Natural Resources for Human Health

visaga publishing house

Original Research

View Article Online

Check for updates

Received 24 August 2024
Revised 15 October 2024
Accepted 22 November 2024
Available Online 08 April 2025

Edited by Ricardo Diego de Albuquerque

KEYWORDS:
Tagetes erecta Linn
Similax zeylanica
In situ gel
Nasal formulation
Box Behnken design
Fungal rhinosinusitis

Natr Resour Human Health 2025; 5 (2):237-244
https://doi.org/10.53365/nrfhh/196299
eISSN: 2583-1194
Copyright © 2025 Visagaa Publishing House

Development of Novel In-Situ Nasal Gels for the Delivery of Herbal Drugs: A Preliminary Study on the Influence of the Residual Mucosal Clearance

Archana Gautam [1,*], Divya Pathak [2]

[1]PhD Research Scholar, IIMT University, MEERUT (U.P), India Pin No- 250001
[2]Associate Professor Departments of Pharmacy, IIMT University, MEERUT (U.P), India, Pin No-250001

ABSTRACT:
In situ gel formulations such as *Tagetes erecta* Linn and *Similax zeylanica* were created and optimized for the administration of herbal medications. The study underscores the potential of *in-situ* nasal gels 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 *in-situ* nasal gel formulations for the administration of herbal medications such as *Similax zeylanica* and Tagetes to treat allergic rhinitis. The in-situ gel was prepared by a cold method, and different concentrations of polymers were used, such as HPMC K4M (0.5-1.5 %), PEG 4000 (1.5-3% w/v), and Carbopol 934 (0.5-1.5%) The optimized formulation, batch F-6, 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 (TEM). The analysis of variance (ANOVA) and the response surface models confirmed the significance and suitability of the developed formulations. The study concluded by demonstrating the effective creation and enhancement of in-situ nasal gel formulations for the administration of herbal medications such as *Similax zeylanica* and *Tagetes erecta* Linn. 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 effects were improved by the formulations' usage of mucoadhesive polymers, which extended the drug's residence duration on the nasal mucosa.

1. INTRODUCTION

A revolutionary drug delivery technology known as an in-situ gel is a solution that, when exposed to physiological fluids or pH changes, turns into a gel. Drug release can be controlled and sustained due to this special feature. These are the main facts regarding in-situ gels. A formulation that is in solution form prior to entering the body but transforms into a gel form under specific physiological conditions is known as an in-situ gelling system (B. Safirstein, 1976). In-situ gels are easy to administer and reduce the need for frequent dosing, patients find them more convenient and comfortable (Kuhn & Javer, 1998). In-situ gels are used in various drug delivery applications, including ocular drug delivery, oral drug delivery, and more (Kuhn & Javer, 2000). The fungal illness known as allergic fungal rhinosinusitis (AFRS) affects the sinuses and nasal passages. It happens as a result of an allergic response or hypersensitivity to certain fungus in the sinuses. Manning and Holman (1998) they are some Symptoms Nasal congestion and stuffiness, sneezing, nasal polyps, itchy or watery eyes, facial pain or pressure, changes to facial structure (in severe cases) (Ryan & Marple, 2007). A thorough medical history is necessary for certain diagnoses. Nasal endoscopy, which uses a thin tube with a light and camera to visualise the sinuses and identify nasal polyps, is one method used by doctors to confirm the extent of sinus involvement and find fungal masses. Blood or allergy tests are also sometimes used. Find particular allergies caused by fungi (Marple, 2001). Some treatment as an **Antifungal medication:** These are used to treat AFRS. However, topical antifungals may not be very effective. **Corticosteroids:** Medications like fluticasone (Flonase) help reduce inflammation and manage symptoms. **Biologics:** Dupilumab (Dupixent) and omalizumab (Xolair) can reduce inflammation, minimizing the need for steroids and antifungals. **Nasal irrigation:** Regular sinus flushes with saline

* Corresponding author.
E-mail address: archna.gautam909@gmail.com (Archana Gautam)

This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

solutions improve sinus health by removing mucus and irritants (Bent & Kuhn, 1994). In-situ nasal gel formulations have been extensively studied for enhancing drug delivery efficiency. These formulations can be beneficial for treating allergic rhinitis by providing sustained release and improved bioavailability of herbal drugs like *Smilax zeylanica* and *Tagetes erecta* (Manning et al., 1997). The use of mucoadhesive polymers in in-situ gels can prolong drug residence time on nasal mucosa, enhancing drug absorption and therapeutic effects. Additionally, in-situ gels can overcome challenges like rapid mucociliary clearance, ensuring prolonged drug action. By optimizing factors like polymer concentrations and gelation properties, these formulations can be tailored to sustain drug release and improve nasal drug delivery. Therefore, in-situ nasal gel formulations hold promise for effectively delivering herbal drugs to treat allergic rhinitis by enhancing drug bioavailability and providing sustained therapeutic action (Campbell et al., 2006; Ghegan et al., 2006a; Mabry & Mabry, 2000; Mabry et al., 1997, 1998; McClay et al., 2002; Schubert, 2001; Zinreich et al., 1988). *Tagetes erecta* Linn (marigold) and Similax zeylanica are two herbal extracts known for their antioxidant and anti-inflammatory properties (B.H. Safirstein, 1976). These extracts have the potential to alleviate allergic rhinitis symptoms by reducing inflammation and modulating immune responses (Ponikau et al., 1999).

