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Review Article

A Comprehensive Review on Transdermal Drug Delivery Systems

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ABSTRACT

Transdermal drug delivery systems (TDDS) are an effective and non-invasive method of delivering drugs through the skin into systemic circulation. These systems provide controlled and sustained drug release, improve bioavailability, and enhance patient compliance by avoiding first-pass metabolism. The stratum corneum acts as a major barrier, allowing only drugs with suitable physicochemical properties to penetrate effectively. Different types of patches, including matrix, reservoir, and drug-in-adhesive systems, are used based on the desired release profile. TDDS offers advantages such as reduced dosing frequency and minimized side effects, but limitations like skin irritation and restricted drug selection remain. Recent advancements, including microneedles and nanotechnology-based approaches, have further improved the efficiency and scope of transdermal drug delivery.

INTRODUCTION

Definition of Transdermal Patches

Transdermal patch is a medicated patch which is applied on the skin to deliver drug into the body. It is a type of drug delivery system where drug passes slowly through the skin layers and enters into the blood circulation. These patches are specially designed to release drug in a controlled and steady manner for long period of time¹⁻³. Because of this, it can maintain constant drug level in the body.

In simple words, transdermal patch is like a small sticker or bandage which contains medicine. When it is placed on the skin, the medicine moves from patch into the body slowly^{4,5}. It does not need swallowing tablets or taking injections. So it is more comfortable for many patients. Some people may feel little irritation sometimes, but mostly it is easy to use.

These patches are made with different layers. The outer layer is called backing layer which protects the patch from environment. Inside there is drug layer which contains the medicine. There is also

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adhesive layer which helps patch to stick on the skin properly. One more layer called release liner is present, which is removed before applying the patch⁶⁻⁸. All these layers work together to deliver the drug effectively.

Different types of transdermal patches are available in the market. Some patches are used for pain relief, some for hormone therapy, and some for quitting smoking like nicotine patches^{9,10}. There are also patches for heart diseases and other chronic conditions. The design and composition of patch may vary depending on the drug used.

Even though the concept looks simple, the design of patch is complex. Scientists need to select proper drug, materials and method to make it effective¹¹⁻¹³. Not all drugs can be given by this method, only certain drugs which can pass through skin are suitable. So, careful selection is required.

Basic Concept (Drug Delivery Through Skin)

The basic concept of transdermal drug delivery is to deliver drug through the skin into systemic circulation. Skin is the largest organ of the body and it acts as a protective barrier^{14,15}. It protects the body from external environment like dust, microbes and chemicals. Because of this, drug cannot easily pass through the skin.

The outermost layer of skin is called stratum corneum. This layer is very strong and acts like a main barrier for drug entry¹⁶⁻¹⁸. It is made up of dead cells and lipids, which makes it difficult for drug molecules to pass. Only small, lipophilic and potent drugs can easily penetrate through this layer.

When a transdermal patch is applied on skin, drug starts releasing from the patch. The drug moves from high concentration area (patch) to low concentration area (skin). This process is called

passive diffusion^{19,20}. It is the main mechanism in most transdermal systems.

After crossing stratum corneum, drug enters deeper layers like epidermis and dermis. From dermis, drug reaches blood vessels and enters into systemic circulation^{21,22}. Then it is distributed throughout the body and produces therapeutic effect. This process takes some time, so the onset of action may be slow compared to injections.

There are many factors which affect drug absorption through skin. These include molecular size of drug, solubility, skin thickness, hydration of skin and site of application²³⁻²⁵. For example, drug absorption is more in areas where skin is thin. Also, damaged or hydrated skin may allow more drug to pass.

Sometimes, special techniques are used to increase drug permeation. Chemical enhancers are added to break the barrier of skin. Physical methods like iontophoresis and microneedles are also used in advanced systems²⁶⁻²⁸. But even with these methods, the main concept remains same, that is delivering drug through skin in controlled way.

One small problem is that if patch is not applied properly, drug delivery may not happen correctly. Also if patch is removed early, dose may not be complete. So proper usage is important.

Importance in Modern Drug Delivery Systems

Transdermal patches have become very important in modern drug delivery systems. In earlier days, most drugs were given in form of tablets or injections. These methods have some disadvantages like pain, frequent dosing, and side effects^{29,30}. Transdermal system provides an alternative way to overcome some of these issues.

