International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 30-10-2021, Accepted: 16-11-2021, Published: 01-12-2021
Volume 6, Issue 6, 2021, Page No. 1-6

Review on gel– A semisolid dosage form

P Rajalakshmi[1*], M Sakthivel[2], B Prathap[3], R Saranya Devi[4], R Rasiga[4]

[1] Associate Professor, Department of Pharmaceutics, Dhanalakshmi Srinivasan College of Pharmacy, Perambalur, Tamil Nadu, India

[2] Professor, Department of Pharmaceutics, Dhanalakshmi Srinivasan College of Pharmacy, Perambalur, Tamil Nadu, India.

[3] Principal, Dhanalakshmi Srinivasan College of Pharmacy, Perambalur, Tamil Nadu, India

[4] Department of Pharmaceutics, Dhanalakshmi Srinivasan College of Pharmacy, Perambalur, Tamil Nadu, India

Abstract
Gels are getting popularity nowadays when compared with other semisolid dosage form like ointments, creams, lotion and pastes due to their stability and controlled release. Stability of drug and better absorption can provide by gel formulation. Gels formulation are substitute for oral route of administration and avoid first pass metabolism. Topical gels are intended for skin application, to certain mucosal surfaces for local action or percutaneous penetration of medicament, for their emollient or protective action. Topical drug delivery has advantage such as applying the drug directly into the skin and it also provides prolonged action on the targeted site. Gels are evaluated by following parameter such as pH, homogeneity, grittiness, drug content, viscosity, spreadability, extrudability, skin irritation studies, invitro and stability study. This review includes deep immense on fundamental advantage of gel formulation over other semisolid preparation and also other aspects like terms, characteristic, classification, preparation, mechanism, evaluation and applications of gel formulation.

Keywords: gels, imbibition, swelling, syneresis, thixotropy

Introduction

Semisolid dosage forms are the topical dosage form which is used for the therapeutic, protective or cosmetic functions. The dosage form was administrated through the skin, ophthalmic, nasal, vaginal or rectal route. Examples of semi-solid dosage forms are Ointments, pastes, cream, lotion and gels. They act as carriers for drugs that are topically delivered by way of the skin, ophthalmic, rectal tissue, nasal mucosa, vagina, buccal tissue, urethral membrane and external ear lining. A semisolid dosage form is advantageous in terms of its easy application, rapid preparation and capable to topically deliver a large variety of drug molecules. Topical semisolid dosage forms are normally presented in the form of creams, gels, ointments or paste. It contain one or more active ingredients uniformly dissolved in a suitable base and any suitable excipients such as emulsifiers, viscosity enhancing agents, anti-microbial agents, antioxidants, or stabilizer.

Ointments are semisolid preparations for external application to skin or mucous membranes. The ingredient softens but does not melt upon application to the skin. Therapeutically, ointments act as a skin protectives and moisturizer, but they are used as vehicles for the topical application of drug substances. Creams are semisolid dosage forms that contain one or more drug substances dissolved in a suitable base, usually oil in- water emulsion or aqueous microcrystalline dispersion of long- chain fatty acids or alcohols that are water washable. Pastes are semisolid dosage forms that consist of one or more drug substances absorb in a base with large quantity of finely dispersed solids.

A large range of raw materials is available for the preparation of a semisolid dosage form. Apart from the normal pharmaceutical ingredients such as antimicrobial agent, antioxidants, and solubilizers the basic ingredients of a semisolid dosage form are special to its composition. The choice of suitable raw materials is made on the basis of the drug delivery requirements and the particular need to impart sufficient emolliency or other quasi-medicinal qualities in the formulation. In general, semisolid dosage forms are complex formulations having complex structural elements. Often they are composed of two phases (oil and water), one of which is a continuous (external) phase, and the other of which is a dissolved (internal) phase.

