RESEARCH PAPER

Transdermal Drug Delivery: Enhancers and Penetration Mechanisms

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ABSTRACT
Transdermal drug delivery (TDD) is a hopeful way to give medicines because it avoids first-pass digestion and allows for the drug to be released slowly over time. But the skin's natural protective qualities make it hard for drugs to get through. Several penetration boosters and methods have been created to make the skin more permeable and reach acceptable drug concentrations. Penetration boosters are chemicals that temporarily break down the skin's protective function. This makes it easier for active medicinal ingredients to get through the epidermis and into the bloodstream. We look at the different kinds of penetration enhancers in this paper. These include chemical enhancers like fatty acids, detergents, and alcohols; physical ways like iontophoresis, microneedles, and ultrasound; and new approaches like nanocarriers and lipid-based systems. Each booster works by going after different layers of skin, mainly the stratum corneum, to either make the lipid bilayers more fluid or open up brief channels for drugs to move through. It is talked about in depth how these enhancers work, such as by changing the structure of proteins or lipids in the skin or by starting electrical currents. The paper also talks about how hard it can be to choose the right enhancers because of things like skin itching, drug safety, and the need for exact dose control. Hybrid methods, which combine more than one technique, are also looked into because they might be able to get better results with fewer side effects. One more thing that is looked at is how transdermal drug delivery methods could be used to treat long-term diseases like pain and hormone replacement therapy. New ideas in how to make drugs and improve them are likely to make TDD systems much more useful and useful in more situations
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INTRODUCTION

Therapeutic agents can now be delivered through the skin for systemic circulation in a new way with transdermal drug delivery (TDD). This method has many advantages, such as keeping the drug out of the digestive system and first-pass metabolism, which can break it down or change how well it works. TDD also allows for controlled, long-lasting release of medicine, which lowers the number of times it needs to be given and increases patient cooperation. The skin is a great shield for keeping the body safe from outside threats, but because it is impenetrable, it makes it hard for drugs to get to where they need to go. The top layer of skin, called stratum corneum, is the main barrier that keeps drugs from penetrating. This makes delivering healing agents through this method complicated and hard. Different penetration boosters have been created to get around the skin's protective features and allow enough drug entry [1]. Penetration enhancers are chemicals that make it easier for drugs to pass through the skin by changing its structure or making it more permeable for a short time. These boosters can be roughly put into two groups: chemical and physical. Chemical boosters are made up of different substances, like fatty acids, detergents, alcohols, and other chemical molecules. They work by reacting with the skin's lipids and proteins to lower the barrier resistance.

Physical ways, on the other hand, use mechanical forces to help drugs get into cells better. These include iontophoresis, electroporation, microneedles, and ultrasound. It is very important to choose the right boosters and methods for transdermal drug delivery based on the drug's properties, the type of skin, and the treatment result that is wanted. Usually, chemical boosters are easy to make and add to transdermal patches. Physical ways, on the other hand, are more difficult, but they can be applied without any harm and don't need any extra chemicals. In the past few years, progress in nanotechnology has led to new tactics using

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nanocarriers and lipid-based delivery systems [2]. These offer even better ways to improve drug penetration. These boosters and methods work in a lot of different and complicated ways. Chemical boosters often work by changing the protein structure of the epidermis or the lipid bilayer structure of the stratum corneum.

This makes it easier for drugs to reach the deeper layers of the skin. Physical means, on the other hand, use outside forces to make brief passageways or damage the skin layers so that drugs can get through. For example, iontophoresis uses a small electric current to move charged molecules through the skin. Ultrasound, on the other hand, uses waves to help drugs get deeper into the body. Transdermal drug delivery has come a long way, but there are still some problems that need to be fixed. These include skin itching, drug safety, and making sure that the drug is released slowly and consistently [3]. Some boosters can irritate or inflame the skin if used in large amounts, and others might not work with all drug types because of how they are chemically made or how they dissolve. It is also necessary to fine-tune recipes because the skin naturally changes in different people or body parts, which can affect how well drugs are delivered. Getting around these problems with new and better enhancement technologies and delivery methods is what the future of transdermal drug delivery lies in. Researchers want to make better, more patient-friendly transdermal systems that can deliver a wide range of medicines, from small chemicals to biologics [4]. They plan to do this by learning how penetration enhancers work and always looking for new ways to make them work better.

