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Transdermal Drug Delivery System: A Review

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Abstract:

Transdermal patches are now widely used as cosmetic, topical and transdermal delivery systems. These patches represent a key outcome from the growth in skin science, technology and expertise developed through trial and error, clinical observation and evidence-based studies that date back to the first existing human records. This review begins with the earliest topical therapies and traces topical delivery to the present-day transdermal patches, describing along the way the initial trials, devices and drug delivery systems that underpin current transdermal patches and their actives. This is followed by consideration of the evolution in the various patch designs and their limitations as well as requirements for actives to be used for transdermal delivery.

Keywords: Transdermal,drug delivery,patch, matrix system, reservoir ,first pass metabolism bypass.

Indroduction

The human skin is a multilayeredstructure that primarily consists of the epidermis, dermis, and subcutaneous tissue.15 The epidermis, mainly composed of cuticles, is the outermost layer of skin. It could resist environmental disturbances such as ultraviolet radiation, pathogenic bacteria, and uncontrollable mechanical damage.16 It can also prevent dehydration by regulating moisture.15 The dermis, a thick,collagen-rich connective tissue, is the close-by layer. The extracellular matrix (ECM), living cells, nerve endings, and blood vessels that are abundant in the dermis support the skin's structural integrity, elasticity, and nutrition.16,17 The communication between the epidermis and dermis could establish, maintain, and restore tissue homeostasis 18 The deepest layer is subcutaneous tissue. It is mainly composed of vascularized loose peri areolar connective tissue and adipose tissue,19 which provides thermal isolation and protection to the body.16 A schematic diagram of the skin structure.

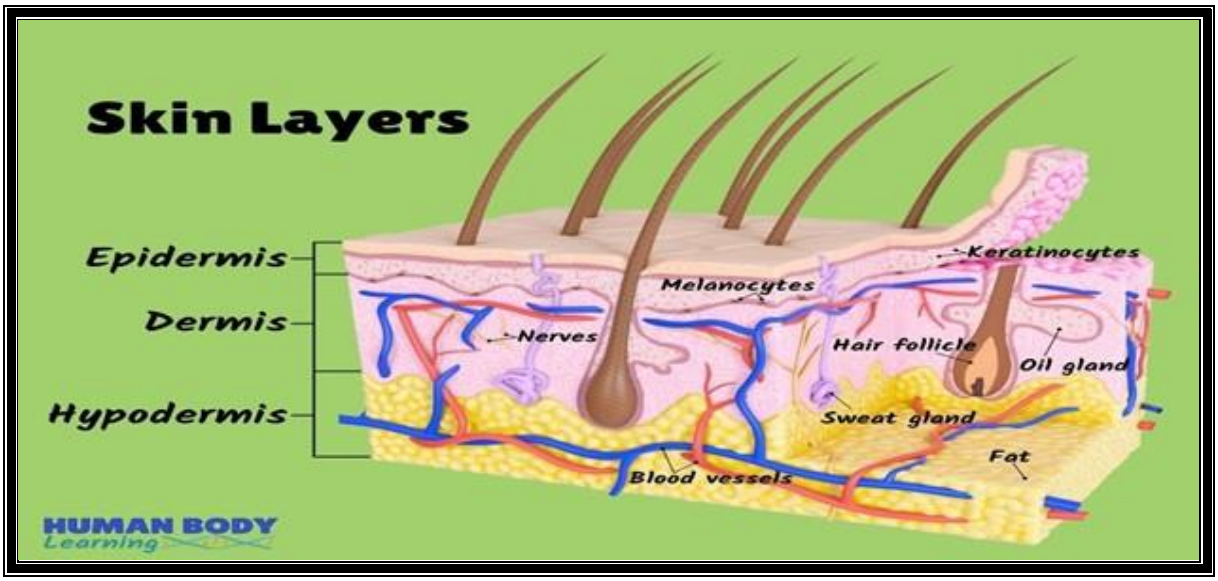


Fig. no.01; structure of skin

1.Epidermis (Top Layer):

This is the outermost layer of your skin — the part you can see and touch. It protects your body from germs, sunlight (UV rays), and injuries. It also helps keep water inside your body so you don't dry out.

2. Dermis (Middle Layer):

This layer lies just under the epidermis. It's thicker and contains things like:

Blood vessels (to bring nutrients and oxygen)

Nerve endings (to help you feel touch, pain, and temperature)

Hair roots

Sweat and oil glands

The dermis keeps your skin strong and stretchy.