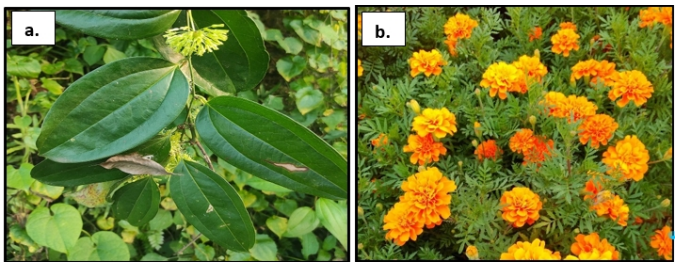

Figure 1. a) *Similax zeylanica* (Kumarika leave), **b)** *Tagetes erecta* (Genda leave)

2. MATERIALS AND METHODOLOGY

The plant materials used in this study were unripe fruits of *Tagetes erecta* Linn (Common name Genda) and leaves of *Similax zeylanica* (common name kumarika) were collected from the local markets and local area of Dehradun and identified Forest Research Institute Dehradun. Pluronic F127 (Thermo fisher chem.), Carbopol 934 (Lubrizol. chem.), Poly ethylene glycol-4000 (Miralax lab.), Hydroxypropyl Methylcellulose [HPMC K4M] (Alisha lab.), Benzalkonium (Thermo fisher chem.) etc.

2.1. Preparation of extract of Tagetes erecta Linn

The gathered plant leaves were cleaned with water and allowed to dry in the shade. A mixer grinder was then used to powder the plant material. The 100g of powder was extracted in a Soxhlet extractor at 40°C using several solvents. Until the solvent in the thimble became clear, the extraction process was continued. This extract was used for additional phytochemical research after being kept in a desiccator. The initial photochemical investigation was carried out (Ferguson et al., 2000; Laury & Wise, 2013; Wise et al., 2008).

2.2. Preparation of extract of Similax zeylanica

After washing the leaves (1000g) with distilled water to get rid of dirt and grime, they were well dried in the shade for 5-7 days. After that, they were dried in a tray dryer set at 400°C and ground into powder. They were then extracted using an independent solvent using a Soxhlet apparatus for 72 hours at 55–60°C. The extract was heated to less than 50°C and centrifuged at 85 rpm while being filtered and concentrated under vacuum in a rotary evaporator (Ghegan et al., 2006b, 2007; Manning et al., 1991; Wise et al., 2004).

2.3. Preparation Methods of In-situ gel:

The preparation of in situ gels involves various methods, including:

- **Cold Method-** This method involves slow addition of a polymer solution to a solvent, allowing for the formation of a gel.
- **Solvent Evaporation Method-** This method involves dissolving a polymer in a solvent, followed by evaporation of the solvent to form a gel.
- **Emulsification Method-** This method involves mixing a polymer with a solvent and an emulsifier, allowing for the formation of a gel (Li & Li, 2007; Manning et al., 1993; Schillen et al., 1993).

2.4. Preparation of Gel Base:

Pluronic F127: Dissolve a predetermined amount of Pluronic F127 in distilled water with constant stirring. Heating may be required to ensure complete dissolution. Allow the solution to cool down to room temperature.

Carbopol 934: Disperse Carbopol 934 in water with constant stirring to avoid lump formation. Allow the dispersion to swell for a few hours, then neutralize with a suitable base (e.g., triethanolamine) to achieve the desired viscosity and pH.

HPMC K4M and PEG 4000: Dissolve HPMC K4M and PEG 4000 in water under constant stirring to achieve a clear solution.

Incorporation of Herbal Extract: Add the standardized herbal extracts of *Similax Zeylanica* and *Tagetes Erecta* to the respective polymer solutions/dispersions. Stir gently to ensure uniform dispersion of the herbal extracts in the polymer matrices (Abu-Huwaij et al., 2011; Basu & Bandyopadhyay, 2010; Mainardes et al., 2006; Swathi, 2015).

Using a cold technique, in situ gel was created. Various polymer concentrations were employed, including PEG 4000 (1.5–3% w/v), Carbopol 934 (0.5–1.5 % w/w), and HPMC K4M (0.5–1.5 % w/v) to find the ideal concentration of Pluronic-F127 and other polymers needed for thermotriggered gelling. which, when heated to 32°C, formed thermotriggered

gel. By continually stirring on a magnetic stirrer set at 400 rpm, 0.5-1.5% PEG 4000 and 0.5-1.5% Carbopol 934 were dissolved in the aqueous phase to create a thermotriggered in situ gel.