II. Basics of Transdermal Drug Delivery

A. Structure and function of the skin

When it comes to protecting the body's internal systems from the outside world, the skin is the biggest organ. Three primary layers are the epidermis, dermis, and hypodermis subcutaneous layer. The top layer, the epidermis, is very vital if the skin is to defend itself. There are numerous layers to it, one of which is the stratum corneum, which blocks medications from passing. Made mostly of keratinocytes, melanocytes, and Langerhans cells, the epidermis lacks blood vessels [5]. These cells all contribute to skin's functions including pigment synthesis and immune system protection. Underlying the skin lays the dermis. It has lymphatic veins, blood arteries, and connective tissue. This layer gives the epidermis food and keeps the skin's structure in place. The hypodermis, or subcutaneous layer, is made up of fat tissue and helps keep the body warm and cool. The main job of the skin is to protect the body from germs, chemicals, and damage. It also keeps the body's temperature stable, keeps it from drying out, and helps nerve ends feel things. The stratum corneum is the most important layer to target for transdermal drug delivery (TDD) [6]. Its highly organised lipid barrier stops most things, including drugs, from getting through. To get around this block or briefly stop it, successful TDD methods try to get the drug to deeper layers so it can enter the systemic circulation.

B. Mechanisms of drug absorption through the skin

Drugs that are absorbed through the skin have to get past several layers, with the stratum corneum being the toughest. Drugs can be taken in in a number of ways, such as through passive diffusion, active movement, and assisted diffusion. Concentration differences drive passive diffusion, which is the most common way things move. Because the stratum corneum is mostly made up of lipids, lipophilic (fat-soluble) drugs are better taken through the skin. It is harder for hydrophilic (water-soluble) drugs to get through the lipid-rich upper layers, which makes their problems even worse [7]. Aside from passive diffusion, active transport methods like carrier-mediated transport can also help drugs get into the body. Figure 1 shows how drugs get into the skin through active transport, silent diffusion, and microporation

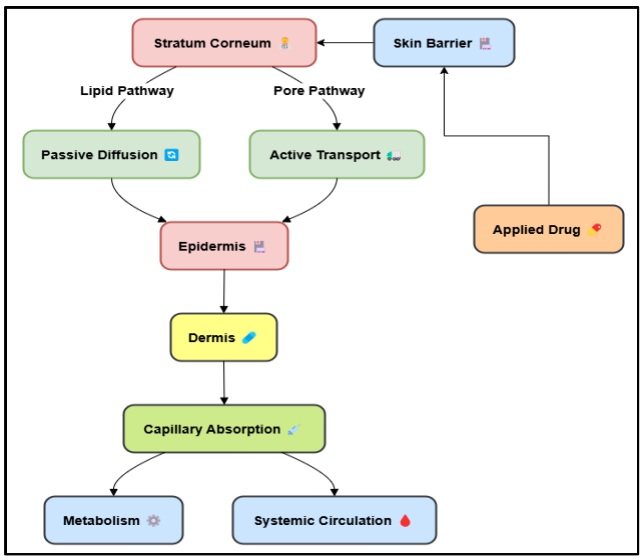

Figure 1: Illustrating the mechanisms of drug absorption through the skin

In this case, skin cells have special proteins or transporters that move drugs against differences in concentration. Drugs' ionisation can also be very important for their ability to pass through the skin, especially when iontophoresis is used, a method that uses an electric field to push charged particles through the skin. Drugs are taken in through vesicular transport, which involves putting them in small bubble-like structures (like liposomes) and moving them across the skin. Transdermal patches often use these methods by including boosters that change the structure of the skin or briefly make it more permeable.

