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RESEARCH ARTICLE

Development and Physicochemical Characterization of a Poly-Herbal Hydrosol-Based Intranasal Spray for the Management of Rhinosinusitis

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Abstract: Rhinosinusitis is characterized by the inflammation of the paranasal sinus mucosa, often resulting from microbial infections, environmental allergens, or structural obstructions. While conventional pharmacotherapy involving synthetic decongestants and corticosteroids provides symptomatic relief, prolonged administration frequently leads to adverse effects such as rhinitis medicamentosa, mucosal atrophy, and systemic absorption. A natural therapeutic alternative was developed by utilizing the synergistic properties of medicinal plant hydrosols. A poly-herbal nasal spray was formulated incorporating aromatic distillates of *Eucalyptus globulus, Matricaria chamomilla, Zingiber officinale, Ocimum sanctum,* and *Mentha piperita*. These plant sources were selected for their established antimicrobial, anti-inflammatory, mucolytic, and decongestant activities. The formulation was stabilized using sodium chloride for isotonicity, glycerin as a humectant, and sodium benzoate as a preservative, with the final pH adjusted to maintain compatibility with the nasal microenvironment. Evaluation of the physicochemical parameters revealed a pH of 6.0, optimal viscosity for mucosal retention, and a uniform spray pattern ensuring effective drug distribution. *In-vitro* diffusion and sterility testing confirmed the controlled release profile and safety of the preparation. The absence of irritation in safety models suggests that the multi-hydrosol spray is a biocompatible alternative to synthetic formulations. This natural method addresses the effects of sinusitis by simultaneously reducing inflammation, facilitating mucus clearance, and inhibiting pathogenic growth. The results from this study show the potential for utilizing herbal distillates as a primary or adjunctive treatment in upper respiratory inflammatory conditions.

Keywords: Rhinosinusitis; Herbal Hydrosols; Intranasal Delivery; Steam Distillation; Physicochemical Evaluation.

1. Introduction

The intranasal route is a non-invasive and highly efficient pathway for drug administration, particularly for conditions localized to the respiratory tract. The anatomical structure of the nasal cavity, characterized by a highly vascularized subepithelial layer and a relatively large surface area, allows for the rapid absorption of therapeutic agents and a prompt onset of clinical action [1]. Unlike oral administration, the nasal route bypasses the hepatic first-pass metabolism, thereby enhancing the bioavailability of various compounds. However, the management of chronic inflammatory conditions like sinusitis remains complicated by the limitations of current synthetic options. Sinusitis involves the inflammation of the mucous membranes lining the paranasal sinuses. It is frequently associated with the obstruction of the ostiomeatal complex, leading to the accumulation of secretions and subsequent bacterial overgrowth [2]. Patients typically present with nasal congestion, facial pain, and purulent discharge. Standard treatments involve the use of alpha-adrenergic agonists and topical steroids. Although effective in the short term, these agents can cause rebound congestion and localized irritation. The development of antibiotic resistance also necessitates the exploration of phytochemical alternatives that possess broad-spectrum antimicrobial properties without inducing microbial adaptation [3]. Hydrosols, also referred to as floral waters or herbal distillates, are the aqueous co-products of the steam distillation of aromatic plants. Unlike essential oils, which are highly concentrated and potentially irritating to sensitive tissues, hydrosols contain water-soluble volatile components and trace amounts of essential oils in a diluted, mild form [4]. This makes them exceptionally suitable for application to the delicate nasal mucosa. The selection of *Ocimum sanctum* (Tulasi), *Eucalyptus globulus*, and *Mentha piperita* provides a multi-targeted approach. *Ocimum sanctum* is recognized for its immunomodulatory and anti-allergic effects, while *Eucalyptus* and *Mentha* species provide potent decongestant and cooling sensations through the activation of cold-sensitive receptors and the thinning of viscid secretions [5].

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The integration of multiple botanical distillates aims to achieve a synergistic effect, where the combined efficacy exceeds the sum of individual components. *Zingiber officinale* (Ginger) contributes antioxidant and warming properties that enhance local circulation, whereas *Matricaria chamomilla* (Chamomile) provides a soothing effect, counteracting the potential dryness associated with nasal inflammation [6]. By balancing these diverse pharmacological profiles, a poly-herbal spray can address both the underlying infection and the symptomatic discomfort associated with sinus congestion.