In cold circumstances, 10% Pluronic-F127 was added to the aqueous phase gradually while being constantly stirred. The gel was then filled with this aqueous phase dropwise. To obtain the thermotriggered gel, the solution was kept at 4°C for an entire night following the full solubilisation of Pluronic-F127 (Pratibha et al., 2003). Pluronic-F127 was employed as the thermosensitive agent to produce in situ gel after spraying into the nostrils; carbopol 934 was used as the mucoadhesive agent due to its mucoadhesive capabilities to make the formulation adhere to the mucosal system. Based on the quantity of formulation which the spray pump was capable of to deliver, the active medication had been added.Use of Box Behnken design showing Table 1 and Table 2 shows the composition of the *In situ* gel (Krishnamoorthy & Mitra, 1998).

Table 1
BBD for optimization range of In-situ gel

Independent variables	Symbol	Level of variation	
		Low	High
Carbopol 934	X1	0.5	1.5
Polyethylene glycol-4000	X2	1.5	3
HPMC K4 M	X3	0.5	1.5
Dependent variables	**Symbol**	**Constraint**	
Drug content (%)	Y1	Maximize	
Viscosity (cP)	Y2	Minimize	
In- vitro diffusion Studies (%)	Y3	Maximize	

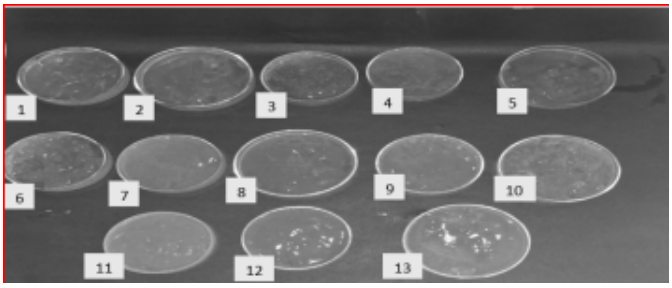

Figure 2. Formulation of in-situ gel batch (F1-F13)

3. METHOD OF EVOLUTION PARAMETER IN IN-SITU GEL

Physical appearance: As a visual in gel like colour and transparency.

pH determination: The pH values of the gel samples were measured using a pH meter (Remi Equipment Pvt. Ltd., Kolkata, India). The pH meter was calibrated with buffer solutions with pH values of 4.0, 7.0, and 9.0 before to each use. The pH of the formulation was checked three times, and the mean was calculated.

Drug content: By adding a little quantity of methanol to a 100 mL volumetric flask, which solubilises the gel, one dose (10 mg) equivalent gel formulation was added in order to evaluate the drug concentration. Ultimately, a pH 6.4 phosphate buffer was added to get the volume up to 100 mL. It was thoroughly shaken in a shaker for approximately one hour, then centrifuged and examined. After passing the resulting solution through Whatman filter paper, a UV-visible spectrophotometer was used to determine the absorbance at 228 nm.

Viscosity: The viscosities of the gel were measured using a Brookfield viscometer DVpluse viscometer. equipped with a spindle number DV-II+ PRO. LV1's spindle code is 61. After being immersed in the mixture, the spindle rotated at room temperature for five minutes at a speed of 100 rpm.

In- vitro diffusion Studies: A drug diffusion research conducted in vitro using Hi Media (molecular weight 5000 Daltons) employed a dialysis membrane and a Franz diffusion cell. The membrane used for dialysis was saturated with simulated nasal fluid (SNF) for a whole night. The upper (donor) and lower (receptor) compartments of the Franz diffusion cell were then fitted with the dialysis membrane. The formulation equal to 10 mg of the dose was applied to the dialysis membrane's donor compartment side. The receptor compartment of the Franz diffusion cell was filled with 18 mL of simulated nasal fluid (SNF). Throughout the experiment, the diffusion cells (Remi, India) were kept at 37 ± 0.5°C and stirred at 600 rpm. Using a side tube, 1 mL of aliquots was taken out of the receptor compartment every 15 minutes, 30 minutes, 45 minutes, 60 minutes, 120 minutes, and 180 minutes at predetermined intervals. To keep the sink condition, the same volume of SNF was then added back. The removed samples were examined using 280 nm UV-visible spectrophotometry.

Transmission Electron Microscopy: In order to investigate the morphology of the final gel formulation, transmission electron microscopy (TEM) (H-7500, Hitachi, Kyoto, Japan) was utilised to look at the morphology of the enhanced formulation. The gel was coloured with 1% (w/v) phosphotungstic acid and then placed on copper grids for observation. The shape of the globule was determined by looking at the TEM pictures.

