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Review On Topical Drug Delivery System

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Abstract

Topical drug delivery is a broad-based method used for the topical administration of drug agents to the skin for regional or systemic effects. Topical drug delivery presents several benefits in the form of increased bioavailability, prevention from first-pass metabolism, decreased system side effects, and increased compliance by the patients. Topical drug delivery mainly depends on the characteristics of stratum corneum, which represents a major drug permeation barrier.

This review discusses different topical drug delivery systems like conventional semi-solid, liquid, and solid systems in the form of creams, ointments, gels, pastes, lotions, and powders. It also deals with new drug delivery technologies such as liposomes, nanoemulsions, dendrimers, microsponges, fullerenes, solid lipid nanoparticles (SLNs), and microneedles, which have transformed transdermal drug delivery by promoting drug penetration and activity.

In addition, several pharmaceutical methods aimed at enhancing drug permeation—iontophoresis, sonophoresis, electroporation, laser-assisted delivery, radio-frequency techniques, and magnetophoresis—are discussed for their ability to bypass the skin's natural barrier. The use of permeation enhancers and the prodrug strategy in enhancing drug absorption is also emphasized.

With ongoing advances in pharmaceutical sciences and material science, topical drug delivery is set to get even more innovative. The incorporation of new drug carriers, permeation enhancement techniques, and targeted drug preparations will expand the therapeutic efficacy of dermatological and transdermal therapies significantly, leading to more efficient and patient-friendly drug delivery systems.

Keywords: Topical drug delivery, dermatological bases, permeation enhancers, novel drug carriers, skin absorption techniques

Introduction

Topical drug delivery is the application of a pharmaceutical dosage form to the skin for the treatment of dermatological disorders or cutaneous symptoms of systemic diseases, with the aim of localizing the pharmacological action at the surface of the skin. The skin is an extremely accessible route for drug administration, and therefore topical drug delivery systems are one of the most commonly used systems. Permeation of chemicals into and across the skin is largely controlled by the stratum corneum, long established as the key barrier to percutaneous absorption. Nevertheless, having a stratum corneum affects drug selectivity as well, preventing the activity of previously delivered drugs or modes of delivery.

Human beings throughout history have been suffering from various physiological and psychological ailments. Nevertheless, strict scientific inquiry worldwide has allowed for considerable advancement in the prevention, treatment, and eradication of many diseases. Pharmaceutical sciences have continued to develop, being a key element in health preservation and disease prevention. Over the last few decades, the therapeutic use of biomolecules, such as pharmaceutical

compounds, proteins, and other biologically active substances, has undergone tremendous progress. Originally, their clinical use was limited by the difficulties involved in drug delivery in physiologically unfavorable conditions[1-3].

Topical drug delivery offers several key advantages, including enhanced bioavailability, more consistent plasma concentrations, prolonged drug action leading to reduced dosing frequency, minimized systemic adverse effects, and improved therapeutic efficacy by maintaining plasma levels throughout the dosing interval, unlike the declining plasma concentrations observed with conventional oral formulations.

A primary benefit of topical administration is the circumvention of first-pass hepatic metabolism. Additionally, topical formulations mitigate the risks and limitations associated with intravenous therapy while also avoiding physiological barriers to absorption such as pH variations, enzymatic degradation, and gastric emptying time. Although semi-solid formulations dominate topical drug delivery, other dosage forms such as foams, sprays, medicated powders, solutions, and transdermal adhesive systems are also utilized. When conventional routes of drug administration prove inadequate, topical delivery is employed for conditions such as pain management, contraception, and urinary incontinence. Over the years, pharmaceuticals have been administered through various routes, including oral, sublingual, rectal, parenteral, topical, and inhalational methods.

Topical drug delivery systems are categorized into externally applied formulations and internally administered topicals intended for localized activity. The benefits of these systems include avoidance of first-pass metabolism, elimination of gastrointestinal incompatibilities, enhanced patient adherence, suitability for self-administration, and improved stability of drugs with limited shelf life. Despite the inherent challenges posed by the skin barrier, several physiological and physicochemical factors influence the effectiveness of topical drug delivery. These include skin thickness, hydration status, inflammation, pH, lipid composition, density of hair follicles and sweat glands, cutaneous blood flow, and drug-related properties such as partition coefficient, molecular weight, and degree of ionization.

