

Detailed Review on Nasal In Situ Gel: Novel Approach To Enhance Therapeutic Benifites of Herbal Drug

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ABSTRACT: The study underscores the potential of insitu nasal gel as a promising approach for enhancing drug delivery To treat allergic rhinitis, offering sustained drug release and prolonged therapeutic action. The estimate and compare different formulation of insitu nasal gel formulation for the administration of herbal medication to treat allergic rhinitis. The in situ gel was prepared by a cold method and different concentration of polymer were used, such as HPMC K4M, PEG 4000 and Carbopol 934 The optimized formulation exhibited excellent properties in terms of physical appearance, pH range, drug content and viscosity, making it a stable and effective formulation for nasal drug delivery. The morphology, size and shape of the optimized formulation were investigated using transmission Electron microscopy. The study concluded by demonstrating the effective creation and enhancement of in situ nasal gel formulation for the administration of herbal medication. Promising outcomes in terms of extended therapeutic effect enhanced bioavailability and sustained drug release were demonstrated by the in situ gels. Drug absorption and therapeutic effect were improved by the formulation usage of mucoadhesive polymers, which extended the drug's residence duration on the nasal mucosa.

KEYWORDS: Nasal Drug Delivery, In Situ gel, Herbal Drug, Natural Polymers.

I. INTRODUCTION

1.1 Nasal Drug Delivery System:

[1] The nasal route of drug administration has gained considerable attention in recent years as an alternative to conventional drug delivery systems. In pharmaceuticals, the design of effective drug delivery systems is essential to maximize therapeutic efficacy while minimizing systemic side effects. The nasal cavity, due to its unique

anatomy and physiology, provides an attractive route for both local and systemic drug delivery.

1. Local:

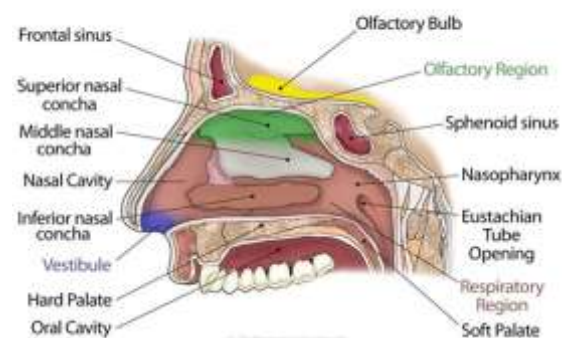
Intranasal administration of medicines is the natural choice for the treatment of topical nasal Disorders. Among the most common examples are antihistamines and corticosteroids for cold symptoms. In these cases, the intranasal route is the primary option for drug delivery because it allows a rapid symptoms relief with less side effect.

2. Systemic:

The intranasal administration is an effective way to systemically deliver drug as an alternative to oral and intravascular routes. Consequently, by nasal formulation, as the number of drugs administered intended to achieve systemic effects has widely increased. Some prominent examples include analgesics [morphine], cardiovascular drugs as Propranolol and carvedilol, hormones such as levonorgestrel, progesterone and insulin, anti-inflammatory agents as indomethacin and Ketorolac, and antiviral drugs.

1.2 Anatomy and Physiology of Nose

Nasal Cavity



[2,3] Three regions can be distinguished in each part

1. Respiratory region:

The nasal respiratory region is the largest part of the nasal cavity, also called conchae. The respiratory region is the most important for systemic drug delivery.¹⁰⁻¹² The respiratory epithelium is composed of four types of cells, namely, non-ciliated and ciliated columnar cells, basal cells and goblet cells. The respiratory region contains three nasal turbinates superior, middle, and inferior which project from the lateral wall of each of the nasal cavity. For systemic drug delivery, nasal respiratory mucosa is considered the most important section.

2. Vestibular region:

Most anterior part of the nasal cavity is nasal vestibule, just inside the nostrils, and presents an area about 0.6 cm this nasal portion is covered by a stratified squamous and keratinized epithelium with sebaceous glands is responsible for filtering out the airborne particles. It is considered to be less important in the three regions concerning drug absorption.

