

## Chapter 2

# Role of Herbal Polymers in Enhancing Permeability

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## Abstract

The skin is a strong protective barrier that challenges drug delivery. Among the key parameters determining drug permeation, the role of polymers is also becoming increasingly important in skin permeation. Polymers increase the permeability of the skin by interacting with the stratum corneum, the outermost skin layer, and adjusting the structure to allow easier drug diffusion. Herbal polymers, such as chitosan and alginate, along with cellulose derivatives, receive special attention due to their natural origin, being biodegradable, and biocompatible. These polymers ensure improvement in drug solubility, sustained release system establishment, and reduction in the degradation of drugs. An example is chitosan, which interacts with lipids in the skin by enhancing permeability and having a gel-like matrix developed by alginate that establishes steady drug release. Other hydroxypropyl methyl celluloses are cellulose derivatives that work like viscosity modifiers and could raise skin retention in formulations. Additional factors like polymer compatibility with the active drug govern size in terms of molecular charge which determines effectiveness in penetration with the skin. These help overcome inherent resistance in a controlled, targeted delivery with minimal systemic side effects by the skin. Thus, such polymer-based formulations could now promise advanced transdermal therapy solutions with better therapeutic efficacy and patient compliance.

**Keywords:** Polymer, Stratum Corneum, Chitosan, Cellulose, Skin Permeability, Biodegradable.

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## Introduction

Drug facilitators known as "bioavailability enhancers" are molecules that, when combined, increase a drug's activity in several ways, such as by acting as receptors for the drug, potentiating the drug through conformational interaction, increasing the drug's bioavailability across membranes, and increasing target cells' receptiveness to drugs. A "bioenhancer" is an agent that, at the dose employed, has no normal pharmacological effect of its own but can increase the bioavailability and bioefficacy of a specific medicine with which it is coupled [1]. These functional excipients, often known as "absorption enhancers," are added to formulations to increase the absorption of pharmacologically active medications. Indian researchers at the Regional Research Laboratory, Jammu (RRL, now known as the Indian Institute of Integrative Medicine, Jammu) initially used the term "bioavailability enhancer" when they identified and confirmed piperine as the first bioavailability enhancer in history in 1979 [2]. Although the general health-promoting properties of many plant products have long been established by phytochemical and phytopharmacological studies, increasing the bioavailability of numerous herbal drugs and plant extracts that are poorly lipid soluble and thus less accessible is of great medical necessity and interest [3]. Despite their remarkable potential in vitro, many herbal medications and extracts show little to no in vivo activity because of their poor lipid solubility, incorrect molecular size, or both. This leads to poor absorption and bioavailability. Since the majority of plant components, particularly phenolics, are soluble in water, their in capacity to pass through intestinal lipid membranes is the main cause of their lower bioavailability. Various innovative delivery systems, such as

liposomes, marinosomes, niosomes, and lipid-based systems, can increase the bioavailability by improving the rate of release and the ability to pass through lipid-rich biomembranes [4]. It has been discovered that phospholipid-based drug delivery systems hold promise for the efficient and successful delivery of herbal medications. A sufficient amount of the active ingredients must be delivered for any herbal product (or medication) to be effective [5].

