TRANSDERMAL DRUG DELIVERY SYSTEM: A BRIEF OVERVIEW

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ABSTRACT:

Transdermal drug delivery system is the way of delivering the drug via a skin it provide the best alternative for delivery the medication at a targeted site this transdermal drug delivery system are providing the tremendous growth in pharmaceutical field which is well accepted and is a very popular approach to a novel drug delivery system this drug delivery system has various advantages over the conventional medications like easy administration ,can be easily handle ,it by passes the first pass metabolism least chances of toxicity having control as well as prolong therapeutic effect .hence this system will be most widely acceptable system in coming recent years. The only complication in the transdermal drug delivery system is the penetration due to the compact packing of the skin layer called as stratum cornium which limits the penetration of the drug is the main issues with this system but by applying various method like use of liposome microneedle, ionophorosis, electrophorasis, etc methods we can able to enhance penetration of drug through the skin.

Keyword: Transdermal drug delivery system, ionophoresis, liposomes, microneedles, electrophoresis.

1. INTRODUCTION

The TDDS allows the release of drug to pass into the skin layer and this is one of the best methods to deliver the drug without any pain and provide the targeted action. This method provides the best method to transfer the drug with controlled and pre determine rate. This system overcomes the limitations of traditional system like oral and parental as this system contain various disadvantages. this system allows to minimize the peak and valley phenomena which lead to plasma drug concentration level flucations, here the main issue comes is the penetration of the drug into the skin. Largest organ is skin which cover almost 15% of total body weight. layers of skin include stratum cornium, stratum granulsum and stratum pinosum and stratum basale and stratum cornium being the most major barrier for the penetration of drug due to its hydrophilicity. Major component which is responsible for its hydrophilicity includes ceramides -50% , cholesterol -25% , fatty acid. Also, it contains densely packed dead corneocytes filled with keratin. which provide Barrer for skin penetration.[1]

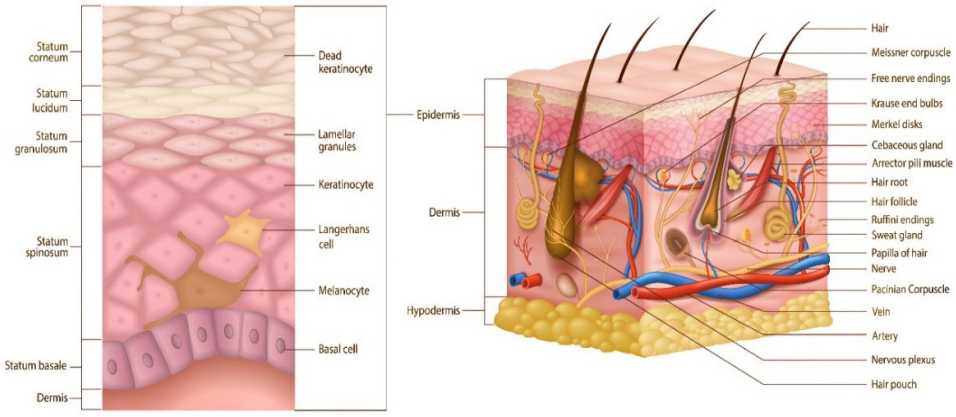


Figure 1: Anatomy of Skin Layer.[2]

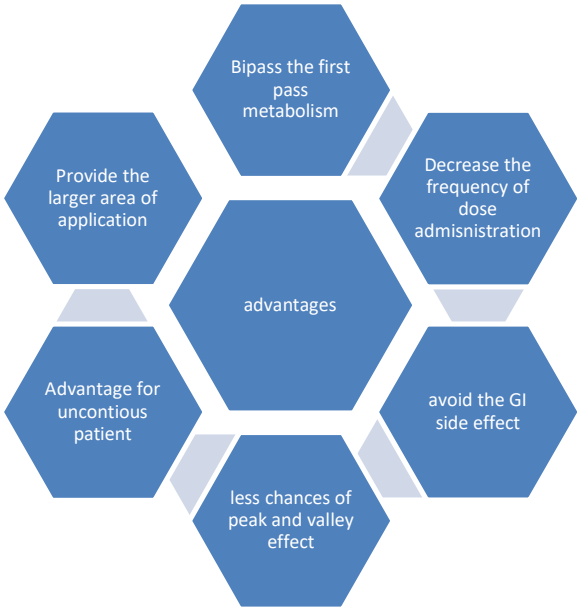


Figure:2 Advantages of TDDS[3]