The active ingredient is often dissolved in one phase, although sometimes the drug is partially soluble in the system and is dispersed in one or both phases, thus creating a three-phase system. The physical properties of the dosage form depend upon various factors, including the size of the dispersed particles, the interfacial tension between the phases, the partition coefficient of the active ingredient between the phases, and the product rheology. These factors combine to identify the release characteristics of the drug, as well as other characteristics, such as viscosity. [4]

Advantage of semi-solid dosage form [4]

- It is used externally
- possible side effect can be reducing
- Local action
- Suitable dosage form for bitter drugs
- First pass gut and hepatic metabolism is avoided.
- Patient compliance is increased; the drug termination is problematic cases is facilitated as compared with other routes of drug administration. [4]

Disadvantages of semi-solid dosage form [4]

- There is no dosage accuracy in this type of dosage form. The base which is used in the semi-solid dosage form can be easily oxidized.
- May cause irritation or allergy to some patients [4]

GELS [3]

The word "gel" is derived from "gelatin" and both "gel" and "jelly" can be derived from the Latin gelu for "frost" and gel are meaning "freeze" or "congeal". This origin indicates the essential idea of a liquid setting to a solid like material that does not flow, but is elastic and remains some liquid characteristics.

The USP defines gel as a semisolid system containing either suspensions made up of small inorganic particles, or large organic molecules diffuse by a liquid. The gel mass consists of networks of small separate particles, the gel is classified as a two phase system. In a two phase system, if the particle size of the dispersed phase is comparatively large, the gel mass is sometimes called as magma. Single-phase gels consist of organic macromolecules uniformly circulated throughout a liquid in such a way that no apparent boundaries occur between the dispersed macromolecules as the liquid.

Some gel systems are as clear as water and others are muddy because the ingredients partially molecularly dispersed [soluble or insoluble] or they may form aggregates, which disperse light. The concentration of the gelling agents is mostly less than 10 % usually in 0.5% to 2.0% range, with some exceptions [3]

Fig 1: GEL

Terms Related To Gel [3]

A number of terms are commonly used in some of the characteristics of gels, including

- Imbibition
- Swelling
- Syneresis
- Thixotropy
- Xerogel

Imbibition

Imbibition is the use of a fixed amount of liquid without a measurable increases the volume.

Swelling

Swelling is using of a liquid by a gel with increases the volume. Only liquids that diffuse a gel can cause swelling. The swelling of protein gels is determined by pH and the presence of electrolytes.

Syneresis

Syneresis occurs when the interaction between particles of the dispersed phase becomes so great that on standing, the dispersing medium is express in droplets and the gel shrinks. It is a form of not able to predict in aqueous and non-aqueous gels. Dissociation of a solvent phase is perception to occur because of the elastic contraction of the polymeric molecules; in the swelling process during gel preparation the macromolecules become expand and the elastic forces increase as swelling proceeds. At equilibrium the restoring force of the macromolecules is evaluate by the swelling forces determined by the osmotic pressure. If the osmotic pressure decreases as a cooling, water may be squeezed out of the gel.

Thixotropy

Thixotropy is a reversible gel – sol formed with no alteration in volume or temperature, a type of non-Newtonian flow.

Xerogel

Xerogel is formed in the liquid that is eliminating from the gel and only their frame work remains. E.g.: Gelatin sheets, tragacanth ribbons, acacia tears, etc. [3]

Properties [3]

- Ideally, the gelling agent must be inert, safe and cannot react with other formulationconstituents.
- The gelling agent should produce a sensible solid-like nature at the time of storage which is easily broken when exposed to shear forces produced by squeezing the tube, trembling the bottle or at the time topicalapplication.
- It should possess suitable antimicrobial activity against microbial attack.
- The topical gel must not besticky.
- The ophthalmic gel must besterile.
- The apparent viscosity or gel strength increases with an increase in the effective crosslink density of the gel. However, a rise in temperature may increase or decrease the apparent viscosity, depending on the molecular interactions between the polymer andsolvent.
- They exhibit the mechanical characteristics of the solid state.
- Each component is continuous throughout thesystem.
- There is high degree of attraction amongst the dispersed phase and water medium so the gels remain equally uniform upon standing and doesn't freely settle. [3]

