IJMPR 2025, 9(4), 68-72

International Journal of Modern Pharmaceutical Research
www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Review Article
SJIF Impact Factor: 6.669

# A REVIEW: PHARMACEUTICAL GELS AND ITS TYPES WITH ROLE OF ITS DRUG DELIVERY SYSTEMS

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**Article Received on: 13/02/2025**
**Article Revised on: 04/03/2025**
**Article Published on: 25/03/2025**

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**ABSTRACT**
The goal of this review was to compile recent literature with a special emphasis on a rational approach to topical formulation and basic components of topical drug delivery systems. Topical drug delivery systems include a wide range of pharmaceutical dosage forms such as semisolids, liquid preparations, sprays, and solid powders. A gelis across linked polymer net work that has swollen in a liquid medium. Its properties are heavily influenced by the interaction of the solid-state polymer and the liquid component. The I.P. defines Gels are homogeneous, semisolid preparations usually consisting of solutions or dispersions of one or more medicaments in suitable hydrophilic or hydrophobic bases. Gels consist of two-phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase and large organic particles are dissolved in the continuous phase, randomly coiled in the flexible chains. Gels are typically formed from a liquid phase that has been thickened with other components.

**KEYWORDS:** Gel, Semi solid, Topical drug delivery systems.

## I. TOPICAL DRUG DELIVERY SYSTEM[1]

Any drug delivery system must deliver a therapeutic dose of medication to the right location in the body in order to quickly reach and then sustain the intended drug concentrations. The therapeutic outcome of a medicine is significantly influenced by the route of delivery. The primary route of topical medication delivery is through the skin, one of the most easily accessible organs on the human body for topical administration.

Topical delivery defined as, the application of a drug-containing formulation to the skin to treat cutaneous disorders (such as acne) or the cutaneous manifestations of a general disease (such as psoriasis),In order to confine the pharmacological or other effect of the drug to the skin's surface or inside the skin, topical delivery is the application of a drug-containing formulation to the skin to treat cutaneous disorders (such as acne) or the cutaneous manifestations of a general disease (such as psoriasis). For topical distribution, semi-solid formulations in all its varieties predominate, but foams, sprays, medicated powders, solutions, and medicated adhesive systems are also used.

- External topical that are applied to the cutaneous tissues by spreading, spraying, orothermeans in order to cover the affected area.
- Internal topicals for local activity, which are given to the mucosal membrane orally, vaginally, or on anorectal tissues.
- External topical that are spread, sprayed ,or otherwise dispersed onto cutaneous tissues to cover the affected area.
- Internal topical that are applied to the mucous membrane orally, vaginally or on anorectal tissues for local activity.

### ADVANTAGES OF TOPICAL DRUG DELIVERY SYSTEM

- Avoidance of first pass metabolism.
- Ability to easily terminate those edications, when needed.
- A relatively large area of application in comparison with buccal or nasal cavity
- Ability to deliver drug more selectively to a specific site.
- Providing utilization of drugs with short biological half-life
- Improving physiological and pharmacological response.
- Improve patient compliance.
- Provide suitability for self-medication

### DISADVANTAGES OF TOPICAL DRUG DELIVERY SYSTEM

- Skin irritation of contact dermatitis may occur due to the drug and/or excipients.
- Poor permeability of some drugs through the skin.
- Possibility of allergenic reactions.
- Can be used only for drugs which require every small plasma concentration for action
- Enzyme in epidermis may denature the drugs

- Drugs of larger particle size not easy to absorb through the skin

## II. GELS

Gels are defined as semi-rigid systems in which the strength of the dispersion medium is limited by the three-dimensional interaction of particles or the solubility of macromolecules in the dispersed phase. The word "gel" is derived from "gelatin", and both "gel" and "jelly" can be traced back to. In Latin gelu means "drop" and gel means freeze or "freeze". This origin shows the basic principle of liquids as solids that do not flow but are elastic and retain some liquid properties. Use of the term "gel" to describe began in the late 1800s, when chemists tried to separate the semisolids of based on their phenomenological properties rather than their molecular composition. The analytical methods required to identify drug samples are not currently available.[10]

Gels are harder than jellies because they have more cross links, higher physical density or simply less liquid. Gel-forming polymers form materials of different hardness, starting from sols to slimes, jellies, gels and hydrogels.

Some gel systems are as clear as water, while others are cloudy because the material is not completely molecularly dispersed (soluble or insoluble) or does not form light-scattering aggregates.

