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An Overview Of The Transdermal Drug Delivery System

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Abstract: Transdermal drug delivery systems have been used as safe and effective drug delivery devices. Various non-invasive administrations have recently emerged as an alternative to conventional needle injections. The transdermal drug delivery system (TDDS) represents the most attractive method among these due to its low refusal, easy handling. The advantage of the drug delivery route over the other types of delivery systems such as oral, topical, intravenous, intramuscular, etc. that's the patch may essentially can provide controlled release of the drug to the patient, usually through either a porous membrane. A transdermal patch is an adhesive patch with medication applied to the skin to deliver a specific dose to the skin and blood. It works best when the medicine is put inside the patch and worn on the skin for a long time. By this constant concentration of drug remain in blood for long time. TDDS could be applicable in not only pharmaceuticals but also in the skin care industry, including cosmetics. Transdermal drug delivery provides a controlled release of the drug to the patient, enhances a stable blood level profile, leading to a reduction in systemic side effects and, in some cases, improved performance in other dosage forms. The main purpose of the transdermal drug delivery system is to bring drugs into the circulation of the skin system at a predetermined level with minimal inter and interpatient variations.

Keywords: - Skin, TDDS, Reservoir, Epidermis, Penetration

INTRODUCTION:

The Drug Delivery System (DDS) is a standard term for a physicochemical series technology that can control the delivery and release of pharmacological substances from cells, tissues and organs, so that these active substances can have positive effects[1,2]. Depending on the route of delivery, there are several types of treatment options, such as oral administration, transdermal administration, lung inhalation, mucosal administration, and intravenous injection. Among them, the transdermal drug delivery system (TDDS) represents the attraction approach[3]. Any drug delivery system aims to provide the right amount of medication for the drug site in the body and then maintain desired drug concentration.

The formulation of substances containing drugs that reflect systemic action is called (TDDS) or transdermal therapeutic systems. Transdermal drug delivery system is a highly regulated drug in the form of leaflets that deliver systemic drugs at a fixed and controlled rate. The acquisition of the (TDDS) is a breakthrough in the field of regulated drug delivery system. It became a large field of interest. TDDS has become the most widely investigated route for the delivery of anti-inflammatory drugs, unlike conventional control injections. Today about 74% of drugs are taken orally again found to be ineffective. Improving drug delivery system of such a character emerged. The drug is used in an extremely relatively high quantity in the middle of the patch, which is worn on the skin for long time. TDDS are dosage forms that contain only, which, when applied to sensitive skin, deliver the drug, through the skin with a degree of control over the circulation of the system[4]. In 1965 Stoughton First conceived with percutaneous drug ingestion. The FDA approved the first Transdermal-SCOP program in 1979. The FDA approved this to prevent nausea and vomiting[5]. The polymer matrix, drugs, permeation enhancers are key components of TDDS; polymers include Zein, Shellac (as natural) to synthetic (Polybutadiene, Polysiloxane, PVC, Polyvinyl alcohol etc.). TDDS is a multidisciplinary genus from a single-layer drug to a multi-layer adhesive drug and some are reservoir and matrix systems. The TDDS has been around for long time. In the past, most widely used systems were creams and ointments for treating skin diseases. TDDS is the non-invasive delivery of drugs from the skin surface - a large and very accessible organ in the human body - through its layers, in the circulatory system.

Advantage of TDDS: -

1) Improved bioavailability

2) Prolonged duration of action leading to a decrease in dosing frequency[6].

3) is suitable for a drug candidate with a short half-life

5) Reduced side effects.

6) many plasma levels are the same.

7) painless and easy use and flexibility to eliminate drug treatment by removing the patch from the skin[7].

8) Self-regulation is possible with these systems[8].

9) They no invasive; they avoid disruption of Parenteral therapy[9].

Disadvantage of TDDS: -

1. Transdermal treatment route is not suitable for drug irritation or skin sensitivity.

2. Many drugs especially drugs with hydrophilic properties enter the skin very slowly and may not reach the level of treatment[10].

