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QUALIFICATION WORK

on the topic: **«DEVELOPMENT OF THE COMPOSITION OF A THROAT SPRAY WITH SOOTHING AND ANTISEPTIC ACTION BASED ON LICORICE EXTRACT AND EUCALYPTUS ESSENTIAL OIL»**

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ANNOTATION

This thesis presents the development of a throat spray with soothing and antiseptic action based on licorice extract and eucalyptus essential oil. The study included formulation design, selection of excipients, and evaluation of key parameters such as pH, viscosity, sprayability, and stability. The final composition demonstrated favorable technological characteristics and user acceptability. The research confirms the feasibility of creating effective mucosal sprays using herbal substances and simple experimental methods.

The work consists of the following parts: introduction, literature review, choice of research methods, experimental part, general conclusions, list of used literature sources, total volume of 56 pages, contains 25 tables, 31 references.

Key words: throat spray, licorice extract, eucalyptus essential oil, pharmaceutical technology, mucosal dosage form.

АНОТАЦІЯ

Робота присвячена розробці спрею для горла з пом'якшувальною та антисептичною дією на основі екстракту солодки та ефірної олії евкаліпта. Дослідження охоплювало підбір допоміжних речовин, проєктування складу та оцінку фізико-хімічних і функціональних властивостей із використанням стандартних методів фармацевтичної технології. Оптимальна лікарська форма для слизової оболонки продемонструвала належну стабільність, зручність у застосуванні та гарну переносимість, що підтверджує її потенціал як ефективного засобу на основі рослинної сировини.

Робота складається з таких частин: вступ, огляд літератури, вибір методів дослідження, експериментальна частина, загальні висновки, список використаних літературних джерел, загальний обсяг 56 сторінок, містить 25 таблиць, 31 посилання.

Ключові слова: спрей для горла, екстракт солодки, ефірна олія евкаліпта, фармацевтична технологія, лікарська форма для слизової оболонки.

CONTENT

LIST OF ABBREVIATIONS

API – active pharmaceutical ingredient

EMA – European Medicines Agency

EU – European Union

FDA – Food and Drug Administration

GMP – good manufacturing practice

HPLC – high-performance liquid chromatography

ICH – International Council for Harmonisation

NF-κB – nuclear factor kappa-light-chain-enhancer of activated B cells

Ph.Eur. – European Pharmacopoeia

SPhU – State Pharmacopoeia of Ukraine

SNEDDS – self-nanoemulsifying drug delivery system

TNF-α – tumor necrosis factor alpha

WHO – World Health Organization

INTRODUCTION

The relevance of the topic

The development of locally acting dosage forms, particularly for oropharyngeal conditions, remains a relevant direction in pharmaceutical technology due to the high prevalence of sore throat, pharyngitis, and upper respiratory tract infections. Throat sprays offer targeted delivery to the mucosa, rapid onset of action, and reduced systemic exposure. Among plant-derived agents, licorice extract has demonstrated mucosal protective and anti-inflammatory effects, while eucalyptus essential oil is known for its antiseptic and decongestant properties. Combining these agents into a throat spray aligns with modern trends in phytotherapy, patient-friendly delivery systems, and non-antibiotic symptom management.

The purpose of the study

To develop and experimentally justify the composition of a throat spray with soothing and antiseptic action based on licorice extract and eucalyptus essential oil.

Research tasks are

1. To analyze the pharmaceutical and technological properties of the selected active and auxiliary substances;

2. To formulate and optimize experimental spray compositions;

3. To evaluate the physical characteristics, sprayability, and stability of the developed formulations;

4. To assess sensory acceptability and justify the selection of the final composition.

The object of research

The object of the study was the process of developing a non-sterile mucosal pharmaceutical form for local application to the throat.

The subject of the study

The subject of the study was the composition and performance of throat spray formulations containing licorice extract and eucalyptus essential oil.

Research methods

The study employed technological research methods typical for liquid and emulsion-type dosage forms. These included pH determination using a digital meter, viscosity evaluation via capillary flow, sprayability testing with manual pump bottles, and storage stability assessment at different temperatures. Organoleptic and usability testing were carried out with human volunteers to evaluate taste, mouthfeel, and comfort of application.

Practical significance of the obtained results

The proposed formulation may serve as a basis for further development of soothing and antiseptic oropharyngeal sprays, especially in the context of increased demand for non-antibiotic and plant-based remedies.

Elements of scientific research

The study provides a technologically justified approach to formulating a throat spray with herbal actives, using accessible excipients and reproducible methods.

Structure and scope of qualification work

Qualification work consists of the following parts: introduction, literature review, choice of research methods, experimental part, general conclusions, list of used literature sources, total volume of 56 pages, contains 25 tables, 31 references.

