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RESEARCH

Formulation and Evaluation of Fluticasone Furoate and Oxymetazoline Hydrochloride Nasal Spray for treatment of Allergic rhinitis

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ABSTRACT

The aim of this study was to develop and assess a nasal delivery system containing Fluticasone furoate and oxymetazoline hydrochloride for treating allergic rhinitis. A colloidal dispersion of fluticasone furoate and oxymetazoline hydrochloride was utilized for the nasal drug delivery system, with Benzalkonium chloride (BKC) included as a preservative. The final formulation incorporated citric acid as an acid-modifying agent, sodium citrate as a buffering agent, polysorbate 80 as a surfactant, and MCC and CMC (Avicel 591) as viscosity-modifying agents. The formulation underwent evaluation for various parameters including pH, clarity, viscosity, drug content, spray content uniformity, pump delivery, spray pattern, plume geometry, droplet size distribution, priming, and repriming. Spray content uniformity ranged from 85% to 115%, while the pH was between 4 and 6. The spray pattern had an ovality of 1.121, with a perimeter of 113.42 mm and an area of 9.671 mm². The plume geometry had a mean spray angle of 59.0°, Plume Width 67.83 mm and Plume Length: 60 mm. The repriming efficiency varied between 83.9% and 100.1%, indicating satisfactory performance. Droplet size distribution was found to be between 25 and 30 µm. The formulation, along with its container, was tested for stability under accelerated conditions for up to three months. The results suggest that this formulation is a viable option for allergic rhinitis treatment, demonstrating comparable performance to existing marketed products.

Keywords: Nasal delivery, Plume geometry, Spray pattern, Droplet size, Priming efficiency

INTRODUCTION

Allergic rhinitis (AR) is a prevalent health issue affecting individuals of all ages worldwide. It is characterized by inflammation of the upper airway, resulting in symptoms such as nasal congestion, rhinorrhea, sneezing, and a reduced sense of smell (1). In addition to these nasal symptoms, patients may also experience non-nasal symptoms, including itching of the ears, palate, and throat, headaches, fatigue, and ear congestion. These symptoms are believed to be triggered by antigen-antibody reactions involving mast cells in the nasal epithelium (2).

Fluticasone furoate (FF) is a highly potent, synthetic glucocorticoid with a strong affinity for the glucocorticoid receptor and minimal systemic absorption. It is a next-generation intranasal corticosteroid, developed through modifications to the 17-ester moiety of fluticasone propionate (3). FF has been approved for managing allergic rhinitis symptoms in various countries and is known for its enhanced pharmacodynamic and physicochemical properties (4). Oxymetazoline (OH) is an adrenomimetic agent that agonizes α1 and α2-adrenergic receptors, leading to vasoconstriction in the nasal blood vessels. This results in relief from nasal congestion by increasing the airway lumen diameter. OH acts quickly, with effects observable within 5 to 10 minutes and lasting between 5 and 6 hours (5). Due to its effectiveness and the potential for nasal congestion to disrupt sleep, OH is often administered once daily at night. However, long-term use can lead to rhinitis medicamentosa, characterized by rebound congestion and histological changes in the nasal mucosa (6,7). This study hypothesizes that combining OH with FF could provide better symptom relief for perennial allergic rhinitis without inducing rhinitis medicamentosa.

Exposure to allergens triggers an IgE-mediated immune response in the nasal mucosa, potentially leading to chronic inflammatory conditions like allergic rhinitis. Symptoms may be seasonal or perennial and include sneezing, postnasal drip, rhinorrhea, nasal irritation, and nasal congestion, along with non-nasal symptoms such as itchy or watery eyes (8). Nasal congestion, a significant and troublesome symptom, can impact sleep quality, cognitive function, health-related quality of life, and psychosocial well-being. Seasonal allergic rhinitis is commonly caused by allergens like pollen or mold, while perennial allergic rhinitis is often triggered by indoor allergens such as dust mites, molds, and animal dander. Both conditions involve inflammatory cell infiltration in the nasal mucosa and the release of inflammatory mediators from mast cells (9,10).

The primary goal of AR treatment is to alleviate symptoms as effectively and safely as possible. Intranasal corticosteroids are the first-line treatment for chronic AR due to their ability to reduce both early and late immune responses. These medications work by inhibiting cytokine production, blocking mediator release from mast cells and basophils, and decreasing pro-inflammatory cell numbers, thereby reducing nasal secretions and mucous membrane permeability (11,12). FF and OH represent a powerful combination for managing AR. This combination not only improves symptoms significantly but also maintains high receptor concentrations within the nasal mucosa, has a rapid onset of action, and exhibits low systemic absorption with a favourable safety profile (13,14).

The pharmaceutical industry continually seeks innovative drug delivery systems to address existing challenges. Nasal drug delivery systems are particularly promising due to the large surface area of the nasal cavity, which enhances drug absorption compared to other routes. The nasal route also bypasses presystemic metabolism, improving drug bioavailability. This study was aimed to assess the efficacy of an intranasal corticosteroid combined with OH in treating AR, focusing on preventing rebound congestion and rhinitis medicamentosa with long-term use. Additionally, the study will evaluate the enhanced drug delivery using a Bona pump, which is noted for its cost-effectiveness.