3. Drugs, adhesives or other substances that aid in patch formation can cause erythema, itching, and local edema.

4. Ionic drugs cannot be delivered by the body's immune system.

5. Skin rejuvenation function varies from place to place in the same person, from person to person and in age.

6) The drug should have the desired the physicochemical properties of stratum corneum infiltration and when dose of the drug required for treatment is more than 10mg / day, TDDS will be more difficult.

7) Loss of dose may be due to the binding of medicine on the skin.

Limitation of TDDS: -

• TDDS cannot deliver ionic drugs.

• High dosage will not be achieved through this program.

• It will not develop a cellular drug.

• TDDS is unable to deliver medication in a way that affects the heart.

• TDDS cannot develop if the drug or texture causes irritation to the skin.

• Skin rejuvenation function changes from place to place, from person to person and up to 6 years.

• Transdermal drug delivery system limited to strong drug[11].

Anatomy and physiology of skin: -

The skin is the largest organ in the body of about 20sq feet and receives about one-third of the blood circulating in the body. which helps control important signals, and allows body sensitivity to cold and warmth. The skin is a barrier to stopping excess water and sweating throughout the body. The skin is a multi-layered outer layer, and the role of the skin is to protect our body by preventing natural hazards such as chemicals, heat, and toxins[12,13]. Such skin can be divided into epidermis, which we have a protective function, as well as the dermis, where there are blood vessels dermis, where blood vessels are present, and produce skin cells, and each layer has features that interfere with transdermal delivery.

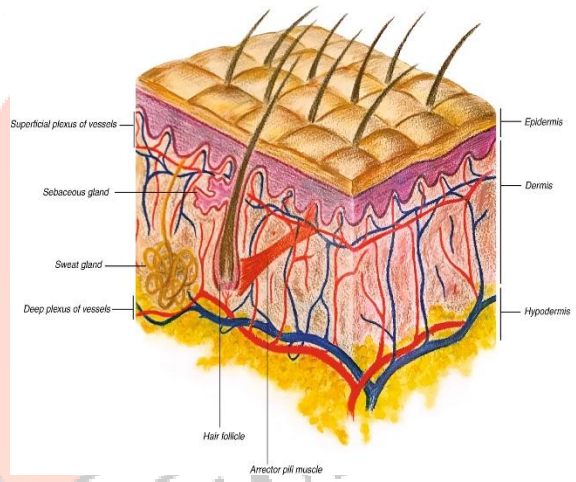

Fig: - Anatomy and physiology of skin

The skin structure is made up of a tortuous network which is the body's first barrier against germs, UV light, chemicals, and mechanical damage. The epidermis is further divided into two parts - the non-living epidermis (stratum corneum) and the active epidermis. The active epidermis is divided into four layers, namely, stratum lucidium, stratum granulosum, stratum spinosum and stratum germinativum. First, the protective effect of the epidermis skin comes from the stratum corneum, the outer layer, and is a protective material for foreign substances. The inhibitory effect is very important for the transport of substances with high molecular weight[14]. In TDDS, it is generally accepted that the delivery of molecular weights uses an intracellular

method. However, in objects with high molecular weight, various methods and techniques that use the intracellular method over the intercellular method are introduced and used[15,16]. This is due to the formation of the skin because the part called lipid that contains both cells and hydrophilic substances and hydrophobic substances does not have a completely normal but normal surface[16]. These structural elements can be explained by the principles of physicochemical structures that attempt to improve the delivery of drugs through the skin. Next, a vascular system in the dermal layer can prevent transdermal delivery. The thick layer of single endothelial cells that cut through the papillary loops of the upper arteriovenous plexus near the dermal-epidermal area in the upper dermis represents the connection between the tissues around the skin and the human vasculature. The role of the endothelium in the skin is similar to that of the whole body. Actively reacts to stress, shear, osmotic pressure, heat, chemokines, and cytokines by modifying maturation and inducing vasodilation or constriction[17]. Therefore, the main problem of TDDS is to resolve the inhibitory effect of stratum corneum, deliver the drug to the skin tissue, and pass through the cellular tissues and vascular tissue to reach the target tissue. The problem is that only a small amount of the drug can be delivered through the skin tissue[18,19].

