



A Brief Review on Topical Gels as Drug Delivery System

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Authors' contributions

This work was carried out in collaboration among all authors. Author CB was responsible for study design, literature search, prepared and revised the manuscript. Author DS helped in study design, literature search, and preparation of the manuscript. Authors BR and DS was responsible for critical review and editing of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

The method of applying prescription dosage forms to the skin for direct treatment of a cutaneous disorder is known as a topical drug delivery system. Topical gels are semisolid dosage forms in which a liquid phase is constrained within a three-dimensional polymeric matrix derived from natural or semi-synthetic sources with high physical or chemical cross-linking. Because of their intermediate behavior between solid and liquid materials, topical gels are an excellent candidate for transdermal drug delivery. Clinical evidence indicates that topical gel is a safe and effective treatment choice for the management of skin-related diseases, especially when used for local action to avoid the side effects of other conventional dosage forms. Gels, cream, ointment, and paste are the most commonly used semi-solid formulations for topical drug delivery. Gels are colloids in which the liquid medium has thickened to the extent that it behaves like a solid. Since topical gel formulations are less greasy and can be quickly removed from the skin, they offer better drug delivery. In comparison to cream, ointment, and paste, gel formulations have improved application properties and consistency. This article aims to review the principles and recent developments in topical gels, including classification, methods of preparation, applications, and so on.

Keywords: Topical drug delivery; skin; gels; anatomy; hydrogel.

1. INTRODUCTION

Research has made it possible to treat, prevent and eradicate many of these diseases that plague man [1]. The treatment of diseases via biomolecules such as drugs, proteins, etc. has progressed a great deal in the past few decades. These carriers allow for the release of drugs in sites that were previously inaccessible [1,2]. Ceramics, natural, and synthetic materials have all been used to make these carriers over the years. Integrity, biocompatibility, and durability were all taken into account, resulting in the use of three-dimensional matrices as carrier materials. The term "gels" refers to a group of materials. Large volumes of water and biological fluids can be absorbed by these three-dimensional polymer matrices. Gels have a wide range of uses, from food additives to pharmaceuticals and medicinal applications, due to this property [3,4].

The material that brings a particular drug into contact with and through the skin is referred to as a topical delivery system. These topical drug delivery systems are typically used for localized skin infections, such as fungal infections, or in situations where other routes of administration are ineffective [5]. It can penetrate deeper into the tissue, allowing for better absorption. The topical application offers a number of benefits over conventional dosage forms. Because of their bilayered composition and structure, they are considered more effective and less toxic than traditional formulations. The topical preparation reduces GI irritation and inhibits drug metabolism in the liver, thereby increasing the drug's bioavailability. Gels are described by United States Pharmacopoeia as a semisolid system made up of dispersion of small inorganic particles or large organic molecules enclosing and interpenetrated by a liquid. Gels are a two-phase mechanism in which inorganic particles are distributed in the continuous phase rather than dissolved, and large organic particles are dissolved in the continuous phase and coiled randomly in the flexible chains [6].

2. GELS AS PHARMACEUTICAL DOSAGE FORMS

In the late 1800s, the word "Gel" was coined to describe certain semisolid materials based on physiological properties rather than molecular composition [7]. Gels are a highly dilute cross-

linked network that does not flow in its steady-state [8]. They are made up of a two-part semi-solid structure with a lot of liquid. One of their distinguishing characteristics is the existence of a continuous structure with solid-like properties. Due to the biocompatibility, network structure, and molecular stability of the integrated bioactive agent, gels have become a preferred material for drug delivery formulations [9]. The majority of topical gels are made with organic polymers like carbomers, which give the products an aesthetically pleasing, clear, sparkling appearance and are easily washed off the skin with water. The type of base used in the formulation of a topical dermatological product has a significant impact on its efficacy. Emollient properties are given to dry, irritated skin by bases containing large quantities of oleaginous substances. More specifically, bases containing non-volatile oleaginous substances (for example, hydrocarbon bases) can create an occlusive barrier on the skin, preventing moisture from escaping into the atmosphere. As a result, moisture builds up between the skin and the ointment layer, causing the stratum corneum to become hydrated. The hydration of the stratum corneum causes intra- and inter-cellular channels and pathways to open up, allowing drug molecules to pass through more easily. The moisture layer also acts as a dissolution medium for the drug, which is otherwise distributed as fine particles in the ointment base. Since only the dissolved substance introduced to the skin will penetrate the stratum corneum as an individual molecular object, skin occlusion usually results in increased percutaneous drug absorption [10].

The essence of the polymer-solvent affinity determines the gel's integrity. According to classical gel theory, there are three types of solvents:

- i. A solvent that is both free and mobile.
- ii. A solvation layer that is solvent bound, normally by hydrogen bonding, and
- iii. A solvent that has been stuck within the network structure.

The proportions of the three solvent forms in a given gel are determined by the polymer concentration, and the solvent affinity for the polymer determines the random coil's extension. The more the coils stretch and entangle with neighboring coils to form crosslinks, the greater the solvent affinity [11].