C. Advantages and limitations of TDD

When compared to more standard ways of giving drugs, like by mouth or injection, transdermal drug delivery (TDD) has a number of clear benefits. One big benefit is that first-pass metabolism is avoided. This is when the liver breaks down a lot of the drug before it gets to the rest of the body's blood system. TDD makes sure that the drug is more consistently bioavailable by skipping the digestive system. This is especially important for drugs that don't absorb well when taken by mouth or are broken down a lot in the liver [8]. One more benefit is that drugs can be released slowly over time. This can cut down on the need for regular doses and make patients more likely to take their medicine as

prescribed, especially for managing chronic diseases. In addition, TDD makes it possible to give drugs without puncturing the skin, which is easier and less painful than giving shots. This makes it perfect for people who have trouble with needles or who need treatment for a long time. Because TDD can control drug release, it can also be used in situations that need a steady effective concentration, like hormone replacement treatment or pain management. But, even though TDD has some benefits, it also has some problems. The main problem is that the skin's natural protection makes it hard to deliver some types of drugs through the skin [9]. Only small molecules that are attracted to fat can effectively pass through the layer corneum. Large chemicals that don't like water, like many biologics and peptides, can't usually be carried well through the skin. Some people can also get skin inflammation or sensitisation from using transdermal methods for a long time. Lastly, creating and making transdermal delivery methods can be more expensive than other ways to give medicine, which makes them less common. Table 1 summarizes transdermal drug delivery basics, highlighting findings, limitations, and their clinical impact. Even with these problems, progress in enhancement technologies and drug composition keeps making TDD more useful

Table 1: Summary of Basics of Transdermal Drug Delivery

Study	Key Findings	Limitations	Impact
Lipid-Based Enhancers	Lipid-based enhancers improve permeability of lipophilic drugs.	Limited effectiveness for hydrophilic drugs.	Increases the effectiveness of lipophilic drug delivery.
Surfactant and Co-Solvent Use	Surfactants and co-solvents significantly increase solubility and permeability.	May cause skin irritation or toxicity with long-term use.	Enhances solubility and stability of various drugs.
Microneedle Patches for Drug Delivery [10]	Microneedle patches allow painless delivery of drugs including biologics.	Requires precise design and manufacturing, potential for incomplete drug delivery.	Offers a painless and efficient delivery system, especially for large molecules.
Electroporation for Enhancing Drug Permeation	Electroporation enhances delivery of both small molecules and biologics.	Can cause discomfort, and electrical parameters need precise optimization.	Improves the efficiency of drug delivery, especially for biologics.
Combination of Microneedles and Chemical Enhancers	Combination of microneedles and chemical enhancers offers synergistic effects.	Complex to formulate, may result in inconsistent drug delivery.	Provides better and more efficient transdermal drug delivery systems.
Nanocarriers in Transdermal Delivery	Nanocarriers improve stability and controlled release of drugs.	Production and formulation of nanocarriers can be expensive and time-consuming.	Improves drug stability and release control, increasing therapeutic efficacy.
Iontophoresis for Controlled Drug Release [11]	Iontophoresis enables controlled release and effective permeation for charged molecules.	Requires specialized equipment, limited patient-friendliness.	Enables controlled and efficient drug delivery, particularly for charged compounds.
Microdialysis for Monitoring Drug Absorption	Microdialysis can be used to monitor real-time drug delivery.	Requires expensive equipment and trained professionals.	Provides valuable insights for optimizing drug delivery in clinical settings.
Liposomal Delivery Systems	Liposomal systems improve drug solubility and stability, enhancing permeation.	Liposomes may be unstable under certain conditions, requiring careful formulation.	Increases drug stability, improving overall therapeutic outcomes.
Hydrogels for Drug Delivery [12]	Hydrogels provide controlled release and reduce irritation in transdermal systems.	Hydrogel formulations may not be suitable for all drug types.	Improves patient compliance with controlled, non-invasive drug delivery.
Role of Temperature in Transdermal Delivery	Temperature-controlled transdermal systems improve drug absorption and efficacy.	Temperature-sensitive systems may face challenges in maintaining stability during transport.	Helps optimize transdermal drug systems for different clinical conditions.

