REVIEW ARTICLE

# An analysis of medical gel

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**Abstract**

With a focus on sensible topical formulation techniques and the essential components of topical drug delivery systems, the goal of this review is to provide an overview of recent research. The advantage of administering medication topically is that it reaches the site of action directly and remains longer there. Topical medications are primarily administered through the skin, which is one of the body's most accessible and widely distributed organs. Topical medications are usually very sticky and uncomfortable to apply, which presents a number of challenges. Ointments, lotions, and creams are common topical medications. They also have a lower spreading coefficient, require rubbing, and have a stability problem when compared to other semisolid preparations in the main category. All of these factors have led to an increase in the use of gas in preparations for pharmaceutical and cosmetic uses. The surface tension between a 99% liquid-by-weight colloid and a network of macromolecules composed of minuscule amounts of the surrounding gelatinous substance immobilizes the colloid, forming a gel.

**Key words:** Assessment of gels, attributes, categorization, formulation, nomenclature, patents, pharmaceutical gels

## INTRODUCTION

Gels resemble semi-frozen systems in which the liquid portion is less mobile due to the microscopic particles or molecules stuck in a network. The Latin terms for "freeze" and "congeal" are "gel" and "jelly," while the word "gel" itself is derived from "gelatin." When scientists were unable to investigate the molecular features of semi-solid materials in the late 1800s, they coined the word "gel" to refer to substances that functioned something like a combination of liquid and solid. They utilized this term to classify materials that behave like a liquid changing into a stretchable, non-flowing substance.

Gels, also called jellies, are semisolid systems made of liquid-interpenetrated suspensions of large organic molecules or small inorganic particles, according to the USP. A gel is classified as a two-phase system when its mass contains a network of discrete, small particles. A magma is a mass of gel in two-phase systems where the dispersed phase has relatively large particle sizes. Gels in one phase are characterized by the uniform distribution of organic macromolecules in the liquid, making it impossible for the liquid to discern boundaries from the dispersed macromolecules. Water and hydroalcoholic solutions are most frequently used in pharmaceutical applications. Numerous polymer gels have the ability to alternate between a liquid sol phase, in which the macromolecule is dissolved, and a solid gel phase. Nevertheless, some polymer gels cannot have their formation reversed because of their covalently bonded chains. To produce two-phase gels and jellies, a three-dimensional network of layers of various inorganic colloidal clays is used. Preventing these inorganic gels from forming is possible. Because they are less liquid and have more chemical or physical linkages, gels are often stiffer than jelly. Gel-forming materials can be used to create a variety of materials with varying degrees of stiffness, such as liquids, gummy mixtures, jelly, solid gels, and hydrogels. Certain gels can lose their transparency and become hazy when molecules or small particles are mixed in. The gelling agents have a concentration ranging from 0.5% to 2.0%, with a few noteworthy exceptions, typically <10%.

## TERMINOLOGIES RELATED TO GELS[1]

We refer to the unique characteristics of gels by terms such as swelling, imbibition, syneresis, thixotropy, and xerogel.

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A gel that absorbs liquid without expanding is said to be imbibition. Swelling is the volume increase that happens when a liquid absorbs into a gel. Gels can only swell when they are dissolved by liquids. Protein gel swelling is influenced by pH and electrolyte availability. Syneresis is the result of strong particle interactions in the dispersed phase, which cause the gel to contract and while the gel is still, push the dispersion medium out in droplets. This type of erratic behavior can be seen in gels that are aqueous or non-aqueous. The polymeric molecules' elastic contraction may lead to solvent phase separation; as gel formation swelling increases, the macromolecules stretch and the elastic forces intensify. The internal water pressure and the gel's own force equalize when the gel is in equilibrium. As the gel cools, the water may be forced out if this pressure decreases. Additives can be added to an acidic gel made from Plantagoalbicans seed gum to prevent this, such as salt, sugar, and more gel material. The pH level has a big impact on how water separates. Low pH levels cause significant syneresis, which could be caused by water loss, the creation of intramolecular hydrogen bonds, and the suppression of carboxylic acid group ionization. This would lessen the solvent's attraction to the macromolecule. Reversible gel-sol formation in the absence of temperature or volume variations is the hallmark of thixotropy, A gel is transformed into a xerogel when the liquid is removed, leaving just the solid structure. Xerogels can be formed from materials such as acacia tears, tragacanth ribbons, and gelatin sheets.