CHAPTER 1
CURRENT STATE OF THE TECHNOLOGY OF THROAT SPRAYS

1.1. Throat sprays in modern pharmaceutical technology

Throat sprays represent a specific group of oromucosal drug delivery systems designed primarily for localized action in the oropharyngeal region. Based on their therapeutic action, throat sprays can be broadly classified into several categories. Antiseptic sprays are formulated to reduce microbial load, targeting bacteria, viruses, and fungi that colonize the mucosal surfaces. Anesthetic sprays focus on providing temporary relief from pain by numbing the irritated tissues. Anti-inflammatory sprays aim to reduce swelling, redness, and discomfort associated with conditions such as pharyngitis and tonsillitis. Additionally, moisturizing sprays are intended to hydrate dry mucosal membranes, which is particularly important in patients suffering from chronic dry throat or xerostomia. Finally, many commercial formulations adopt a combined approach, integrating antiseptic, anti-inflammatory, and anesthetic agents to address multiple symptoms simultaneously.

In clinical practice, throat sprays are commonly indicated for conditions involving infection, inflammation, or mechanical irritation of the upper respiratory tract. These include acute and chronic pharyngitis, tonsillitis, laryngitis, and aphthous ulcers. Some sprays are also recommended as supportive treatment after surgical procedures like tonsillectomy or dental surgeries involving the soft palate. Importantly, sprays provide direct, localized drug delivery to the inflamed area, allowing for a higher concentration of the active ingredient at the site of action with reduced systemic exposure. This local administration route helps to minimize systemic side effects, making throat sprays an attractive therapeutic option in both adult and pediatric populations.

One notable trend in recent pharmaceutical research is the increasing interest in plant-based throat sprays. Herbal ingredients like licorice extract, propolis, chamomile, and sage have been integrated into formulations to provide natural

antiseptic, anti-inflammatory, and soothing effects. The move towards natural-origin actives is driven by patient demand for safer, milder alternatives to synthetic antiseptics and corticosteroids. As natural components often have multi-targeted mechanisms of action, they are particularly suitable for treating complex oropharyngeal conditions where both microbial control and tissue repair are needed.

Another important classification feature of throat sprays is their intended use in acute versus chronic therapy. Acute-use sprays are typically formulated for short-term symptom relief during infections, while chronic-use sprays are optimized for long-term management of dry mouth, allergic irritation, or chronic inflammatory diseases. Formulation strategies vary accordingly: acute sprays prioritize immediate action and potent antiseptics, while chronic-use sprays focus on mucosal protection and maintaining hydration over extended periods.

Oromucosal sprays are subject to stringent regulatory standards to ensure their safety, efficacy, and quality. Regulatory agencies such as the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) provide comprehensive guidelines for the development and approval of these products. These guidelines encompass various aspects, including the selection of active pharmaceutical ingredients (APIs), excipients, manufacturing processes, and quality control measures. For instance, the EMA's "Guideline on quality of oral modified release products" outlines the necessary quality attributes and testing requirements for oromucosal formulations. Similarly, the FDA's "Guidance for Industry: Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products" provides detailed recommendations for the development of nasal and oromucosal sprays [1].

One critical quality attribute for oromucosal sprays is the uniformity of dosage units. This ensures that each actuation delivers a consistent amount of the API, which is vital for maintaining therapeutic efficacy and patient safety. The European Pharmacopoeia specifies tests for uniformity of delivered dose, which involve collecting multiple doses from the spray and analyzing the API content.

Additionally, the spray's droplet size distribution is crucial, as it affects the deposition and absorption of the drug on the mucosal surface. Techniques such as laser diffraction and cascade impaction are employed to characterize droplet size and distribution.

Microbiological quality is another essential consideration, especially for formulations containing water or other aqueous components that can support microbial growth. Preservatives are often included to inhibit microbial contamination, and their efficacy must be demonstrated through antimicrobial effectiveness testing. The choice of preservative and its concentration must balance antimicrobial activity with patient safety, as some preservatives can cause irritation or allergic reactions [2].

Stability testing is conducted to determine the shelf life and storage conditions of oromucosal sprays. These tests assess the physical, chemical, and microbiological stability of the product over time under various environmental conditions. Parameters such as pH, viscosity, API content, and preservative efficacy are monitored. Stability studies must comply with the International Council for Harmonisation (ICH) guidelines, which provide standardized protocols for conducting and reporting stability data.

Throat sprays offer several advantages that make them a preferred choice for delivering medications directly to the oropharyngeal region. One of the primary benefits is the rapid onset of action due to the direct application of the drug to the affected area, bypassing the gastrointestinal tract and first-pass metabolism. This localized delivery ensures higher drug concentrations at the site of infection or inflammation, enhancing therapeutic efficacy while minimizing systemic side effects. Moreover, the ease of administration and non-invasive nature of sprays improve patient compliance, especially among populations that may have difficulty swallowing tablets or capsules. The ability to formulate sprays with pleasant flavors and soothing agents further enhances their acceptability [3].

However, despite these advantages, throat sprays also present certain limitations. One significant challenge is the short residence time of the medication

on the mucosal surface, primarily due to the constant movement and saliva flow in the oral cavity, which can lead to rapid clearance of the drug. This necessitates frequent reapplication to maintain therapeutic levels, potentially impacting patient adherence. Additionally, ensuring uniform distribution and dosage accuracy with each spray actuation can be challenging, requiring precise formulation and device engineering. There's also the consideration of potential irritation or allergic reactions to certain excipients or preservatives used in the formulation.

