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A Comprehensive Review on The Transdermal Drug Delivery System

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ABSTRACT

Today about 74% of drugs are taken orally and are found not to be as effective as desired. To improve such characters transdermal drug delivery system has emerged. Drug delivery through the skin to achieve a systemic effect of a drug is commonly known as transdermal drug delivery and differs from traditional topical drug delivery. Transdermal drug delivery systems (TDDS) are dosage forms that involve drug transport to viable epidermal and or dermal tissues of the skin for local therapeutic effect while a very major fraction of drug is transported into the systemic blood circulation. Transdermal delivery provides a leading edge over injectables and oral routes by increasing patient compliance and avoiding the first-pass metabolism respectively. Transdermal delivery not only provides controlled, constant administration of the drug, but also allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into the systemic circulation, which often causes undesirable side effects. Earlier we use a convectional dosage form but now we use a novel drug delivery system. One of the greatest innovations of novel drug delivery is the transdermal patch. The advantage of the transdermal drug delivery system is that it is a painless technique of administration of drugs.

INTRODUCTION:

Transdermal drug delivery systems (TDDS), also known as patches, are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin. To deliver therapeutic agents through the human skin for systemic effects, the comprehensive morphological, biophysical, and physicochemical properties of the skin are to be considered. Transdermal delivery provides a leading edge over injectables and oral routes by increasing patient compliance and avoiding first-pass metabolism espectively1. Transdermal delivery not only provides controlled, constant administration of the drug, but also allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into the systemic circulation, which often causes undesirable side effects. Thus various forms of Novel drug delivery systems such as Transdermal drug delivery systems, Controlled release systems, Transmucosal delivery systems, etc. emerged. Several important advantages of transdermal drug delivery are limitation of hepatic first-pass metabolism, enhancement of therapeutic efficiency, and maintenance of steady plasma level of the drug. The first Transdermal system, Transderm-SCOP was approved by FDA in 1979 for the prevention of nausea and vomiting associated with ravel, particularly by sea. The evidence of percutaneous drug absorption may be found through measurable blood levels of the drug, detectable excretion of the drug and its metabolites in the urine, and through the clinical response of the patient to the administered drug therapy.2

Advantages of Transdermal Drug Delivery System (TDDS)

The advantages of transdermal delivery over other delivery systems are as follows:

1. Avoidance of the first-pass metabolism of drugs.

2. Reduced plasma concentration levels of drugs, with decreased side effects.

3. Reduction of fluctuations in plasma levels of drugs, Utilization of drug candidates with a short half-life and low therapeutic index.

4. Easy elimination of drug delivery in case of toxicity.

5. Reduction of dosing frequency and enhancement of patient compliance.

6. Transdermal medications deliver a steady infusion of a drug over an extended period. Adverse effects or therapeutic failure frequently associated with intermittent dosing can also be avoided.

7. Transdermal delivery can increase the therapeutic value of many drugs by avoiding specific problems associated with the drug. E.g. GI irritation, lower absorption, decomposition due to 'hepatic first-pass effect.

Limitation of TDDS

 Heavy drugs molecules (>500 Da) are usually difficult to penetrate the stratum cornea.

 Drugs with very low or high partition coefficients fail to reach blood circulation.

 Drugs that are highly melting can be given by this route due to their low solubility both in water and fat. 3

 Many approaches have been attempted to deliver medicament across skin barriers and enhance efficacy.

COMPARISON BETWEEN ORAL, INTRAVENOUS, AND TRANSDERMAL

Oral administration remains the most commonly used route for medication. An oral medication generally becomes active when it passes from the gastrointestinal tract and the liver into the blood. Most newly approved medications are developed in oral forms to improve patient access and adherence, especially for oncology-related medications.4

Topical administration allows drug absorption at specific areas of the skin, thereby limiting systemic absorption. Systemic absorption varies based on factors such as the site of application, the area of the skin, and the specific medication.5 Among the various forms of topical administration, transdermal administration remains innovative and historically safe.

Parenteral preparations are sterile preparations intended for administration by, infusion, or implantation into the human body or animal body. The term „parenteral" is applied to the preparations administered by injection through one or more layers of skin tissue. The word is derived from the Greek words, para, and enteron, meaning outside of the intestine, and is used for those dosage forms administered by routes other than the oral route.