2. Materials and Methods

2.1. Collection and Authentication of Plant Material

The botanical specimens, including the leaves of *Eucalyptus globulus* and *Ocimum sanctum*, the rhizomes of *Zingiber officinale*, and the flowering tops of *Matricaria chamomilla* and *Mentha piperita*, were procured from authenticated herbal suppliers. The plant materials were subjected to thorough cleaning to remove foreign organic matter and were subsequently air-dried under controlled conditions to preserve the integrity of the volatile constituents.

Table 1. Therapeutic Rationale for Selected Herbal Components

Botanical Component	Part Used	Active Phytoconstituents	Therapeutic Action in Sinusitis
Eucalyptus globulus	Leaves	1,8-Cineole (Eucalyptol)	Strong decongestant; promotes airway dilation and clearance.
Ocimum sanctum	Leaves	Eugenol, Methyl chavicol	Immunomodulatory; reduces allergic response and microbial load.
Mentha piperita	Flowering tops	Menthol, Menthone	Natural cooling agent; provides immediate symptomatic relief of congestion.
Zingiber officinale	Rhizomes	Gingerols, Shogaols	Mucolytic; thins viscid secretions and exerts anti-inflammatory effects.
Matricaria chamomilla	Flowers	Chamazulene, Bisabolol	Soothing agent; prevents mucosal drying and reduces irritation.

2.2. Extraction of Hydrosols

The extraction process was conducted using a standardized steam distillation apparatus. A specific quantity of each plant material was placed in the distillation flask with a sufficient volume of deionized water. As steam passed through the plant matrix, the volatile compounds were vaporized and subsequently condensed through a water-cooled condenser. The resulting distillate, consisting of an aqueous phase (hydrosol) and a thin oily layer, was collected. The hydrosols were separated using a separating funnel and filtered through a 0.22 μm membrane filter to ensure the removal of any particulate matter and to maintain initial sterility [7].

2.3. Formulation of the Nasal Spray

The multi-hydrosol nasal spray was developed by mixing the individual distillates in specific proportions based on their therapeutic concentrations. The base of the formulation was prepared by dissolving 0.09 g of sodium chloride in a portion of distilled water to achieve an isotonic concentration of 0.9%, which prevents osmotic shock to the nasal cilia.

Table 2. Composition of the Poly-Herbal Nasal Spray (30 mL)

Ingredient	Quantity	Functional Role
Chamomile Hydrosol	10.0 mL	Anti-inflammatory and Soothing Base
Peppermint Hydrosol	8.0 mL	Decongestant and Sensory Profile
Tulasi Hydrosol	5.0 mL	Antimicrobial Agent
Ginger Hydrosol	3.0 mL	Mucolytic and Warming Component
Eucalyptus Hydrosol	4.0 mL	Principal Airway Dilator
Sodium Chloride	0.09 g	Isotonicity Adjuster (0.9% w/v)
Glycerin	0.5 mL	Humectant and Viscosity Modifier
Sodium Benzoate	0.05 g	Preservative
Citric Acid	q.s.	pH Adjuster (Target: 6.0)
Distilled Water	Up to 30 mL	Vehicle/Diluent

Glycerin was incorporated at a concentration of 0.5 mL as a humectant to ensure the mucosa remains hydrated during treatment. Sodium benzoate was added as a preservative to prevent microbial contamination during multi-dose usage. The pH of the final solution was measured and adjusted using citric acid to fall within the physiological range of 5.5 to 6.5. The final volume was made up to 30 mL with distilled water, followed by a final filtration step.