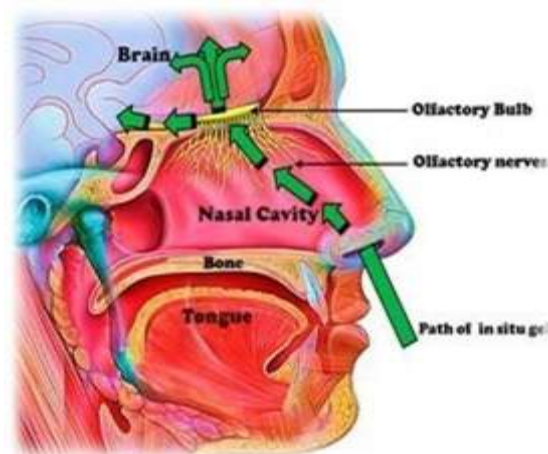
3. Olfactory region:

The olfactory region is located in the roof of the nasal cavity and extends a short way down the septum and lateral wall it is of about 10 cm² in surface area and it plays a vital role in the transportation of drugs to the brain and the CSF. When the drug is administered by the nasal route, it can enter into the brain by three different paths. The first one is the systemic path, by this route the drug is absorbed into the systemic circulation and subsequently reaches the brain by crossing BBB [especially lipophilic drug]. The other pathways are the olfactory region and the trigeminal neural pathway by which the drug is directly transported from the nasal cavity to CNS [cerebrospinal fluid and brain tissue]. There is a different mechanism by which the drugs across the olfactory membrane reach CNS. The first mechanism involves a direct transfer of the drug to primary neurons of the olfactory epithelium and transport to the olfactory bulb by intracellular axonal transport with subsequent possible distribution into more distant brain tissues. The second mechanism depends on the drug permeation across the olfactory sustentacular epithelial cells, either by transcellular or paracellular mechanisms followed by uptake into CNS. The last one employs pinocytosis by olfactory neurons.

1.3 Mechanism of Nasal Drug Delivery

[4,5,6] The first stage in the drug's absorption in the nasal cavity is traversing the mucous membrane. However, the mucous barrier makes it difficult for charged big molecules to flow through. Mucin, a protein found in the mucus layer, binds to solutes to slow down diffusion. Environmental factors, such as variations in pH and temperature, can also trigger structural changes in the mucus layer. simple diffusion, paracellular transport across cells, and transcytosis via vesicle carriers are some of the methods for drug absorption across the mucosa during mucus passage. Prior to entering the systemic circulation, the drug's metabolism depends on the limitations on its absorption.

I. MECHANISM OF NASAL DRUG ABSORPTION



Duration of stay in the cavity. Although several Mechanism have been put out, that two follow have received the most attention. The first Mechanism uses an aqueous pathway for transfer and is referred to as a paracellular route. Second mechanism, referred to as a transcellular route, which includes transportation via the lipid pathway.

1.4.[8] Aspect affecting Nasal Drug Delivery System

1. Physicochemical properties of a drug

- Molecular weight:** Nasal delivery of a is expected to decrease with an increasing molecular weight of the drug molecule
- Chemical form:** It is an important factor for drug absorption. By changing the drug into salt or an ester form can change its absorption.

- c) **Size:** Particle size and morphology of a drug are important tools for the design of nasal drug delivery. Generally, particles in the 5-10 microns range should be deposited in the nostrils.
- d) **Solubility:** it is important to learn about the relationship between a drug's saturation solubility and its absorption.
- e) **Lipophilicity:** The permeation of the compound normally increases through nasal mucosa by increasing lipophilicity.
- f) **Polymorphism:** It can affect the rate of drug dissolution, solubility, and absorption through biological membranes.