The application of a drug-containing formulation to the skin for the treatment of dermatological conditions (e.g., acne) or cutaneous manifestations of systemic diseases (e.g., psoriasis) is referred to as topical drug delivery. The objective is to localize the pharmacological action within the skin or on its surface, although in some cases, intracutaneous injections may be utilized[4,5]. Pharmaceutical dosage forms employed in topical drug delivery include semisolids, liquids, sprays, and powders, with the most frequently used semisolid formulations being gels, creams, and ointments[6].

Topical therapies exert their effects by directly targeting the affected area. Gels, which are three-dimensional cross-linked networks of structural components, may be composed of inorganic particles or organic macromolecules such as polymers[7]. Topical drug delivery systems are further classified into internal and external applications. Internal topicals, designed for localized activity, are applied to mucosal membranes in oral, vaginal, or anorectal regions. External topicals are applied to the skin via sprays, lotions, or other formulations, ensuring direct interaction with the affected site. While a fraction of the drug may be systemically absorbed, it is typically minimal and unlikely to produce significant systemic effects[8,9].

Novel Topical Drug Delivery Systems:

Following are some types of topical drug delivery systems

Liposomes:

Liposomes are artificially constructed vesicular structures made of a lipid bilayer, widely used in pharmaceutical and cosmetic products for

controlled and targeted drug delivery to particular areas of the skin or underlying layers. These vesicular spheres have membranes made of amphiphilic lipids, which have both hydrophilic and lipophilic characteristics—resembling the bilayer structure of biological cell membranes—while having an aqueous core inside.

Because of their amphiphilic character, liposomes are capable of trapping hydrophilic materials inside their aqueous interior and incorporating lipophilic drugs into their lipid bilayer. This unique dual-compartmentalization feature enables the concurrent release of both hydrophilic and lipophilic molecules upon skin application, each acting independently on skin permeability. This action increases the therapeutic effectiveness of the administered drugs, theoretically maximizing pharmacological effects[10,11].

Nanoemulsions:

Nanoemulsions are a specialized class of emulsions that can exist as either water-in-oil or oil-in-water formulations, characterized by the dispersion of ultrafine droplets within the continuous phase. Unlike conventional emulsions, nanoemulsions do not form spontaneously; their production necessitates specific thermodynamic conditions, advanced manufacturing techniques, and the use of surfactants that effectively stabilize the nanodroplets.

There formulations serve as efficient carriers for lipophilic compounds, facilitating their transport into the skin. Consequently, nanoemulsions are considered an optimal vehicle for acne treatment, as they enhance the penetration of active pharmaceutical ingredients into the lipophilic milieu of the pilosebaceous unit. Moreover, nanoemulsion particles do not obstruct pores, and they confer additional dermatological benefits such as improved skin hydration and enhanced viscoelastic properties[12].

Dendrimer:

Dendrimers have found recent applications in novel topical and transdermal delivery systems, providing benefits such as improved drug solubilization, controlled release, and drug polymer conjugates like prodrugs. The viscosity generation-number property of a dendrimer solution allows for ease of handling of highly concentrated dendrimer formulations for these applications. Dendrimers have been shown to be useful as transdermal and topical drug delivery systems for nonsteroidal anti-inflammatory drugs (NSAIDs), antiviral, antimicrobial, anticancer, or antihypertensive drugs. PAMAM dendrimers have been studied as carrier transdermal systems for the model NSAIDs: ketoprofen and diflunisal. It was found that the PAMAM dendrimer-drug formulations showed increased transdermal drug delivery compared with formulations lacking dendrimers. In vivo studies in mice showed prolonged pharmacodynamic responses and 2.73-fold higher bioavailability over 24 h for certain dendrimer-containing drug solutions[13,14].