Optimization Statistical Analysis: One-way analysis of variance (ANOVA) was employed in the statistical analysis to compare the outcomes of various formulations. Statistical significance was defined as a p value of 0.05 (GraphPad Prism version 6.03, Boston, MA, USA). The characterisation results were presented as the three experiments' means ± standard deviation (Amkar et al., 2024; Hu et al., 2002; Raut et al., 2023)

4. RESULT AND DISCUSSION

- **Physical appearance:** As a visual in gel like colour and transparency as result in optimized formulation F-6 is better compare to other formation. (++++) is reparented in excellent property in formulation. its good compatibility and transparency. it showing of observation Table 4.

Table 2
Use for optimization of Box Behnken design (BBD)

Formulation code	**X1** (CP 934)%		**X2** (PEG-4000)%		**X3** (HPMCK4M)%	
	Code value	Actual value	Code value	Actual value	Code value	Actual value
F1	-1	0.5	-1	1.5	0	1
F2	+1	1.5	-1	1.5	0	1
F3	-1	0.5	+1	3	0	1
F4	+1	1.5	+1	3	0	1
F5	-1	0.5	0	2.25	-1	0.5
F6	+1	1.5	0	2.25	-1	0.5
F7	-1	0.5	0	2.25	+1	1.5
F8	+1	1.5	0	2.25	+1	1.5
F9	0	1	-1	1.5	-1	0.5
F10	0	1	+1	3	-1	0.5
F11	0	1	-1	1.5	+1	1.5
F12	0	1	+1	3	+1	1.5

Table 3
Composition of different quantity in situ gel with their responses using BBD

S. No.	API & Excipients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Tagetes erectalinn(%w/v)	2	2	2	2	2	2	2	2	2	2	2	2
2	Similax zeylanica(%w/v)	2	2	2	2	2	2	2	2	2	2	2	2
3	Pluronic F127(%w/v)	10	10	10	10	10	10	10	10	10	10	10	10
4	Carbopol 934(%w/v)	0.5	1.5	0.5	1.5	0.5	1.5	0.5	1.5	1	1	1	1
5	PEG 4000(%w/v)	1.5	1.5	3	3	2.25	2.25	2.25	2.25	1.5	3	1.5	3
6	HPMC K4M(%w/v)	1	1	1	1	0.5	0.5	1.5	1.5	0.5	0.5	1.5	1.5
7	Benzalkonium chloride (%v/v)	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
8	Distilled Water (ml)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

- **pH determination:** In- situ gel formulation of topical used so skin pH range 5.8 - 7.0 and this formulation best and optimize pH range 6.8 ±0.5 in this formulation batch no. F-6.it is mention of Table 4.

- **Drug content:**The impact of Tagetes erectalinn and similax zeylanica on the drug content in the *in situ* gel varies. The formulation batch F-6, which includes Carbopol 934 (1.5%), PEG 4000 (2.25%), and HPMC K4M (0.5%), showed the best results for the *in-situ* gel. The drug content in batch F6 was optimized at 86±0.2%, making it a stable formulation.

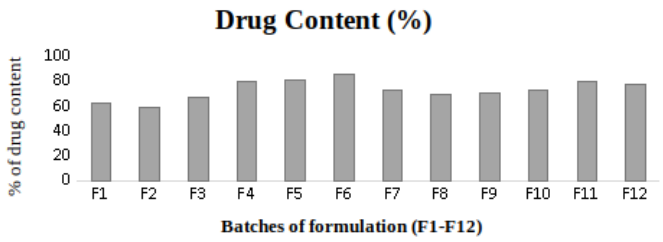

Figure 3. Graph of Drug content formulation (F1-F12)

- **Viscosity:**The in-situ gel formulation should have a viscosity range of 2322.36 ± 56.4cP for batch F-6, as indicated in Table 4 and Figure 4. This formulation contains a higher concentration of Carbopol 934.

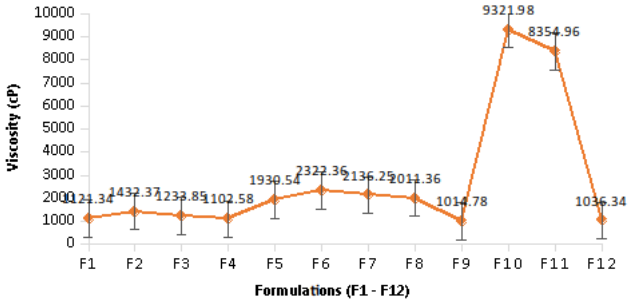

Figure 4. Graph of Viscosity formulation (F1-F12)

- **In- vitro diffusion Studies:** Figure 5 shows how the in-situ gel releases over time after being optimized. The pure drug released quickly, with almost 98% released within 3 hours. On the other hand, the optimized herbal-loaded in-situ gel released about 96.97% after 180 minutes. The optimized formulation (batch F-6) had two phases of

Table 4
Results of gel formulation batch (F1 to F12)