2. Physicochemical properties of a formulation

- a) **Drug concentration, dose, and dose-volume:** Drug concentration, dose, and dose-volume of administration are three interlinked parameters that affect the performance of the nasal delivery system.
- b) **Antioxidants:** Antioxidants have not any effect on drug absorption or cause nasal irritation.
- c) **Preservatives:** Nasal formulations mostly contain preservatives to protect them from microbial contamination. Preservatives are used in small quantities and are not likely to affect drug absorption.
- d) **Humectants:** humectants can be added mostly in gel-based nasal products to avoid irritation of the nasal cavity. Humectants do not affect drug absorption. Examples like glycerin, sorbitol, and mannitol
- e) **Viscosity:** The higher viscosity of the formulation increases contact time between the drug and therefore the nasal mucosa, thereby increasing permeation time.

3. Physiological factors

- a) **Blood flow/ supply:** Nasal mucosa has a larger surface area and rich with blood supply which makes nasal an optimum place for drug absorption. The blood flow influences significantly the systemic nasal absorption of the medicine so that because it enhances more drug passes through the membrane
- b) **Nasal cycle:** In this process congestion and relaxation regulate the rise and fall in the amount of drug permeation process
- c) **A pH of the nasal cavity:** Nasal cavity pH in the adult is 5.5-6.5 and 5.0-7.0 in infants. A change in the pH mucus affect the ionization.

- d) **Effect of enzymatic activity:** Many enzymes affect the stability of drug that are present on the nasal mucosa. For Example protein and peptides are subjected to degradation by protease and aminopeptides at the mucosal membrane.

1.5 [8] Ideal properties of drug candidate for nasal drug delivery system

II. IDEAL PROPERTIES



2.5 [9] Advantages of nasal drug delivery System

- Nasal drug administration is one way to get medications that are not absorbed when taken orally into the bloodstream.
- It avoids hepatic first pass metabolism.
- In contrast to parenteral approaches, self-medication is made easier by easy accessibility and needle free drug administration that eliminates the requirement for trained staff, enhancing patient compliance.
- There is no drug breakdown in the gastrointestinal system.
- Absorption enhancers and other methods can be used to increase the bioavailability of big medicinal molecules.
- It is possible to obtain a rapid start of action and rapid medication absorption.

- ☐ For smaller pharmacological molecules, the nasal bioavailability is good.
- ☐ Drug degradation that is observed in the gastrointestinal tract is absent.
- ☐ The nasal bioavailability for smaller drug molecules is good.
- ☐ Drugs that are orally not absorbed can be delivered to the systemic circulation by nasal drug delivery.
- ☐ Self-administration

1.7 Disadvantages of Nasal Drug Delivery System[10,11]

- ☐ The histological toxicity of absorption enhancers used in nasal drug delivery system is not yet clearly established.
- ☐ Relatively inconvenient to patients when compared to oral delivery systems since there is a possibility of nasal irritation.
- ☐ Nasal cavity provides smaller absorption surface area when compared to GIT.
- ☐ Compared to oral administration systems, this method is rather uncomfortable for patients since it may cause discomfort.
- ☐ The substance and the ingredients added to the dosage form carry the danger of local side effects and permanent damage to the cilia on the nasal mucosa.
- ☐ Inappropriate delivery strategy may result in a mechanical loss of the dose to other areas of the respiratory system, such as the lungs.
- ☐ Difficulty in delivering new drug compounds with high molecular weight or low lipophilicity.

II. INTRODUCTION OF HERBAL MEDICINE

[12] Herbal medicines are naturally occurring, plant-derived substances that are used to treat illnesses within local or regional healing practices. These products are complex mixtures of organic chemicals that may come from any raw or processed part of a plant. Herbal medicine has its roots in every culture around the world. There are many different systems of traditional medicine, and the philosophy and practices of each are influenced by social conditions, environment and geographic location, but these systems all agree on a holistic approach to life. Well-known systems of herbal medicine like Traditional Chinese Medicine and Ayurvedic Medicine believe in the central idea that there should be an emphasis on health rather than on disease. Herbs are used for the treatment of chronic and acute conditions and various ailments,

including major health concerns like cardiovascular disease, prostate problems, depression, inflammation and weakened immune system. Herbs are used around the world to treat conditions and diseases, and many studies prove their efficacy.