One major advantage is that it avoids first-pass metabolism in the liver. When drugs are taken



orally, they pass through liver before reaching circulation, which reduces drug effectiveness^{31,32}. In transdermal delivery, drug directly enters into systemic circulation, so bioavailability can be improved.

Another important benefit is controlled drug release. The patch releases drug slowly over long time, so there is no need to take medicine again and again³³⁻³⁵. This helps in maintaining constant drug levels in the blood. Because of this, side effects due to fluctuations in drug levels can be reduced.

Patient compliance is also improved. It is easy to apply and remove the patch. There is no pain like injections and no difficulty like swallowing tablets³⁶. This is especially useful for elderly patients, children and patients with chronic diseases. Sometimes patients may forget to take tablets, but patch can work continuously for many hours or even days.

Transdermal patches are also useful in conditions where long-term therapy is required. For example, in pain management, hormone therapy, and cardiovascular diseases, patches can provide continuous drug supply. This makes treatment more effective.

In recent years, many advancements are happening in this field. New technologies like microneedle

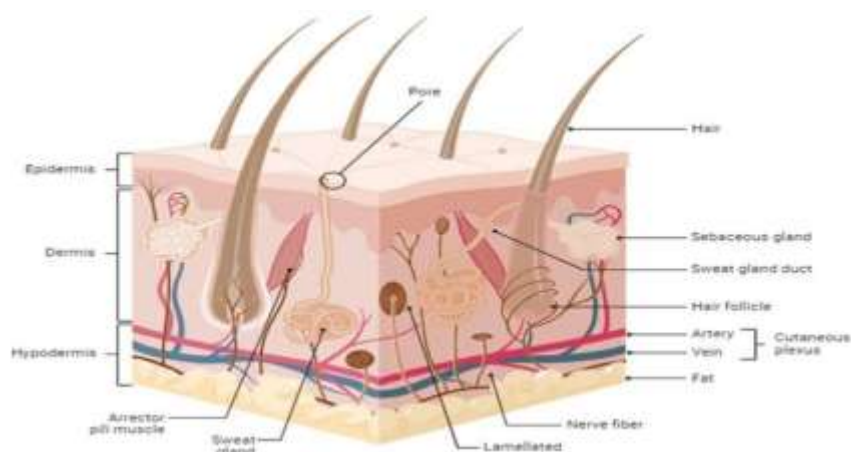
patches, smart patches and electrically assisted systems are being developed^{37,38}. These systems can deliver more types of drugs including large molecules. It is still under research but shows good future scope.

However, transdermal patches also have some limitations. Not all drugs are suitable for this system. Drugs with high molecular weight or high dose cannot be delivered easily. Also some people may get skin irritation or allergy due to patch. But still, the advantages are more compared to disadvantages in many cases.

Structure of Skin

Skin is the largest organ of the human body. It covers the entire body and acts as a protective barrier between internal organs and external environment¹⁻³. It protects the body from dust, microbes, harmful chemicals and physical damage. Skin also helps in maintaining body temperature, prevents excessive water loss and plays role in sensation like touch, pain and heat.

For understanding transdermal drug delivery, it is very important to study the structure of skin. Skin is mainly divided into three layers: epidermis, dermis and hypodermis⁴⁻⁶. Each layer has different structure and function, and together they control the movement of drug through the skin.



Epidermis

Epidermis is the outermost layer of the skin. It is the first layer which comes in contact with environment. Even though it is thin, it plays very important role in protection^{7,8}. It is made up of stratified squamous epithelial cells. This layer does not contain blood vessels, so nutrients are supplied from dermis by diffusion.

Epidermis is further divided into different sublayers such as stratum basale, stratum spinosum, stratum granulosum and stratum corneum⁹⁻¹¹. Among all these, stratum corneum is the most important for transdermal drug delivery.

Cells in epidermis are continuously produced in the lower layer and move upwards. As they move towards surface, they lose their nucleus and become dead cells filled with keratin^{12,13}. Finally, they form the stratum corneum layer. This process is continuous, so skin is always renewing itself.

Epidermis acts as a barrier to prevent entry of foreign substances. Because of this barrier nature, only limited amount of drug can pass through it¹⁴⁻¹⁶. Sometimes, the permeability of epidermis can change due to factors like hydration, temperature or skin condition. For example, wet or damaged skin may allow more drug to enter.

Dermis

Dermis is the middle layer of the skin, present below the epidermis. It is thicker and stronger compared to epidermis^{17,18}. This layer is mainly composed of connective tissue which contains collagen and elastin fibers. These fibers provide strength, flexibility and elasticity to the skin.