With some exceptions, the concentration of gelling agent is usually less than 10% and is usually in the range of 0.5% to 2%. 0% more.[3]

## III. STRUCTURE OF GELS[4]

The rigidity of a gel arises from the presence of a network formed by the interlinking of particles gelling agent. The nature of the particles and the type of force that is responsible for the linkages, which determines the structure of the net work and the properties of the gel.

The individual particles of the hydrophilic colloid may consist of either spherical or an isometric aggregate of small molecules, or single macromolecules. Possible arrangements of such particles in a gel network are shown in (Figure 1).[5]

In linear macro molecules the net work is comprised of entangled molecules, the point of contact between which may either be relatively small or consist of several molecules aligned in a crystalline order, as shown in Figure 1 (c) and (d), respectively.

The forces of attraction responsible for the linkage between gelling agent particles may range from strong primary valencies, as in silicicacid gels, to weaker hydrogen bonds and Vander Waals forces. The weaker nature of these latter forces is indicated by the fact that a slight increase in temperature often causes liquefaction of gel.

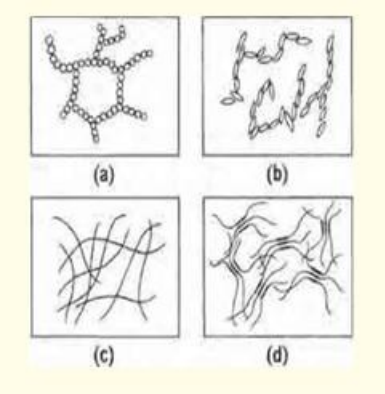



**Figure 1: Representations of gelstructures. (a) Flocculated particles in a two-phasegels tructure. (b) Network of elongated particles orrods forming a gelstructure. (c)Mattedfibersasfoundinsoap gels. (d) Crystalline and amorphous regions in a gel of carboxymethylcellulose.**

## IV. IDEAL PROPERTIES OF TOPICAL GEL[6]

- The gel should be clear and homogenous.
- The gel should be inert in nature.
- The gel should be non-sticky.
- The gel should not interact with any other formulation component.
- The gel should be stable.
- It should be non-irritate to the skin or any part where the gel is applied.
- The viscosity is should be optimum.
- It should have anti-microbial activity.

## V. CHARACTERISTICS OF GELS[7,8]

**Swelling**

The gel expands and absorbs liquid as it increases in volume. This can be considered the initial stage of decomposition. The solvent penetrates the gel matrix so that gel-gel interactions are replaced by gel-solvent interactions. The limited swelling is usually the result of the degree of cross-linking in the gel matrix at around degrees preventing complete dissolution. This gel swells significantly when the solvent mixture has a solubility parameter comparable to that of the gelling agent.

**Syneresis**
Many gel systems shrink when standing. The interstitial liquid is expelled and accumulates on the surface of the gel. This process, called syneresis, is not limited to organic hydrogels, but occurs in both organic and inorganic hydrogels. In general, syneresis becomes more pronounced as the polymer concentration decreases. The shrinkage mechanism of is related to the relaxation of elastic stresses that occur during gel solidification.

**Ageing**
Colloidal systems generally exhibit slow spontaneous aggregation. This process is called aging. In gels, aging causes to gradually form a dense gelling network. Inner showed that the process is similar to the initial gelation process and continues after the initial gelation when the fluid medium of the newly formed gel is lost.

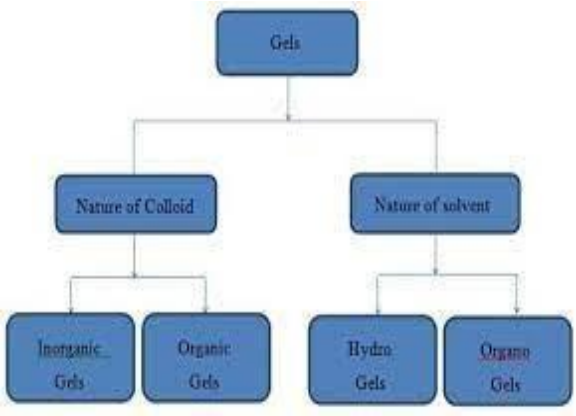
Structure: The rigidity of gels results from the presence of a network of interconnected gelling particles. The nature of the particles and the type of bond strength determine the network structure and properties of the gel.

**Rheology**
Solutions of gelling agents and dispersions of flocculated solids are pseudo plastic, i.e. they exhibit non-Newtonian flow behavior, and is characterized by a decrease in viscosity with increasing shear rate. The elongated structure of inorganic particles dispersed in water is disturbed by the applied shear stress due to the breaking of inter particulate bonds, showing a greater tendency to flow.