To address the issue of limited mucosal adhesion and prolonged drug retention, the incorporation of mucoadhesive polymers into throat spray formulations has been explored. These polymers can form a protective film over the mucosal surface, enhancing the residence time of the drug and allowing for sustained release. Such formulations not only improve therapeutic outcomes but also reduce the frequency of administration. However, the selection of appropriate mucoadhesive agents is critical, as they must be non-irritating, biocompatible, and capable of forming a stable formulation without compromising the spray's rheological properties [4].

While throat sprays present a convenient and effective means of delivering medications for oropharyngeal conditions, careful consideration must be given to their formulation to overcome inherent limitations. Advancements in formulation technologies, such as the use of mucoadhesive polymers and optimized spray devices, hold promise in enhancing the efficacy and patient acceptability of throat sprays. Ongoing research and development are essential to fully harness the potential of this dosage form in clinical practice.

1.2. Licorice extract: pharmaceutical and therapeutic applications

Licorice (*Glycyrrhiza glabra*) has been extensively studied for its diverse pharmacological properties, largely attributed to its rich composition of bioactive compounds. The primary constituents include glycyrrhizin (also known as glycyrrhizic acid), liquiritin, glabridin, and liquiritigenin. Glycyrrhizin, a triterpenoid saponin, is renowned for its anti-inflammatory, antiviral, and

hepatoprotective effects. Liquiritin and liquiritigenin, both flavonoids, exhibit significant antioxidant and anti-inflammatory activities. Glabridin, another prominent flavonoid, has been identified for its potent antioxidant and anti-inflammatory properties. These compounds collectively contribute to the therapeutic potential of licorice in various clinical applications [5].

The anti-inflammatory effects of licorice's active compounds have been demonstrated in multiple studies. For instance, glycyrrhizin has been shown to inhibit the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. Liquiritin and liquiritigenin have been observed to suppress the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), enzymes pivotal in the inflammatory process. Glabridin, in particular, has been reported to inhibit the NF-κB signaling pathway, a key regulator of inflammation. These mechanisms underscore the potential of licorice compounds in managing inflammatory conditions [6].

Beyond their anti-inflammatory properties, licorice constituents exhibit notable antimicrobial activities. Glycyrrhizin has demonstrated antiviral effects against various viruses, including hepatitis C and herpes simplex. Liquiritin and glabridin have shown antibacterial activity against pathogens such as Staphylococcus aureus and Escherichia coli. These antimicrobial properties enhance the therapeutic versatility of licorice, particularly in formulations aimed at treating infections [5].

The antioxidant capacity of licorice compounds further contributes to their therapeutic efficacy. Liquiritin and liquiritigenin have been found to scavenge free radicals, thereby protecting cells from oxidative stress-induced damage. Glabridin also exhibits strong antioxidant activity, which may play a role in its protective effects against various diseases. These antioxidant properties are particularly beneficial in conditions where oxidative stress is a contributing factor [7].

The pharmacological activities of licorice's active compounds glycyrrhizin, liquiritin, glabridin, and liquiritigenin are well-documented and multifaceted. Their anti-inflammatory, antimicrobial, and antioxidant properties make them valuable

components in therapeutic formulations, including throat sprays designed to soothe and protect the oropharyngeal mucosa. Understanding these compounds' mechanisms of action is crucial for optimizing their use in pharmaceutical applications.

Licorice (*Glycyrrhiza glabra*) has been traditionally used to alleviate symptoms associated with oropharyngeal conditions such as sore throat, cough, and inflammation. Recent clinical studies have provided evidence supporting its efficacy in modern medical applications. For instance, a randomized controlled trial demonstrated that patients who gargled with licorice solution before undergoing general anesthesia experienced a significant reduction in the incidence and severity of postoperative sore throat compared to those who used a sugar-water solution. This suggests that licorice's anti-inflammatory properties can be beneficial in managing throat discomfort following medical procedures [8].

The therapeutic effects of licorice in oropharyngeal conditions are primarily attributed to its active compounds, such as glycyrrhizin and glabridin. These constituents exhibit anti-inflammatory, antimicrobial, and soothing properties, which can help reduce throat irritation and suppress cough reflexes. Moreover, licorice has been found to inhibit the growth of certain bacteria and viruses responsible for respiratory infections, thereby potentially reducing the duration and severity of symptoms [5].

In addition to its anti-inflammatory and antimicrobial effects, licorice has demonstrated analgesic properties that can alleviate pain associated with sore throats. A study evaluating the effectiveness of licorice pastilles in patients with chronic cough found that regular use led to a significant decrease in cough frequency and throat discomfort. These findings underscore the potential of licorice-based formulations in providing symptomatic relief for individuals suffering from persistent oropharyngeal irritation.

