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FORMULATION AND EVALUATION OF MICROEMULSION BASED GEL FOR NASAL DRUG DELIVERY SYSTEM

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ABSTRACT:

The present study aims to formulate and evaluate a microemulsion-based gel for intranasal delivery of capsaicin, a poorly water-soluble drug known for its analgesic and anti-inflammatory effects. Drug absorption is, however, hampered by issues including mucociliary clearance and a short nasal residence duration.

Based on solubility tests, a microemulsion was created to overcome these restrictions utilising isopropyl myristate (oil phase), Tween 80 (surfactant), and PEG 400 (co-surfactant). Using Carbopol 934, the optimised microemulsion was then combined with a gel to create a spreadable, pH-compatible, and thermally stable formulation that could be used in the nose.

The formulation was tested for stability, drug content, in vitro drug release, pH, viscosity, and spreadability. The formulation was evaluated for pH, viscosity, spreadability, drug content, in vitro drug release, and stability. Results demonstrated that the microemulsion-based gel achieved sustained drug release over 8 hours and maintained physical and chemical stability under accelerated conditions. This novel drug delivery platform has potential for enhanced therapeutic efficacy, patient compliance, and bioavailability of lipophilic drugs delivered via the nasal route.

Introduction

Nasal Drug Administration System

Medications like proteins and peptides that are active at low dosages and do not have minimal oral bioavailability, it is a helpful delivery technique. The mucociliary clearance mechanism's quick departure from the absorption site in the nasal cavity is one of the causes of the low degree of peptide and protein absorption via the nasal route (Mahalaxmi R et al., 2007).
Numerous animal models have been used to test drug candidates, ranging in size from tiny metal ions to massive macromolecular proteins (Chien YW et al., 1989).

Certain hormones and steroids have been shown to be more fully absorbed when administered by the nose. This suggests that the nasal route may be useful for both administering systemic drugs and using it for local effects. Nasal administration of medications for both topical and systemic effect has been used for many years. Topical administration has led to the development of a wide range of drugs, including corticoids, antihistamines, anticholinergic, and vasoconstrictors, and is used to treat congestion, rhinitis, sinusitis, and associated allergy or chronic diseases. More research on the nasal route has been conducted recently, with a particular emphasis on nasal application for systemic drug delivery (Kublik H et al., 1998).
These include dry powder inhalers, aqueous nasal sprays, nasal gel pumps, pressured MDIs, and nasal drops in multiple or single-dose formulations. Additional therapeutic areas that are being developed or may benefit from nasal administration include rheumatoid arthritis, cancer treatment, epilepsy, antiemetics, and insulin-dependent diabetes.

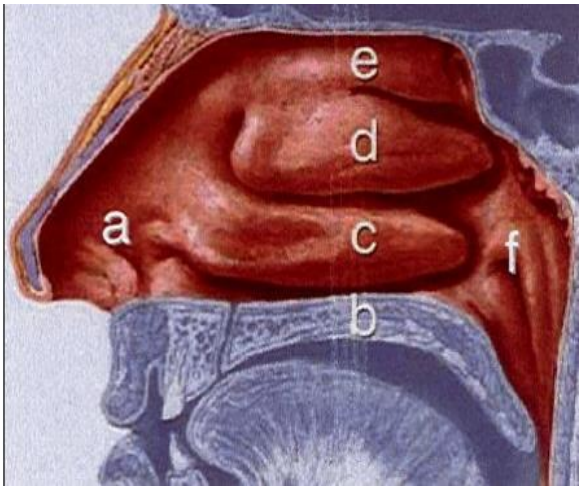
Advantages

- There is no evidence of drug breakdown in the gastrointestinal tract.
- It is possible to produce a rapid beginning of action and rapid medication absorption.
- Absorption enhancers or other methods can be used to increase the bioavailability of bigger medication molecules.
- For smaller pharmacological molecules, the nasal bioavailability is good.
- Nasal drug delivery is a method of delivering oral medications that are not absorbed to the systemic circulation.
- Research to date suggests that the nasal route is a viable alternative to the parenteral route, particularly for medications containing proteins and peptides.
- When compared to parenteral medication, it is more convenient for patients, particularly those undergoing long-term therapy.

Anatomy & Physiology of Nasal Cavity

The nasal depression is divided into two halves by the nasal septum and extends posterior to the nasopharynx, while the most anterior part of the nasal depression, the nasal entranceway, opens to the face through the nostril.

The nasal depression consists of three main regions nasal entranceway, olfactory region, and respiratory region. The face area in the nose can be enlarged about 150cm2 by the side walls of the nasal depression including a folded structure, it's a veritably high face area compared to its small volume. The main nasal airway has narrow passages, generally it is 1- 3 mm wide and these narrows structures are useful to the nose to carry out its main functions.



Parts of Nasal Cavity Consists	Parts Name
	Nasal vestibule
	Palate
	Inferior Turbinate
	Middle Turbinate
	Superior Turbinate (Olfactory Mucosa)
	Nasopharynx

Factors Influencing Nasal Drug Absorption

Medicine immersion Several factors affect the systemic bioavailability of medicines that are administered through the nasal route. These factors play a crucial part for the utmost of the medicines to reach therapeutically effective blood situations after nasal administration. The factors impacting nasal medicine immersion are described as follows.