III. Penetration Mechanisms

A. Passive diffusion

Most people know that drugs are absorbed through the skin through a process called passive diffusion. Following Fick's Law of Diffusion, molecules move from a place where there are a lot of them to a place where there are not as many of them. The concentration gradient, the surface area that can be absorbed, and the drug's diffusion coefficient are some of the things that affect the rate of diffusion. Lipophilic (fat-soluble) drugs work especially well for passive diffusion because the stratum corneum is mostly made up of lipid-rich layers, which make it hard for drugs to get through. These lipids make it easy for molecules that are attracted to fat to move through the skin's barrier [13]. To be taken by passive diffusion, a drug needs to be able to break down in the fatty matrix of the skin and move across the epidermis to get to the bloodstream. Since the process doesn't need energy or carrying proteins, it is a natural way to move drugs around that uses little energy. Passive spread does have some problems, though. Drugs that dissolve in water usually don't pass through the skin well because they can't easily get into the lipid-rich stratum corneum.

B. Active transport

Active transport is another way that drugs can be absorbed through the skin. This is when molecules move across the skin barrier against the difference in their concentration. Active transport, on the other hand, needs energy in the form of ATP and the help of certain carrier proteins or transporters that are found in the cell membranes of the skin. This method is often used for drugs that are too big, too water-loving, or otherwise can't get through the skin through passive diffusion alone. In the skin, carrier-mediated transporters help move these molecules into and through the epidermal layers so they can get to the dermis and then the bloodstream [14]. Molecules like peptides, proteins, and other polymers would not be able to get through the skin barrier without active transport because they are too big or don't dissolve in water. This process also lets you finetune the amount of drug that gets into the bloodstream, which makes it good for specific drug delivery systems. But because this process needs certain carriers and energy input, it only works if there are good carriers in the skin. In addition, the process may be slower than passive diffusion, which could make it less useful in some therapy settings.

C. Vesicular transport

Drugs are put into small bubble-like structures called vesicles, which are then moved across the layers of skin. This process is also called transcytosis. These particles, like liposomes or niosomes, are made of lipids and can carry hydrophilic drugs. This lets the drugs get through the lipid-rich stratum corneum. The spheres connect with skin cells, like keratinocytes, which makes it easier for the drug to move from one layer of skin to another. When the vesicles get to the skin layer, the drugs can be let out into the bloodstream. It is especially helpful for hydrophilic drugs that would have a hard time getting through the skin barrier through passive diffusion [15]. As the vesicles break down over time, the drug inside can be slowly released, this allows for controlled and long-lasting drug release. In addition, vesicular systems can protect medicines that are easily broken down by enzymes or things in the surroundings. But making vesicular carriers can be hard, and they need to be carefully planned to make sure they are stable, that they encapsulate well, and that they release drugs at the right rates. In addition, the skin may be able to receive these cells in different ways, based on their size and shape.

D. Intercellular and intracellular penetration routes

There are two main ways for drugs to get through the skin: intercellularly (between skin cells) and intracellularly (through skin cells). The most usual path is through cells, especially for drugs that are lipophilic. For this method to work, drug molecules have to go through the lipid bilayers that cover the epidermal cells. The main thing that stops drugs from spreading is the stratum corneum, which is made up of corneocytes anchored in a fatty framework. The drug molecules move through the fatty layers instead of going through the cells. Smaller molecules that are lipophilic and can easily dissolve in the skin's lipid-rich surroundings are more likely to take the intercellular route. The internal path, on the other hand, has drug molecules go inside the skin cells (keratinocytes) instead of going between them. It's not very usual for chemicals that are small enough to move into and through skin cells to use this route. For example, hydrophilic drugs may go this way, though it may take longer for them to get inside cells because of the way they are made up of fats. Depending on the features of the drug, both methods can help with absorption. Many successful transdermal versions use a mix of both to improve drug release and absorption.

DRUG PENETRATION ENHANCERS

A. Chemical enhancers

Chemical boosters are chemicals that make the skin more permeable so that drugs can get through the stratum corneum more easily. They work by briefly breaking down the skin's barrier function. This can happen by working with the lipids in the skin or by changing the way proteins are structured in the epidermis. These boosters help make the skin less resistant to drugs, which makes transdermal drug release more efficient and effective. Chemical enhancers can be broken down into different groups based on how they work. Two of the most common groups are lipid-based enhancers and surfactants/co-solvents.