Incorporating licorice extract into pharmaceutical sprays presents several formulation challenges, primarily due to the physicochemical properties of its active constituents. Glycyrrhizin, the principal bioactive compound in licorice,

exhibits limited water solubility, which can hinder its effective dispersion in aqueous spray formulations. This poor solubility necessitates the use of solubilizing agents or alternative formulation strategies to ensure uniform distribution and bioavailability of the active ingredient in the final product. Moreover, the stability of glycyrrhizin in solution is influenced by factors such as pH and temperature, requiring careful optimization of formulation conditions to maintain its therapeutic efficacy over the product's shelf life.

Beyond solubility and stability concerns, the potential toxicity associated with glycyrrhizin poses significant considerations in the development of licorice-based pharmaceutical sprays. Excessive intake of glycyrrhizin has been linked to adverse effects such as hypertension, hypokalemia, and edema, primarily due to its mineralocorticoid-like activity. These effects underscore the importance of precise dosing and thorough safety evaluations in the formulation process to mitigate the risk of toxicity, especially in populations susceptible to these side effects [9].

To address these challenges, innovative formulation approaches have been explored. For instance, the use of glycyrrhizin as a multifunctional drug carrier has been investigated to enhance the solubility and stability of hydrophobic drugs, suggesting its potential utility in improving the delivery of active compounds in spray formulations. Additionally, microencapsulation techniques have been employed to protect sensitive bioactive compounds, like those found in licorice extract, from degradation and to control their release profiles, thereby enhancing the overall efficacy and safety of the pharmaceutical product [10, 11].

1.3. Eucalyptus essential oil: antiseptic potential and pharmaceutical use

Eucalyptus essential oil, predominantly extracted from *Eucalyptus globulus* leaves, is rich in bioactive compounds that contribute to its therapeutic properties. The primary constituent is 1,8-cineole (eucalyptol), comprising approximately 70–90% of the oil's composition. Other significant components include α-pinene, limonene, p-cymene, and α-terpineol. These constituents are mainly monoterpenes and sesquiterpenes, known for their volatility and bioactivity. The high

concentration of 1,8-cineole is particularly noteworthy, as it imparts the characteristic aroma and is largely responsible for the oil's pharmacological effects [12].

The antimicrobial activity of eucalyptus essential oil is well-documented. Studies have demonstrated its efficacy against a broad spectrum of microorganisms, including Gram-positive bacteria like Staphylococcus aureus and Gram-negative bacteria such as Escherichia coli. The mechanism involves the disruption of microbial cell membranes, leading to increased permeability and leakage of cellular contents, ultimately resulting in cell death. This property makes eucalyptus oil a potential natural preservative and antimicrobial agent in pharmaceutical formulations.

In addition to its antimicrobial properties, eucalyptus essential oil exhibits significant anti-inflammatory effects. 1,8-cineole has been shown to inhibit the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukins IL-1β and IL-6. This inhibition occurs through the suppression of the nuclear factor-kappa B (NF-κB) signaling pathway, a key regulator of inflammatory responses. Such anti-inflammatory activity is beneficial in managing conditions like bronchitis, sinusitis, and other inflammatory disorders of the respiratory tract [13].

Furthermore, eucalyptus essential oil possesses **antioxidant** properties, which contribute to its therapeutic potential. The oil's constituents can scavenge free radicals and reduce oxidative stress, thereby protecting cells from damage. This antioxidant activity complements its anti-inflammatory effects, offering a multifaceted approach to managing respiratory ailments and enhancing overall health.

The chemical composition of eucalyptus essential oil, dominated by 1,8-cineole, underpins its pharmacological activities, including antimicrobial, anti-inflammatory, and antioxidant effects. These properties make it a valuable component in pharmaceutical applications, particularly in formulations aimed at treating respiratory and oropharyngeal conditions [14].

Eucalyptus essential oil has been traditionally used to alleviate symptoms associated with respiratory conditions, including those affecting the oropharyngeal region. Recent studies have explored its incorporation into various formulations such as mouthwashes and sprays aimed at treating oropharyngeal infections. For instance, a study developed a eucalyptus essential oil-based nanoemulsion and evaluated its antimicrobial properties against *Streptococcus mutans*, a common oral pathogen. The nanoemulsion demonstrated significant antimicrobial activity, suggesting its potential as an innovative material in preventive dentistry and oropharyngeal health [15].

In addition to its antibacterial properties, eucalyptus essential oil exhibits antiviral activities that are beneficial in treating viral infections of the oropharyngeal region. A comprehensive review highlighted the effectiveness of eucalyptus essential oil and its major monoterpenes in preventing and treating infectious diseases caused by viruses. The mechanisms involve direct inactivation of viruses and modulation of the host's immune response, making eucalyptus oil a promising agent in managing viral oropharyngeal conditions [16].

Clinical studies have also demonstrated the efficacy of eucalyptus oil in relieving cough symptoms, which are often associated with oropharyngeal infections. A systematic review and meta-analysis of randomized controlled trials found that eucalyptus is effective in relieving cough symptoms, supporting its use in managing oropharyngeal conditions that involve coughing [17].