MATERIALS AND METHOD

Materials

Fluticasone furoate and Oxymetazoline hydrochloride gifted by Sava Healthcare Pvt. Limited. Benzalkonium chloride, Citric acid, Sodium citrate, Polysorbate 80, Microcrystalline cellulose (Avicel RC-591), Sodium citrate dihydrate and Glycerine were purchased from Merck Chemicals, India.

Preformulation studies

Preformulation studies were conducted to assess drug-excipient interactions and solubility. These studies included UV absorption spectroscopy to identify any potential interactions between the drug and excipients. Viscosity measurements of the formulation were performed using a Brookfield Viscometer to evaluate the impact of viscosity on drug release. Additionally, infrared spectroscopy was used to analyze the spectra of pure FF and OH. Drug-excipient compatibility tests were conducted to confirm the chemical stability of FF and OH with the excipients used in the formulation (15).

Preparation of colloidal dispersion

All the twelve batches of the prepared formulations contained OH 0.50 mg and FF 0.28 mg of drug per ml. Benzalkonium chloride used as preservative. Citric acid used as buffering agent to maintain pH. Microcrystalline cellulose (MCC) (Avicel RC-591) used as viscosity modifying agent. Polysorbate 80 used as tonicity agent and surfactant. Anhydrous disodium hydrogen phosphate (ADHP) and sodium dihydrogen phosphate (SDP) was used as buffering agent. The different compositions of all formulation were given in table 1. Total quantity of 100 ml of formulation was prepared for each batch. The 120-gram filtered purified water was taken in stainless steel (SS) vessel and MCC and sodium carboxy methyl cellulose (Na CMC) (Avicel RC-591) were dispersed in it slowly under stirring to form homogenous slurry. It was further allowed to hydrate with continuous stirring for 2 hrs (stirring speed 1200-1500). This step was recorded as **1.1**. Further, 20 gm of purified water in separate beaker was taken and disodium edetate was dissolved in it. This step was recorded as **1.2**. Then 15 gram of purified water is taken in separate beaker and citric acid monohydrate was dissolved into it and then ADHP and SDP was added under continuous stirring for 10 minutes. This step was recorded as **1.3**. The 5 gram of purified water was taken in separate beaker and benzalkonium chloride (BKC) solution (50%) was dissolved to it under continuous stirring for 10 minutes. (stirring speed 1000 RPM, stirring time: 10 minutes). This step was said to be **1.4**. Further, step 1.1, step 1.2 and step 1.3 were mixed under continuous stirring for 10 minutes. In the second phase of formulation 15 gram of purified water is taken in separate beaker and polysorbate 80 was dissolved into it. This step was said to be **2.1**. Further, FF was added and dispersed to above step of polysorbate 80 solution. (Stirring speed 500-800 RPM) which was considered as step **2.2**. Transfer slurry of step **2.2** to **1.1** of MCC & sodium CMC dispersion with continuous homogenization for 30 minutes (stirring speed 500-1000 RPM, stirring time: 30 minutes) which was considered as step **3.1**. Further, final volume was adjusted with purified water. Throughout the formulation the temperature was maintained at room temperature.

Evaluation of colloidal dispersion

The prepared colloidal dispersions were assessed for various parameters including pH, viscosity, pump delivery, spray content uniformity, spray pattern, plume geometry, droplet size distribution, and priming and repriming efficiency. Additionally, stability studies were conducted to evaluate the formulations performance over time.

pH

The pH of the nasal formulation is crucial for several reasons: it helps prevent irritation of the nasal mucosa, inhibits the growth of pathogenic microorganisms, and supports normal physiological ciliary function (16).

Clarity

The sterility test was conducted to detect microorganisms in the colloidal dispersions. For this purpose, soyabean casein digest medium was utilized to identify both bacteria and fungi. One portion of the medium was incubated at 37°C for 24 hours to detect bacterial contamination while another portion was incubated at 23°C for seven days to identify fungal contamination (17).

Content uniformity

Content uniformity studies were conducted to assess the drug content across different formulations. To perform this, 1 mL of the colloidal dispersion (containing 12 mg of drug) was pipetted into volumetric flask and diluted to 100 mL with distilled water. Then, 1 mL of this diluted solution was transferred into a 50 mL volumetric flask and further diluted to 50 mL using the mobile phase. The drug content of FF and OH was determined using an high-performance liquid chromatography (HPLC) method. The chromatographic conditions were as follows: a Bakerbond Q2100 C18 column (250 × 4.6 mm, 5 µm), a flow rate of 1 mL/min, an injection volume of 20 µL, at wavelength of 240 nm and a run time of 25 minutes. Detection was performed using a UV detector. The drug concentration in the formulation was calculated by comparing the content to a calibration curve prepared with standard FF and OH under