Dermis contains many important structures like blood vessels, lymph vessels, nerve endings, hair follicles and sweat glands¹⁹⁻²¹. Because of the presence of blood vessels, dermis plays a major

role in systemic drug absorption. Once drug crosses the epidermis and enters dermis, it can easily reach the bloodstream.

The blood circulation in dermis helps in distribution of drug throughout the body^{22,23}. This is the main reason why transdermal patches are effective, even though drug is applied on skin surface.

Dermis also plays role in regulating body temperature by controlling blood flow and sweat production. It is also responsible for sensation, as it contains nerve endings which detect pain, pressure and temperature²⁴.

Even though dermis is not a major barrier like epidermis, it supports the drug absorption process and helps in drug distribution.

Hypodermis

Hypodermis is the innermost layer of the skin. It is also known as subcutaneous tissue²⁵. This layer is mainly made up of adipose (fat) tissue and loose connective tissue. It lies below the dermis and connects skin to underlying muscles and bones.

The main function of hypodermis is to store fat, which acts as an energy reserve. It also provides insulation and helps in maintaining body temperature^{26,27}. In addition, it acts as a shock absorber and protects internal organs from mechanical injury.

Hypodermis also contains larger blood vessels and nerves. Even though it is not directly involved in initial drug absorption, it supports overall structure and function of the skin.

In transdermal drug delivery, drug usually acts before reaching this layer, but in some cases small amount of drug may reach this region.



Role of Stratum Corneum as Barrier

Stratum corneum is the outermost layer of the epidermis and it is the most important barrier for drug penetration^{28–30}. It is made up of dead, flattened cells called corneocytes. These cells are filled with keratin and are tightly packed together. Surrounding these cells is a lipid matrix composed of lipids like ceramides, cholesterol and fatty acids.

This structure is often described as “brick and mortar” model³¹. In this model, corneocytes act as bricks and lipids act as mortar. This arrangement makes the layer very compact and highly resistant to penetration. Because of this, most drugs cannot easily pass through this layer.

Stratum corneum mainly functions to prevent entry of harmful substances like bacteria, chemicals and toxins. At the same time, it also prevents loss of water from the body³². But this protective nature becomes a major challenge in transdermal drug delivery.

Only drugs with suitable properties such as low molecular weight, moderate lipophilicity and high potency can cross this barrier effectively^{33–35}. Drugs that are too large or too hydrophilic cannot penetrate easily.

Drug can pass through stratum corneum by different pathways such as:

- Intercellular route (between cells)
- Transcellular route (through cells)
- Appendageal route (through hair follicles and sweat glands)

Among these, intercellular route is most common³⁶. Even then, the process is slow and limited.

To overcome this barrier, different techniques are used. Chemical permeation enhancers can disturb lipid structure and increase permeability. Hydration of skin can also make the layer more permeable³⁷. Advanced methods like microneedles, iontophoresis and sonophoresis are also used to improve drug delivery³⁸.

Even with all these methods, stratum corneum remains the main limiting factor in transdermal drug delivery. So, proper understanding of this layer is very important while designing transdermal patches.

Overall, the structure of skin plays a key role in transdermal drug delivery. Among all layers,

Principle of Transdermal Drug Delivery

Transdermal drug delivery is based on the principle of delivering drug through the skin into the systemic circulation^{1–3}. In this method, drug is applied on the skin surface in the form of a patch, and it slowly passes through different layers of skin to reach the blood. From blood, drug is distributed to different parts of the body and produces its effect.

The main idea of this system is to provide controlled and continuous release of drug for a

long period of time^{4–6}. Unlike tablets which give sudden release of drug, transdermal patches release drug slowly and maintain constant drug level in the body. This helps in improving therapeutic effect and reducing side effects.

In this system, skin acts as both a route and a barrier^{7,8}. Drug must cross the outermost layer of skin, which is very strong and resistant. Because of this, only certain drugs which have suitable properties can be delivered through this route.

The movement of drug through the skin mainly depends on concentration gradient^{9–11}. Drug moves from high concentration area (patch) to low concentration area (skin and blood). This process continues until equilibrium is reached.

Another important principle is that the drug should have proper balance between lipophilicity and hydrophilicity^{12,13}. If drug is too lipophilic, it may stay in skin and not reach blood. If it is too hydrophilic, it may not cross the lipid-rich barrier of skin. So, balance is very important.