Formulation code	Physical appearance	pH range	Drug content (%)	Viscosity (cP)
F1	++	6.4±0.2	63±0.5%	1121.34±14.1
F2	+	6.3±0.3	60±0.2%	1432.37±15.8
F3	+	6.2±0.5	68±0.5%	1233.85±13.5
F4	+++	6.4±0.1	80±0.2%	1102.58±11.3
F5	++	6.5±0.6	82±0.3%	1930.54±54.3
F6	++++	6.8±0.5	86±0.2%	2322.36±56.4
F7	+	6.3±0.4	74±0.4%	2136.25±36.5
F8	++	6.4±0.3	70±0.3%	2011.36±24.3
F9	++	6.3±0.2	71±0.5%	1014.78±54.8
F10	++	6.7±0.4	73±0.5%	9321.98±23.3
F11	+++	6.6±0.7	81±0.4%	8354.96±19.3
F12	+++	6.2±0.6	78±0.1%	1036.34±36.4

release: fast release in the first 180 minutes and then a continuous release afterwards. The herbal gel release was steady over 180 minutes, showing that can trap the herbal drug.

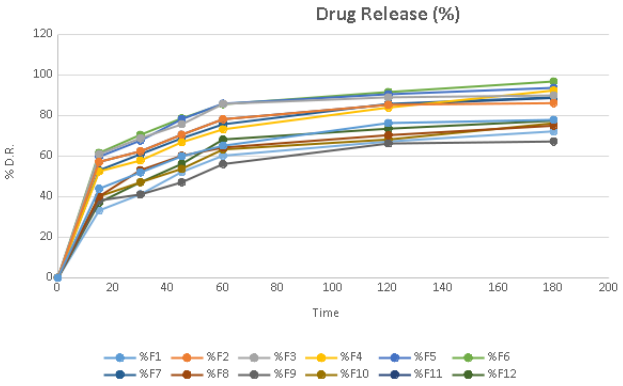

Figure 5. Graph of gel formulation batch (F1- F12)

- **Transmission Electron Microscopy:** TEM was used to examine the optimised In-situ gel formulation's size, shape, and structure. As observed in Figure 6, the in-situ gel was condensed into spherical vesicles with distinct walls. The result estimated by TEM was equivalent to the VS obtained using the dynamic light scattering approach. It is representative optimize batch F-6 showing Figure 6.

- **Optimization statistical analysis:** One way ANOVA was applied to the measured values of the examined responses for each of the BBD designs in order to get model equations for the responses that were then analysed using the appropriate statistical tool, Design-Expert 10.0.1 software. Table 6 displays the results of an ANOVA analysis of the chosen replies, which showed that each response surface model was significant and suitable. Based on the two cubic models, the ANOVA results showed that these models were significant for

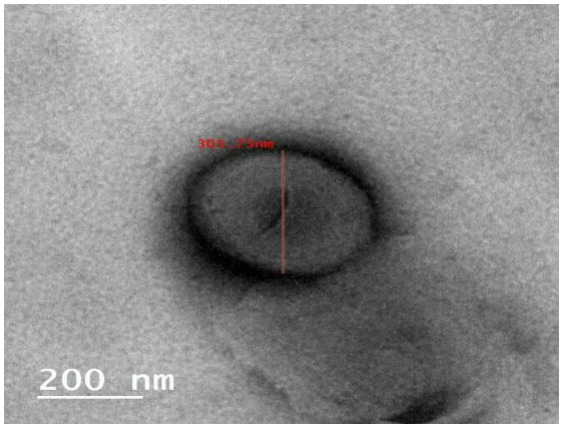

Figure 6. TEM representative in optimize batch F-6

every response parameter. All of the model equation's coefficients are visible. The model equation all response shown in –

Drug content (%) = $0.31+ 0.22\ X_1 + 1.75\ X_2 + (0.223x1.758)\ X_1\ X_2 + (- 0.040)\ X_1^2 + [(-0.040)\ x(1.75)]X_1^2\ X_2 + [(0.223)x(-0.040)]\ X_1\ X_1^2 + [(-0.040)x(-0.040)]\ X_1^2X_1^2$

Viscosity (cP)= $(-0.25) + 0.31\ X_1 + 0.12\ X_2 + (-0.014)\ X_1\ X_2 + (-0.049)\ X_1^2 + [(-0.014)\ x\ (0.128)\ X_1^2\ X_2 + [(0.316)\ x(-0.049)]\ X_1\ X_1^2 + [(-0.049)x(-0.049)]\ X_1^2X_1^2$

Cumulative Drug release at 180 min = $32.2+ 32.8\ X_1 + 55.7\ X_2 + (-10.04)X_1\ X_2 + (-5.38)\ X_1^2 + [(-5.38)\ x(55.7)]X_1^2\ X_2 + [(32.8)x(-5.38)]\ X_1\ X_1^2 + [(-5.38)x(-5.38)]\ X_1^2X_1^2$

The Contour and 3D response surface graphs were generated by the design expert 10.0.1 software.