Knowing the problems with each compound's bioavailability may help develop strategies to get around its drawbacks. Numerous investigations have determined that low bioavailability is mostly caused by a compound's quick conjugation, particularly by glucuronidation in the liver and intestine [6]. Uridine diphosphate-glucuronosyltransferases (UDP-UGTs) mediate glucuronidation [7] and when combined with cytochrome P450 enzyme activities, they account for about 80% of chemical metabolic pathways. It is acknowledged that the cytochrome P450 and glucuronidation pathways are significant clearance processes [8]. Co-delivery of drugs that alter the activity of such pathways or, more generally, block the tested compound's metabolism in vivo could be one strategy to boost the bioavailability of chemopreventives. Due to their low permeability across epithelia and/or low water solubility, several medications have poor bioavailability. Others cannot be used by the method that patients choose because of enzymatic breakdown or acidic pHs that make them labile when taken orally. Others lack specificity and may need localization techniques at the site of action to optimize their therapeutic index, even though routes supply them with lower proteolytic activity. Polymers have long been used in medicine delivery [9–11] and are necessary to increase patient compliance as well as the pharmacokinetics and pharmacodynamics of drugs [12]. About 60% of people worldwide utilize plant-based medications, while the majority of third-world nations continue to rely on herbal remedies. Nearly 25% of medications in contemporary pharmacopoeias also contain substances derived from plants [13]. Polymers protect drugs through conjugation, adsorption onto the particle surface, encapsulation, or entrapment (within the core) [14]. Natural polymers are often biocompatible, biodegradable, and harmless. Polysaccharides are frequently utilized to create polymer-based nanoparticles [15]. Trikatu is the collective word for ginger (*Zingiber officinalis*), long pepper (*Piper longum*), and black pepper (*Piper nigrum*) in Ayurveda. These three substances were listed as necessary components of numerous prescriptions and formulations used to treat a variety of illnesses in the ancient, documented Ayurvedic Material Medica. The scientific rationale behind the usage of three herbs has been the subject of some contemporary Ayurvedic practitioners' investigations. It was discovered that when taken orally, trikatu plays a significant role in boosting medication bioavailability [16].

