A REVIEW ON PHARMACEUTICAL GELS

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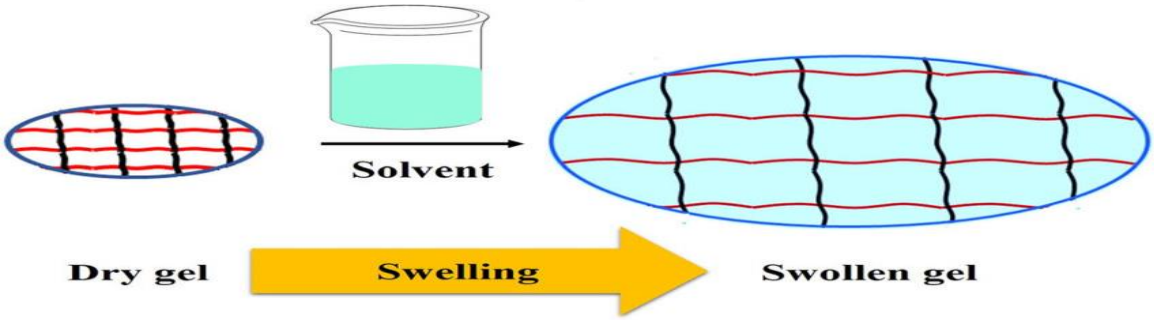
ABSTRACT

The purpose of writing this review was to compile the recent literature with a special focus on a rational approach to topical formulation and basic components of topical drug delivery systems. Topical applications of drugs have advantages of delivering the drug directly to the site of action and acting for a longer period of time. A gel is colloid that is typically 99% by weight liquid, which is immobilized by surface tension between it and a macromolecular network of fibers built from a small amount of a gelatinous substance present. Skin is one of the most widespread and readily accessible organs on the human body for topical administration and is the main route of topical drug delivery system. A gel is a cross-linked polymer network that has swollen in a liquid medium 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.

KEY WORDS: *Pharmaceutical gels; Terminologies; Classification; Preparation; Evaluation of Gels; Patent; methods :Topical drug delivery system .*

INTRODUCTION:

Gels are semisolid preparations intended for application on the skin or the accessible mucous membranes like oral cavity. Gels are composed of two interpenetrating systems where the colloidal particles, also known as the gelatos or gallant, are uniformly distributed throughout a dispersion medium or solvent forming a three-dimensional matrix known as the gel. The reversible gels are generally hydrogen bonded systems whereas irreversible gels are usually covalently bonded. A gel may either appear as a single system with no apparent boundaries or as a two-phase system with floccules of discrete particles. The gels are formed using synthetic polymers such as Carbomcelluloses such as hydroxypropyl cellulose and hydroxypropyl methylcellulose, Tragacanth gum, pectin and natural agars gum are used in the gel formulation.



FIGURE;1: Swelling of gelling agent in solvent.

GELS:

Gels are attractive delivery systems as they are simple to manufacture and suitable for administering drugs through skin, oral, bucal, ophthalmic, nasal, otic, and vaginal routes. Gels are semisolid preparations that contain small inorganic particles or large organic molecules interpenetrated by a liquid. In a typical polar gel, a natural or synthetic polymer builds a three-dimensional matrix throughout a hydrophilic liquid.

FIGURE; 2: Gels

ADVANTAGES OF GELS:

