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A REVIEW ON GEL AS A RECENT APPROACH FOR TOPICAL DRUG DELIVERY

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ABSTRACT

The basic network of gel is a combination of a gelling agent and water/ solvents in which the drug molecules are embedded/ entwined evenly. The nature of the solvent classify gels into two basic types i.e. organogels and hydrogels. Gel is a thick, clear, slightly sticky substance, especially one used in cosmetic or medicinal products. Gel is applied topically for topical drug delivery system. There are so many advantages of delivering the drug directly to the site of action and acting for a longer period. Skin is one of the most largely spread and easily accessible site on the human body for topical administration and more effective or rapid action. Gel formulation provides better application property and stability in comparison to cream and ointment, many products used topical like ointments, creams and lotions have less disadvantages as they are usually very sticky causing oily skin orgrassy feeling to the patient when applied on skin. Gels are formulated by using methods like Thermal changes, Flocculation, Chemical reaction. Gels are evaluated by following parameters such as pH, homogeneity, grittiness drug content, viscosity, spreadability, extrudability, skin irritation studies, in- vitro release, in Stability.

KEYWORDS: Gel, Topical Administration, Spreadability, Viscosity etc.

INTRODUCTION[1,2,3,4]

Gel is defined semi-solid formulation that is rigid system in which solid or liquid drug easily interrupted in matrix. A gel is a two-segment, cross three-dimensional system comprising of auxiliary materials. Topical drug delivery is easily route of administration for local and systemic treatment. There are drug delivered onto the skin. It has more effective means the therapy for local dermatologic diseases. It can penetrate deeper into skin and enhance the therapeutic effect. Topical application has been many advantages over the conventional dosage forms. In general, it has less toxic effect due to the bilayer composition and structure. In the formulation of topical dosage forms, to ensure adequate percutaneous absorption. Topical formulation avoids the GI-irritation, prevent the metabolism of drug in the liver and increase the bioavailability of the drug. Topical preparations give its action directly at the site of action. A gel is a two-component, cross linked three-dimensional network consisting of structural materials interspersed by an adequate but proportionally large amount of liquid to form an infinite rigid network structure which immobilizes the liquid continuous phase. The structural materials that form the gel network can be composed of inorganic particles or organic macromolecules, primarily polymers. Cross links can be formed via chemical or physical interactions. This leads to gel classification into chemical and physical gel systems, respectively. Chemical gels are associated with permanent covalent bonding while physical gels result from relatively. The U.S.P. defines gels as a semisolid system consisting of dispersion made up of either small inorganic particle or large organic molecule enclosing and interpenetrated by liquid. Gels consist of two phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase.

Anatomy of Skin: The skin is the largest organ of the body. Its large surface area in direct contact with the environment presents tremendous opportunities for drug delivery there are mainly three layer of skin.

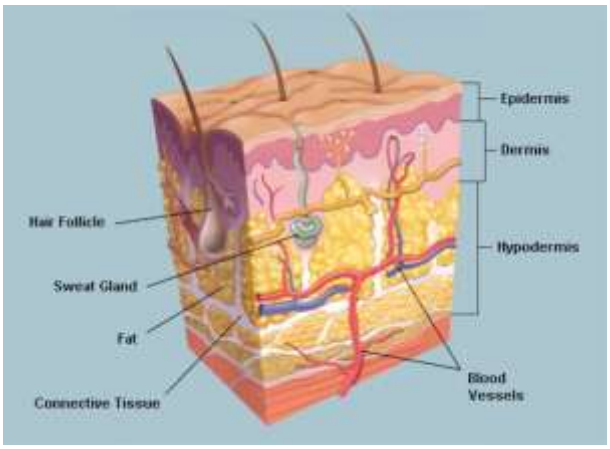

Fig. (1): Skin anatomy.