Microsponges:

It is a unique technology for the controlled release of topical agents and consists of microporous beads, typically 10-25 microns in diameter, loaded with active agent. When applied to the skin, the MDS releases its active ingredient on a time mode and also in response to other stimuli like rubbing, temperature, pH, etc. MDS technology is being used in cosmetics, over-the-counter skin care, sunscreens and prescription products. These are biologically inert particles that are made of synthetic polymers with the capacity to store a volume of an active agent up to their own weight. Furthermore, the particles serve to protect the entrapped active compound from physical and environmental degradation.

The microsponge technology can be utilized in a variety of formulations but is more frequently manufactured as gels. Once applied on the skin, microsponges slowly release the active agents.

Fullerenes:

Fullerenes have a wide range of biological activities and show significant antioxidant activity and the capacity to efficiently eliminate reactive oxygen species (ROS), rendering them useful active ingredients in dermatological products. Fullerenes are structurally made up of pure carbon atoms in a hollow spherical structure.

When in contact with the skin, fullerenes tend to move through intercellular routes more than transcellular diffusion. This property makes them useful as carriers, trapping active ingredients and releasing them in a controlled manner into the epidermis when applied. In addition, fullerenes themselves are thought to have strong antioxidant properties. Current studies show that fullerenes exhibit good biocompatibility and have great potential for use in dermatology and cosmetics[15,16].

Solid Lipid Nanoparticles (SLNs):

Solid lipid nanoparticles (SLNs) have demonstrated significant potential as a novel drug delivery system for the topical administration of various pharmaceutical agents. However, their cutaneous performance remains incompletely understood due to the complexity of their structural composition and physicochemical properties.

In theory, drug delivery via SLNs can be directed systemically to the dermal vasculature, locally to the different layers of the skin, or superficially to the skin’s surface. Therefore, the formulation of a topical delivery system should be tailored to the intended therapeutic objective. Understanding the permeation dynamics of drugs through the skin necessitates an in-depth analysis of drug release mechanisms from SLN formulations. Several distinct drug release profiles have been documented in the literature, with variations primarily attributed to differences in manufacturing processes and formulation parameters[17].

Microneedles:

The traditional needle-syringe device has long been the major vehicle for administering ineffective drugs and vaccines via other routes of administration. Streamlined as a universally standardized medical device, the technology has led to the emergence of microdevice-based drug delivery systems, particularly microneedles.

Microneedles are designed to be painless and minimally invasive yet efficient at circumventing the skin's inherent barrier function. The novel strategy facilitates transdermal drug delivery without inducing major epidermal disruption. Fabrication techniques for microneedles involve micromolding, microfabrication, microshaping, and hybrid methods that integrate these processes.

Relative to traditional delivery systems, microneedles have a number of benefits for patients, medical professionals, and pharmaceutical companies. One key advantage is decreased discomfort, and thus they are especially well-suited for people with needle anxiety, like children, and those who need injections repeatedly, like diabetics. Microneedles also offer a convenient means of delivering therapeutic agents transdermally, and their use in mass vaccination campaigns—particularly during pandemics—may increase immunization effectiveness.

The use of microneedle technology holds possibilities for the development of miniaturized, economical, pain-free, and convenient drug delivery systems with extensive biomedical applications. Remarkably, ALZA Corporation has already brought on the market a microneedle system termed Macroflux that can be applied either with an accompanying drug reservoir or through dry-coated drugs directly deposited on the microprojection array. The latter option has been promising to enhance the efficacy of vaccine administration by intracutaneous immunization[18-20].

Skin Abrasion:

Skin abrasion techniques involve the deliberate removal or disruption of the outermost layers of the epidermis to enhance the transdermal absorption of topically applied pharmacological agents. Certain devices utilized for this purpose are adaptations of dermatological procedures, such as microdermabrasion, which is commonly employed in the treatment of acne, scarring, hyperpigmentation, and other dermatological conditions.

Microscissuining is a novel approach that generates microchannels in the skin by eroding the impermeable outermost layer using sharp, microscopic metal granules. Carlisle Scientific is currently developing a pen-like handheld instrument, termed the microscissioner, for this purpose.