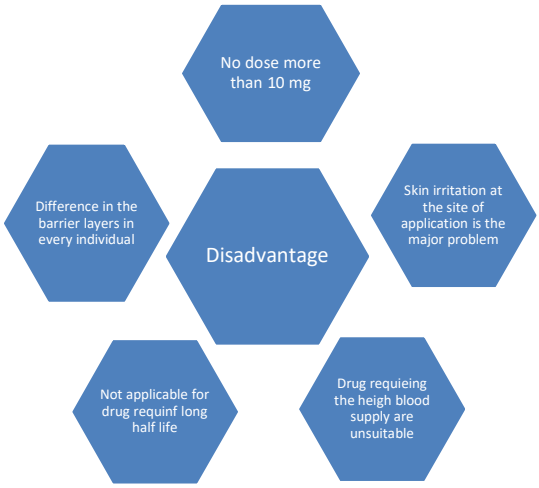


Figure:3 Disadvantages of TDDS[3]

2. MARKETED PRODUCT OF TRANSDERMAL PATCHS:

BRAND NAME	DRUG	MANUFATURER	INDICATIONS
NICOTINE®	Nicotine	Novartis	Smoking cessation
MATRIFEN®	Fentanyl	Nycomed	Pain relief patch
ORTHO EVRA®	Norelgostromin	Ortho-Mcneil	Post menstrual syndrome,
NuPatch 100	Diclofenac Diethylamine	Zydus	Anti inflammatory
Neupro	Rigotine	UCB And Schwarz Pharma	Earlystage idiopathic Parkinson disease
ALORA	Estradiol	Thera Tech	Post menstrual syndrome
Androderm	Testosterone	Thera Tech	Hypogonadism in males
TRansderm-scope	Scopolamine	Alza	Motion sickness

Table 1:Marketed product of transdermal patch[14]

3. BASIC COMPONENTS OF TRANSDERMAL DRUG DELIVARY

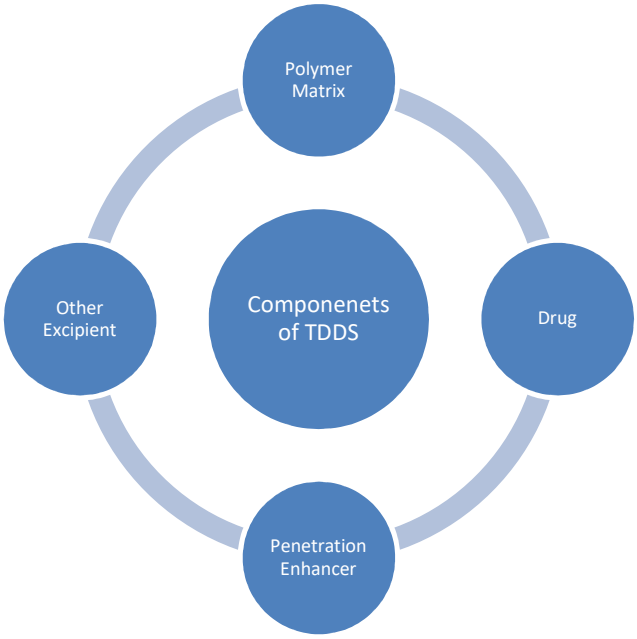


Figure 4: Components of TDDS

3.1 POLYMER MATRIX: This is one in which there is the presence of the polymer incorporated with the drug. This polymer is design as such it can release the drug in its controlled rate. The polymer in cooperate into the patch are designed as such it can't interfere with the drugs activity.[5]

A) Degradable Polymers: This include natural or synthetic hydrolytic polymer which is used to perform hydrolysis in the body. The most widely used polymer includes chitosan and hydroxy acids. Generally, the synthetic polymer general has less batch-to-batch variability and less immunogenicity as compare to the natural polymer. The mechanism involved in degradable polymer include surface erosion and diffusion [6]