1. Lipid-based enhancers

Lipid-based boosters are chemicals that change the shape of the skin's lipid bilayer and make it easier for drugs to be absorbed. The stratum corneum is mostly made up of a lipid-rich structure that keeps drugs from getting into the skin. Lipid-based boosters are made up of fatty acids, esters, and alcohols. These chemicals are known to be able to mix with the skin's lipid layers and change how the skin's lipid bilayers are organised. This change temporarily breaks down the barrier, making it easier for the drug molecules to move into the deeper layers of skin. Oleic acid, linoleic acid, and isopropyl myristate are all common lipid-based stimulants. These chemicals are often used to help

lipophilic drugs (drugs that break easily in lipids) get deeper into cells. Figure 2 shows different drug entry boosters that make the skin more permeable so that drugs can be absorbed better.

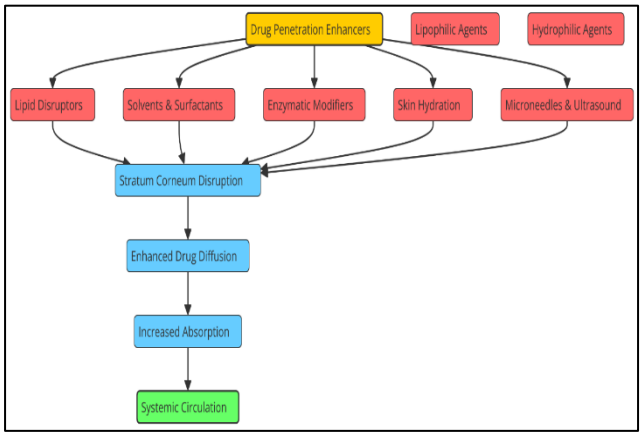

Figure 2: Illustrating Drug Penetration Enhancers

The good thing about lipid-based boosters is that they are mild and non-toxic. However, how well they work can depend on things like dosage and formulation stability. It's possible that they won't work as well on big or lipophilic molecules or molecules that don't fit through the skin as well with these. If lipid-based boosters are used in large amounts, they may irritate or damage the skin. Because of this, they need to be carefully formulated and dosed.

2. Surfactants and co-solvents

Surfactants and co-solvents are another type of chemical enhancers that help the skin's ability to let substances through by lowering surface tension and changing how drugs dissolve. Surface-active agents, also known as surfactants, lower the surface tension between the drug and the skin. This makes it easier for the drug to move through the stratum corneum. Surfactants can also change the structure of the skin's lipids by breaking down the stability of the lipid bilayers. This makes the skin more permeable. Polysorbates, cetyl alcohol, and sodium lauryl sulphate are all common detergents that are used in transdermal products. These chemicals can really help both water-loving and fat-loving drugs get into cells better. But they need to be used with care because high amounts can irritate the skin or break down the skin's natural protection too much, which could make it more sensitive or harmful. Co-solvents, like glycerin, ethanol, and propylene glycol, are often used with detergents to make drugs more soluble and help them get deeper into the skin. Co-solvents dissolve both the drug and the booster. This lets more of the drug be in the mixture and makes it easier for it to cross the skin barrier. Co-solvents like ethanol are often used because they can lower skin barrier by changing the flexibility of the skin's lipid structure. Using detergents and co-solvents together can make it much easier for hydrophilic drugs to be absorbed, which means they can be used for a wider range of medicinal purposes.

B. Physical methods

Using mechanical or electrical forces to get past the skin's natural protective features is one way to improve medicine penetration through the skin. Chemical boosters change the molecular structure of the skin, but physical means are more direct and often easier to control when it comes to making the skin more permeable. Microneedles and electroporation are two of the most studied and used physical ways.

1. Microneedles

Microneedles are very small structures that look like needles. They make tiny holes or channels in the skin so drugs can get to the deeper layers without causing a lot of pain or discomfort. Most of these microneedles are less than 1 millimetre long. This is small enough to go through the stratum corneum, the top layer of skin, but not deep enough to reach the nerve ends below, which reduces pain. Nanoneedles are tiny needles that can be made from silicon, metals, or plastics. They can be used in groups to cover more skin. The best thing about microneedles is that they let drugs go straight into the skin, which is where the blood vessels are. This makes it easier for the drugs to get into the general circulation quickly. For example, biologics, vaccines, and proteins that can't get through the skin through passive diffusion can be delivered this way. Microneedles can also be used for drugs that are either hydrophilic or lipophilic, based on how they are made.

