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A REVIEW ON PHARMACEUTICAL GEL

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ABSTRACT

The study focuses on the formulation and evaluation of topical gels designed for the treatment of mouth ulcers. Topical gels, which are semi-solid solutions composed of synthetic or natural polymers, provide an effective delivery mechanism for localized treatment. Mouth ulcers, caused by trauma, nutritional deficiencies, or infections, are often treated using gels due to their ability to enhance bioavailability and bypass first-pass metabolism. This paper explores various gel formulation techniques and ingredients, such as benzocaine, hydrocortisone, and aloe vera, which contribute to pain relief, inflammation reduction, and accelerated healing. The study also evaluates the ideal properties of gels, including viscosity, spreadability, and drug release profiles, ensuring efficacy and patient comfort. The findings suggest that gels are an optimal method for treating mouth ulcers due to their ease of application, biocompatibility, and controlled drug release capabilities.

Keywords: Mouth, Sores, Mucosa, Gel.

I. INTRODUCTION

A mouth ulcer is the loss or erosion of part of the delicate tissue that lines the inside of the mouth (mucous membrane).[1]An ulcer is derived from the Latin word "ulcus," which means sore. [2]The oral mucosa is the "skin" that covers the majority of the mouth cavity, excluding the teeth.[3]The "skin" covering majority of the oral cavity—aside from the teeth—is called the oral mucosa. Its primary function is to act as a interference t. [4]Mouth ulcers are frequent and typically result from trauma, such as shattered teeth, poorly fitted dentures, or fillings.[5]Mouth ulcers can be caused by a variety of factors, including biting the inner cheek, food sensitivities, hard tooth brushing, hormonal fluctuations, vitamin shortages, bacterial infections, and illnesses. [6]Treating mouth ulcers efficiently involves the use of various topical therapeutic approaches. Nonetheless, a few issues arising from the drug's brief half-life may contribute to its restricted therapeutic effectiveness and need to be addressed.[7,8]

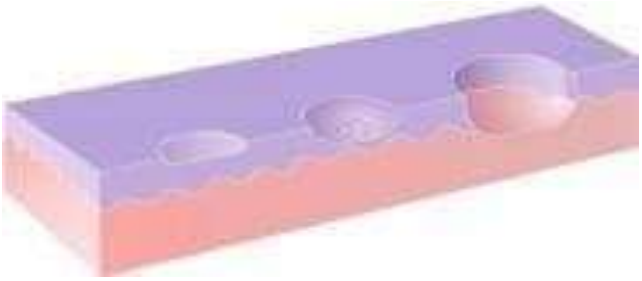

Fig 1: Diagrammatic representation of mucosal erosion (left), excoriation (centre), and ulceration (right).An

Types

There are five types of mouth ulcer

1. **Canker sores:**-Canker blisters cancer blisters is a common form of mouth ulcer, which appears as a painful white or unheroic ulcer girdled by a bright red area.

Canker sore subgroups that comprise the following include:-

a. **Mild:** Less than 1 centimeter in diameter sores that heal in a week or two
b. **Major:** Sores can take weeks or months to heal since they are larger, deeper, and have a diameter of two to three centimeters.
c. **Herpetiform:** Sores have a diameter of one to two millimeters, are seen in clusters of ten to one hundred, and can last for several weeks.[9]

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2. **Oral lichen planus:** Oral lichen is an ongoing (chronic) inflammatory condition that affects mucous membranes inside your mouth.[10]
3. **Leukoplakia:** Leukoplakia is a White or gray patches inside your mouth thant is ymptom of this illness.
4. **Erythroplakia:** Erythraplakia is an abnormal patch of red tissue that usually forms on the inside of the mouth, especially on the tongue, inside of the cheek, and under the tongue.
5. **Oral thrush:** Oral thrush Inside your mouth, a yeast overgrowth known as Candida albicans is the source of this fungal infection.[11].