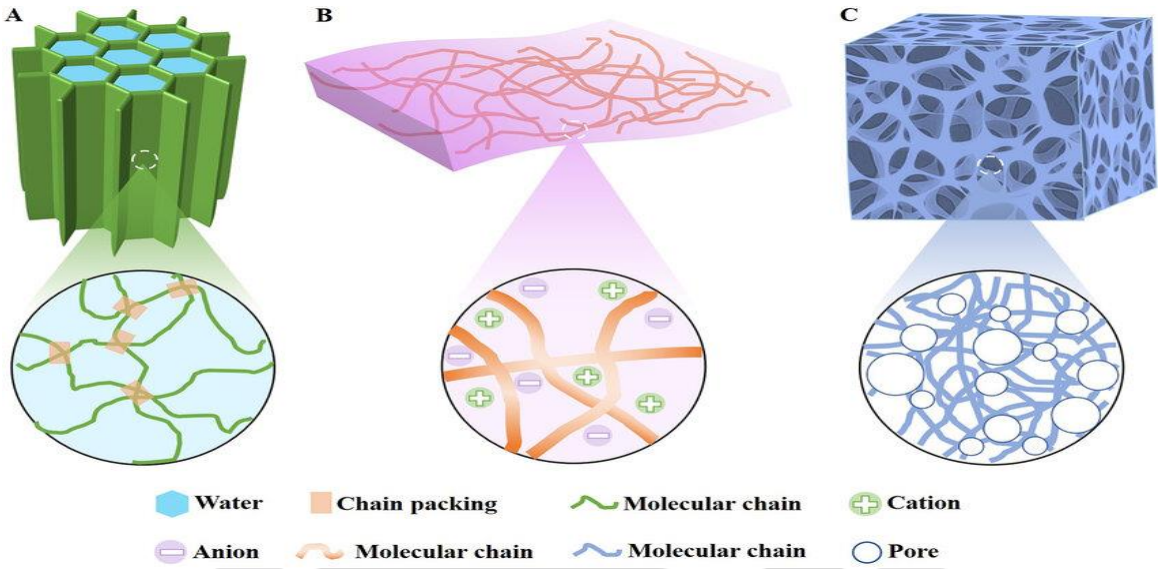
- they are easy to create with active substances and have a non-greasy application.
- Non-toxic and easily washable.
- By passing via the digestive system, undesired side effects are avoided.
- It is simple to disseminate.
- Retention of the skin
- It has a calming effect on the skin.

DISADVANTAGES OF GELS

- There was a chance of having an allergic reaction
- Gels have a slower onset impact.
- The gel's additives may irritate the skin.
- Reactions at the application location must be observed.
- Temperature, humidity, and other environmental conditions may have an influence on effectiveness.
- Some medications are difficult to absorb through the skin.

STUCTURE OF GELS:

A gel consists of a natural or synthetic polymer forming a three-dimensional matrix throughout a dispersion medium or hydrophilic liquid. As soon as the liquid is applied, it evaporates, leaving the medication contained in a thin layer of the gel-forming matrix that physically covers the skin.