2.1 Mentha Piperita

[13] Mentha piperita, commonly known as peppermint, is a popular herb used in various traditional medicine formulations due to its therapeutic properties. Its essential oil contains active compounds like menthol and menthone, which provide cooling, anti-inflammatory and antimicrobial benefits in nasal gel formulation.

- ☐ **Decongestant Properties:** Mentha piperita's menthol content may help relieve nasal congestion by promoting nasal airflow and reducing swelling in the nasal passages.
- ☐ **Cooling Sensation:** The cooling effect of menthol may provide symptomatic relief from nasal irritation and discomfort

2.2 Eucalyptus oil

[14] Eucalyptus oil is an essential oil extracted from the leaves of the Eucalyptus tree, particularly Eucalyptus globulus. It is widely known for its medicinal properties, especially in respiratory ailments. Eucalyptus oil contains active compounds such as eucalyptol (1,8-cineole). Eucalyptus oil-based nasal gels are designed as in-situ gelling systems, which are typically liquid at room temperature and transform into a gel upon contact with nasal mucosa due to temperature, pH, or ion-triggered gelation. Such formulations can help relieve nasal congestion, promote easier breathing, and exhibit antimicrobial action against pathogens in the nasal cavity.

2.3 Advantages of herbal drug [15]

- ☐ Natural Healing Properties
- ☐ Holistic Wellness:
- ☐ Fewer Side Effects:
- ☐ Support for a Wide Range of Health Conditions:
- ☐ Enhanced Nutrient Density:

2.4 Disadvantages of herbal drug [15]

- ☐ Variability in Potency
- ☐ Potential Interactions with Medications
- ☐ Limitations in Scientific Research
- ☐ Quality and Purity Concerns
- ☐ Delayed Effects

III. INTRODUCTION OF IN-SITU NASAL GEL [16]

a) Gel-

Gel is the state which exists between solid and liquid phase. The solid component comprises a three-dimensional network of interlinked molecules which immobilizes the liquid phase.

b) In-Situ delivery system:

In-Situ gelation is a process of gel formation at the site of action after the formulation has been applied at the site. In-Situ gel phenomenon based upon liquid solution of drug formulation and converted into semi-solid Mucoadhesive key depot. It permits the drug must be delivered in a liquid form or solution form. In the field of human and animal medicine, the sites, topical application sites, surgical sites and other agents are brought into contact with tissues or body fluids.

3.1 Principle of In-Situ Gel:

[17] The principle of in situ gelling system is of solid nasal formulations are that the nasal formulations absorb the nasal fluid after administration and form a gel within the cavity. The foreign body sensation can avoid by the formation of nasal gel within the cavity. Due to bioadhesive nature, the gel adheres to the nasal mucosa. It acts as a release controlling matrix and thus acts as a sustained drug delivery system.

3.2 Importance of In Situ Gelling System [18]

- ☐ In-situ forming polymeric delivery system such as ease of administration and reduced frequency of administration improved patient compliance and comfort.
- ☐ Liquid dosage form that can sustain drug release and remain in contact with cornea of eye for extended period of time is ideal.
- ☐ The major importance is the possibilities of administering accurate and reproducible quantities compared to already formed gel.

3.3 Various Approach To Enhance In-Situ Gelling System [19,20]

The various approaches for in-situ gelling system.

A) Stimuli Responsive In-Situ Gelling System

1. Temperature induced in-situ gel systems.
2. pH induced in-situ gel system.

B) Osmotically Induced In-Situ Gelling System

C) Chemically Induced In-Situ Gelling System

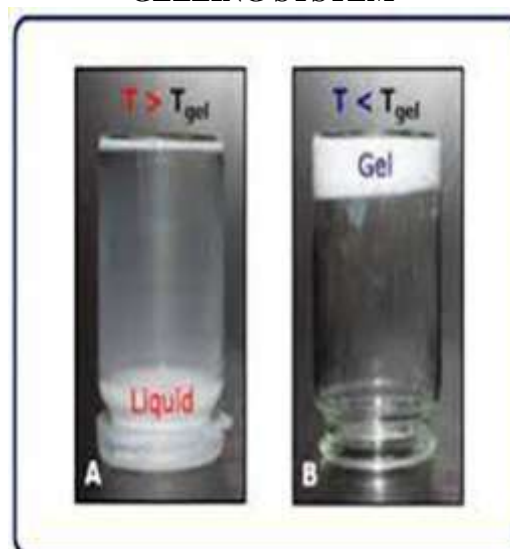
1. Ionic cross linking.
2. Enzymatic cross linking.