Fig 2: Mouth Ulcer

Causes

Mouth ulcers can have many causes, including things you can try to avoid and other factors:

- **Injuries**

Injuries Biting your cheek or tongue, cuts or burns from eating or drinking, or damage from a toothbrush or dentures

- **Food**

Food intolerances or allergies, eating certain foods like chocolate, spicy foods, or acidic foods, or stopping smoking

- **Medications**

Reactions to certain medications or toothpaste containing sodium lauryl sulfate

- **Other factors**

Hormonal changes, stress, anxiety, lack of sleep, or a weakened immune system

- **Diseases**

Viral infections like the herpes simplex viral infection (cold sore virus) or diseases like chronic inflammatory bowel disease or Behçet's disease[12]

Gel:-Gels are classified as semi-rigid systems where the solubility of macromolecules in the dispersed phase or the three-dimensional particle interaction limit the dispersion medium's strength. The word "gel" comes from the word "gelatin," and there is a history for both "gel" and "jelly." Gelu means "drop" and gel means "freeze" in Latin. This source demonstrates the fundamental idea that liquids are solids with some liquid characteristics that are elastic and do not flow. The word "gel" was first used to characterize semisolids in the late 1800s when scientists attempted to distinguish between them using their phenomenological characteristics rather than their chemical makeup. There isn't yet a method for identifying drug samples analytically.[13]

Fig 3: Gel

Structure of Gel:-The network created by the granular gelling agent's connections amongst one another gives the gel its toughness. The network structure of the gel and product is determined by the nature of the product

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and the type of oil used for the coupling.Single or small macromolecules may be arranged in spherical or evenly spaced clusters inside a single hydrocolloid product. Getting these goods ready in gel wax.[14]

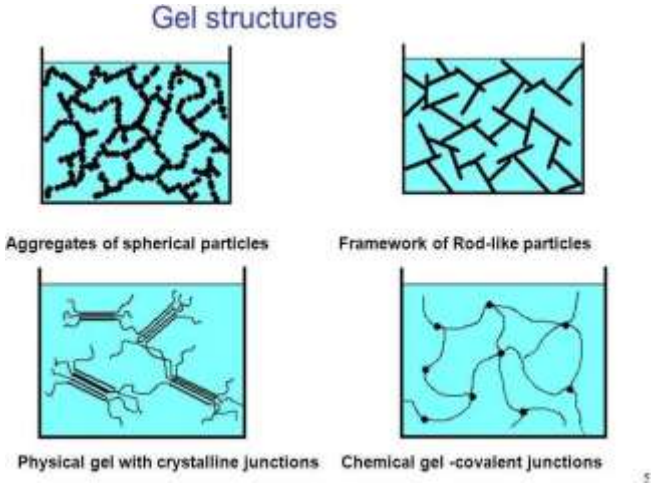

Fig 4: Gel structure

Classification of Gels:-[15]

a) Based on Number of Phases:-

1. Colloid Phase:- They are separated into:

a. Inorganic (two-phase) system: -

This type of system, which resembles a system that produces the three-dimensional structure of the entire gel, exists if the dispersion size of the dispersed phase is too great. little flocks. This body is not necessarily stable, in contrast to bigger molecules and gel formations. When left alone, they ought to be thixotropic semi-solids, which melt into liquid when combined.

b. Organic (Single phase) system:-

These comprise big organic molecules dissolved in a continuous phase in the form of a helix. Historically, large organic molecules—whether they are synthetic or natural polymers—were referred to as gels because they tended to assemble in competition with one another or to be bound together by van der Walls.

2. Based on Nature of Gelling Agent:

a. Hydrogel (Water Based):-

Water serves as the dispersing agent in networks of hydrophilic polymer chains, which make up hydrogels. These are networks of natural or artificial polymers that are very absorbent. They have a high water content, which also makes them rather flexible.