Similarly, is used for large molecules, and the applied shear stress aligns the molecules in the direction of the stress, straightening them and reducing the resistance to flow.

## V. CLASSIFICATION OFGELS

Gels can be classified based on colloidal phases, nature of solvent used, physical nature and rheological properties.[9]




### 1. Based On Colloidal Phases

They are classified into:
a. Inorganic(Two phase system)
b. Organic(Single phase system)

**Inorganic (Two-Phase System)**
The system consist of floccules of tiny particles rather than larger molecules and the gel structure will be unstable if the dispersed phase partition size is especially large and develops a three-dimensional structure throughout the gel. They must be thixotropic, which means that when disturbed, they transform from a semisolid to a liquid. Gel made of aluminium hydroxide and bentonite magma are two examples.

**Organic (Single Phase System)**
On the twisted threads, there are large organic molecules that are continuously dissolved. The majority of organic gels are single-phase solutions made up of organic liquids such Plastic base and gelling agents like carbomer and tragacanthin.

### 2. Based on Nature of the Solvent

**Hydrogels: (water based)**
A hydrogel is a three-dimensional network of hydrophilic polymers that can grows in water and contain a significant quantity of water while maintaining their structural integrity due to the chemical or physical cross-linking of individual polymer chains. Hydro philic colloids like silica, bentonite, tragacanth, pectin, sodium alginate, etc. provide an example. The hydrogel may be utilised as an ECG medical electrode, rectal medication delivery system, and sustained release drug delivery system.

**Organogel: (With a non-aqueous solvent)**: A liquid organic phase is contained within a three-dimensional, cross-linked network in an organo gel, a type of gel. The addition of a polar solvent causes the organo gelling or gelation of lecithin solution in organic solvents.

**Xerogels**: Xerogels are solid-formed gels created by allowing materials to gently dry at room temperature while experiencing unrestricted shrinking. Viscous sintering takes place when a xerogel is heated over a certain point, thereby turning the porous gel into a thick glass. Examples include polystyrene, dry cellulose, and tragacanth ribbons. Gels are occasionally categorized as plastic gels, pseudo-plastic gels, and thixotropic gels because they display non- Newtonian flow.

### 3. Based on Physical Nature

**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. Eg.: Alginate and Carbopol.

**Rigid gels**: This can be made from macromolecules with primary valence bonds connecting the framework. Eg.

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.

## VI. GELS CAN BE PREPARED BY FOLLOWING METHODS[10]

1) **Thermalchange:** When the lipophilic colloids (solvated polymers) are exposed to thermal changes, gelatin results. In comparison to cold water, several hydrogen formers are more soluble in heat. When the temperature drops, the amount of moisture decreases and gelatin forms. (A gel will form when a concentrated hot solution is cooled). For examples, cellulose derivatives, gelatin, agar sodium oleate, and guar gum. Some substances, such as cellulose ether, on the other hand, have their water solubility due to hydrogen bonding with the water. These solutions' lower solubility and broken hydrogen bonds will result in gelation when the temperature is raised. As a result, this technique cannot be used as a standard for creating gels.
2) **Flocculation:** Here, gelation is created by adding just the right amount of salt to cause age state precipitation, but not enough to cause complete precipitation. In order to prevent a particular high concentration of precipitant, fast mixing must be ensured. For instance, ethyl cellulose and polystyrene solutions in benzene can be gelled by combining them quickly with the right quantity of a non-solvent, such petroleum ether. Salts cause coagulation and gelation when added to hydrophobic solutions, respectively. The gels created using the flocculation process behave in a thixotropic way. Hydrophilic colloids like gelatin, proteins, and acacia are only impacted by high electrolyte concentrations; typically, the colloidal state becomes "salted out," and gelation is prevented.
3) **Chemical reaction:** Using this technique, the solute and solvent interact chemically to form gel. A higher concentration of the reactants will result in a gel structure, as in the formation of aluminium hydroxide gel by interaction of an aluminium salt and sodium carbonate in an aqueous solution. A few more instances in which the polymeric chain has been cross-linked include PVA, cyanoacrylates with glycidol ether (Glycidol), toluene diisocyanates (TDI), and methane diphenyl isocyanine (MDI).
4) **Fusion method:** In this technique, the medication, vehicles, and gelling agents are all mixed together at high heat until a semi-solid texture is not produced.
5) **Cold method**: All the components, excluding the medication or active pharmaceutical ingredient, are heated and mixed concurrently in this approach. After lowering the formulation's temperature, the drug is added, and the blending process is repeated until the gel has not formed.
6) **Dispersion method**: In this technique, the medication is dissolved in the medium and mixed in while the gelling agentis agitated with water until it begins to swell. If required, add buffer solution to the gel to change the pH.