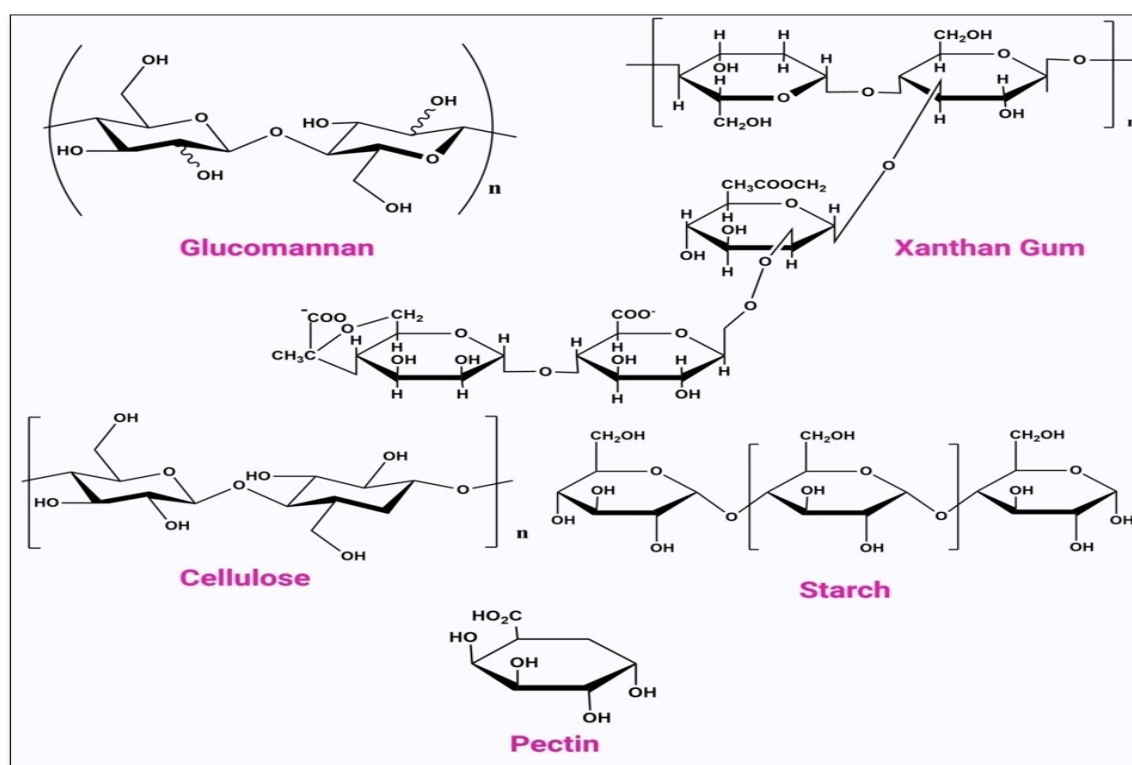


Figure 1: Molecular structures of widely used herbal polymers

## Herbal Polymers: Properties and Advantages

Herbal polymers are highly in demand in the pharmaceutical and cosmetic industry based on easy availability, biodegradability, non-immunogenicity, biocompatibility, elasticity, and highwater solubility. Besides this, they are reportedly showing properties like adhesives, thickeners, stabilizers, disintegrants, binders, and lubricants with excellent film-forming properties that make them potential materials for transdermal and topical applications [17]. The sources and properties of herbal polymers used in the current scenario are provided in Table 1 [18–25].

**Table 1:** Herbal polymers source, properties and application

Herbal Polymer	Source	Properties	Application	References
Alginates	Brown algae cell walls	Thickening agent, mucoadhesiveness	Wound dressings, controlled drug delivery, and dental impressions	18
Pectin	Citrus peels and apple pomace	Thickening agent, Stabilizing agent	Gelling agent in food, wound healing patches, and oral drug delivery systems	18
Starch	Grains (such as corn, wheat, rice, etc), tubers (such as yam, potato, etc)	Disintegrant, binder, lubricant, and film-forming agent	Tablets, capsules, and biodegradable packaging	19
Agar	Varieties of red seaweeds	Thickening agent, gelling agent, laxative, appetite suppressant	Microbiological culture media, dental molds, and cosmetics	19
Carrageenan	Red edible seaweeds	Thickening agent, Stabilizing agent, Binding agent	Lotions, creams, and emulsions for cosmetics and food stabilizers	20
Cellulose	Green plants cell walls, algae, and Oomycetes	Thickening agent, Stabilizing agent	Sustained-release tablets, viscosity modifiers in liquids	21
Psyllium	Husks of the seeds of <i>Plantago ovata</i>	Thickening agent, mucilage production	Laxatives, dietary fiber supplements, and colon-targeted delivery systems	22
Aloe Vera Mucilage	Aloe vera	Shooting agent, mucilage production, emulsifying agent, film-forming agent	Wound healing gels, moisturizers, and hydrating creams	23
Chitosan	Crab shells, plants such as oak, hop, etc, and brown algae	Bioadhesive, film-forming properties	Drug delivery, wound healing materials, and antimicrobial coatings	24
Xanthan Gum	From plant pathogen bacteria named <i>Xanthomonas campestris</i>	Thickening agent, Stabilizing agent, emulsifying agent	Toothpaste, suspensions, and stabilizers in beverages	25
Tragacanth	Dried gum obtained sap of <i>Astragalus</i> genus of legumes	Thickening agent, Stabilizing agent, Binding agent, cross-linking ability	Syrups, emulsions, and tablet binders	25
Guar Gum	Seeds of <i>Cyamopsis tetragonolobus</i>	Thickening agent, Stabilizing agent, emulsifying agent	Pharmaceutical suspensions	25

## Biocompatibility and Biodegradability

Herbal polymers have various benefits over the ones derived synthetically. They are owed largely to biodegradability and biocompatibility. Biodegradable polymers easily degrade biologically into harmless products, thereby minimizing ecological waste and pollution. This attribute is highly important in medical and pharmaceutical uses. Biocompatibility ascertains that these polymers can safely react with the body without inducing side effects or toxicity. This is particularly important for drug delivery and tissue engineering applications where materials directly interacting with the body tissues cannot trigger any adverse immune response.

Herb-based polymers are biodegradable and biocompatible, thus having the potential for biomedical applications. Herb-based polymers are used in the food industry in the form of emulsions and edible films as well as packaging material. In the biomedical field as materials for drug delivery, wound healing, tissue scaffolding, and medical implants. The recent trend as well as steadily increasing interest in herbal polymers, such as cellulose, gelatin, chitosan, and alginate, have added promise for application in herbal medical devices as a greener alternative for synthetic polymers in regenerative medicine and drug delivery systems. Their remarkable attributes, including nontoxicity, stability, and bioactivity, regulate their use in various biomedical applications with significant continuing research and development [26].