These gels have special physicochemical characteristics, such as the following:

- Capacity to hold a three-dimensional structure while absorbing vast amounts of aqueous fluid (usually 100 times the initial mass).
- Strong mechanical characteristics and resistance to fracture are displayed by hydrogel, even after repeated exposure to pressures as high as 1 kPa.
- Hydrogel demonstrates remarkable pliability.

1) Hydrogel Dressing:-The capacity of hydrogel dressings to saturate dry wounds with moisture sets them apart from other dressings. Because of this, they are employed to maintain a moist healing environment in gritty wounds, which helps to promote autolytic debridement (the production of protein-rich exudate from wound surface capillaries containing phagocytes and other components that consume dead cell debris and germs). A swelling three-dimensional network of hydrophilic polymers with a sizable water content in their structure makes up the hydrogel dressing.

Hydrogels can be administered to wounds in a variety of ways, each with unique benefits and applications for wound care: -

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1. Amorphous gel filler that has the ability to resemble a wound.
2. A piece of fabric or elastic.

Fig 5: Hydrogel Dressing

2) Amorphous Gel for wounds (Filter): Comprises 70–95% water and is produced by synthetic (polyvinylpyrrolidone, polyacrylamide) or natural (alginate, carboxymethylcellulose) polymerization that is acquired by dispersion in water. The precise polymer employed and its content in the dressing determine the rheological qualities of the gel, which differ significantly between various commercial goods. These variations might have an impact on clinical handling and usage traits. For instance, an amorphous gel's apparent viscosity may have an impact on its capacity to completely or partially fill a wound cavity and then stay on the wound bed. The way the dressing is packaged after that, such as in a foil pouch, spray bottle, or tube, will depend on how the dressing behaves under shear.

Fig 6: Amorphous gels for wound

b. Organogel: Organogel is a non-crystalline, non-vitreous, thermoreversible solid made up of an organic liquid phase that is confined in a three-dimensional network of cross-links. Mineral oil, vegetable oil, or organic solvents are examples of fluids.

Fig 7: Organogel

c. Xerogel: This gel is firm and dry, and it will always shrink. It often keeps a large surface area (m2/g) and high porosity (15–50%). For instance, beta-cyclodextrin, acacia tears, dry cellulose and polystyrene strips, gelatin sheets, and gum tragacanth.

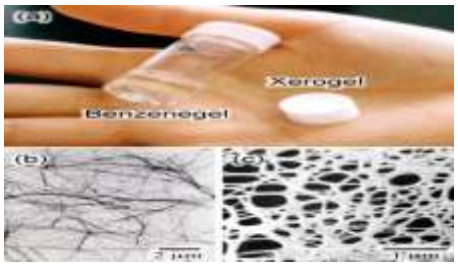

Fig 8: Xerogel

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3. **Based on theological properties:-**Generally gels exihibit non - Newtonian flow properties They are classified as:

a. **Plastic gels:**-The term "plastic flow" refers to the behavior of flocculated suspensions, such as tragacanth gum, sodium alginate, and sodium CMC dispersions, according to the Bingham Body. The rheogram indicates the characteristics of the gel that will cause elastic gel to deform and start to flow.

b. **Pseudoplastic gel:-** These gels have no yield value, and their viscosity diminishes as the shear rate increases. Cutting the linear polymer's molecular chain length yields the rheogram. The solvent is discharged from the gel matrix as the shear stress increases and the chaotic molecules start to align their long axes downstream.

c. **Thixotropic gel-**These gels' particle bonds are so weak that they can be broken by shaking. The solution will revert to the gel upon particle collision and reconnect (reverse isothermal gel-sol-gel transition). This results in the formation of scaffold-like structures in colloidal systems containing spherical particles.

eg.kaolin, bentonite, agar etc

4. **Based on physical strength:-**

They are divided into:

a. **Elastic gels:-**Agar, pectin, guar gum, and alginates gels behave elastically. At certain locations, weak forces like dipole attraction and hydrogen bonds hold fiber molecules together. Additional connections between two neighboring chains of a COO-X-COO type salt bridge occur if the molecule has a free COOH group. Eg. Alginate and Carbopol.

b. **Rigid gels:-**Macromolecules to which primary bonds bind the framework can form this. For instance, Si-O-Si-O bonds hold silicic acid molecules together in silica gel, creating a polymer structure with a pore network.