Mechanism of Drug Permeation

Drug permeation through the skin is a step by step process^{14–16}. When a transdermal patch is applied, drug is released from the patch and comes in contact with the skin surface. From there, it starts entering into the skin layers.

The process mainly involves three steps:

- Release of drug from the patch
- Penetration through stratum corneum
- Absorption into systemic circulation^{17,18}

First, drug is released from the formulation and reaches the surface of skin. Then it penetrates through the stratum corneum, which is the main barrier. After crossing this layer, drug moves through epidermis and dermis.

Once drug reaches the dermis, it enters into blood vessels and becomes available for systemic action^{19,20}. The rate of this process depends on drug properties and condition of skin.

Drug permeation can occur through different pathways^{21–23}:

- Intercellular route – drug passes between the cells

- Transcellular route – drug passes through the cells
- Appendageal route – drug passes through hair follicles and sweat glands

Among these, intercellular route is most common because lipid matrix is present between cells²⁴. However, all routes may contribute to some extent.

Passive Diffusion

Passive diffusion is the main mechanism by which drug passes through the skin in transdermal drug delivery^{25–27}. It does not require any energy. Drug molecules move from region of higher concentration to region of lower concentration.

In transdermal patch, drug concentration is high in the patch and low in the skin. So drug naturally moves into the skin. This movement continues until concentration becomes equal on both sides.

Passive diffusion follows Fick's law of diffusion^{28,29}. According to this law, the rate of diffusion depends on factors like concentration gradient, surface area, thickness of membrane and diffusion coefficient.

The process of passive diffusion includes:

- Drug dissolves in the patch matrix
- Drug diffuses to the skin surface
- Drug partitions into stratum corneum
- Drug moves across skin layers
- Drug enters into blood circulation^{30–32}

This process is slow and controlled, which is useful for maintaining steady drug levels. However, because it is slow, onset of action may be delayed compared to other routes like injection.

Factors Affecting Absorption

Absorption of drug through the skin depends on many factors^{33–35}. These factors can be related to drug, skin or formulation.

1. Drug-related factors

Molecular size: Small molecules can pass easily, while large molecules cannot pass easily

Lipophilicity: Drug should have moderate lipophilicity to cross lipid layer

Solubility: Drug should be soluble in both lipids and water

Dose: Drugs with low dose are more suitable for transdermal delivery³⁶

2. Skin-related factors

Thickness of skin: Thin skin allows more absorption

Hydration: Hydrated skin increases permeability

Condition of skin: Damaged or diseased skin may increase absorption

Age: Skin properties change with age

Site of application: Different body parts have different permeability³⁷

3. Formulation-related factors

Type of patch: Design of patch affects drug release

Use of permeation enhancers: Chemicals can increase drug penetration

Adhesive properties: Proper adhesion ensures good contact with skin

Drug concentration: Higher concentration increases diffusion rate

4. Environmental factors

Temperature: Higher temperature can increase absorption

Blood flow: Increased blood flow improves drug uptake³⁸

All these factors together determine how much drug enters into the body and how fast it acts.

Types of Transdermal Patches

Transdermal patches are classified based on their design and method of drug release^{1–3}. Different types of patches are developed to control the rate of drug delivery and improve effectiveness. The main types are matrix type, reservoir type, drug-in-adhesive type and microreservoir type.

Matrix Type Transdermal Patch

Matrix type patch is one of the most commonly used systems^{4,5}. In this type, drug is uniformly dispersed in a polymer matrix. The polymer acts as a support and also controls the release of drug.

In this system, there is no separate drug reservoir. The drug is mixed directly with the polymer and forms a homogeneous layer. This layer is then placed between backing layer and adhesive layer⁶.

When the patch is applied on skin, drug slowly diffuses out from the matrix and enters into the skin^{7,8}. The release of drug mainly depends on the diffusion process through the polymer.

One advantage of matrix system is that it is simple to prepare and less chances of dose dumping. But sometimes the release rate is not very precise. Also drug may not be completely released from the matrix.

Reservoir Type Transdermal Patch

Reservoir type patch contains a separate drug reservoir^{9,10}. In this system, drug is present in liquid or gel form and enclosed between backing layer and a rate controlling membrane.

The rate controlling membrane plays very important role. It controls the amount of drug that is released from the reservoir¹¹. Because of this, drug release can be more uniform and controlled.

When the patch is applied, drug passes through the membrane and then enters the skin¹². This system can provide zero-order release, meaning constant drug release over time.