1) Physiochemical properties of drug.

- Molecular size.
- Lipophilic
- hydrophilic balance.
- Enzymatic declination in nasal depression.

2) Nasal Effect

- Membrane permeability.
- Environmental pH
- Mucociliary concurrence
- Cold, rhinitis.

3) Delivery Effect

- Expression (Attention, Ph, Osmolarity)
- Delivery Goods
- Medicines Distribution and Deposit.
- Density

Pathways For Nasal Absorption

The Paracellular route

The paracellular permeability of the nasal epithelium is roughly the same as that of the intestine, therefore small hydrophilic motes can passively diffuse between conterminous cells.

The transcellular route

The transport across the epithelial cells, which can be done by unresistant prolixity, carrier-intermediated transport, and endocytic processes (e.g., transcytosis). Traditionally, the transcellular route of the nasal mucosa has been simply viewed as primarily crossing the “Lipoidal Hedge”, in which the immersion of a medicine is determined by the magnitude of its partition measure and its molecular size.

Transcellular passive diffusion

For utmost conventional medicine motes, which tend to be small and lipophilic, immersion occurs transcellularly, by unresistant prolixity across the cells of the epithelium. Again, movement occurs down an attention grade, according to Fick’s first law of prolixity. The degree of ionization of a medicine species is an important property for immersion via unresistant transcellular prolixity and is dependent on the pKa of the medicine and the pH of the terrain; the pH of nasal concealment is typically in the region 5.5- 6.5.

Formulation Development In Nasal Drug Delivery

Specific types of lozenge forms that are used to deliver phrasings into the nose are important in determining the nasal immersion biographies of medicines. The choice of a certain lozenge form generally depends on the medicine being developed, the suggestion being pursued, the patient population, and marketing aspects. colourful different nasal lozenge forms that have been developed and considered reported include the following Specific types of lozenge forms that are used to deliver phrasings into the nose are important in determining the nasal immersion biographies of medicines. The choice of a certain lozenge form generally depends on the medicine being developed, suggestions being pursued, patient population, and marketing aspects. colourful different nasal lozenge forms that have been developed and considered reported include the following Specific types of lozenge forms that are used to deliver phrasings into the nose are important in determining the nasal immersion biographies of medicines. The choice of a certain lozenge form generally depends on the medicine being developed, the suggestion being pursued, the patient population, and marketing aspects. colourful different nasal lozenge forms that have been developed and considered reported include the following Specific types of lozenge

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Nasal drops

Nasal drops are one of the most simple and accessible systems developed for nasal delivery. The main disadvantage of this system is the lack of cure perfection and thus nasal drops may not be suitable for traditional products. Nasal drops, if administered rightly deposit medicine throughout the nasal depression, which offers a larger effective area for immediate immersion than if the medicine is delivered in the form of a spray. Some medicine is deposited on the ciliated regions of the mucosa and is thus incontinently available for concurrence.

Nasal sprays

Nasal sprays are available as squeeze bottles which would not be anticipated to give reproducible dosing. They're also available as metered cure bias which would be anticipated to give further reproducible dosing as a mechanical actuation delivers a determined volume to the case. therefore, the cure of medicine entered by the case will be dependent on the attention of medicine in the expression. Nasal region sprays tend to deposit at their impaction point, in the anterior, non-ciliated regions of the nasal depression where air-inflow associated with alleviation is high and mucociliary concurrence is slow or erratic.

Nasal powder

This lozenge form may be developed if result and suspense lozenge forms cannot be developed e.g., due to lack of medicine stability. The advantages to the nasal greasepaint lozenge form are the absence of preservatives and superior stability of the expression. still, the felicity of the greasepaint expression is dependent on the solubility patch size, aerodynamic parcels, and nasal irritancy of the active medicine and or excipients. The original operation of medicine is another advantage of this system.

Nasal gels

Nasal gels are high-density thickened results or dormancies. Until the recent development of precise dosing devices, there wasn't an important interest in this system. Reduction of vexation by using soothing/ emollient excipients and target to mucosa for better immersion.

Nanoparticles

Lately, important attention has been given to nanotechnology in numerous areas. Nanoparticle systems are being delved into to ameliorate medicine delivery and intranasal medicine administration. Nanoparticles are solid colloidal patches with periphery ranging from 1- 1000nm. They correspond to macromolecule accoutrements and can be therapeutically used as adjuvants in vaccines or as medicine carriers, in which the active substance is dissolved, entangled, reprised, adsorbed, or chemically attached. Nanoparticles may offer several advantages due to their small size, but only the lowest nanoparticles access the mucosal membrane by paracellular route and in a limited volume because the tight junctions are in the order of 3.9- 8.4. The low bioavailability attained can be because patches are presumably taken up by M- cells in the nasal-associated lymphoid towel and thus, transported into the lymphatic system and blood sluice.