Table 1: Composition of colloidal dispersion

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Oxymetazoline hydrochloride	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Fluticasone furoate	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28
BKC	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30
Polysorbate 80	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Disodium edetate	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
MCC & CMC Sodium	15	10	15	15	15	15	15	15
Dextrose anhydrous	50	37	37	37				
Sodium chloride				4	4	8	8	8
ADHP (Anhydrous disodium hydrogen phosphate)				0.08	1.15	1.15	1.20	0.60
SDP (Sodium dihydrogen phosphate)				0.08	1.15	1.15	1.20	0.60
Citric acid				0.50	0.50	0.60	0.60	0.60
Purified water	q.s. to1gm	q.s. to1gm	q.s. to1gm	q.s. to1gm	q.s. to1gm	q.s. to1gm	q.s. to1gm	q.s. to1gm
All quantities in mg/gm								

the same conditions (18).

Viscosity

The rheological properties and viscosity of the formulations were evaluated using a Brookfield viscometer (Model DV-RV-I, Brookfield Engineering Laboratories, Massachusetts, USA) with spindle SC4-21. A sample volume of 10 mL was used, and the torque was maintained within the range of 10–100 % of 0.067 mN. Due to the low viscosity of the nasal sprays, the rotational speed was adjusted to achieve 50% torque. Viscosity measurements were taken at a rotational speed of 250 rpm and at a temperature of 25°C. Flow behavior was assessed at 25°C with a shear rate ranging from 17 to 85 s^{-1}. Viscosity influences the residence time of the formulation, which in turn affects the rate of drug absorption through the nasal mucosa (19).

Spray content uniformity

Spray content uniformity, a critical parameter for nasal sprays, was evaluated to determine the amount of active ingredient dispensed from the nozzle. The assessment involved testing multiple sprays from a single container and from different containers to ensure consistency. The acceptance criteria should be within 80-120 % of the label claim for not more than one out of ten containers. None of the individual measurements should fall outside the range of 75-125% of the label claim. The mean active ingredient content should be within 85-115% of the label claim. (20)

Pump delivery

The performance of the nasal spray was evaluated by assessing both pump delivery and spray content uniformity which were crucial for product efficacy. To determine pump-to-pump reproducibility and the metering capability of the pump, the formulation was filled into the container, which was then actuated ten times into a pre-weighed bottle. After ten actuations, the weight of the bottle was measured again. The difference in weight was calculated to assess the amount of formulation delivered per actuation. Spray content uniformity was assessed using the SprayVIEW system (Proveris, Model NOSP, USA) to ensure consistency and uniformity in the spray output. Both tests ensure that the nasal spray dispenses the correct amount of active ingredient reliably and uniformly, impacting overall product performance (20).

Spray pattern

Characterizing the spray was crucial for assessing the performance of the pump and nozzle within the container closure system. The spray pattern evaluation involves specific parameters such as the distance between the nozzle and the collection surface, as well as the orientation of the nozzle. The spray pattern was assessed by actuating the container at distances of 3 cm and 6 cm from the actuator orifice. The spray pattern of the nasal formulation was analyzed using the SprayVIEW system (Proveris, Model NOSP, USA). Key parameters measured included Height is 30 mm, Evacuation Time: 15,000 milliseconds, Inclination: 65.4°. These measurements were helpful to determine the uniformity and effectiveness of the spray delivery (21).

Plume geometry

Plume geometry measures the plume angle at the origin of the plume and was determined for plume lengths of 3 cm and 6 cm from the origin, at two side views (90^0 to each other relative to the axis of the plane). Plumes of nasal sprays were influenced by the presence of excipients and their levels in the formulation. A nasal spray formulation that shows a uniform plume does not drip down the nose and considered as a desirable formulation (22).

Droplet size distribution

The deposition of a nasal formulation within the nasal cavity is significantly influenced by the droplet size distribution. Both the delivery device and the formulation play crucial roles in determining this distribution. To ensure effective delivery, controlling the droplet size distribution of the emitted plume is essential. The droplet size distribution was assessed using laser diffraction, focusing on key parameters such as D10, D50, and D90. Measurements were taken at distances of 3 cm and 6 cm from the actuator orifice. This analysis was performed using the SPRAYTECH system (Malvern Instruments, Model STP5313, UK) (23).

Priming and Repriming

Priming is conducted to establish the initial amount of drug released from the product, while repriming assesses the product's ability to deliver the same amount of drug content after a period of storage. For this study, the storage durations were set at 5, 10, and 30 days. During priming, the number of actuations required to achieve drug content within the specified limits (80-120% of the label claim) was determined. Similarly, during repriming, the number of actuations needed to ensure that subsequent doses remain within the specified limits was also evaluated (24). This process helps to verify the consistency and reliability of drug delivery throughout the product's shelf life.