- **Drug Content (%):**
- **Viscosity (cP):**
- **Cumulative drug release (%):**

Table 5
Table of *In vitro* drug release all formulation (F1- F12)

Time (min.)	Formulation Code											
	%F1	%F2	%F3	%F4	%F5	%F6	%F7	%F8	%F9	%F10	%F11	%F12
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
15	44.05± 0.32	57.29± 0.28	61.09± 0.3	52.62± 0.12	59.82± 0.35	61.74± 0.16	53.14± 0.22	40.25± 0.34	38.23± 0.73	40.25± 0.30	57.29± 0.40	37.25± 0.42
30	52.09± 0.46	62.52± 0.32	68.95± 0.18	57.97± 0.24	67.85± 0.67	70.65± 0.52	61.09± 029	53.20± 0.65	41.22± 0.62	47.23± 0.33	62.52± 0.35	47.25± 0.38
45	60.04± 0.64	70.74± 0.41	75.85± 0.25	67.01± 0.68	78.37± 0.76	78.77± 0.56	68.95± 0.67	60.32± 0.65	47.23± 0.71	53.89± 0.45	70.74± 0.46	56.27± 0.42
60	65.29± 0.65	78.34± 0.52	85.92± 0.59	73.37± 0.42	86.04± 0.65	85.76± 0.45	75.85± 0.57	64.37± 0.43	56.21± 0.48	63.45± 0.70	78.34± 0.43	68.35± 0.66
120	76.46± 0.61	85.48± 0.73	89.16± 0.61	84.11± 0.38	90.67± 0.71	91.77± 0.64	85.92± 0.76	70.47± 0.49	66.35± 0.51	68.33± 0.34	85.48± 0.52	73.69± 0.72
180	78.05± 0.75	86.29± 0.74	90.09± 0.40	92.52± .60	93.83± 0.62	96.97± 0.58	89.16± 0.61	75.16± 0.72	67.35± 0.64	76.35± 0.57	88.86± 0.58	77.60± 0.75

Table 6
Summary of ANOVA for the response parameters

Response Factor	Sum of square	d.f.	Mean square	F-Value	Prob.>F
Drug content (%)	1.25	4	0.37	635.42	<0.0001
Viscosity (cP)	0.045	4	3.25	10.56	0.0307
Cumulative drug release (CDR $_{60min.\%}$)	632.32	4	145.40	41.84	0.0036

5. DISCUSSIONS AND CONCLUSION

The study concluded by demonstrating the effective creation and enhancement of in-situ nasal gel formulations for the administration of herbal medications such as Similax zeylanica and Tagetes erecta Linn. 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 effects were improved by the formulations' usage of mucoadhesive polymers, which extended the drug's residence duration on the nasal mucosa. The in-situ gels also overcome obstacles such quick mucociliary clearance, guaranteeing sustained drug action. The batch F-6 formulation was shown to be stable and efficacious for nasal drug delivery because to its exceptional physical appearance, pH range, drug content, and viscosity.

The significance and applicability of the developed formulations were validated by means of statistical analysis employing ANOVA and response surface models. The viscosity, cumulative drug release, and drug content model equations showed how independent variables affected the responses, offering insightful information for future research and optimisation. The Design Expert 10.0.1 software produced contour and three-dimensional response surface graphs that demonstrated how the independent variables interacted with one another and affected the responses. Overall, the study highlights how in-situ nasal gel formulations, which provide sustained drug release, enhanced bioavailability, and longer therapeutic activity, could be a promising method for improving the delivery of herbal medications to treat allergic rhinitis.

ETHICS APPROVAL AND STANDARDS

Not applicable.

REPORTING STANDARDS

The study followed the PRISMA/STROBE guidelines for reporting research findings.

AVAILABILITY OF DATA AND MATERIALS, FUNDING, AND CONFLICT OF INTEREST

Data and materials availability were not applicable, and the study received no specific funding. The authors declared no conflicts of interest.

ACKNOWLEDGEMENTS

The authors express their gratitude to Prof. Dr. Divya Pathak and Vice Chancellor of IIMT University, Meerut (U.P), India, for his invaluable support throughout the research work.