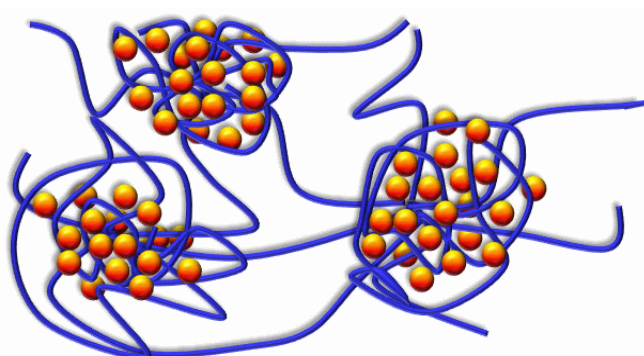


Fig. 1. Structure of gels

2.1 Drug Absorption from Topical Formulations

The total amount of active ingredients absorbed in topical applications varies greatly depending on many factors, including the region of application, the frequency with which it is applied, and the viscosity or thickness of the applied vehicle. Other factors that influence drug absorption include the application location, age, and skin condition. An active ingredient can reach the dermis more easily if it is not keratinized. The drug diffusion through the skin is managed in the best topical formulations by ensuring that the drug is only soluble enough in the vehicle to allow drug release at the desired rate. This is accomplished by assuring that the whole drug is dissolved in water.

2.2 Topical Vehicles

Topical vehicles, in general, do not penetrate the skin; instead, they keep the active ingredient in place on the skin to allow for drug absorption. The vehicle should be carefully chosen because it can affect the drug's absorption through the skin. When choosing a topical delivery system, the activity of the drug in that vehicle is the most important thing to consider. If the drug is weakly acidic or weakly basic, the pH of the vehicle may be significant, as weakly acidic drugs have higher activity in acidic vehicles and weakly basic drugs have higher activity in basic vehicles [12].

2.3 Different forms of Topical Drug Products

Dermatological products for application to the skin come in a variety of formulations and consistencies, ranging from liquids to solid powders, but semisolid preparations are the most common.

Topical Liquids: Aqueous solutions, hydro alcoholic solutions or tinctures (iodine tincture), organic solvent-based collodions (salicylic acid collodion), and other topical liquids are examples.

Solid Powders: A powder is a mixture of finely divided drugs and/or chemicals in dry form. These are solid dosage forms of medicament which are meant for internal and external use.

Ointments: Ointments are semi-solid preparations meant for external application to the skin or mucous membrane. They usually contain a medicament or medicaments dissolved, suspended, or emulsified in an ointment base. The ointments are mainly used as protective or emollient for the skin.

Creams: Creams are emulsions of oleaginous substance(s) and water that spread more quickly than ointments over the skin. Water-in-oil (w/o) creams are conveniently water-washable, but oil-in-water (o/w) creams are not. Cold cream and hydrous lanolin are w/o emulsions with small water absorption ability.

Gels: Gels are a more recent class of dosage forms that are made by trapping a large volume of aqueous or hydro alcoholic liquid in a network of colloidal solid particles. In comparison to ointments and creams, gel formulations typically include quicker drug release. These are superior in terms of patient acceptability and ease of use [13].

3. STRUCTURE OF GELS

A gel is a three-dimensional matrix formed by a natural or synthetic polymer distributed in a dispersion medium or hydrophilic liquid. The configuration of the network and the properties of the gel are determined by the existence of the

particles and the form of force responsible for the linkages. The hydrophilic colloids of individual particles may be spherical or isometric aggregates of small molecules or single macromolecules. The following diagram illustrates possible particle configurations in a gel network (Fig. 1). The network in linear macromolecules is made up of entangled molecules, each of which has a point of contact that can be small or consist of several molecules aligned in a crystalline order, as shown in Figs. 1 (c) and (d), respectively.

Gels may be prepared from natural gums, such as tragacanth, pectin, sodium alginates, or from synthetic derivatives of natural substances, such as methylcellulose and sodium carboxy methylcellulose. These are similar to mucilages because they may be prepared from gums, but they differ from mucilages in having jelly-like consistency [14,15].

3.1 Advantages of Topical Drug Delivery [16]

- The first fast metabolism is avoided
- It's convenient and easy to use.
- Easily terminates the medications, when needed
- Deliver the medication to a precise location with good specificity.
- Gastrointestinal incompatibility is avoided.

- Patient compliance can be improved
- Allowing for the use of medications with a short biological half-life and a limited therapeutic window.

3.2 Disadvantages of Topical Drug Delivery [16,17]

- The drug or its excipients can cause skin irritation or dermatitis.
- Some medications have low permeability through the skin.
- Larger particle size drugs are more difficult to absorb through the skin.
- Allergic reactions may occur
- Drugs that irritate or sensitize the skin are not appropriate for this route.

4. CLASSIFICATION OF GELS

Gels can be classified based on colloidal phases, nature of the solvent used, physical nature and rheological properties, etc.