## Sustainable Sourcing and Environmental Impact

The sourcing of herbal polymers must be done sustainably so the environmental impact can be kept at a minimum, and they remain available for long-term pharmaceutical and cosmetic applications. The polymers from natural plant sources have increased in value due to their biocompatibility, biodegradability, and environmental properties. However, the exploitation at this rate would degrade habitats, result in loss of biodiversity, and lead to the depletion of those species that are essential.

For sustainability, responsible sourcing practices must be pursued having ethical harvesting, cultivation, and management of resources. Sustainable agriculture is an approach that can be directed toward agroforestry, organic farming, is very effective in conserving healthy soils, and reducing the usage of pesticide use while improving biodiversity. Other strategies for sustainable sourcing include fast-growing or high-yielding plant sources that reduce environmental costs. Another approach is the utilization of green chemistry in the extraction and processing of herbal polymers, thereby minimizing the use of harmful chemicals to reduce energy consumption. Moreover, empowering the local community and promoting the indigenous knowledge system through fair trade can be sustainable approach toward adequate economic benefits for the participants within the supply chain. The pharmaceutical and cosmetics industries will thus minimize their ecological footprint without compromising supply base diversity and quality [27].

## Benefits of herbal Polymers over Synthetic Polymers

**Eco-friendly:** Herbal polymers come from plants and marine sources, mainly biodegradable, so it is considered safe for the environment. This is in contrast to synthetic polymers that are obtained through chemical processing related to heavy environmental effects, mainly pollution, and non-biodegradability.

**Lower Production Costs:** Herbal polymers tend to be comparatively less expensive than synthetic polymers. The reason is that they occur straight from natural resources, so they have minimal complex production processes, and the cost is reduced during the production process.

**Biocompatibility and Non-toxicity:** Herbal polymers are biocompatible and non-toxic by nature, inherently making them safer for human use and the environment. Synthetic polymers, because of their chemical identity, have the risk of toxicity and other health problems.

**Sustainability:** The demand for herbal polymers is very high in the pharmaceutical, cosmetic, and food industries of the world, therefore many countries cultivate these polymers as herbs and renewable resources. This makes them quite a sustainable alternative to synthetic polymers.

**Less Adverse Effects:** Herbal polymers are constituted by naturally occurring substances and appear less or without any adverse effects on humans, while synthetic polymers contain harmful chemicals that might be adverse to human health.

## Disadvantages of herbal Polymers

**Variation in Composition:** The chemical composition is bound to change with climate, geographical conditions, and nutrient availability in herbal polymers. This becomes a bit inconvenient for standardization .

**Risk of Microbial Contamination:** Because they are produced directly exposed to the environment, the risk of microbial contamination is slightly higher with herbal polymers. This might affect the product safety and efficiency.

**Uses of Pesticides:** Certain pesticides like DDT, have been found in some applications in herbs to avoid the invasion of pests. These may be harmful to human health. Such dangerous chemicals are present in herbal products too, increasing the degree of risk in usage.

**Environmental Factors:** The growth rates of the plants or herbs that are being used in natural polymers depend on environmental factors, which comprise altitude, humidity, and nutrients. This will affect the consistency and availability of the polymers.

**Adulteration:** Herbal polymers often expose a risk of adulteration with herbs that are seemingly similar but not the same as those used. This affects the quality and efficacy of the final product, so validation must be intense.

**Standardization:** Since the chemical constituents of herbs may be extracted previously or altered, standardization and validation of natural polymers are a must. This will ensure their purity, quality, and safety [28].

## Mechanisms of Drug Delivery through Skin: Permeation Pathways

The three routes by which pharmaceuticals can penetrate the stratum corneum layer the intercellular route, the transcellular route, and the appendageal route are the main categories into which the drug absorption pathways of skin-mediated drug delivery techniques can be divided. The most popular path is the intercellular one. Through this pathway, the medication molecules enter the stratum corneum layer through the intercellular gaps between the corneocytes.

