

FORMULATION AND EVALUATION OF ANTIVIRAL TOPICAL GEL

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ABSTRACT : Gel formulations are becoming pre-eminent among the various semi-solid dosage forms utilized for topical treatment. These preparations are known as semi-solids because the medication is dissolved in the liquid media. Gels consist of natural or manufactured polymers joined by ionic, chemical or physical interactions to form three-dimensional structure. A family of medications known as antiviral drugs is specifically intended to treat viral infections. Antiviral medications are those that fight viral infections. The aim of the study was to create a topical antiviral gel. Compared to oral and intravenous delivery, topical application of drugs offers numerous benefits. In addition to avoiding the risk of gastrointestinal disorders and the discomfort of intravenous therapy, it stops the liver from metabolizing drugs. Applying the medication topically allows it to enter the skin more deeply, improving the absorption and bioavailability. Antiviral medications that specifically target viruses include those that block virus attachment, entrance, uncoating, polymerase, protease, nucleoside and nucleotide reverse transcriptase, and integrase inhibitors. The gel's maximal medication content was achieved by employing 1%- Carbopol. The compositions viscosity ranged from 36,000-51,000 cps, while their pH ranged from 6.8-7.2. The Carbopol and CMC gels were more extrudable than the sodium CMC gel. According to the spreadability statistics, the formulation containing 1% Carbopol-934 has the highest value, whereas the other formulations have significant value.

INTRODUCTION

Gels are semi-solid, three-dimensional structures made of polymeric matrices. Despite having a higher proportion of liquid component than solid dispersions, these behave similarly to solid systems. Long, random chains with reversible linkages at specific locations make up gel systems. These systems are colloidal dispersion systems that are essentially coherent and consist of at least two components [1]. A number of medications have been effectively administered using topical drug delivery systems for both local and systemic effects, and these methods are becoming more and more popular [2]. Typically, gels are semi-solid mixtures with a liquid phase that has been thickened with additional ingredients. Since molecules can freely diffuse through the polymer scaffold in the liquid phase, the release should be comparable to that from a straightforward solution [3]. Depending on the kind of bonding, gels can be either irreversible or reversible. While irreversible gels are often covalently bonded, reversible gels are typically hydrogen-bonded system [4]. Topical application is

specific to a certain skin surface area and only has an impact on that area. The use of topical formulations is intended to produce two main results. Supporting and reestablishing the skin's barrier function is the first result. Enhancing skin condition is the second result, which is achieved by both delivering an active ingredient to the skin and optimizing its efficacy. Because topical medicines are non-invasive, painless, easy to use, and have less adverse effects than other methods, they are more beneficial [5]. The use of a suitable gelling ingredient, often a polymer, is necessary for the creation of an efficient gel. Such polymers are recommended for their inertness, safety, and biocompatibility with other substances; they also have strong mucous membrane adhesion, allow medication penetration without being absorbed by the body, are irritation-free and are ideally biodegradable [6]. The most prevalent living organisms on earth are viruses. Human society is still in danger due to their tremendous diversity, which is frequently accompanied by extremely high mutation rates. Even though over 99.99 percent of viruses on earth are not

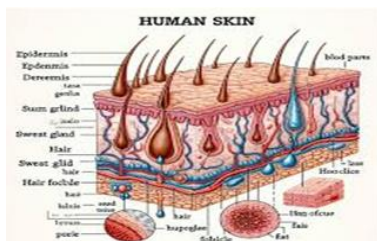
harmful to people or species associated with human activity. Some viruses can have disastrous consequences, especially in densely populated areas or intense farming[7]. The nose, mouth, eyes, and skin are just a few of the many ways that these viruses can enter the human body. Major pathogenic viruses that cause a significant amount of human immunodeficiency virus(HIV), norovirus, hepatitis viruses, human papillomavirus (HPV), herpes simplex virus(HSV) and corona virus[8]. Human immunodeficiency viruses 1(HIV-1 and herpes simplex virus 2(HSV-2) have been shown to have a complicated interaction during the past three decades. HIV-1 and HSV-2 are spread through sexual contact [9]. Viral infections are treated with antiviral medications [10]. Antiviral medications are acyclovir, valacyclovir, penciclovir, famciclovir, foscarnet, ribavirin, lamivudine, amantadine etc[11].