3. photo-polymerization.

(A) Stimuli Responsive In-Situ Gelling System

Physical or chemical changes in response to small external changes in the environmental conditions.

TEMPERATURE INDUCED IN SITU GELLING SYSTEM



Temperature is the most widely used stimulus in environmentally responsive polymer systems. The change of temperature is not only relatively easy to control, but also easily applicable both in-vivo and in-vitro. In this system, gelling of the solution is triggered by change in temperature, thus sustaining the drug release. These hydrogels are liquid at room temperature (20° - 25° C) and undergoes gelation when in contact with body fluids (35° - 37° C) due to increase in temperature. The polymers which show temperature induced gelation are poloxamers or pluronics, cellulose derivatives (methyl cellulose)

1. pH induced system in In-Situ gelling system

Polymers containing acidic or alkaline functional groups that respond to changes in pH are called pH sensitive polymers. The pH is an important signal, which can be addressed through pH-responsive materials. Gelling of the solution is triggered by change in pH. At pH 4.4 the formulation is free from is a free running solution which undergoes coagulation when the pH is raised by the body fluid to pH 7.4. The polymers which shows pH induced gelation are cellulose and its derivatives polyvinyl acetate, polyethylene glycol.

(B) Osmotically Induced In-Situ Gelling System

In this method, gelling of the solution instilled is triggered by changes in the ionic strength. It is assumed that the rate of gelation depends on the osmotic gradient across the surface of the gel. The aqueous polymer solution forms a clear solution, which forms a clear gel in the presence of the mono or divalent cations. The polymer which shows osmotically induced gelation is gellan gum, alginates.

(C) Chemically Induced In-Situ Gelling System

The chemical reaction which forms in-situ gel systems are ionic crosslinking, enzymatic crosslinking and photopolymerization.

1) Ionic cross linking

Certain ion sensitive polysaccharides such as carrageenan, gellan gum, pectin, sodium alginate undergo phase transition in presence of various ions such as K^+ , Ca^{2+} , Na^+ . These polysaccharides fall into the class of ion-sensitive ones. For example, Alginic acid undergoes gelation in presence of divalent cations example- Ca^{2+} due to the interaction with guluronic acid block in alginate chains.

2) Enzymatic cross linking

In-Situ formation catalyzed by natural enzymes has not been investigated widely but seems to have some advantages over chemical and physicochemical approaches. For example an enzymatic process operates efficiently under physiologic conditions without need for potentially harmful chemicals such as monomers and initiators.

3) Photo polymerization

In-Situ photo polymerization has been used in biomedical applications for over more than decade. A solution of monomers can be injected into a tissue site and the application of electromagnetic radiation used to form gel. Acrylate or similar polymerizable functional groups are typically used as the polymerizable groups on the individual monomers and macromere because they rapidly undergo photo-polymerization in the presence of suitable photo initiator. Photo polymerizable systems when introduced to the desired site via injection get photo cured in-situ with the help of fiber optic cables and then release the drug for prolonged period of time. A photo polymerization, biodegradable hydro gels as a tissue contacting material and controlled release carrier.

3.4 Properties on Nasal In-Situ Gel:[21]

- It should have a long residence time.
- It should be low viscous
- Free-flowing allows for reproducible administration to the nasal cavity.
- The nasal in-situ gel follows the phase transition mechanism and shear forces in nasal cavity wall.