Hydrophilic molecules can be delivered, and drug molecules that go through this pathway may be large. By moving completely through the lipid bilayers of the cell membranes, the drug molecules are transported via the stratum corneum layer in the transcellular route Figure 2. The medication molecules then enter the systemic circulation after diffusing through the epidermis layer and arriving at the dermis layer. Only lipophilic and relatively tiny medications can be administered via the transcellular route because the molecules must pass through the lipid matrix of the cell membranes. Drugs are administered by the appendage route via the skin's sebaceous glands, sweat glands, and hair follicles. Because these structures are found in comparatively deeper places than the stratum corneum layer, drug molecules can enter the dermis layer more deeply when administered via this method. The benefits of using these channels for drug delivery include the ability to transport bigger drug molecules as well as polar or ionizable compounds. However, few skin-mediated drug delivery techniques use these routes because these structures only cover a small percentage (about 0.1% of the total skin area) [29]. Table 2 shows mechanism of drug delivery through skin.

## Factors Influencing Drug Delivery through Skin

**Molecular Size:** Drugs with a molecular size of less than 500 Da have preferential permeation through the stratum corneum in the skin. Larger molecular size provides greater resistance as the lipid matrix in the skin is very tight.

**Polymer Structure:** The polymer structure (for example, linear, branched, or cross-linked) determines the interaction of the polymer with the drug and the skin. Generally, linear polymers provide a more uniform release of the drug than highly branched or cross-linked polymers, which can hinder free movement.

**Lipophilicity:** Drugs with balanced lipophilicity (log P between 1 and 3) are better permeable in the skin. Lipophilic drugs can penetrate the lipid bilayers of the skin; however, hydrophilic drugs commonly require permeation enhancers.

**Ionization State:** The non-ionized drugs cross the skin's lipid-rich layers more efficiently than the ionized drugs. The stratum corneum's lipid environment favors neutral molecule absorption.

**Diffusion coefficient:** Drug penetration depends on the diffusion coefficient of a drug. The diffusion coefficient of the drug at constant temperatures mainly dependent on the properties of the drug, diffusion medium, and their interaction [30].

## Different Techniques via drugs are administered

The stratum corneum limits the amount of medication that may be absorbed via the skin when it is applied. Therefore, by increasing the permeability of medications via the stratum corneum layer, different techniques have been devised to permit the administration of drugs into the dermis layer. These techniques, which fall into three categories—chemically enhanced, physically enhanced, and stimuli enhanced.