1. Epidermis
2. Dermis
3. Hypodermis

The highly vascular dermis is made up of a connective tissue matrix containing the nerves, hair follicles, skin contain sweat glands that excrete the sweat from pore. The epidermis is avascular and its outermost layer, the stratum corneum, consists of keratinrich, dead epidermal cells called corneocytes embedded within a lipid rich matrix. The stratum corneum forms the primary barrier for drug permeation especially to watersoluble compounds. Consequently, drug delivery across the stratum corneum has become the essence in the design of many dermal delivery systems.

Advantages of Gel

- Gel can easy to formulate as compared to other semisolid dosage forms.
- A gel is attractive non-greasy formulation.
- It can be used as controlled release dosage form by using the polymer more than once.
- Gels have good adhere property to the site of application.
- It has good bioavailability.
- It has good retention time of gels is higher than other topical dosage forms.
- They are easily washable and nontoxic.
- They produce excellent spreadability and cooling effect.
- They can be used to administer both polar and non-polar drugs.
- They form a protective layer on the application site.
- Meets the highest regulatory and quality requirements.

Disadvantages of gel

- The effect of gels slower orless longer than sustained dosages form
- The additives may produce irritation.
- The water content may increase the chancesof microbial contamination.
- Syneresis (expulsion of solvent from the gel matrix) may occur in gels during storage.
- Solvent evaporation from the formulation may result in dryness of the gel.
- Flocculation in some gels may produce unitability in gel formulation.
- Due to the presence of polymers some drugs may degrade in gel formulation.
- Rheology of some gels may alter because of temperature, humidity and other environmental factors.
- The gelling agents may precipitate and result.

Properties of gel

- The ophthalmic gel should be sterile or clear.
- It should carries suitable anti-microbial to prevent from microbial attack.
- The formulation of topical gel should not be tacky.
- The gelling agent is pharmaceutical or cosmetic use itshould be inert as well as safe.
- It should not be reacting with other excipients.
- It should be easily spread on to the skin.

Uses

- To directly deliver of drug by applied on skin, mucous membrane or the eye.
- It also use as binding agent in tablet granulation, protective colloids in suspensions, thickeners in oral liquid and suppository bases.
- It used incosmetics preparations like shampoos, fragrance products, dentifrices, skin and hair care preparation
- Lubricant for catheters tube.
- NaCl gel for electrocardiography
- Sodium fluoride & Phosphoric acid gel for dental care.

Characteristics of gels[4,5]

- **Swelling:** Gelling agent in combination with liquid that solvates it, then an appreciable amount of liquid is taken up by the agent and the volume increases. This process is called as swelling. This phenomenon occurs as the solvent penetrates the matrix. Gel-gel interactions are replaced by gel solvent interactions. The degree of swelling depends on the number of linkages between individual molecules of gelling agent and on the strength of these linkages.

- **Syneresis:** Several gels often contract suddenly on standing and exude some fluid medium. This effect is recognized as syneresis. The degree to which syneresis occurs, increases as the concentration of gelling agent decreases. The occurrence of syneresis indicates that the original gel was thermodynamically unstable. The mechanism of contraction has been related to the relaxation of elastic stress developed during the setting of the gels. As these stresses are relieved, the interstitial space available for the solvent is reduced, forcing the liquid out.

- **Ageing:** Colloidal systems usually exhibit slow spontaneous aggregation. This method is referred to as ageing. In gels, ageing results in gradual formation of a denser network of the gelling agent.

- **Structure:** The rigidity of a gel arises from the presence of a network formed by the interlinking of particles of the gelling agents. The nature of the particle and the stress, straightening them out and lessening the resistance to flow.

- **Rheology:** Solutions of the gelling agents and dispersion of flocculated solid are pseudo plastic i.e. exhibiting Non-Newtonian flow behaviour, characterized by a decrease in viscosity with increase in shear rate. The tenuous structure of inorganic particles dispersed in water is disrupted by applied shear stress due to breaking down of interparticulate association, exhibiting a greater

tendency to flow. Similarly, for macromolecules the applied shear stress aligns the molecules in the direction of Organic (single phase system).