## STRUCTURE OF GELS[4]

The connections between the gelling agent particles give a gel its structure, which gives it its stiffness. The composition and adhesion of the particles determine the properties and structure of the gel. Particles in a hydrophilic colloid might be spherical, composed of tiny molecules grouped together, or big molecules connected together.

## PROPERTIES OF GELS[1,2,4,6]

1. The gelling agent should ideally be safe, non-toxic, and unable to interact with any other ingredients in the mixture.
2. When a bottle is shaken or a tube is squeezed, the gelling ingredient should produce a solid that breaks readily.
3. An appropriate antimicrobial agent should be on hand.
4. The topical gel cannot have any stickiness to it.
5. Sanitized eye gel is required.
6. The gel seems thicker or stronger as the molecular bonds are strengthened. However, the viscosity can alter with heating, contingent upon the degree of solvent and polymer interaction.
7. They provide an illustration of the gels' mechanical properties.[4,7]

### Swelling

Gels have the ability to expand and absorb liquid to gain volume. This may be considered the first stage of the disintegration. Gel matrix elution through the solvent pen replaces gel-gel interactions with gel-solvent interactions. A certain level of cross-linking in the gel matrix, which keeps the material from completely dissolving, is typically the cause of limited swelling. When the gel reaches a solubility parameter similar to the gallant's, it swells significantly.

### Syneresis

Gel systems contract when stored upright. The interstitial liquid congregates at the gel's surface after being expressed. In addition to organic hydrogels, it has also been shown that inorganic and organogel hydrogels exhibit the syneresis phenomenon. In general, as the polymer concentration drops, syneresis becomes more noticeable. The amount of space that the liquid may occupy in the gel decreases when the stretching stress is released. We relate this to the procedure of gel setting. We have also found a correlation between the amount of liquid that is squeezed out of gels that contain ionic gelling agents such as gelatin or psyllium seed gum and pH and salt content.

### Aging

Colloidal systems usually spontaneously agglomerate over time. What is commonly known as "aging," the gelling ingredient gives gels a firm structure that they build over time. Removing liquid from a freshly produced gel is similar to carrying out the same gel-making procedure again. The network that the gelling agent's particles generate gives a gel its rigidity. The types of particles and the forces connecting them determine the properties of the gel and its structure.

### Rheology

Stirring some solutions that defy the standard flow laws causes them to get thinner and flow more. This occurs in mixtures containing solid particle clumps and gelling agents. The microscopic particles in the liquid flow more easily when you agitate them because their loose structure dissolves. Similar to this, shear stress straightens out macromolecules by positioning the molecules to face the stress, which lowers flow resistance.

## USES OF GELS[7]

1. As a method of giving oral medicine
2. For topical medications administered topically to the skin, mucosa, or eyes
3. Long-acting medication implants or intramuscular injections

4. In tablet granulation, suppository bases, oral fluid thickeners, tablet binders, and suspension protective colloids
5. In cosmetics, such as hair and skin care products, toothpaste, shampoos, and perfumes
6. Catalyst lubricant
7. Bases for testing patches
8. NaCl gel for electrocardiograms
9. Preventive dental care using sodium fluoride and phosphoric acid gel.

### Gels are categorized[1,6,8]

Gels can be categorized according to various factors such as their physical characteristics, rheological properties, solvent type, and colloidal phases. They are categorized into the following based on colloidal phases:

a. Two-phase system (inorganic)
b. Organic (one-phase structure)
c. Inorganic (having two phases).

Here, clusters of tiny particles replace large molecules. It is possible that the system will not always remain stable when these large aggregates form a three-dimensional structure inside the gel. When left in a semisolid state, they must dissolve into a liquid and form a semisolid phase known as the thixotropic phase.

### Organic (Single phase system)

Large organic molecules, such as synthetic or natural polymers, are what form gels. Because these molecules cling to one another or become twisted, they create linkages and are referred to as "gel formers."

### Based on nature of solvent

#### *Hydrogels (water based)*

It is rare to find a hydrogel that is dispersed in water like a colloidal gel. Instead, hydrogels are chains of hydrophilic polymers. These are networks of polymers, either natural or artificial, with a large absorption capacity. Because they contain a lot of water, they are also relatively flexible, much like natural tissue.

#### *Uses for hydrogels*

1. Methods for administering medications with a gradual release
2. Rectal diagnosis and drug administration
3. Cell culture experiments have made use of wells coated with hydrogel
4. As tissue engineering scaffolds
5. As a sensor of environmental sensitivity
6. Polymacon, silicone hydrogel, and polyacrylamide contact lenses
7. Medical ECG electrode
8. Remedial cream.