ANATOMY AND PHYSIOLOGY OF SKIN

The skin is the largest organ of the human body which covers a surface area of approximately 2 sq.m. and receives about one-third of the blood circulation through the body. (6) It serves as a permeability barrier against the transdermal absorption of various chemical and biological agents. It is one of the most readily available organs of the body with a thickness of few millimeters (2.97 0.28 mm) which,

 Separates the underlying blood circulation network from the outside environment.

 Serves as a barrier against physical, chemical, and microbiological attacks.

 Acts as a thermostat in maintaining body temperature.

 Plays role in the regulation of blood pressure.

 Protects against the penetration of UV rays.

 Skin is a major factor in determining the various drug delivery aspects like permeation and absorption of drugs across the dermis. The diffusional resistance of the skin is greatly dependent on its anatomy and ultrastructure. 7

Anatomy of Skin: The structure of human skin (fig.1) can be categorized into four main layers:

 The epidermis

 The viable epidermis

 A non-viable epidermis (Stratum corneum)

 The overlying dermis

The innermost subcutaneous fat layer (Hypodermis) 8

The Epidermis:

The epidermis is a continually self-renewing, stratified squamous epithelium covering the entire outer surface of the body and primarily composed of two parts: the living or viable cells of the malpighian layer (viable epidermis) and the dead cells of the stratum corneum commonly referred to as the horny layer 8. The viable epidermis is further.

Classified into four distinct layers as shown in Fig. 2. 7

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

Dermis:

Dermis is the layer of skin just beneath the epidermis which is 3 to 5 mm thick layer and is composed of a matrix of connective tissues, which contains blood vessels, lymph vessels, and nerves. The cutaneous blood supply has an essential function in the regulation of body temperature. It also provides nutrients and oxygen to the skin, while removing toxins and waste products. Capillaries reach within 0.2 mm of the skin surface and provide sink conditions for most molecules penetrating the skin barrier. The blood supply thus keeps the dermal concentration of permeate very low, and the resulting concentration difference across the epidermis provides the essential driving force for transdermal permeation. In terms of transdermal drug delivery, this layer is often viewed as essentially gelled water, and thus provides a minimal barrier to the delivery of most polar drugs, although the dermal barrier may be significant when delivering highly lipophilic molecules.8

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 mechanical protection. It carries principal blood vessels and nerves to the skin and may contain sensory pressure organs. For transdermal drug delivery, the drug has to penetrate through all three layers and reach the systemic circulation.9

Drug Permeation Through the Skin

The skin is a selectively permeable barrier. As such, different drugs permeate through the skin at different rates. The rate of drug permeation is expressed as the flux (J), i.e. the amount of drug permeated per unit area, per unit time (usually µg cm−2 h−1). The flux is determined by (a) the permeability of the skin to the permeant and (b) the concentration gradient (ΔC) of the permeant across the skin (usually µgmL−1), according to Eq. 1:

$$J = Kp \cdot \Delta C \quad (1)$$

In Eq. 1, skin permeability is defined by the permeability coefficient, Kp (usually cm h−1). Assuming passive drug absorption, the permeability coefficient is a combined measure of the partition coefficient (P, which depicts how readily the permeant partitions from the formulation into the skin), the diffusion coefficient (D, which measures how readily the permeant diffuses through the skin) and the diffusional path length (h), according to Eq. 2:

$$Kp = P \cdot D\ h \quad (2)$$

The processes of partitioning and diffusion (and thus skin permeability, according to Eq. 2) are highly dependent on the physicochemical properties of the permeant, such as molecular mass and hydrophilicity. As a general rule, molecules that permeate the skin most readily have a molecular mass of <500 Da and are moderately hydrophilic, with an octanol-water partition coefficient (log Poctanol–water) of 1–3. The quantitative relationship between skin permeability (defined by Kp), molecular mass (MW), and hydrophilicity (defined by log Poctanol–water) is widely described using Eq. 3 [10]:

$$\log Kp = 0.71 \cdot \log P_{octanol\text{-}water} - 0.0061 \cdot MW - 2.74 \quad (3)$$

Other factors that may influence skin permeation include hydrogen bond activity, molecular volume, melting point, and solubility. Other mathematical models have been devised to relate the role of these parameters to skin permeation. [11, 12]

Permeation Pathways

A molecule can permeate through the skin via either the transepidermal pathway (diffusing across the skin layers) or the appendageal pathway (through hair follicles or sweat ducts) (Fig. 3). The combined flux of these two pathways determines the overall observed flux across the skin.

