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Formulation and Evaluation of Topical Gels: An Updated Review

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ABSTRACT:
Topical gels offer a substantial development in transdermal drug delivery methods, combining the therapeutic advantages of targeted therapy with the ease and compliance of non-invasive administration. This paper fully covers the present landscape of topical gel formulations, including their categorization into hydrogels, organogels, and emulgels based on their physicochemical qualities. Key formulation components such as gelling agents, permeation enhancers, and preservatives are examined for their roles in establishing appropriate viscosity, stability, and drug release characteristics. The paper also dives into the mechanics of skin penetration and the effect of formulation factors on medicationbioavailability.
Recent advancements in gel technology—such as nanogels, thermoresponsive and pH-sensitive gels—are reviewed for their potential to enable regulated and targeted medication delivery. Additionally, this article includes in vitro and in vivo assessment methodologies, including rheological analysis, spreadability testing, and skin penetration investigations, which are critical for assuring the effectiveness and safety of gel compositions. Applications in dermatology, pain management, wound healing, and cosmeceuticals are studied, emphasizing the vast therapeutic value of gels.
Finally, regulatory considerations, obstacles in large-scale production, and future approaches, including customized and smart gel-based therapeutics, are reviewed to offer a thorough picture of the present trends and future prospects in topical gel development.
KEY WORDS: Topical drug delivery, Semi-solid preparations, Gel Formulation,Drug Absorption.

I. INTRODUCTION

Topical drug delivery is the technique of applying drugs directly onto the skin or mucosal surfaces to provide a localized therapeutic impact. Commonly used for the treatment of dermatological diseases, eye infections, nasal and vaginal issues, and for pain relief (1).Among various clinical applications, topical drug delivery systems are among the most frequently applied because skin is one of the most accessible pathways for drug delivery. On the other hand, topical medical treatments range from simple liquids and ointments to multiphase nanotechnology-based therapies.

Advantage of topical administration system is bypass first pass metabolism. Topical preparations have other advantages as well: they allow one to bypass the risks and inconveniences of IV therapy and the variableabsorption conditions such as alterations in pH, if enzymes are present or not, stomach emptying time.(2)

Pharmaceutical dosage form, from semisolids to liquid preparation, sprays, and solid powders, are used as topically acting medications. Semisolid preparations for topical administration of drugs consist mainly of gels, creams, anointments(3). A gel-based product called topical gel is administered straight to the skin or mucous membranes. Designed to provide active components to a specific location for localized therapy, it provides advantages including pain alleviation, inflammation reduction, or treatment of skin disorders. Usually clear, smooth, and non-greasy, topical gels let the skin quickly absorb them without leaving residue.(4)

A gel is a two component, crosslinked three-dimensional network of structural elements separated by a suitable, but comparatively massive content of fluid to make a boundless inflexible network structure that ‘clogs’ the fluid constant

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stage inside. A gel is a state of matter intermediate between those of a solid and a liquid that contains properties of both solids and liquids, known as viscoelasticity The structural components forming a gel network may be inorganic particles or organic macromolecules, generally-sized polymers.(5)

The topical delivery system is occasionally used if other routes of drug administration fails or primarily it is used in pain relief, contraception and urine incontinence. In last decades the approach towards treating any sort of disease has been administration of anti-biotic drugs in human body by various routes such as oral, sublingual, rectal, parental, topical, aerosolic etc.(6)

Topical drug delivery is defined as the topical application of the drug containing formulation to the skin for the treatment of cutaneous disorders (eg, acne) or for the treatment of the cutaneous lesions of a systemic disease (eg, psoriasis), with the aim of restricting the pharmacological or other action of the drug to the skin surface or to the skin.(7)

CLASSIFICATION OF GELS:

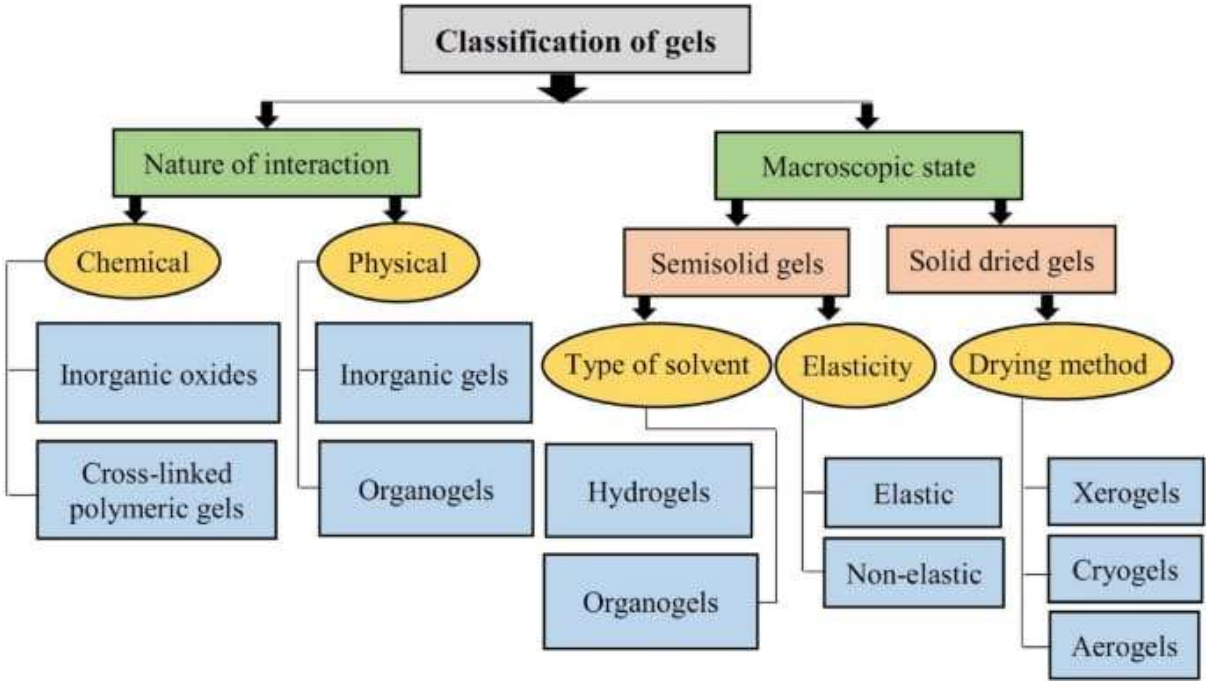

Fig. 1 CLASSIFICATION OF GELS:

CLASSIFICATION OF GELS (8,9,10,11)

Gels are mainly classified by two methods which are as follows:

1)Nature of the colloid phase

a. Inorganic gels (Two phase system)
b. Organic gels (single phase system)

2)Based on the nature of solvent

a. Hydrogel (Aqueous gels)
b. Xerogel
c. Organic gel (Non aqueous gels)

3. Based on rheological properties

Usually gels exhibit non-Newtonian flow properties. They are classified as,

a. Plastic gels
b. Pseudo plastic gels
c. Thixotropic gels

4. Based upon physical nature

a. Elastic gel
b. rigid gel

Hydrogel - A hydrogel is a three-dimensional (3D) network of hydrophilic polymers that can expand in water and retain a high quantity of water while keeping the structure owing to chemical or physical cross-linking of individual polymer chains.

Organogels - These are solid materials made out of a three dimensionally cross-linked network trapping a liquid organic phase.

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Xerogels - Xerogels are solid substances made from gels including linked particles or polymers spread in a liquid.

STRUCTURE OF GELS:

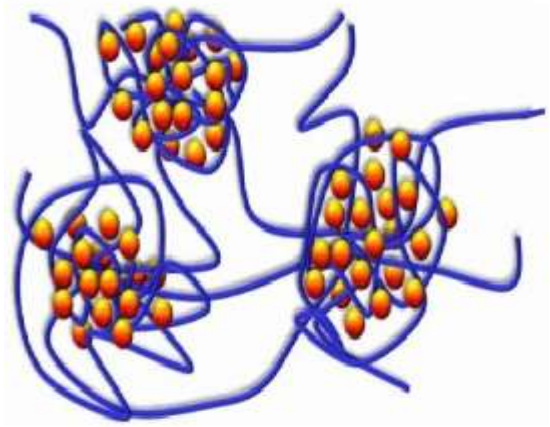

Fig. 2 STRUCTURE OF GELS

The stiffness of a gel structure derives from a network constructed by physical or chemical interlinking of particles and the kind of force responsible for interlinking defines the structure and characteristics of gel. While there may be many components in a gel, the primary component necessary to build the structural network of the gel are polymers.(12)

PROPERTIES OF GELS:

1. Ideally, the gelling agent for pharmaceutical or cosmetic usage should be inert, safe, and should not react with other formulation components. (13)
2. The gelling agent contained in the preparation should provide a tolerable solid-like character during storage that may be readily broken when exposed to shear forces produced by shaking the container, squeezing the tube, or during topical application. (14)
3. It should contain adequate anti-microbial to avoid from microbial assault.
4. The topical gel should not be sticky.
5. The ophthalmic gel should be sterile.(15)

Advantages:(16)

1. Avoid primary metabolism.
2. simple to use and simple to apply.
3. Easy to quit medicine.
4. Drugs are selectively supplied to certain areas.
5. Avoid gastrointestinal intolerance.
6. Allow the use of medicines with short biological half-lives and restricted therapeutic windows.
7. Better patient compliance.
8. Self-medication.

