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A REVIEW ON TRANSDERMAL DRUG DELIVERY SYSTEM

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ABSTRACT

Today about 74% of drugs are taken orally and found to be ineffective. Developing such characters transdermal drug delivery system emerged. Delivery of drugs through the skin to achieve the effect of the drug system more commonly known as transdermal drug delivery and different from traditional drug delivery. Transdermal Drug Delivery systems (TDDS) dosage forms that involve the transport of drugs to the epidermal and / or local functional skin tissues. Therapeutic effect while the bulk of the drug is transferred to a systematic circulation. Adhesive for The transdermal drug delivery system is critical to the safety, efficacy and quality of the product. Title management for therapeutic agents offer more benefits than conventional oral and aggressive drug delivery methods. Several important. The benefits of transdermal drug delivery are limited to hepatic first pass metabolism, improving therapeutic efficacy. And maintaining a stable plasma level of the drug.

Keywords*: TDDS, delivery of high quality drugs, systematic blood circulation.*

1. INTRODUCTION

Transdermal drug delivery systems (TDDS), also known as patches, which are volume forms designed to deliver the effective dose of the drug in the entire patient skin. To bring therapeutic agents through human skin of systemic effects, complete morphological, biophysical and physicochemical properties of skin should be considered. Transdermal Delivery provides a leading edge over injections and oral routes with increasing patient compliance and avoiding early on average (1). Transdermal delivery not only provides control, regular administration of the drug, however and allows for continuous input of drugs with short biological half-lives and eliminates pulsed penetration into the systemic circulation, which often causes unpleasant side effects. So different types of Novel drug delivery system such as Transdermal Drug Delivery Systems, Controlled Release systems, Trans mucosal delivery systems etc. A few important benefits of transdermal drug delivery reduce hepatic pass metabolism, development therapeutic efficacy and maintenance of consistent plasma dose of the drug. The first version of Transdermal, Transderm-SCOP was approved by the FDA in 1979 for bans nausea and vomiting associated with ravel, especially in the sea (2). Evidence of percutaneous drug absorption can be found in the measured blood levels of the drug visible release of the drug and its metabolites in urine and clinical response of the patient to drug administration. Common ingredients that used for TDDS fixes are as follows (3).

Medicine: The drug is directly linked to the release liner Ex: Nicotine, Methotrexate and Estrogen Lines: Protects the pond at the last moment. Example: polyesterfilm.

Adhesive: It works to attach the patch the skin systematic drug delivery.

Example: Acrylates, Polyisobutylene, Silicones.

Permeation Enhancements: Control Releas tree. Ex: Terpenes, Terpenoids, Pyrrolidones.Solvents such as alcohol, Ethanol, Methanol.The same surfactantsSodium Lauryl sulfate, Pluronic F127, Pluronic F68. Support layer: Protect the patch from the outside.Example: Exit from cellulose, poly vinyl alcohol,Polypropylene Silicon Rubber.

Advantages (4-10) :

1. It is very easy as drug use is very easy.

2. Completes the first pass path.

3. Reduce formal drug interactions.

4. Provides long working life.

5. Self-regulation can be done.

6. Prevents hepatic pass metabolism.

7. Keeps blood levels stable for a long time.

8. Improving bioavailability.

Disadvantages (11-13):

1. Many drugs especially hydrophilic drugs properties penetrate the skin very little to be profit.

2. Not suitable for high doses of drugs.

3. Adhesion may vary by patch type once natural conditions.

4. Skin irritation and hypersensitivity reactions are possible they happen.

5. Drugs that require high blood pressure cannot be is treated. Along with these limitations are high product costs and the great error of widespread acceptance of this product.

PROPERTIES:

Physiochemical properties (14,15):

1. The drug must have a certain level solubility in both oil and water (preferably greater than 1 mg / ml)

2. The object must have a point of melting and be small above 200°F. Concentration gradient across the membrane is directly proportional to entry of the drug log into the lipid phase membrane, which is straight equal to the melting point (with full dose of the drug). To find the best TDD candidates, an effort should be made to keep melting point down as much as possible.