Step 1: Fick's First Law of Diffusion

Fick's law can be expressed as:

$$J = -D * \left(\frac{dC}{dx}\right)$$

Where:

- J is the flux (amount of drug per unit area per unit time),
- D is the diffusion coefficient of the drug,
- (dC/dx) is the concentration gradient of the drug across the skin.

Step 2: Microneedle-Assisted Diffusion

In the presence of microneedles, the flux J can be enhanced by a factor depending on the effective volume of drug delivered through the microchannels created by the needles. The enhanced flux through the microneedle channels is given by:

$$J_{enhanced} = \alpha * J$$

Where:

- α is the enhancement factor (which depends on microneedle properties such as length, diameter, and density).

Step 3: Drug Concentration Gradient

The concentration gradient is modified due to the disruption in the stratum corneum by microneedles. The effective concentration gradient can be defined as:

$$\left(\frac{dC_{effective}}{dx}\right) = \frac{C_{drug}}{h}$$

Where:

- C_drug is the concentration of the drug in the microneedle reservoir,
- h is the penetration depth of the microneedles into the skin (the distance the drug travels through the skin layers).

Step 4: Rate of Drug Delivery

The rate of drug delivery through the skin using microneedles can be determined by multiplying the enhanced flux by the area of the microneedles that are in contact with the skin:

$$Rate_o = J_{enhanced} * A$$

Where:

- A is the total area of the microneedles in contact with the skin.

Step 5: Final Equation for Drug Delivery

Combining the above expressions, the final equation for the rate of drug delivery through microneedles is:

$$Rate_o = \alpha * \left(-D * \left(\frac{C_{drug}}{h}\right)\right) * A$$

2. Electroporation

In electroporation, quick, high-voltage electrical shocks are applied to the skin to briefly make holes in the cell membranes. This makes it easier for drug molecules to pass through the skin. The electrical shocks break up the skin's lipid bilayer in a way that can be undone. This makes holes that drugs that are more water-loving can get through. This method is often used with other drug delivery methods to help molecules that would normally have trouble getting through the skin be absorbed better. Electroporation has many benefits, one of which is that it can improve the release of both small molecules and bigger biologics like DNA or proteins. You can fine tune the method by changing the voltage, pulse frequency, and pulse length. This makes it very useful for a wide range of drugs and skin diseases. Also, chemical boosters are not needed for electroporation, so there is less chance of skin injury or toxins. It's also not painful, so patients will feel better about it than standard treatments that use injections. Even though electroporation has some benefits, it also has some problems. The electrical bursts needed for the process can be painful for a short time, and if the settings are not optimised, there is a chance that the skin will become irritated or damaged.

V. Mechanisms of Action of Penetration Enhancers

A. Effects on the stratum corneum

The stratum corneum, which is the top layer of the epidermis, is the main thing that stops drugs from getting through the skin. Changes in the structure and function of the stratum corneum are what penetration boosters do. The fatty matrix between the densely packed keratinized cells largely serves to provide protection for the skin. Penetration enhancers momentarily weaken the stratum corneum without causing any lasting damage. Drug molecules therefore pass through more easily. Penetration enhancers have many mechanisms of action with the stratum corneum. Some boosters increase the moisture of the skin, which promotes the growth and lessening of rigidity of the coenocytes. Drugs therefore find it simpler to enter the skin. Some alter the protein structure of the corneocytes, therefore increasing their accessibility. Several boosters also alter the stratum corneum's lipid components.