Transepidermal Pathway

In the transepidermal pathway, the permeant traverses the intracellular and/or extracellular spaces, from the epidermis to the dermis and hypodermis. The molecule may do so either transcellular or intercellularly. The transcellular route requires that the permeant traverse the alternating layers of cells and extracellular matrix.

This involves a sequence of partitioning and diffusion into alternating hydrophilic and lipophilic domains. The cells and substances that comprise the hydrophilic or lipophilic domains vary between skin layers, but generally, the interiors of cells are more hydrophilic than the extracellular matrix. In the intercellular route, the permeant navigates the tortuous path within the extracellular matrix, without traversing the cells. Small hydrophilic molecules generally favor the transcellular route over the intercellular route and vice versa for lipophilic molecules.

Appendageal Pathway

The appendageal (or shunt) pathway encompasses permeation through hair follicles (the transfollicular route) or sweat ducts. The transfollicular route has gained significant research interest in recent years and is covered in a separate chapter. [13]

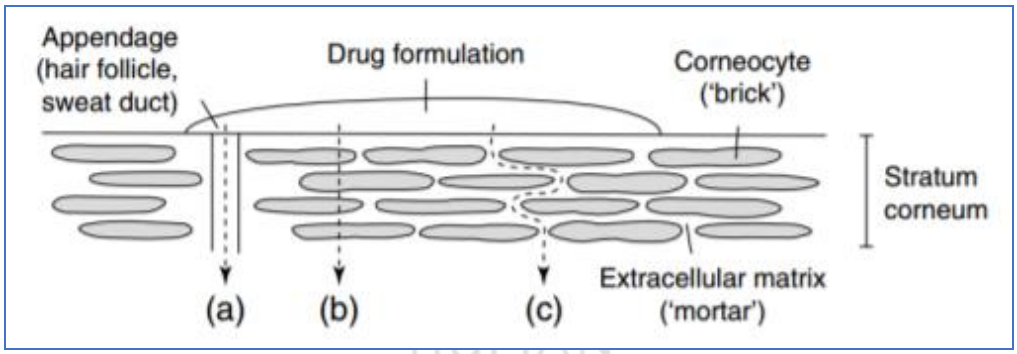

Figure No. 1: Drug permeation pathways in the skin (stratum corneum shown): (a) the appendageal route, (b) the transcellular route

Strategies for the Enhancement of Penetration:

The SPE strategies investigated include chemical skin penetration enhancers (CPEs), physical skin penetration enhancers (PPEs), nanocarrier systems, and a combination of SPE strategies (cream). Of these, PPEs and cream are the most advanced approaches in terms of preclinical and clinical studies, respectively.