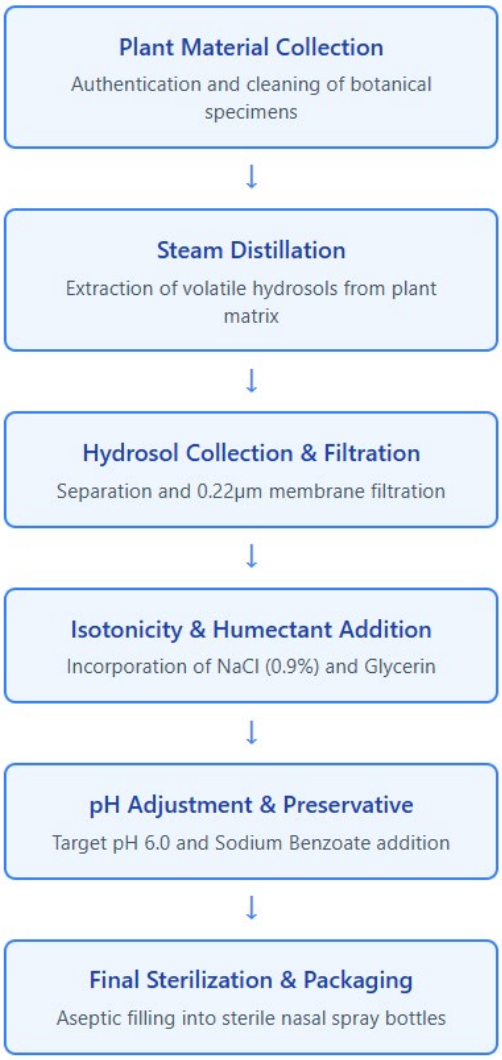

Figure 1. Experimental Methodology for the Preparation of Multi-Hydrosol Nasal Spray

2.4. Physicochemical Characterization and Quality Control

The prepared formulation underwent a series of rigorous quality control tests. The pH was determined using a digital pH meter calibrated with standard buffers. Viscosity, a critical factor for the residence time of the spray on the nasal mucosa, was measured using a Brookfield viscometer at 25 °C. The spray pattern and droplet size distribution were evaluated by actuating the spray onto a target surface at a distance of 10 cm, followed by visual and microscopic analysis to ensure uniform distribution and optimal atomization.

2.5. Sterility and Safety

Sterility testing was conducted in accordance with pharmacopoeial standards using fluid thioglycolate and soybean-casein digest media to confirm the absence of aerobic and anaerobic bacteria as well as fungi. A standardized nasal irritation study was performed using an *in-vivo* model involving healthy Wistar rats (weighing 180–220 g) to assess the biocompatibility of the poly-herbal formulation (Institutional Animal Ethical Committee Approval No. KGRL/IAEC/Ceu/25219). The animals were divided into three groups: a negative control receiving normal saline, a positive control receiving a known irritant (1% v/v sodium lauryl sulfate), and a test group receiving the multi-hydrosol nasal spray.

Table 3. Experimental Grouping for the *In-Vivo* Nasal Irritation Study

Group Designation	Test Substance	Dose/Frequency	Rationale
Group I (Negative Control)	Normal Saline (0.9% NaCl)	20 µL / twice daily	Establish baseline mucosal histology.
Group II (Positive Control)	1% Sodium Lauryl Sulfate	20 µL / twice daily	Induce observable mucosal irritation.
Group III (Test Group)	Poly-Herbal Nasal Spray	20 µL / twice daily	Evaluate biocompatibility of formulation.

Each group consisted of six animals maintained under standard laboratory conditions with free access to food and water. The formulation was administered intranasally twice daily for 24 hours. The subjects were monitored for clinical signs of toxicity, including frequent sneezing, nasal rubbing, and behavioral changes. Following the treatment period, the nasal tissues were examined for signs of mucosal edema, erythema, and ulceration to ensure the safety of the herbal ingredients within the sensitive nasal microenvironment

3. Results and Discussion

The developed multi-hydrosol nasal spray was subjected to a comprehensive evaluation to determine its suitability for the management of sinusitis. The integration of various botanical distillates necessitated a rigorous assessment of both the individual properties of the hydrosols and the performance of the final combined formulation.

3.1. Physicochemical and Organoleptic Characteristics

The organoleptic assessment of the formulation revealed an amber-brown liquid with a golden yellow base, which is characteristic of the concentrated phytoconstituents present in the hydrosols. The preparation exhibited a pleasant, herbal odor, primarily attributed to the volatile terpenoids in *Eucalyptus* and *Mentha* species. This aromatic profile is an essential factor in patient compliance, as the cooling sensation of menthol and eucalyptol provides immediate sensory relief from congestion [8]. The formulation was found to be clear and devoid of any visible particulate matter or precipitation, confirming the effectiveness of the 0.22 µm filtration process and the compatibility of the blended hydrosols.

