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REVIEW ARTICLE

A Review on Topical Gels as Drug Delivery System

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Abstract: The skin serves as a formidable barrier to drug penetration, primarily due to the stratum corneum. For successful transdermal drug delivery, the drug must overcome this barrier and reach the target site in sufficient concentrations. Drug molecules can penetrate the skin via the transcellular, intercellular, and appendageal pathways. The extent of drug permeation is influenced by factors such as the physicochemical properties of the drug, the nature of the vehicle, and the condition of the skin. Gels, being hydrophilic, can enhance drug permeation by increasing the hydration of the stratum corneum. Permeation enhancers, which reversibly alter the structure of the stratum corneum, can also improve drug permeation. Recent advancements in topical gel drug delivery include the use of nanotechnology, stimuli-responsive gels, combination therapy, natural polymers, and biodegradable materials. The delivery of biomolecules through the skin remains a challenge, and strategies such as iontophoresis, microneedles, and nanocarriers are being investigated. 3D printing technology enables the personalized fabrication of gels with precise drug dosing and customized release profiles. Despite significant advancements, challenges such as limited drug permeability, potential for skin irritation, and the need for long-term stability studies persist. Future research should focus on developing innovative strategies to overcome these challenges and optimize the performance of topical gels, involving the exploration of new drug-polymer combinations, advanced drug delivery technologies, and in silico modeling tools.

Keywords: Topical gels; Skin disorders; Patient compliance; Controlled release; 3D Printing.

1. Introduction

Over the past few decades, the administration of drugs through various routes has been the primary focus of pharmaceutical research. Topical drug delivery, which involves the application of formulations directly to the skin, has gained significant attention due to its potential to treat cutaneous disorders and deliver drugs locally [1]. Topical delivery systems offer several advantages over oral and parenteral routes, such as avoiding first-pass metabolism, minimizing systemic side effects, and improving patient compliance [2-4].

Among the various topical formulations, gels have emerged as a promising drug delivery system. Gels are semi-solid preparations that consist of a three-dimensional network of natural or synthetic polymers, which immobilize a large amount of aqueous or hydroalcoholic liquid [5]. The unique properties of gels, such as their non-greasy nature, ease of application, and ability to provide controlled drug release, have made them an attractive option for topical drug delivery [6]. This comprehensive review aims to provide an in-depth understanding of topical gels as drug delivery systems.

1.1. Advantages and Disadvantages

Topical gels offer several advantages over other topical formulations. One of the main benefits is their ability to avoid the first-pass metabolism, which is a major limitation of oral drug delivery [7]. The drug can be delivered locally, minimizing systemic exposure and reducing the risk of side effects by applying the gel directly to the skin [8]. Gels also provide a convenient and easy-to-apply option for patients, leading to improved patient compliance [9]. The non-greasy and easily washable nature of gels makes them more acceptable to patients compared to ointments and creams [10]. Moreover, gels can be easily terminated if any adverse reactions occur, providing a safer alternative to systemic medications [11].

Another advantage of topical gels is their ability to deliver drugs with short biological half-lives and narrow therapeutic windows [12]. The controlled release properties of gels allow for a sustained and continuous drug input, maintaining the drug concentration within the therapeutic range and avoiding fluctuations in drug levels [13]. However, topical gels also have certain limitations. Some drugs with poor permeability may be difficult to deliver through the skin, requiring the use of permeation enhancers [14]. The possibility of local skin irritation or contact dermatitis at the application site is another concern associated with topical gels [15]. Additionally, drugs with larger particle sizes may face challenges in penetrating the skin barrier [16]

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2. Methods of Preparation

Several methods are employed for the preparation of topical gels, including the cold mechanical method, hot mechanical method, and chemical cross-linking method [17]. Among these, the cold mechanical method is widely used due to its simplicity and effectiveness [18].

The cold mechanical method involves the following steps:

- The required quantity of polymer (natural or synthetic) is weighed and sprinkled slowly on the surface of purified water. The mixture is allowed to stand for 2 hours to ensure proper soaking of the polymer [19].
- The mixture is then continuously stirred using a mechanical stirrer until a homogeneous dispersion is obtained. Triethanolamine is added to neutralize the gel and maintain the desired pH [20].
- Penetration enhancers, such as dimethyl sulfoxide (DMSO), and preservatives, like methyl paraben, are incorporated into the gel with continuous stirring [21].
- Finally, the active drug ingredient is added to the gel and mixed thoroughly until a homogeneous dispersion is achieved [22]

3. Formulation

Permeation enhancers play a key role in the preparation of topical gels which are listed in Table 1. Polymers which are used in the preparation of topical gels are described in Table 2 and the novel strategies used for formulation of topical gels are given in Table 3.

