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# Evaluation of Mucoadhesive Polymers for Nasal Delivery of Herbal Bioactives

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***Abstract***

*A study assessed mucoadhesive polymers for intranasal herbal bioactive administration with higher residence time and mucosal permeability. Chitosan, Carbopol® 934P, and HPMC K15M were utilized to manufacture mucoadhesive nasal gels with standardized herbal bioactive fractions. Formulations were examined for pH, viscosity, spreadability, drug content, mucoadhesive strength, in-vitro release, ex-vivo penetration, and short-term stability. All formulations demonstrated a suitable pH for nasal usage and uniform drug content (97.48 ± 1.12% to 101.26 ± 0.94%). Pseudoplastic flow behavior (1820 ± 95 to 3540 ± 140 cP at 25 °C) indicates strong nasal retention from chitosan to Carbopol 934P to HPMC, but mucoadhesive strength varies. Chitosan-based formulation showed the maximum mucoadhesive force (39.4 ± 2.1 g), followed by Carbopol (32.6 ± 1.8 g) and HPMC (23.7 ± 1.5 g). In-vitro experiments revealed sustained herbal bioactive release over 8 hours, with chitosan releasing (85.9 ± 2.7%), Carbopol (74.8 ± 2.3%), and HPMC (79.6 ± 2.5%). Chitosan formulation was found to outperform HPMC-based systems in ex-vivo permeation investigations on freshly excised sheep nasal mucosa, with cumulative permeation of 68.4 ± 3.2% and apparent permeability coefficient of 3.87 ± 0.29 × $10^{-5}$ cm/s, 1.71-fold higher ($p < 0.05$). Fourier-transform infrared spectroscopy and differential scanning calorimetry indicated herbal bioactive molecule dispersion in polymeric matrix and no chemical incompatibility. Stability studies at 25 ± 2 °C for 30 days showed no significant pH, drug content, or release behavior changes. Due to its superior mucoadhesion, rheology, and mucosal penetration, chitosan is the best polymeric carrier for herbal bioactive nasal administration.*

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**Keywords:** Carbopol 934P, chitosan, ex-vivo permeation, herbal bioactives, HPMC, mucoadhesive polymers, nasal drug delivery, polymeric nasal gel

## INTRODUCTION

Nasal drug delivery systems represent a unique class of soft polymer-based biomedical composites designed to operate at a complex biological interface. From a materials science perspective, these systems are not merely pharmaceutical formulations but structured polymer networks engineered to control adhesion, hydration, mechanical stability, and mass transport. Although the nasal route offers rapid systemic absorption and

 

potential nose-to-brain delivery, conventional liquid formulations suffer from rapid mucociliary clearance, poor epithelial penetration, and limited residence time. These limitations arise primarily from inadequate interfacial interactions and insufficient structural integrity of the delivery matrix [1].

Herbal bioactives present additional formulation challenges due to poor aqueous solubility, chemical instability, and limited bioavailability. Addressing these issues requires rational design of polymer composite matrices capable of simultaneously providing structural support, controlled swelling, diffusion regulation, and strong biointerfacial adhesion. In polymer engineering terms, such systems can be considered biofunctional composites in which the herbal bioactive acts as the dispersed phase, while the hydrated polymer network functions as the continuous phase governing mechanical and transport behavior [2].

Mucoadhesive polymers belong to an important category of functional soft materials whose adhesion performance depends on physicochemical interactions at the polymer–mucin interface. Electrostatic attraction, hydrogen bonding, van der Waals forces, and chain interpenetration collectively determine adhesion strength. The density and spatial distribution of functional groups, such as amine ($–NH_2$), carboxyl (–COOH), and hydroxyl (–OH) moieties influence interfacial bonding and hydration-driven swelling. Simultaneously, bulk network characteristics—crosslink density, porosity, viscoelastic relaxation, and diffusion resistance—govern drug release kinetics and permeation behavior. Thus, both interfacial and bulk structural parameters dictate the overall performance of these composite systems [3,4].