Basic elements of transdermal Drug Delivery Systems[20,21]: -

1. compound matrix
2. The drug
3. Permeation enhancers
4. different excipients

1) Polymer Matrix:

The chemical compound controls the release of the drug on the wire. The following conditions must be met for the polymer to be applied to transdermal patches.

(i)The polymer should be stable.

(ii) The polymer must be non-toxic

(iii) The polymer should be easily made

(iv) The polymer should be inexpensive

Polymers that can be useful for stratum devices are:

Natural Polymers: Gelatin from Cellulose, Wax, Natural Rubber, Starch etc.

Synthetic Elastomers: e.g., polybutadiene, Hydrin rubber, Polysiloxane, synthetic rubber, Nitrile, propenonitrile, synthetic rubber, Styrenebutadieine rubber, synthetic rubber etc.

Synthetic Polymers: e.g., polyvinyl alcohol, PVC, synthetic resin, plastic, Polyacrylate, Polyamide, Polyurea, Polyvinyl Pyrrolidone, Polymethylmethacrylate, Epoxy Etc.

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2) The Drug:

Because of the success of the drug delivery system, the drug must be selectively charged. the following is a list of the attractive features of stratum Delivery[22].

Physiochemical properties

(a) A drug must have a molecular weight of less than 1000 Dalton.

(b) The drug should be compatible in both lipophilic and hydrophilic phases.

(c) The tree should have a low melting point.

Biological properties

(a) The drug should be intensified with a daily dose of a few mg / days.

(b) The life span (t½) of a tree should be short.

(c) Medication should not cause allergies.

3) Permeation Enhancers:

These compounds promote skin porosity by altering the skin as a barrier to the flow of desired penetration. The dehydrator is thought to have touched one or more of these layers to achieve improved skin penetration. A large number of computers have been investigated for their ability to improve stratum corneum permeability[23].

The following topics:

a. Solvents:

These compounds increase Inflammation almost by inflammation of the polar pathway and / or by excretion of lipids. Examples accept liquid alcohol - wood and ethanol; radical alkyl sulfoxides - dimethyl sulfoxide, radical homologs of alkyl sulfoxide dimethyl amide and dimethyl formamide; pyrrolid-Ones- a pair of pyrrolidone, N-methyl, 2-purrolidone; Laurocapram (Azone), solvents — Propylene glycol, glycerol, siloxane liquid, Isopropyl palmitate.

b. Surfactants

These compounds are expected to improve the transport of the polar pathway, especially fluid drugs. the power of the top acting agent to change the input can be the function of a cool head unit and consequently the length of the integrated biological chain. Anionic Surfactants: eg, Dioctylsulpho-Succinate, Na lauryl salt, Decodecyl-Methyl sulphoxide etc.

c. Nonionic Surfactants:

e.g., Pluronic F127, Pluronic F68, etc. Bile Salts: e.g., Na mstaurocholate, Na Deoxycholate, Na tauroglycocholate.

d. Bile salt: sodium taurocholate, sodium deoxycholate.

e) Various Chemicals: These include urea, hydrating and keratolytic agent

f) other helpful items

(i) Adhesives: - A pressure-sensitive adhesive can be applied to the surface of the phone or to the back of the device.

- ❖ It should not be irritant.
- ❖ It should be easily removed.

- ❖ It should not leave a residue unwashed on the skin.
- ❖ It should blend well with the skin.
- ❖ Physical and chemical interactions with medicine.
- ❖ Drug overdose should not affect.

(ii) Linear: Protect the pond at the last moment. Linear is removed before use.

(iii) Backing: - Protect the patch from the outside.

FACTORS AFFECTING TRANSDERMAL DRUG DELIVERY [4,24]: -

Effective transdermal drug delivery can be built by considering three factors such as Drug, Skin, and vehicles. Therefore, affecting factors can be classified into classes such as biological and physicochemical factors.