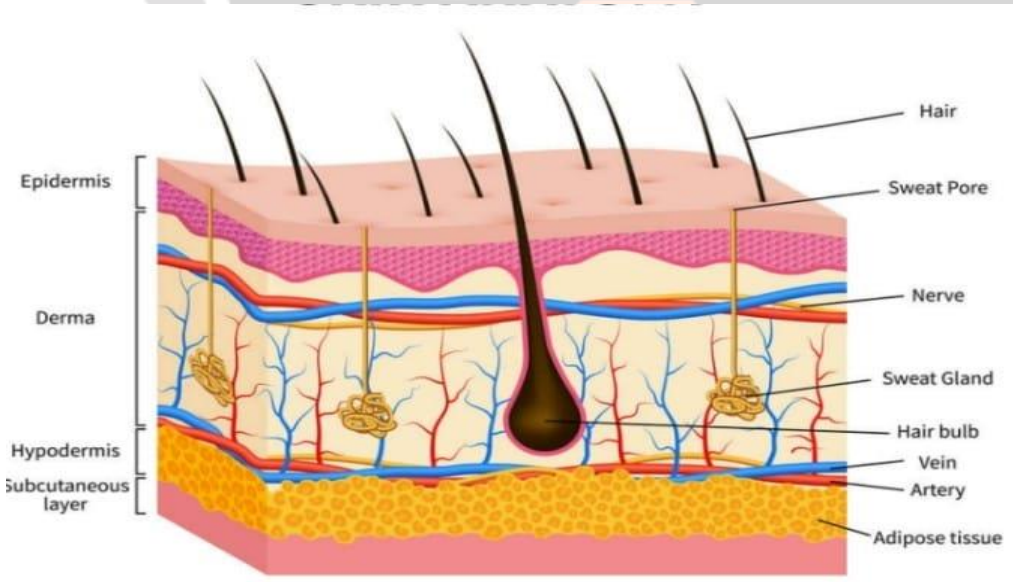


FIGURE; 3: STRUCTURE OF GELS

TOPICAL GELS OF DRUG DELIVEY SYSTEM:

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 .The human skin is organized into two distinct layers, namely the epidermis and dermis directly beneath. The highly vascular dermis is made up of a connective tissue matrix containing the nerves, hair follicles, pilosebaceous units and sweat glands.



FIGURE; 4ANATOMY OF THE SKIN

EPIDERMIS:

Epithelial cells that forms the epidermis. Both live and dead cells can be detected among these cells. The older cells are pushed forward by the younger cells at the bottom of the epidermis, which divide quickly. There are no direct blood vessels that supply nutrients to the epidermis.

DERMIS:

The dermis, which lies beneath the epidermis, is distinguished by a dense network of fibers that gives the skin its ability to stretch and a dense network of collagen that gives the skin its strength. The dermis is crucial for monitoring body temperature. There are nerves that provide pressure and pain feelings. The dermis is 3 to 5 mm thick.

HYPODERMIS:

The innermost layer of skin is known as the hypodermis. It is the layer of skin that has contact with the body's deeper tissues, such muscles and bone. Sebaceous glands, sweat glands, and hair follicles all originate in the dermis but are enclosed in the epidermis.

Factors affecting topical absorption of drug:

The factors that affect the topical absorption of drug are as follows;

- Physiological factors.
- Skin thickness.
- Lipid content.
- Density of hair follicles.
- Density of sweat glands.
- Skin pH.
- Blood flow.
- Hydration of skin.
- Inflammation of skin.
- .Physiochemical factors.
- Molecular weight Partition coefficient.

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.

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 collusions (salicylic acid collusions), and other topical liquids are examples.

Creams: Creams are emulsions of oleaginous substance(s) and water that spread more quickly than ointments over the skin.

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

Terminologies Related to Gels:

A number of terms are commonly used in discussing some of the characteristics of gels, including imbibitions, swelling, syneresis, thixotropy, and Xerogels.

Imbibitions: Is the taking up of a certain amount of liquid without a measurable increase in volume.

Swelling: Is taking up of a liquid by a gel with a rise in the volume

Syneresis happens when the interaction between particles of the dispersed phase becomes so great that on standing, the dispersing medium is pressed out in droplets and the gel shrinks.

Thixotropy: Is a reversible gel-sol formation with no change in volume or temperature, a type of non-Newtonian flow.

Xerogels: Is formed when the liquid is removed from a gel and only the framework remains. E.g., Gelatin sheets, tragacanth ribbons, acacia tears, etc.

Materials use for preparation of gels:

- Aqueous material: Commonly used agents e.g. water, alcohol.
- Gelling agent: The thickness of the formulation is increased by using a gel forming agent. This is where carbopol 934, crabapple 940, and hydroxyl propyl methyl cellulose (HPMC) come in handy.
- Preservatives: e.g. Propyl paraben, methyl paraben, benzoic acid, benzyl alcohol etc.
- Humectant: e.g. Glycerine, Propylene glycol.

IDEAL CHARACTERISTICS OF GELS:

Ageing: Colloidal systems usually show slow aggregation naturally. This process is known as ageing. In gels, ageing causes gradual formation of a denser network of the gelling agent.

Rheology: Solutions of the gelling agents and dispersion of flocculated solid are pseudo plastic in nature, i.e. follow NonNewtonian flow behavior, characterized by a reduction in viscosity with increase in shear rate.