Structure of Gels [1]

A gel contains a natural or synthetic polymer establish a three dimensional matrix all over a dispersion medium or hydrophilic liquid. After application, liquid evaporate leaving the drug entrapped in a thin film of the gel –forming matrix physically converting the skin. The presence of a network formed by interlocking of particle of gelling agent gives rise to the rigidity of a gel. The nature of the particle and type of form that is responsible for the linkages determine the structure of the network and the property of the gel. [1]

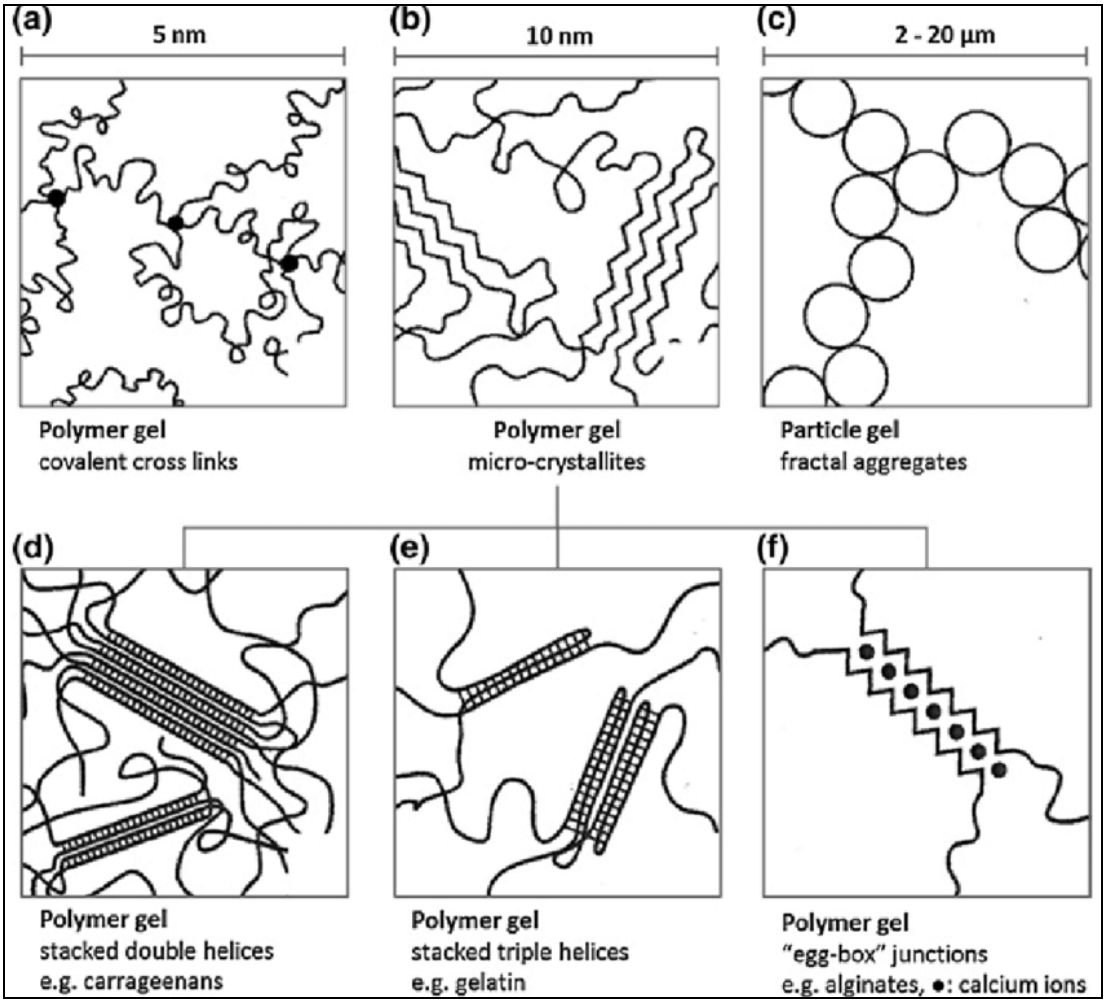

Fig 2: Types and scales of gel structures, showing various types of gel junctions [9]