Polysaccharide- and acrylic-based polymers, such as chitosan, cross-linked poly(acrylic acid) derivatives (Carbopol®), and cellulose ethers (HPMC) are widely investigated matrix-forming materials in mucoadhesive systems. Their molecular architecture, ionic character, chain flexibility, and hydration behavior enable the formation of three-dimensional polymer networks with tunable swelling and mechanical properties. Variation in molecular weight, degree of ionization, and network organization directly influences viscoelasticity, mucoadhesive strength, and mass transport pathways. When herbal bioactives are incorporated into these matrices, the resulting system behaves as a polymer composite in which phase compatibility, molecular dispersion, and polymer–bioactive interactions critically determine stability and release performance [5].

A central objective in polymer and composite research is to establish clear structure–property–performance relationships. In mucoadhesive nasal composites, polymer chemistry and network architecture dictate rheological adaptability under physiological shear, interfacial adhesion to mucosal tissues, and diffusion-controlled transport of the encapsulated bioactive. Parameters, such as crosslink density, hydration kinetics, and polymer charge density influence mechanical durability, swelling behavior, and permeability. Therefore, these systems provide an excellent model for studying how polymer network design translates into functional biomedical performance [6,7].

Growing interest in sustainable and biocompatible materials has further accelerated the exploration of natural and semi-synthetic polymers in biomedical composites. Biopolymers, such as chitosan offer inherent bioadhesive properties, biodegradability, and favorable interfacial interactions, while synthetic and semi-synthetic polymers provide structural tunability and mechanical robustness. The integration of herbal bioactives within such polymer matrices exemplifies the convergence of sustainable material science and advanced functional composite design [8].

In this context, the present study aims to comparatively evaluate chitosan, Carbopol® 934P, and HPMC K15M as matrix-forming polymers in mucoadhesive nasal composite systems. Emphasis is placed on correlating polymer chemistry, network organization, rheological behavior, interfacial adhesion, and mass transport characteristics with overall functional performance. By systematically analyzing these structure–property–performance relationships, this work contributes to the rational

 

design of polymer-based biofunctional composites for intranasal biomedical applications, aligning closely with the scientific scope of polymer and composite research. Therefore, this study aims to comparatively evaluate chitosan, Carbopol® 934P, and HPMC K15M as mucoadhesive polymeric carriers and to establish structure–property–performance relationships governing the nasal delivery of herbal bioactive compounds.

## MATERIAL AND METHODS

### Materials

Chitosan, Carbopol® 934P, and HPMC K15M were selected as representative mucoadhesive polymers because they possess distinct ionic characteristics (cationic, anionic, and non-ionic, respectively) and different network-forming behaviors, allowing systematic comparison of their effects on mucoadhesion, rheology, drug release, and nasal permeation. These polymers were chosen based on their distinct molecular architecture, ionic character (cationic, anionic, and non-ionic, respectively), and network-forming capabilities. A standardized herbal bioactive fraction was used as the dispersed functional phase within the polymer matrices. Glycerol and propylene glycol were incorporated as plasticizers and wetting agents to modulate matrix flexibility and hydration behavior. Hydrochloric acid and sodium hydroxide were employed for pH adjustment and regulation of polymer ionization state. All other reagents and solvents were of analytical grade and used as received.

### Preparation of Polymer-Based Mucoadhesive Composite Matrices

Polymer composite nasal gels were prepared using individual matrix-forming polymers to comparatively evaluate their network architecture and functional performance. Chitosan (1.0–1.5% w/v) was dispersed in 1% v/v acetic acid and stirred for 12 hours to ensure complete solvation and formation of a homogeneous cationic polymer network. Carbopol® 934P (0.5–1.0% w/v) and HPMC K15M (1.5–2.0% w/v) were separately dispersed in purified water and allowed to hydrate for 24 hours to achieve full network swelling and structural relaxation. The herbal bioactive was either dissolved or uniformly dispersed in a minimal volume of aqueous co-solvent and incorporated into each polymeric dispersion under mechanical stirring (800 rpm) to ensure uniform phase distribution. The systems were subsequently neutralized where required to induce gel network formation (particularly for Carbopol) and adjusted to a physiologically compatible pH range (5.5–6.5), thereby optimizing polymer ionization and interfacial adhesion characteristics. The resulting systems were allowed to equilibrate for 24 hours to ensure uniform dispersion of the bioactive within the continuous polymer phase and stabilization of the composite matrix structure [9].