B) Biodegradable Polymers: The biodegradable polymer breakdown into the body into the short period of time which provide the temporary support. These are the kind of polymer which generally includes polysaccharide and protein like starch, alginate, chitosan, collagine, gelatine etc. This kind of polymer are used in TDDS to provide the control release of drug. This is used as it is available and are generally cheap.[7]

C) Cellulose and its derivatives: Various derivatives of cellulose like ethyl cellulose, HPMC, HPC, CMC, and MC, used for the fabrication of transdermal patches.

D) Polyethylene glycol: Polyethylene glycol (PEG) is an excellent polymer in terms of its bioavailability and biocompatibility.

3.2 DRUG USED:

There are some basic criteria for the selection of the drug .and this selection depends upon various physiochemical properties like:

1) the drug should have its molecular weight which can be less than or approx. 1000 Dalton.

2) The melting point of drug should be low.

3) The drug must possess boat lipophilic and hydrophilic property.

4) The drug should show its property within minimum daily dose less than (10 mg/day).

5) The half life of the drug should be shorter.

3.3 PENETRATION ENHANCER:

The penetration enhancer is the major component in the patch which is responsible for enhancing the chances of penetrating drug into skin .as penetration of the drug into the skin is the major concern in the case of TDDS. penetration enhancer do not provide any of the therapeutic effect but only help the drug to penetrate into the skin[8].

There is various method which are used to enhance the penetration of drug into the skin which includes:

1) Use of certain penetration enhancers like: ethanol, fatty acid, polyethylene glycol, super refined oleic acid, various surfactant.

2) By various method like use of:

1) Use of microneedles

2) Iontophoresis

3) Sonophoresis

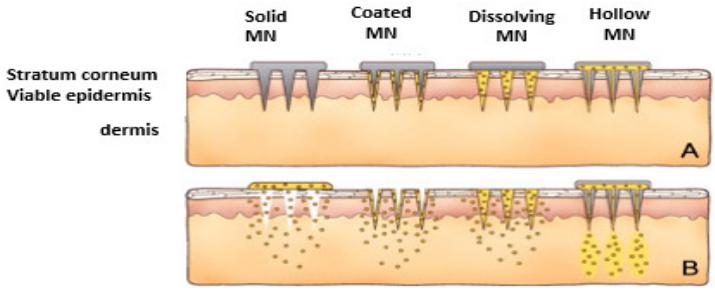
4) Electroporation

3.3.1 MICRONEEDALS:

In microneedle technology it consists of a microscopic microneedle which are responsible for delivering the drug across the subcutaneous layer. They consist of the small needle embedded with the drug which are attached to the small patch.[9]

MECHANISM OF MICRONEEDLE:

The mechanism which is involved in the penetration of drug into the skin via microneedle mechanism is by diffusion mechanism[10].in order to introduce the sufficient amount of medicine and provide the best therapeutic response the hundreds of microneedle are arranged as such which are and are integrated into the patches. This mechanism avoid the issues related to penetration of drug into skin after the application this microneedle it penetrates into epidermis and the drug is send to the systemic circulation and provide the therapeutic response.[11]



ure 5: Mechanism of Microneedle Penetration[12]

TYPES OF MICRONEEDLES:

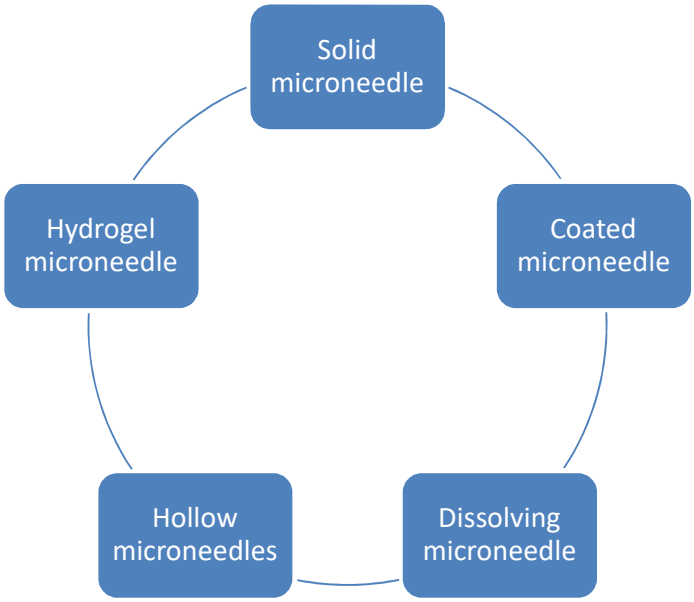


Figure 6: Types of Microneedles

A) SOLID MICRONEEDLE

It is used to penetrate the drug into the skin and produce pore in the skin. When drug patch is applied into the skin it enters into skin due to previous created pore by needles pointed points. Where the drug is absorb by capillaries which result in systemic action. This are also used for the local effect[9].

B) COATED MICRONEEDLE:

The microneedles are enclosed with the drug solution or drug dispersion. The medicine dissolves from the layer later on, and it is rapidly administered. Coating size and thickness of patch , which is typically quite small, determine how much medication can be loaded. [5]

C)DISSOLVING MICRONEEDLE:

The dissolving microneedle is the method which is based on the diffusion mechanism. Which the drug gets diffused into the skin y creating the membrane and causes the drug penetration into the

skin.it crosses the hardest layer to pass through that is stratum cornium and reaches he site of action. [11]

D)HOLLOW MICRONEEDLE:

In this mechanism here the medication in the form of solution or dispersion are filled into the empty space present inside the hollow microneedle further the tip of the microneedle is punctured. where after puncture the medication are deposited into the epidermis or higher epidermis. This type is microneedle are applicable to higher molecular weight oligonucleotide, protein, vaccines. More number of the medication can be filled into the empty area this method ca be use to delivers higher number of microneedle.to strengthen the microneedle metal coating can be done which ca lead to sharpen the microneedle.[11]

E) HYDROGEL FORMING MICRONEEDLE:

This microneedle has the super swelling property as this type of microneedle contain super-swelling polymer. The polymer is hydrophilic in nature which is responsible to absorb the higher amount of water into three-dimensional network of polymers. When this polymer come in the contact with intestinal fluid this polymer gets swell. Which causes the creation of passage between medication patch and capillary circulation. This patches are used as rate controlling membrane as they are having property of swelling .this patch have the advantage as thy can be easily sterilized and can be removed from the intact of skin. [11]

3.3.2 IONTOPHORESIS:

It is the process of introducing the ions or charged molecule inside the tissue by passing the direct current or otherwise by passing periodic electric current through an electrolyte solution which contain the ionic molecules which is being delivered using an electrode is known as iontophoresis.it can be also define as the permeation of drug molecule across biological membrane under the influence of electric current is known as iontophoresis. [13]It is the method which uses the reduced current for the prolong period of time and this type of system is used to enhance the penetration of the drugs containing proteins and peptides. By passing the direct current through the electrode the ions are passed into the skin. The current which is applied is a medically tolerable electric current i.e. (0.5 mA/cm2 or less). The mechanism involve that when the current is applied the electrostatic repulsion pushes the drug inside the skin it enhances the transfer of drug in predetermined rate[14].this method is best for transfer the ionic medication .[15]

TYPES OF IONTOPHORESIS METHODS:

- REVERSE
- PULSATIVE
- IONTOPHORESIS AND ELECTROPORATION COMBINATION

A) REVERSE IONTOPHORESIS:

The reverse iontophoresis is the method which is widely used in diagnostic purpose to withdraw the intestinal fluid via a skin with the help of low electric current. this method offers the simultaneous estimation and effective monitoring desired substances. For example, Glucowatch®,it is an device which uses an electric signals which is equal to the amount of glucose in the extracellular fluid which provide the needleless method for the monitoring of blood glucose level in the diabetic patient.[15]

B) PULSATIVE IONTOPHORESIS:

Here there is a use of DC by the help of short pulse.[15]

C) IONTOPHORESIS AND ELECTROPORATION IN COMBINATION:

They are used in the combination with the use of electroporation which uses the high voltage of current for the short duration of time for the drug to penetrate into the skin the increased drug penetration is cause by the formation of the pores .[15]

ADVANTAGES:

1) Sterile procedure

2) Painless

3) Non-invasive technique. Etc

3.3.3 SONOPHORASIS:

Sonophorasis is the method which is use in increasing the penetration of the drug into the skin by the use of ultra sound which work by increasing the kinetic energy of molecules which causes the drug mor permeable into the skin. The ultrasound causes the cavitation, microstreaming, and by heating. This method is widely use in the physical therapy.[16]

APPLICATION:

1] Ultrasound help to treat bone related problems

2] Sonophoresis is used in the treatment of damaged skin

3] Painful muscular condition responds to non-invasive Ultrasound treatment

4] Hormone Delivery

5] US with Topical anaesthesia rapidly decreases Pain of intravenous cannulation

6] Low-Frequency Ultrasonic Gene Delivery

7] Ultrasound is used for Calcific Tendinitis of the Shoulder

8] The dolphin therapy and sonophoretic model.[16]

4) OTHER EXCIPIENTS:

1) Adhesive layer

2) Backing layer

3) Release line

1)ADHESIVE LAYER:

This is the layer which are used to stick the patch to the skin and to protect the patch from displacement, dust, water etc. Here the pressure sensitive adhesive is used.[17]

IDEAL CHARACTER OD ADHESIVE:

1) It should be highly biocompatible with low or no irritations, toxic, and should not produce any allergic reactions.

2) should provide good sticking even with oily, hairy skin.

3)Should be easily removed from the skin

4)Should be non-reactive with the drug.[17]

2) BACKING LAYER:

This are used to hold the entire system together and also prevent the drug reservoir system from the exposed atmosphere. The most widely used backing material are polyester, aluminized polyethylene tetra phthalate etc.[18]

3) RELEASE LINE:

This are the layer which are being peel or removed during the time of placing the patch to the skin. This are used to protect the loss of drug which is present into the patch[18].

4. EVALUATION PARAMETER OF TRANSDERMAL DRUG DELIVARY SYSTEM:

Parameter	Instrument\Method	Purpose	Remarks
Thickness	Micrometers, screw gauge, dial gauge, etc.	To determine uniform thickness of patch	Avg.thickness should be ± SD calculated from multiple variables
Weight Uniformity	Digital balance	To check consistency in weight	Patches dried at 60°C for 4 hrs.
Folding Endurance	Manual repeated folding	To determine mechanical strength of patch	No.of folds until break indicated endurance
% Moisture Content	Desiccator with calcium chloride	To evaluate water content in patch	Stored for 24 hrs. weight before and after is compared
Content uniformity	UV or HPLC are used	To conform even distribution of drug	Must be between 85 to 115 percent limit

Moisture uptake	Desiccator with KCL 84%RH	To test ability of patch to observed moisture	Weigh until constant until constant weight achieved
Drug content determination	Solvent extraction/HLC	To quantify total drug in patch	Specific area dissolved, filtered and analyzed
In-vitro drug release	USP apparatus V(paddle over disc)	To measure drug release rate	Buffer 7.4, 32±0.5°C,50 rpm analysed over time
In-vitro skin permeation	Franz diffusion cell	To study skin penetration of drug	Rat skin used, flux and permeability coefficient calculated
Skin irritation study	Rabbit skin is used	To check the biocompatibility	Patch applied 24hrs, irritation graded on scale

Table 2: evaluation test with its instrument, purpose and remark[19–22]

CONCLUSION:

The (TDDS) offers promising alternative to traditional drug administration methods by enabling controlled and sustained drug release through the skin. Its advantages include improved patient compliance, bypassing of the gastrointestinal tract, and minimization of side effects. With various types such as reservoir, matrix, and adhesive patches, TDDS is versatile for different therapeutic needs. Despite challenges like skin permeability and formulation stability, advancements in technology and novel approaches such as microneedles and iontophoresis are expanding its scope. Overall, TDDS holds significant potential for revolutionizing drug delivery, particularly for chronic conditions and localized treatments.

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