As an example, consider carpooling, gelatin, cellulose derivatives, poloxamer gel, and bentonite magma.

### Organogels (solved without aqueous solvent)

An organic phase in liquid form is entangled in a three-dimensional network of cross-links to forman organogel, a thermoreversible solid that is non-crystalline and non-glassy. Among the liquids are vegetable and mineral oils as well as organic solvents. An organogel's firmness and elasticity are determined by the size of its particles and how efficiently the structure dissolves. These gels frequently rely on molecules joining forces to form their shape.

### Xerogels

Dashing a gel that has shrunk quickly yields an aerogel. Small pore size, high porosity, and big surface area are all retained. An extremely porous, light-weight substance known as an aerogel is created when the solvent is removed under supercritical circumstances without causing the structure to contract. Xerogel can be successfully heated to a temperature that results in viscous sintering, which turns the porous gel into a thick glass.

Examples include gelatin sheets, acacia tears, dry cellulose and polystyrene, β-cyclodextrin, and tragacanth ribbons.

### Relying on rheological characteristics

Gels usually exhibit non-Newtonian flow properties. Their classifications are as follows: (a) plastic gels, (b) pseudoplastic gels, and (c) thixotropic gels.

### Plastic gels

Bingham bodies have plastic-like behavior when aluminum hydroxide suspensions are present. The solid gel's yield value – the point at which it begins to flow and deform – is displayed on the rheogram plot.

### Pseudo-plastic gels

For example, tragacanth, sodium alginate, Na CMC, and other liquid dispersions exhibit pseudo-plastic flow. These gels have no yield value, and as the shear rate rises, their viscosity falls. When linear polymer long-chain molecules are subjected to force, the rheogram results. Because the solvent is exiting the gel as you push, the disordered molecules begin to align in the force's direction.

### Thixotropic gels

The incredibly weak particle bonds in these gels are readily broken by shaking. A structure that forms when particles join together can undergo a reversible metamorphosis, switching back and forth between a gel and a solution. This structure resembles a scaffold and occurs in systems such as agar, bentonite, or kaolin that contain non-round particles. For instance, an agar combination can solidify as a gel upon cooling and then reconstitute as a solution upon heating.

E.g., Kaolin, bentonite, agar, etc.

## BASED ON PHYSICAL NATURE

### Flexible gels

Alginates gels behave elastically, as do guar gum, pectin, and agar. Weak connections, such as hydrogen bonds and dipole attraction, cause the fibrous molecules to adhere to one another at the junction. A molecule with a -COOH group can link two neighboring strand networks using a salt bridge like-COO-X-COO.

### Rigid gels

A macromolecule can use strong primary bonds to connect the structure. For instance, the Si-O-Si-O link in silica gel forms a polymer structure with holes by holding the silica molecules together.

## PREPARATION OF GELS[8]

Usually, gels are prepared at room temperature in an industrial environment. However, not all polymers need to be handled carefully before processing. The procedures listed below can be used to make gels:

1. Alterations in temperature
2. Intermingling
3. Chemical reactions

### Thermal changes

Solvated polymers, sometimes referred to as lipophilic colloids, are heated to create gelatin. In hotter water than in colder water, many hydrogen formers dissolve more readily. Gelation occurs when there is a reduction in both temperature and moisture content. Concentrated hot solution gels upon cooling.

Agar sodium oleate, guar gum, gelatin, and cellulose derivatives are a few examples of substances that gel when combined with water. However, certain materials, like cellulose ether, dissolve in water instead of mixing with it to form hydrogen bonds. Raising the temperature of these solutions will cause them to lose solubility and break the hydrogen bond, causing gelation. Gel preparation cannot therefore be done with this technique in a reliable manner.

### Flocculation

Here, the mixture is treated with a small amount of salt (not enough to cause full precipitation), causing gelation and the formation of a precipitate that results in an age state. Rapid mixing is required to avoid a localized high precipitant concentration. Polystyrene and ethyl cellulose do not gel when combined with benzene. However, they can gel if a non-solvent, such as petroleum ether, is added rapidly. On the other hand, if salt is added to a solution that is incompatible with water, the result is less frequently a gel but rather a clumping of the particles. Thixotropic gels are produced by the flocculation method. Hydrophilic colloids (acacia, gelatin, proteins) are only affected by high electrolyte concentrations; otherwise, the processes of gelation and colloidal formation are inhibited.