In vitro drug diffusion study

The in vitro drug diffusion profile of the formulations was assessed using a Franz diffusion cell setup (Variomag Telesystem, Thermo Fisher Scientific Inc., Waltham, MA, USA). In this procedure, three puffs of the formulation were sprayed onto a nylon membrane (1.77 cm^2, MW cut-off 250 kDa, pore size 0.45 µm). This membrane was then placed in contact with 23 mL of dissolution medium in the lower chamber of the Franz diffusion cell. The donor compartment containing the membrane was secured on top of the receptor compartment and clamped tightly. The dissolution medium, continuously stirred with a magnetic bar (5 x 2 mm) at 400 rpm, was adapted from the US Pharmacopeia, consisting of 0.5% sodium dodecyl sulfate in water (U.S. Pharmacopeial Convention, 2016). The Franz cells were maintained in a preheated water bath (PolyScience, Niles, IL, USA) at 37°C (25).

Sampling was conducted by withdrawing 1 mL from the receptor compartment at intervals of 0. 2.5, 5, 10, 15, 20 and 25 hours. After each sample withdrawal, an equal volume of fresh medium at 37°C was added to the receptor compartment. The samples were then analyzed using HPLC Bakerbond Q2100 C18 column (250 × 4.6 mm, 5 µm), a flow rate of 1 mL/min, an injection volume of 20 µL, at wavelength of 240 nm and a run time of 25 minutes to determine the drug release profile (26).

Table 2: Results for preliminary trials of formulation

Sr. no.	Test Parameter	F1	F2	F3	F4	F5	F6	F7	F8
1	Clarity	Clear solution	Clear solution	Clear solution	Clear solution	Clear solution	Clear solution	Clear solution	Clear solution
2	pH	6.08± 0.21	6.00± 0.20	4.17± 0.22	5.65± 0.21	5.4± 0.21	5.15± 0.20	5.19± 0.25	5.20± 0.23
3	Drug content (%)	100.62±2.3	98.63 ±2.8	98.80 ±3.9	95.19 ±3.4	97.90 ±3.1	98.44 ±2.2	99.14 ±2.8	99.59 ±3.1
4	Viscosity (cP)	42.5 ±2.6	18 ±1.9	17.5 ±1.7	11.15 ±1.1	18 ±2.0	18.5 ±1.95	22.5 ±2.2	21 ±2.1
5	Osmolality (mOsmol/kg)	370±10	345±8	352±9	320±7	323±6	319±6	320±7	325±8

Stability study

The stability studies were conducted under accelerated conditions at 40±2°C and 75±5% relative humidity (RH). The evaluation was performed at the 0, 1, 2, and 3 months (27).

Statistical analysis

The findings were reported as the standard deviation using Graph Pad Prism 7®. A two-way ANOVA was employed to assess significance of variances. Throughout all the experiments statistical significance was defined as $p < 0.05$.

RESULTS AND DISCUSSION

Preliminary trials and composition of nasal formulation

The initial formulation trials were conducted to determine the optimal concentrations of surfactants and co-solvents. Key preliminary parameters evaluated included clarity, pH, drug content, viscosity, and osmolality as detailed in Table 2. Additional evaluation parameters, including spray content uniformity, pump delivery, spray pattern, plume geometry, droplet size distribution and both priming and repriming were also assessed to ensure the formulation met the required specifications.

pH

The pH of a nasal formulation was crucial to ensure it does not irritate the nasal mucosa, inhibit microbial growth, and maintain normal ciliary function. Nasal secretions contain lysozyme, an enzyme that helps destroy certain pathogens at an acidic pH. If the pH becomes alkaline, lysozyme activity decreases, making the nasal tissue more vulnerable to infections. Therefore, it is important to adjust the pH of the formulation to fall within the range of 4.5 to 6.5. In the formulations prepared, the pH was specifically adjusted to between 4 and 6, as detailed in the table no 2 (25).

Clarity

The appearance of the contents within the container and closure system was assessed for all twelve formulations. No changes were observed in color, size, shape, texture, or clarity of the formulations indicating the drug product's integrity across all batches. These observations are detailed in Table 2 (28).

Drug content and Viscosity

The drug content across all batches of the formulations was consistently uniform, ranging from 95.19 ± 0.1% to 100.62 ± 0.2% as shown in Table 2. The low viscosity of the formulations ensures effective spreadability of the solution within the nasal cavity. All formulations fell within the acceptable viscosity range of 20-30 cps, as detailed in Table 2 (29).

Spray content uniformity

The formulations were evaluated for emitted dose content uniformity to ensure consistent drug delivery and the data for the spray content uniformity is specified in the table 3. This assessment involved examining the performance of the formulation, valve, and actuator. The data revealed that the drug content sprayed from both the same container and across different containers fell within the acceptable range of 85-115%, demonstrating uniform medication delivery per spray (30).

Pump delivery

To evaluate the pump's reproducibility and dosing consistency, a test was performed using the nasal spray product. The spray was filled into a container with a single nozzle, and the pump was actuated 10 times into a pre-weighed bottle. After these actuations, the bottle was reweighed to determine the weight difference, ensuring consistent dose delivery. In this test, the initial weight of the filled nasal spray container was 15 grams. After 10 actuations, the weight of the spray container was recorded as 13.5 grams. Given that each actuation dispensed a volume of 100 µl, the weight loss of 1.5 grams corresponds to the total volume dispensed, confirming the pump's reproducibility and the accurate delivery of the specified dose (31).