B. Disruption of lipid bilayers

Penetration enhancers break down the lipid bilayers of the stratum corneum, therefore facilitating the passage of medicines over the skin. Ceramides, cholesterol, and fatty acids make up the bulk of the lipid matrix found in stratum corneum. It creates a rather ordered and impenetrable barrier that protects the body from harmful substances, germs, and dehydration. However, many therapeutic molecules find it difficult to migrate using the same shape heavy in lipids. Drugs may pass this lipid bilayer more readily because penetration agents either modify its structure or increase its flexibility. Among the lipid-based stimulants sometimes used to target the lipid matrix include fatty acids, alcohols, and esters. These boosters interact with the lipid layers of the skin to alter the packing density of the lipid molecules, therefore increasing the flexibility of the bilayer. This relaxation of the lipid bilayer facilitates the passage of molecules dissolving in fat and those dissolving in water over the skin. Some enhancers can also temporarily break down the lipid bilayer, creating small holes or pathways that let bigger drug molecules pass through.

RESULT AND DISCUSSION

By getting past the skin's natural defences, penetration boosters make transdermal drug administration much more effective. Lipid-based boosters work well to break up the stratum corneum's lipid barrier, which makes it easier for lipophilic drugs to get into the skin. Surfactants and co-solvents make drugs more soluble, which makes it easier for hydrophilic molecules to be absorbed. Table 2: Evaluation of Penetration Enhancers

Penetration Enhancer	Skin Permeability Enhancement (%)	Solubility Enhancement (%)	Irritation Potential (%)
Oleic Acid	45	60	44
Isopropyl Myristate	50	55	60
Ethanol	40	70	25
Surfactant (Sodium Lauryl Sulfate)	35	65	4
Glycerin	30	50	2

In Table 2, different penetration enhancers are rated by how well they improve solubility, how well they increase skin permeability, and how likely they are to cause discomfort. It is a lipid-based booster called oleic acid. It has a middling discomfort potential of 44% but a fairly high skin permeability enhancement of 45% and a large solubility enhancement of 60%. Figure 3 compares penetration enhancers based on how well they work by looking at how permeable, soluble, and likely to irritate the skin they are on

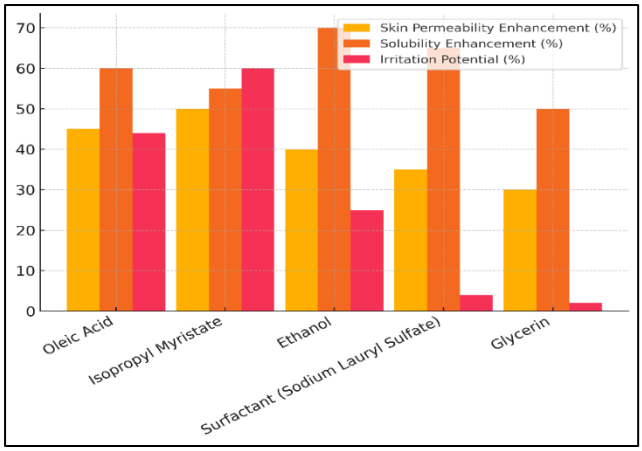

Figure 3: Comparison of Penetration Enhancers: Skin Permeability, Solubility, and Irritation Potential

This makes it useful for delivering lipophilic drugs, but it should be used with care because it could irritate the skin. Similar to isopropyl myristate, it increases skin absorption by 50% and solubility by 55%, but it also has a higher itching potential of 60%. Figure 4 shows the balance between the ability to improve entry and the chance of soreness, which shows how effective and safe enhancers are.

