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Research Paper

Formulation And Evaluation of Nanoemulgel for Mouth Ulcer

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ABSTRACT

The present study aimed to formulate and evaluate a nanoemulgel for treating mouth ulcers. Mouth ulcers are painful lesions in the oral cavity causing discomfort and affecting daily activities like eating and speaking. Conventional topical treatments such as gels and mouthwashes provide only temporary relief due to limited mucosal retention and poor drug penetration. To address these limitations, a novel nanoemulgel drug delivery system was developed to enhance drug bioavailability and retention at the application site. The nanoemulgel was prepared by incorporating lignocaine-loaded nanoemulsion into a carbopol-based gel. The formulation included an oil phase, surfactant, water, and a gelling agent. It was evaluated for physicochemical properties such as pH, viscosity, spreadability, drug content, and stability. Results showed the nanoemulgel had a suitable pH for oral use, uniform drug distribution, acceptable viscosity, and good spreadability. It remained stable under accelerated conditions for three months. The nanoemulgel provided prolonged retention on the mucosal surface and was easy to apply, which could improve patient comfort and treatment compliance. In conclusion, this formulation represents an effective, safe, and economical topical drug delivery system for mouth ulcers. Its ease of use and potential for enhanced therapeutic effect make it a promising alternative to conventional products. However, further clinical studies are necessary to confirm its efficacy and safety in humans.

INTRODUCTION

In recent years, the development of advanced drug delivery systems has become a focal point in pharmaceutical research due to their potential to enhance the therapeutic efficacy and patient compliance of existing treatments. Among these systems, nanoemulgels have garnered attention for

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their ability to combine the advantages of nanoemulsions - such as increased solubility, enhanced stability, and improved mucosal permeability - with the beneficial characteristics of gels, including mucoadhesion and sustained drug release. This synergistic combination enables prolonged residence time at the site of application and controlled drug release, making nanoemulgels particularly suitable for localized treatment of conditions such as mouth ulcers.

MOUTH ULCER:

Mouth ulcers, also known as aphthous ulcers or canker sores, are painful, open lesions that appear on the soft tissues of the oral cavity, including the inner cheeks, lips, tongue, gums, and the roof of the mouth. These lesions are usually round or oval with a white or yellow center and a red, inflamed border. Although typically small and self-limiting, mouth ulcers can cause significant discomfort, particularly while eating, drinking, or speaking.

Causes:

Mouth ulcers may arise from various factors, including:

1. Minor tissue injury caused by dental procedures.
2. Accidental biting of the cheek or tongue.
3. Allergic reactions to specific oral bacteria.
4. Mechanical irritation from orthodontic appliances such as braces or retainers.
5. Use of harsh or abrasive toothpaste formulations.
6. Consumption of acidic foods, including oranges, pineapples, and strawberries.
7. Hormonal changes, particularly during the menstrual cycle.
8. Psychological stress and lack of adequate sleep.
9. Use of certain immunosuppressant medications.

Treatment:

Management of mouth ulcers focuses on relieving symptoms and promoting healing. Common treatment strategies include:

1. Drink plenty of water to maintain hydration and support overall oral health.
2. Practice good oral hygiene to prevent secondary infection and promote healing.
3. Rinse the mouth with warm salt water several times a day to reduce irritation and cleanse the area.
4. Avoid hot, spicy, or acidic foods until the ulcer heals to prevent further irritation.
5. Use a hydrogen peroxide rinse (prepared by mixing equal parts hydrogen peroxide and water) twice daily to disinfect the ulcer and reduce bacterial load.
6. Apply over-the-counter (OTC) topical anesthetics, such as Orajel™ or Anbesol®, to numb the area and relieve pain.
7. Use corticosteroid-based ointments, such as Triamcinolone, in severe or persistent cases to reduce inflammation and accelerate healing.