Spray pattern

The performance of the pump can be evaluated through a spray pattern test, which assesses how effectively the pump dispenses the formulation. This test considers various factors, including the nozzle size and shape, pump design, and formulation properties. For the nasal spray formulation, the following parameters were recorded: Ovality was found to be 1.131, perimeter was 193.31 mm, area 2662.2 mm² at the height of 60 mm. These parameters describe the spray pattern's geometry and distribution. An image actuation graph and an intensity graph, provided in the figure 1, demonstrated that the pump dispensed the medication correctly. The consistent spray pattern and intensity indicate that the pump functioned as intended, ensuring effective delivery of the formulation (32, 33).

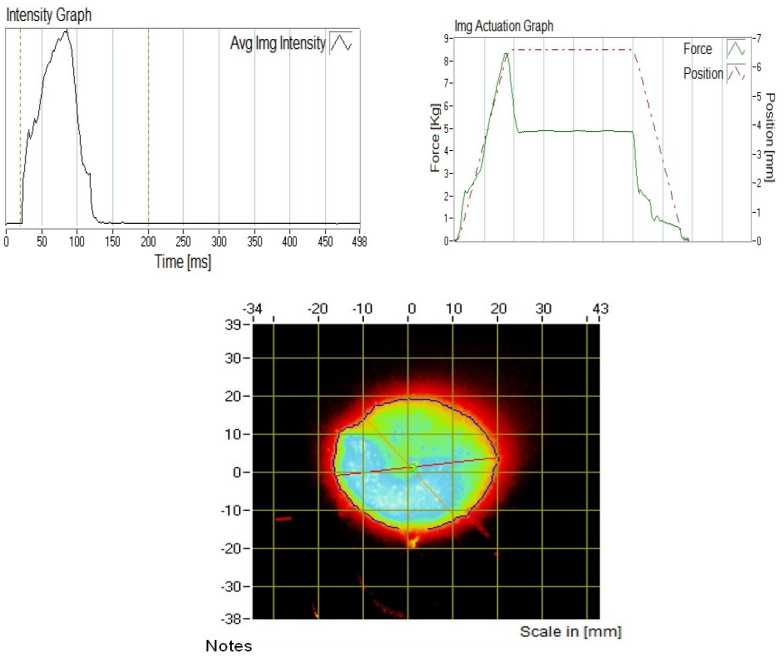

Figure 1: Spray pattern, Image actuation and intensity graph of formulation

Table 3: Spray content among different and same containers

Sr. No.	Batch no.	F1*	F2*	F3*
1	F7	102%	97%	99%
1	F7	100%	95%	99%
* Indicates different containers labelled as F1, F2 and F3 used for spray content test.				
# Indicates different sprays S1, S2 and S3 from container F7.				

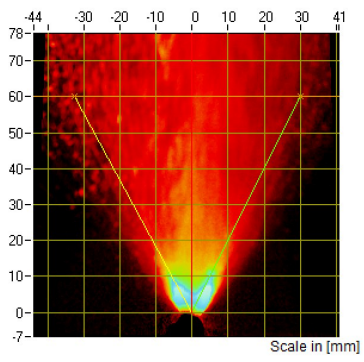

Figure 2 : Plume geometry analysis of formulation

Plume geometry

The Figure 2 illustrated the plume geometry analysis conducted at a 6 cm tip offset. The data, highlighted the key parameters of the spray plume: Mean spray

Droplet Size Distribution

Droplet size distribution was analyzed using the laser diffraction method with an automatic nasal actuator (Malvern Instruments, UK), integrated with Spraytech. Containers labelled F1 to F5 from the batch were tested with each container actuated at distances of 3 cm and 6 cm from the orifice of the actuator. Single scans were performed during the stable phase of spraying. The results, specifically the median droplet size (D50) for actuation at a 6 cm distance were summarized in Table 5 (35).

angle: 59.0°, Plume width: 67.83 mm. Plume length: 60 mm. These measurements confirmed that the plume was fully developed, reflecting an effective and consistent spray pattern. The results from the plume geometry study underscore the reliability and quality of the FF and OH nasal spray device during actuation (34).

Droplet Size Distribution

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Priming and repriming study

- **Priming study**

The priming study was conducted to determine the number of actuations required before the nasal spray formulation was ready for use by the end-user. The results indicated that the drug content released during the first actuation ranged from 70.49% to 80.54% of the label claim. After six actuations, the formulation achieved a drug content of 100.6% (36) as detailed in Table 6.

- **Repriming study**

The repriming study assessed the nasal spray formulation's performance after storage periods of 5, 10, and 30 days. The results revealed that the repriming values ranged from a minimum of 83.9% to a maximum of 100.1% of the label claim. These findings indicate that a single actuation was sufficient to ensure proper delivery of the drug after storage (37). The detailed results of the repriming study were presented in Table 7.