Classification of Gels [2]

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

Based on colloidal phases

They are classified into inorganic [two phase system] type of force that is responsible for the linkages find out the structure of the network and the properties of the gel.

Two phase system

If particle sizes of the dispersed phase are moderately large and form the three dimensional structure all over gel, such a system consists of floccules of small particles rather than larger molecules and gel structure, in this system is not always stable. They must be thyrotrophic-forming semisolid on standing and become liquid on trouble.

Single phase system

These consist of large organic molecules existing on the twisted strands dissolved in a continuous phase. This larger organic either natural or synthetic polymer are mention as gel formers, they tend to twist with each other their random motion or bound together by Vander Waals forces [2].

Based on nature of solvent

Hydro gels (water based)

They contain water as their continuous liquid phase. E.g. bentonite magma, gelatin, cellulose derived from carpooler and poloxamer gel.

Organic gels (with a non-aqueous solvent)

This contains a non-aqueous solvent on their continuous phase. E.g. plastibase (low molecular wt. Polyethylene dissolved in mineral oil & short cooled) Olag (aerosal) gel and dispersion of metallic stearate in oils.

Xerogel

Solid gels with low solvent concentration are known as Xerogel. These are produced by evaporation of solvent or freeze drying, leaving the gel frame work behind on contact with fresh fluid; they swell and can be reconstituted. E.g. Tragacanth ribbons, acacia tear beta cyclotdextrine, dry cellulose and polystyrene [2].

Based on rheological properties

Usually gels shows an non-Newtonian flow properties

They are classified into,

a. Plastic gels
b. Pseudo plastic gel
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 twist and starts to flow.

(b) Pseudo plastic gels

E.g. Liquid dispersion of tragacanth, sodium alginate, Na

CMC etc. is exhibit 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 start 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 resulting solution will return back to gel due to the particle colliding and connect together again (the reversible isothermal gel-sol-gel transformation). This occurs in colloidal system with non-spherical particles to build up a scaffold like structure. E.g. kaolin, Bentonite and agar [2].

Based on physical nature

(a) Elastic gels

Gel of agar, pectin, guar gum and alginates are exhibiting an elastic character. The fibrous molecules are being linked at the point of junction by enough 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 groups.

(b) Rigid gels

This can be formed from macromolecule in which the frame work linked by primary valence bond. E.g.: In silica gel, Silica acid molecules are held by Si-o-Si-o bond to give a polymer structure have a network of pores [2].

Preparation of Gels [7]

Gels are normally in the industrial scale prepared under a room temperature. through few of polymers need special treatment before process.

Gels can be prepared by following methods

- Thermal changes
- Flocculation
- Chemical reaction [7]

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. (Cooling of a concentrated hot solution will produce a gel). E.g.: -Gelatin, agar sodium oleate, guar gummed and cellulose derivations 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.

Flocculation

Here gelation is produced by adding just sufficient quantity of salt to precipitate to produce age state but insufficient to bring about complete precipitation. It is essential to ensure quick mixing to avoid local high concentration of precipitant. E.g.: solution of ethyl cellulose, polystyrene in benzene can be gelled by quick mixing with suitable amounts of a non-solvent such as petroleum ether. The adding of salts to hydrophobic solution brings about coagulation, gelation is infrequently 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

Chemical Reaction

IN this method gels are formed by chemical interaction between the solute and solvent. E.g.: aluminium hydroxide gel can be prepared by interchange in aqueous solution of an aluminium salt and sodium carbonate an increased concentration of reactants will produce a gel structure. [7]