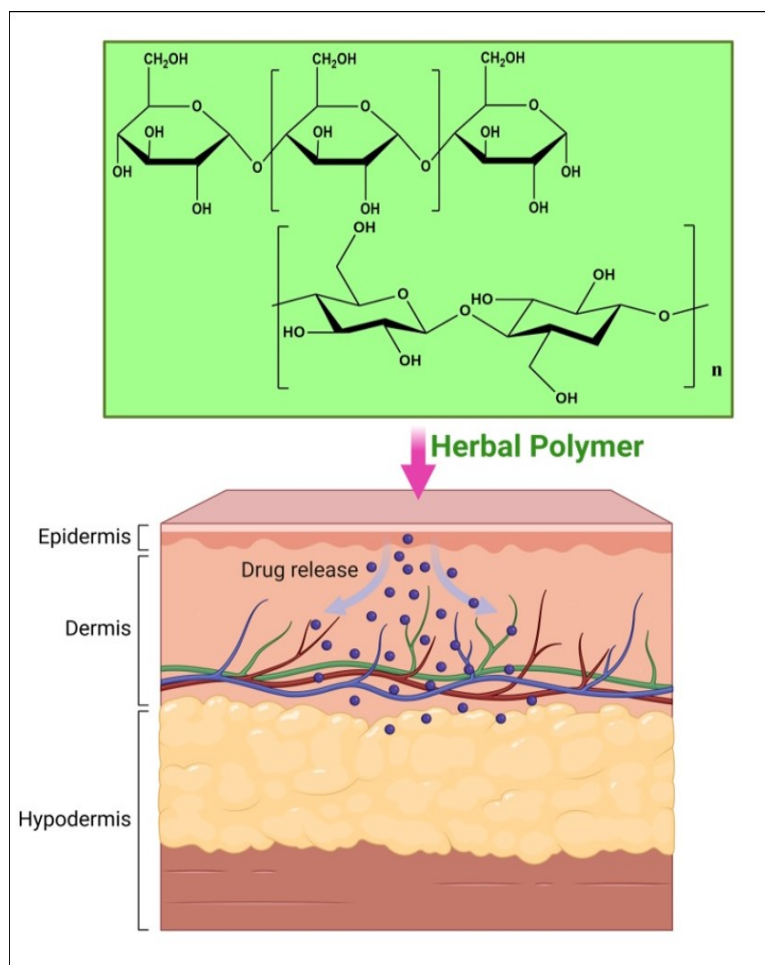


Figure 2: Permeation Pathways in Skin-Mediated Herbal Polymers

### Chemically-Enhanced Methods

Instead of being injected into the skin, chemically enhanced skin-mediated drug delivery uses a diffusion-based technique where medications enter the skin via altering the stratum corneum layer's structure. This method increases the permeability of medications by using chemical enhancers. Absorption enhancers decrease the skin's barrier function, increasing skin permeability. Water-soluble organic solvents, such as ethanol and propylene glycol, are a frequent family of absorption enhancers. These solvents make lipophilic compounds more soluble and facilitate their skin absorption. Furthermore, by hydrating and softening the stratum corneum layer, substances including hyaluronic acid, urea derivatives, and salicylic acid are primarily employed to break down keratin and facilitate the absorption of medication molecules. Higher alcohols, fatty acids, esters, glycerine, and lecithin are examples of surfactants that work on lipids to break down the hard stratum corneum layer [31].

### Physically-Enhanced Methods

In order to increase the permeability of pharmaceuticals through the skin, physically-enhanced skin-mediated drug delivery strategies include triggering systems and procedures that remove or penetrate the stratum corneum layer. Drug delivery methods that bypass the stratum corneum or flow through it directly to the inner layer have been investigated as a result of this layer. Furthermore, physical-enhanced medication delivery techniques have been created, such as triggering systems that can release pharmaceuticals when needed.

The most basic technique to improve drug permeability is ablation, which includes the tape-stripping approach, and microdermabrasion, which removes the stratum corneum layer directly. The stratum corneum layer is removed using the tape-stripping technique, which involves applying and removing adhesive tape to the skin. These procedures must be repeated multiple times in order to fully exfoliate the stratum corneum layer. Another technique for directly removing the stratum corneum layer is microdermabrasion, which involves simultaneously drawing the abraded skin cells back to the device and ejecting abrasive particles, such as sodium chloride or aluminium oxide particles, at a high velocity to ablate the stratum corneum layer. Despite being easy to use and inexpensive, these ablation techniques are not widely used due to their low repeatability and discomfort to patients. Furthermore, these techniques cause skin redness or irritation right after the ablation process, which can result in infections. As a result, they are only used on individuals without sensitive or damaged skin [32]. The ablation method's drawback the potential for skin damage can be addressed using microneedles. By establishing direct channels through the stratum corneum layer, microneedles enable medications to enter the underlying layers of the skin and be applied directly to the dermis layer. Their height ranges from 25 to 1500  $\mu\text{m}$ , and they are composed of a variety of elements, including silicon, metals, and polymers, allowing them to pass through the stratum corneum layer, which is 10 to 20  $\mu\text{m}$  thick but excludes the pain receptors found in the dermis layer. Among the many benefits of micro needles are their simplicity of usage, low level of pain or discomfort, and the possibility of patient