Table 1. Common Permeation Enhancers

Class of Enhancer	Examples	Mechanism of Action
Fatty acids	Oleic acid, Linoleic acid, Lauric acid	Disruption of lipid bilayers
Alcohols	Ethanol, Propylene glycol, Menthol	Extraction of lipids, Increase in drug solubility
Surfactants	Sodium lauryl sulfate, Tween 80, Span 20	Interaction with keratin, Fluidization of lipids
Terpenes	Limonene, Menthol, Cineole	Interaction with intercellular lipids
Urea and its derivatives	Urea, Dimethyl sulfoxide (DMSO)	Keratolytic effect, Increase in hydration
Enzymes	Papain, Trypsin, Bromelain	Hydrolysis of peptide bonds in corneocytes

Table 2. Polymers used in the formulation of topical gels

Polymer Class	Examples	Properties
Natural polymers	Chitosan, Alginate, Pectin, Xanthan gum	Biocompatibility, Biodegradability, Mucoadhesion
Synthetic polymers	Carbopol, Poloxamer, Polyvinylpyrrolidone (PVP)	pH-sensitivity, Thermoreversibility, Bioadhesion
Cellulose derivatives	Hydroxypropyl methylcellulose (HPMC), Carboxymethylcellulose (CMC)	Viscosity enhancing, Gelling agents
Acrylic polymers	Eudragit, Polyacrylic acid	pH-dependent solubility, Controlled release
Polyethylene glycols (PEGs)	PEG 400, PEG 4000	Solubilizing agents, Penetration enhancers

Table 3. Novel drug delivery strategies for topical gels

Strategy	Description	Advantages
Nanoparticles	Incorporation of drug-loaded nanoparticles into gels	Enhanced drug penetration, Controlled release, Protection of sensitive drugs
Liposomes	Encapsulation of drugs within lipid vesicles	Improved drug solubility, Targeted delivery, Reduced side effects
Microemulsions	Thermodynamically stable, transparent dispersions of oil and water	Enhanced drug solubility, Increased permeation, Ease of preparation
Iontophoresis	Application of electric current to drive charged drugs into the skin	Controlled drug delivery, Enhanced permeation, Reduced variability
Microneedles	Microscopic needles that create transient pores in the stratum corneum	Painless administration, Enhanced permeation, Delivery of macromolecules
Stimuli-responsive gels	Gels that respond to external stimuli (e.g., pH, temperature)	Targeted drug release, Improved patient compliance, Enhanced therapeutic efficacy

4. Evaluation of topical gels

The evaluation of topical gels is crucial to ensure their quality, safety, and efficacy. Various parameters are assessed during the evaluation process, including physical appearance, pH, spreadability, viscosity, drug content, and in vitro drug release [23].

3.1 Physical evaluation

Physical evaluation involves the assessment of organoleptic characteristics, such as color, odor, and consistency, as well as the occlusiveness and washability of the gel [24]. The pH of the gel is measured using a digital pH meter to ensure compatibility with the skin and avoid irritation [25].

3.2 Spreadability

Spreadability is an important parameter that determines the ease of application and distribution of the gel on the skin. It is measured by pressing a sample of the gel between two slides and measuring the diameter of the spread [26].

3.3 Viscosity

Viscosity is another critical parameter that affects the flow properties and stability of the gel. It is determined using a Brookfield viscometer at different rpm, and the apparent viscosity is recorded [27].

3.4 Drug Content

Drug content estimation is performed by dissolving a known quantity of the gel in a suitable solvent and analyzing the solution using UV-visible spectrophotometry [28]. This ensures that the desired amount of drug is present in the formulation.

3.5 *In vitro* drug release studies

In vitro drug release studies are conducted to assess the release profile of the drug from the gel. The gel is placed in a dissolution apparatus containing a suitable receptor medium, and samples are withdrawn at predetermined intervals [29]. The amount of drug released is quantified using UV-visible spectrophotometry, and the release kinetics are analyzed [30]

5. Conclusion

Topical gels have emerged as a promising drug delivery system for the localized treatment of various skin disorders. Their unique properties, such as ease of application, non-greasy nature, and controlled release characteristics, have made them an attractive option for both patients and healthcare professionals. As the field of dermatology continues to evolve, topical gels are expected to play an increasingly important role in the management of skin disorders. With their ability to deliver drugs directly to the site of action, minimize systemic side effects, and improve patient compliance, topical gels hold great promise for the future of topical drug delivery.

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