Uses of Gel:- [15]

- Use as a medication delivery method oral.
- External formulations meant to be applied directly to the eyes, mucous membranes, or skin.
- A long-acting medication that is implanted in the body or injected into a muscle.
- Tablet granulation binder, suspension protective colloids, oral liquid thickeners, and suppository bases.
- In cosmetic items, including shampoos, conditioners, fragrances, and skin and hair care products.
- Catheter lubricant.
- The patch test foundation.
- NaCl gel for ECG purposes.
- Dental prophylactic using phosphate gel and sodium fluoride.

IDEAL PROPERTIES OF TOPICAL GEL :- [16]

The ideal gel should have the following qualities:

- It should be clear and homogenous.
- It should be inert in nature.
- It should not stick to surfaces or interact with other formulation ingredients.
- It should be stable.
- It should not irritate skin or other areas where it is applied.
- It should have the ideal viscosity; and it should have antimicrobial activity.

ADVANTAGES OF GEL FORMULATIONS:-[17,18]

The gel formulation has a few key advantages over other semisolid dosing formulations:

- Gels require less work to prepare than other formulations.
- Gel has a sophisticated, non-greasy composition.
- Gels adhere exceptionally well to the application location

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- .Gels are environmentally benign and biocompatible.
- Are incredibly resilient to stressful situations.

DISADVANTAGES OF GEL FORMULATION:- [19,20]

- Gels have a slower, more persistent effect.
- Additives or gelators could irritate skin.
- The likelihood of a microbial or fungal attack in gel is increased by water content.
- The gel dries out due to solvent loss in the formulation.
- In certain gels, flocculation results in an unstable gel.

Ingredients:-

The ingredients commonly used in gels for treatment of mouth ulcers(also known as cancer sores or apthus ulcer) often aim to provide pain relief,promot healing ,and create a protective barrier over the ulcer to prevent irritation.Here are some key ingredients frequently found in mouth ulcer treatment gels:

Sr.no	Name	Purpose	Reference
1.	Benzocaine (Topical anaesthetic)	Provide localized pain relief by numbing the	Benzocaine Is commonly used in
		Affecting area.	Over- the-counter products like orajel as it is an effective Local anaesthetic .
2.	Hydrocortisone (Anti-inflammatory)	Reduce inflammation and can help alleviate pain and swelling in the ulcerated area.	Hydrocortisone is used in prescription gels and ointments to treat more severe or persistent mouth ulcers
3.	Chlorhexidine (Antiseptic)	Helps to prevent infection and reduce bacteria in the mouth, pramoting faster healing.	Chlorhexidine is often used in mouth wash and gels, such as peridex or paroex, for oral hygiene and ulcer treatment.
4.	Alo vera (Healing and soothing Agent)	Know for its healing properties, alovera can reduce pain and inflammation , and pramot faster healing of mouth ulcers.	Alo Vera gels or mouthwashs are commonly used as natural remidies for soothing and healing oral ulcers.
5.	Carbomer (Gelling Agent)	Used as thickening agent to give the gel it's consistency and to create a protective layer over the ulcer.	Carbomer is often used in Pharmaceutical and cosmetic formulations for creating gels,such as in oral care products.
6.	Pectin (Protective agent)	Forms a protective film over the ulcer to shield it form irritants and prevent further	Pectin is used in some gels to provide a soothing barrier and help in the healing
		Discomfort.	Process.
7.	Sodium bicarbonate (Alkaline agent)	Neutralizes acids in the mouth and helps reduce the irritation that can exacerbate mouth ulcers.	Sodium bicarbonate is used in some gels to pramote healing by balancing the oral environment.
8.	Vitamin B complex (B1,B2,B6,B12)	Supports tissue healing and may help reduce the recurrence of mouth ulcers by addressing potential deficiencies.	Some mouth ulcer treatment gels include B complex vitamins to aid in the regeneration of dameged tissues.
9.	Cetrimide (Antiseptic)	A mild antiseptic used to cleans the ulcer and reduce the risk of infection.	Cetrimide is often included in oral gels that aim to treat ulcers and reduce microbial activity in the affected area.