SKIN STRUCTURE

With a surface area of between 1.5 to 2 square meters in adults, the skin is the biggest organ in the body. The body has accessory structures including glands, hair, and nails in various places its thickness varies, with the palms of the hands and the soles of the feet having the thickest texture [12]. There are two primary:the dermis is the layer beneath the epidermis, which is the outermost layer.Asubcutaneous layer made up of adipose and areolar tissue lies between the dermis and underlying tissues [13].

EPIDERMIS:

This is made up of keratinized squamous epithelium that is stratified. The epidermis lacks blood vessels and nerve endings, but the interstitial fluid from the dermis, which supplies oxygen and nutrients and drains away as lymph, is made up of many layer of cells. From the most basal layer to the most superficial stratum corneum, the epidermis is made up of many layers of cells [14].



STRUCTURE OF SKIN

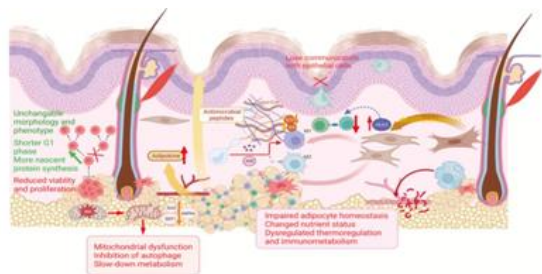
The basal layer, which is composed of cuboidal, nucleated, highly active, and continuously dividing epithelial cells, is the where the cells of the epidermis begin. New cells are forced upward during formation, up from their source of nutrients and blood. Their structure and form gradually alter as they move closer to the skin's surface, with the fibrous protein keratin having taken the place of the cytoplasm. The cells are continuously scraped off the surface and replaced by those under-neath. It takes roughly a month for the epidermis to completely regenerate. The epidermis is thicker and lacks hairs in areas of the skin that are more prone to deterioration, such as the palms and fingers of the hands and the soles of the feet [15]. The skin surface appears ridged in some regions due to the parallel arrangement of dermal papillae. Every person has a different pattern of ridges on their fingertips, and this is known as their "fingerprint". The dermal papillae, which are upward projections of the dermal layer, firmly anchor the dermis to the epidermis and permit waste products and nutrients to pass through to the lower epidermis. By stabilizing the two layers, this structure guards against shearing force damage. When the dermis and epidermis are separated by trauma and significant fluid builds up between them [15].

DERMIS:The dermis is the skin's innermost layer. Collagen fibers interwoven with elastic fibers make up the dermis, which is both robust and elastic. Collagen fibers have the ability to hold water and exhibit flexible characteristics. They also include the enzyme collagenase, which is responsible for wound healing. Fibroblasts and mast cells are found in the dermis. The dermis has two layers. The deeper reticular layer, the superficial papillary layer, and those layers this layer extends to cells in the epidermis that carry pigment. In addition to nerve fibers, blood arteries, and lymphatics, this layer contains what are known as chromatophores. The reticular layer is deeper this is made up of reticular and elastic fibers. These fibers are found close to the hair bulbs, sweat glands and sebaceous glands. There are glands in the skin's dermal layer [16].

HYPODERMIS:

The subcutaneous layer beneath the dermis is called the hypodermis, and it is mostly made up of fat. In addition to protecting the body from cold and facilitating shock absorption, it serves as the primary structural support for the skin. It is

entwined with neurons and blood vessels [17]. Researchers have recently proposed the concept of human dermal white adipose tissue (dWAT) to characterize the adipose tissue surrounding the proximal half of the hair follicles. This phrase describes the structural structure of the skin and has important implications for the study of adipose tissue and associated skin problems [18]. Over time, the hypodermis thins out compared to other fat depots [18].



CHARACTERISTICS OF GELS:

1. When exposed to shear forces created by shaking the containers, squeezing the tube and applying the preparation topically, the gelling ingredient should produce a reasonable solid like character during storage that is easily broken [19].
2. Topical gel mustn't be sticky [19].
3. The gels used in ophthalmic formulations should be sterile [19].
4. In pharmaceutical or cosmetics compositions, the gelling agent would be safe, inert and would not react with other substances [19].
5. To defend against microbial attacks, it should possess sufficient anti-microbial activity [19].

