functions of the skin

The top layer of the skin is the most important function maintaining the effectiveness of the barrier. Here the individual cells overlap and are well packaged, which prevents bacteria from entering e preservation of the water retention properties of the leather14. The stratum corneum consists mainly of the the content of dead cells and keratinized water is also lowercompared to other components of the skin.15 Lipids are secreted by the cells of the basal layer of the skin on. These lipid molecules come together and form a strong network of connection, by acting in fact like mortar between the bricks of a wall

Basic Principal of Transdermal permeation-

Transdermal permeation is based on passivity Broadcast
The skin is the most intense and willing accessible organ of the body than a simple fractionmillimeters of fabric separate its surface from that underlying capillary network. The output of a therapeutic agent of a formulation applied Surface of the skin and its transport to the systemic Circulation is a multi-step process including

1. Diffusion of the drug from one drug to anothercontrol membrane.
2. Dissolution in and exemption fromFormulation.
3. Adsorption and penetration of the stratum corneumthrough a viable epidermis.
4. Absorption of the drug through the capillary network in thedermal papillary layer. 5) Effect on the target organ.
5. Separation in the outer skin layerstratum corneum.
6. Diffusion through the stratum corneum, mainly through an intercellular lipid pathway.
7.

Formulation of transdermal drug delivery system: Drug substance:

For the successful development of a transdermal drug Administration system with which the drug should be selected great care. Here are some of the most desirable Properties of a drug for transdermal administration.28 12.1.1 Physico- chemical properties: The drugmust have a molecular weightless than 1000 daltons.The drug must have an affinity for bothlipophilic and hydrophilic phasea. Extreme Partitioning characteristics are not driver for successful drug delivery the skin

The drug should have a low melting point. Along with these properties the drugit must bepowerful, have a short half-life anddon't be irritating.

Biological properties:

The medicine must be very powerful, that is, it should beeffective in a few mg / day
The drug should have a short biological half-life

- The drug should not be irritating and notallergic to human skin.
- The drug must be stable in contact withSkin. • They must not provoke an immune responseto the skin.Tolerance to the drug should not develop belowtransdermal releaseprofile of close to zero orderdelivery
- The dose is less than 50 mg per day and ideallyless than 10 mg per day.
- The drug must not be irreversibly boundthe subcutaneous tissue.
- The drug must not be expandedmetabolized in the skin

Polymer matrix:

Polymers are the backbone of transdermal drugs delivery system. Transdermal delivery system are manufactured as multilayer polymer laminates in each a drug reservoir or a drug-polymer matrix integrated between two layers of polymer waterproof outer support layer that prevents this Loss of drug through the substrate surface and onto inner layer of polymer that acts as an adhesive, or flow-controlled diaphragm.

Other excipients:

Various solvents such as chloroform, methanol acetone, isopropanol and dichloromethane used to prepare the drug reservoir. In addition Plasticizers such as dibutyl phthalate, propylene Glycol is added to give plasticity patch

Pressure sensitive adhesive:

A pressure sensitive adhesive (PSA) is a material it helps to maintain intimate contact between the transdermal system and the surface of the skin. This should stick with no more than an outstretched finger Pressure to be aggressive and constantly tachy exert a strong holding force. Moreover, it should be removable from the smooth surface without leaving a residuee.g. e.g. polyacrylates,

Polyacrylates, polyisobutylene, silicone-based Adhesive.

The choice of an adhesive is based on many factors, including patch design and drug formulation. PPE must be physico-chemical and biologically compatible and should not change drug release. The PSA can be positioned on the in front of the device or at the back of the device and expand to the periphery.

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