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10.	Zinc sulphate (Mineral supplement)	Aids in healing and may reduce the recurrence of mouth ulcers by supporting tissue repair.	Zinc is an essential mineral often found in oral care products designed to aid healing and prevent ulcer formation.

GELS CAN BE PREPARED BY FOLLOWING METHODS: [21]

1. **Thermal change:-**Gelatin is produced when thermally altered lipophilic colloids (solvated polymers) are exposed. Several hydrogen formers are more soluble in heat than they are in cold water. Gelatin formed as the temperature drops and there is less moisture present. When a concentrated hot solution is cooled, a gel will form. Guar gum, cellulose derivatives, gelatin, and agar sodium oleate are a few examples. On the other hand, other materials, like cellulose ether, are soluble in water because of hydrogen bonds with the water. As the temperature rises, the dissolved hydrogen bonds in these liquids will cause them to gel. Therefore, this method cannot be applied as a standard for making gels.
2. **Flocculation**:-In this case, the ideal amount of salt is added to induce age-state precipitation but not enough to cause total precipitation in order to create gelation. Quick mixing is necessary to avoid very high precipitant concentrations. For example, solutions of ethylcellulose and polystyrene in benzene can be gelled by rapidly mixing them with the appropriate amount of a non-solvent, like petroleum ether. When added to hydrophobic fluids, salts induce gelation and coagulation, respectively. The gels that are produced by the flocculation process exhibit thixotropic behavior. High electrolyte concentrations are the only conditions that affect hydrophilic colloids, such as proteins, gelatin, and acacia; otherwise, the colloidal state gets "salted out," preventing gelation.
3. **Chemical reaction:**-This method creates gel by the chemical interaction of the solute and solvent. A larger concentration of the reactants will produce a gel structure, similar to how an aluminum salt and sodium carbonate interacting in an aqueous solution forms aluminum hydroxide gel. Other examples of cross-linked polymeric chains are PVA, methane diphenyl isocyanine (MDI), cyanoacrylates with glycidol ether (Glycidol), and toluene diisocyanates (TDI).
4. **Fusion method**:-In this technique, the medication, vehicles, and gelling agents are all mixed together at high heat until a semi-solid texture is not produced.
5. **Cold method:**-In this method, every component—aside from the drug or active pharmaceutical ingredient—is simultaneously heated and combined**.** The medicine is added, and the mixing process is continued until the gel has not formed after the formulation's temperature has lowered.
6. **Dispersion method:-**With this method, the gelling agent is stirred with water until it starts to swell, then the drug is dissolved in the medium and combined with it. If necessary, adjust the pH of the gel by adding buffer solution.

EVALUATION PARAEMETERS OF TOPICAL GELS: [22,23,24,25,26,27]

1. PH measurement:

An electronic pH meter is employed to determine the pH of various gel compositions. One gram of gel is mixed with 100 milliliters of freshly prepared distilled water, and it is left to dissolve for two hours. The pH of each formulation is measured three times, and the average values are calculated.

2. 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. The relevant dial reading is noted for each speed. By multiplying the dial measurement with a factor listed in the Brookfield viscometer catalogs, one may determine the viscosity of gel.