### Physicochemical Characterization

#### *pH and Drug Content*

The pH of each composite formulation was measured at 25 ± 1 °C using a calibrated digital pH meter to assess compatibility with the nasal mucosal environment and polymer ionization behavior. Drug content uniformity was determined by dissolving an accurately weighed quantity of the composite in a suitable solvent, followed by filtration and spectrophotometric analysis at the characteristic absorption wavelength of the herbal marker compound. Results were expressed as percentage drug content relative to the theoretical value, indicating phase homogeneity within the composite matrix [10].

### Rheological and Viscosity Analysis

Rheological behavior of the hydrated polymer composite systems was evaluated using a rotational viscometer at 25 ± 1 °C. Viscosity measurements were recorded over a range of shear rates to characterize flow behavior and viscoelastic response. Shear-dependent viscosity profiles were analyzed to determine pseudoplasticity and structural recovery, reflecting network integrity and polymer chain entanglement within the composite matrix. The correlation between polymer type, molecular architecture, and viscoelastic performance was systematically examined [11].

### Mucoadhesive Strength Measurement

Mucoadhesive performance was evaluated using freshly excised sheep nasal mucosa and a modified two-arm balance method. The polymer composite formulation was placed between two mucosal

 

surfaces mounted on glass supports. The minimum force required to detach the surfaces was recorded as mucoadhesive strength (g). This measurement reflects interfacial bonding arising from electrostatic interactions, hydrogen bonding, and polymer chain interpenetration at the polymer–mucin interface. All experiments were performed in triplicate to ensure reproducibility [12].

**In-Vitro Release Studies**

Drug release behavior from the polymer composite matrices was studied using a Franz diffusion cell apparatus. A dialysis membrane (molecular weight cut-off 12–14 kDa) separated the donor and receptor compartments. Phosphate buffer saline (pH 6.4) maintained at 37 ± 0.5 °C served as the receptor medium under continuous stirring. Samples were withdrawn at predetermined intervals up to 8 hours and analyzed spectrophotometrically. Cumulative release data were used to evaluate diffusion-controlled transport through the hydrated polymer networks [13].

**Ex-Vivo Nasal Permeation Study**

Ex-vivo permeation experiments were conducted using freshly excised sheep nasal mucosa mounted in Franz diffusion cells. The polymer composite formulation was placed in the donor compartment, while phosphate buffer (pH 6.4) was used as the receptor medium at 37 ± 0.5 °C under constant stirring. Samples were collected at defined intervals and analyzed spectrophotometrically. Steady-state flux and apparent permeability coefficient ($P_{app}$) were calculated from the linear portion of the permeation profile, providing insight into composite-controlled transport across the biological barrier [14].

**Fourier-Transform Infrared Spectroscopy (FTIR)**

FTIR analysis was performed to investigate molecular interactions and phase compatibility between the polymer matrix and the herbal bioactive. Spectra of individual polymers, pure bioactive, and optimized composite formulations were recorded using the KBr pellet method in the range of 4000–400 $cm^{-1}$. Shifts, broadening, or disappearance of characteristic peaks were analyzed to assess intermolecular interactions within the composite system [15].

**Differential Scanning Calorimetry (DSC)**

Thermal behavior and phase characteristics of the polymers, pure bioactive, and selected composite formulations were evaluated using differential scanning calorimetry. Samples were heated from 30 to 300 °C at a rate of 10 °C/min under a nitrogen atmosphere. Changes in melting endotherms and thermal transitions were analyzed to determine crystallinity reduction, molecular dispersion, and possible amorphization of the bioactive within the polymer matrix [16].

**Short-Term Stability Studies**

Optimized polymer composite formulations were subjected to stability studies at 25 ± 2 °C and 60 ± 5% relative humidity for 30 days. Periodic evaluation included pH, drug content, visual appearance, and in-vitro release behavior to assess structural integrity and functional stability of the composite networks during storage [17].