In vitro drug diffusion study

The in vitro drug diffusion study for the nasal spray formulations demonstrated a slow-release profile, with release times ranging from 20 to 30 minutes. The Figure 5 illustrated the release characteristics for formulation F7 and the marketed product, Fluticone-OX. Drug release from the recipient medium decreased over time, with the rate influenced by both the spray characteristics and the binder ratio used. Sodium chloride was included in the formulation for its role as a washing agent and to ensure isotonicity, while the buffered solution served as a bioavailability enhancer, improving drug absorption in the nasal mucosa. The nasal spray formulation containing FF and OH showed promising delivery to the nasal cavity. Formulation F7 proved to be satisfactory in all evaluated aspects, with its drug release profile aligning closely with the reference product, Fluticone-OX, achieving release within 25 minutes (38).

Stability studies

The stability of the optimized nasal spray formulation was assessed under accelerated conditions at 40 ± 2ºC and 75 ± 5% relative humidity over periods of 0, 1, 2, and 3 months. The findings from these stability studies were summarized in Table 8. The results demonstrated that the formulation maintained satisfactory performance in terms of appearance, pH, viscosity, and drug assay throughout the study period, confirming the formulation's stability under the tested conditions (39).

CONCLUSION

The study highlighted the importance of various evaluation tests in the formulation development of the nasal spray containing fluticasone furoate and oxymetazoline hydrochloride. The pre-formulation phase included drug-excipient compatibility assessments, ensuring stability and effectiveness. Comprehensive evaluation of the formulation was conducted, addressing key parameters such as drug content, pH and viscosity to ensure suitability for nasal mucosa. Further, spray content uniformity, pump delivery efficiency and spray pattern demonstrated an effective spray distribution. Further, plume geometry analysis revealed the spray angle of 59.0^0, plume width of 67.83 mm and the plume length of 60 mm. The droplet size distribution was ranged from 25-30 µm across different containers which affects drug deposition. The repriming study showed satisfactory performance, with repriming values between 83.9% and 100.1%, indicating that a single actuation was adequate for repriming. Stability testing over a 3-month period under accelerated conditions confirmed that both the formulation and its container remained stable and met the required specifications.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Data will be made available on prior request.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Table 4: Results for droplet size (D50) distribution

Container no.	D_{50} value (µm) Droplet size distribution
F1	27.8
F2	27.3
F3	28.0
F4	28.4
F5	27.9

Table 5: Results for priming study

Container no.	Priming	Priming result actuation 1	Priming result actuation 6
1	Yes	70.49%	98.90%
2	Yes	80.54%	101.6%

REFERENCES

1. Antila MA, Castro FM, Sano F, Machado A, Fernandes F, Rosário Filho NA, Stelmach R. Mometasone furoate in the treatment of mild, moderate, or severe persistent allergic rhinitis: a non-inferiority study (PUMA). Brazilian Journal of Otorhinolaryngology. 2016 Sep 1;82(5):580-8.

2. Baroody FM, Brown D, Gavanescu L, DeTineo M, Naclerio RM. Oxymetazoline adds to the effectiveness of fluticasone furoate in the treatment of perennial allergic rhinitis. Journal of Allergy and Clinical Immunology. 2011 Apr 1;127(4):927-34.

3. Ramey JT, Bailen E, Lockey RF. Rhinitis medicamentosa. Journal of Investigational Allergology and Clinical Immunology. 2006 Jan 1;16(3):148.

4.Allen A, Bareille PJ, Rousell VM. Fluticasone furoate, a novel inhaled corticosteroid, demonstrates prolonged lung absorption kinetics in man compared with inhaled fluticasone propionate. Clinical pharmacokinetics. 2013 Jan;52 (1):37-42.

5.Salter M, Biggadike K, Matthews JL, West MR, Haase MV, Farrow SN, Uings IJ, Gray DW. Pharmacological properties of the enhanced-affinity glucocorticoid fluticasone furoate in vitro and in an in vivo model of respiratory inflammatory disease. American Journal of Physiology-Lung Cellular and Molecular Physiology. 2007 Sep;293(3):L660-7.

6. Baroody FM, Brown D, Gavanescu L, DeTineo M, Naclerio RM. Oxymetazoline adds to the effectiveness of fluticasone furoate in the treatment of perennial allergic rhinitis. Journal of Allergy and Clinical Immunology. 2011 Apr 1;127(4):927-34.

7. Bhattachan S, Neupane Y, Pradhan B, Thapa N. Comparison of outcomes between mometasone furoate intranasal spray and oral montelukast in patients with allergic rhinitis. Journal of Nepal Health Research Council. 2020 Sep 8;18(02):268-70.

8. Bhuva F, Patel LD, Patel K. Factorial design methodology for development of pediatric nasal spray: study on xylometazoline nasal solution used for treatment of nasal congestion. Indian J Pharm Edu Res. 2018 Apr 1;52(2):218-29.

