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TRANSDERMAL DRUG DELIVERY SYSTEM: AREVIEW

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ABSTRACT
Nowadays 74 % of medication are taken orally. This are observed now no longer to be as powerful as desired. Transdermal dermal drug shipping (TDDS) is important a part of novel drug distribution system. TDDS drug are without problemscapable of penetrate the pores and skin and attain the goal site. The pores and skin is the biggest organ with inside the body. This shipping gadget enhance healing efficacy and protection of drug. The drug are brought in predetermined in managed rate. Various strategies are to be had to put together the transdermal patches inclusiveof solvent evaporation, solvent casting strategies. It offer greater bioavailability thandifferent direction of management respectively.

INTRODUCTION
Transdermal Drug Delivery System
Transdermal drug delivery system (TTDS) is an essential a part of novel drug transport system. TTDS is to supply a drug throughout the patient's pores and skin. Transdermal delivery presents controlled, regular administration of drug. This machine is handiest method and the transdermal path has emerge as one of the a success and revolutionary drug transport system. In theory, transdermal patches paintings very simply. A drug is carried out in a surprisingly excessive dosage to theinner of patch, that's worn at the pores and skin for an prolonged length of time. Through a selection process, drug enters the bloodstream at once via the pores and skin. Since, there's a excessive attention at the patch and occasional attention in blood. TDDS does now no longer contain passage of medicine via the GIT tract. Thus there's no loss because of first by skip metabolism, and drug may be without difficulty added with none interference from PH, enzyme, and intestinal bacteria.

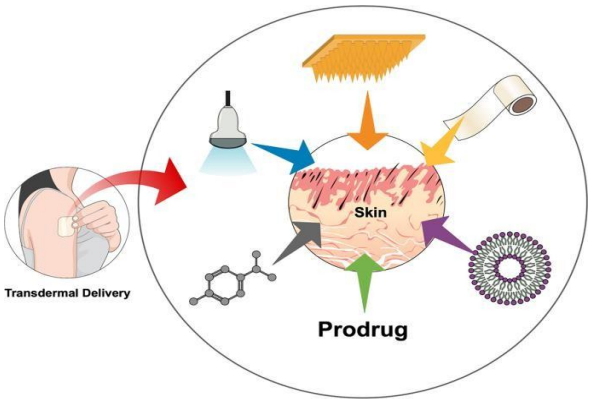


Figure 1: Transdermal Drug Delivery System.

FACTORS THAT INFLUNCE TDDS
Biological Factors Includes
- Skin condition.
- Skin age.
- Blood flow.
- Regional skin sites.
- Skin metabolism.

Physiological Factors Includes
- Skin hydration.
- Temperature and Ph.
- Diffusion coefficient
- Drug concentration
- Partition coefficient

BASIC COMPONENTS of TDDS
- The drug.
- Polymer matrix or matrices.
- Permeation enhancers.

1. **DRUG:** For developing transdermal drug delivery system, there should a greatcare in choosing of the drug. The following are the some of the properties of drug.

Desirable properties
The molecular weight should be less than approximately 1000 Daltons The drug should have affinity for both lipophilic and hydrophilic phases. The drug should have low melting point.

2. **POLYMER MATRIX:** The polymer controls the release of drug from the device. For transdermal patches the following criteria should be satisfied.

a. The polymer should be stable.
b. The polymer should be nontoxic.

c. The polymer should be inexpensive and should be easily manufactured.

3. PERMEATION ENHANCERS: Some of the compounds which promote theskin permeability may be classified under following headings:

a. Solvents: These compounds increase penetration by fluidizing lipids. Example water alcohol-methanol and ethanol.

b. Surfactants: These ranging from hydrophobic agents such as oleic acid to hydrophilic sodium lauryl sulfate has been tested as permeation enhancer to improve drug delivery

4. OTHER EXCIPIENTS

a. Adhesive: The fastening of all transdermal devices to the skin has so far beendone by using a pressure sensitive adhesive which can be positioned on the faceof the device and extending peripherally.

b. Backing membrane: Backing membranes are flexible and they provide a good bond to the drug reservoir, prevent drug from leaving the dosage form

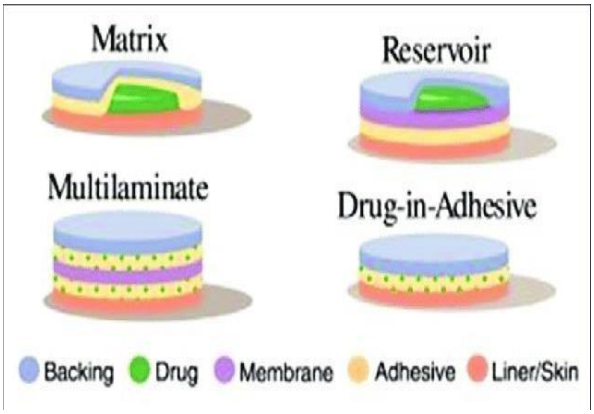


Figure 2: Components of TddsTransdermal Pateches.