3.5 Advantages of Nasal In-Situ Gel: [22]

- Increased residence time of drug in nasal cavity.
- Offers lower risk of overdose of CNS acting drugs.
- Reduced systemic side effect.
- Prolong drug release.
- Ease of administration.
- Reduced frequency of administration.
- Better patient compliance.
- Gels can afford the use of soothing agents or emollients which may not be suitable for solutions, suspensions or powder dosage form so can reduce irritation potential.
- Reduction in anterior leakage of the drug out of the nasal cavity.

3.6 Disadvantages of Nasal In-Situ Gel:[23]

- It requires a high level of fluids.
- The sol form of the drug is more susceptible to degradation.
- Chances of stability problems due to chemical degradation.
- After placing the drug eating and drinking may become restricted up to a few hours.
- The quantity and homogeneity of drug loading into hydrogels may be limited, particularly for hydrophobic drugs.
- Only drugs with small dose requirements can be given.
- Lower mechanical strength, may result in premature dissolution or flow away of the hydrogel from a targeted local site.

3.7 Various polymer to use in nasal in situ gel

a) Carbopol:[24]

Carbopol polymers are having excellent water sorption property. Carbopol polymer swells in water up to 1000 times by its original volume and 10 times their original diameter to form a gel when exposed to a pH environment above 4.0-6.0 because the pKa of those polymers is 6.0 ± 0.5 . It is a high relative molecular weight, a cross-linked polyacrylic acid derivative and has a strong mucoadhesive property. If there's an addition of

cellulose then it'll reduce polymer concentration and improve a gelling property. Carbopol 934 and Carbopol 981 are mostly used as gelling agents.

b) Poloxamer:[25]

Poloxamer is a water-soluble tri-block copolymer consisting of two polyethylene oxide and polypropylene oxide core in an ABA configuration. Poloxamer is also known as pluronic. Poloxamer has good thermal setting property and increased residence time of the drug. It acts as a gelling agent and solubilizing agent. Poloxamer gives colorless, transparent gel. Depending on the ratio and distribution of hydrophilic and hydrophobic chain different molecular weights are available and it has different gelling properties.

c) Chitosan:[26]

Chitosan is obtained by alkaline deacetylation of chitin, a natural component of shrimp and crab shell. Chitosan has a biodegradable, thermosensitive, polycationic polymer. Chitosan is a pH-dependent cationic polymer. Chitosan has biocompatible property, which remains dissolved in aqueous solutions up to a pH of 6.2. Neutralization of aqueous solution of chitosan to a pH exceeding up to 6.2 leads to the formation of a hydrated gel-like precipitate.

d) Xanthumgum:[27]

Xanthan gum is a high molecular weight extracellular polysaccharide produced by the fermentation of the gram negative bacterium *Xanthomonas campestris*. The primary structure of this naturally produced cellulose derivative contains a cellulosic backbone (β -D-glucose residues) and a trisaccharide side chain of β -D-mannose- β -D-glucuronic acid- α -D-mannose attached with alternate glucose residues of the main chain.

e) Gellangum:[28]

Gellan gum polymer is an anionic deacetylated exocellular polysaccharide obtained by *Pseudomonas elodea* with a tetrasaccharide repeating unit of one α -L rhamnose, one β D-glucuronic acid, and two β -D-glucuronic acid residues. Gellan gum has the property of gelation which is both temperature-dependent or cations induced. This gelation process involves the formation of double-helical junction zones followed by aggregation of the double-helical segments to make a three-dimensional network by

complexation with cations and hydrogen bonding with water.

f) Sodium alginate: [29]

Sodium alginate is a salt of alginic acid. It is extracted from brown algae. It has a linear block polysaccharide containing two type monomers β -D Mannuronic acid and α -L glucuronic acid residues connected by 1,4 glycosidic linkages. Sodium alginate biodegradable and non-toxic which exhibit good mucoadhesive property due to the presence of the carboxylic group. The mechanism of polymer is the monomers of alginate β -D-Mannuronic acid and α -L glucuronic acid are arranged as M-M block with altering sequence (M-G) block. Upon interaction of G block of polymer with calcium, moieties give in the formation of a gel. On G: M ratio the mechanical strength and porosity of hydrogel depends, type of crosslinker used and concentration of alginate polymer solution.