NANOEMULGEL:

Nanoemulgels are advanced topical or mucosal drug delivery systems specifically formulated to enhance both the penetration of active pharmaceutical ingredients and their retention at the site of application. This dual-action capability makes them particularly effective for localized therapies, such as the treatment of mouth ulcers. The nanoemulsion component, composed of nano-sized droplets, facilitates improved drug solubility and permeation across biological barriers. Incorporation into a gel base not only enhances the viscosity and spreadability of the formulation but also extends its residence time on mucosal or dermal surfaces, allowing for prolonged therapeutic action. Moreover, nanoemulgels reduce surface and interfacial tension, which

contributes to their thermodynamic stability and ensures a more uniform and sustained drug release profile.

Components:

1. **Oil phase:** Used to dissolve lipophilic drugs and stabilize the emulsion; common oils include olive oil, castor oil, and maize oil.
2. **Aqueous phase:** Serves as the continuous phase, typically consisting of distilled or purified water.
3. **Surfactants:** Stabilize the emulsion by reducing interfacial tension. Non-ionic surfactants like Tween 80 and Span 20 are preferred for their safety and efficiency.
4. **Co-surfactant:** Agents like ethanol and PEG 400 enhance emulsion stability and reduce the required surfactant concentration.
5. **Penetration enhancers:** Improve drug permeation across mucosal or skin barriers. Examples include alcohols, terpenes, and esters.
6. **Gelling agent:** Provide gel consistency and spreadability. Commonly used agents are Carbopol and HPMC.
7. **Preservatives:** Prevent microbial growth. Typical preservatives include methylparaben and propylparaben.
8. **pH modifiers:** Maintain pH within a biocompatible range, often using triethanolamine.

Method of preparation:

1. High-pressure homogenization method
2. Ultrasonication method
3. Microfluidization method
4. Self-emulsifying gel method
5. Solvent evaporation method
6. Phase inversion method
7. Coacervation method

Advantages:

- High drug-loading capacity.
- Improved drug penetration and diffusion.
- Low skin irritation compared to traditional carriers.
- Suitable for both hydrophilic and lipophilic drugs.
- Easy application and good patient compliance.

Disadvantages:

- Some drugs may have poor skin absorption.
- May cause irritation in patients with contact dermatitis.
- Larger drug molecules may not permeate easily.
- Potential for allergic reactions.

MATERIALS AND METHODS:

MATERIALS	USE
Lignocaine	Active pharmaceutical ingredient (API)
Carbopol-940	Gelling agent
Castor oil	Oil phase component
Tween-80	Surfactant
Triethanolamine	pH adjuster
Distilled water	Aqueous phase/Solvent

METHOD OF PREPARATION:

Preparation of Nanoemulsion:

The oil phase was prepared by mixing castor oil with tween-80, followed by the incorporation of lignocaine. Separately, tween-80 was also mixed with distilled water to prepare the aqueous phase. Both phases were heated to 70°C using a water bath. The oil phase was then added drop wise into the aqueous phase under high-speed homogenization to form a stable nanoemulsion.

Preparation of Nanoemulgel:

Carbopol-940 was dispersed in distilled water using high-speed magnetic stirrer to form the gel base. The prepared nanoemulsion was then incorporated into the gel base in a 1:1 ratio with continuous stirring. The pH of the final formulation was adjusted using a few drops of triethanolamine to obtain the desired consistency and skin/mucosal compatability.

Formulation development:

INGREDIENTS	QUANTITY TO BE TAKEN		
	F1	F2	F3
Lignocaine	0.6 g	0.6 g	0.6 g
Carbopol-940	0.2 g	0.3 g	0.4 g
Castor oil	2.6 ml	3.6 ml	4.6 ml
Tween 80	2.6 ml	3.6 ml	4.6 ml
Triethanolamine	2 drops	2 drops	2 drops
Water	q.s	q.s	q.s

EVALUATION OF NANOEMULSION:

1. Physical appearance:

The physical appearance of the nanoemulsion was evaluated by visual inspection to assess clarity, color and homogeneity.

2. Dilution test:

The maximum amount of water was added to the oil-in-water (O/W) nanoemulsion, and the formulation was visually inspected for clarity and any signs of phase separation.

3. Determination of viscosity:

Viscosity was measured to evaluate the rheological properties of the formulation using a Brookfield rheometer with spindle no. 63 at 50 rpm. The measurement was conducted at 30℃.