The incorporation of eucalyptus essential oil into oropharyngeal treatments offers multiple therapeutic benefits, including antimicrobial, antiviral, and anti-inflammatory effects. These properties make it a valuable component in formulations aimed at managing various oropharyngeal conditions.

Eucalyptus essential oil, while renowned for its therapeutic properties, presents several safety considerations that must be addressed in pharmaceutical formulations. The primary constituent, 1,8-cineole (eucalyptol), is effective in treating respiratory ailments but can be toxic in high concentrations. Ingestion of even small amounts (2–3 mL) of pure eucalyptus oil has been associated with

severe symptoms, including central nervous system depression and respiratory compromise. These effects are particularly pronounced in children, necessitating stringent dosage controls and clear labeling on products containing eucalyptus oil [18].

Topical application of eucalyptus oil can also lead to adverse reactions. While generally considered safe when diluted appropriately, there have been reports of contact dermatitis and allergic reactions in sensitive individuals. The oil's high volatility and lipophilicity can facilitate rapid skin penetration, potentially leading to systemic exposure. Therefore, formulations intended for mucosal application, such as throat sprays, must ensure proper dilution and include excipients that mitigate irritation [19].

Inhalation of eucalyptus oil vapors, a common method of administration for respiratory conditions, is not without risks. Cases of eucalyptus oil-induced seizures have been documented, particularly in individuals with a history of epilepsy or other neurological disorders. These incidents underscore the need for caution when recommending eucalyptus oil inhalation, especially in vulnerable populations [20].

From a formulation perspective, eucalyptus oil's hydrophobic nature poses challenges in developing stable aqueous-based sprays. Its poor solubility in water necessitates the use of emulsifiers or the development of nanoemulsion systems to ensure uniform dispersion and bioavailability. Moreover, the oil's volatility can lead to rapid evaporation, affecting the consistency and efficacy of the product over time. Advanced formulation techniques, such as encapsulation, have been explored to enhance stability and control the release of active compounds.

1.4. Role of auxiliary substances in throat spray development

In the formulation of throat sprays, the incorporation of solubilizers is essential to ensure the uniform dispersion of hydrophobic active pharmaceutical ingredients (APIs) within aqueous systems. Many plant-derived compounds, such

as essential oils and certain flavonoids, exhibit limited water solubility, posing challenges for their effective delivery. Solubilizers, including non-ionic surfactants like polysorbates (e.g., Polysorbate 80) and co-solvents such as propylene glycol, are employed to enhance the solubility of these hydrophobic substances. By reducing the interfacial tension between the hydrophobic APIs and the aqueous medium, solubilizers facilitate the formation of stable, homogenous mixtures, thereby improving the bioavailability and therapeutic efficacy of the active compounds [21].

Stabilizers play a pivotal role in maintaining the physical and chemical stability of throat spray formulations over their shelf life. They prevent the degradation of sensitive APIs and inhibit undesirable interactions between formulation components. Antioxidants such as tocopherols (vitamin E) and ascorbic acid are commonly used to protect APIs from oxidative degradation. Additionally, chelating agents like ethylenediaminetetraacetic acid (EDTA) are incorporated to sequester metal ions that could catalyze degradation reactions. The selection of appropriate stabilizers ensures the preservation of the formulation's efficacy and safety throughout its intended use period.

Preservatives are integral to throat spray formulations, particularly those containing water, as they inhibit microbial growth and extend the product's shelf life. Commonly used preservatives include benzalkonium chloride, phenoxyethanol, and parabens, which exhibit broad-spectrum antimicrobial activity. The choice of preservative depends on factors such as the formulation's pH, the presence of other excipients, and regulatory considerations. It's crucial to balance antimicrobial efficacy with the potential for irritation or allergic reactions, especially given the sensitivity of the oropharyngeal mucosa.

The synergistic use of solubilizers, stabilizers, and preservatives is fundamental to the development of effective and safe throat spray formulations. Solubilizers ensure the uniform distribution of hydrophobic APIs, stabilizers maintain the integrity of the formulation, and preservatives protect against microbial contamination. A comprehensive understanding of these excipients'

functions and interactions is essential for pharmaceutical scientists aiming to optimize throat spray formulations for therapeutic use.

The palatability of throat sprays significantly influences patient compliance, especially in pediatric and geriatric populations. Sweeteners such as xylitol and sorbitol are commonly incorporated to mask the often bitter taste of active pharmaceutical ingredients. Xylitol, a naturally occurring sugar alcohol, not only imparts sweetness comparable to sucrose but also offers dental health benefits by inhibiting the growth of cariogenic bacteria. Its non-cariogenic nature and low glycemic index make it suitable for diabetic patients and those concerned with oral health. Sorbitol, another sugar alcohol, provides a sweet taste and acts as a humectant, helping to retain moisture in the oral mucosa. However, excessive consumption of these polyols can lead to gastrointestinal discomfort, necessitating careful dosage considerations in formulation [22].