ORCID

Archana Gautam 0009-0007-8181-6413

Divya Pathak 0000-0002-6818-8244

REFERENCES

Abu-Huwaij, R., Obaidat, R.M., Sweidan, K., Al-Hiari, Y., 2011. Formulation and in vitro evaluation of xanthan gum or carbopol 934-based mucoadhesive patches, loaded with nicotine. American Association of Pharmaceutical Scientists Pharmaceutical Science & Technology. 12, 21-27. https://doi.org/10.1208/s12249-010-9560-3

Amkar, A., Waghchoure, P., Rane, B., Jain, A., 2024. Development and optimization of polymeric nanoparticles and its in vitro deposition studies using modified tsi. Current Applied Materials. 3. (Scopus indexed). https://doi.org/10.2174/0126667312289623240327073342

Basu, S., Bandyopadhyay, A.K., 2010. Development and characterization of mucoadhesive in-situ nasal gel of midazolam prepared with ficus carica mucilage. American Association of Pharmaceutical Scientists Pharmaceutical Science & Technology. 11, 1223-1231. https://doi.org/10.1208/s12249-010-9478-9

Bent, J.P., Kuhn, F.A., 1994. Diagnosis of allergic fungal sinusitis. Otolaryngology–Head and Neck Surgery. 111(5), 580-588. https://doi.org/10.1177/019459989411100508

Campbell, J.M., Graham, M., Gray, H.C., Bower, C., Blaiss, M.S., Jones, S.M., 2006. Allergic fungal sinusitis in children. Annals of Allergy, Asthma & Immunology. 96(2), 286-290. https://doi.org/10.1016/S1081-1206(10)61236-7

Ferguson, B.J., Barnes, L., Bernstein, J.M., 2000. Geographic variation in allergic fungal rhinosinusitis. Otolaryngologic Clinics of North America. 33, 441-449. https://doi.org/10.1016/S0030-6665(05)70215-6

Ghegan, M.D., Lee, F.S., Schlosser, R.J., 2006a. Incidence of skull base and orbital erosion in allergic fungal rhinosinusitis (afrs) and non-afrs. Otolaryngology–Head and Neck Surgery. 134(4), 592-595. https://doi.org/10.1016/j.otohns.2005.11.040

Ghegan, M.D., Lee, F.S., Schlosser, R.J., 2006b. Incidence of skull base and orbital erosion in allergic fungal rhinosinusitis (afrs) and non-afrs. Otolaryngology–Head and Neck Surgery. 134, 592-595. https://doi.org/10.1016/j.otohns.2005.11.040

Ghegan, M.D., Wise, S.K., Gorham, E., Schlosser, R.J., 2007. Socioeconomic factors in allergic fungal rhinosinusitis with bone erosion. American Journal of Rhinology & Allergy. 21, 560-563. https://doi.org/10.2500/ajr.2007.21.3045

Hu, G., Walls, R.S., Bass, D., Bullock, R., Grayson, D., Jones, M., et al., 2002. The chinese herbal formulation biminne in management of perennial allergic rhinitis: a randomized, double-blind, placebo-controlled, 12-week clinical trial. Annals of Allergy, Asthma & Immunology. 88, 478-487. https://doi.org/10.1016/S1081-1206(10)62380-5

Krishnamoorthy, R., Mitra, A.K., 1998. Prodrugs for nasal drug delivery. Advanced Drug Delivery Reviews. 29, 135-139. https://doi.org/10.1016/S0169-409X(97)00069-3

Kuhn, F.A., Javer, A.R., 1998. Allergic fungal rhinosinusitis: our experience. Archives of Otorhinolaryngology-Head & Neck Surgery. 124(10), 1179-1180. https://doi.org/10.1001/archotol.124.10.1179

Kuhn, F.A., Javer, A.R., 2000. Allergic fungal rhinosinusitis: perioperative management, prevention of recurrence, and role of steroids and antifungal agents. Otolaryngologic Clinics of North America. 33(2), 419-433. https://doi.org/10.1016/S0030-6665(05)70213-2

Laury, A.M., Wise, S.K., 2013. Chapter 7: allergic fungal rhinosinusitis. American Journal of Rhinology & Allergy. 27, 26-27. https://doi.org/10.2500/ajra.2013.27.3937

Li, G.L., Li, M., 2007. Preparation and evaluation of ophthalmic thermosensitive in-situ gels of penciclovir. Journal of Chinese Pharmaceutical Sciences. 16, 90-95. https://doi.org/10.5246/jcps.2007.02.012

Mabry, R.L., Mabry, C.S., 2000. Allergic fungal sinusitis: the role of immunotherapy. Otolaryngologic Clinics of North America. 33(2), 433-440. https://doi.org/10.1016/S0030-6665(05)70214-4

Mabry, R.L., Manning, S.C., Mabry, C.S., 1997. Immunotherapy in the treatment of allergic fungal sinusitis. Otolaryngology–Head and Neck Surgery. 116(1), 31-35. https://doi.org/10.1016/S0194-5998(97)70350-0

Mabry, R.L., Marple, B.F., Folker, R.J., Mabry, C.S., 1998. Immunotherapy for allergic fungal sinusitis: three years' experience. Otolaryngology–Head and Neck Surgery. 119(6), 648-651. https://doi.org/10.1016/S0194-5998(98)70063-6