A. Swelling:

The gel has the ability to expand absorbing fluids with greater volume. The dissolution process may be started at this point, Gel-Gel interactions are replaced by gel solvent interactions. The quantity and strength of the bonds that are created between the individual gelling agents molecules influence and they much swelling occurs [20].

B. Syneresis:

On standing, many gels frequently compress spontaneously and release a fluid medium. Syneresis is the term to this effect. As the concentration of the gelling agent drops, the degree of syneresis increase. The initial gel was thermodynamically

unstable, as evidenced by the occurrence of syneresis. The relaxation of elastic stress created during gel setting has been linked to the contraction process. The liquid is forced out when these strain are released because there is less interstitial space available for the solvent [21].

C. Aging:

Typically, slow spontaneous aggregation is seen in colloidal systems. Aging is the term used to describe this process. A denser network of the gelling agent gradually forms in gels as they age. Age causes a denser network of the gelling ingredient to gradually accumulate in gels. According to their, as fluid medium is lost from the freshly formed gel, this process is comparable to the original gelling process and continues after the initial gelation [22].

D. Structure:

The network created by the interlinking of gelling agent particles gives a gel its stiffness. The composition of the particles and the kind of force that creates the connections define the network's structure and gel's characteristics. Single macromolecules or spherical or isometric aggregates of tiny molecules might make up the individual hydrophilic colloid particles [23].

E. Rheology:

The dispersion of flocculated solid and gelling agent solutions are pseudoplastic, or displaying Non-Newtonian flow behaviour, which is defined by a drop in viscosity with an increase in shear rate. Gels break the filmy structure of inorganic particles scattered in water and as people age, a thicker network of the gelling agent gradually forms [22].

PROPERTIES:

- There should be no sticky topical gels [24].
- Gelling agents should ideally be safe, inert and non-reactive with the formulation's other constituents [24].
- When exposed to shear stresses via squeeze tubes, shaken bottles or topical application, the gelling agent should readily fracture and acquire a definite solid-like quality [24].
- The gel should be non-irritating, non-toxic and non-allergenic [25].
- The gel should be sterile, in the case of ophthalmic use [25].
- The gel should possess suitable activity [25].

ADVANTAGES:

- Rapid clearance [3].
- Enhance skin absorption [3].
- Pain free treatment [3].
- Forming mucoadhesive polymeric delivery systems including ease of administration, improved bioavailability [25].
- Investment and manufacturing cost will be reduced [25].
- Less frequent administration [25].
- By passing the first pass effect may help in preventing deactivation by digestive and liver enzymes [26].
- Decreased amounts in comparison to oral dosage forms [26].
- Convenient and easy to use [19].
- Permitting the use of drugs that have a brief biological half-life and narrow therapeutic range [19].
- Avoidance of the gastro-intestinal incompatibility [27].
- A quite large area of application in comparison with buccal cavity [27].
- They are less greasy and can be easily removed from the skin [23].
- They are non-invasive and have patient compliance [23].
- Avoidance of risks and inconveniences of intravenous drug delivery [28].
- Cost effective [23].
- Localized effect with minimum side effects [28].
- Improving physiological and pharmacological response [26].

DISADVANTAGES:

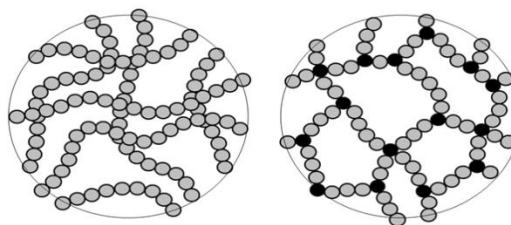
- There could be allergic reactions [19].
- Dermatitis or skin irritation may result from the medication or its excipient 95 [19].
- Certain drug don't pass easily through the skin [19].
- Large-particle drugs are more difficult for the skin to absorb [27].
- Only medications that require extremely low plasma concentrations to function can be used [27].
- Gels works more subtly and last longer [29].
- The presence of water increases the likelihood pH fungal or microbial attacks on gels [27].
- Age and physical conditions are two examples of characteristics that can alter the system's dependability in delivering medication [28].