Transdermal patches are the patches that stick firmly to the pores and skin as a manner to supply drugs. They offer a specific, predetermined dose of medicine that's absorbed thru the pores and skin and into the bloodstream. Nowadays, severa transdermal patches for energetic dealers are to be had withinside the market (e.g. nitroglycerin, nicotine, scopolamine, clonidine, fentanyl, estradiol, testosterone, andoxybutynin).

Types of transdermal patches

- Single layer drug in adhesive.
- Multiple layer drug in adhesive.
- Reservoir.
- Matrix.

Single layer drug in adhesive: This adhesive layer of this gadget consists of the medication. This layer now no longer simply serves to stick the numerous layers together, further in change of discharging the medication to the skin. This glue layeris surrounded by a temporary liner and a support.

Multiple layer drug in adhesive: The multiple layer in adhesive is similar to the single layer system and it contains a quick medication discharge layer. But it is different however that adds another layer of drug in – adhesive. The cement layer isin charge of discharging of the medication. This patch also has temporary liner- layer and a permanent backing.

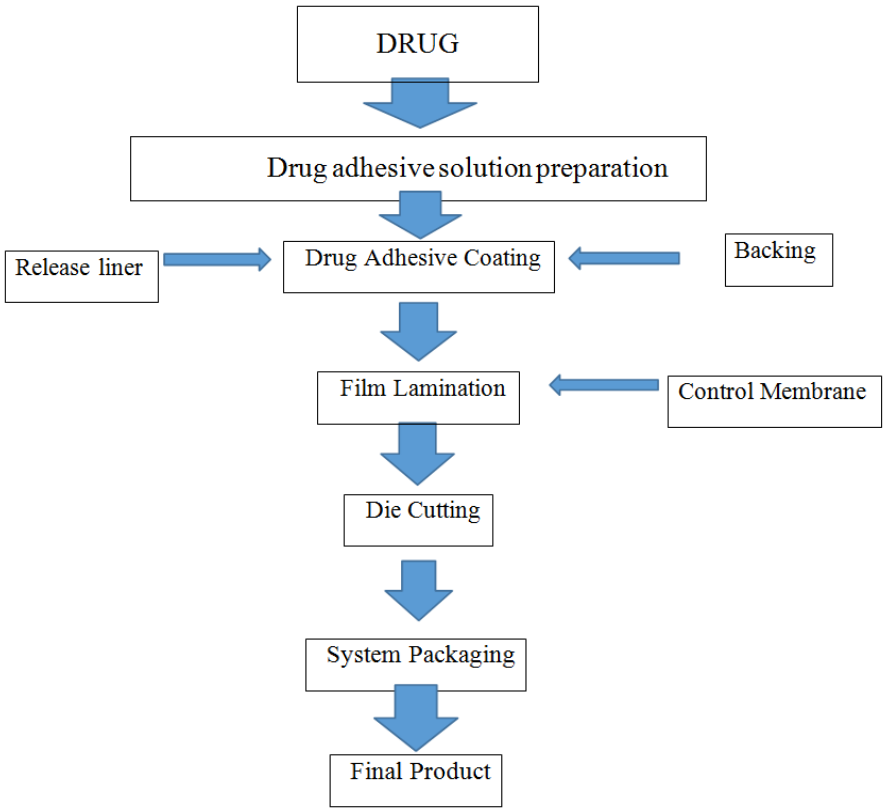
Reservoir: This transdermal system has a separate drug layer. The medication discharge just through the rate of controlling film, which can be permeable or nonporous. In the medication compartment, the drug can be as solution, suspension, gel or scattered in a strong polymer grid. In this type of system the rate is zero order.

Matrix: The matrix system is characterized by inclusion of semisolid matrix containing a drug solution or suspension. The components responsible for skin adhesion is incorporated in an overlay and form a concentric configuration around the semisolid matrix. This kind of medication is scattered homogenously in a hydrophilic or lipophilic polymer grid.

Methods of formulation of transdermal patches

1. **Circular Teflon mould method:** Solutions containing polymers in various ratio are used in organic solvents. In a organic solvent the calculated amount of drug is dissolved. The drug dissolved in half the quantity of same organic compound. Enhancers in different concentration are added, then Di-N- butylphthalate is added as a plasticizer into drug polymer solution. The total contents are to be stirred for 12 hours and then poured into a circular teflon mould. These are leveled and covered with inverted funnel to control vaporization in a laminar flow hood with an air speedof 0.5 m/s.
2. **Mercury substrate method:** The drug this method are dissolved in polymer solution along with plasticizers. When a solution is stirred for 10- 15 minutes it produce a homogenous dispersion. Finally it is poured to a leveled mercury surface, to control the solvent evaporation covered with inverted funnel.
3. **By using 'EVAC membranes' method:** For rate control membrane 1% carbopol reservoir gel, polyethylene (PE), ethylene vinyl acetate copolymer (EVAC) membranes are used.