Microspheres

Microspheres are generally grounded on mucoadhesive polymers (chitosan, alginate), which present advantages for intranasal medicine delivery. likewise, microspheres may also cover the medicine from enzymatic metabolism and sustained medicine release, dragging its effect.

Nasal inserts

The principle of the lozenge form is to imbibe nasal fluid from the mucosa after administration and to form a gel in the nasal depression to avoid foreign body sensation.

Microemulsion

lately, there has been an increased interest in microemulsions, for the delivery of hydrophilic and lipophilic medicine as medicine carriers because of their bettered medicine solubilization, longer shelf life, The nature of the factors of the system like oil painting, surfactant, cosurfactant, and water, as well as temperature and pressure which affect the microemulsion systems are known as the expression variables. Interest in this field is increasing and their operations have been diversified to colorful administration routes in addition to the conventional oral route. Microemulsions have drawn attention

to their use as new vehicles for medicine delivery. Microemulsion systems are also now being extensively used for transdermal, optical, nasal, and intravenous medicine delivery.

INTRODUCTION OF MICROEMULSION:

The essential distinction between normal conflation and microemulsion is their drop size and stability; the former is 'kinetically stable' whereas the ultimate is 'thermodynamically stable'. The stability of microemulsion can be told by the addition of swabs, other complements, temperature or pressure. Microemulsions can be prepared by controlled addition of lower alkanols (butanol, pentanol, and hexanol) to milky mixes to produce transparent results comprising dissipations of either water-in-oil painting (w/ o) or oil painting-in-water (o/ w) in nanometer or colloidal dissipations (100 nm). The lower alkanols are called cosurfactants; they lower the interfacial pressure between oil painting and water sufficiently low for nearly robotic conformation of the said micro miscellaneous systems. The miscibility of oil painting, water, and amphiphile (surfactant plus cosurfactant) depends on the overall composition which is system-specific. To gain an understanding of the reasons for microemulsion conformation, it's demanded first to consider the parcels of amphiphiles, similar as surfactants in the result. Conventional surfactant motes comprise a polar head region and polar tail region, the ultimate having the larger molecular volume, particularly in the case of ionic surfactants. On disbandment in water, surfactants tone-associate into a variety of equilibrium phases, the nature of which stems directly from the interplay of the colorful inter and intermolecular forces as well as entropy considerations. Surfactants are also tone-associated with nonaqueous detergents, particularly polar liquids similar to alkanes. In this case, the exposures of the surfactant motes are reversed compared to those espoused in the waterless results. The reorientations serve to optimize the deliverance conditions of the surfactant and minimize the free energy of the overall system.

Theories of microemulsion formation

Historically, three approaches have been used to explain microemulsion conformation and stability. These are (i) interfacial or mixed film propositions (ii) Solubilization propositions and (iii) thermodynamic treatments. An in-depth discussion of these propositions is beyond the compass of this review but has been addressed by others. still, a simplified thermodynamic vindication is presented below. The free energy of microemulsion conformation can be considered to depend on the extent to which surfactant lowers the face pressure of the oil painting water interface

ΔGf1/4 ΔA - TΔS

It should be noted that when a microemulsion is formed the change in Δ A is veritably large due to the large number of veritably small driblets formed. Firstly, workers proposed that for a microemulsion to be formed a (flash) negative value of was needed, it's now honored that while the value of is positive at all times, it's tiny (of the order of fragments of mm/ m), and is neutralized by the entropic element.

Microemulsion structure

The structure of microemulsion can be effectively explained by the drop model where in the driblets of microemulsion are girdled by interfacial film conforming of both surfactant and co-surfactant motes. The exposure of these amphiphiles will be different for o/ w and w o microemulsions. The nonpolar portion of these motes will live in the dispersed phase of o/ w system, while the polar group's pooch in the nonstop phase, while the contrary is true for w/ o microemulsion.

Types of microemulsions

Micro mixes are thermodynamically stable but are only set up under precisely defined conditions. One way to characterize these systems is by whether the disciplines are in driblets or nonstop. Characterizing the systems in this way results in three types of microemulsions

Oil-In-Water (o/w)

Water-In-Oil (w/o)

BI continuous

Oil-In-Water (o/w)

This type of microemulsion generally has a larger commerce volume than the w o microemulsions. The monolayer of surfactant forms the interfacial film that's acquainted in a "positive" wind, where the polar head-groups face the nonstop water phase and the lipophilic tails face into the oil painting driblets. The o/ w systems are intriguing because they enable a hydrophobic medicine to be more answerable in a waterless grounded system, by solubilizing it in the internal oil painting driblets.

Water-In-Oil (w/o)

Microemulsion used orally or parenterally may be destabilized by the waterless natural system.

BI continuous

BI continuous microemulsions, as mentioned ahead, may show on Newtonian inflow and malleability. These parcels make them especially useful for topical delivery of medicines or for intravenous administration, where upon dilution with waterless natural fluids, form an o/ w microemulsion.