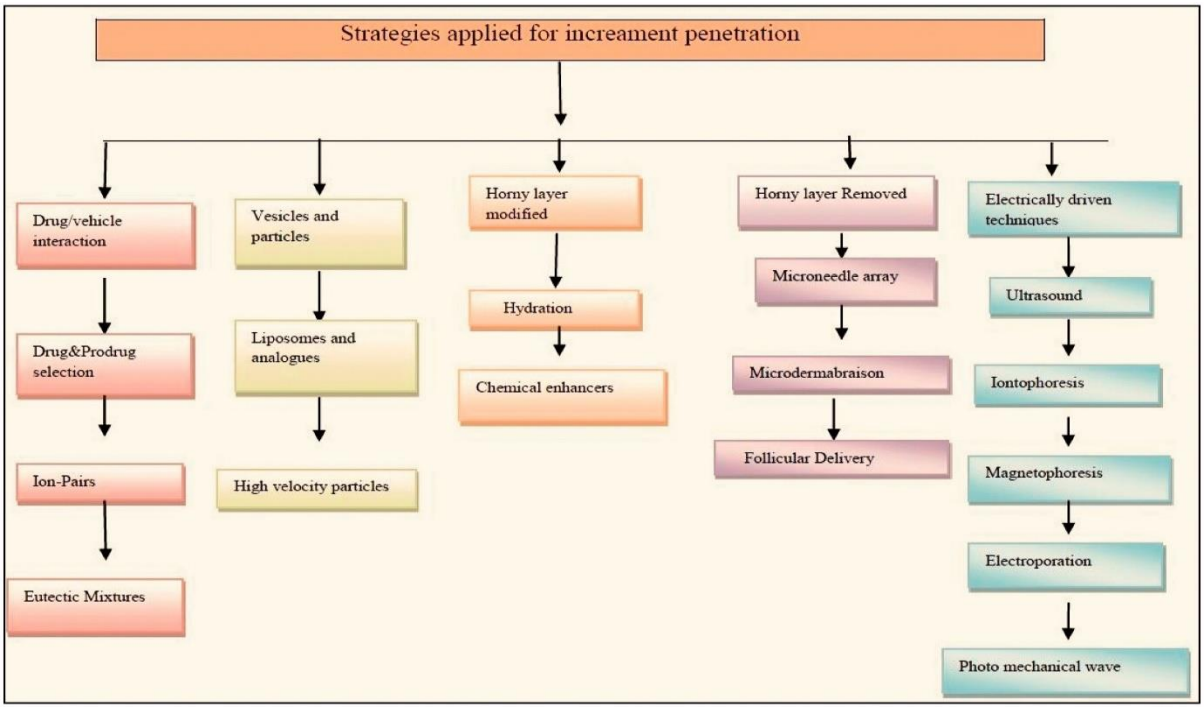

Figure No. 2: Strategies for the Enhancement of Penetration

CLASSIFICATION OF TDDS

Based On Their Technical Sophistication

A) Rate pre-programmed drug delivery system

B) Activation modulated drug delivery system

C) Feedback regulated drug delivery system

D) Carrier-based drug delivery system

A) Rate Pre-Programmed Drug Delivery System

It involves the system design that delivers medicaments by controlling the molecular diffusion of drug molecules across the skin barrier within or surrounding the delivery system.

1. Polymer membrane permeation controlled drug delivery system

It involves the system in which the drug is enclosed within a drug reservoir. This is covered by the semi-permeable membrane of polymer that regulates the release and having a specific permeability. There are some potential development with the process of membrane permeation are as microporous membrane permeation controlled gastrointestinal delivery

device, gastric fluid resistance intestinal targeted controlled release gastrointestinal device, and gel diffusion controlled drug delivery system.14

2. Polymer matrix diffusion controlled drug delivery system-

It is developed by dispersing drug particles in a carrier matrix (in a homogenous manner) that is rate-controlling i.e. NitroDur. It is designed for application onto intact skin for 24 hrs that provide a consistent transdermal infusion of nitroglycerine. 15

3. Microreservoir partitioned controlled drug delivery system-

It involves dispersion of microparticles of suspension of the drug (aqueous) in a polymer using high energy dispersion. e.g. Syncromate implant. Engineered to deliver subdermal administration of norgestomet.15

B) Activation Modulated Drug Delivery System

This type of delivery system can be achieved by-

1-Physical means

- ✓ Osmotic pressure-activated drug delivery system.
- ✓ Hydrodynamic pressure controlled drug delivery system.
- ✓ Vapour pressure-activated drug delivery system.
- ✓ Mechanically activated drug delivery system.
- ✓ Magnetically activated drug delivery system.
- ✓ Electrically activated drug delivery system.
- ✓ Ultrasound-activated drug delivery system.
- ✓ Hydration activated drug delivery system.

2-Chemical means

- ✓ pH activated drug delivery system
- ✓ Ion activated drug delivery system
- ✓ Hydrolysis activated drug delivery system

3-Biochemical means

- Enzymes activated drug delivery system

C) Feedback Regulated Drug Delivery System

The release of the drug molecules from the transdermal system is facilitated by an agent that triggers the release of the drug, such as biochemicals in the body, and also regulated by its concentration through some feedback mechanism.

- ✓ Bio-erosion regulated drug delivery system.
- ✓ Bio-responsive drug delivery system.
- ✓ Self-regulated drug delivery system. 16

D) Carrier-Based Drug Delivery System

Colloidal particulates carrier system:

This involves vesicular systems like hydrogels, liposomes, niosomes, nanocapsules, nanoparticles, polymeric complexes, microspheres, nanoerythrosomes, transferosomes, dendrimers, aquasomes, etc. 17

TRANSDERMAL PATCHES

A transdermal patch or skin adhesive patch is a device that is loaded with a drug candidate and usually applied on the skin to transport a specific dose of medication across the skin and into the blood circulation. 17

The adhesive serves two functions: It is the glue in nature that keeps the patch adhered to the skin, and it acts as the suspension that holds the drug. The problem associated with this is the concentration of the drug within the adhesive directly affects the "stickiness" of the adhesive so if the large quantities of the drug are to be administered, either the size of the patch has to be increased or the patch needs to be reapplied again and again. Several pharmaceuticals are usually combined with substances, like alcohol, within the patch to improve their penetration via skin to improve absorption. 18

Components of Transdermal Patch:-

Liner - Protects the patch during storage. The liner should be removed before its use.