3. Substances with less molecular weight more than 1000 units are eligible.

4. Hydrogen bonding groups should be low 2.

Biological properties (16):

1. The drug should be very strong, that is, it should be works with a few mg a day (preferably less than 25 mg / day)

2. A tree should have a short part of living organism's life

3. The medicine should not be irritating and unhealthy allergy to human skin

4. The drug should be stable when in contact on the skin

5. Medication should not stimulate the immune system skin reaction

ANATOMY OF SKIN :

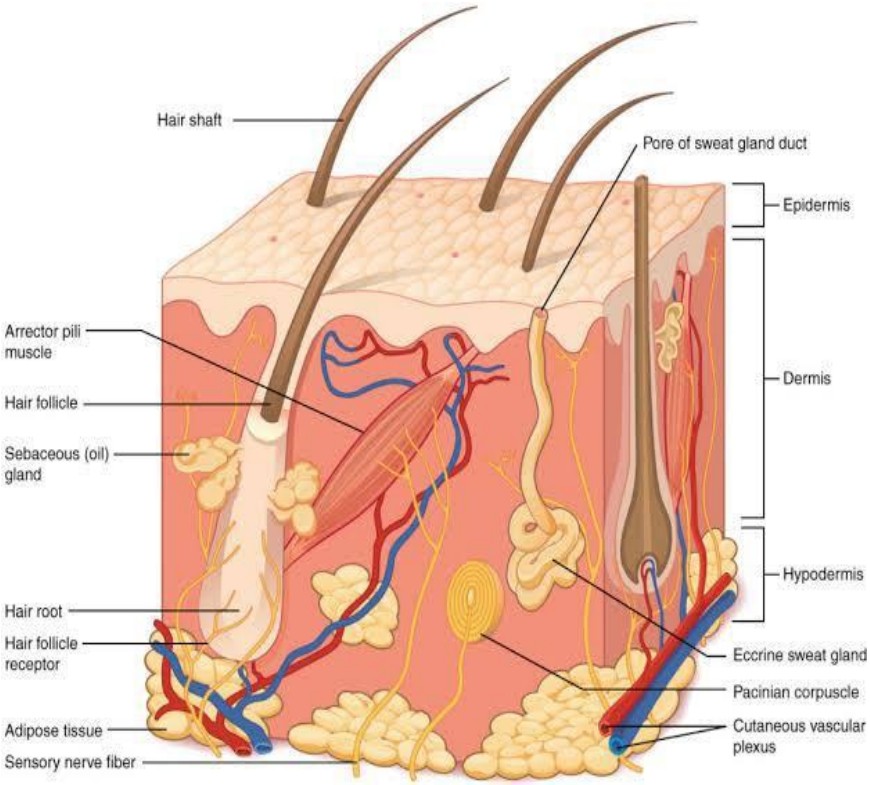

Fig1: Schematic representation of skin and its appendages

The structure of the human skin (fig.1) can be divided into four main categories:

- The epidermis
- The viable epidermis
- A non-viable epidermis (stratum corneum)
- The overlying dermis A layer of subcutaneous oil(Hypodermis)

THE EPIDERMIS:

The epidermis is always rejuvenating stratified squamous epithelium covering the whole the outer surface of the body and is mainly covered of two parts: living or active cells of a layer of malpighian (active epidermis) and dead stratum corneum cells are often referred to like a horned horn(17,18). The active epidermis into four different layers as shown in Fig.2

- Stratum lucidum
- Stratum granulosum
- Stratum spinosum
- Stratum basale

Stratum corneum: This is the outer layer of the skin also called a layer of horns. It is an obstacle that reduces the level of that restricts internal and external movements of chemical substances. Type of block for the horny layer is highly dependent on the catch:

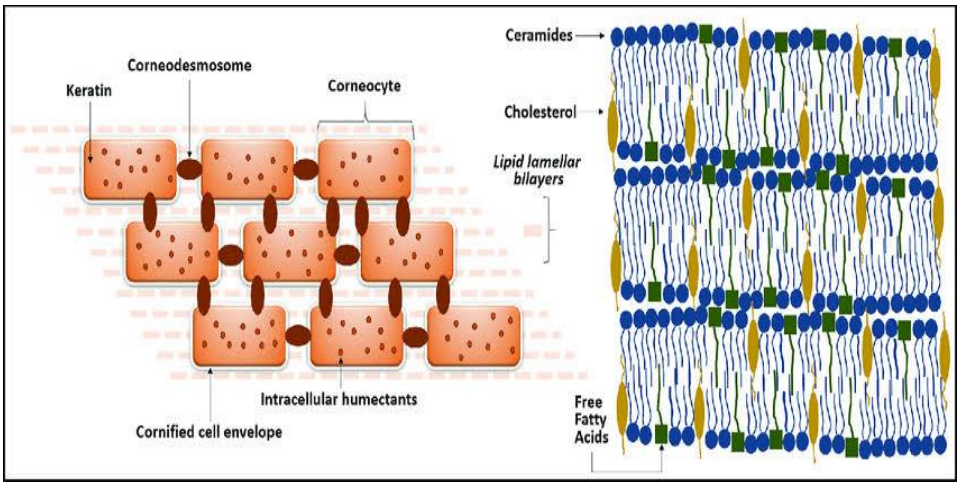

Fig : 2 Schematic representation of microstructure of stratum corneum

75-80% protein, 5-15% lipids, and 5-10% ondasetron material on the basis of dry weight. The stratum corneum is about 10 mm thick if dry but swollen several times when full water. It is flexible but not approachable. A horny layer structure is possible modelled as a wall-like structure with protein bricks and lipid mud. It contains horned skin ki cells(corneocytes) connected by desmosomes (appendages rich in protein membrane proteins).Corneocytes are embedded in the lipid matrixplaying an important role in determining the hardness of the object on the skin.

- **The Viable epidermis**

This is found under the stratum corneum as well varies in thickness from 0.06 mm on eyelids to 0.8mm on the palms of the hands. Inside, it contains various layers such as stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale. It is in the basal layer, mitosis of cells it always stimulates the epidermis and this the increase compensates for the loss of dead horns cells from the surface of the skin. As cells are produced by the basal out,ichanges by itself morphologically and histochemically, continuously keratinization to form the outer layer of stratum corneum.(19)

2. THE HOUSES NEAR EPIDERMIS

•Dermis:

The Dermis is a layer of skin just below the skin epidermis with a thickness of 3 to 5 mm formed by a matrix of connective tissue, viz contains blood vessels, lymph nodes, and nerves. The blood found in the skin has a special functioning controlling body temperature. It also offers nutrients and oxygen in the skin, while removing toxins and waste products. Capillaries reach up to within 0.2 mm of skin surface and provide sink conditions of many molecules entering the skin barrier. Therefore, blood retains dermal the permeate concentration is very low, too difference in concentration throughout the epidermis provides vital driving force transdermal pe(20,21) About transdermal drug delivery, this layer is often considered as gelled water is actually, and thus provides a minor obstacle to the delivery of many polar drugs, although the skin barrier may be significant when presenting highly lipophilic molecules.

•Hypodermis:

The hypodermis or subcutaneous tissue is supportive skin and epidermis. It serves as a fuel depot place. This layer helps to control the temperature, provides nutritional support and equipmentrotation. It carries the main blood vessels as well nerves in the skin and may contain nerve pressure body parts. Delivery of antiretroviral drugs, the drug should go through all three layers and get to the middle system rotation

PERCUTANEOUS ABSORPTION:

Before the above-mentioned drug can work anything locally or systematically, it should enter stratum corneum. Percutaneous absorption is defined as the entry of various objects layers of skin and penetration into the skin penetrated system rotation. Percutaneous absorption drug molecules are very important transdermal drug delivery system for drug it should be absorbed at a sufficient level and balancedacquire and maintain a uniform, program, treatment levels throughout use. general and molecule of the drug crosses the stratum corneal barrier, extends to deeper layers of skin and system capture takes place quickly again easily.

PERCUTANEOUS PERMISSION:

Release of a therapeutic agent from a in the composition applied to the surface of the skin and its moving to system streaming is a number of steps process (figure 5) which includes:

- Internal dispersion and release from make-up
- Separating the outer layer of skin,stratum corneum (SC)
- Distribution by SC, especially by a lipidic intercellular pathway
- Separation from SC to water active epidermis, spreading through active use .epidermis and upper dermis, take in the papillary dermis (capillary system) as well in microcirculation.

3 ways to get drugs into the skin:

Through the process of percutaneous permeation, medicine.The molecule may pass through the epidermis itself or it may spread with shunts, especially those supplied with widely distributed hair follicles and eccrine glands as shown in Figure 6. In the first phase of the temporary distribution, drug molecules it may penetrate the skin near the hair follicles or sweat ducts then absorbed by follicular epithelium and sebaceous glands.If stability is reached in the broadcast through the unstable Stratum corneum becomes main method of transdermal permeation In any molecule applied to the skin, two main ones ways to get rid of the skin can be explained:

- Transepidermal route
- Transfollicular Route

• Transepidermal Route

In transepidermal transport, molecules collapse a solid layer of horns. There are two possible alternatives to is an input, transcellular (or intracellular) as well both polar and non-polar objects are distributed through transcellular and intercellular lines in different ways methods. Tropical molecules are widely distributed through a polar method that includes “arrest water ”inside the hydrated stratum corneum while non-polar molecules melt again dispersed by a non-aqueous lipid matrix for stratum corneum. So the main approach has been taken the entry is determined mainly by separation coefficient (log K). Hydrophilic drug classification especially on intracellular domains,while lipophilic permeants (octanol / water log K> 2) cut the stratum corneum with intercellular route. Many molecules pass through the stratum corneum in both directions.