However, this type of patch is more complex in design. There is also risk of leakage if the membrane is damaged. Because of this, careful handling is required.

Drug-in-Adhesive Type Transdermal Patch

Drug-in-adhesive system is a modified form of matrix system^{13,14}. In this type, drug is directly incorporated into the adhesive layer. The adhesive layer not only sticks the patch to skin but also acts as a drug reservoir.

This type of patch is thinner and more comfortable compared to other types. It is easy to apply and has good patient acceptability.

There are two types in this system:

- Single layer drug-in-adhesive
- Multi-layer drug-in-adhesive¹⁵

In single layer, drug is present in one adhesive layer. In multi-layer, more than one adhesive layer

is used, which can control release more effectively.

Drug release occurs when drug diffuses from adhesive layer into the skin^{16,17}. The rate of release depends on properties of adhesive and drug.

Microreservoir Type Transdermal Patch

Microreservoir system is a combination of matrix and reservoir systems^{18,19}. In this type, drug is present in the form of small microscopic reservoirs within a polymer matrix.

These microreservoirs are formed by dispersing drug solution into polymer and then solidifying it. So drug exists as small droplets surrounded by polymer.

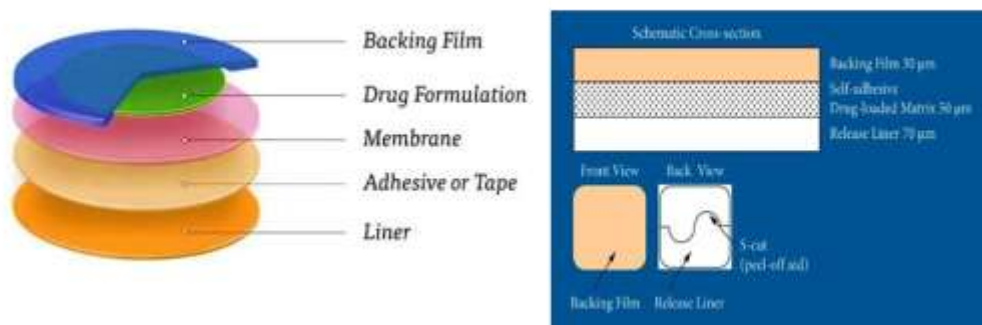
When the patch is applied, drug is released from these microreservoirs and diffuses through the matrix into the skin^{20,21}. This system provides controlled and sustained release of drug.

One advantage of this system is better control over drug release compared to simple matrix system. But preparation process is more complicated and requires proper technique.

Components of Transdermal Patch

Transdermal patch is made up of different layers and components which work together to deliver the drug through the skin¹⁻³. Each component has a specific function and plays an important role in the overall performance of the patch. Proper selection of these components is necessary to achieve effective and controlled drug delivery.





Backing Membrane

Backing membrane is the outermost layer of the transdermal patch^{4,5}. It is present on the side opposite to the skin. The main function of backing membrane is to protect the patch from the external environment such as moisture, air and contamination.

This layer should be impermeable to the drug, so that drug does not escape from the patch⁶. It also provides mechanical support and strength to the patch. Backing membrane should be flexible so that it can easily adjust to body movements.

Materials used for backing membrane include plastic films like polyethylene, polyester and polyvinyl chloride^{7,8}. The selection of material depends on drug properties and required flexibility.

If backing membrane is not proper, drug may get lost or patch may get damaged. So it is very important component.

Drug Reservoir

Drug reservoir is the part of the patch which contains the active drug^{9–11}. It can be present in different forms like solution, gel or solid matrix, depending on the type of patch.

In reservoir type system, drug is stored in a separate compartment. In matrix type system, drug

is uniformly dispersed in polymer matrix. In drug-in-adhesive system, drug is directly mixed with adhesive layer^{12,13}.

The main function of drug reservoir is to hold the drug and release it in controlled manner¹⁴. The release of drug depends on the design of reservoir and properties of drug.

Proper formulation of drug reservoir is important to maintain stability and effectiveness of drug. If drug is not stable, it may degrade and reduce therapeutic effect.

Adhesive Layer

Adhesive layer helps the patch to stick to the skin surface^{15,16}. It ensures proper contact between patch and skin, which is necessary for drug absorption.

In some systems, adhesive layer only provides sticking property. In drug-in-adhesive systems, it also contains the drug. So it performs dual function.