Additionally, MedPharm Ltd. has engineered an advanced dermal abrasion device (D3S) designed to enhance the delivery of therapeutics that are traditionally difficult to formulate, including hydrophilic low-molecular-weight compounds and biopharmaceutical agents. In vitro studies indicate that this device can increase the dermal penetration of angiotensin by a factor of 100 compared to untreated human skin. The device operates through a non-invasive mechanism, and histological evaluations confirm that its impact on the stratum corneum is reversible and non-irritating.

Cyclodextrins:

Cyclodextrins possess a hydrophilic outer surface along with a relatively lipophilic central cavity, enabling them to form water-soluble inclusion complexes with numerous hydrophobic, poorly water-soluble drugs. In aqueous solutions, the drug molecules within the cyclodextrin cavity exist in a dynamic equilibrium with free drug molecules. The presence of multiple lipophilic compounds in solution results in competitive interactions for inclusion within the cyclodextrin cavity.

Due to their molecular size and hydrophilic nature, cyclodextrins and their drug-complexed forms exhibit limited permeability across lipophilic biological barriers such as intact skin. However, they enhance topical drug delivery by increasing the drug concentration at the surface of the skin barrier. At this interface, the drug molecules dissociate from the cyclodextrin cavity and partition into the lipophilic barrier. Consequently, drug delivery from aqueous cyclodextrin formulations is governed by both diffusion and membrane-controlled processes. Notably, the efficacy of cyclodextrins in facilitating topical drug penetration is contingent upon the presence of water[21].

Aquasomes:

Aquasomes represent a novel class of nanoparticulate delivery systems designed for the transport of peptides and protein-based therapeutics. Structurally, aquasomes are self-assembled, multilayered carriers composed of a solid nanocrystalline core coated with polyhydroxy oligomers onto which bioactive molecules are adsorbed.

The solid core serves as a stabilizing scaffold, while the carbohydrate coating preserves the hydration state and structural integrity of the biologically active compounds. This unique stabilization mechanism enables aquasomes to maintain the conformational integrity of bioactive molecules, thereby rendering them a promising carrier system for peptide-based pharmaceuticals. The technology has been successfully employed for the targeted delivery of biomolecules such as insulin, hemoglobin, and various antigens[22].

Dermatological Bases:

Topical formulations intended for either systemic absorption or localized therapeutic effects can be categorized as follows:

Solid Dosage Forms – Dusting powders.

Semi-solid dosage Forms – Creams, gels, ointments, pastes, and related formulations.

Liquid Dosage Forms – Solutions, emulsions, liniments, suspensions, medicated soaps, shakes, collodions, lotions, topical paints, and similar preparations[23].

Among these, semi-solid formulations offer significant advantages over solids and liquids due to their enhanced ability to adhere to the site of application, thereby prolonging the duration of action before being removed.

Pharmaceutical semi-solid preparations include ointments, pastes, cream emulsions, gels, and rigid formulations, all of which serve as effective drug delivery systems in dermatological and transdermal applications[24].

Ointments:

Ointments are semisolid drug formulations consisting mainly of liquid hydrocarbons distributed in a higher-melting solid hydrocarbon matrix. They act as a vehicle for the delivery of active pharmaceutical ingredients (APIs), which can be dissolved, suspended, or emulsified in the ointment base. Owing to their nature, ointments have a greasy feel[25].

Ointment Bases:

The ointment base serves as the carrier or vehicle for the active ingredient(s). The choice of a suitable base relies on several factors, such as the desired therapeutic effect, the physicochemical characteristics of the drug, and the formulation stability.

A good ointment base should have the following attributes:

1. It must be chemically inert, odourless, and smooth.
2. It should be physically and chemically stable in the long term.
3. It must be compatible with the skin and the active ingredients included.
4. It must have a proper consistency to ensure ease of use and proper adhesion to the skin.
5. It should promote wound healing without any delay in the healing process.

Classification of Ointment Bases:

As per the United States Pharmacopeia (USP) XX, ointment bases can be categorized under four broad types: hydrocarbon bases, absorption bases (in anhydrous and emulsion form), water-removable bases, and water-soluble bases.