4.1 Based on Colloidal Phases [18]

They are classified into:

- a. Inorganic (Two-phase system)
- b. Organic (Single phases system)

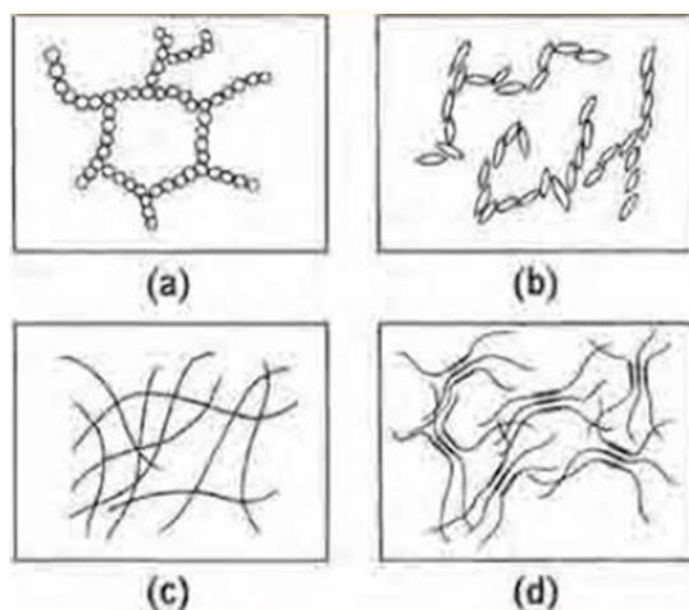


Fig. 2. Crosslinking of gel structures; (a) Flocculated particles in a two-phase gel structure; (b) Network of elongated particles or rods forming gel structure; (c) Matted fibers as found in soap gels; (d) Crystalline and amorphous regions in a gel of carboxy methylcellulose

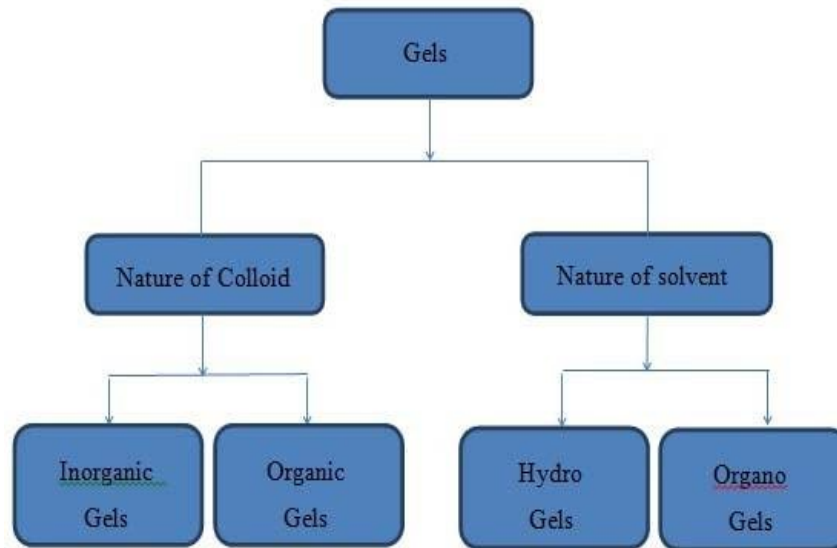


Fig. 3.General classification of gels

4.2 Inorganic (Two- Phase System)

If the dispersed phase partition size is very big and forms a three-dimensional structure throughout the gel, the system will consist of floccules of small particles rather than bigger molecules and the gel structure will be unstable. They must be thixotropic, meaning they form a semisolid on standing and turn liquid when agitated. Examples are aluminum hydroxide gel and bentonite magma.

4.3 Organic (Single Phase System)

These are large organic molecules that are dissolved in a continuous phase on the twisted strands. Most organic gels are single-phase solutions that comprise gelling ingredients such as carbomer and tragacanth, as well as organic liquids like Plastibase.

4.4 Based on Nature of the Solvent

4.4.1 Hydrogels (water- based)

Due to the chemical or physical cross-linking of individual polymer chains, a hydrogel is a three-dimensional network of hydrophilic polymers that can swell in water and hold a large amount of water while keeping their structure. An example includes hydrophilic colloids such as silica, bentonite, tragacanth, pectin, sodium alginate, etc. The hydrogel can be used for sustained release drug delivery, rectal drug delivery, ECG medical electrode.

4.4.2 Organogels (With a non-aqueous solvent)

An organogel is a class of gel composed of a liquid organic phase within a three-dimensional, cross-linked network. The organo gelling or gelation of lecithin solution in organic solvents is induced as a result of the incorporation of a polar solvent.