Mainardes, R.M., Urban, M.C., Cinto, P.O., Chaud, M.V., Evangelista, R.C., Gremiao, M.P., 2006. Liposomes and micro/nanoparticles as colloidal carriers for nasal drug delivery. Current Drug Delivery. 3, 275-285. https://doi.org/10.2174/156720106777731034

Manning, S.C., Holman, M., 1998. Further evidence for allergic pathophysiology in allergic fungal sinusitis. Laryngoscope. 108(10), 1485-1496. https://doi.org/10.1097/00005537-199810000-00010

Manning, S.C., Mabry, R.L., Schaefer, S.D., Close, L.G., 1993. Evidence of ige-mediated hypersensitivity in allergic fungal sinusitis. Laryngoscope. 103, 717-721. https://doi.org/10.1288/00005537-199307000-00001

Manning, S.C., Merkel, M., Kriesel, K., Vuitch, F., Marple, B., 1997. Computed tomography and magnetic resonance diagnosis of allergic fungal sinusitis. Laryngoscope. 107(2), 170-176. https://doi.org/10.1097/00005537-199702000-00007

Manning, S.C., Schaefer, S.D., Close, L.G., Vuitch, F., 1991. Culture-positive allergic fungal sinusitis. Archives of Otorhinolaryngology-Head & Neck Surgery. 117, 174-178. https://doi.org/10.1001/archotol.1991.01870140060014

Marple, B.F., 2001. Allergic fungal rhinosinusitis: current theories and management strategies. Laryngoscope. 111(6), 1006-1019. https://doi.org/10.1097/00005537-200106000-00014

McClay, J.E., Marple, B., Kapadia, L., 2002. Clinical presentation of allergic fungal sinusitis in children. Laryngoscope. 112(3), 565-569. https://doi.org/10.1097/00005537-200203000-00028

Ponikau, J.U., Sherris, D.A., Kern, E.B., et al., 1999. The diagnosis and incidence of allergic fungal sinusitis. Mayo Clinic Proceedings. 74(9), 877-884. https://doi.org/10.4065/74.9.877

Pratibha, N., Saxena, V.S., Amit, A., D'souza, P., Bagchi, M., Bagchi, D., 2003. Anti-inflammatory activities of aller-7, a novel polyherbal formulation for allergic rhinitis. International Journal of Tissue Reactions. 26, 43-51. https://doi.org/10.1007/s10787-003-0010-3

Raut, S.S., Rane, B.R., Jain, A.S., 2023. Development and evaluation of ebastine loaded transfersomal nanogel for the treatment of urticaria (autoimmune disease). Engineering Proceedings. 56, 101. (Scopus indexed). https://doi.org/10.3390/ASEC2023-15286

Ryan, M.W., Marple, B.F., 2007. Allergic fungal rhinosinusitis: diagnosis and management. Current Opinion in Otolaryngology & Head and Neck Surgery. 15(1), 18-22. https://doi.org/10.1097/MOO.0b013e328011bc85

Safirstein, B., 1976. Allergic bronchopulmonary aspergillosis with obstruction of the upper respiratory tract. Chest. 70, 788-790. https://doi.org/10.1378/chest.70.6.788

Safirstein, B.H., 1976. Allergic bronchopulmonary aspergillosis with obstruction of the upper respiratory tract. Chest. 70(6), 788-790. https://doi.org/10.1378/chest.70.6.788

Schillen, K., Glatter, O., Brown, W., 1993. Characterization of a peo-ppo-peo block copolymer system. Progress in Colloid and Polymer Science. 93, 66-71. https://doi.org/10.1007/BFb0118520

Schubert, M.S., 2001. A superantigen hypothesis for the pathogenesis of chronic hypertrophic rhinosinusitis, allergic fungal sinusitis, and

related disorders. Annals of Allergy, Asthma & Immunology. 87(3), 181-188. https://doi.org/10.1016/S1081-1206(10)62223-4

Swathi, S., 2015. Phytochemical screening and tlc studies of moringa oleifera extract: their antibacterial and anti-oxidant activities. International Journal of Current Pharmaceutical Research. 1, 46-49. https://doi.org/10.22159/ijcpr.2015v7i1.14896

Wise, S.K., Ghegan, M.D., Gorham, E., Schlosser, R.J., 2008. Socioeconomic factors in the diagnosis of allergic fungal rhinosinusitis. Otolaryngology–Head and Neck Surgery. 138, 38-42. https://doi.org/10.1016/j.otohns.2007.09.006

Wise, S.K., Venkatraman, G., Wise, J.C., DelGaudio, J.M., 2004. Ethnic and gender differences in bone erosion in allergic fungal sinusitis. American Journal of Rhinology & Allergy. 18, 397-404. https://doi.org/10.1177/194589240401800403

Zinreich, S.J., Kennedy, D.W., Malat, J., 1988. Fungal sinusitis: diagnosis with ct and mr imaging. Radiology. 169(2), 439-444. https://doi.org/10.1148/radiology.169.2.3051118