Biological traits:

i) Skin condition: Acids and alkalis, many solvents such as chloroform methanol damage skin cells and promote penetration. The patient's medical condition changes skin conditions. Solid leather is a better barrier but the conditions listed above affect penetration.

ii) Skin age: smaller skin is more accessible than old ones. Children are very sensitive to toxic skin. Therefore, skin age is one of the factors drug entries into TDDS.

iii) Blood supply: Changes in peripheral circulation can affect transdermal absorption.

iv) Skin temperature: The human body maintains skin temperature from about 37ºC to about 32ºC on the outside. Since stratum corneum proliferation is an inactive process, high skin temperature can cause structural changes within the stratum corneum, and these changes can also increase tissue proliferation.

v) Types of animal species: Density of the skin, congestion of the appendages, and keratinization of the skin vary in species, thus affecting penetration.

Physicochemical Features:

i) Skin hydration: When in contact with water the skin maturation increases dramatically. Hydration is a very important factor that increases skin fullness. Therefore, the use of humectants is carried out in transdermal delivery.

ii) Melting point / melting point: It is known that most organisms with high melting points have low water solubility at normal temperatures and pressures. Lipophilic molecules usually penetrate the skin faster than most hydrophilic molecules. However, although lipophilicity is desirable for flexible individuals, it is also necessary for the molecule to exhibit a certain liquid solubility as topical drugs are commonly used from water composition.

iii) Diffusion coefficient: Ingestion of a drugs depend differentiation of the drug coefficient. At constant temperatures the distribution coefficient of the drug depends on location of the drug, the diffusion medium and the interaction between them.

iv) Cell size: The absorption of the drug is related to the weight of cells; small molecules enter faster than hundreds. is a key factor to determining the flow of material through human skin the molecular size. However, for the convenience of cells the weight of cells is usually taken as a measure of cell size. It has been suggested that a negative relationship exists between the transdermal flux and the molecular weight of the molecule.

v) Partition coefficient: the partition coefficient is important in determining the distribution of a tree to an organism in order to perform its biological function. Hydrophilic drugs are not absorbed

when used topically, due to the lower lipid matrix of the stratum corneum.

TYPES OF TDDS[7, 25,26]: -

1. The drug in TDDS adhesive: - In this system the drug is dispersed in the adhesive layer of the pond. Not only layer of adhesive works to attach parts of the patch to the skin but also regulates the rate of drug delivery on the skin. The adhesive layer is the surrounded by a liner.

Two types of there,

a) Single-layer adhesive: In this process the tree is dispersed in the adhesive layer of the pond. In these types of patches, the adhesive layer works to attach various layers together and oversees drug release. The paste layer is surrounded by a temporary liner and support

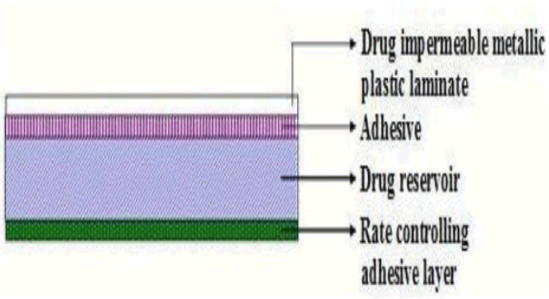

Fig: - Single–layer adhesive

b. TDDS multi-layer adhesive: This type is similar to a single layer but contains a quicker a drug withdrawal layer and another layer will be a controlled release and an adhesive layer. The adhesive layer is responsible drug release. This clip has a temporary liner layer and endless support.

2. Reservoir-controlled TDDS: - The transdermal system of the reservoir has a different layer of drugs enclosed by a number of microporous or non-nonporous membranes and a non-concentrated laminate. A drug layer is a liquid that contains a drug solution or suspension separated by a supporting layer. The rate of release of the drug is determined by the degree of abrasion, maturation, spread and firmness of the membrane. In this type of system, the release rate is zero order.