4.4.3 Xerogels

Xerogels are solid-formed gels that are made by slowly drying at room temperature with unconstrained shrinkage. When a xerogel is heated to a higher temperature, viscous sintering occurs, effectively transforming the porous gel into a thick glass. Example: Tragacanth ribbons, dry cellulose, and polystyrene. As gels exhibit non-newtonian flow therefore, sometimes they are also classified as plastic gel, pseudo-plastic gels, and thixotropic gels.

4.5 Based on Physical Nature

4.5.1 Elastic gels

Agar, pectin, Guar gum, and alginates gels have an elastic property. At the point of junction, the fibrous molecules are joined by comparably weak connections such as hydrogen bonds and dipole attraction. If the molecule has a free -COOH group, a salt bridge of the type -COO-X-COO forms an extra bond between two adjacent strand networks. E.g: Alginate and carbopol.

4.5.2 Rigid gels

This can be made from macromolecules with primary valence bonds connecting the framework. E.g: Silic acid molecules are kept together in a silica gel by the Si-O-Si-O link, resulting in a polymer structure with a network of pores.

4.6 Characteristics of Gels [18,19,20]

Gels should possess the following ideal properties-

- The gelling agent used in pharmaceutical or cosmetic formulations would be inert, safe, and not react with other ingredients.
- It should have an adequate antimicrobial activity to protect against microbial attacks.
- The gels used in ophthalmic formulations should be sterile.
- During storage, the gelling ingredient in the preparation should generate a reasonable solid-like consistency that can be easily broken when subjected to shear stress.
- Topical gel mustn't be sticky.

4.6.1 Swelling

The gel can swell, absorbing liquid with an increase in volume. This can be considered the beginning of the dissolution process. Gel solvent interactions take the place of gel-gel interactions. The amount of swelling is determined by the number of linkages formed between individual gelling agent molecules and the strength of these linkages.

4.6.2 Syneresis

On standing, many gels contract spontaneously and exude a fluid medium, which is known as syneresis. As the concentration of gelling agents decreases, the degree of syneresis increases. Syneresis means the original gel was thermodynamically unstable.

4.6.3 Ageing

Slow spontaneous aggregation in colloidal systems results in Ageing. In gels, ageing causes a thick network of the gelling agent to form over time.

4.6.4 Structure

The presence of a network generated by the interlinking of gelling agent particles gives a gel

its stiffness. The structure of the network and the properties of the gel are determined by the nature of the particle and the kind of force responsible for the connections.

4.6.5 Rheology

Rheology is the science of fluid flow and deformation. Solutions of the gelling agents and dispersion of flocculated solid are pseudoplastic i.e. exhibiting Non-Newtonian flow behavior.

5. USES OF GELS

- Used as topical drug delivery system for direct application of skin, mucous membrane, or the eye.
- As tablet granulators, protective colloids in suspensions, and thickeners in oral liquid and suppository bases.
- Gels can be used for the preparation of Shampoos, dentifrices, skin and hair care preparations.
- Lubricant for catheters.
- NaCl gel for electrocardiography
- Phosphoric acid gel and sodium fluoride for dental care products.

6. ANATOMY AND PHYSIOLOGY OF SKIN [21]

Two systems in the human body protect it from hazardous organisms found in the environment. Microorganisms and bacteria that have already invaded the body are destroyed by the internal defense system. The body's exterior defense mechanism keeps microbial germs out. The largest exterior defense system is the skin. Skin not only protects the outside of the body, but also serves additional purposes. It acts as a mechanical barrier between the body's inner workings and the outside world.

6.1 Anatomy of the Skin

Skin is the largest organ in the body. It consists of three different layers. The epidermis is the outermost layer, the dermis is the intermediate layer, and the hypodermis is the innermost layer.

6.2 Epidermis

It consists of epithelial cells and is made up of five different layers. Stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum and stratum germinativum. The epidermis lacks a direct source of nutrients in the form of blood

vessels. It gets its nourishment from a dense circulatory network in the underlying dermis, which allows essential chemicals to diffuse. Desmosomes bind epidermal cells together very tightly. Desmosomes come into contact with keratin filaments within the cell.

The stratum corneum is the outermost layer of the epidermis having a thickness of 10-20µm when it is dry and 40µm when wet and swollen. Cell types that exist in the epidermis are-

- Keratinocytes: Primary cells of epidermis about 95%

- Melanocytes: These are pigment-producing cells located in the epidermis's basal layers.
- Langerhans cells: Merkel cells, which are situated in the basal layer of the epidermis and are part of the amine precursor and decarboxylation system, are key immunological cells that can be found in the mid dermis [22,23].

The structure of the stratum corneum is made up of "bricks and mortar." The keratin-rich corneocytes (bricks) in this model are sitting in a lipid-rich intracellular matrix (mortar).