- The skin's barrier qualities and dosage size restrict this administration method to a small medication population [28].
- Drug-induced contact dermatitis could happen [30].
- This method is not suitable for medications that cause skin irritation or sensitization [14].
- Gels have relatively slower and longer lasting effects [31].
- Temperature, humidity and other environmental conditions can change the rheology of various gels [31].
- Gels controlled release characteristics enable a continuous and prolonged medication input, preventing drug level variation and preserving the drug concentration within the therapeutic range [22].
- Solvent loss from the formulations dries to gels [29].
- Some gels become unstable due to flocculation [29].

APPLICATIONS:

1. Gels function as long-acting medications that can be implanted or administered intramuscularly [19].
2. Gels have greater potential as a drug delivery system for topical applications [19].
3. Gelling agents are helpful suppository bases, thickeners in oral fluids, protective colloids in suspension, and binders in the tablet granulation [26].
4. In cosmetics such as dentifrices, shampoos, fragrances, skin and hair items [27].
5. As drug delivery systems for orally administered drugs [27].
6. To offer local actions, gels are administered directly to the skin mucous membrane or eye [32].
7. Drugs with anti-inflammatory steroids in gel form are used to treat scalp is an area of the body where lotions and ointments are too greasy for patient to handle [26].
8. Compared to ointments, gels offer greater potential as a drug delivery system since they are stable, non-sticky require less energy to formulate, and have aesthetic value [26].

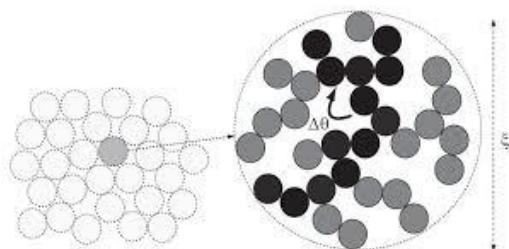
STRUCTURE OF GELS:



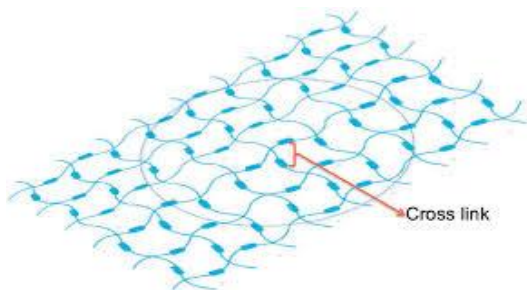
TYPES OF GELS:

The gels are divided into five different types

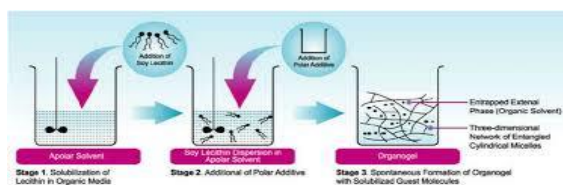
COLLOIDAL GELS: Colloidal gels' varied elements, network-supporting attractive forces, and gelation paths make them essentially and technologically interesting. They consequently display peculiar combinations of characteristics that would be difficult to observe in their types of materials [33]. Colloidal gels are a significant class of materials with numerous used and in a variety of settings [34].



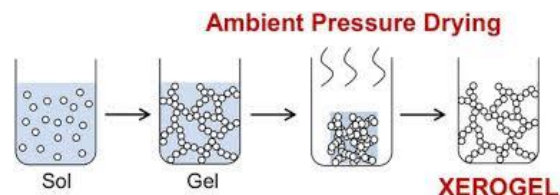
HYDROGELS: Hydro gels are network of chains of hydrophilic polymers that are dispersed by water. These networks of natural or artificial polymers are very absorbent. They have a high- water content, which also makes them slightly flexible [35]. Since the beginning of life on earth, hydrogels have been present in nature. Two common examples of water-swollen motifs in nature are plant structures and bacterial biofilm, which are hydrated extracellular matrix component [36].