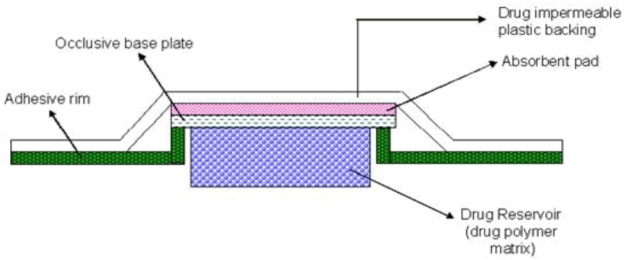

Fig: - Reservoir controlled TDDS

3. Matrix controlled TDDS: - In this way, the drug reservoir is the prepared by dissolving the drug particles in a hydrophilic or lipophilic polymer matrix. The adhesive layer on this clip surrounds the layer of the drug that covers it slightly. It also has an occlusive base plate, an absorbent pad and a backing laminate on the back.

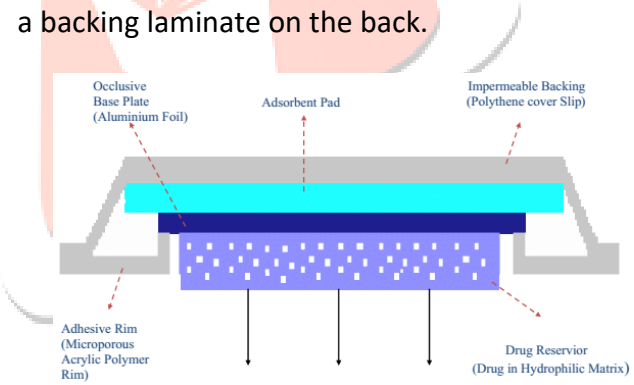

Fig: - Matrix controlled TDDS

4) Micro reservoir TDDS: - This program is a combination of reservoir and matrix-dispersion system. The drug reservoir is first developed by dissolving the drug in the liquid solution of a water-soluble polymer and then dispersing the solution evenly into a lipophilic polymer to form thousands of inaccessible spheres, very small of the drug dams. This thermodynamically unstable dispersion is rapidly stabilized by rapid bonding of the polymer in situ by means of bonding agents.

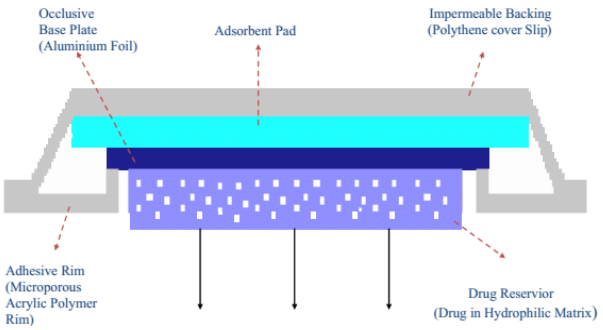

Fig: - Micro reservoir TDDS

Evaluation of Transdermal drug delivery system[27,28,29]: -

1) Pack size: - Pack size can be measured using a micrometer screw gauge at three different points and the average value is calculated.

2) Weight loss: - The prepared pieces were dried at 60 ° C for 4 hours before testing. The specified area of the pond should be cut into different parts of the pond and measured with a digital balance. Medium weight and standard deviation values should be calculated on an individual weight[30].

3) Percentage of moisture content: - Films weigh separately and are left in a desiccator containing anhydrous calcium chloride or silica activated at room temperature for 24 hours. Individual films are repeated over and over again until they show a consistent weight. The calculation of% of moisture content is done as the difference between the initial and final weight in relation to the final weight.

4) Percentage of moisture absorption: - Weighed films are stored in a desiccator containing a complete mixture of potassium chloride to retain 84% RH. After 24 hours, re-evaluate the films and determine the selected moisture content from the formula mentioned below[31].

5) Drug content: - A specific area of the patch should be dissolved in the appropriate solvent by a certain volume. Then, the solution is filtered through a filter and then analyzed the drug content accordingly as a UV or HPLC process.