**Statistical Analysis**

All experiments were conducted in triplicate, and results were expressed as mean ± standard deviation. Statistical comparisons among different polymer composite systems were performed using one-way analysis of variance (ANOVA), with significance considered at $p < 0.05$.

## RESULTS

**Physicochemical Properties, Rheology, and Mucoadhesion**

The physicochemical properties and repeatability of performance were satisfactory in all of the nasal formulations that were made of polymer-herbal bioactive composites. The formulations made using chitosan (F1), Carbopol 934P (F2), and HPMC K15M (F3) are reported in Table 1 with respect to pH, drug content, viscosity, and mucoadhesive strength.

 

**Table 1.** Physicochemical and mucoadhesive characteristics of polymer composite nasal formulations.

| Formulation | Polymer used | pH (25 °C) | Drug content (%) | Viscosity at 25 °C (cP) | Mucoadhesive strength (g) |
|---|---|---|---|---|---|
| F1 | Chitosan | 5.6 ± 0.1 | 101.26 ± 0.94 | 3540 ± 140 | 39.4 ± 2.1 |
| F2 | Carbopol 934P | 5.9 ± 0.2 | 98.74 ± 1.08 | 3120 ± 125 | 32.6 ± 1.8 |
| F3 | HPMC K15M | 6.1 ± 0.1 | 97.48 ± 1.12 | 1820 ± 95 | 23.7 ± 1.5 |

The nasal compatibility pH range was 5.6–6.1 and the medication concentration was consistently over 97% in all formulations. Composites based on chitosan had the greatest viscosity, although all of the matrices demonstrated appropriate viscosity levels for intranasal administration. The interfacial adhesion was highly affected by polymer chemistry and chain functionality, as indicated by the significantly different mucoadhesive strengths ($p < 0.05$) of the polymers F1, F2, and F3. Viscosity profiles that vary with shear are shown in Figure 1 for all three composite systems. A distinct pseudoplastic (shear-thinning) characteristic was displayed by all formulations. Composites made of chitosan and carbopol showed less viscosity under higher shear, making them easier to administer, and they maintained a higher viscosity at low shear rates, making them ideal for extended nasal residence.

## In-Vitro Release Behavior

Figure 2 shows the comparative release profiles, while Table 2 shows the total in-vitro release of the herbal bioactive from the polymer composite matrices. There was an 8-hour period of sustained release in every polymer composite system. By 8 hours, the chitosan composite (F1) had released 85.9 ± 2.7% of its total weight, while the carbopol composite (F2) had released 74.8 ± 2.3%. Figure 2 clearly shows that the diffusional transport inside the composite matrices was substantially regulated by polymer hydration and network density, as seen by the intermediate release pattern found for the HPMC composite (F3).