Table 1: Gelling Concentrations for Substances Used In Pharmaceutical Products

Substances	Gel-forming concentrations
Collagen	0.2-0.4
Gelatin	2-15
Agar	0.1-1
Alginates	0.5-1
K-carrageenan	1-2
Gellum gum	0.5-1
Carboxy methyl cellulose	4-6
Hydroxyl propyl cellulose	8-10
Hydroxyl propyl methylcellulose	2-10
Aluminium hydroxide	3-5
Bentonite	5
Laponite	2
Poloxamer	15-50

Mechanism of gel formation [5]

Gels are formed via three types of cross linking

- chemical cross-linking
- physical cross – linking
- ionic cross- linking

Chemical Cross-Linking

Chemical cross-linkage is found also with polymer possessing bonded group in their assembly. When cross-linkage compounds are bringing together such polymers cause an irreversible reaction among the added compound and free group. After attaining a specific concentration viscosity increases in this type of reaction and results in gel formation. Eg: Polyacrylic acid (with multiple carboxylic acid)

Physical Cross- Linking

By hydrogen bond formation solution to gel transition can be obtain also in cases like concentration variation, temperature variation transition, crystalline component solubilisation. Physical cross-linking is shown in Eg: Cellulose gels, Dextran gels.

Ion Cross- Linking

Here cross-connecting occur by making charge on polymer(S) or different particles (Solvent) that attract one another resulting in gel. Charges on the molecules result in Ionic bonds formation. Eg: Polysaccharide alginate produce gel matrix in company of calcium ions result in gel matrix of calcium ions result in gel matrix that encapsulates some compounds (enzymes). [5]

Evaluation Parameters of Gel [5]

- Measurement of pH
- Drug content
- Viscosity study
- Spread ability
- Extrudability study
- Skin irritation study
- In-vitro dissolution studies
- Stability
- Homogeneity
- Grittiness

Measurement of Ph

PH can be determined by using digital pH meter.

Drug Content

Mix 1g of the gel formulation with 100 ml of suitable solvent. Filter the stock solution. Then prepared the aliquots of different concentration by suitable dilutions and measure the absorbance. Linear regression analysis of calibration curve is used to calculate the drug content [6].

Viscosity Study

It is carried out by using Brookfield viscometer. Rotate 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 spreadability. The following formula is used to calculate the spreadability:

Spreadability (S) = M × L / T

Where,
M = Weight tied to upper slide
L = Length of glass slides
T = Time taken to separate the slides

Extrudability Studies

The formulations are filled 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 Test

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 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 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 (500 mg/ 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**.**

Table 2

0	**No reaction**
1	Minor patchy erythema
2	Minor but confluent or modest but patchy erythema
3	Severe erythema with or without edema

***In-Vitro* Diffusion Studies**

It is done by using Franz diffusion cell to determine the dissolution release of gels through a cellophane membrane. 0.5 of gel sample occupied in cellophane membrane. Diffusion studies were done at 37±1°C using pH buffer (pH7.4) 250 ml as dissolution medium.

***In-Vivo* Studies**

It is done in 6 male Wister albino rats divided into 3groups. Rubbing 100mg of prepared gel carefully twice at 1 and 2 h on each paw and calculate the percentage of inhibition by using mercury plethysmo meter**.**

Stability

It is done by freeze-thaw cycling. The products are kept under temperature of 4°c for 1 month again 25°C for 1 month and next at 40°C for one month, and syneresis have being detected. The gels are kept under room temperature and find the liquefied exudates separately. [5]

Application of Gel [3, 5]