Formulation considerations and potential ingredients

In general, the miracle of micro emulsification is substantially governed by factors similar as

- Nature and attention of the oil painting, surfactant, cosurfactant, and waterless phase
- oil painting/ surfactant and surfactant/ cosurfactant rate
- Physicochemical parcels of the medicine similar as hydrophilicity/ lipophilicity, pKa, and opposition. Hence, these factors should be given due consideration while expressing the microemulsions. expression considerations concerning the factors of the microemulsions are bandied below.

Oily phase

Selection of an applicable unctuous phase is veritably important as it influences the selection of the other constituents of microemulsions, substantially in the case of o/ w microemulsions. generally, the oil painting, which has maximum solubilizing eventuality for the named medicine seeker, is named as an unctuous phase for the expression of microemulsions. This helps to achieve minimal medicine lading in the microemulsions. At the same time, the capability of the named oil painting to yield systems with larger microemulsion actuality regions is also important. It's delicate for a single unctuous element to merge both these conditions. It's a known fact that canvases with exorbitantly long hydrocarbon chains (or high molecular volume) similar as soybean oil painting are delicate to microemulsion whereas canvases with shorter chain (or low molecular volume) similar as medium chain triglycerides (MCT), adipose acid esters (like ethyl oleate) are easy to micro emulsify. On the negative, the capacity of solubilization of lipophilic halves generally increases with the chain length of the unctuous phase. The choice of the unctuous phase is frequently a concession between its capability to solubilize the medicine and its capability to grease conformation of microemulsions of asked characteristics. In certain cases, an admixture of canvases is also used to meet both conditions. For illustration, an admixture of fixed oil painting and medium chain triglyceride is used in certain cases to have a good balance between medicine lading and emulsification. lately, vitamin E (d- tocopherol) grounded mixes are proposed in some examinations substantially due to their solubilizing eventuality. It has been reported that vitamin E can solubilize API similar to itraconazole, Saquinavir, and paclitaxel which are delicate to solubilize by using conventional unctuous factors. There are no reports on the vitamin E grounded microemulsions but there's a great compass to develop similar systems. lately, microemulsions grounded on medium-chain mono- and diglycerides have also been reported. Medium chain mono- and diglycerides similar to Capmul MCM have much more advanced solubilization eventuality than that of the fixed canvases and MCT and they're easy to microemulsion.

Methods of microemulsion preparation

Phase titration method (water titration method)

The construction of phase illustration is a needful approach to study the complex series of relations that can happen when different factors are incorporated in a system. Microemulsion expression goes on with colorful association structures (conflation, micelles, hexagonal, patellar, boxy, gel, and unctuous dissipation) depending on the chemical composition and attention of each element. Mock ternary phase illustration is frequently constructed to find the different zones, including the microemulsion region, in which each corner of the triangle represents 100 of one particular element. The region can be separated into o/w or w o microemulsion by simply considering the composition, whether it is water-rich or oil painting-rich. Compliances must be made precisely so that the metastable systems aren't included.

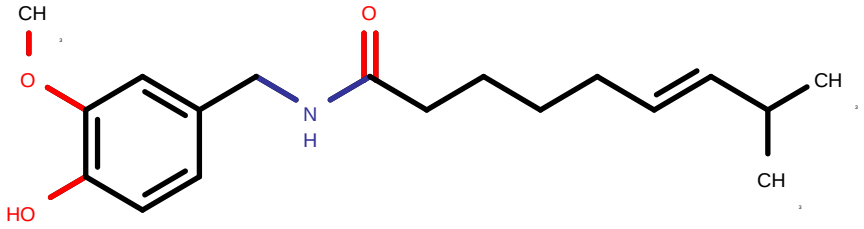
Phase inversion system

During phase inversion physical changes occur, including flyspeck size changes that can affect medicine release in vivo and in vitro. These styles make use of changing the curve of the product. At the time of cooling, the system reaches a point of zero curve and minimum face pressure, promoting the conformation of fine oil painting driblets that are dispersed. This system is also known as the phase inversion temperature(hole) system. Other parameters such as swab attention or pH value may be considered as well rather than the temperature alone. Also, a transition in the robotic compass of the curve can be attained by changing the water bit. By adding water into the oil painting phase, originally water driblets are formed in a nonstop oil painting phase. Short-chain surfactants form monolayers at the o/w interface performing in a BI continuous microemulsion at the inversion point.

- **Drug Profile: Capsaicin**

Capsaicin ($C_{18}H_{27}NO_3$) Parameter	Details
Drug Name	**Capsaicin**
Chemical Formula	**$C_{18}H_{27}NO_3$**
Molecular Weight	**305.41 g/mol**
Category	**Analgesic, Counterirritant**
Mechanism of Action	**Acts on TRPV1 (transient receptor potential vanilloid 1) receptors in sensory neurons, depleting substance P, thereby reducing pain sensation.**
Solubility	**Insoluble in water; soluble in alcohol, oils, and organic solvents**
Half-Life	**Approximately 1.5–2 hours (topical/nasal)**
Therapeutic Use	**Neuropathic pain, migraine, arthritis, post-herpetic neuralgia**
Challenges in Delivery	**Low water solubility, rapid metabolism, limited absorption orally**
Advantages via Nasal Route	**Avoids first-pass metabolism, allows rapid systemic or local effect**

Structure



Capsaicin ($C_{18}H_{27}NO_3$)

Capsaicin

- Capsaicin is a topical analgesic that is used to treat several types of muscle and joint pain, including the neuropathic pain associated with post-herpetic neuralgia.