3. Spreadability:

The spreadability of a gel is the area to which it readily spreads after application. It is assessed using a wooden block measurement tool and a glass slide. Spreadability is the time it takes for two slides to separate from gel placed in their interstices when subjected to a particular force. It is measured in seconds. Shorter intervals between two slides result in better spreadability. To calculate spreadability, use the following formula:

S is equal to M.

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The spread ability is L/TT S.

M = Top slide tide's weight L is the length of the glass slide.

T is the time required to completely isolate one slide from the others.

4. Homogeneity:

All gels are inspected visually to assess uniformity after formation.

5. Screening for stability:

One method for examining stability is freeze-thaw cycling. For a duration of one month, the product is heated to 40 degrees, followed by 25 degrees, and finally 40 degrees. Syneresis is present. After exposing the gel to room temperature, distinct liquid exudates are seen.

6. Drug Diffusion Study in Vitro:-

Drug release tests are carried out in vitro using Franz diffusion cells. 0.5 grams of gel are contained in a cellophane membrane. In diffusion studies, the dissolving medium is a 250 mg phosphate buffer with a pH of 7.4 conducted at 370 °C to 10 °C. Every hour, a 1 ml sample is collected and replaced with a new buffer solution. The gathered samples are appropriately evaluated.

7. Skin irritation test:-

For a skin irritation test, ten volunteers—a male and a female—in good health were chosen. A 2 cm area of the internal surface of the upper arm was wrapped with a cotton bandage after 100 mg of gel was applied and left on for six hours. Following a six-hour period, the locations were cleaned using acetone, and measurements were taken using Draize's scale. Not irritated: 0. A little annoyance: 1 Two points of irritation

8. In-vivo Study:-

Male Wistar albino rats are used to investigate the inhibition of carrageenan-induced rat paw edema using a mercury plethysmometer. The experimental animals' unilateral hind paw volume is assessed both before and after carrageenan is administered. Exhibition is observed.

9. Drug content:-

To 100 milliliters of an appropriate solvent containing the medication, 1 g of gel is added. After a suitable dilution at max nm, absorbance is measured using a UV spectrophotometer.

Marketed Formulations:

Sr.no	Name	Ingredients
1.	Bonjela	Choline salicylate ,, cetalkonium chloride and also contains ethano,glycerol, menthol, hypromellose , anise oil, sodium saccharin and water
2.	Orasore	Lignocaine hydrochloride, choline
		Salicylate, and benzalkonium chloride.
3.	Anbesol	Lidocaine hydrochloride , Chlrocresol and cetylpyridinium chloride.
4.	Choline salicylate &lignocaine	Choline Salicylate+ Lidocaine / Lignocaine.
5.	Biolone	Choline salicylate, Cetalkonium chloride, Ethanol.
6.	Quick cool	Choline Salicylate, Lignocaine Hydrochloride, Benzalkonium Chloride.
7.	Zytee	Benzalkonium chloride, Choline salicylate and Lignocaine hydrochloride .
8.	Chorhexidne gluconate	Chorhexidne gluconate, Gaur gum, sodium acetate trihydrate, purified water, alcohol, glycerine, sodium saccharine.

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9.	Difflam	Benzydamine Hydrochloride., Cetylpyridium Chloride, sodium saccharin.
10.	Hiora-SG	Jasmine, Licorice, Triphala, Spreading Hogweed.

II. CONCLUSION

Because pharmaceutical gels are more stable and offer controlled release compared to other semisolid dosage forms, their use is growing in popularity these days. The topical gel increases the bioavailability of the drug by enhancing the skin's ability to absorb it. The primary benefit of a topical delivery approach is that first-pass metabolism is avoided. It also provides a high level of patient acceptance. Topical distribution is usually the preferred method of medicine administration when another technique has a lesser bioavailability. The clinical data suggests that topical gel is a safe and useful therapeutic alternative for the management of disorders connected to the skin.

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