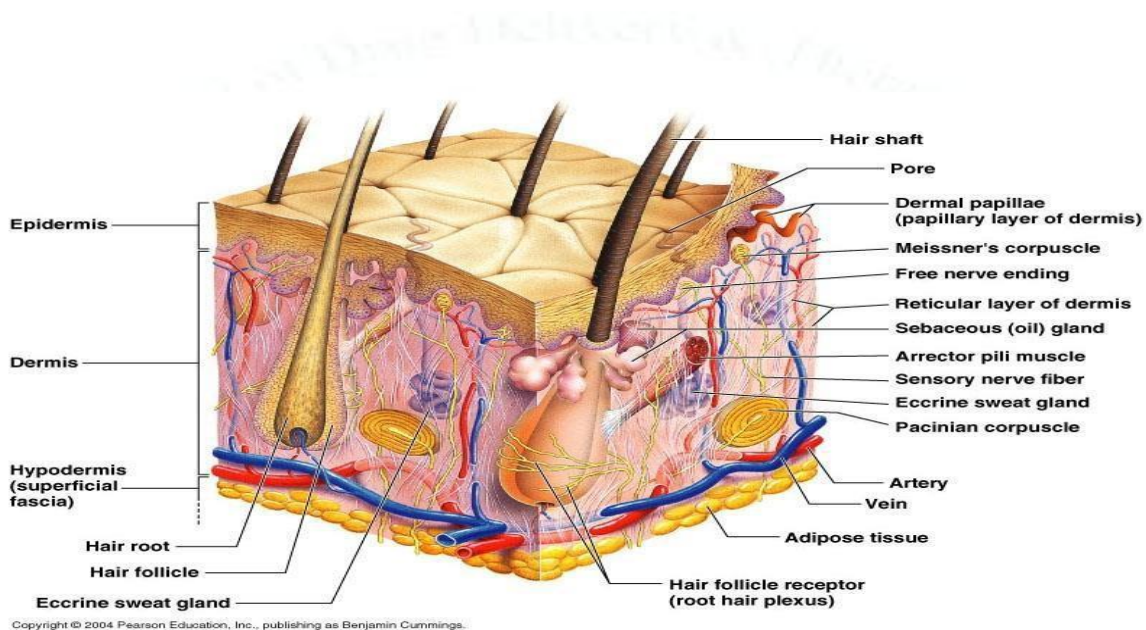


Fig. 4. Anatomy of skin

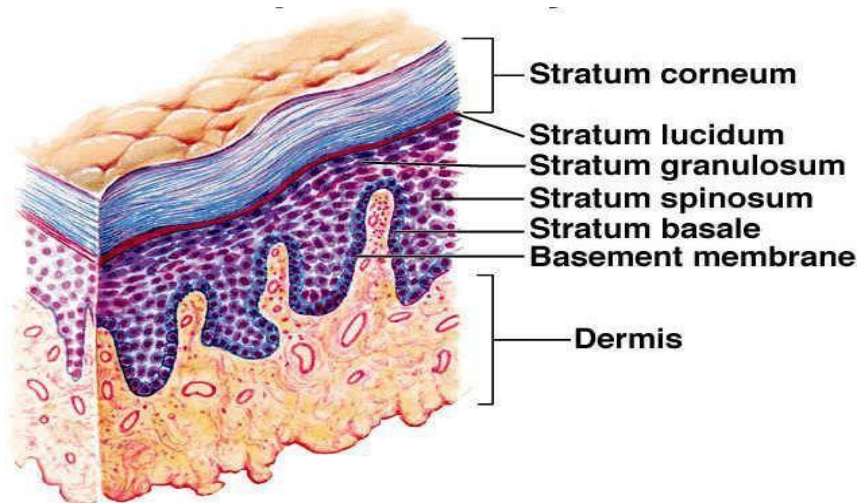


Fig. 5. Structure of epidermis

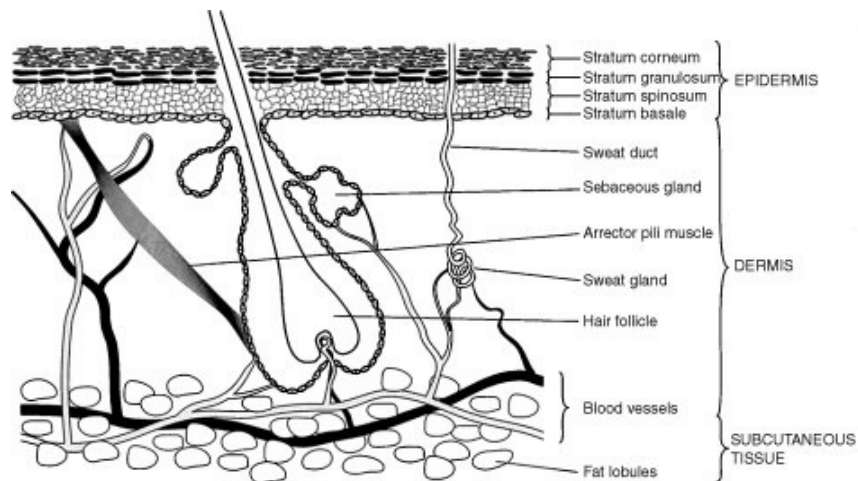


Fig. 6. Epidermal and skin layers

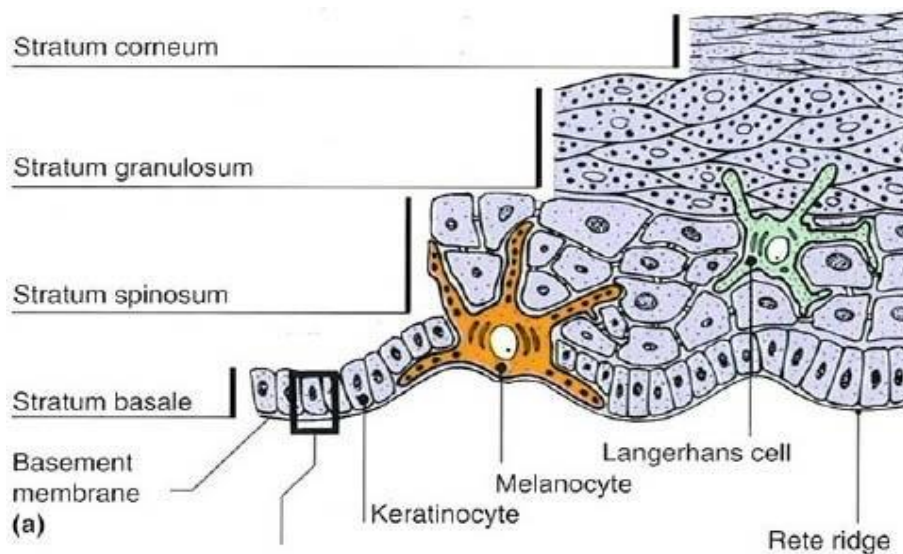


Fig. 7. Different layers of the epidermis

Corneocytes (the bricks) are made up 85 percent of the stratum corneum, which is organized in 15-20 layers with internal lipids (15 percent). 70% of the stratum corneum is made up of proteins, 15% lipids, and only 15% water.

6.3 Dermis

The dermis is located beneath the epidermis and is distinguished by a large number of elastin fibers that allow the skin to stretch and a large amount of collagen that gives it strength. Nerve endings, sweat glands, oil glands, hair follicles, and blood arteries are all found in the dermis [24]. The dermis is also important for temperature regulation. Pressure and pain sensations are caused by the presence of nerves

[25]. The thickness of the dermis is 3-5 mm. The dermis contains elastin fibers, blood arteries, and nerves, as well as an interfibrillar gel comprising glycosamino glycan, salt, water, lymphatic cells, and sweat glands are parts of the dermis. Cell types found in the dermis are-

- Fibroblasts: The cell which produces collagen
- Macrophages: Scavenger cells
- Mast cells: Responsible for immunological reactions

6.4 Hypodermis

The hypodermis is the skin's innermost layer. It is the layer that connects the skin to the body's

underlying tissues, such as muscles and bone. Sweat glands, sebaceous glands, and hair follicles all have their origins in the dermis, although they are enclosed in the epidermis. Sweat glands secrete a dilute salt solution on the skin's surface. The evaporation of this weak salt solution cools the skin, which is crucial for body and skin temperature regulation.

7. PERCUTANEOUS ABSORPTION AND KINETICS OF DRUG PERMEATION [26]

The following steps are involved in topical permeation of a drug: sorption by stratum corneum, Penetration of the drug through viable epidermis, uptake of the drug by the capillary network in the dermal papillary layer.