Brand Names

- Capzasin Quick Relief, Capzasin- HP, Castiva Warming, Dendracin Neurodendraxcin, Lidopro, Medi- derm, Medi- derm With Lidocaine, Medrox, Qutenza, Rematex, Xoten- C, Zostrix

Generic Name

- Capsaicin

Background

- Capsaicin is a topical analgesic that is used to treat several types of muscle and joint pain, including the neuropathic pain associated with post-herpetic neuralgia.
- Capsaicin is a naturally- being botanical inconvenience in chili peppers, synthetically deduced for pharmaceutical phrasings. The most recent capsaicin FDA blessing was Qutenza, an 8-capsaicin patch dermal-delivery system, indicated for neuropathic pain associated with post-herpetic neuralgia.

Properties

- Lipophilic, poorly soluble in water

- Strong affinity for lipid membranes
- Volatile and pungent; requires careful formulation for mucosal use

Role in Formulation

- Active pharmaceutical ingredient (API)
- Delivered via nasal mucosa for rapid local or systemic effect
- **Therapeutic Uses**

- Neuropathic pain, arthritis, post-herpetic neuralgia, and migraine
- **Formulation Challenge**

- Low aqueous solubility necessitates the use of solubilizing systems like microemulsions

Aim and Objectives

Aim

- To formulate and estimate a microemulsion-grounded gel for nasal delivery of a named medicine.

Objectives

- To prepare a stable capsaicin-loaded microemulsion.
- To incorporate the microemulsion into a nasal gel base.
- To evaluate the gel formulation for pH, viscosity, spreadability, drug content, in vitro drug release, and stability.

Materials and Methods

Materials Used

- Drug: Capsaicin
- Oil Phase: Isopropyl Myristate
- Surfactant: Tween 80
- Co-surfactant: PEG 400
- Gelling Agent: Carbopol 934
- Other Reagents: Distilled water, NaOH

Equipment

- Magnetic stirrer
- pH meter
- Brookfield viscometer
- Franz diffusion cell
- UV-spectrophotometer

Steps

- **Solubility Study**
- The solubility of capsaicin was determined in different oils and surfactants to select suitable components for the microemulsion.
- **Microemulsion Preparation**
- Mixtures of oil, surfactant, and co-surfactant (Smix) were made in the proper proportions. A transparent microemulsion was created by adding water drop by drop. In the ideal formulation, the medication was dissolved.
- **Creation of Gel**
- Throughout the night, carbopol 934 was wet. The gel base and the prepared microemulsion were combined. Using NaOH, the pH was brought down to 5.5–6.5.
- **Materials Used**
- Oil Phase: Isopropyl Myristate (IPM)
- Type: Lipophilic ester
- Structure: Isopropyl alcohol ester of myristic acid
- **Function**
- Solubilizes lipophilic drugs (like capsaicin)
- Enhances skin and mucosal permeability

- **Properties**:

- Non-toxic, colorless, non-greasy
- Good spreading properties
- **Role in Microemulsion:**
- Provides an internal phase for drug solubilization
- Helps form stable o/w microemulsions when paired with suitable surfactants

Surfactant: Tween 80 (Polysorbate 80)

- **Type**: Non-ionic surfactant
- **HLB Value**: ~15 (high, suitable for oil-in-water microemulsions)
- **Function**
  - Stabilizes the microemulsion droplets
  - Enhances solubility and dispersion of capsaicin
- **Properties**
  - Biocompatible and widely used in pharmaceuticals
  - Suitable for mucosal use with minimal irritation
- **Rationale for Use**
  - Its high HLB value supports the formation of transparent, stable o/w microemulsions

Co-Surfactant: PEG 400 (Polyethylene Glycol 400)

- Type: Hydrophilic liquid co-surfactant
- **Function**
- Works synergistically with Tween 80 to lower the interfacial tension further
- Helps to form a thermodynamically stable and clear microemulsion
- Modifies the flexibility and curvature of the surfactant film at the oil–water interface
- **Properties**
- Miscible with water and ethanol
- Non-toxic, non-irritating, and pharmaceutically accepted
- Why Used with Tween 80
- Alone, Tween 80 might not produce sufficient emulsification; PEG 400 enhances emulsification and droplet size control

Gelling Agent: Carbopol 934

- Type: Crosslinked polyacrylic acid polymer
- **Function**:
- Converts the liquid microemulsion into a gel form
- Provides viscosity and consistency for nasal administration
- Ensures prolonged residence time on the nasal mucosa (enhanced absorption)
- **Properties**:
- Forms clear gels in water upon neutralization with a base (e.g., NaOH)
- Requires hydration and pH adjustment (to ~5.5–6.5 for nasal compatibility)
- **Reason for Selection:**
- Exhibits pseudoplastic rheology (shear-thinning), ideal for easy application and nasal spread
- Distilled Water
- **Role**:
- Aqueous phase of the microemulsion
- Solvent for hydrophilic components
- **Importance**:
- Purified to prevent microbial contamination and unwanted interactions
- Sodium Hydroxide (NaOH)
- **Function**:
- Neutralizes Carbopol 934 to induce gelation
- **Use**:
- Added dropwise to avoid abrupt pH changes and ensure consistent viscosity