Polymer used in gel formulation[6,7]

1. Natural polymer

a) Proteins

1. Gelatin
2. Collagen

b) Polysaccharides

i. Alginic acid
ii. Agar
iii. Tragacanth Sodium or Potassium
iv. carrageenan
v. Pectin
vi. Gillum Gum
vii. Xanthine
viii. Cassia tore
ix. Guar Gum

2. Semisynthetic polymers

a) Cellulose derivatives
i. Hydroxyethyl cellulose
ii. Methylcellulose
iii. Hydroxypropyl methyl cellulose
iv. Hydroxypropyl cellulose
v. Carboxymethyl cellulose

3. Synthetic polymers

a) Carbomer
i. Carbopol -941
ii. Carbopol -940
iii. Carbopol -934

b) Poloxamer
c) Polyvinyl alcohol
d) Polyacrylamide
e) Polyethylene and its co-polymers

4. Inorganic substances

a) Bentonite
b) Aluminum hydroxide

5. Surfactants

a) Brij-96
b) Cetostearyl alcohol

Different types of gel

1. Based on colloidal phases

They are classified into
• Inorganic (two phase system)
• Organic (single phase system)

Two phase system: When partial size of the dispersed phase is relatively large and forms the three-dimensional structure throughout gel, such a system consists of floccules of small particles rather than larger molecules and structure, in this system is not always stable. They must be Thixotropic-forming semisolids on standing and become liquid on agitation.

Single-phase system: These consist of bulky organic molecules existing on the twisted strands dissolved in a continuous phase. This larger organic molecule either natural or synthetic polymers are referred as gel formers, they tend to entangle with each other their random motion or bound together by Vander walls forces.

2. Based on nature of solvent

a) Hydro gels (water based): Hydro-gel contains water as their continuous liquid phase.
E.g.: bentonite magma, Gelatin, cellulose derivatives, carpooler, and poloxamer gel.

b) Organic Gels (with a non-aqueous solvent): These contain a non-aqueous solvent on their continuous phase. E.g. pl-astibase (low molecular wt polyethylene dissolved in mineral oil & short Cooled), Olag (Aerosol) gel and dispersion of metallic stearate in oils

c) Xerogels: These are Solid gels with low solvent concentration are known as xerogels. These are produced by evaporation of solvent or freeze drying, leaving the gel framework behind on contact with fresh fluid, they swells and can be reconstituted. E.g. Tragacanth ribbons, acacia tear β-cyclodextrin, dry cellulose and polystyrene.

3. Based on rheological properties: Usually gels exhibit non-Newtonian flow properties.

According to rheological properties they are classified into

a) Plastic gels
b) Pseudo plastic gels
c) Thixotropic gels.
(a) Plastic gels:

E.g.: Bingham bodies, flocculated suspensions of Aluminum hydroxide exhibit a plastic flow and the plot of rheogram gives the yield value of the gels above which the elastic gel distorts and begins to flow.

(b) Pseudo-plastic gels: E.g.: - Liquid dispersion of tragacanth, sodium alginate, Na CMC etc. exhibits pseudo-plastic flow. The viscosity of these gels decreases with increasing rate of shear, with no yield value. The rheogram results from a shearing action on the long chain molecules of the linear polymers. As the shearing stress is increased the disarranged molecules begin to align their long axis in the direction of flow with release of solvent from gel matrix.

(c) Thixotropic gels: The bonds between particles in these gels are very weak and can be broken down by shaking. The resultant solution will revert back to gel due to the particles colliding and linking together again.This occurs in colloidal system with non-spherical particles to build up a scaffold like structure.

E.g.: Kaolin, baronet and agar.

4. Based on physical nature

(a) Elastic gels: Gels of agar, pectin, Guar gum and alginates exhibit an elastic behavior. The fibrous molecules being linked at the point of junction by relatively weak bonds such as hydrogen bonds and dipole attraction. If the molecule possesses free –COOH group then additional bonding takes place by salt bridge of type –COO-X-COO between two adjacent strand networks.

E.g.: Alginate and Carbapol.