Flavoring agents are integral to enhancing the sensory experience of throat sprays. Natural flavors such as mint, lemon, and honey are frequently used to provide a pleasant taste and aroma, which can soothe the throat and encourage regular use. For instance, Manuka honey, derived from the *Leptospermum scoparium* plant, is renowned for its unique antibacterial properties and is often included in throat sprays for its therapeutic and flavor-enhancing qualities. The inclusion of such natural flavors not only improves taste but may also contribute additional health benefits, aligning with the growing consumer preference for natural and multifunctional products.

Mucosal comfort enhancers are critical components in throat spray formulations, aiming to alleviate irritation and dryness in the oropharyngeal region. Glycerin, a trihydroxy alcohol, is widely utilized for its hygroscopic properties, drawing moisture into the mucosal tissues and providing a soothing effect. Its lubricating action helps in reducing friction and discomfort during swallowing. Additionally, honey derivatives are employed not only for their sweetening and flavoring capabilities but also for their demulcent properties, forming a protective film over the mucous membranes to shield against irritants and pathogens. These

agents collectively enhance the therapeutic efficacy of throat sprays by addressing both the symptoms and the underlying mucosal irritation.

The incorporation of sweeteners, flavors, and mucosal comfort enhancers in throat spray formulations is pivotal in ensuring patient adherence and therapeutic success. These excipients not only improve the organoleptic properties of the product but also contribute to the overall soothing and protective effects on the oropharyngeal mucosa. A judicious selection and combination of these agents, tailored to the target patient population, can significantly enhance the acceptability and effectiveness of throat spray therapies.

The development of plant-based throat sprays necessitates meticulous selection of auxiliary substances to ensure efficacy, stability, and patient compliance. One primary consideration is the biocompatibility of excipients with the oropharyngeal mucosa. Excipients should be non-irritating and safe for mucosal application. For instance, glycerin is commonly used for its soothing properties and ability to maintain moisture, enhancing patient comfort. Similarly, propylene glycol serves as a solvent and humectant, facilitating the solubilization of hydrophobic plant extracts like eucalyptus oil and licorice derivatives. The selection of such excipients is crucial to maintain the therapeutic properties of the active ingredients while ensuring user safety.

Another critical factor is the impact of excipients on the physicochemical properties of the spray, such as viscosity, pH, and osmolarity. These parameters influence the spray's performance, including droplet size, spray pattern, and residence time on the mucosal surface. For example, incorporating mucoadhesive polymers like hydroxyethyl cellulose can enhance the spray's adherence to the mucosa, prolonging the contact time of active ingredients and potentially improving therapeutic outcomes. However, the concentration of such polymers must be optimized to prevent excessive viscosity, which could impede sprayability and patient comfort [2].

The stability of plant-based formulations is another paramount consideration. Plant extracts are often susceptible to degradation due to

environmental factors like light, heat, and oxygen. To mitigate this, antioxidants such as ascorbic acid or tocopherols can be included to preserve the integrity of sensitive compounds. Additionally, the use of appropriate preservatives is essential to prevent microbial contamination, especially in aqueous formulations. However, the choice of preservatives must balance antimicrobial efficacy with the potential for mucosal irritation, necessitating thorough evaluation during formulation development.

Furthermore, the regulatory status and consumer perception of excipients play a significant role in their selection. There is a growing preference for natural and plant-derived excipients among consumers seeking holistic and organic products. This trend encourages formulators to consider natural alternatives to synthetic excipients, such as using plant-based emulsifiers or natural sweeteners like stevia. However, the functionality and stability of these natural excipients must be rigorously assessed to ensure they meet the necessary pharmaceutical standards.

The selection of auxiliary substances in plant-based throat sprays is a multifaceted process that requires balancing efficacy, safety, stability, and consumer preferences. A thorough understanding of the interactions between excipients and active plant compounds, as well as their collective impact on the final product's performance, is essential for the successful development of effective and acceptable throat spray formulations.

1.5. Challenges in the development of plant-based throat sprays

The formulation of plant-based throat sprays presents significant challenges, primarily due to the inherent properties of plant extracts. Many bioactive compounds derived from plants, such as essential oils and flavonoids, exhibit poor water solubility, which hampers their incorporation into aqueous-based spray formulations. This limited solubility not only affects the uniform distribution of the active ingredients but also compromises their bioavailability, leading to suboptimal therapeutic outcomes. For instance, compounds like eucalyptol and glycyrrhizin,

found in eucalyptus oil and licorice extract respectively, are hydrophobic, making their dispersion in water-based sprays particularly challenging.

To address these solubility issues, various formulation strategies have been explored. One such approach involves the use of self-nanoemulsifying drug delivery systems (SNEDDS), which are isotropic mixtures of oils, surfactants, and solvents that spontaneously form nanoemulsions upon contact with aqueous media. These systems enhance the solubility and bioavailability of hydrophobic plant compounds, facilitating their effective delivery through throat sprays [23, 24].

Another critical challenge in the development of plant-based throat sprays is the standardization of plant extracts. The chemical composition of these extracts can vary significantly due to factors such as plant species, geographical origin, harvesting time, and extraction methods. This variability leads to inconsistencies in the concentration of active constituents, making it difficult to ensure batch-to-batch uniformity and consistent therapeutic efficacy. For example, the concentration of glycyrrhizin in licorice root can fluctuate based on environmental conditions and processing techniques.