Adhesive should be non-irritating and should not cause allergy to the skin¹⁷. It should have good tack, meaning it should stick easily but also should be removed without causing pain or damage to the skin.

Common adhesives used include acrylic, silicone and rubber-based adhesives¹⁸. Selection depends on compatibility with drug and skin safety.

If adhesive is not good, patch may not stick properly and drug delivery may be affected.

Release Liner

Release liner is a protective layer which covers the adhesive layer before the patch is applied^{19, 20}. It is removed just before use.

The main function of release liner is to protect the adhesive and drug layer from contamination and damage during storage. It also prevents the patch from sticking to other surfaces before application.

Release liner should be easy to remove without disturbing the patch structure. It should not interact with drug or adhesive²¹.

Materials used for release liner include siliconized paper or plastic films. These materials allow easy removal without sticking strongly²².

Even though it is removed before use, it is still an important component for maintaining quality of patch.

Permeation Enhancers

Permeation enhancers are substances added to the patch to increase the penetration of drug through the skin^{23–25}. Since the skin acts as a strong barrier, these agents help in improving drug absorption.

They work by temporarily modifying the structure of stratum corneum. They may disrupt lipid arrangement, increase fluidity or improve drug solubility in skin^{26, 27}. Because of this, drug can pass more easily.

Common permeation enhancers include alcohols, fatty acids, surfactants and solvents²⁸. The selection depends on drug and formulation.

Permeation enhancers should be safe and should not cause irritation or damage to the skin²⁹. Their effect should be reversible, meaning skin should return to normal condition after some time.

If permeation enhancers are not used properly, it may cause skin irritation or excessive drug absorption. So careful selection is required.

Ideal Properties of Drugs for Transdermal Delivery

Not all drugs are suitable for transdermal drug delivery. Only drugs with certain properties can easily pass through the skin and produce effective action^{1–3}. Since skin acts as a strong barrier, drug must have specific characteristics to penetrate through it. If drug does not have these properties, it may not be effective in transdermal form.

Some important ideal properties of drugs for transdermal delivery are given below:

Molecular Weight

Molecular weight of the drug plays an important role in its ability to pass through the skin^{4–6}. Drugs with low molecular weight can easily penetrate through the skin layers, especially the stratum corneum.

Generally, drugs with molecular weight less than 500 Dalton are considered suitable for transdermal delivery^{7, 8}. Smaller molecules can move faster and diffuse easily through the lipid matrix of the skin.

On the other hand, drugs with high molecular weight face difficulty in crossing the skin barrier⁹. They move slowly and may not reach the systemic circulation in sufficient amount. Because of this,

large molecules like proteins and peptides are not easily delivered through transdermal patches.

So, low molecular weight is an important requirement for effective transdermal drug delivery.

Lipophilicity

Lipophilicity means the ability of a drug to dissolve in lipids or fats¹⁰⁻¹². Since the outer layer of skin (stratum corneum) is rich in lipids, drug must have some lipophilic nature to pass through it.

If the drug is too hydrophilic (water-loving), it cannot easily cross the lipid barrier. If it is too lipophilic, it may remain in the skin and not reach the blood circulation¹³. So, drug should have balanced lipophilicity.

This balance helps the drug to first penetrate through the lipid layer and then move into aqueous layers of the skin. Partition coefficient is often used to measure this property¹⁴.

Therefore, moderate lipophilicity is ideal for transdermal delivery.

Low Dose Requirement

Drugs used in transdermal patches should require only small dose^{15,16}. This is because only limited amount of drug can pass through the skin at a time.

If the drug requires high dose, it cannot be delivered effectively through a patch. The patch size would become very large, which is not practical. Also, skin permeability limits the amount of drug entering the body.

Usually, drugs with daily dose in milligram range are suitable for transdermal delivery¹⁷. Potent

drugs are more preferred because small quantity is enough to produce therapeutic effect.

So, low dose requirement is an important factor in selecting drugs for transdermal systems.

Short Half-Life

Half-life of a drug is the time required for its concentration in the body to reduce by half^{18,19}. Drugs with short half-life are good candidates for transdermal delivery.

Such drugs need frequent dosing when given orally or by other routes. Transdermal patch can provide continuous and controlled release of these drugs, maintaining constant plasma concentration²⁰⁻²².

This reduces the need for repeated dosing and improves patient compliance. It also helps in reducing fluctuations in drug levels, which can decrease side effects.

However, drugs with very long half-life may not require controlled release system, so transdermal delivery may not be necessary.