### Chemical reaction

This process uses a chemical reaction between the solute and solvent to create gel. For instance, a higher reactant concentration will result in the formation of the gel structure when an aluminum salt and sodium carbonate are reacted in an aqueous solution to create aluminum hydroxide gel. Other chemical reactions that cross-link the polymeric chain are PVA, methane diphenyl isocyanine, toluene diisocyanates, and cyanoacrylates with glycidol ether (Glycidol).

## FORMULATION CONSIDERATIONS FOR PHARMACEUTICAL GELS[11]

The selection of a solvent or vehicle purified water is usually combined with a solvent. Co-solvents can be added to a dosage form to increase the therapeutic agent's solubility or to enhance drug penetration through the skin. PG, alcohol, glycerol, and PEG 400 are examples of co-solvents.

### Inclusion of buffers

In hydroalcoholic and aqueous gel formulations, buffers are used to regulate the mixture's pH. Buffer salt solubility declines in hydroalcoholic-based vehicles.

### Reserving agents

Utilize preservatives that interact with the hydrophilic polymers used to make gels to reduce the amount of free preservative – an antimicrobially active preservative – in the mixture. The initial concentration of the preservatives needs to be increased to make up for this.

### Antioxidants

It might be used to strengthen the chemical stability of medicinal components that are susceptible to oxidative degradation during the formulation stage. It is common practice to use water-soluble antioxidants since most gels are naturally aqueous.

Examples include sodium metabisulphite and sodium formaldehyde sulfoxylate.

### Flavors/sweetening agents[3,5,10]

Only gels meant to be injected into the oral cavity – like those used to treat ulcers, infections, inflammations, etc. – have flavors and sweeteners in them.

E.g.

Sweeteners: Xylitol, Agave nectar, Monk fruit extract, Maple syrup, Honey, Erythritol, and Xylitol.

Flavors: Caramel, Lemon, Blueberry, Coffee, Coconut, Chocolate, and Strawberry.

## MANUFACTURE OF GELS[11]

When creating a combination, the first step is often to use a stirrer to dissolve materials that are soluble in water in a liquid. The hydrophilic polymer is then added gradually to prevent clumps, and stirring is necessary until the polymer dissolves fully. Air becomes trapped when stirring too much. A mixing vessel with a vacuum attachment can be used to prevent trapped air, or the mixing rate should not be too high.

## FACTORS AFFECTING TOPICAL DRUG DELIVERY[12-15]

The interaction of these factors – the physicochemical properties of the medication, (b) Physiological elements, and (c) formulation components and their interactions – determines the effectiveness of topical drug delivery.

Physiological variables largely dictate the properties of the skin, including its moisture content, follicle density, and thickness. Individual variability in these characteristics may be significant depending on variables such as age, gender, race, anatomical location, general health, and environmental factors such as temperature and humidity. Identifying the rate-limiting step in the formulation for topical drug administration, as opposed to the biological barrier, might help minimize such physiological variability.

How efficiently a medication penetrates a topical substance and enters the skin or mucous membranes depends on how it acts both chemically and physically. The molecular weight, which is a proxy for molecular size, stability, melting point, partition coefficient between the skin and the vehicle, and chemical functionality are a few of the important variables. These variables all have an impact on the drug's solubility in the vehicle, binding affinity, and ionization potential.

Its significance is evident in the way that the vehicle formulation affects both the drug and the application site. Drug dispersion, stability, thermodynamic activity, and the degree to which weakly basic or acidic drugs ionize all have an impact on the medication. Changes in the barrier property brought about by the simultaneous absorption of formulation ingredients and physical occlusion have an effect on the application site. These treatments promote skin hydration or changes that enhance the absorption of medications.

The vehicle's thickness and sticking power are influenced by the formulation factor, which also affects the vehicle's ability to stick and maintain its position.

For effective medication delivery and to guarantee the vehicle's retention at the application site, these features were essential. There are three primary categories of topical products: Semisolids, liquids, and solids. Semisolid materials are the most often utilized among them.

## EVALUATION PARAMETERS OF THE FORMULATED GELS[9,16]

### Measurement of pH

We measured the pH with digital pH meters. Let 1 gram of gel dissolve in 100 ml of distilled water and then let it sit for 2 h. Calculated average values and verified pH measurement twice.