Ingredients and Their Quantities (for 100 g of Final Product)

Sr. No.	Ingredient	Function	Quantity (% w/w)	Quantity (g)
1	Capsaicin	Active Drug	0.1%	0.1 g
2	Isopropyl Myristate	Oil Phase	5.0%	5.0 g
3	Tween 80	Surfactant	20.0%	20.0 g
4	PEG 400	Co-surfactant	20.0%	20.0 g
5	Carbopol 934	Gelling Agent	0.5%	0.5 g
6	Sodium Hydroxide (0.5 N)	pH Adjustment	q.s.(to pH 5.5–6.5)	~0.2–0.4 mL
7	Distilled Water	Aqueous Phase (vehicle)	q.s. to 100 g	~54.4 g

Formulation Procedure

Step 1: Solubility Determination (Preformulation Study)

- Determine the solubility of Capsaicin in various oils, surfactants, and co-surfactants.
- Select Isopropyl Myristate (oil), Tween 80 (surfactant), and PEG 400 (co-surfactant) based on the highest solubility and compatibility.

Step 2: Preparation of Surfactant-Co-surfactant Blend (Smix)

- Accurately weigh 20 g of Tween 80 and 20 g of PEG 400.
- Mix them thoroughly in a beaker using a magnetic stirrer until a uniform Smix (1:1) is formed.

Step 3: Oil Phase Addition

- Add 5 g of Isopropyl Myristate to the above Smix.
- Stir continuously to obtain a clear homogeneous oil phase mixture.

Step 4: Drug Incorporation

- Weigh 0.1 g of Capsaicin.
- Dissolve it completely in the Smix + oil phase under continuous stirring until a transparent solution is achieved.

Step 5: Formation of Microemulsion

- Using continuous magnetic st. Using continuous magnetic stirring, gradually add 54.4 g of distilled water dropwise to the oil phase mixture at room temperature.irring, gradually add 54.4 g of distilled water dropwise to the oil phase mixture at room temperature.
- A clear, transparent oil-in-water microemulsion should form.
- Continue stirring for 15–20 minutes to ensure stability and uniform dispersion.

Step 6: Preparation of Gel Base

- In 10–15 millilitres of distilled water, dissolve 0.5 grammes of carbopol 934.
- Leave it at room temperature to hydrate for at least two hours or overnight.
- To avoid the production of air bubbles, stir gently.

Step 7: pH Adjustment of Gel Base

- Add 0.5 N Sodium Hydroxide solution dropwise to the Carbopol dispersion.
- Adjust until the final pH reaches 5.5–6.5, ideal for nasal mucosa.

Step 8: Incorporation of Microemulsion into Gel Base

- Gradually add the prepared microemulsion into the neutralized Carbopol gel base.
- Mix gently using a glass rod or mechanical stirrer to avoid foam formation.
- Ensure a uniform, transparent, and smooth gel is formed.

Step 9: Final Makeup and Packaging

- Bring the total weight up to 100 g with distilled water if necessary.
- Mix gently to ensure homogeneity.
- Transfer the final formulation into sterile, light-protective nasal tubes or containers.

Evaluation Parameters

Test	Result/Requirement
Appearance	**Transparent, uniform gel**
pH	**Within 5.0–6.5**
Viscosity	**Evaluated using Brookfield Viscometer**
Spreadability	**Acceptable with minimal force required**
Drug Content	**> 90% by UV-spectrophotometric assay**
In vitro Drug Release	**Sustained over 8 hours (Franz diffusion cell)**
Stability	**No phase separation or drug loss after 2 weeks**

Results and Discussion

- Solubility studies revealed Isopropyl Myristate, Tween 80, and PEG 400 as the most effective components for drug incorporation.
- The resulting microemulsion-based gel was clear, stable, and had appropriate pH and viscosity.
- In vitro release studies demonstrated sustained drug release, which is beneficial for prolonged therapeutic action.
- Stability studies showed no significant changes in viscosity, clarity, or drug content, indicating good shelf-life potential.