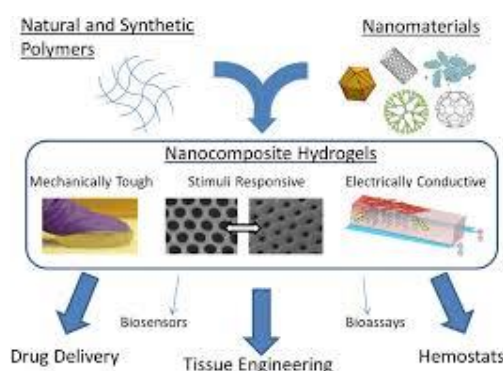
ORGANO GELS: Organo gels are often made using the direct approach, which involves in mixing gelator into the oil phase at temperature higher than the gelator's melting point. On the other hand, the multi-step solvent exchange method (also known as indirect method) [37]. Because of it, a three-dimensional network is created [38].



XEROGELS: This gel is firm and dry, and it will always shrink. Large surface area (m^2/g) and high porosity (15-20%) are typically retained [35]. Xero gels are solid materials made from gels, which are made up of polymers or linked particles scattered throughout a liquid. A drying procedure (such as gradual evaporation or freeze-drying) is applied to this gel structure, which removes the liquid phase and leaves behind a solid substance. The liquid is removed from the gel throughout this drying process, making every effort to maintain the gel's original structure and form[39].



NANOCOMPOSITEHYDROGELS: Advanced biomaterials known as nanocomposite hydrogels combine nanocomposite hydrogels combine nanotechnology and biomaterial science. They consist of water, organic polymers, and nanoparticles and have a wide ranges of possible use[4].

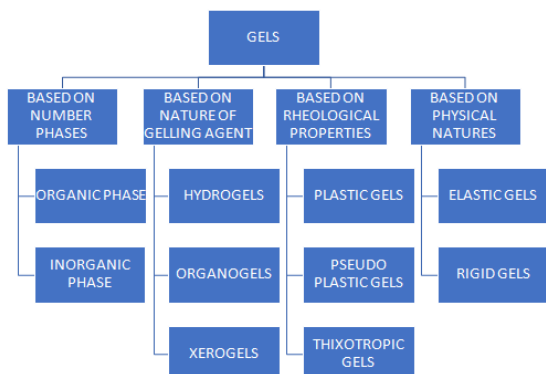
**CLASSIFICATION OF GELS:****BASED ON NUMBER OF PHASES:**

Organic phase: It is also known as “single phase system”. Large organic molecules in a helix are dissolved in a continuous phase in these. Previously referred to as gels, large organic molecules, whether natural or man-made polymers, have a tendency to bind together due to van der Waals' competition or holding forces [35].

Inorganic phase: It is also known as “Two phase system”. This system is made up of flocs of small particles rather than a large-molecules, and if the dispersed phase partition size is very large and forms a three-dimensional structure across the gel, the gel structure will become unstable. Their thixotropic

nature necessities that, the semi-solid state gives way to the liquid state when disturbed [41].

Examples include: Bentonite magma, and gel composed of aluminium hydroxide.



BASED ON NATURE OF GELLING AGENT:

Hydro gels: Hydrogels are network of hydrophilic polymer chains in which water is the dispersing medium. These are highly absorbent natural or synthetic polymers networks. They are also somewhat flexible because of their high-water content [35].

Organo gels: A non-crystalline, non-vitreous thermos reversible solid consisting of liquid organic phase trapped in 3D cross-linked network fluid can be vegetable oil, organic solvent or mineral oil [37].

Xero gels: This is dried solid gel that shrinks indefinitely. It generally retains high porosity [15-50%] and large surface area [m²g] [39].

Example: Gum tragacanth strips beta-cyclodextrin anhydrous cellulose and polystyrene, gelatin acacia tears.

BASED ON RHEOLOGICAL PROPERTIES:

Plastic gels: The bingham body is thought to undergo plastic flow in to that of aluminium in plastic deformation. Dish consistency often referred to as a flocculated suspension, such as of tragacanth gum, sodium alginate and sodium CMC dispersions is referred to as “plastic flow” or plastic as the complete rheogram points out that the gel has elastic gel that will yield and begin to flow[20].

Pseudoplastic gels: For instance, a liquid dispersion containing sodium alginate, tragacanth, Na, CMC, etc., shows pseudo-plastic flow. With an increasing rate of shear, these gels’ viscosity falls without producing any yield value. Shearing action on the rheogram. With an increase in shearing force , the

disorganised molecules start orient their long axis in the direction of flow as the gel matrix releases solvent [42].