Gel Uses:

1. As an oral drug delivery system.
2. External preparations intended for direct application to the skin, mucous membranes or eyes.
3. A long-acting form of the drug that is injected into a muscle or implanted in the body.
4. Binders in tablet granulation, protective colloids in suspensions, thickeners in oral liquids and suppository bases.

CLASSIFICATION OF GELS:

- **Gels can be classified:**
- **based on colloidal phases:**

- nature of the solvent used
- physical nature and
- rheological properties,etc

Based on Colloidal Phases:

They are classified into:

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

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. Examples are aluminum hydroxide gel and betonies magma.

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.

Based on Nature of the Solvent:

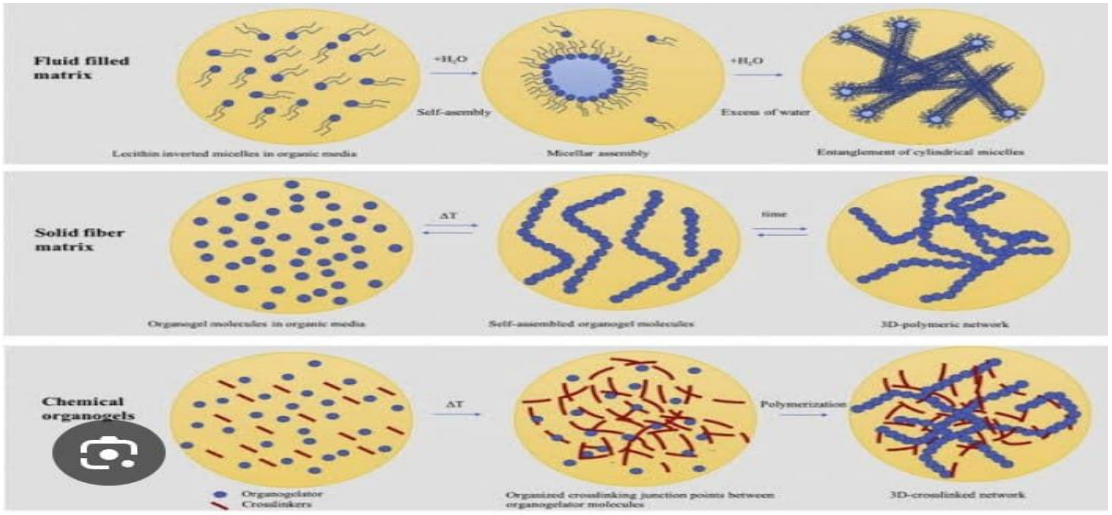
Hydro gels :(water based):

A hydrogel is three-dimensional networks 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.

FIGURE; 5: Hydro gels

Organ gel: (With a non-aqueous solvent):

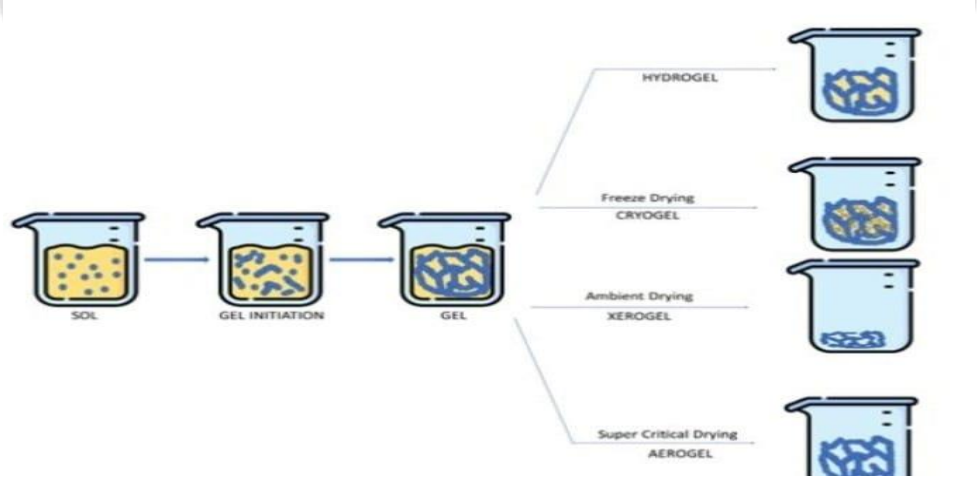
A liquid organic phase is contained within a three-dimensional, cross-linked network in an organ gel, a type of gel