3.1.1. pH and Buffer Capacity

The pH of the formulation was recorded at 6.0, which aligns precisely with the physiological pH of the nasal mucosa, typically ranging from 5.5 to 6.5. Maintaining this pH is critical to avoid damaging the nasal cilia, which are sensitive to extreme acidity or alkalinity [9]. A pH outside this range can lead to ciliary stasis, reducing the natural clearance mechanisms of the respiratory tract [10]. The successful adjustment to pH 6.0 indicates that the spray is likely to be non-irritating and biocompatible for long-term administration.

3.1.2. Rheological Properties and Spray Performance

The viscosity of the nasal spray was found to be low and uniform, measured at approximately 1.3 cP. While a very high viscosity can impede the atomization process, a moderate level is required to ensure the droplets remain on the mucosal surface long enough for absorption [11]. The results suggest that the inclusion of glycerin provided sufficient humectancy and a slight increase in viscosity compared to pure water, balancing sprayability with mucosal retention.

Table 4. Results for Various Evaluation Tests of Poly-Herbal Nasal Spray

Parameter	Observed Value	Standard/Acceptable Limits	Inference
Physical Appearance	Clear, amber-brown	Clear, free from particles	Passed
Odor	Pleasant, Herbal	Acceptable to consumer	Passed
pH Value	6.0 ± 0.1	4.5 – 6.5 (Physiological)	Compatible
Viscosity	1.32 ± 0.05 cP	Low/Moderate flow	Optimal for spray
Spray Pattern	Uniform/Circular	Reproducible distribution	Optimized
Foam Height	1.2 mL	Minimal foam formation	Non-interfering
Foam Collapse Time	45 Seconds	< 60 Seconds	Rapid dissipation

The spray pattern analysis showed a uniform, circular distribution upon actuation at a distance of 10 cm. This uniformity ensures that the therapeutic dose is distributed across a wide area of the nasal epithelium, maximizing the surface area available for drug

uptake [12]. The foam test resulted in a minimal foam height (1.2 mL), which collapsed within 45 seconds. The absence of persistent foaming is a positive indicator, as excessive foam can interfere with dose accuracy and lead to discomfort during inhalation.

3.2. *In-Vitro* Diffusion and Drug Release Kinetics

The *in-vitro* diffusion studies conducted using a Franz diffusion cell showed a gradual and sustained release of the active phytoconstituents over the study period. The release profile followed a controlled pattern, which is desirable for the symptomatic relief of sinusitis. A sustained release mechanism allows for a prolonged therapeutic effect, potentially reducing the frequency of administration [13]. The presence of glycerin likely played a role in modulating this release, acting as a mild barrier that controls the diffusion of the water-soluble volatile compounds across the membrane.