**Table 2:** Permeation Pathways in Skin-Mediated Herbal Polymers

Pathway/Method	Description	Advantages	Examples
Intercellular Route	Drug molecules pass through intercellular gaps in the stratum corneum	Allows delivery of hydrophilic and large molecules	Topical creams, gels
Transcellular Route	Drug molecules traverse through the lipid bilayers of cell membranes	Suitable for lipophilic and small drugs	Lipid-based formulations
Appendageal Route	Drug enters via sebaceous glands, sweat glands, and hair follicles	Enables deeper penetration for large/polar molecules	Hair treatments, deep-tissue applications
Chemically Enhanced	Uses chemical enhancers like ethanol to alter the stratum corneum structure	Increases skin permeability	Hyaluronic acid-based formulations
Physically Enhanced	Techniques like microneedles or tape stripping to bypass stratum corneum	Direct channels to deeper layers, less invasive	Microneedle patches, abrasion devices
Stimuli Enhanced	Methods like electroporation and iontophoresis using electrical or thermal stimuli	Improves penetration of charged or large molecules	Electrical patches, ultrasound-assisted delivery

self-administration. Additionally, they can be manufactured as individual needles, arrays, or patches. Sterilization problems and preserving the stability of medications, as well as their capacity to retain their chemical, physical, and biological characteristics during the delivery process, are some constraints that must be addressed [33].

### Stimuli-Enhanced Methods

External stimuli are used in stimuli-enhanced skin-mediated drug delivery techniques to improve medication penetration through the skin. These techniques use a variety of stimuli, including ultrasonic, electric, and thermal stimulation, to help transfer medications through the stratum corneum and into the skin's underlying layers.

High-voltage pulses are used in electroporation, a technique for skin-mediated drug delivery, to penetrate medications from tiny molecules to macromolecules. By immediately altering the structure, a voltage gradient of 30 to 100 V across the skin layer causes the lipid bilayer membrane to reorganize, creating holes and aqueous channels that let high-molecular medications pass through. Skin resistance reduces during pulsing, which is partially reversible, and pores as small as 10 nm are created. These pores have a brief lifespan of a few microseconds to a few seconds. It depends on a number of variables, including the drug's physicochemical characteristics and the electrical pulse circumstances. Increased pulse voltage or duration improves medication delivery through the epidermal layer [34].

Iontophoresis is a stimuli-enhanced technique that uses two electrodes to create a voltage gradient across the skin to promote medication penetration. Electro osmosis and electro repulsion are the two mechanisms at action here. When a voltage differential is placed across a charged membrane, a bulk flow known as electro osmotic flow takes place. The counter ion is a positive ion and electro osmotic flow takes place from anode to cathode because human skin is negatively charged above pH 4. To improve and regulate the passage of charged medications through the epidermal barriers and into the tissues, electrical current is utilized. By adjusting the stimulating current's strength and duration, drug dosages can be readily managed. To avoid pain, irritation, or skin burns, a small patch of skin is exposed to a low voltage, low current electric current. Since electric fields accelerate drug transport more quickly than passive diffusion-based techniques, iontophoresis is frequently used [35].

### Role of Herbal Polymers in Enhancing Permeability

In the last few decades, the transdermal drug delivery system has developed significantly, but the absorption of active ingredients via the stratum cornea remains a primary challenge. The synthetic permeability enhancers are well-documented and exhibit drawbacks like poor biocompatibility, no biodegradability, cost, low recyclability, etc. In contrast, herbal polymers emerge as promising alternatives because they can offer improved biocompatibility, high-level safety, high efficacy, biodegradability, water retention, non-toxicity, cost-effectiveness, and low risk of skin irritation making them safer and more suitable options.

Herbal polymerase obtained from plant (starch, cellulose, and pectin) sources as well as marine sources (agarose, alginate, chitosan, and carrageenan) to enhance the permeability of drugs in transdermal and topical drug delivery systems through various mechanisms. They provide a moist environment that supports skin and increases drug absorption by reducing the stratum corneum barrier and facilitating drug diffusion. Such polymers interact with the lipid bilayer by disrupting its structure to allow better drug penetration. Moreover, herbal polymers can create polymeric gels that retain active ingredients close to the skin for a long period of time, resulting in enhanced drug residence time and absorption. Herbal polymers also possess bioadhesive properties, which contribute to improved contact between the formulation and the skin, thus improving permeability. These polymers modulate the rate of drug release and provide for controlled delivery, thus optimizing therapeutic outcomes with minimum side effects, making them ideal for transdermal and topical applications. The following mechanisms explain how they enhance permeability: Herbal permeability enhancer and its role/mechanism:

## Chitosan

Chitosan is a non-toxic and biocompatible polymer and can facilitate the transport of drugs across mucosal epithelium. However, it is ineffective as a permeation enhancer at  $pH > 6.5$  due to its poor solubility. To improve such drawbacks in chitosan, several studies synthesized N-trimethyl chitosan. N-trimethyl chitosan represents an improved polymer type for changing the aqueous solubility and permeability mainly in basic environments. Moreover, the molecular weight, degree of deacetylation, and quaternization degree are also critical points to decide the effectiveness of N-trimethyl chitosan. The formulation of low molecular weight chitosans showed enhanced permeability across the skin. Parameters such as deacetylation degree, pH (optimum  $\sim 7.0$ ), and molecular weight demonstrate significant importance. Another derivative, N-arginine chitosan derivatives, demonstrates cell uptake functions and has promising results in transdermal delivery at optimal molecular weights (5 and 10 kDa), concentrations 2% (w/v) concentration, and pH 7.0 [36].

## Alginate

Alginate is a colloidal polysaccharide, commercially extracted from brown seaweeds presents biodegradable, biocompatible, and bioadhesive characteristics. Alginate-based films are water-soluble, have high water vapor permeability, and work as effective moisture barriers. Alginate has enhanced drug diffusion due to its hydrophilic nature, whereas the presence of  $\alpha - (1 \rightarrow 4)$ -linked L-guluronic acid residues improves the moisture barrier property through cross-linking with divalent cations. Chemically modified alginate, for example, 3-aminophenyl boronic acid-modified alginate, has been applied within the microneedle patch to enhance drug permeation and control release significantly. Alginate was also used as a drug-delivery approach that can encapsulate drugs such as insulin, providing effective transdermal delivery with fewer side effects, stability, and mechanical strength [37].

## Cellulose derivatives

Cellulose derivatives, such as ethyl cellulose and hydroxypropyl methylcellulose, have demonstrated great potential as permeability enhancers in transdermal drug delivery. In the preparation of the transdermal film of furosemide, the combination of these cellulose-based polymers was reported to be crucial in improving skin permeability. For instance, a binary mixture containing ethyl cellulose and hydroxypropyl methylcellulose in the ratio of 8.5:1.5 considerably increased drug permeation. Such polymers possess film-forming properties with suitable skin adhesion that allow for better and controlled release of drugs and improved diffusion across the skin [38].

## Pectin derivatives

Pectin is one of the plant-derived polysaccharides that plays an important role as a permeability enhancer in dermal drug delivery systems. Pectin derivatives with highly esterified galacturonic acid residues exhibit increased hydrophobicity, allowing them to sustain the release of incorporated substances. In contrast, less esterified pectin derivatives are more permeable, enabling deeper penetration into the skin, and making them ideal for applications in transdermal drug delivery [39].

## Carrageenan

Carrageenan is a polysaccharide that acts as a permeability enhancer because of its gelling and adhesive properties toward the skin. In microemulsions, carrageenan improves viscosity and modifies rheological properties so that formulations become more appropriate for topical delivery. It enhances drug permeation by altering the stratum corneum and allows better diffusion for both hydrophilic as well as lipophilic compounds. It also increases the skin contact time with the drug, thus enhancing its retention and absorption. Studies show that formulations preparations containing carrageenan exhibits increased skin permeation, similar to that with sodium fluorescein. Therefore, it is a promising excipient in improving delivery in pharmaceutical and cosmetic applications [40].

## Conclusion

Polymers, especially herbal ones like chitosan, alginate, and cellulose, are key to the improvement of drug delivery through the skin. They help drugs get absorbed better and control how they are released. These polymers are safe for the body and environmentally friendly, making them a good choice for natural medicine. They offer a better way of delivering treatments by addressing such issues as poor drug absorption and reducing side effects. The introduction of new technologies, such as microneedles and electrical methods, will improve the use of polymers in drug delivery. As more research is done, these polymers can become even more critical in the treatment of diseases, vaccines, and even cosmetic products by providing safer treatments for patients.

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