METHOD FOR PREPARATION OF GEL

Gels can be made in three different methods.

- Fusion process:** In this technique, the medications, ingredients, gelling agents and vehicles are mixed at a high temperature until a semi-firm texture is obtained [29].
- Cold method:** This approach involves heating and blending every component aside from the drug or active ingredient all at once, lowering the formulation’s temperature, adding the drug, and then continuing to blend until the gel does not form [43].
- Dispersion method:** In this method, the gelling agent is mixed with water until starts to swell. The medication is then added after it has been dissolved in the medium. If required, adjust the pH of the gel by adding buffer solution [43].
- Flocculation method:** By adding a suitable amount of salt, the flocculation method creates gelatin by including by adding a suitable amount of salt the flocculation method creates gelatin by inducing an aging state without full precipitation. When it comes to creating the structural foundation required for gel preparation[48].

CLASSIFICATION OF ANTIVIRAL DRUGS

The Antiviral drugs are divided into two types, they are:

- Retroviral drugs
- Non-retroviral drugs

Retroviral Drugs:

They are divided into six types.

1.Nucleoside reverse transcriptase inhibitors (NRTIs):

- Zidovudine (AZT)
- Didanosine (dd1)
- Stavudine (d4T)
- Lamivudine (3TC)
- Abacavir (ABC)
- Emtricitabine (FTC)
- Tenofovir (TDF)

2.Non-nucleoside reverse transcriptase inhibitors (NNRTIs):

- Nevirapine (NVP)
- Efavirenz (EFV)
- Delavirdine (DLV)
- Etravirine (ETV)
- Rilpivirine

3.Protease inhibitors (Pis):

- Ritonavir (RTV)
- Atazanavir (ATV)
- Indinavir (INV)
- Saquinvir (SQV)

5.Fosamprenvir (FPV)6.Lopinavir (LPV)

7.Darunavir (DRV)

4.Entry inhibitors:

Enfuvirtide (T-20)

CCR-5 receptor inhibitor:

Maraviroc

Integrase inhibitor:

1.Raltegravir2.Dolutegravir (DTG)

Non-retroviral Drugs:

They are divided into three types.

Anti-herpes virus drugs:

1.Idoxuridine2.Trifluridine

3.Acyclovir4.Valacyclovir

5.Famciclovir6.Ganciclovir

7.Valganciclovir8.Cidofovir

9.Foscarnet

Anti-influenza virus drugs:

1.Amantadine2.Rimantadine

3.Oseltamivir4.Zanamivir

5.Peramivir

Anti-hepatitis virus drugs:

It is divided on two basis hepatitis B and hepatitis C

Hepatitis B:

1. Lamivudine2.Entecavir

3.Adefovir dipivoxil4.Tenofovir

5.Telbivudine

Hepatitis C:

1.Ribavirin2. Interferon α

3.Sofosbuvir4.Simeprevir

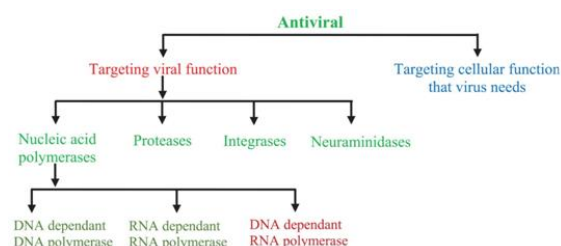
5.Daclatasvir6.Ledipasvir

7.Velpatasvir

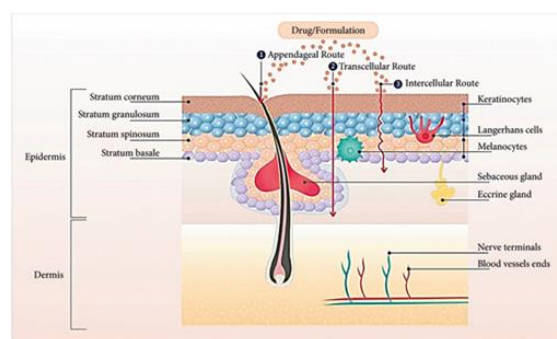
MECHANISM OF ACTION:

The antiviral substances that specifically target virus reproduction are the subject of this article. Following a quick historical review, we go over the ideas and difficulties that have influenced and helped advance antiviral treatment specificity [45]. It has been believed that viruses rigorously adhere to the cells regular metabolic processes during their replicative cycle and that it is difficult to stop virus multiplication without interfering with regular cell metabolism [46]. Viral DNA enters a host cell, replicates there and releases new viruses as part of a viral infection. Viral attachment, invasion, uncoating,

replication, assembly and release are the six stages of viral replication. The following describes the stages of the virus life cycle, emphasizing the virus's entry and exit[47]. Antiviral medications work by converting it in to triphosphate after inhibiting the synthesis of viral DNA. According to an analysis of the mechanism of action of well-known antiviral medications, they can suppress the virus's adsorption or diffusion into the cell, increase the cell's resistance to the virus (interferons), and de-proteinise the virus in the cell (amantadine). They can also inhibit the synthesis of nucleic acids by producing anti-metabolites.



MECHANISM OF DRUG PENETRATION:



FACTORS AFFECTING

Factors affecting how efficiently the drug is going to penetrate the skin to eventually reach its action site. The major ones are follows:

1.Physicochemical properties of the Drug

- **Molecular Size and Molecular Weight:** Such small molecules easily diffuse in the skin compared to those bigger molecules.
- **Lipophilicity:** Lipid-soluble drugs, simply put, lipophilic drugs absorb well just because the outmost stratum corneum of the skin is made up of lipids.
- **Ionization:** Non-ionised drugs tend to absorb through skin more efficiently than their corresponding ionized forms.
- **Solubility:** Drugs soluble both in water and the lipid tend to be more absorbed.

2.The Concentration of the Drug

Higher the concentration of the drug increases the rate of absorption, which results in developing the greater concentration gradient on the skin.

3. Vehicle:

- Choice of the formulation may influence the rates of absorption as bases show different abilities to deliver their drug.
- Vehicles also contain penetration enhancers, some alcohols, etc., to enhance permeability through the skin.

4. Skin Condition and Integrity:

- Skin Moisture: Moist skin penetrates drugs much better than a dry one.
- Thickness and stratum corneum: It has a lesser permeation because the skin is much thicker on palms. Thinner skin, such as on the face, permits greater permeation.
- Skin Damage: Absorption increases with damage in the skin or inflammation as they modify the barrier function.

GEL FORMING AGENTS:

POLYMERS : In addition to being utilised to produce controlled release, improve stability, and increased bioavailability, polymers are essential in the production of tablets because they are used as coating materials that conceal and mask the bitterness, bad odours, and taste that make the patient reluctant to the medication [49]. In drug development, polymers play a crucial role because they aid in the long term release of drugs. Applications of polymers are widely used in the medical sectors by developing numerous medical devices, such as scaffolds in tissue engineering, medication delivery systems, implants, etc [50].

Polymers are divided into three types:

S NO	TYPES OF POLYMERS	EXAMPLES
1	NATURAL POLYMER : Natural polymers are those that can be extracted from natural resources like plants and materials and are found in nature. Starch, wool, proteins, cellulose, chitin, DNA, polysaccharides, [suga	A] Starch: A plant's food store, starch is a polymer of glucose. Cellulose is polymer found in plants[52]. B] Chitin: The most prevalent organic component in the skeleton of invertebrates in chitin, a polysaccharides derivative with acetyl and amino groups. It is mostly found in arthropods, mollusks, and