●Transfollicular Route (Shunt pathway)

This route includes transportation through sweat glands and the hair follicles associated with it sebaceous glands. Although these methods give up permeability, are considered minorvalue because of their very small space,about 0.1% of total skin area. This the line appears to be very important for ions and is large polar molecules easily penetrate water stratum corne, um.

3. TYPES OF TRANSDERMAL PATCHES (22,27)

1. Single-layer drug -in-Adhesive

The adhesive layer of this system also contains wood. Ku this type of pool adhesive layer does not just work with adhesive various layers together, and the whole system in skin, but also responsible for the release of the drug. the adhesive layer is surrounded by a temporary liner and a support.

2. Multi-layer Drug-in-Adhesive

The multi-layer drug-in adhesive patch is similar to a single layer system in that both adhesive layers are also responsible drug extraction. Multi-horizontal system different however is that it adds another layer of wood -adhesive, usually separated by a membrane (but not at all charges). This clip also has a temporary liner layer and permanent support.

3. Reservoir

Unlike Single-layer and Multi-layer Drug-inadhesive systems reservoir transdermal system has a different drug layer. The drug layer is a fluid that contains a drug solution or suspension separated by a coating layer. This clip is also supported by a supporting layer. In this type of system release rate is zero order.

4. Matrix

The Matrix system consists of a drug matrix of semisolid matrix containing a drug solution or suspension. Paste layer in between this clip wraps around a thin layer of wood.

5. Vapor Patch

In this type of patch the adhesive layer is not only functional sticking different layers together but also releasing vapor. Vapor patches are new to the market and are releasing essential oils for up to 6 hours. Vapors patches are released essential oils and are used in congestion conditions in particular.Some steam sheets on the market are steam controller pamphlets improve sleep quality. The vapor closes that reduce the amount of cigarettes a person smokes per month are also available in the market.

Preparation Method :

The method for preparing TDDS was summarized as to correct previously reported methods. The tracts were like that prepared in the form of a solvent extractor. Polymer (e.g.PVP / HPMC) is taken from a small quantity bank of solvent. Then 2 / 3rd of the solvent was added to other polymers (for example PVA) and were first added with shaking at low rpm and later at high speed. The plasticizer was added and mixed in the same way with the drug it was fitted with tolerant turbulence and volume was available done. Films are placed in a well-designed area as well mold moulded and dried in the oven at 40 oC. The films were extracted using sharp edges by isolation on the edge of the film. The dried films were wrapped in butterpaper and stored in a sealed container away from light and inside

4. MECHANISM ACTION OF TRANSDERMAL PATCHES

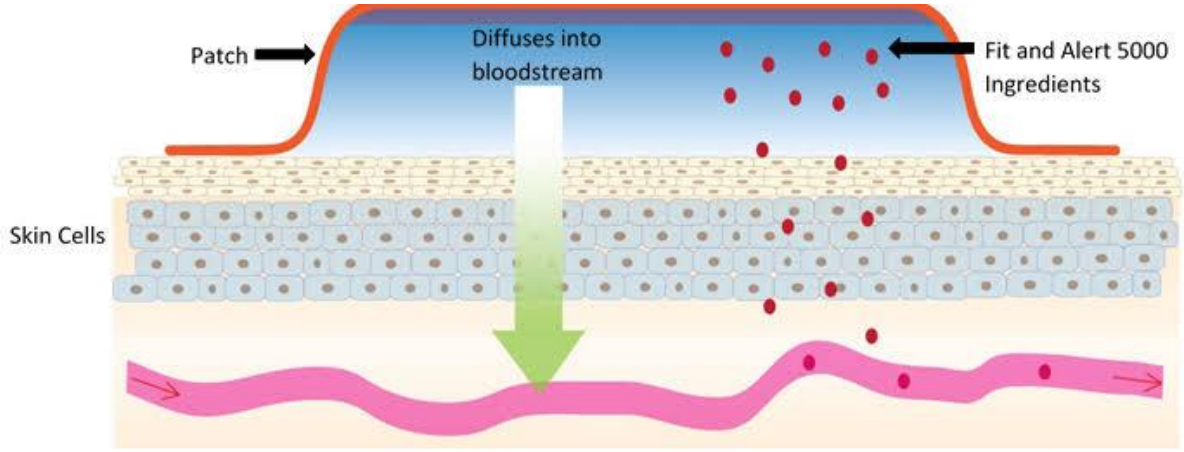

Fig : 3 Mechanism of action of transdermal patches

Use of transdermal patch and the flow of the active substance of the drug from the pond in the circulatory system through the skin occurs different ways.