(b) Rigid gels:

This can be formed from macromolecule in which the framework linked by primary valance bond.

E.g.: In silica gel, silica acid molecules are held by Si-O-Si-O bond to give a polymer structure possessing a network of pores

Formulation of gel[8]

Gel are prepared by using following methods like

1)Thermal changes

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 reducing, the degree of hydration is reduced and gelatin occurs. When Cooling of a concentrated hot solution will result in the formation of a gel.

E.g.: - Gelatin, agar sodium oleate, guar gummed and cellulose derivatives etc. In contrast to this, some materials like cellulose ether have their water solubility to hydrogen bonding with the water. Raising the temperature of these solutions will disrupt the hydrogen bonding and reduced solubility, which will cause gelation. Hence this method cannot be adopted to prepare gels as a general method.

2)Flocculation: Gelation is produced by adding enough quantity of salt to precipitate to produce age state but insufficient to bring about complete precipitation. It is essential to ensure rapid mixing to avoid local high concentration of precipitant.

E.g.: Solution of ethyl cellulose, polystyrene in benzene can be gelled by rapid mixing with suitable amounts of a non-solvent such as petroleum ether. The addition of salts to hydrophobic solution brings about coagulation and gelation is rarely observed. The gels formed by flocculation method are Thixotropic in behaviour. Hydrophilic colloids such as gelatin, proteins and acacia are only affected by high concentration of electrolytes, when the effect is to “salt out”, the colloidal and gelation doesn’t occur.

3)Chemical reaction: This method involve formation of gel by chemical inter action between the solute and solvent.

E.g.:- aluminum hydroxide gel can be prepared by contact in aqueous solution of an aluminum salt and sodium carbonate an increased concentration of reactants will produce gel structure. Few other examples that involve chemical reaction between PVA, cyanoacrylates with glycidol ether (Glycidol), toluene diisocyanates (TDI), methane diphenyl isocyanine (MDI) that cross-links the polymeric chain.

Evaluation of gel[9]

Homogeneity: formulation of gel has determine some physical parameters and appearance like homogeneity milkyness after the gel formulation settling in the container and aggregation of formulation.

Grittiness: The gel formulations are evaluated microscopically for the presence of particles size if there is no particle observed that can be seen under light microscope. Hence obviously the gel preparation fulfils the requirement of freedom from particular matter and from grittiness as required for any topical preparation.

Viscosity: The determination of gel formulation viscosity by the Brookfield viscometer. The gels have were rotate at 50 rpm using spindle no. 95. At each speed. The reading is note.

Spreadability: Spreadability is evaluate in terms of time in seconds using by two slides to slip off from gel and placed in between the slides under the direction of certain load, lesser the time taken for separation of two slides, better the spreadability.

It is calculated by using the formula

$S = M. L / T$

Where M = weight tied to upper slide

L = length of glass slides

T = time taken to separate the slides.

Skin Irritation test: for the irritation test determination the wister rat is use and weight is required 150-200 of a rat.gel is applies on the back side of rat where applies hair are removed.gel is applie intack of askin continuously seven day and determine the erythema edema.

Stability study: For the evaluation of stability study, gel formulation are put into the stability chamber maintain condition over a period of three months.

Applications[10,11]

Many substances can form gels when a suitable thickener or gelling agent is added to their formula. This approach is common in manufacture of wide range of products, from foods to paints and adhesives. In fiber optics communications, a soft gel resembling "hair gel" in

viscosity is used to fill the plastic tubes containing the fibers. The main purpose of the gel is to prevent water intrusion if the buffer tube is breached, but the gel also buffers the fibers against mechanical damage when the tube is bent around corners during installation, or flexed. Gel is used for the treatment of following diseases.

- Acne
- Bedbugs
- Cold Sores
- Eczema
- Fungal Infections
- Hair Loss
- Healthy Beauty
- Lice
- Psoriasis
- Psoriatic Arthritis
- Poison Ivy
- Shingles
- Skin Cancer

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