1. **Hydrocarbon Bases**

These bases are hydrophobic, thus being immiscible with water and being minimally absorbent. They create an occlusive film on the skin that does not allow moisture loss and increases hydration, which could allow drug absorption. Examples include petrolatum and white ointment (petrolatum mixed with 5% beeswax). Hydrocarbon-based ointments are largely only to be recommended for chronic dermatological disorders because of their very occlusive nature[26].

2. **Absorption Bases:**

Absorption bases are composed by the addition of hydrocarbon-miscible substances with polar functional groups like sulphate, sulfonate, carboxyl, hydroxyl, or ether linkages. They are grouped into two categories:

Anhydrous Absorption Bases: These bases allow the addition of aqueous solutions to form water-in-oil (W/O) emulsions. Hydrophilic petrolatum and anhydrous lanolin are examples.

Emulsion Bases: These are established water-in-oil emulsions that facilitate the incorporation of small quantities of aqueous solutions. Examples of these include cold cream and lanolin.

3. **Water-Removable Bases:**

Water-removable bases are oil-in-water (O/W) emulsions that are readily removable from the skin or clothing with water and, therefore, are referred to as "water-washable" ointment bases. These bases are similar to creams and are water-dilutable or dilutable with aqueous solutions. Therapeutically, they are useful in absorbing exudates in dermatological conditions. Some active ingredients show improved percutaneous absorption when formulated in these bases[27].

4. **Water-Soluble Bases**

Water-soluble bases are prepared with a blend of high and low molecular weight polyethylene glycols, which provide an ointment-like texture that melts or softens on contact with the skin. Water is not needed in their preparation, unlike in other bases. These bases are fully soluble in water because they contain large numbers of polar groups. They are also known as "greaseless ointment bases" and provide benefits like being non-toxic, non-irritating, non-occlusive, and removable easily without staining.

Creams:

Creams are semi-solid emulsions with an opaque appearance, as opposed to the translucent nature of ointments. Their rheological properties and consistency are a function of the type of emulsion.

Oil-in-Water (O/W) Creams: They exist as water-washable bases. They are patient favorites because they are not greasy and easy to apply. When the water phase dries, the concentration of the active drug is increased in the residual film, leading to increased percutaneous absorption. Formulators can add non-volatile, water-soluble co-solvents like propylene glycol to suppress the precipitation of the drug.

Water-in-Oil (W/O) Creams: They are emollients and cleansers. Not occlusive, they leave lipids and humectants on the stratum corneum to restore water[28].

Pastes:

Pastes are semi-solid dermatological preparations that resemble ointments but have a larger amount of solid material and so are thicker, stiff, and more absorbent. Unlike ointments, they are less greasy and do not drip from the application area once applied, with little tendency to soften or flow. Their high absorptive ability makes them particularly suitable for the control of acute dermatologic lesions with exudation, crusting, or vesiculation. Since they are stiff, pastes are not appropriate for administration onto hairy regions.

Illustration: Zinc oxide pastes, usually applied for protective and calming effects in dermatology.

Gels:

Gels are a fairly recent category of semi-solid dosage forms made up of extensive quantities of aqueous or hydro-alcoholic liquid trapped in a network of colloidal solid particles. These particles can be either from inorganic materials like aluminum salts or from organic natural and synthetic polymers. The optical appearance of gels ranges from totally transparent to opaque, based on the type of colloidal substances and liquid phase.

The majority of topical gels are made from organic polymers like carbomers, which have a clear, cosmetic appearance and can easily be washed away with water. Gels are generally a two-phase semi-solid system consisting of natural or synthetic polymers as a three-dimensional network in a hydrophilic liquid. Polymers used commonly are natural gums (tragacanth, carrageenan, pectin, agar, alginic acid), semi-synthetic cellulose derivatives (methylcellulose, hydroxyethyl cellulose, hydroxypropyl methyl cellulose, carboxymethylcellulose), and synthetic polymers (carbopol). Some clays, bentonite and veegum, are employed as gelling agents, but only if they do not disrupt drug release.

Types of Gels:

Single-phase gels: These contain macromolecules dispersed uniformly in a liquid medium, with no clear boundaries between the dispersed phase and the liquid.

Double-phase gels: These are flocculated small particles present in the gel mass, usually termed magmas (e.g., milk of magnesia).