If the medicine has particular physicochemical properties, penetration may be feasible. The rate of permeation across the skin (dQ/dt) can be calculated as follows:

$$dQ/dt=Ps(C_d - C_r) \dots \dots \dots (i)$$

Where,

C_d =Concentration of skin penetrant in the donor compartment (e.g., on the surface of stratum corneum)
 C_r =Concentration in the receptor compartment (e.g., body) respectively
 Ps = Overall permeability constant of the skin tissue to the penetrant

$$Ps=(K_s D_{ss})/h_s \dots \dots \dots (ii)$$

Where,

K_s is the partition coefficient for the interfacial partitioning of the penetrant molecule from a solution medium.

D_{ss} is the apparent diffusivity for the steady-state diffusion of the penetrant molecule through a thickness of skin tissues.

h_s is the overall thickness of skin tissues.

A_s , K_s , D_{ss} , and h_s are constant under given conditions, the permeability coefficient (Ps) for a skin penetrant can be considered to be constant.

From Eq.(I) it is clear that a constant rate of drug permeation can be obtained only when $C_d \gg C_r$ i.e., the drug concentration at the surface of the

stratum corneum(C_d) is consistently and substantially greater than the drug concentration in the body(C_r), then Eq. (i) becomes:

$$dQ/dt=PsC_s \dots \dots \dots (iii)$$

8. FORMULATION DESIGN

The topical gel may consist of the following components-

- a) Gel forming agent or polymer
- b) Drug substances
- c) Penetration enhancer

a) Gel forming agent or polymer

Polymers are employed to provide the structural network that is required for gel preparation. Gel forming polymers are classified below-

Natural polymers

- (i) Proteins: E.g: Gelatin, collagen, Xanthum gum
- (ii) Polysaccharides: E.g: Agar, Alginic acid, Tragacanth, Pectin, Guar gum

Semi-synthetic polymers

- (i) Cellulose derivatives: E.g: Carboxymethyl cellulose, Methylcellulose, Hydroxypropyl methylcellulose, Hydroxyethyl cellulose.