Drug-Drug solution is in direct contact with release liner.

Adhesive- It serves to adhere the components of the patch together along with adhering the patch to the skin. E.g.- Acrylic, polyisobutylene (PIB), and silicone are adhesives that have many pharmaceutical applications. For applications in which the adhesive, the drug, and perhaps enhancers are compounded, the selection of a PSA is more complex (e.g., a matrix design).

Membrane- It controls the release of the drug from the reservoir and multi-layer patches.

Backing- The film protects the patch from the outer environment 19-20.

FACTORS AFFECTING TRANSDERMAL PERMEATION

Biological factor:

Skin conditions: The intact skin itself acts as a barrier but many agents like acids, alkali cross the barrier cells and penetrates through the skin, many solvents open the complex dense structure of horny layer Solvents like methanol, chloroform remove lipid fraction, forming artificial shunts through which drug molecules can pass easily.

Skin age: It is seen that the skin of adults and young ones are more permeable than the older ones but there is no dramatic difference. Children show toxic effects because of the greater surface area per unit body weight. Thus, potent steroids, boric acid, hexachlorophene have produced severe side effects.

Blood Supply: Changes in peripheral circulation can affect transdermal absorption.

Skin metabolism: Skin metabolizes steroids, hormones, chemical carcinogens and some drugs. So, skin metabolism determines the efficacy of drug permeated through the skin.

Species differences: The skin thickness, density of appendages, and keratinization of skin vary from species to species, so affects the penetration.

10 Physicochemical factors: 21

Skin hydration: In contact with water the permeability of skin increases significantly. Hydration is most important factor in increasing the permeation of skin. So use of humectant is done in transdermal delivery.

Temperature and pH: The permeation of the drug increases ten folds with temperature variation. The diffusion coefficient decreases as the temperature falls. Weak acids and weak bases dissociate depending on the pH and pKa or pKb values. The proportion of unionized drug determines the drug concentration in skin. Thus, temperature and pH are important factors affecting drug penetration

Diffusion coefficient: Penetration of drug depends on the diffusion coefficient of the drug. At a constant temperature, the diffusion coefficient of the drug depends on the properties of the drug, the diffusion medium, and the interaction between them.

Drug Concentration: The flux is proportional to the concentration gradient across the barrier and the concentration gradient will be higher if the concentration of the drug will be more across the barrier.

Partition coefficient: The optimal partition coefficient (K) is required for good action. Drugs with high K are not ready to leave the lipid portion of the skin. Also, drugs with low K will not be permeated.

Molecular size and shape: Drug absorption is inversely related to molecular weight, small molecules penetrate faster than large ones.

Environmental factors: 22

Sunlight: Due to Sunlight the walls of blood vessels become thinner leading to bruising with only minor trauma in sun-exposed areas. Also, pigmentation: The most noticeable sun-induced pigment change is a freckle or solar lentigo.

Cold Season: Often result in itchy, dry skin. Skin responds by increasing oil production to compensate for the weather's drying effects. A good moisturizer will help ease symptoms of dry skin. Also, drinking lots of water can keep your skin hydrated and looking radiant.

Air Pollution: Dust can clog pores and increase bacteria on the face and surface of the skin, both of which lead to acne or spots. This affects drug delivery through the skin. Invisible chemical pollutants in the air can interfere with the skin's natural protection system, breaking down the natural skin's oils that normally trap moisture in the skin and keep it supple.