1. Iontophoresis:

Oontophoresis exceeds a few milliamperes current to a few square inches of skin through an electrode set to connect with construction, which facilitates drug delivery across the bar. (28) Mainly used pilocarpine delivery to cause sweating as part of cystic acid diagnostic fibrosis diagnosis. Iontophoretic delivery lidocaine appears to be a promising alternative immediate onset of anesthesia

2. Electro oration:

Electroporation is a method of useshort, high-voltage electric shocks to the skin.After electroporation, the permeability of the skinin drug distribution increases by 4 orders of size. (29) pulses are believed to they form watery passages that pass through the stratum corneum, where drug transport takes place. It safe and electric pulses can be it is administered painless using a nearby area electrodes to force the electric field inside the nerve stratum corneum.

3. Application by ultrasound :

Use of ultrasound, especially low frequency ultrasound, has been shown to improve transdermal transport of various drugs. Also known as sonophoresis. Katz et al. reported the use of low-frequency sonophoresis for topical delivery EMLA cream.

APPROACHES:

I. Membrane moderate system :

Various technologies have been developed to provide quality control the release and transdermal permeation of the drug.They are referred to as Membrane moderate system: Solid drug dissolves in a solid polymer matrix or in a viscous liquid again coveredin a shallow area associated with the drugStainless steel plastic laminate and quality control

polymeric membrane.Drug molecules enter just to release polymeric membrane control level rate limit . membrane can be microporous or non porous polymeric membrane with known anti-drug properties. To access to close links to the drug delivery system with skin, a thin layer of hypoallergenic drug adhesive polymer can be used. Drug withdrawal rate from the transdermal drug delivery system can be maintained by changing the composition of the polymer, consistency efficiency or thickening of the reducing membrane once adhesive. Internal level of drug release in this type of the drug delivery system is provided as

dQ / dT = CR / 1 / Pm + 1 / Pa

There,

CR = Drug overflow in water storage.

Pa = Collaborative work of the strength of the attachment layer.

Pm = Co-operation to measure the level of membrane control.

II. Adhesive Diffusion Control System:

In this program the drug directly disperses the drug to adhesive polymer and spread the adhesive glue in the reservoir layer form a reservoir. In this non-layer medicated dose controlled polymer adhesive of regular thickness is used . The drug release rate of this type of system is defined as

dQ / dT = (Ka / r) X Da X CR / δa

There,

Ka / r = Partition co-efficient separation by face

drugs form a reservoir layer to the adhesive layer.

Da = Diffusion co-operation in the attachment layer.

δa = The strength of the adhesive layer.

CR = Drug overflow in water storage.

III. Matrix dispersion type system:

In this project, the reservoir was formed by disbanding the similar drugs in polymer hydrophilic or lipophilic matrix and then converted into a medical disc with precise location and controlled stiffness. The disc is attached to the top of the occlusive base plate in a commissioned area from a non-slip plastic base. Glue the polymer is distributed circularly to form an adhesive edge next to a disc with trees The rate of drug release in this matrix distribution system is defined as

dQ / dT = √A * Cp * Dp / 2t

A = The initial load of the drug is dispersed in the polymer matrix,Cp & Dp is a solubility and drug variant polymer respectively.

IV. Microreservoir system:

In this program the drug store is created first suspension of the drug (solid form) in aqueous solution of a polymer dissolved in water and then dispersed evenly drug suspension in lipophilic polymer with high shear mechanical force. Linking a polymer chain, in this case a composite polymer disc of a permanent and defined surface thickening quickly strengthens this dispersion .

5. CONCLUSION

This review article concludes that, the old tree in to make it with new dosage forms produced interest among pharmacologists to develop new volume forms. In addition, new dosage forms are important in other drugs to improve their effectiveness by saying reduce their volume, increase absorption, bring to target location etc. New patented in transdermal tree the delivery platform aims at these objectives. However, the final test that the new process must pass is related to it effective in vivo.

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