2	<p>r polymers], and polypeptides like silk, keratin, hair, and rubber [derived from a tropical plant's latex] are examples of natural polymer[51].</p> <p>SYNTHETIC POLYMER: Synthetic fibers are produced in laboratories through the polymerization of basic chemical components[53].</p>	<p>annelids. It is also a compound of many fungi's spores and mycelia[52].</p> <p>A] Carbopol: First proposed in 1955, Carbopol polymers were granted a patent in 1957. A crosslinked acrylic acid polymer with a high molecular weight is used to make these polymers. All members of the Carbopol polymer family share a high molecular weight and are crosslinked polymers with polyacrylic acid. Carbopol are polyacrylic acid polymers that could be utilized as bioadhesive drug delivery vehicles. Allyl sucrose crosslinked with Carbopol [54]. B] Nylon: Nylon is the least stable of the more widely used commercially produced polyamides (nylon 6,6 and 6,10) at and above the polymers industrial processing temperatures. The chain's adipic acid component has been blamed for this decreased heat stability [55].</p>
3	<p>SEMI-SYNTHETIC POLYMERS: These are polymers made from natural fibre that have undergone a straightforward chemical process to enhance their tensile strength and durability[53].</p>	<p>A] Hydroxypropylmethylcellulose: HPMC is frequently utilized in the ophthalmic preparations as a thickening ingredient, film coating, extended-release tablet matrix, and capsule shell. The hydroxyl groups of cellulose in this polymer are partially methylated and 2-hydroxypropylated. The degree of substitution and molecular weight dispersion (about 10-1500kDa) of the various HPMC variants vary. Because of this variety, it is challenging to create a straight forward approach that takes into account each of these factors [56].</p>

EVALUTION TESTS

1.SPREADABILITY TEST: When applied to the skin or affected area, it shows the size of the area that gel spreads easily. Spreading value is another factor that affects therapeutic potency. Spreadability is the speed in seconds at which two slides separate from gel positioned between them when subjected to a specific stress. The spreadability improves with a shorter time required to separate two slides [1].

To determine the spreadability, using the formula below:

$$\text{Spreadability (S)} = M \cdot L / T$$

Where,

M = Weight attached to the upper slide.

L = Glass slide length.

T = Duration needed to separate the slides.

2.Viscosity test: Using a Brookfield viscometer, the viscosity of the gel measured at room temperature at 5, 10, 15, 20, 50, 70 & 90 rpm. At 5, 10, 15, 20, 50, 70 & 90 degrees at temperature, spindle number six was turned after being dipped in the preparation. The viscosity and particle size are influenced by a number of variables, including temperature and pressure[57].

3.Ph: A calibrated Ph meter was used to measure the gel's Ph. The Ph of the gel was calculated by taking the average of the three separate measurements that were made [57].

4.Drug content: By dissolving precisely weighed one-gram gels in 0.1N NaOH, the drug concentration of the gel was ascertained. At 254 nm, absorbance was measured using a visible spectrometer following an appropriate dilution. The slope of the standard curve was used to calculate the drug content [5].

The following formula was used to calculate the drug content:

$$\text{Drug content} = (\text{concentration} \cdot \text{volume taken}) \cdot \text{conversion factor}$$

5. Extrudability study: When a little pressure is applied, a good gel extrudes from the gel as it best it can. Using a universal tube filling machine, the extrudability of formulations made from aluminium collapsible tubes was assessed. Teng gel-filled aluminium collapsible tubes were clamped between two clamps. The formulation's extrudability was assessed by compressing a tube and measuring the weight in grams needed to extrude a 0.5 cm gel ribbon in 10 sec[50].

6. Visual examination: The colour, look, homogeneity, and consistency of the made gal were visually assessed [50].

7. Invitro diffusion studies:

In vitro diffusion studies: A Franz diffusion cell equipped with a cellophane membrane will be used for the diffusion tests. There will be a set quantity of the formulation in the donor compartment. The receptor compartment, which contains phosphate buffer (pH 7.4) kept at 37 ± 1 °C, will submerge the donor compartment. At a predetermined interval, the sample will be periodically removed from the receptor compartment. The same volume of fresh medium will be added when the sample is removed at each interval. Phosphate buffer will be used as a blank in a spectroscopic analysis to evaluate the drug content.

8.Grittiness:

A light microscope will be used to measure it under a microscope. The prepared gel is deemed grittiness-free based on the lack of particle matter.

9.Homogeneity:

The gels' appearance and the existence of any aggregates will be examined visually to determine their homogeneity.

CONCLUSION:

Gel formulations have become more popular recently than other topical preparations because they are easier to wash, have a simpler preparation process, offer stability and controlled release, are more patient-acceptable, have fewer side effects, avoid gastrointestinal tract, and improve bioavailability through increased absorption. With active targeting, they improve drug absorption while reducing adverse effects. To improve stability and effectiveness, the gel formulations need to optimised. According to the recent research, topical gels are quite safe and effective.

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