FIGURE; 6: ORGANOGELS

Xerogels:

Xerogels are solid-formed gels created by allowing materials to gently dry at room temperature while experiencing unrestricted shrinking.



FIGURE; 7: XEROGELS

Based on physical nature:

Elastic Gels:

Gels like agar, pectin, guar gum, and alginates possess elastic properties. Fibrous molecules• are connected at junction points through relatively weak interactions like hydrogen bonds and dipole attraction.

If Rigid Gels: These gels are formed from macromolecules with primary valence bonds connecting the framework.

Based on rheological properties:

Generally, gels exhibit non-Newtonian flow properties.

They are classified as:

. Plastic gels: The Bingham body sees plastic flow as aluminum hydroxide, Flocculated suspensions, such as tragacanth gum, sodium alginate and sodium CMC dispersions, is the so-called plastic flow and the rheogram gives the results of the gel on which elastic Gel will deform and begin to flow.

Pseudo plastic gel: The viscosity of these gels decreases with increasing shear rate and has no yield value. The rheogram is given by cutting the length of the molecular chain of the linear polymer. As shear stress increases, solvent is released from the gel matrix as the chaotic molecules begin to align their long axes downstream.

Thyrotrophic Gels: The bonds between particles in these gels are so weak that can be broken by shaking. When particles collide and reconnect (reverse isothermal gel-sol-gel transition) the solution will return to the gel. For example kaolin, betonies, agar etc.

Method of preparation of gels:

Fusion Method:- In this method, vehicles, gelling agents, additives, and the drug are blended at high temperatures until a semi-solid texture is formed.

Cold Method:- In this approach, all components except the drug or active pharmaceutical ingredient are heated and blended simultaneously. The temperature of the formulation is then lowered, the drug is added, and blending continues until the gel is formed.

Dispersion Method: - In this approach, the gelling agent is stirred with water until it swells up. The drug is then dissolved in the medium and incorporated into the swollen gelling agent

Formulation design:

Gel forming agent or polymer:

r• Drug Substance

- Penetration Enhancers

Gel forming agent or polymer:

These agents increase the viscosity of a liquid substance without substantially altering other properties like taste . The addition of a gelling agent to certain formulations results in a gelled structure.

Drug Substance Physicochemical Properties:

The drug should possess a molecular weight of less than 1000 Daltons.

It should exhibit an affinity for both lipophilic and hydrophilic phases.

Biological Properties:

Penetration Enhancer Penetration enhancers are substances designed to enhance the drug's ability to penetrate the skin. Formulations often include ingredients that temporarily disrupt the highly ordered structure of the stratum corneum skin barrier.

Properties of Permeation Enhancer:

Permeation enhancers must be non-toxic, non-irritating, and non-allergenic

MECHANISM OFGEL FORMULATION:

Gels consist of three types of cross links,

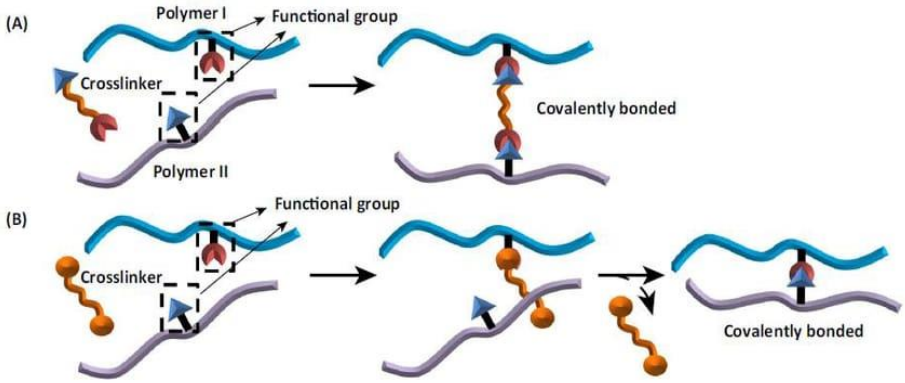
a) Chemical crosslink

b) Physical cross links

c) Ionic crosslinking

a)Chemical crosslinking:

Chemical crosslinking is also found there in the assembly of groups. When cross-linking compounds bring the polymers together, it causes a negative reaction between the additive compounds and free radicals. After reaching a certain concentration, this reaction increases the viscosity and causes gel formation34. For example: Polyacrylic acid (contains polycarboxylic acids).

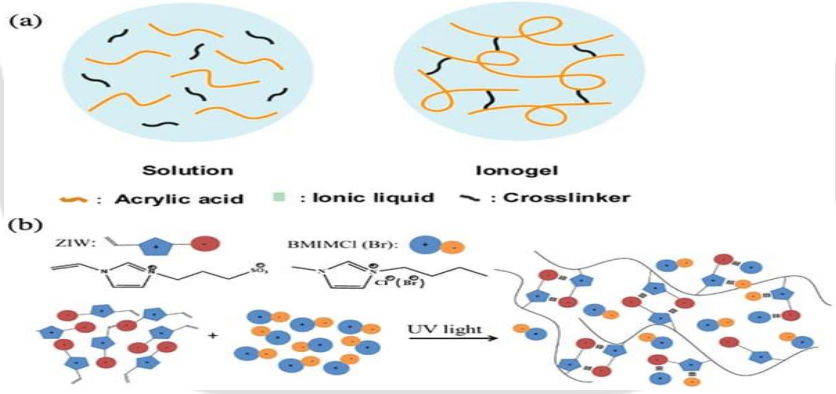


FIGURE; 8: CHEMICAL CROSS LINKING

b) Physical crosslinking: Concentration change, temperature change, dissolution of crystalline components etc. In such cases it is also possible to obtain a hydrogen gel solution. Communication The physical crosslinking is shown as: Cellulose gel, Sephadex 34.

c) Ionic crosslinking:

Here crosslinking takes place costing like polymer(S) or different particles (exchange) another result the



FIGURE;9: IONIC CROSS LINKING

FORMULATION OF GELS:

Gel Formation:

FIGURE;10:GEL FORMATION

A gel is formed by creating a balance between the polymer and the solvent. A critical concentration yields the gel, also known as the gelling point, below this point the gel cannot be formed while above this point the viscosity increases greatly.

Preparation of gels:

Generally, the gels in the industrial scale are manufactured at room temperature. Nevertheless, some polymers require unique treatment before processing. Gels are manufactured by the given below

methods:

1. Thermal changes: Solvated polymers (lipophilic colloids) when subjected to thermal changes causes gelatin e.g. gelatin, agar sodium locate, guar gummed and cellulose derivatives etc.

2. Flocculation: In flocculation, gelatin is produced by adding just enough quantity of salt to precipitate to produce age state but insufficient to bring about complete precipitation. e.g.: Solution of ethyl cellulose, polystyrene.

3. Chemical reaction: In this method, gel is prepared by chemical reaction between the solute and solvent. e.g.: aluminum hydroxide gel is precipitated by interaction in aqueous solution of an aluminums salt and sodium carbonate. An increased concentration of reactants will produce a gel structure.

Application of Gels:

To offer location 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.