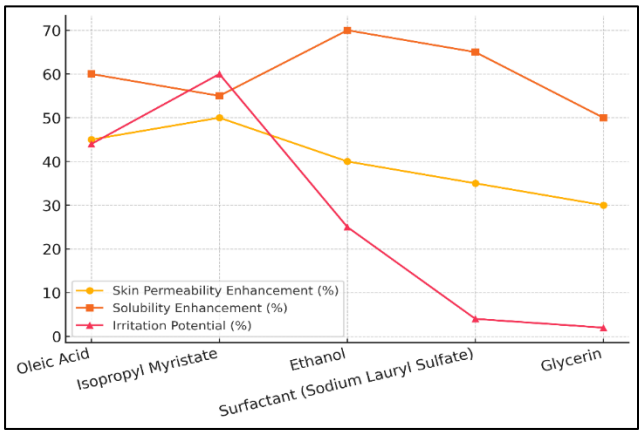

Figure 4: Effectiveness of Penetration Enhancers: Enhancement vs. Irritation

This means it might be better at improving drug administration, especially for lipophilic drugs, but it should be used with care to avoid discomfort. Ethanol is a co-solvent that improves solubility 70% of the time while increasing skin permeability only 40%. It also has a low discomfort potential of 25%, which makes it a good choice for making a wider range of drugs more soluble. Surfactant (sodium lauryl sulphate) improves skin permeability only slightly (35%), but it improves solubility significantly (65%) and has a very low irritation potential (4%). This makes it a good choice for products that need to improve solubility without causing major skin irritation

Table 3: Evaluation of Physical Methods

Physical Method	Delivery Efficiency (%)	Drug Type Compatibility	Ease of Application (%)
Microneedles	85	Lipophilic & Hydrophilic	82
Electroporation	75	Lipophilic & Biologics	60

Table 3 compares microneedles and electroporation, two physical ways that can improve transdermal drug delivery. Microneedles are very good at delivering drugs because they work 85% of the time for both lipophilic and hydrophilic drugs. They are very good at what they do because they can make tiny openings in the skin. This lets drugs get to the right places faster and more directly, especially for bigger molecules or biologics. The rating for how easy it is to use is 4 out of 5, which means that even though the method is pretty simple and doesn't hurt, it may still need careful device design and application technique. Figure 5 shows a comparison of different ways to give drugs physically, focussing on how well they work, how invasive they are, and where they can be used

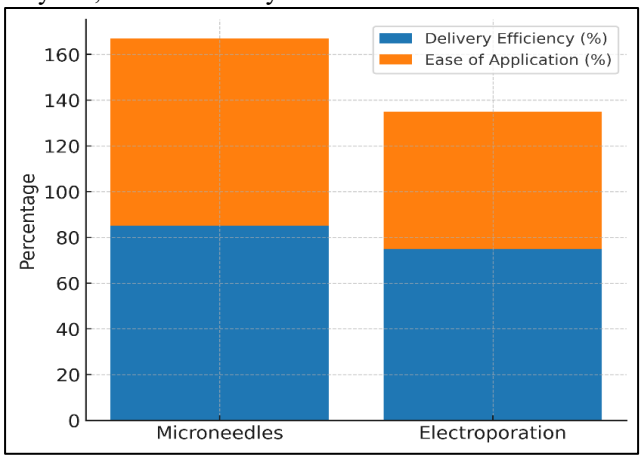

Figure 5: Comparison of Physical Drug Delivery Methods

However, electroporation only works 75% of the time, which is a little less than other methods. It still works, but it mostly helps lipophilic drugs and biologics, which are hard to get through the skin otherwise. Electroporation uses an electric field to briefly make the skin permeable, which makes it easier for drugs to get into the body. The rating for ease of use is 3, which means that the method is fairly hard to understand and needs special tools and knowledge to make the electric field settings work best and cause the least amount of pain. Even with these problems, electroporation is useful for improved drug delivery methods because it can transport biologics.

CONCLUSION

Transdermal drug delivery (TDD) has become an interesting option to traditional ways. It has many benefits, such as longer-lasting drug release, avoiding first-pass metabolism, and better patient cooperation. But the protected layer of the skin, especially the stratum corneum, makes it hard for many drugs to get through and into the

systemic blood. To get around this problem, many penetration boosters have been created, using both chemical and physical ways to make skin more permeable. Chemical boosters, like detergents, co-solvents, and lipid-based agents, work on the fatty layers of the skin to make medicines more stable and easy to dissolve. These factors make it easier for both water-loving and fat-loving drugs to be absorbed, which makes transdermal systems work better. Microneedles and electroporation, on the other hand, directly break through the skin's barrier, making ways for drug molecules to pass through without hurting the skin too much. These ways work especially well for sending big molecules like proteins and biologics that would have a hard time getting through the skin the old way. There are still some problems with enhancement devices, even though they have come a long way. Care must be taken to avoid skin inflammation and tissue damage, especially when boosters are used in higher amounts or for a long time.

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