Future Scope

The successful development and evaluation of a capsaicin-loaded microemulsion-based gel highlight multiple future research and application opportunities:

- In Vivo Evaluation: Future studies should include pharmacokinetic and pharmacodynamic testing in animal models or clinical trials to assess bioavailability and therapeutic outcomes.
- Mucoadhesive Enhancement: Incorporating mucoadhesive polymers (e.g., chitosan, HPMC) could improve nasal retention time and drug absorption by resisting mucociliary clearance.
- Thermoresponsive Gels: Exploring temperature-sensitive polymers (e.g., Pluronic F127) can enable sol-to-gel transitions at nasal temperatures, enhancing drug residence time and patient comfort.
- Targeted Brain Delivery: Intranasal microemulsion systems can be optimized for nose-to-brain delivery, particularly useful for central nervous system (CNS) disorders like migraine, epilepsy, and neurodegenerative diseases.
- Broader Drug Application: The delivery system can be extended to other hydrophobic drugs or biomolecules such as peptides, vaccines, or hormones requiring rapid absorption and non-oral routes.
- Patient-Centric Formulations: Development of portable nasal devices for accurate dosing and ease of self-administration could make these formulations more commercially viable.
- Regulatory and Commercial Translation: Addressing regulatory compliance and scaling up the formulation for clinical or market-level production is crucial for real-world application.

Conclusion

The present research successfully demonstrates the feasibility of using a microemulsion-based gel for the nasal delivery of capsaicin, achieving enhanced solubility, improved mucosal retention, and controlled drug release. The optimized formulation showed favorable characteristics in terms of pH, viscosity, spreadability, drug content, and in vitro performance.

Compared to conventional nasal formulations, the microemulsion-based gel provides multiple advantages—including increased bioavailability, reduced dosing frequency, and improved patient compliance. By integrating both solubilization and gelling technologies, this system can overcome many limitations associated with nasal drug delivery of poorly soluble compounds.

The formulation showed excellent stability and reproducibility, indicating its potential for long-term storage and large-scale manufacturing. Furthermore, the modular nature of this approach allows adaptation for a wide range of therapeutic agents.

In conclusion, this study paves the way for a new generation of intranasal drug delivery systems that are efficient, patient-friendly, and pharmaceutically robust. With further refinement and in vivo validation, microemulsion-based gels may significantly contribute to the advancement of non-invasive drug delivery technologies.

Appendices

Appendix A: Composition of the Final Formulation (100 g Batch)

S. No.	Ingredient	Purpose	Quantity (% w/w)	Amount (g)
1	Capsaicin	Active drug	0.1%	0.1 g
2	Tween 80	Surfactant	20.0%	20.0 g
3	PEG 400	Co-surfactant	20.0%	20.0 g
4	Sodium Hydroxide (0.5N)	pH adjustment	q.s.	~0.2–0.4 mL
5	Distilled Water	Vehicle	q.s. to 100%	~54.4 g

Appendix B: Observation Table

Parameter	Test Method	Observation	Specification
Appearance	Visual inspection	Clear, transparent gel	Should be free of particles
Viscosity	Brookfield viscometer	2300 ± 100 cps	Suitable for nasal use
Spreadability	Glass slide method	6.5 cm	≥ 5 cm preferred
Drug content	UV-spectrophotometry (λ = 281 nm)	97.8%	≥ 90%
Stability (14 days)	Physical observation	No phase separation	Stable at 40°C

Appendix C: Solubility Screening of Capsaicin

Solvent	Solubility of Capsaicin
Isopropyl Myristate	High
Tween 80	High
PEG 400	High
Water	Very low
Ethanol	Moderate

Conclusion: Isopropyl Myristate, Tween 80, and PEG 400 were selected based on solubility and compatibility.

Appendix D: List of Equipment Used

Instrument	Purpose
Digital pH Meter	pH measurement of gel
Magnetic Stirrer	Mixing and emulsification
Brookfield Viscometer	Viscosity measurement
UV-Visible Spectrophotometer	Drug content analysis
Franz Diffusion Cell	In vitro drug release study
Analytical Balance	Accurate weighing of ingredients

Appendix E: Safety and Handling Information

Material	Precaution
Capsaicin	Use gloves and mask; avoid eye/skin contact
Carbopol 934	Use dust mask to avoid inhalation
NaOH (0.5N)	Corrosive—use gloves and handle with care
Organic solvents	Handle in ventilated areas to avoid vapor inhalation

Appendix F: Abbreviations

Abbreviation	Full Form
API	Active Pharmaceutical Ingredient
PEG	Polyethylene Glycol
HLB	Hydrophilic-Lipophilic Balance
IPM	Isopropyl Myristate
UV	Ultraviolet
CPS	Centipoise (unit of viscosity)
q.s.	Quantum satis (amount sufficient to make)

REFERENCES

1. Khan, A. W., Kotta, S., Ansari, S. H., Sharma, R. K., & Ali, J. (2013). Formulation development, optimization and evaluation of aloe vera gel for wound healing. Pharmacognosy Magazine, 9(1), S6–S10. https://doi.org/10.4103/0973-1296.117846
2. Raut, S. Y., & Bhalekar, M. R. (2016). Nasal drug delivery system: Formulation and evaluation of microemulsion-based gel for intranasal delivery of drug. International Journal of Pharmaceutical Sciences and Research, 7(2), 835–841. https://doi.org/10.13040/IJPSR.0975-8232.7(2).835-41
3. Zaki, N. M., & Awad, G. A. (2008). Preparation and in-vitro/in-vivo evaluation of a thermally reversible nasal gel containing microemulsion of tramadol. European Journal of Pharmaceutics and Biopharmaceutics, 70(2), 614–622. https://doi.org/10.1016/j.ejpb.2008.06.019
4. Gupta, R., Kompella, U. B. (2006). Nanoparticle formulation for ocular delivery of lipophilic drugs. Drug Delivery and Translational Research, 6(5), 475–491. https://doi.org/10.1208/s12249-006-0012-z
5. Tiwari, G., Tiwari, R., Sriwastawa, B., Bhati, L., Pandey, S., & Bannerjee, S. K. (2012). Drug delivery systems: An updated review. International Journal of Pharmaceutical Investigation, 2(1), 2–11. https://doi.org/10.4103/2230-973X.96920
6. Madhav, N. V. S., & Shakya, A. K. (2009). Nasal drug delivery system: An overview. International Journal of Pharmaceutical Sciences and Research, 1(2), 1–8.