9. Mali AJ, Pawar AP, Purohit RN. Development of budesonide loaded biopolymer based dry powder inhaler: optimization, in vitro deposition, and cytotoxicity study. Journal of Pharmaceutics. 2014;2014(1):795371.

10. Mali AJ, Pawar AP, Bothiraja C. Improved lung delivery of budesonide from biopolymer based dry powder inhaler through natural inhalation of rat. Materials technology. 2014 Nov 1;29(6):350-7.

11. Dai J, Ruan BH, Zhu Y, Liang X, Su F, Su W. Preparation of nanosized Fluticasone Propionate nasal spray with improved stability and uniformity. Chemical Industry and Chemical Engineering Quarterly. 2015;21(3):457-64.

Table 6: Results for Repriming study

Container no.	Duration	Repriming	No. of actuation	Assay results
1	5 d	Yes	1	86%
2	5 d	Yes	1	84.5%
1	10 d	Yes	1	90.08%
2	10 d	Yes	1	83.9%
1	30 d	Yes	1	100.1%
2	30 d	Yes	1	99.6%

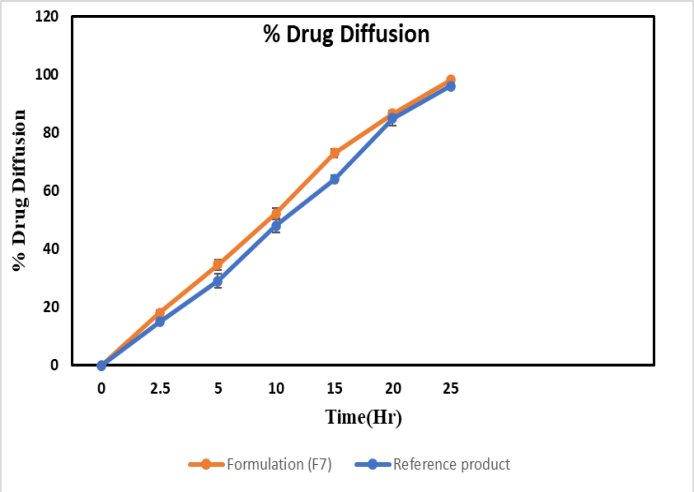

Figure 3: In vitro drug diffusion

Table 7: Results of Accelerated stability study at 40 ± 2ºC/75±5%RH

Accelerated stability studies						
Parameters		**Limits**	**Initial results of analysis**	**Results of analysis**		
				$40^0C \pm 2^0C/75\% \pm 5\%$ RH		
				1M	**2M**	**3M**
Description		***	Complies	Complies	Complies	Complies
pH		4-6	5.12	5.12	5.10	5.19
Assay (%)	**Fluticasone furoate IH**	90.0 % to 110.0 % of the label claim	99.6	101.8	101.4	101.1
	Oxymetazoline hydrochloride IP	90.0 % to 110.0 % of the label claim	99.2	101.2	100.4	100.0
	Benzalkonium chloride IP	80.0 % to 120.0 % of the label claim	99.3	98.0	98.0	99.6
Related substances	**Highest unknown impurity**	NMT 1.0%	0.165	0.247	0.192	0.165
	Total impurity	NMT 1.0%	0.46	0.585	0.588	0.658