Standardization efforts often involve the identification and quantification of marker compounds within the plant extracts. However, the complex nature of plant matrices, which contain numerous bioactive and inactive constituents, complicates this process. Advanced analytical techniques, such as high-performance liquid chromatography (HPLC) and mass spectrometry, are employed to achieve precise quantification, but these methods require specialized equipment and expertise.

Moreover, regulatory frameworks for herbal products vary across regions, further complicating standardization efforts. In some jurisdictions, herbal products are regulated as dietary supplements, while in others, they are treated as medicinal products, each with distinct requirements for quality control and standardization. This lack of harmonization poses challenges for manufacturers aiming to market plant-based throat sprays internationally [25].

The development of plant-based throat sprays is hindered by challenges related to the solubility and bioavailability of plant extracts, as well as the

standardization of their chemical composition. Addressing these issues requires the application of innovative formulation strategies and advanced analytical techniques, alongside a comprehensive understanding of regulatory requirements.

Plant-based throat sprays, while offering therapeutic benefits, often face significant challenges related to stability and shelf life. The natural constituents, such as essential oils and plant extracts, are susceptible to degradation processes like oxidation and hydrolysis, which can compromise the efficacy and safety of the product over time. Oxidation, in particular, leads to the formation of peroxides and other reactive compounds that can alter the chemical composition and sensory properties of the formulation. Hydrolysis, on the other hand, can result in the breakdown of active compounds, especially in aqueous environments, further diminishing the product's effectiveness. These degradation pathways are influenced by factors such as exposure to light, heat, and oxygen, necessitating careful consideration during formulation and storage.

To mitigate these stability issues, formulators often incorporate antioxidants into the formulation. Natural antioxidants, such as tocopherols (vitamin E) and ascorbic acid (vitamin C), are commonly used to inhibit oxidative degradation by scavenging free radicals and reactive oxygen species. These compounds help preserve the integrity of sensitive plant-derived ingredients, thereby extending the shelf life of the product. Additionally, the use of chelating agents like ethylenediaminetetraacetic acid (EDTA) can sequester metal ions that catalyze oxidative reactions, further enhancing the stability of the formulation [26].

Packaging also plays a crucial role in maintaining the stability of plant-based throat sprays. Selecting appropriate packaging materials that provide barriers against light, oxygen, and moisture is essential to protect the formulation from environmental factors that can accelerate degradation. For instance, amber-colored glass bottles can shield the product from ultraviolet light, while airtight containers can minimize oxygen exposure. Moreover, incorporating active packaging technologies, such as oxygen scavengers or antioxidant-releasing materials, can

offer additional protection by actively neutralizing oxidative agents within the packaging environment [27].

Storage conditions significantly impact the shelf life of natural formulations. Maintaining optimal temperature and humidity levels is vital to prevent degradation processes. Refrigeration can slow down chemical reactions, thereby prolonging the stability of the product. Furthermore, controlling the pH of the formulation within a range that minimizes hydrolytic activity can enhance the longevity of the active compounds. Implementing these storage strategies, alongside robust formulation and packaging approaches, is essential to ensure the efficacy and safety of plant-based throat sprays throughout their intended shelf life.

The development of plant-based throat sprays often encounters significant challenges related to taste and overall sensory experience. Many herbal extracts, such as those derived from licorice and eucalyptus, possess inherently bitter or astringent flavors that can be off-putting to consumers. This bitterness is primarily due to the presence of compounds like glycyrrhizin in licorice and eucalyptol in eucalyptus oil. These compounds, while therapeutically beneficial, can activate bitter taste receptors, leading to reduced patient compliance, especially among children and sensitive individuals. Addressing these taste-related issues is crucial for the successful formulation of palatable and effective throat sprays.

To mitigate the bitterness of herbal extracts, various taste-masking strategies have been employed in pharmaceutical formulations. One common approach involves the use of sweeteners and flavor enhancers to overshadow the unpleasant taste. Natural sweeteners like xylitol and sorbitol not only provide sweetness but also offer additional benefits such as dental health promotion and moisture retention in the oral cavity. Flavoring agents, including mint, honey, and citrus flavors, can further enhance the palatability of the spray. However, the selection of appropriate sweeteners and flavors must consider factors like patient preferences, potential allergies, and interactions with active ingredients [28, 29].

Organoleptic properties, including texture, mouthfeel, and aftertaste, also play a pivotal role in the acceptability of throat sprays. The incorporation of certain

herbal extracts can impart a gritty or oily sensation, which may be undesirable to users. Formulators must carefully balance the concentration of active ingredients and excipients to achieve a pleasant mouthfeel. The use of mucoadhesive agents like glycerin can improve the viscosity and adherence of the spray to the mucosal surface, enhancing its soothing effect while minimizing negative sensory attributes. Furthermore, the optimization of spray characteristics, such as droplet size and spray pattern, is essential to ensure uniform distribution and minimize irritation [30].