4. Preparation of TDDS by using proliposomes



EVALUATION OF TRANSDERMAL PATCH

The evaluation method for transdermal dosage form can be classified into followingtype:

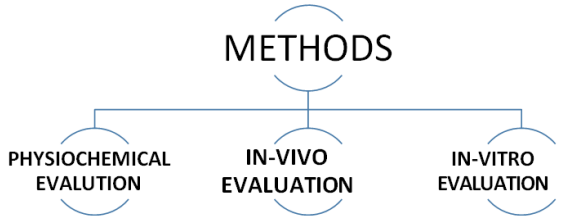


Figure No: 3 Methods of Evaluation Physiochemical Evalution.

a) **Drug content uniformity**: It is determined by suitable validated analytical method. Take specific no. of patches and completely dissolve in specific media. Then the whole sample is sonicated. The sample so obtained is analyzed by HPLC or U. V. spectrophotometer.

b) **Folding endurance:** A piece of specific region is to be cut equally, keep collapsing in the same spot until it broke. The number of times the film could be folded the same place without breaking gave the estimation of folding endurance.

c) **Thickness of the patch**: The thickness of the patch loaded with drug is measured at various points with a screw gauge and the average thickness and standard deviation is determined.

d) **Weight variation:** The prepared plasters should be dried for 4 hours at 60° C before testing. A specific patch area is to be incised different parts of the patch and weigh them in the digital scale. The mean weight and standard deviation values are to be calculated from the individual weights.

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e) **Moisture content:** The prepared patches are to be weighed and closed individually stored in a desiccator with molten calcium chloride at room temperature for 24 hours. After 24 hours the patches

are weighed back and the percentage moisture content is determined from the formula mentioned below.

Percentage moisture content = (Initial weight –Final weight/ Final weight) × 100.

IN-VIVO EVALUATION

In-vivo evaluation can be carried out using– 1) Animal models, 2) Humanvolunteers.

1) **Animal Models:** *In- vivo* animal models are preferred because of the considerable time and resources are required to conduct human studies. Some of the species are used like mouse, rat, guinea pig, rabbit, cat, dog, pig, monkey etc… For *in-vivo* evaluation of transdermal patches radiotracer methodology used. The application site is generally abdomen, which least hairy part of the animal body.
2) **Human models:** Human subjects should provide relevant information with minimal risk the subjects within the responsible period. It is first described by Fieldman and Maibach. This includes the determination of percutaneous absorption by an indirect measurement method radioactivity in excretion after tropical administration requires the investigator to know the amount of radioactivity retained or excreted in the body Stretch. The percentage of the transdermally absorbed dose is then calculated as, Percentage absorbed dose = total radio activity administered after topical administration / Total radioactivity excercised through intervention management.

IN-VITRO EVALUATION

The *in-vitro* permeation investigation of created transdermal patches studied under drug launch and pores and skin permeation studies.

***In-vitro* drug release studies:** The paddle over disc method is used for employing the drug release study. Dry films thickness to be in definite shape, weight and fixed over the glass plate with an adhesive. The glass plate was placed in 500 ml of dissolution medium or phosphate buffer (pH 7.4) and the apparatus equilibrated to 32±0.5. The paddle should place at a distance of 2.5 cm away from glass plate operating speed of 50 rpm. Samples of 5ml can be withdrawn at suitable time intervals up to 24 hrs. and viewed by UV spectrophotometer or HPLC. The experiment performed with triplicate and mean value calculated.

***In-vitro* skin permeation studies:** *In-vitro* permeation study can be viewed by diffusion cell. Abdominal skin of male thickness wistar rats weighed by 200-250 g. Abdominal region of hairs removed carefully with a help of electric clipper ; The dermal site of the skin should be clean with distilled water in order to remove any unwanted tissues or blood vessels, equilibrated for an hrs. in dissolution medium or phosphate buffer having a pH of 7.4 before starting the experiment and it was placed in a magnetic stirrer having a small magnetic needle with constant distribution of thediffusant. The cell temperature was maintained at 32±0.5℃ using a controlled heater. The rat skin piece was isolated between the compartments of the diffusion cell, Theepidermis should faced upward in to the donor compartment some sample volume as been removed from the receptor compartment at regular intervals, each volume of fresh medium should be placed. Samples to be filtered and analysed by HPLC method. Flux can be determined by having a slope curve between the steady state vstime

REACENT ADVANCES IN THE FIELD OF TDDS:

Many research works havebeen and only a few going in this area. Some of the latest research done in the fieldof transdermal patches are listed below:

- Patch technology for protein delivery.
- Pain-free diabetic monitoring using transdermal patches.
- Testosterone transdermal patch system in young women with spontaneouspremature ovarian failure.
- Patches used for pain relief

DEVELOPMENT OF TDDS MARKET

Pain management segment is anticipated to hold the largest market share in transdermal drug delivery system devices in the forecast period. Higher adoption ofopioid medication patches in pain management, especially among cancer patients one of the major factor for the development of the segment in global market.