12. Day J, Carrillo T. Comparison of the efficacy of budesonide and fluticasone propionate aqueous nasal spray for once daily treatment of perennial allergic rhinitis. Journal of allergy and clinical immunology. 1998 Dec 1;102(6):902-8.
13. Dibildox J. Safety and efficacy of mometasone furoate aqueous nasal spray in children with allergic rhinitis: results of recent clinical trials. Journal of allergy and clinical immunology. 2001 Jul 1;108(1):S54-8.
14. Gaddipatti RC, Rao SP, Rajiv K, Jain M. Isotonic nasal spray versus fluticasone nasal spray in treatment of allergic rhinitis. International Journal of Otolaryngology. 2017 Jul;3(3):581-4.
15. Ilyina NI, Edin AS, Astafieva NG, Lopatin AS, Sidorenko IV, Ukhanova OP, Khanova FM. Efficacy of a novel intranasal formulation of azelastine hydrochloride and fluticasone propionate, delivered in a single spray, for the treatment of seasonal allergic rhinitis: results from Russia. International Archives of Allergy and Immunology. 2019 Mar 18;178(3):255-63.
16. Jullaphant T, Nakpeng T, Srichana T. Montelukast nasal spray: formulation development and in vitro evaluation. Pharmaceutical Development and Technology. 2019 Apr 21;24(4):494-503.
17. Lungare, S., J. Bowen and R. Badhan (2016). "Development and Evaluation of a Novel Intranasal Spray for the Delivery of Amantadine." J Pharm Sci **105** (3): 1209-1220.
18. Mak KK, Ku MS, Lu KH, Sun HL, Lue KH. Comparison of mometasone furoate monohydrate (Nasonex) and fluticasone propionate (Flixonase) nasal sprays in the treatment of dust mite-sensitive children with perennial allergic rhinitis. Pediatrics & Neonatology. 2013 Aug 1;54(4):239-45.
19. Mehmood Y, Shahid H, Tariq A, Ali SO. Efficacy and safety of a new mometasone furoate nasal spray formulation in patients with acute rhinosinusitis: A randomized clinical trial. Italian Journal of Medicine. 2022 Nov 28;16(1).
20. Menaka M, Pandey VP. Formulation development and evaluation of cinnarizine nasal spray. Int. J. Pharma Res. Health Sci. 2014;2:339-46.
21. Menaka M, Pandey VP, Anton Smith A. Formulation development and evaluation of ondansetron hydrochloride nasal spray. International Journal of pharmacy and pharmaceutical sciences. 2013;5(4):150-4.
22. Mirmoezzi MS, Yazdi MS, Gholami OM. Comparative study on the efficacy of mometasone and fluticasone nasal sprays for treatment of allergic rhinitis. Int J Pharm Pharm Sci. 2017;9(3):211-4.
23. Okubo K, Okamasa A, Honma G, Komatsubara M. Safety and efficacy of fluticasone furoate nasal spray in Japanese children 2 to< 15 years of age with perennial allergic rhinitis: a multicentre, open-label trial. Allergology international. 2015;64(1):60-5.
24. Patel P, Salapatek AM, Tantry SK. Effect of olopatadine-mometasone combination nasal spray on seasonal allergic rhinitis symptoms in an environmental exposure chamber study. Annals of Allergy, Asthma & Immunology. 2019 Feb 1;122(2):160-6.
25. Mali AJ, Rokade A, Kamble R, Pawar A, Bothiraja C. Resveratrol-loaded microsponge as a novel biodegradable carrier for dry powder inhaler: A new strategy in lung delivery. Bionanoscience. 2021 Mar;11(1):32-43.
26. Patel K, Bothiraja C, Mali A, Kamble R. Investigation of sorafenib tosylate loaded liposomal dry powder inhaler for the treatment of non-small cell lung cancer. Particulate Science and Technology. 2021 Nov 17;39(8):990-9.
27. Nandedkar J, Masane M, Mali AJ. An optimisation of critical quality attributes for acyclovir dispersible tablets: a quality by design approach. International Journal of Experimental Design and Process Optimisation. 2020;6(3):253-74.
28. Shah A, Shelat P. Development of ipratropium bromide and budesonide thixotropic nasal spray using quality by design approach.
29. Shrestha S, Joshi RR, Shrestha S. Efficacy of mometasone furoate nasal spray in the treatment of acute rhinosinusitis. The Egyptian Journal of Otolaryngology. 2023 Jan 17;39(1):14.
30. Aneeza WH, Husain S, Rahman RA, Van Dort D, Abdullah A, Gendeh BS. Efficacy of mometasone furoate and fluticasone furoate on persistent allergic rhinoconjunctivitis. Allergy & Rhinology. 2013 Sep;4(3):ar-2013.
31. Yanez A, Dimitroff A, Bremner P, Rhee CS, Luscombe G, Prillaman BA, Johnson N. A patient preference study that evaluated fluticasone furoate and mometasone furoate nasal sprays for allergic rhinitis. Allergy & Rhinology. 2016 Oct;7(4):ar-2016.
32. Yang P, Li Y, Li W, Zhang H, Gao J, Sun J, Yin X, Zheng A. Preparation and evaluation of carfentanil nasal spray employing cyclodextrin inclusion technology. Drug Development and Industrial Pharmacy. 2018 Jun 3;44(6):953-60.
33. Bhuva F, Patel LD. Xylometazoline nasal spray solution: novel composition used for treatment of nasal congestion. MOJ Drug Des Develop Ther. 2018;2(5):246-56.
34. Jullaphant T, Nakpeng T, Srichana T. Montelukast nasal spray: formulation development and in vitro evaluation. Pharmaceutical Development and Technology. 2019 Apr 21;24(4):494-503.
35. Menaka M, Pandey VP. Formulation development and evaluation of cinnarizine nasal spray. Int. J. Pharma Res. Health Sci. 2014;2:339-46.
36. Bhuva F, Patel L. Pediatric nasal spray solution: factorial design development and evaluation. J. Drug Deliv. Ther. 2018 Sep 2;8:355-65.
37. Menaka M, Pandey VP, Anton Smith A. Formulation development and evaluation of ondansetron hydrochloride nasal spray. International Journal of pharmacy and pharmaceutical sciences. 2013;5(4):150-4.
38. Kulkarni V, Shaw C. Formulation and characterization of nasal sprays. An examination of nasal spray formulation parameters and excipients and their influence on key in vitro tests. Inhalation. 2012 Dec 21;1015.
49. Mali AJ, Patil S, Chellampillai B. Investigation of polyvinyl alcohol-polyethylene glycol graft copolymer as an advanced functional polymer in the development of perampanel orodispersible film. Journal of Polymer Research. 2022 Apr;29(4):130.