## VII. EVALUATION PARAMETERS OF THE FORMULATED GELS[11,12]

**Measurement of pH**

The Ph was determined by using a digital pH meter. Dissolve1g of gel in 100ml of distilled water and stored for 2h. done the mea-surement of pH in triplicate and calculate the average values.

**Drug content**

Mixed1g of the gel with 100ml of suitable solvent. Filter the stock solution. Then prepared the aliquots of different concentration by suitable dilutions and measure the absorbance. Drug content was calculated by using the equation, which was got by line arregres-sion analysis of calibration curve.

**Viscosity study**

It is carried out by using Brookfield viscometer. Rotated the gels at 0.3, 0.6 and 1.5 RPM. Note down the corresponding dial reading at each speed. The viscosity was obtained by dial reading × factor given in the Brookfield viscometer catalogues.

**Spreadability**

It indicates the extent of the area to which gel readily spreads on application to the skin or affected part. The therapeutic potency also depends upon spreading value. 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 taken for the separation of two slides, better the spreadabil-ity. The following formula is used to calculate the spreadability:

Spreadability(S)=M×L/TWhere,

M=weight tied to upper slide L = length of glass slides

T=time taken to separate the slides

**Extrudability study**

The formulations are fill in the collapsible tubes, after it was set in the container. Extrudability is determine in terms of weight in gm required to extrude a 0.5 cm ribbon of gel in 10 second.

**Skin irritation study**

For skin irritation study, Guinea pigs (400-500g; either sex) were used. The animals were maintained on the standard animal feed and had free access to water. The animals were kept under standard conditions. Hair was shaved from the back. Five ml of each sample was with drawn 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 as guinea pigs and an area of 4 cm was marked blank on both the sides, one side served as control while the other side was test. The gel was applied (500mg/guinea pig) twice a day for 7 days and the site was observed for any sensitivity and the reaction if any. It was graded as:

| | |
|---|---|
| 0 | No reaction |
| 1 | Minor patch yerythema |
| 2 | Minor but confluent or modest but patch yerythema |
| 3 | Severe erythema with or with out edema |

***In-vitro* Diffusion studies**

It can be carried out in a Franz diffusion cell, for studying the dissolution release of gels through a cellophane membrane. 0.5g of gel sample was taken in cellophane membrane. Carried out the diffusion studies at 37±1° C using 250 ml of phosphate buffer (pH7.4) as the dissolution medium.

***In-vivo* studies**

Inhibition of carrageen an induced rat pawedema: 3groups of 6 male Wistaralbino rats were used.

| Group | Sample |
|---|---|
| 1 | Marketed sample (Reference) |
| 2 | For the test formulation |
| 3 | For control |

Measure the volume of unilateral hind paw test animal. Before the carrageenan administration, rubbed 100 mg of preparation carefully twice at 1 and 2 h on each paw. Placed them in cages with copo graphy meshes. Inject 0.1 ml of 1% w/v carrageen an subcuta-neously in to the paw. The volume of hind paw measured a thourly inter mission for 5h. Use mercury plethysmo meter for that. Calculate the percentage of inhibition.

**Stability**

It was carried out by freeze-thaw cycling. Here, the product to a temperature of 4°C for 1 month, then at 25°C for 1 month and then at 40°C for 1 month, syneresis was observed. Then the gel is exposed to ambient room temperature. Note the liquid exudates separated.

**Homogeneity**

Set the gel in container and then it were tested for homogeneity by visual inspection. They were tested for their appearance and presence of any aggregates.

**Grittiness**

The formulations were evaluated microscopically to check the presence of any visible particulate matter which was seen under light microscope.

## CONCLUSION

The use of pharmaceutical gel getting more popular nowadays because they are more stable and also provide control release than other semi solid dosages forms. The skin is the most accessible part of the body and as such is also highly vulnerable to injuries. In case of cuts, burns and wounds, topical formulations such as gels are the most preferred for treatment. A topical administration system's main advantage is that it avoids first-pass metabolism. Additionally, it offers high patient acceptance. The majority of the time, when another method of medication administration has a lower bioavailability, topical distribution is preferred. The demand of herbal constituents based gels are also increased day by day.

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