Synthetic Polymers

- (i) Carbomer: E.g: Carbopol-934, Carbopol-940, Carbopol-941, Polaxomer, Polyacrylamide, Polyvinyl Alcohol, Polyethylene, and its copolymers.

Inorganic Substances

An example includes Aluminum hydroxide, Bentonite.

Surfactant:

Sodium lauryl sulphate, Cetosteryl Alcohol.

b) Drug Substances [27]

During the formulation of a topical product, drug substances play a major role. The important drug properties that effect its diffusion through gels as well as through skin are as follows:

1. Physicochemical Properties

The drug should have a molecular weight of less than 400 daltons

Highly acidic or alkaline drugs are not suitable candidates for topical drug delivery

The drug should have adequate lipophilicity

Drug candidates should have pH in between 5-9

2. Biological Properties

The drug should not be irritating to the skin

Drugs which degraded in the GI tract are suitable for topical drug delivery

Drugs should not stimulate an immune reaction to the skin

c) Penetration Enhancer

Penetration enhancers are also called accelerants or sorption promoters are defined as substances that are capable of promoting the penetration of drugs into the skin. An ideal penetration enhancer should have the following properties-

It should be pharmacologically and chemically inert

It should be non-toxic, non-irritant and non-allergenic

It should be odorless, colorless, tasteless, and inexpensive

It should have a rapid onset of action, predictable duration of activity

8.1 Formulation Consideration for Pharmaceutical Gel [28]

8.1.1 The choice of vehicle or solvent

Water is a common solvent for all types of dosage forms. To improve the solubility across the skin, co-solvents may be used. E.g: Alcohol, Glycerin, PEG-400 etc.

8.1.2 Inclusion of buffers

Buffers may be incorporated in the gel formulation to control the pH of the formulation. The solubility of buffer salts decreases in hydro alcoholic based vehicles. E.g: Phosphate, Citrate, etc.

8.1.3 Preservatives

Preservatives are used for the formulation of pharmaceutical gel to prevent decomposition by

microbial growth or by undesirable chemical changes. E.g: Methyl paraben, Propyl paraben, phenolics, etc.

8.1.4 Antioxidant

These are used to improve the chemical stability of the therapeutic agents that are prone to oxidative degradation. Generally, water-soluble antioxidants are preferred during the formulation of pharmaceutical gel. E.g: Sodium metabisulphite, Sodium formaldehyde

8.1.5 Sweetening Agents/ Flavors

Gels which are manufactured especially for oral cavity in such cases these agents are used (For ulceration of mouth, Inflammation, Infection, etc.)

8.2 Manufacture of Gels

Initially, water-soluble excipients are dissolved in a vehicle in a mixing vessel with the help of a magnetic stirrer. To prevent aggregation hydrophilic polymers are added slowly. Stirring is continued until the dissolution of the polymer has occurred.

Table 1. Gel forming substances

Natural Polymers	A	Proteins
		Gelatin
		Collagen
	B	Polysaccharides:
		Pectin
		Gellum Gum
		Alginic acid
		Agar
		Xanthin
		Cassiatora
		Tragacanth
		Sodium or Potassium carrageenan
	Guar Gum	

8.3 Application of Gels [29]

- To offer local action gels are applied directly to the skin, mucus membrane, or eye.
- Gels have been used in a wide range of cosmetic goods, including shampoos, fragrances, dentifrices, and skin and hair care treatments.
- Gels offer more potential as a vehicle for topically administering drugs.

- Gels act as long- acting forms of drug injected intramuscularly or implanted into the body.

8.4 Evaluation of Gels [30,31]

pH Measurement: pH of gel formulation is determined by using a digital pH meter. 1 gm of gel is dissolved in 100ml of distilled water and stored for two hours. Each formulation pH is measured three times and the average readings are calculated.

Drug Content: 1gm of gel is dissolved in 100 ml suitable solvent. Filter the stock solution and absorbance is measured after suitable dilution at λ max nm using a UV visible spectrophotometer.

Viscosity Study: Brookfield digital viscometer can be used to calculate the viscosity of prepared gel formulation. Gels are rotated at 0.3, 0.6, and 1.5 rotations per minute. At each speed corresponding, dial reading is noted. Viscosity is calculated by multiplication of dial reading with a factor given in the viscometer catalogs.