EVALUATION PARAMETERS OF TDDS

□ Thickness:

The thickness of the transdermal film is determined by traveling microscope, dial gauge, screw gauge, or micrometer at different points of the film.23

□ Uniformity of weight:

Weight variation is studied by individually weighing 10 randomly selected patches and calculating the average weight. The individual weight should not deviate significantly from the average weight.24, 25

□ Drug content determination:

An accurately weighed portion of the film (about 100 mg) is dissolved in 100 mL of suitable solvent in which the drug is soluble and then the solution is shaken continuously for 24 h in a shaker incubator. Then the whole solution is sonicated. After sonication and subsequent filtration, the drug in solution is estimated spectrophotometrically by appropriate dilution. 26, 27

□ Content uniformity test:

10 patches are selected and content is determined for individual patches. If 9 out of 10 patches have content between 85% to 115% of the specified value and one has content not less than 75% to125% of the specified value, then transdermal patches pass the test of content uniformity. But if 3 patches have content in the range of 75% to 125%, then additional 20 patches are tested for drug content. If these 20 patches have ranged from 85% to 115%, then the transdermal patches pass the test.28

□ Moisture content:

The prepared films are weighed individually and kept in a desiccator containing calcium chloride at room temperature for 24 h. The films are weighed again after a specified interval until they show a constant weight. The percent moisture content is calculated using the following formula. 23

% Moisture content = Initial weight – Final weight X 100

Moisture Uptake:

Weighed films are kept in a desiccator at room temperature for 24 h. These are then taken out and exposed to 84% relative humidity using a saturated solution of Potassium chloride in a desiccator until a constant weight is achieved. % moisture uptake is calculated as given below.24

% moisture uptake = Final weight – Initial weight X 100

Folding Endurance:

Evaluation of folding endurance involves determining the folding capacity of the films subjected to frequent extreme conditions of folding. Folding endurance is determined by repeatedly folding the film at the same place until it breaks. The number of times the films could be folded at the same place without breaking is folding endurance value.29, 30

 Tensile Strength:

To determine tensile strength, polymeric films are sandwiched separately by corked linear iron plates. One end of the film is kept fixed with the help of an iron screen and the other end is connected to a freely movable thread over a pulley. The weights are added gradually to the pan attached to the hanging end of the thread. A pointer on the thread is used to measure the elongation of the film. The weight just sufficient to break the film is noted.24

***IN-VITRO* RELEASE STUDIES:**

Transdermal patches can be in vitro evaluated in terms of Franz diffusion cell the cell is composed of two compartments: donor and receptor. The receptor compartment has a volume of 5-12ml and an effective surface area of 1-5 cm2. The diffusion buffer is continuously stirred at 600rpm by a magnetic bar. The temperature in the bulk of the solution is maintained by circulating thermostated water through a water jacket that surrounds the receptor compartment. The drug content is analyzed using a suitable method, maintenance of sink condition is essential.31

***IN-VIVO* STUDIES:**

Transdermal patches can be in vivo evaluated in terms of In vivo evaluations are the true depiction of the drug performance. The variables which cannot be taken into account during

in vitro studies can be fully explored during in vivo studies. *In-vivo* evaluation of TDDS can be carried out using animal models human volunteers.24

Animal models:

Considerable time and resources are required to carry out human studies, so animal studies are preferred at a small scale. The most common animal species used for evaluating transdermal drug delivery systems are mouse, hairless rat, hairless dog, hairless rhesus monkey, rabbit, guinea pig, etc. Various experiments conducted lead to a conclusion that hairless animals are preferred over hairy animals in both *in-vitro* and *in-vivo* experiments. Rhesus monkey is one of the most reliable models for *in-vivo* evaluation of transdermal drug delivery in man.24

Human model:

The final stage of the development of a transdermal device involves the collection of pharmacokinetic and pharmacodynamic data following the application of the patch to human volunteers.39 Clinical trials have been conducted to assess the efficacy, risk involved, side effects, patient compliance, etc. Phase I clinical trials are conducted to determine mainly safety in volunteers and phase II clinical trials determine short-term safety and mainly effectiveness in patients. Phase III trials indicate the safety and effectiveness in a large number of patient populations and phase IV trials at post-marketing surveillance are done for marketed patches to detect adverse drug reactions. Though human studies require considerable resources best to assess the performance of the drug.24

APPLICATION OF TDDS [32]

✓ The antihypertensive drug like clonidine and ketoprofen, the non-steroidal anti-inflammatory drug are also available in the form of transdermal patches.

✓ Estrogen patches are sometimes prescribed to treat menopausal symptoms as well as postmenopausal osteoporosis.

✓ Other transdermal patches for hormone delivery include the contraceptive patch.

✓ Transdermal delivery agent for Attention Deficit Hyperactivity Disorder (ADHD).