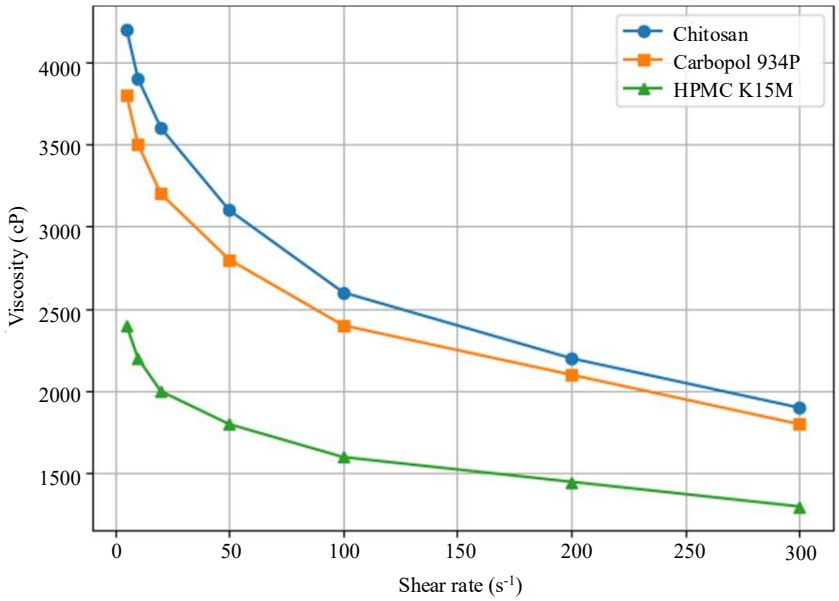


**Figure 1.** Rheological profiles of polymer composite nasal formulations.

**Table 2.** Cumulative in-vitro release (%) of herbal bioactive from polymer composites.

| Time (h) | F1 – Chitosan | F2 – Carbopol | F3 – HPMC |
|---|---|---|---|
| 1 | 18.6 ± 1.4 | 12.8 ± 1.1 | 15.3 ± 1.2 |
| 2 | 31.9 ± 1.8 | 24.6 ± 1.5 | 27.8 ± 1.6 |
| 4 | 55.4 ± 2.3 | 43.2 ± 1.9 | 48.7 ± 2.1 |
| 6 | 71.8 ± 2.5 | 61.5 ± 2.2 | 66.4 ± 2.3 |
| 8 | 85.9 ± 2.7 | 74.8 ± 2.3 | 79.6 ± 2.5 |

 

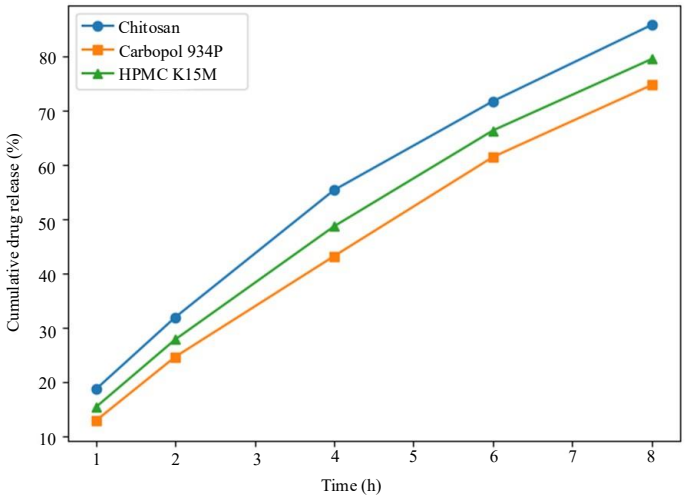


**Figure 2.** Comparative in-vitro release profiles of herbal bioactive from polymer composite nasal formulations.

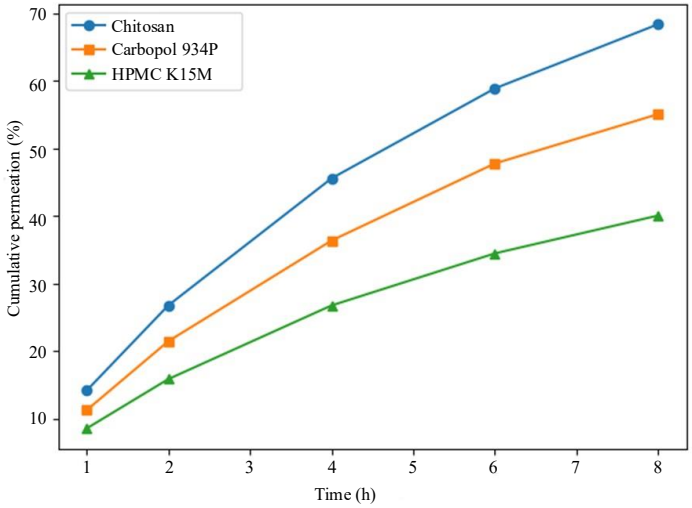


**Figure 3.** Ex-vivo permeation profiles of herbal bioactive from polymer composite nasal formulations across sheep nasal mucosa.