3.subcutaneous layer (Bottom layer):

This is the deepest layer. It's made of fat and soft tissue. It helps:

Keep your body warm

Protect your muscles and bones from bumps and falls

Store energy

Principle :

The TDDS works by slowly releasing a drug through the skin into the blood. It keeps the drug level steady, avoids frequent dosing, and reduces side effects.

Ideal properties:

➢ Drug Properties	➢ Patch or System Properties
➢ Skin Safety	➢ Treatment Benefits
➢ Other Qualities	

Type of TDDS

1. **Membrane-Controlled System (Reservoir Type)**

- Structure: Drug is in a reservoir (gel/solution) and released through a membrane.
- Control: Rate of drug release is controlled by the membrane.
- Example: Nitroglycerin patch.

2.Matrix-Controlled System

- Structure: Drug is mixed within a polymer matrix.
- Control: Drug slowly diffuses out of the matrix onto the skin.
- Example: Fentanyl patch.

3.Drug-in-Adhesive System

- Structure: Drug is directly mixed in the adhesive layer that sticks to the skin.
- Control: Adhesive layer controls drug release.
- Advantages: Thin, flexible, and simpler design.

4.Micro-reservoir System

- Structure: Drug is suspended in micro-reservoirs (tiny drug-filled compartments) within the adhesive.
- Control: Combines features of reservoir and matrix types.
- Provides: Controlled release and better stability.

Formulations components

Sr. No.	Component	Example(s)	Function in TDDS
1	**Drug**	Nitroglycerin, Fentanyl, Nicotine	Provides the therapeutic effect
2	**Polymer matrix / Film former**	Eudragit, PVP, HPMC, EC, PVA	Controls drug release and provides structural integrity
3	**Permeation enhancer**	Oleic acid, DMSO, Propylene glycol, Menthol	Increases drug permeability through the skin

Sr. No.	Component	Example(s)	Function in TDDS
4	**Pressure-sensitive adhesive (PSA)**	Polyisobutylene, Silicone, Acrylates	Adheres the patch to the skin and can act as a drug reservoi
5	**Backing layer**	Polyethylene, Polyester, Aluminum foil	Protects the patch from external environment and prevents drug loss
6	**Release liner**	Silicone-coated polyester film	Covers the adhesive layer; removed before application
7	**Plasticizer**	Glycerol, Dibutyl phthalate, PEG	Improves flexibility and mechanical strength of film
8	**Solvent / Co-solvent**	Ethanol, Chloroform, Acetone	Helps in dissolving polymers and drugs during patch preparation
9	**Stabilizers / Antioxidants**	Butylated hydroxytoluene (BHT), Butylated hydroxyanisole (BHA)	Prevents degradation of drug and excipients
10	**Rate-controlling membrane** (in reservoir type)	Ethylene-vinyl acetate (EVA), Polyurethane	Controls the release rate of drug from reservoir to skin

Methods of preparation

- Solvent Casting Method.
- Hot Melt Extrusion Method.
- Other Fabrication Methods.

1. Solvent Casting Method

- Most commonly used method
- **Steps**:

1.Drug + polymers are dissolved in a suitable solvent (e.g., ethanol, chloroform).

2.Plasticizers or enhancers may be added.

3.The solution is poured onto a flat surface (like glass or Teflon plate).

4.Solvent is evaporated at room temp or in an oven.

5.A thin film/patch is formed.

6.Patch is peeled off and cut into desired sizes.

Advantages:

- Uniform film thickness
- Suitable for heat-sensitive drugs

Disadvantages:

- Use of toxic solvents
- Solvent residues may remain

2. Hot Melt Extrusion Method

Solvent-free method (uses heat)

🔹 Steps:

1.Drug and polymer are melted together using heat.

2.Mixture is blended until uniform.

3.The hot mass is spread or cast into a film.

4.Film is cooled and then cut into patches.

Advantages:

- No solvents required (eco-friendly)
- Faster production
- Better drug-polymer mixing

Disadvantages:

- Not suitable for heat-sensitive drugs
- May cause drug degradation at high temperature

3. Other Fabrication Methods

a. Microneedle Fabrication

- Uses micro-molds to form drug-loaded microneedles.
- Made using polymers, metals, or sugar-based materials.

b. Electrospraying or Electrospinning

- High-voltage is used to make nanofibers or thin films.
- Useful for targeted or rapid drug release.

c. 3D Printing

- Customizable patches printed with drug-loaded materials.
- Allows personalized medicine.

d. Layer-by-Layer Assembly

- Films made by alternating layers of drug and polymer.
- Offers controlled release and flexibility.