Disadvantages:(17)

1. Skin Irritation
2. Stability Concerns
3. Not Suitable for All Types of Skin
4. Limited Penetration

Drug absorption from topical formulations:

In topical applications the total amount of active ingredient absorbed varies substantially dependent on various aspects including application area size, the frequency and strength of application and the viscosity or thickness of the applied vehicle. Other variables impacting medication absorption include application place, age and condition of the skin. Non-keratinized dermis is more readily penetrated by an active substance. In the best topical formulations, the drug diffusion through skin is managed by ensuring that the drug is just soluble enough in the vehicle to induce drug release at the correct pace. This is accomplished by ensuring that the full medication is insolution. (18)

Formulation Consideration for Pharmaceutical Gel:

The choice of vehicle or solvent:

Water is a typical solvent for all sorts of dosage formulations. To increase the solubility over the skin, co-solvents may be utilized. E.g: Alcohol, Glycerin, PEG-400 etc. (19)

Inclusion of buffers:

Buffers may be used in the gel formulation to adjust the pH of the formulation. The solubility of buffer salts falls in hydroalcoholic based vehicles. E.g: Phosphate, Citrate, etc.(20)

Preservatives:

Preservatives are utilized for the manufacture of pharmaceutical gel to avoid degradation by microbial growth or by undesired chemical changes. E.g: Methyl paraben, Propyl paraben, phenolics, etc.(21)

Antioxidant:

These are utilized to increase the chemical stability of the medicinal compounds that are prone to oxidative degradation. Generally, water-soluble antioxidants are selected during the formulation of medicinal gel. E.g: Sodium metabisulphite, Sodium formaldehyde.(22)

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Sweetening Agents/ Flavors:

Gels which are created specifically for oral cavity in such instances these agents are employed (For ulceration of mouth, Inflammation, Infection, etc.).(23)

METHODS OF PREPARATION OF GELS:

Gels are generally at the industrial scale manufactured under room temperature. However,few of polymers require specific treatment before processing. Gels may be created via following ways.

1)Thermalchanges
2)Flocculation
3) Chemical reaction

1)**Thermal changes**: Solvated polymers (lipophilic colloids) when subjected to thermal changes causes gelatin. Many hydrogen formers are more soluble in hot than cold water. If the temperature is decreasing, the degree of hydration is reduced and gelatin occurs (cooling of a concentrated hot solution will produce a gel).(24)

2) **Flocculation:** Here gelation is produced by adding just sufficient quantity of salt to precipitate to produce gel state but insufficient to bring about complete precipitation. It is needed to ensure rapid mixing to avoid local high concentration of precipitant.

3) **Chemical reaction**: In this method, gel is produced by chemical interaction between the solute and solvent. (25)

EVALUATION PARAEMETERS OF TOPICAL GEL(26,27)

Appearance and homogeneity

Physical appearance and homogeneity were evaluated by visual inspection.

pH of the Gel

The pH of the gel was measured by digital pH meter. 1 gm gel is dissolved in medium and inspect with pH meter.

Viscosity

The viscosity of the gel was measured by the Brookfield Viscometer.

Spreadability

0.5 g of gel was put inside a circle of 2 cm diameter pre-marked on a glass plate, over which a second glass plate was placed. A weight around 500 g was put to rest on the top glass plate for 10 minutes. The increase in the diameter owing to gel spreading was detected.

Extradurability

To assess extradurability a sealed collapsible tube holding gel was pressed immovably at the folded end. At the point when the top was emptied, gel discharged till the weight dispersed. Weight in grams necessary to evacuate a 0.5 cm ribbon of the gel in 10 sec was resolved. The usual expulsion pressure in g was recorded.

Skin Irritation test

The animal model swiss albino mouse strain was utilized for skin irritation test and Guniea pig (400-500gm) of either sex was also used. The hairs are removed by the skin removal cream and then clean the skin with spirit, 3 mice are employed in which normal saline, blank gel and formulation were administered and check the irritation in animals.

Stability Studies

The stability study of the gel was done as per ICH recommendations the gel was store at 30^0 C± 2^0 C/ 60% ± 5% RH and 40^0 C± 2^0 C/ 75% ± 5% RH. The formulation were examined in the change in physical appearance, pH, spread ability and Viscosity.