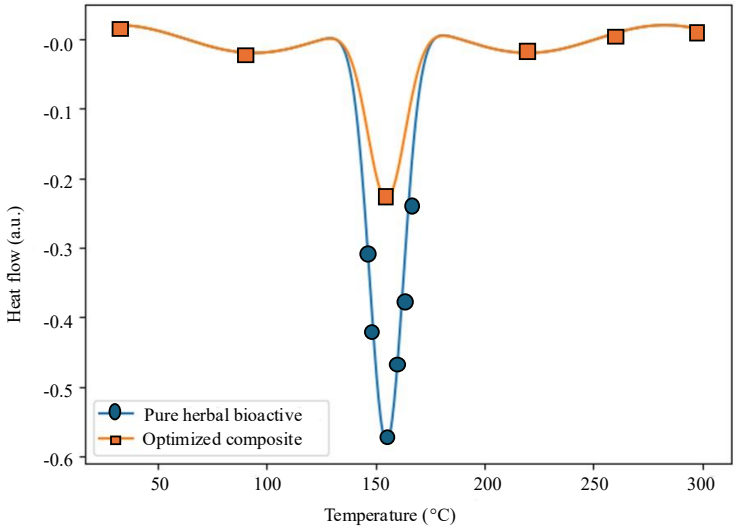


**Figure 4.** DSC thermograms of pure herbal bioactive and optimized polymer composite formulation.

 

**Table 3.** Ex-vivo permeation parameters of polymer composite nasal formulations.

| Formulation | Cumulative permeation at 8 h (%) | Steady-state flux (μg $cm^{-2}$ $h^{-1}$) | P_app (cm $s^{-1}$ $\times 10^{-5}$) |
|---|---|---|---|
| F1 – Chitosan | 68.4 ± 3.2 | 24.6 ± 1.9 | 3.87 ± 0.29 |
| F2 – Carbopol | 55.1 ± 2.8 | 18.3 ± 1.4 | 2.81 ± 0.21 |
| F3 – HPMC | 40.1 ± 2.4 | 14.4 ± 1.2 | 2.26 ± 0.18 |

**Ex-Vivo Nasal Permeation**

Figure 3 shows the permeation profiles, and Table 3 summarizes the ex-vivo permeation performance across the nasal mucosa of excised sheep. Figure 3 shows that throughout the experimental period, the chitosan-based composite (F1) had the highest penetration rate. F1 had a nearly 1.71-fold greater apparent permeability coefficient ($3.87 \pm 0.29 \times 10^{-5}$ cm $s^{-1}$) compared to the HPMC composite (F3), showing a statistically significant improvement in mucosal transit ($p < 0.05$). Based on its increased mucoadhesive strength in Table 1, the improved penetration performance of F1 can be explained by the cationic nature of chitosan and its strong interaction with the negatively charged mucosal surface.

**FTIR and DSC Analysis**

The FTIR spectra of the optimized polymer composite formulations, the pure herbal bioactive, and the individual polymers showed that the bioactive's unique absorption bands were retained, without any new peaks or noticeable shifts in the existing ones. Physically dispersed polymer-bioactive composites may be formed, and the lack of chemical incompatibility is confirmed. In contrast to the pure compound, the improved composite systems' differential scanning calorimetry (DSC) thermograms revealed a weaker herbal bioactive's signature melting endotherm, suggesting molecular-level dispersion of the bioactive inside the polymer matrix and partial amorphization (Figure 4).

**Short-Term Stability**

No evident alterations in appearance or homogeneity were noted over 30 days of storage at 25 ± 2 °C and 60 ± 5% RH. Polymer composite nasal formulations maintained drug content within 98.1–100.4% of initial values, and there was no significant variation in pH or in-vitro release profiles ($p > 0.05$), indicating that the formulations are stable in the short term. The results show that the rheological behavior, interfacial adhesion, release kinetics, and mucosal transport performance of the herbal bioactive-loaded polymer composites are greatly affected by the type of polymer used. Among all the parameters that were evaluated, the chitosan-based composite system was found to have superior functional performance.