Evaluation of TDDS

1. Physicochemical Evaluation:

- **Appearance:** Check color, clarity, smoothness of the patch.
- **Thickness:** Measure uniformity across all patches.
- **Weight variation:** Ensure each patch has consistent weight.
- **Drug content uniformity:** Confirm equal drug amount in each patch.
- **Moisture content:** Determines stability; prevents drying or microbial growth.
- **Folding endurance:** Number of times patch can be folded without breaking.
- **Tensile strength:** Measures patch strength (how much force it can handle).
- **Percentage elongation:** Assesses flexibility/stretching ability.
- **Surface pH:** Should be close to skin pH (~5.5) to avoid irritation.

2. In Vitro Evaluation:

- **Drug release study:** Measures how much drug is released over time using dissolution or diffusion cells.
- **Permeation study:** Measures how much drug passes through synthetic or animal skin.

3.In Vivo evaluation

- **Skin irritation study:** Tests for redness, swelling, itching, or allergy.
- **Pharmacokinetic study:** Measures drug absorption, metabolism, and excretion from the patch.
- **Bioavailability study:** Compares how much drug reaches blood vs. other forms (e.g., oral).

4. Additional Tests:

- **Adhesive property test**: Assesses how well the patch sticks to skin.
- **Shear strength test:** Measures resistance to external forces (e.g., movement).
- **Swelling index:** Assesses how much the patch swells upon contact with moisture.

Recent advances:

1. Microneedle-Based TDDS

- Tiny, painless needles that create micro-channels in the skin.
- Deliver larger molecules like insulin, vaccines, and peptides.
- Types: Solid, coated, dissolvable, and hydrogel microneedles.
- Advantages: Painless, self-administered, better absorption.

2. Iontophoresis

- Uses mild electrical current to push charged drugs through the skin.

- Improves delivery of drugs with poor skin permeability.
- Used in pain management and local anesthesia (e.g., lidocaine).

3. Sonophoresis (Ultrasound-Enhanced Delivery)

- Uses ultrasound waves to temporarily increase skin permeability.
- Helps deliver large or hydrophilic drugs.
- Often used for anti-inflammatory drugs and cosmetic treatments.

4. Nanocarrier-Based TDDS

- Uses nano-sized drug carriers (e.g., liposomes, niosomes, ethosomes, nanoparticles).
- Improve skin penetration, drug stability, and targeted delivery.
- Useful for anti-cancer, anti-inflammatory, and cosmetic drugs.

Future perspective

1. Delivery of Large and Complex Molecules

- Future TDDS will focus on delivering biologics like:
- Insulin
- Vaccines
- Antibodies
- Gene therapy agent
- Microneedles, electroporation, and nanocarriers will help overcome the skin barrier for large molecules.

2. Smart TDDS (Digital & Responsive Patches)

- Sensor-integrated patches that can:
- Monitor body signals (e.g., temperature, glucose, pH).
- Adjust drug release automatically.
- Useful for personalized medicine and chronic diseases (e.g., diabetes, hypertension).

3. Nanotechnology Integration

- Use of nano-carriers (liposomes, nanoparticles, ethosomes) to:
- Improve penetration
- Enhance targeted delivery
- Increase drug stability
- Can deliver drugs, genes, or vaccines more efficiently.

4. Targeted Brain and Cancer Therapy

- TDDS being developed to bypass blood-brain barrier using skin routes.
- Transdermal patches for brain disorders like Parkinson's, Alzheimer's, and brain tumors.
- Cancer patches delivering chemotherapy locally through skin.

5. 3D-Printed & Customizable Patches

- 3D printing will allow:
- Personalized drug doses
- Adjustable patch sizes and shapes
- Ideal for individual patient needs.

Applications

1. **Chronic Disease Management**

TDDS is widely used for long-term therapy where consistent blood levels of the drug are needed.

Examples:Nitroglycerin patches for angina,

Clonidine patches for hypertens

2.Hormone Therapy

Ideal for hormones that need steady delivery over time.

Examples:Estrogen patches for menopause symptoms

3.Smoking Cessation

TDDS provides a controlled dose of nicotine to help reduce withdrawal symptoms.