Methods of Preparation of Transdermal Patches

Preparation of transdermal patches is an important step in developing an effective drug delivery system¹⁻³. Different methods are used depending on the type of patch and drug properties. The main aim is to prepare a uniform patch with proper drug distribution and controlled release.

Some commonly used methods are given below:

Solvent Casting Method

Solvent casting method is one of the most widely used methods for preparing transdermal patches^{4,5}. It is simple and easy to perform. In this method,



polymer is first dissolved in a suitable solvent to form a clear solution. Then drug is added to this solution and mixed properly to get a uniform mixture⁶. Sometimes plasticizers and permeation enhancers are also added.

This solution is then poured into a flat surface like petri dish or glass plate. It is spread uniformly and allowed to dry slowly. During drying, solvent evaporates and a thin film is formed^{7, 8}.

After complete drying, the film is removed and cut into required size patches. These patches are then stored in suitable conditions.

One small problem is that if solvent is not removed properly, it may affect the patch. Also sometimes air bubbles may form during casting. But still this method is commonly used because it is simple.

Mercury Substrate Method

In mercury substrate method, polymer solution containing drug is prepared similar to solvent casting method^{9, 10}. But instead of pouring on glass plate, the solution is poured over a mercury surface.

Mercury provides a smooth and non-sticky surface, so the film formed is uniform and easy to remove¹¹. The solution spreads evenly on mercury and forms a thin layer.

Then solvent is allowed to evaporate slowly. After drying, the film is carefully separated from the mercury surface and cut into patches¹².

This method gives uniform thickness and smooth surface. But use of mercury is toxic and harmful, so it is not commonly used now. It requires careful handling and safety precautions.

Asymmetric TPX Membrane Method

In this method, an asymmetric membrane is prepared using a polymer called TPX (poly(4methyl-1-pentene))^{13, 14}. This membrane acts as a rate controlling barrier.

First, TPX polymer is dissolved in suitable solvent. Then it is casted on a surface to form a membrane. During this process, one side of membrane becomes dense and other side becomes porous, forming asymmetric structure¹⁵.

After preparing the membrane, drug solution is placed in contact with it. The membrane controls the release of drug from the system¹⁶.

This method is mainly used for reservoir type patches. It helps in achieving controlled and uniform drug release.

However, the process is little complex and requires proper control of conditions.

Other Methods (Brief)

Some other methods are also used in preparation of transdermal patches^{17–19}:

Melt extrusion method: Polymer and drug are mixed and heated, then passed through an extruder to form thin film

Hot melt method: Similar to extrusion but involves melting and casting without solvent

Freeze drying method: Used for special formulations

These methods are less common compared to solvent casting but are useful in certain cases.

Merits of Transdermal Patches

Transdermal patches have many advantages compared to traditional drug delivery methods. At the same time, they also have some limitations.



Both merits and demerits should be considered while using this system.

1. Avoids First-Pass Metabolism

Drugs given orally pass through liver before reaching systemic circulation. This reduces drug effectiveness. In transdermal delivery, drug directly enters blood, so first-pass metabolism is avoided. This can improve bioavailability¹⁻⁵.

2. Controlled Drug Release

Transdermal patches provide slow and controlled release of drug over a long period of time. This helps in maintaining constant drug concentration in the body. It reduces fluctuations in drug levels.

3. Improved Patient Compliance

Patches are easy to use and painless. There is no need for injections or swallowing tablets. Patient can apply the patch and leave it for many hours or days. This makes it more convenient, especially for elderly and children.

4. Reduced Dosing Frequency

Since drug is released slowly, there is no need to take medicine frequently. One patch can work for long time. This reduces the burden on patient.

5. Non-Invasive Method

Transdermal delivery does not involve needles or surgical procedures. So it is a safe and noninvasive method. It reduces risk of infection and pain⁵⁻¹⁰.

6. Easy to Terminate Therapy

If any side effect occurs, the patch can be easily removed. This stops further drug entry into the body. It is simple compared to other dosage forms.

7. Suitable for Chronic Conditions

It is useful for diseases which require long-term treatment like pain management, hormone therapy and cardiovascular conditions. It provides continuous drug supply¹¹⁻¹³

Demerits of Transdermal Patches

1. Skin Irritation

Some patients may develop skin irritation, redness or allergy at the site of application. This is one of the common problems in transdermal patches.

2. Limited Drug Selection

Not all drugs can be delivered through transdermal route. Only drugs with suitable properties like low molecular weight and low dose are suitable.