Spreadability: Spreadability indicates the extent area to which gel readily spreads on application to the skin or affected area. Spreadability

generally performs in a glass slide. The time in sec taken by two slides to slip off from gel which is placed in between the slides under the direction of certain load is expressed as spreadability. Lesser the time is taken for separation of two slides better the spreadability. It can be expressed as-

$$\text{Spreadability (S)} = M \times L / T$$

Where,

S = Spreadability

L= Length of glass slides

T = Time taken to separate the slides

Extrudability study: Gel formulations are filled in the collapsible tubes after it was set in the container.

Extrudability is determined in terms of weight in gm required to extrude 0.5cm ribbon of gel in 10 sec.

Homogeneity: Prepared gels are tested for homogeneity by visual inspection after the gels have been set in the container. They are tested for their appearance and presence of any aggregates.

Table 2. Patentable formulations of topical gel

Sr. No.	PatentNo.	Formulation
1	US5939090 A	Gel formulations for topical drug delivery
2	EP1304992B1	Topical gel delivery systems for treating skin disorders
3	US5914334 A	Stable gel formulation for topical treatment of skin conditions
4	EP0183322 A2	Gel-form topical antibiotic compositions
5	WO187276A1	Hydrogel composition for transdermal drug delivery
6	US2014363498 A1	Hydrogel polymeric compositions and methods
7	US8771734B2	Sustained-release hydrogel preparation
8	US2200709 A	Organogel
9	EP2711001 A3	Organogel compositions and processes
10	US2327968 A	Porous xerogel
11	US8703284B1	Aerogel/Xerogel composite material amalgamated with single-walled carbon nanotubes for multipurpose usage
12	US3033686 A	Plastic gels of water and acyl lactic acids and their salts
13	USRE35144E	Thixotropic adhesive gel
14	US2487600 A	Aqueous thixotropic gel composition
15	US6117176 A	Elastic-crystal gel
16	US4643924 A	Protective article comprising an elastic gel
17	US6045814 A	Cosmetic use of a rigid gel, and cosmetic or dermatological composition
18	WO2008014036A1	Aqueous gel formulation and method for inducing topical anesthesia
19	US20070031479 A1	Bioadhesive gel based on hydroxyl ethylcellulose
20	WO2009042231A2	Sol-gel phase-reversible hydrogel templates and uses there of

Table 4. Examples of gels

SI No.	Active Ingredients	Proprietary	Gelling Agent	Route & Use
1	Acetic acid	Aci-jel	Tragacanth,acacia	Vaginal: restoration and maintenance of acidity
2	Becaplermin	Regranex Gel	Na CMC	Dermatologic
3	Benzoly peroxide	Desquam-X Gel	Carbomer940	Acnevulgaris
4	Clobetasol	Termovate Gel	Carbomer934	Antipruritic
5	Clindamycin	Cleocin T Gel	Carbomer	AcneVulgaris
6	Cyanocobalamin	Nascobal	Methyl Cellulose	Nasal:Hematologic
7	Desoximetasone	TopicortGel	Carbomer940	Anti-inflammatory; antipruritic
8	Metronidazole	Metro-Gel	Carbomer	Vaginal:Bacteria
9	Progesteron Supplement	Crinone-Gel	Carbomer	Progesteron
10	Tretinion Cellulose	Retin-A	Hydoxypropyl Cellulose	Acne Vulgaris

Grittiness: All the gel formulations are checked microscopically for the presence of any particulate matter.

In- vitro drug diffusion study: It can be carried out in a Franz diffusion cell. 05gm of gel is taken in a cellophane membrane. Carried out the dissolution studies at 37±1° C using 250 ml of phosphate buffer (pH7.4) as the dissolution medium.

In-vivo study: Inhibition of carrageenan-induced rat paw edema is studied in male Wistar albino rats using mercury plethysmometer. The volume of the unilateral hind paw of experimental animals is measured, before and after administration of carrageenan. % inhibition is noted.

Skin Irritation test: For skin irritation study, guinea pig (400-500gm; either) sex were used. Animals were kept under standard conditions. Hair was shaved from the back. Five ml of each sample was withdrawn periodically at 1,2,3,4,5,6,7 and 8h and each sample was replaced with an equal volume of fresh dissolution medium. Then analyzed the samples for drug content by using phosphate buffer. An area of 4 cm (skin) was marked blank on both sides, one sides as control I while the other side was tested. The gel was applied (500mg/guinea pig) twice a dayfor7days and the site was observed for any sensitivity and the reaction If any. It was graded as: 0 (Non -Reaction), 1 (Minor patchy erythema), 2 (Minor but confluent or modest but patchy erythema), 3 (Severe erythema with or without edema).

9. CONCLUSION

The use of pharmaceutical gel getting more popular nowadays because they are more stable and also provide control release than other semisolid dosages forms. The topical gel provides better absorption to the skin and therefore increases bioavailability. The major benefit of a topical delivery system is to bypass first- pass metabolism. Moreover it also provides excellent patient acceptability. In most cases, topical delivery prefers when another system of drug administration having less bioavailability. The clinical evidence shows that topical gel is a safe and effective treatment choice for use in the management of skin- related diseases.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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