Jellies:

Jellies are soluble bases made by the use of natural gums like tragacanth, pectin, alginate, or

boroglycerin, or synthetic analogs like methylcellulose and carboxymethylcellulose.

Lotions:

Lotions are clear liquid preparations (25-50% alcohol) containing antiseptic, emollient, and haemostatic agents. Some of the common ingredients are witch hazel extract, menthol, glycerine, boric acid, alum, potassium oxyquinoline sulphate, and chloroform. Lotions are not usually rubbed into the skin when applied[29].

Types of Lotions:

1. Hand lotion
2. Face lotion
3. Body lotion
4. After-shave lotion
5. Antiperspirant lotion

Liniments:

Liniments are comparable to lotions but differ from them in that they are rubbed into the skin when applied.

Suppositories:

Suppositories are solid dosage forms for the rectal, vaginal, or urethral delivery of drugs. They are manufactured either by the cold compression process or fusion method, with bases chosen on the basis of compatibility, stability, melting point, and aesthetics. The bases used in suppositories are usually cocoa butter, glycerine, hydrogenated vegetable oils, and polyethylene glycol.

Powders:

Powders are different from liquid skin preparations in their physical state. Their small particle size gives a high surface area, enabling them to cover the skin more effectively. Some of the types of powders are:

1. Body powders (dusting powders or talcum powder)
2. Face powders
3. Compact powders
4. Medicated powders (for prickly heat or antimicrobial use)

Solutions:

Solutions are liquid preparations in which soluble chemicals are dissolved in solvents like water, alcohol, or propylene glycol[30].

Examples of Solutions:

Aromatic waters

Tinctures (e.g., Tincture of iodine)

Sterile Indian ink (surgical application)

Emulsions:

Emulsions are two-phase mixtures in which one phase (dispersed/internal phase) is dispersed in the form of very fine droplets within another (continuous/external phase). Emulsions are oil-in-water (O/W) or water-in-oil (W/O) based on the composition of the dispersed phase. Such systems need stabilizers in the form of surfactants, non-ionic polymers, polyelectrolytes, or biopolymers[31].

Types of Emulsions:

1. Water-in-Oil (W/O) Emulsion
2. Oil-in-Water (O/W) Emulsion
3. Water-in-Oil-in-Water (W/O/W) Emulsion
4. Oil-in-Water-in-Oil (O/W/O) Emulsion

Suspensions:

Suspensions are multi-component heterogeneous systems formed by a semi-solid or liquid continuous phase and an insoluble dispersed phase. The preparations are made to enable drug absorption or coating processes under controlled conditions. Because settling happens over time, preparations are made to retard sedimentation and re-dispersibility after shaking.

Types of Suspensions:

Flocculated suspension: Consists of particles with aggregates that re-disperse easily after shaking.

Deflocculated suspension: Comprises separate particles that settle slowly but can create a hard cake, which is difficult to re-dispense.

Aerosols:

Aerosols are pressurized systems that use compressed or liquefied gases to deliver pharmaceutical formulations when activated. Propellants for topical pharmaceutical aerosols are hydrocarbons (propane, butane, isobutane) and compressed gases (nitrogen, carbon dioxide, nitrous oxide)[32].

Various Techniques to Increase Drug Permeation and Absorption

The progress made in drug delivery technologies in recent times has been inspired by advances in precision engineering, bioengineering, computing, chemical engineering, and materials sciences. This has seen the creation of numerous techniques and equipment that make drug delivery across the skin possible, with the desired therapeutic outcomes[33].

Iontophoresion:

Iontophoresis is a method by which an electric current is used to improve the uptake of topically applied medicinal compounds across the skin. A charged electrode, possessing the same polarity as the drug, is utilized to force the drug molecules into the skin, and an indifferent counter electrode is utilized elsewhere on the body to make a circuit. The method is a way to effectively allow the penetration of the drug into the interior layers of the skin[34,35].