3. Slow Onset of Action

Drug absorption through skin is slow. So the effect may take more time compared to injections or some oral drugs. It is not suitable for emergency conditions.

4. Limited Dose Deliver

Only small amount of drug can pass through the skin. Drugs requiring high dose cannot be given through this^{metho15-19d}.

5. Possibility of Patch Falling Off

Sometimes patch may not stick properly and may fall off due to sweating, movement or improper application. This can affect drug delivery.

6. Cost

Transdermal patches may be more expensive compared to conventional dosage forms like tablets.

7. Variability in Absorption

Drug absorption may vary depending on skin type, age, site of application and environmental conditions. This may affect drug effectiveness²⁰⁻²⁵.

Recent Advances in Transdermal Drug Delivery

In recent years, transdermal drug delivery systems have developed a lot due to new technologies and materials. These advancements are mainly focused on improving drug penetration through skin, increasing efficiency and expanding the range of drugs that can be delivered.

1. Microneedle Patches

Microneedle patches are one of the most important recent advancements. These patches contain very small needles which can penetrate the outer layer of skin without causing pain.

These microneedles create tiny channels in the skin, which helps the drug to bypass the stratum corneum barrier. Because of this, even large molecules like proteins and vaccines can be delivered through the skin.

Different types of microneedles are developed such as solid, hollow, dissolving and hydrogel forming. These systems are easy to use and provide better patient compliance.

2. Iontophoresis

Iontophoresis is a technique where a small electric current is used to enhance drug delivery through the skin. It helps in pushing drug molecules into the skin by electrical force.

This method is useful for drugs which cannot pass easily by passive diffusion. It increases drug absorption and provides controlled delivery.

Recent studies show that iontophoresis is now combined with other technologies like microneedles and nanocarriers to improve efficiency²⁷⁻³⁰.

3. Sonophoresis (Ultrasound Method)

Sonophoresis uses ultrasound waves to increase skin permeability. These waves disturb the lipid structure of skin and allow drug to pass more easily.

This method can significantly increase drug absorption compared to normal patches. It is useful for delivering both small and large molecules.

4. Electroporation

Electroporation involves the use of short electrical pulses to create temporary pores in the skin. These pores allow drug molecules to enter easily.

This method is useful for delivering drugs with high molecular weight. It is often combined with microneedles for better results.

5. Smart Patches

Smart patches are advanced systems which can monitor patient condition and adjust drug release accordingly. These patches contain sensors and electronic components.

For example, some smart patches can monitor glucose levels and release drug automatically based on need. This helps in personalized treatment and better control of disease.

6. Nanotechnology-Based Systems

Nanotechnology is widely used in modern transdermal systems. Nanoparticles, nanoemulsions and nanocarriers are used to improve drug delivery.



These systems help in increasing drug stability, penetration and controlled release. They also allow delivery of drugs which were not suitable earlier.

7. Combination Techniques

Recent research is focusing on combining different technologies to improve drug delivery. For example:

- Microneedles + iontophoresis
- Microneedles + electroporation
- Nanocarriers + patches

These combined systems provide better penetration, higher drug delivery and improved therapeutic effect.

8. Third Generation Transdermal Systems

Transdermal systems are now classified into generations. Third generation systems are the latest and most advanced.

These systems can effectively overcome the skin barrier and deliver drugs like proteins, vaccines and large molecules. They are more efficient and show better results compared to older systems²⁹⁻³⁵.

CONCLUSION

Transdermal drug delivery system is an important and developing area in pharmaceutical field. It provides a simple and effective way to deliver drugs through the skin into the body. This system avoids first-pass metabolism and helps in maintaining constant drug levels for a longer time. Because of this, it improves therapeutic effect and reduces side effects to some extent.

Transdermal patches are easy to use and non-invasive. They improve patient compliance because there is no need of frequent dosing or

painful injections. It is especially useful in long-term treatments like pain management, hormone therapy and chronic diseases. Even small children and old patients can use it easily, but sometimes proper guidance is needed.

However, there are some limitations also. Not all drugs are suitable for transdermal delivery. Only drugs with specific properties like low molecular weight and low dose can be used. Skin irritation and slow onset of action are also some problems in this system.

Recent advances like microneedles, smart patches and nanotechnology are helping to overcome these limitations. These new methods are making it possible to deliver more types of drugs and improve efficiency. Research is still going on, so more improvements can be expected in future.

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