✓ Two opioid medications used to provide round-the-clock relief for severe pain are often prescribed in patch form: Fentanyl and Buprenorphine.

✓ The transdermal patch of nicotine, which releases nicotine in controlled doses to help with the cessation of tobacco smoking.

Popular uses/market study [33]

- The first commercially available vapour patch of nicotine to reduce smoking was approved in Europe in 2007.
- Two opioid medications used to provide round-the-clock relief for severe pain are often prescribed in patch form: Fentanyl (marketed as Duragesic) and Buprenorphine (marketed as Bu Trans).
- Estrogen patches are sometimes prescribed to treat menopausal symptoms as well as post-menopausal osteoporosis.
- Nitro-glycerine patches are used for the treatment of angina instead of sublingual pills.
- The anti-hypertensive drug Clonidine is available in transdermal patch form under the brand name Catapres-TTS.
- Emsam, a transdermal form of the MAO-I selegiline, became the first transdermal delivery agent for an antidepressant approved for use in the US in March 2006.

Transdermal Market Product [34]:

An increasing number of TDD products continue to deliver real therapeutic benefits to patients around the world. Over the past 5 years (2003–2007), that rate has more than tripled to a new transdermal delivery system every 8 months. It is assumed that more than one billion transdermal patches are currently produced every year.

Currently Approved TDDS

Year	Generic (Brand) Names	Indication
1979	Scopolamine (Transderm Scop®)	Motion sickness
1984	Clonidine (Catapress TTS®)	Hypertension
1986	Estradiol (Estraderm®)	Menopausal symptoms
1990	Fentanyl (Duragesic®)	Chronic pain
1991	Nicotine (Nicoderm®, Habitrol®, Prostep®)	Smoking cessation
1993	Testosterone (Androderm®)	Testosterone deficiency
1995	*Lidocaine/epinephrine (Iontocaine®)*	Local dermal analgesia
1998	Estradiol/norethindrone (Combipatch®)	Menopausal symptoms
1999	Lidocaine (Lidoderm®)	Post-herpetic neuralgia pain
2001	Ethinyl estradiol/norelgestromin (OrthoEvra®)	Contraception
2003	Estradiol/levonorgestrel (Climara Pro®)	Menopause
2003	Oxybutynin (Oxytrol®)	Overactive bladder
2004	*Lidocaine/ultrasound (SonoPrep®)*	Local dermal anesthesia
2005	Lidocaine/tetracaine (Synera®)	Local dermal analgesia
2006	*Fentanyl/iontophoresis (Ionsys®)***	Acute postoperative pain
2006	Methylphenidate (Daytrana®)	ADHD
2006	Selegiline (Emsam®)	Depression
2007	Rotigotine (Neupro®)**	Parkinson's disease
2007	Rivastigmine (Exelon®)	Dementia
2008	Granisetron (Sancuso®)	Chemo-induced emesis
2009	*Oxybutynin (Gelnique®)*	Overactive bladder
2010	Buprenorphine (Butrans®)	Chronic pain

Advancement in Transdermal Drug Delivery [5]

From a global view, an advancement that occurs in transdermal delivery systems can be categorized into three generations of development. In the first generation of systems that produced many of today's patches by judicious selection of drugs that can cross the skin at therapeutic rates with little or no enhancement; through the second generation that has yielded additional advances for small molecule delivery by increasing skin permeability and driving forces for transdermal transport; to the third generation that will enable transdermal delivery of small molecule drugs, macromolecules (including proteins and DNA) and virus-based/ other vaccines through targeted permeabilization of the skin's stratum corneum. First-generation transdermal delivery systems.

In almost all transdermal patch designs, the drug is stored in a reservoir that is enclosed on one side with an impermeable backing membrane and has an adhesive layer on the other side that contacts the skin. Some designs involve drugs dissolved in a liquid or gel-based reservoir, which permit the use of liquid chemical enhancers.

CONCLUSION

The purpose of this article was to give valuable information regarding transdermal drug delivery systems. Transdermal drug delivery systems have been used as safe and effective drug delivery devices since 1981. Many drugs have been formulated in TDDS forms, such as hormonal therapy, a wide range of analgesics, drugs for heart diseases, for avoiding GI effects, and first-pass metabolism. TDDS a realistic practical application as the next generation of drug delivery system and due to large advantages, many new types of research are going on in the present day to incorporate newer drugs via the system.

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