### Drug content

First, 100 mL of the suitable solvent were combined with 1 gram of the gel. Clean up the solution in stock. Calculate the absorbance after creating aliquots with different concentrations using the proper dilutions. The drug content was determined using the equation that resulted from the calibration curve's linear regression analysis.

### Viscosity study

For this procedure, a Brookfield viscometer is utilized. 1.5, 0.6, and 0.3 RPMs were used for the gel rotations. When the dial readings correspond with each speed, keep an eye on them. Utilize the dial reading from the Brookfield viscometer

inventory multiplied by the specified amount to determine viscosity.

### Spreadability

Any area where gel spreads easily across the skin is visible, including the affected area. The distribution of the value also influences the therapeutic efficacy. When two slides are subjected to a particular load, spreadability is the amount of time, measured in seconds that it takes for the gel placed between them to separate. Shortening the time between two slides improves spreadabilty. Spreadability is computed using the formula below:

Transparency (S) = M × L/T

Where,
M = weight fastened to the top slide
L = glass slide's length
T = amount of time needed to divide the slides.

### Extrudability study

To T The formulations are inserted into the collapsible tubes, then into the container. Extrudability is the weight in grams required in 10 s to extrude a gel ribbon that is 0.5 cm long.

### Skin irritation study

For the skin irritation study, 400–500 g Guinea pigs of both sexes were employed. The animals were given unlimited access to water and regular animal feed. The housing conditions for the animals were standard. He had shaved his entire back. After 1, 2, 3, 5, 6, 7, and 8 h, 5 mL of each sample were removed and replaced with an equivalent volume of fresh dissolving medium. Phosphate buffer was used as a test subject to determine the drug content of the samples. The test and control areas were separated by 4 cm. The guinea pig was given 500 mg of the gel twice a day for 7 days, and during that time, the application site was watched for any indications of sensitivity or response. As a result:

### *In vitro* diffusion studies

The Franz diffusion cell's cellophane membrane can be used to study gel release upon dissolution. A membrane made of cellophane was inserted into a 0.5 g gel sample. Diffusion experiments were conducted using a dissolution medium consisting of 250 mL of phosphate buffer (pH 7.4) at 37 ± 1°C.

### *In vivo* studies

Rat paw edema produced by carrageenan was inhibited using three sets of six male Wistar albino rats. The volume of the test animal's unilateral hind paw is measured. Before administering the carrageenan, 100 mg of the mixture should be gently massaged into each of the two paws every hour. Place them in mesh-covered cages for topography. Give the paw a subcutaneous injection of 0.1 mL of 1% w/v carrageenan. During the hourly intermission, the hind paw's volume was recorded for 5 h. A mercury plethysmometer can be used for that. Figure out the percentage of inhibition.

### Stability

The item was repeatedly frozen and thawed. A month of heating it at 4°C, 25°C, and 40°C resulted in liquid separation or syneresis. The gel was then allowed to come to room temperature to observe how the liquid detachment occurred.

### Homogeneity

The gel was visually examined to make sure it was homogeneous after being placed in the container. We counted the number of aggregates after examining their appearance.

### Grittiness

To check for visible particulate matter, the formulations were inspected under a light microscope.

| Substance | Gel-forming concentrations (wt%) | Required additives |
|---|---|---|
| Proteins | | |
| Collagen | 0.2–0.4 | |
| Gelatin | 2–15 | |
| Polysaccharides | | |
| Agar | 0.1–1 | |
| Alginates | 0.5–1 | $Ca^{2+}$ |
| | 5–10 | $Na^{-}$ |
| Glycyrrhiza | 2 | |
| Starch | 6 | |
| Tragacanth gum | 2–5 | |

## CONCLUSION

Because gels are more stable and able to provide controlled release compared to other semisolid preparations such as creams, ointments, pastes, etc., they are gaining popularity these days. The gel formulation's enhanced absorption capabilities might make the medication more bioavailable. Long-term stability research may improve the gel's suitability for usage as a therapeutic agent. Because the polymer dissolves in water and forms a washable gel, its potential uses as a topical drug delivery dosage form are increased. Delivering medication topically has the main benefit of

being able to raise high local drug concentrations for better drug action in the tissue and its surrounding areas. When used topically, this is especially helpful for medications with brief biological half-lives and narrow therapeutic windows. Clinical evidence supports the safety and efficaciousness of topical gel as a treatment option for skin-related conditions.

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