APPLICATION OF TDDS[32]: -

I. Nicotine transdermal patch is marketed as Nicodermis to help quit smoking. It is the best-selling episode in the United States.
II. Antihypertensive drugs such as clonidine and ketoprofen, non-steroidal anti-inflammatory drugs are also available in the form of transdermal patches.
III. Two opioid drugs are Fentanyl (marketed as Duragesic) and Buprenorphine (marketed as BuTrans) used to provide day and night relief from severe pain found in patch form.
IV. Estrogen patches are sometimes prescribed to treat the symptoms of menopause and postmenopausal osteoporosis.
V. Transdermal component of clonidine available to treat high blood pressure.
VI. Transdermal Delivery Agency for Attention Deficit Hyperactivity Disorder (ADHD).

Popular uses of transdermal drug delivery system[28]: -

- The first commercially available nicotine-induced tobacco smoke was approved in Europe in 2007.
- Two opioid medications that usually provide uninterrupted relief with a square measure of acute pain are usually defined as a supplement: opiate (marketed as Duragesic) and Buprenorphine (marketed as BuTrans).
- Estrogen tablets are a square measure determined to treat the symptoms of biological period but as a postmenopausal pathology. various transdermic patches for internal secret delivery include contraception (on the market with Ortho Evra or Evra).
- Nitro-glycerine extracts of the standard square prescribed for treating angina in the office of the articulator pills.
- Antihypertensive drug is found in the subcutaneous type of Catapres-TTS product.
- Emsam, a transdermic type of MAOI selegiline, became the main transdermic

delivery agent of the approved drug for use in the U.S. March 2006.

Future technologies and approaches: -

A small needle is inserted a few millimeters into the skin and the drug solution is injected into the skin in controlled doses using a micro-infusion pump contained in a large piece attached to the skin, morphine is delivered to humans using this method.

Ten years ago, the nicotine patch had changed dramatically to stop smoking; patients were treated with nitroglycerin for angina, clonidine hypertension, scopolamine for motion sickness and estradiol for estrogen deficiency, all through patches. Over the past decade, the number of drugs built into patches has not grown significantly, and there has been little change in the design of binding systems. Adjustments are very limited in the development of materials. The reason is that only a limited number of drugs equal the molecular weight and the energy requirements of transdermal absorption.

The ViaDerm application may be used in delivery of topical local medicine applications in the field of dermatology and makeup. The ViaDerm system may also approved vaccination, which provides The ViaDerm system may be used in the delivery of local medicines for use in the skin and cosmetics industry. The ViaDerm system may also allow for improved immunization, providing a painless, safe and effective alternative to current intramuscular or subcutaneous vaccinations.

Over the past decade a number of theories have been made in dealing with chemical compounds and iontophoresis; chemicals and electroporation; chemicals and ultrasound; iontophoresis and ultrasound; electroporation and iontophoresis; and electroporation and ultrasound.

CONCLUSION: - The purpose of this article was to provide valuable information on transdermal drug delivery systems. Transdermal drug delivery systems have been used as a safe and effective drug delivery device since 1981. Many drugs have been developed in the form of TDDS, such as hormonal therapy, various analgesics, drugs for heart disease, to prevent GI side effects and to start over. Alternative Route Indications are many, such as patients who do not like or are unable to swallow medication, oral cancer, throat and GI tract, GI tract disorders, intestinal obstruction, intolerable side effects during administration, local pain treatment, to avoid systemic side effects, newborns / children etc. Transdermal drug delivery is not only about the patch and its use but it is a system that contains other ingredients such as ointments, creams, gels designed for use as a means of delivery of drugs with the help of input enhancements but dosage. the concept cannot be effectively controlled by these semisolid formulations as it can be done elsewhere.

TDDS is a practical application as the next generation of drug delivery system and because of its great benefits, many new research is ongoing today to introduce new drugs through the system. Future development of TDDS will likely focus on further control of therapeutic drugs and the continued increase in available drugs for use. Transdermal drug delivery system is useful for local and local drug action. Drugs that show the effect of initial liver failure and instability in GI conditions are the appropriate TDDS candidate.

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