7. Kumar, M., Misra, A., Babbar, A. K., Mishra, A. K., Pathak, K., & Gupta, K. C. (2008). Intranasal nanoemulsion based brain targeting drug delivery system of risperidone. International Journal of Pharmaceutics, 358(1–2), 285–291. https://doi.org/10.1016/j.ijpharm.2008.03.005
8. Lawrence, M. J., & Rees, G. D. (2000). Microemulsion-based media as novel drug delivery systems. Advanced Drug Delivery Reviews, 45(1), 89–121. https://doi.org/10.1016/S0169-409X(00)00103-4
9. Khan, F., Nazzal, S. (2010). A novel approach for preparing capsaicin microemulsion: Characterization and delivery. Drug Development and Industrial Pharmacy, 36(5), 588–598. https://doi.org/10.3109/03639040903391746
10. Sahoo, S. K., Sahoo, N., Bhattacharya, C., & Barik, B. B. (2010). Formulation and evaluation of microemulsion-based gel of fluconazole for topical drug delivery. Journal of Pharmacy Research, 3(2), 299–303.
11. Martin, A., & Sinko, P. J. (2010). Martin's Physical Pharmacy and Pharmaceutical Sciences (6th ed.). Lippincott Williams & Wilkins.
12. Aulton, M. E., & Taylor, K. M. G. (2017). Aulton's Pharmaceutics: The Design and Manufacture of Medicines (5th ed.). Elsevier Health Sciences.
13. Indian Pharmacopoeia Commission. (2022). Indian Pharmacopoeia (Vols. I–III). Government of India, Ministry of Health and Family Welfare.
14. United States Pharmacopeia (USP 44 – NF 39). (2021). USP-NF Online. The United States Pharmacopeial Convention.
15. Azeem, A., Rizwan, M., Ahmad, F. J., Iqbal, Z., Khar, R. K., & Aqil, M. (2009). Emerging role of microemulsions in cosmetics. Recent Patents on Drug Delivery & Formulation, 3(2), 110–122. https://doi.org/10.2174/187221109788452367
16. Dhawan, S., Aggarwal, G., & Harikumar, S. L. (2011). Enhanced transdermal permeability of piroxicam using microemulsion-based gel. International Journal of Drug Delivery, 3(1), 43–56. https://doi.org/10.5138/ijdd.2010.0975.0215.03004
17. Alam, M. I., & Baboota, S. (2013). Intranasal microemulsion of olanzapine: pharmacokinetic and pharmacodynamic studies. Current Drug Delivery, 10(6), 720–728. https://doi.org/10.2174/1567201811310660009
18. Yadav, K. S., & Sawant, K. K. (2010). Formulation optimization of etodolac microemulsion for topical delivery using response surface methodology. Indian Journal of Pharmaceutical Sciences, 72(4), 447–454. https://doi.org/10.4103/0250-474X.73905
19. Pandey, A., Khuller, G. K. (2005). Liposomal drug delivery systems for tuberculosis. International Journal of Pharmaceutics, 293(1-2), 37–44. https://doi.org/10.1016/j.ijpharm.2004.12.019
20. Shaji, J., & Lodha, S. (2010). Brain-targeted nasal drug delivery: An overview. Pharma Times, 42(1), 19–24.
21. Pathan, I. B., & Setty, C. M. (2009). Chemical penetration enhancers for transdermal drug delivery systems. Tropical Journal of Pharmaceutical Research, 8(2), 173–179. https://doi.org/10.4314/tjpr.v8i2.44527
22. Kohli, A. K., & Alpar, H. O. (2004). Potential use of nanoparticles for transcutaneous vaccine delivery: Effect of particle size and charge. International Journal of Pharmaceutics, 275(1-2), 13–17. https://doi.org/10.1016/j.ijpharm.2003.12.031
23. Sharma, V. D., Sharma, P. R., & Kohli, D. V. (2014). Nasal drug delivery: A promising alternative to oral route. The Pharma Innovation Journal, 3(6), 50–54.
24. Jaiswal, D., Bhattacharya, A., Yadav, A., & Jaiswal, S. (2012). Microemulsion: A potential nanocarrier for the delivery of lipophilic drugs. Journal of Drug Delivery & Therapeutics, 2(5), 29–35. https://doi.org/10.22270/jddt.v2i5.234