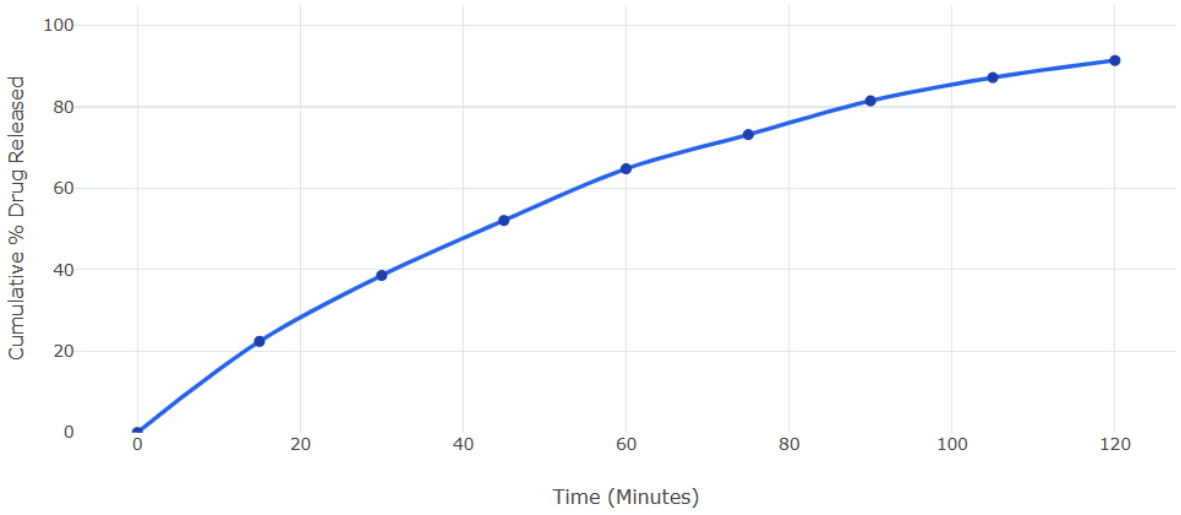

Figure 2. *In vitro* cumulative drug release profile of the prepared formulation

3.3. Sterility and Safety

The sterility testing yielded no microbial growth after a 14-day incubation period in both fluid thioglycolate and soybean-casein digest media. This confirms that the aseptic filtration and the inclusion of sodium benzoate were effective in maintaining the microbiological quality of the formulation [14]. Given that the nasal cavity is a sensitive entry point for pathogens, ensuring the sterility of a multi-dose spray is paramount.

Table 5. Results of Sterility and Microbiological Stability Testing

Medium Used	Incubation Conditions	Observation (14 Days)	Result
Fluid Thioglycolate	30–35°C (Aerobic/Anaerobic)	No Turbidity	Sterile
Soybean-Casein Digest	20–25°C (Fungi/Yeast)	No Growth	Sterile
Nutrient Agar Slant	37°C (General Bacteria)	No Colony Growth	Sterile

The *in-vivo* nasal irritation study in Wistar rats provided critical evidence of the safety of the poly-herbal formulation. No clinical signs of irritation, such as redness, swelling, or excessive sneezing, were observed in the test group. The behavioral patterns of the animals remained normal, and macroscopic examination of the nasal mucosa post-treatment showed no evidence of ulceration or structural damage. In contrast to synthetic decongestants, which can cause mucosal drying and irritation, the herbal hydrosols showed high biocompatibility, likely due to their mild, aqueous nature [15].

3.4. Stability Assessment

Stability studies conducted under specified environmental conditions revealed that the formulation remained physically and chemically stable. There were no significant changes in the pH, color, or clarity of the spray over the observation period. The antimicrobial efficacy remained intact, and no precipitation of the herbal components was noted. These findings suggest that the formulation has a robust shelf-life, provided it is stored at the recommended temperatures (2–8°C), which helps in preserving the delicate volatile components of the hydrosols [16].

4. Conclusion

The present study focused on the development of a poly-herbal nasal spray utilizing a synergistic combination of medicinal hydrosols. The results show that the formulation successfully met all the essential requirements for an effective intranasal delivery system. By integrating the antimicrobial properties of *Tulasi* and *Eucalyptus* with the anti-inflammatory effects of *Chamomile* and *Ginger*, the spray offers a comprehensive approach to managing the symptoms of rhinosinusitis. The physicochemical evaluations confirmed that the spray possesses an optimal pH, uniform spray characteristics, and a controlled release profile. The absence of irritation in animal models and the confirmed sterility highlight its safety for clinical use. This natural alternative addresses the limitations of synthetic nasal sprays, such as rebound congestion and mucosal irritation, providing a biocompatible and potentially more sustainable therapeutic option. The findings support the clinical potential of hydrosol-based preparations as a primary or adjunctive therapy in upper respiratory inflammatory disorders, though further clinical trials are warranted to establish long-term efficacy in human populations.

Compliance with ethical standards

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Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. No funding or support was received from any third-party commercial entities, and there are no conflicts of interest regarding any products or institutional outcomes mentioned in this manuscript.

Statement of ethical approval

The *in-vivo* nasal irritation study involving Wistar rats was conducted in strict accordance with the internationally accepted principles for laboratory animal use and care. The experimental protocol was reviewed and approved by the Institutional Animal Ethics Committee (Approval No. KGRL/IAEC/Ceu/25219). All efforts were made to minimize animal suffering and to reduce the number of animals used in the safety assessment.

Statement of informed consent

The present research work does not contain any studies performed on human subjects or involve any individual participants, surveys, or interviews by any of the authors. Therefore, a statement of informed consent is not applicable to this study.

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