3.8 Different methods for formulation of nasal in situ gel [30]

1. Hot method
2. Cold method

1. Hot Method

This method is used when gellan gum or pectin is used as a gelling polymer. At high temperature, gellan chains dissolve in water and assume a random-coil conformation with high segmental mobility at high temperatures and remain as a solution at a higher temperature. A phase transition occurs on a cooling gellan gum solution in the presence of ions like K^+ or Ca^{2+} . Similarly, pectin also requires a high temperature for its demethoxylation, which helps in the formation of a solution or dissolving of pectin.

2. Cold Method

In this method, the drug is stirred with a sufficient quantity of double distilled water and kept overnight at $4^{\circ}C$ in a refrigerator. The in situ gelling polymers are then added slowly with stirring. The dispersion is stored in a refrigerator till a clear solution is formed and finally volume is adjusted with distilled water. This method is chosen when poloxamer, chitosan or carbopol is used as a gelling polymer. Considering the fact that polymeric dispersion of poloxamer is in solution at lower temperature and gets converted into a gel at higher nasal temperature because the solubility of polypropylene oxide chain of poloxamer decreases at a high temperature which results in precipitation or salting-out of a polymer. Similarly, chitosan also

requires the low temperature to remain as a solution at room temperature, its hydrophobicity increases with an increase in temperature.

3.9 Evaluation Parameter of Nasal in Situ gel^[31]

1. **Clarity:** The clarity of in situ gel is found out by visual inspection under the black and white background.
2. **Gelling capacity:** Mix in-situ gel with simulated nasal fluid to find out the gelling capacity of the ophthalmic product. The gelation may be assessed visually by noting the time for and time is taken for the dissolution of the formed gel.
3. **Viscosity:** The viscosity and rheological properties of the polymeric formulations, either in solution or in a gel made with artificial tissue fluid and may be determined with different viscometers like Brookfield viscometer, cone, and plate viscometer. The viscosity of these formulations should be such that it should be patient compliance.
4. **Texture analysis:** The firmness, consistency, and cohesiveness of formulation may be determined using a texture analyzer which mainly indicates the syringe ability of sol so the formulation can easily be administered in-vivo.
5. **Sterility testing:** Sterility testing is carried out as per the IP 1996. Incubate the formulation for not less than 14 days at 300°-350°C in the fluid thioglycolate medium to find the growth of bacteria and at 200°-250°C in soyabean casein digest medium to find the growth of fungi in the formulation.
6. **Appearance:** In situ nasal gel is examined visually for clarity in sol and gel form.
7. **pH of gel:** With the help of a pH meter pH of in situ nasal gel is measured
8. **Gel strength:** Gel strength may be evaluated using a rheometer. Depending on the mechanism of the gelling agent used a specified amount of gel is prepared in beaker, from the sol form. This gel containing beaker is raised at certain rate, so pushing a probe slowly through the gel. The changes in the load on the probe can be measured as a function of depth of immersion of the probe below gel surface.
9. **Drug content:** Take 1ml of formulation and adjust to 10ml in volumetric flask and then dilute with 10ml of distilled water, 1ml from this solution again diluted with distilled water up to 10ml. after this take absorbance of

prepared solution at a particular wavelength of the drug by using U.V visible spectroscopy.

IV. CONCLUSION

In-situ nasal gel as a novel and effective approach for the delivery of herbal drugs. By combining the therapeutic benefits of herbal bioactives with the advantages of nasal administration, the formulation successfully overcomes limitations such as poor oral bioavailability, rapid metabolism, and low patient compliance associated with conventional dosage forms. The developed in situ gel exhibited desirable gelling capacity, mucoadhesion, and sustained drug release, ensuring prolonged residence time at the nasal mucosa and improved absorption. Furthermore, by bypassing the hepatic first-pass effect, the system enhances the bioavailability and therapeutic efficacy of herbal drugs. This novel strategy not only supports the clinical relevance of nasal in situ gels for herbal drug delivery but also establishes a promising platform for future development of safer, effective, and patient-friendly herbal formulations.

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