- Used in soft and hard gel pills.
- Preparation of suppositories e.g. -glycerine in suppositories BP.
- Gels are used to prepare continuous release formulation.
- Used for drug administration to various routes such as, topical, intranasal, ophthalmic, vaginal, rectal and intramuscular and parenteral in some cases.
- They are largely used in food industry.
- Phosphoric acid and sodium fluoride gels used in dental care.[6]
- As drug delivery systems for orally administered drugs.
- To deliver topical drug applied directly to the skin, eye or mucous membrane.
- Gels are used in cosmetics like shampoos, fragrance products, dentifrices, skin and hair care preparations.
- Sodium chloride gels are used in electrocardiography.
- Sodium fluoride and phosphoric acid gel are used for preventive dental care. [3]

Advantage [5]

- Gels are effortless to prepare when compare to other formulation.
- Gel is elegant, non – greasy formulation.
- Gels are having outstanding sticky property to application site.
- Gels are biocompatible and biodegradable.
- Have magnificent tolerability to stress condition.[5]

Disadvantage [5]

- Effect of gels is proportionally sustained and slower.
- The gelators or excipients may cause irritation on application site.
- Moisture content improves possibility of fungal or

microbial attack in gel.
- Solvent loss from the preparation dries of gel.
- Flocculation in some gel causes an unsteady gel [5].

Table 3: Marketed Available formulations of Gel

Product name	Generic name	Uses
Timoptic-XE	Timolol maleate	Reduce pressure inside the eyes
Akten TM	Lidocaine hydrochloride ophthalmic gel	Relives pain
Pilopine HS	Pilocarpine hydrochloride	Used to treat glaucoma
Volini	Diclofenac Diethyl amine	Relives pain
Ampho gel	Aluminium hydroxide	Heart burn and acid indigestion
Spectazole	Econazole nitrate	Anti-fungal
Regranex gel	Becaplermin	Dermatologic
Desquamate-X GEL	Benzoyl peroxide	Acne vulgaris
Acsi-gel	Magnesium hydroxide	Maintenance of acidity
Termovate Gel	Clobetasol propionate	Relief of inflammation
Metro-Gel	Metronidazole	Treat bacterial infection
Retin- A	Tretinion cellulose	Acne vulgaris

Conclusion

The study clearly revealed about the detailed view on gel formulation including it types, preparation, mechanism involved in gel formation and their Evaluation. Gels are getting more popular nowadays because they are more stable and also can provide controlled release than other semisolid preparations like creams, ointments, pastes, etc. The gel preparation can gives a better absorption and enhance bioavailability of the drug.

Reference

1. Ashni Verma, Sukhdev Singh, Rupinder Kaur, Upendra K Jain. Topical gels as drug delivery system. International journal of pharmaceutical science review and research,2013:23(2):374-382.
2. Loveleen Preet Kaur, Tarun Kumar Guleri. Topical gel. Asian journal of biomedical and pharmaceutical sciences,2013:3(17):1-5.
3. Hemendrasinh J Rathod, Dhruti P Mehta. Acta Scientifica International journal of pharmaceutical science,2015:1(1):33-47.
4. Md. Amman Maqbool, manoj Kumar mishra, supriya pathak,adarsh kesharwani, anuradha kesharwani. Indo American journal of pharmaceutical research, 2017, 7(11).
5. Suchithra ABS, Jeganath E. Jeevitha. Pharmaceutical gels and recent trends-A review,2019:12(12):6181-6186.
6. PB Patil, Datir SK, Saudagar RB. Journal of drug delivery and therapeutics,2019:9(3-s):989-994.
7. Abhishek Soni, Dr. Amit chaudhary, Dr.shivali singla, Dr. sachin goyal. Review on novel approach in pharmaceuticalgel,2019:8(6):429-435.
8. https://www.slideshare.net/laithalasadi/semi-solid-dosage-form-68119310 https://www.google.co.in/imgres?imgurl=https%3A%2F%2Fimg.khoobsurati.com%2Fwp-content%2Fuploads%2F2021%2F05%2FSide-Effects-of-Hair-Gels.jpg&imgrefurl=https%
9. searchgate.net/figure/Types-and-scales-of-gel-structures-showing-various-types-of-gel-junctions-Redrawn-from_fig6_301268765