## DISCUSSION

This research supports the hypothesis that nasal formulations are biofunctional polymer composites because the polymeric matrix's intrinsic physicochemical and structural features considerably impact their functional performance. The comparative investigation shows that polymer chemistry and network architecture regulate herbal bioactives' interfacial adhesion, rheology, and transport. Table 1 shows that the chosen polymers formed stable composite matrices without impacting formulation homogeneity, as all formulations had a consistent drug concentration and nasal-compatible pH [17, 18]. Polymer chain hydration, functional group density, and flexibility affect mucoadhesive strength and viscosity in polymers and composites. Table 1 demonstrates that chitosan and carbopol are more viscous than HPMC. Because hydrated polymers form more ordered and connected networks. All formulations showed shear-thinning behavior (Figure 1), which is good for nasal delivery since it allows smooth flow and speedy structural recovery. Shear breaks polymer chain entanglements and reorients them. Hydrated polymer composites behave this way [19, 20].

The ranking of mucoadhesive performance: chitosan > carbopol > HPMC (Table 1) shows the importance of polymer-substrate interactions in composite design. Chitosan, a cationic polysaccharide, promotes hydrogen bonding, chain interpenetration, and electrostatic interactions with the negatively charged mucin layer. Carbopol relies on hydrogen bonding and hydration-driven swelling, while HPMC, being non-ionic, has weaker interfacial contacts. Results demonstrate that polymer phase surface chemistry and charge density are the most critical determinants in composite adhesion to biological surfaces [21, 22].

 

Figure 2 and Table 2 reveal that all formulations were polymer matrices controlled by diffusion, resulting in 8-hour sustained release. The chitosan composite releases its contents faster than Carbopol because the herbal bioactive diffuses more easily into the polymer phase due to its hydrated network structure. Carbopol composites have slower release due to their diffusionally resistant compact gel structure and increased crosslink density. These results reveal that network density and swelling capacity directly govern mass transfer inside the matrix, a classic structure-transport relationship in polymer composites [23, 24].

The ex-vivo permeation test shows that the polymer phase affects composite performance in many ways. Chitosan-based system had greater cumulative permeation and permeability coefficient than Carbopol and HPMC (Figure 3 and Table 3). This enhancement is due to chitosan's ability to change the mucosal surface's interfacial environment and improved release behavior. Wetting, temporary epithelial tight junction alteration, and strong mucoadhesion help overcome the biological barrier (Table 1) [25]. Chitosan acts as a structural matrix, promotes interfacial adhesion, and changes permeability in polymer composites. High-performance microcapsule (HPC) composites have good rheology but reduced penetration rates due to poorer mucoadhesive contact and limited epithelial barrier effects. Carbopol-based composites improved retention and diffusional path length inside the polymer network due to their high swelling capacity and gel formation, resulting in intermediate performance [26–28].

Chemical incompatibility of herbal bioactive with polymeric matrices was proven by FTIR and DSC investigations. The bioactive was molecularly or partially amorphously dispersed in composite systems. Polymer composites require molecular-level dispersion to make the dispersed phase more compatible with the continuous matrix at the interface, improving physical stability and release behavior. Since short-term stability experiments reveal that polymer networks maintained structural integrity and functional performance during storage, the chosen polymers can preserve this system's rheological and transport capabilities and herbal bioactive's chemical stability [29–32].

The key findings show that polymer structure, network organization, and interfacial behavior greatly influence mucoadhesion, controlled release, and mucosal penetration. Chitosan composites had the best rheological adaptability, biointerfacial adhesion, and transport capability for herbal bioactive nasal administration. Thus, this research provides a materials-oriented approach to developing high-tech biofunctional polymer composites for intranasal delivery [33–35].

## CONCLUSION

The current research shows that the effectiveness of mucoadhesive nasal composites in delivering herbal bioactives is highly dependent on the polymer choice. The chitosan-based formulation outperformed the other systems tested in terms of mucoadhesive strength (39.4 ± 2.1 g), cumulative drug release (85.9 ± 2.7% at 8 h), and nasal permeation when compared to the Carbopol 934P and HPMC structures. The formulations were shown to be suitable for intranasal application due to their acceptable pH, excellent rheological behavior, and high short-term stability. When it comes to creating efficient polymer composite systems for the nasal administration of herbal bioactives, chitosan stood out as a multifunctional polymer matrix that showed great promise.

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None

**Conflict of Interest**

None

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