EVALUATION:

PH measurement: A digital pH meter is used to measure the pH of different gel compositions. Each formulation's pH is examined three times, with the average readings being computed.

Measurement of Viscosity: The viscosity of produced gel formulations may be evaluated using a Brookfield digital viscometer. The rotation rates for the gels are 0.3, 0.6, and 1.5 per minute.

Spread ability: The region that gel spreads to easily after application is referred to as its spread ability. Glass slide and wooden block measuring tools are used to evaluate it. M = Weight of the top slide tide **Homogeneity:** Following development, all gels are examined visually to determine their homogeneity.

Grittiness: All gel formulations are microscopically examined to see whether any particle matter is present.

Extrudability: After being placed in the containers, the gel formulations are filled in collapsible tubes. The weight in grammas needed to extrude a 0.5 cm ribbon of gel in 10 seconds is used to gauge the extrudability of gel compositions.

Screening for stability: Freeze-thaw cycling is used to investigate stability. The product is heated to 40 degrees for one month, then 25 degrees for one month, then 40 degrees for one month.

Drug content: 1g of gel is added to 100 ml of a suitable solvent, which contains the drug. Utilizing a UV spectrophotometer, absorbance is determined following an appropriate dilution at max nm.

Drug Diffusion Study in Vitro: Franz diffusion cells are used to conduct drug release experiments in vitro. A cellophane membrane containing 0.5 g of gel is used.

Skin irritation test: Ten healthy male and female volunteers were selected for skin irritation testing. 100 mg gel was applied on are of 2 cm for 6 hours, on the interior surface of upper arm and covered with cotton bandage

In-vivo Study: Inhibition of carrageen an induced rat paw edema is studied in male Westar arabino rats using mercury plethysmometer.

In-vitro Diffusion studies: Stability Homogeneity Grittiness 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.

Stability Homogeneity: 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.

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 improves the skin's capacity to absorb medication, increasing bioavailability. 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. Topical gel is a safe and effective therapy option for use in the management of skin-related illnesses, according to the clinical data.

REFERENCES:

1. Hemendrasinh J Rathod1 and Dhruti P Mehta, Acta Scientifica International Journal of Pharmaceutical Science, A Review on Pharmaceutical Gel, 2020 1(1).
2. ROYCHOWDHURY SANTANU, SINGH DEEP HUSSAN, GUPTA RAJESH, MASIH DALJISantanu Roychowdhury, IJPRBS, 2021; Volume 1(5): 21-36.
3. Loyd VA, "Ansel's pharmaceutical dosage forms and drug delivery systems. 9th ed. Philadelphia: Lippincott Williams & Will- dns; (2019).
4. Niyaz BB., et al. "Formulation and evaluation of Gel containing Fluconazole-Antifungal agent". International Journal of Drug Devel- opment and Research 3.4 (2022): 109-128.
5. Dow DA., et al. "Dow Pharmaceutical Sciences, Inc., assignee. Topical gel delivery systems for treating skin disorders". European patent 1304992 B1. (2020): 29.
6. International Journal of Creative Research Thoughts (IJCRT)2004565 www.ijcrt.org 3951© 2020 IJCRT | Volume 8, Issue 4 April 2020 | ISSN: 2320-2882.
7. Trimmers H, NeubertRH: Overcoming the stratu corneum: the modulation skin penetration, skin pharmacology and physiology,2006,19:106-121.
8. GS. Sharma, Lankala Anusha, R. Shireesh Kiran, K. Geetha, T. Rama Rao VOLUME 21: ISSUE 12 (Dec) – 2022.

9. Maghraby GM, Barry BW, Williams AC, Liposomes and skin: From drug delivery to model membranes, European Journal of Pharmaceutical Sciences, 34(4), 2023, 203-222.
10. Yang K, Han Q1, Chen B1, Zheng Y1, Zhang K 1, Li Q 1, Wang J1, Antimicrobial hydro gels: promising materials for medical application.2024.