4. Determination of pH:

The pH of the nanoemulsion was measured using a calibrated digital pH meter.

5. Determination of drug content:

Drug content was assessed by UV-visible spectrophotometry. Sample was prepared using ethanol as the diluent, and the absorbance was measured at 228.8 nm.

6. Determination of globule size:

Globule size was analyzed using Scanning Electron Microscopy (SEM) at NISHKA Research Pvt. Ltd., Hyderabad.

7. Stability study:

The stability of the nanoemulsion was assessed by centrifuging the formulation at 5000 rpm for 10 minutes, followed by visual observation for any signs of phase separation.

EVALUATION OF NANOEMULGEL:

1. Determination of homogeneity:

The nanoemulgel was inspected visually for clarity, color, and the presence of particulate matter. A smear was observed under a microscope to check for grittiness.

2. Determination of viscosity:

Viscosity was measured using a Brookfield digital rheometer with spindle no.7 at 200 rpm.

3. Determination of pH:

The pH was determined using a digital pH meter.

4. Determination of spreadability:

Spreadability was determined by applying 0.5 g of the formulation between two glass slides, followed by placing a 100 g weight on the upper slide.
Spreadability(S) was calculated using the formula:

$$S = (M \times L)/T$$

Where, M = weight on the upper slide
L = length of slide
T = time taken to separate the slides

5. Drug release profile:

Drug release was studied using a Franz diffusion apparatus at 37°C. An egg membrane was used as the barrier between the donor and receptor compartments. Phosphate buffer saline (pH 7.4) was added to the receptor compartment, and 1 g of nanoemulgel was placed in the donor compartment. Samples were collected at predetermined intervals and analyzed by UV spectrophotometry at 228.8 nm.

6. Drug content analysis:

A weighed amount of sample was dissolved in 20 ml of ethanol, stirred for 30 minutes, ant the volume was made up to 100 ml. After filtration, a 1 ml aliquot was diluted to 10ml twice, and the absorbance was recorded at 228.8 nm.

7. Accelerated stability study:

Stability was assessed by storing the formulations at 40 ± 2°C and 75 ± 5% RH for three months. Samples were withdrawn at 0, 30, 60, and 90 days and evaluated for physical stability and phase separation.

RESULTS AND DISCUSSION:

EVALUATION OF NANOEMULSION:

1. Physical appearance:

The prepared nanoemulsion was clear, homogeneous, and free from visible particulate matter or phase separation. It exhibited a uniform color with no signs of turbidity, creaming, cracking, or sedimentation, indicating good physical stability.

2. Dilution test:

Formulation	Clarity	Phase separation
Nanoemulsion	Clear	Absent

3. Determination of viscosity:

Formulation	F1	F2	F3
Nanoemulsion	31.66 ± 1.52 cps	40 ± 2 cps	27.33 ± 1.15 cps

F2 formulation had optimal viscosity within the desired range of 20 – 70 cps.

4. Determination of pH:

Formulation	F1	F2	F3
Nanoemulsion	7.16 ± 0.11	6.86 ± 0.05	6.93 ± 0.05

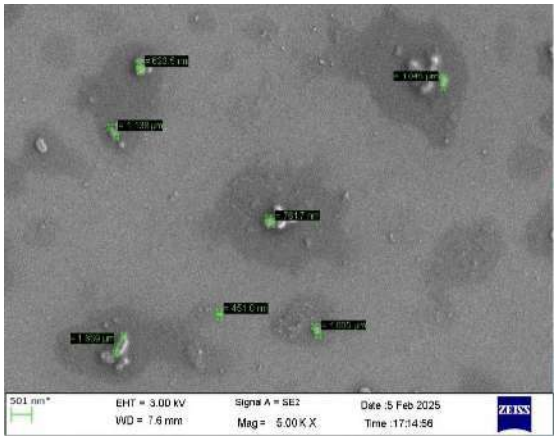
F2 had an ideal pH compatible with topical application.