Ultrasound (Sonophoresis or Phonophoresis):

Ultrasound, or sonophoresis or phonophoresis, is the process of using ultrasonic energy to enhance transdermal drug delivery. Ultrasonic waves interact with intercellular lipids present in the skin, creating gaseous cavities and thus breaking up the skin barrier and increasing permeability. Micro-vibrations produced by the ultrasound waves enhance the kinetic energy of the molecules in topical solutions, enhancing the absorption of the drug. The process is increasingly applied in hospitals for the transdermal delivery of drugs[36].

Laser Radiation and Photomechanical Waves:

Both laser radiation and photomechanical waves increase drug absorption through selective removal of the outermost layer of the skin. The ablation of stratum corneum (SC) with controlled damage to the underlying epidermis has been demonstrated to enhance the administration of lipophilic and hydrophilic drugs[37].

Electroporation:

Electroporation is a method of delivering drugs or genes into cells with the use of a short, high-voltage electrical pulse. The electrical pulse permeabilizes the cell membrane for a temporary period, making it possible for molecules that would not have had access otherwise to enter the cell. It is commonly applied in electrochemotherapy for drug delivery of chemotherapeutic compounds and in gene electro transfer for the delivery of DNA into cells[38].

Radio-Frequency:

Radio-frequency therapy is the process of exposing the skin to a high-frequency alternating current of about 100 kHz, creating heat-induced microchannels in the skin membrane. Like laser radiation, this process creates channels for increased drug penetration. The delivery rate of the drug is based on the characteristics of the microelectrodes employed in the device, which determine the number and depth of the microchannels[39].

Magnetophoresis:

Magnetophoresis employs a magnetic force to promote drug penetration across biological barriers. In vitro and in vivo tests have illustrated its efficacy in transdermal drug delivery. Mechanisms involved in enhanced drug absorption are magnetokinesis and enhanced drug partitioning into the stratum corneum[40].

Microporation:

Microporation is a method whereby microneedles, between 10 and 200 micrometers in length and 10 to 50 micrometers in width, make microscopic holes in the stratum corneum. This method greatly enhances skin permeability without penetrating deeper layers of skin, and it is a safe and efficient drug-delivery method[41].

Application of Permeation Enhancers:

The application of permeation enhancers enhances drug absorption by altering the barrier function of the stratum corneum. An ideal permeation enhancer should be pharmacologically inert, non-toxic, non-irritating, odourless, tasteless, colourless, cost-effective, and compatible with a wide range of drugs and excipients. Since the last two decades, numerous penetration enhancers have been synthesized, among which alcohols and polyols such as ethanol and propylene glycol, surfactants like Tween, Span, and sodium lauryl sulphate, fatty acids like oleic acid, amines and amides like Azone and N-methyl pyrrolidone, terpenes like limonene, sulfoxides like dimethyl sulfoxide (DMSO), and esters like isopropyl myristate have emerged[42-44].

Prodrug Approach:

The pro-drug strategy is also a promising approach to increasing drug penetration. Prodrugs are inactive drugs that are metabolically converted into the active therapeutic agent. Through modulation of the lipophilicity and physicochemical properties of the parent drug, this strategy improves drug absorption and enhances therapeutic effects.

These sophisticated techniques of drug delivery offer creative solutions for increasing drug penetration and absorption across the skin, facilitating more efficient and effective transdermal administration[45].

Conclusion:

Topical and transdermal drug delivery systems have come a long way with a wide variety of formulations that cater to optimal therapeutic effects. From solid, semi-solid, and liquid dosage forms to newer techniques of drug permeation enhancement, the dermatological bases ensure drug stability, efficacy, and compliance. The formulation is based on drug solubility, permeability of the skin, and the desired therapeutic action.

The introduction of new permeation methods—such as iontophoresis, ultrasound, electroporation, and microporation—has further opened up the potential for transdermal drug delivery, bypassing conventional barriers to absorption. Moreover, the use of penetration enhancers and prodrug approaches continues to increase drug bioavailability and therapeutic efficacy.

With advances in pharmaceutical technology, more investigation and innovation in dermatological bases and drug delivery methods will continue to advance and enhance transdermal therapeutics. By maximizing formulation approaches and creating new permeation methods, the discipline can lay the groundwork for improved, patient-friendly, and targeted drug delivery systems in dermatology and beyond.

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