Example:Nicotine patches

4.Pain Management

Useful for chronic and severe pain, providing continuous analgesic effect.

Examples:Fentanyl patches,

Lidocaine patches for localized neuropathic pain

5.**Neurological Disorders**

Certain neurological conditions benefit from steady drug levels delivered transdermally.

Examples:Rivastigmine patches for Alzheimer's disease

6.cardiobascular therapy

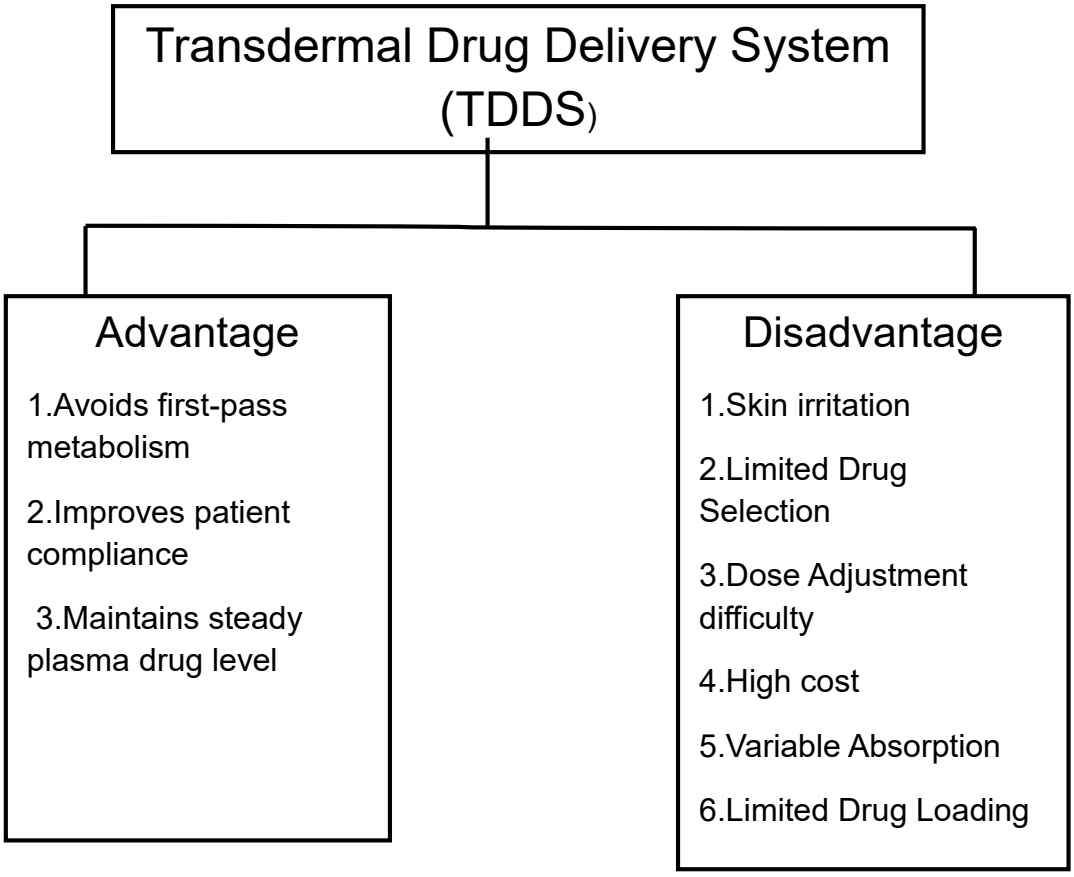
Drugs for heart conditions can be delivered slowly and consistently.

Example:Nitroglycerin patches for angina

7.Motion Sickness

TDDS can provide long-lasting antiemetic effect without frequent dosing.

Example: Scopolamine patch for motion sickness



Conclusion

Transdermal Drug Delivery Systems (TDDS) are an advanced way of delivering medicines through the skin. They offer a safe, painless, and easy method to give drugs without using injections or taking pills.

With new technologies like microneedles, nanotechnology, smart patches, and 3D printing, TDDS can now deliver not just small drugs but also vaccines, insulin, and other large molecules.

Although there are some challenges like skin barrier and irritation, scientists are finding better solutions every day.

In the future, TDDS will become even more important in medicine, helping people take treatments in a more comfortable, effective, and personalized way.

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