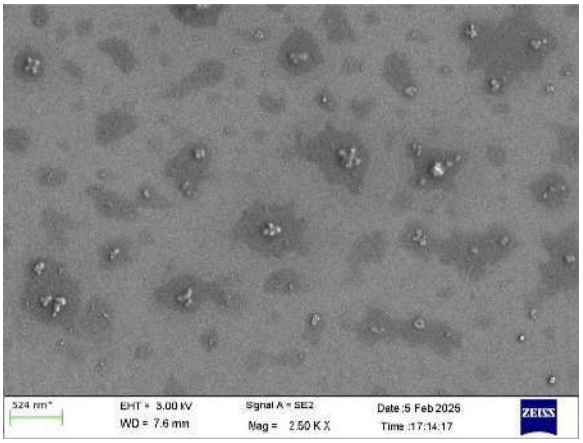
5. Determination of drug content:

Formulation	F1	F2	F3
Nanoemulsion	90.79 ± 0.1 (%)	95.90 ± 0.05 (%)	84.56 ± 0.03 (%)

F2 showed the highest drug content.

6. Determination of globule size:





The average globule size of the nanoemulsion was found to be in the range of 200 – 1000 nm.

7. Stability study:

Formulation	F1	F2	F3
Nanoemulsion	++	+++	+

F2 exhibited excellent phase stability.

EVALUATION OF NANOEMULGEL:

1. Determination of homogeneity:

Formulation	Homogeneity
Nanoemulgel	Homogenous

2. Determination of viscosity:

Formulation	F1	F2	F3
Nanoemulgel	2598 ± 0.694 cps	2860 ± 0.014 cps	2477 ± 0.0061 cps

F2 had optimal viscosity for gel application.

3. Determination of pH:

Formulation	F1	F2	F3
Nanoemulgel	7.39 ± 0.01	6.87 ± 0.51	7.01 ± 0.06

F2 exhibited an ideal pH for mucosal application.

4. Determination of spreadability:

Formulation	F1	F2	F3
Nanoemulgel	70.57 ± 1.3 g.cm/sec	73.32 ± 4.59 g.cm/sec	68.76 ± 3.1 g.cm/sec

F2 showed the better spreadability.

5. Drug release profile:

Formulation	%CDR		
	F1	F2	F3
0	0	0	0
20	35.42	18.25	26.40
40	50.18	32.90	41.87
60	65.35	50.75	60.42
80	78.44	68.31	76.15
100	88.91	84.12	89.03
120	96.12	94.78	95.25

F2 exhibited sustained and controlled drug release.

6. Drug content analysis:

Formulation	F1	F2	F3
Nanoemulgel	90.15 ± 0.12 (%)	99.94 ± 1.70 (%)	95.78 ± 1.4 (%)

F2 had the highest drug content.

7. Accelerated stability study:

Formulation	F1	F2	F3
Nanoemulgel	Stable	No phase separation. Highly stable	Stable

DISCUSSION

Mouth ulcers are common oral lesions that affect the lips, tongue, gums, and inner cheeks. Conventional formulations such as ointments and gels often offer limited efficacy due to poor mucosal retention. To address this, a nanoemulgel was developed by combining the advantages of emulsions and gels, aiming to enhance mucosal adhesion and drug penetration. Lignocaine, a local anesthetic with anti-inflammatory properties, was selected as the active pharmaceutical ingredient. Castor oil was used as the oil phase for its high solubilizing capacity and enhanced permeation, while Carbopol-940 served as the gelling agent due to its viscosity and drug delivery efficiency. Among the three formulations (F1, F2, F3), F2 exhibited optimal performance. It showed ideal pH (6.87 ± 0.51), highest viscosity (2860 ± 0.014 cps), and excellent spreadability (73.32 ± 4.59 g·cm/sec), all of which contribute to better mucosal adherence and ease of application. The drug content of F2 ($99.94 \pm 1.70\%$) and its controlled drug release profile (94.78% at 120 min) further confirmed its therapeutic potential. Stability studies at 40 ± 2 °C and $75 \pm 5\%$ RH demonstrated that F2 remained physically stable with no phase separation over three months. Thus, F2 was identified as the optimized formulation, offering improved stability, drug release, and therapeutic efficacy for the management of mouth ulcers.

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