In vitro Diffusion studies

Franz diffusion cell are used for the research of dissolution release of topical gel. 0.5g of gel sample was collected in membrane and the dissolution release were carried out at 37 ± 1^0 by utilizing phosphate buffer with pH 7.4(250ml) as the dissolving medium. Withdrawn the 5ml sample regularly at 1, 2, 3, 4, 5, 6, 7 and 8 h and each sample is replaced by new buffer solution in equal quantity and then analyze the sample in spectrophotometer and take phosphate buffer as blank reagent.

Drug Content

To assess the drug content in gel, take 1gm of gel dissolve in 100ml appropriate solution and filter it. Then the filtrate is analyzed under spectrophotometer, absorbance was determined and the drug content is carried out by regression linear analysis of calibration curve.

RESEARCH:

Sams, R. L., et al. (2015): The study has revealed that parameters such as the molecular weight of the active component, the gel's viscosity, and the kind of skin (e.g., injured or healthy) strongly impact drug absorption. The development

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of in vitro and in vivo models to explore these aspects has been vital for improving gel compositions. (28)

Koushki et al., (2016): The Research focused on several gel types, including hydrogel, organogel, and microemulsion-based gels, to optimize drug release profiles. Hydrogel-based formulations, including polymers like hydroxypropyl methylcellulose (HPMC) and carbomers, were often explored for their potential to deliver medications in a regulated or sustained way. (29)

Kumar et al., (2016): The research studied the rheological characteristics of topical gels and their effect on the spreadability and application. Viscosity, elasticity, and flow behavior were crucial in producing gels with desirable texture and performance. (30)

El-Khordagui, L. K., et al. (2017): The research focuses on optimizing the polymeric composition of gels, especially in terms of drug release control and bioavailability. Polymers like carbomer, hydroxypropyl methylcellulose (HPMC), and polyvinyl alcohol (PVA) were commonly exploited for their gelation qualities, enhancing the uniformity and durability of compositions. (31)

Patel, M., et al. (2018): The Research on adding nanostructured lipid carriers (NLCs) into gels aims at enhancing the penetration and controlled release of active chemicals. This development gave a more tailored approach to treating skin problems.(32)

Tan et al., (2019): This research emphasizes the use of biocompatible and natural excipients in gel formulations to prevent skin irritation and increase acceptability. Biodegradable polymers, such PLGA (poly (lactic-co-glycolic acid)), were included into gels for prolonged release and increased skin penetration. (33)

Taj, T., et al. (2020): The research focused on improving viscosity, spreadability, and adhesion to enhance patient experience. In particular, yield stress and elastic modulus were examined to determine how gels might respond upon application to the skin. These qualities were crucial for ensuring the gels maintained the optimum consistency for ease of application while preserving medication stability. (34)

Ravi, R., et al. (2021): The study continues to examine the rheological characteristics of topical gels, specifically focused on their spreadability, adhesion, and viscosity. The perfect gel composition has to balance these qualities for ease of application and comfort. (35)

Jadhav et al., (2022): The research focuses on targeted medication delivery employing nanoparticles in gels. Researchers worked on enhancing the ability to target certain skin layers (epidermis and dermis) for targeted therapy. (36)

Pardo, A., et al. (2023): The research focused on creation of acne therapy gels. Retinoids, benzoyl peroxide, and salicylic acid were coupled using nanoencapsulation methods to increase their effectiveness and prevent skin irritation. (37)

Khan MZ, Zafar A, Alam S, et al. (2024): The study on imiquimod-loaded nanoemulsion-based gels aims at increasing the solubility, permeability, and therapeutic efficiency of imiquimod for skin cancer therapy. The nanoemulsion-based gel displayed considerable cytotoxicity against the A431 cell line and decreased tumor parameters in vivo. (38)

II. CONCLUSION:

Topical gels continue to emerge as a viable platform for localized and systemic drug administration, delivering a mix of patient comfort, excellent drug penetration, and convenience of application. Advances in polymer science, nanotechnology, and smart delivery systems have considerably broadened their therapeutic potential beyond conventional dermatological applications. Despite the advances, obstacles persist in obtaining constant skin penetration, long-term stability, and patient-specific personalization. Ongoing research focusing on bioresponsive materials, customized therapy, and regulatory harmonization is likely to further develop gel-based delivery methods. Overall, topical gels lie at the confluence of innovation and clinical usefulness, prepared to play an increasingly crucial role in contemporary pharmaceutical and cosmetic formulations.

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