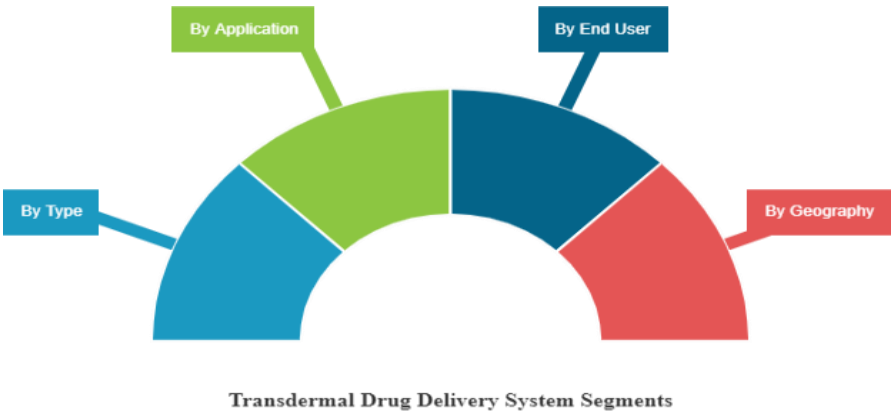

Figure 4: Transdermal Drug Delivery System Segment.

Table No 1: Details about TDDS segments.

Attribute	DETAILS
By Type	• Patches • Gels
By Application	• Pain management • Cardiovascular disease • Central Nervous System Disease • Others
By End User	• Hospitals • Clinics • Home care Settings • Others
By Geography	• North America • Europe • Middle East And Africa

FUTURE TECHNOLOGIES AND APPROACHES

Thermal Poration is the formation of aqueous pathway across stratum corneum by the application of pulsed heat, this approach has been used to deliver traditional drug and to extract intestinal fluid glucose from human body.

Now a days, jet injectors are receiving increased attention, improved device design for control in opening doors, needle free injection of drug solution across the skin and tissues

Small needle is inserted a few millimeter into skin and drug solution is flowedthrough the needle in to the skin at control rate with the help of micro-infusion pump that is contained within a large patch affixed to skin Trans Pharma is focused on products for which our technology will provide clear benefits over existing therapies. Such benefits could include improving safety and compliance through the use of a drug patch or enhancing efficacy with the use of sustained release patch formulations, among others.

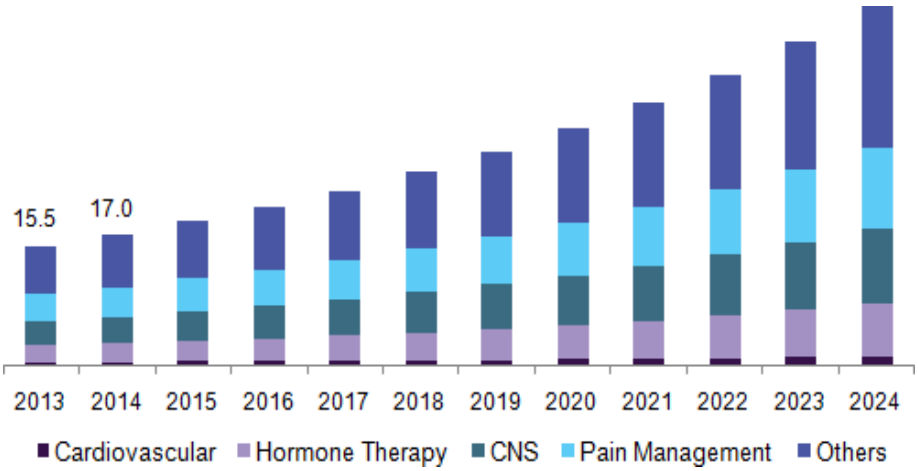

Figure 5: Future Development of Tdds.

CONCLUSION

This article provide an valuable information about the transdermal drug delivery Systems and its evaluation process details. TDDS is may be an old technology but, advanced technology greatly helpful for the society. The transdermal drug delivery system have been used as rational drug therapy (safe, effective and economic) drug delivery system. Nowadays transdermal route is becoming the most widely accepted route of drug administration. It promises to eliminate needles for the delivery of a variety of drugs in future.

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