Overcoming taste-masking and organoleptic challenges in plant-based throat sprays requires a multifaceted approach that combines the use of sweeteners, flavor enhancers, advanced encapsulation techniques, and careful formulation of excipients. By addressing these sensory issues, manufacturers can improve patient compliance and the overall therapeutic efficacy of herbal throat sprays.

Conclusions to chapter 1

1. Throat sprays are valuable dosage forms for local treatment of oropharyngeal conditions, offering rapid symptom relief and targeted drug delivery. Growing interest in natural remedies has highlighted licorice extract and eucalyptus essential oil as promising active substances due to their anti-inflammatory, antimicrobial, and soothing properties.

2. Licorice contains bioactive compounds like glycyrrhizin and glabridin, known for anti-inflammatory and antimicrobial effects. Eucalyptus oil, rich in 1,8-cineole, provides antiseptic and anti-inflammatory actions. Together, they offer a complementary therapeutic profile suitable for throat spray formulations.

3. Auxiliary substances are critical for successful formulation. Solubilizers, preservatives, antioxidants, and flavoring agents ensure stability, microbiological safety, and patient acceptability. Proper selection and combination of these excipients enhance the efficacy and usability of throat sprays based on plant actives.

4. The development of plant-based sprays faces challenges, including poor solubility, variable extract composition, stability concerns, and taste-masking difficulties. Modern formulation approaches, such as nanoemulsions, mucoadhesive systems, and antioxidant protection, are essential to overcome these barriers.

5. An effective plant-based throat spray requires balancing pharmacological activity, technological stability, and patient-centered design. The next chapter will focus on the experimental development of such a formulation based on the insights gained from the literature.

CHAPTER 2
OBJECTS AND RESEARCH METHODS

2.1. General approach to technological research

The development of a pharmaceutical throat spray requires a structured and logical approach based on the principles of pharmaceutical technology. In this study, a stepwise experimental model was applied, which allowed the formulation process to be optimized progressively through a series of practical investigations. The goal was to design a stable, effective, and acceptable throat spray with soothing and antiseptic properties, using licorice extract and eucalyptus essential oil as the main active components.

The chosen methodology emphasized technological simplicity, making use of basic laboratory tools and avoiding complex analytical techniques. This reflects realistic conditions in a university research environment, where access to advanced instrumentation may be limited, but meaningful formulation work can still be carried out using thoughtful design and controlled experimental observation.

The research workflow was divided into four main stages:

1. Characterization of raw materials, including pH, solubility, visual appearance, and organoleptic properties;
2. Formulation of trial compositions, with variation in key excipient concentrations (glycerin and polysorbate-80);
3. Evaluation of spray properties, such as spray angle, droplet uniformity, dose per actuation, and handling convenience;
4. Stability testing and sensory analysis, to determine which formulation remained most acceptable and physically stable over time.

Each experimental phase was designed to provide immediate feedback to guide the next step. For instance, results from viscosity measurements directly informed excipient adjustment, while user evaluations helped determine which prototype offered the most pleasant taste and throat feel. This iterative design process is widely used in pharmaceutical development, especially for oral and

mucosal drug delivery systems, where patient experience is just as critical as product stability.

All investigations were conducted in triplicate, and results were recorded using tables and simple graphs. The emphasis was placed on practical applicability, ease of reproduction, and alignment with technological norms typically used in semi-industrial pharmaceutical settings. The selected methods were appropriate for the type of formulation and consistent with established pharmaceutical research practices.

2.2. Objects of research

The objects of this research were selected based on their pharmaceutical functionality, safety profile, and technological compatibility for use in a non-sterile, topical throat spray formulation. The formulation was designed to provide both soothing and antiseptic effects when applied to the oropharyngeal mucosa.

The primary active pharmaceutical ingredients (APIs) included:

Licorice extract (5%), chosen for its mucoprotective, anti-inflammatory, and mild sweetening properties. The extract was used in liquid form and contained glycyrrhizic acid and flavonoids as the main functional constituents.

Eucalyptus essential oil (0.5%), selected for its volatile terpene content (mainly eucalyptol), which provides a local antiseptic, anti-inflammatory, and refreshing action.

To ensure optimal delivery, dispersion, and physical stability, several pharmaceutically acceptable excipients were incorporated:

Glycerin (5–20%) was used as a humectant and viscosity-modifying agent, improving throat adhesion and softening the formulation’s texture.

Polysorbate-80 (1.5–2.5%), a nonionic surfactant, served as a solubilizer for eucalyptus oil, allowing stable dispersion in the aqueous medium.

Purified water, compliant with pharmacopoeial standards, was used as the primary solvent and vehicle for all formulations.

The formulations tested (F1–F5) differed in the ratios of glycerin and polysorbate-80, while the concentrations of licorice extract and eucalyptus oil remained constant. This allowed the study to focus on the effect of excipients on sprayability, viscosity, and sensory perception.

For packaging and delivery, the formulations were filled into 10 mL amber glass bottles equipped with manual spray pumps. This primary packaging simulated real-world use conditions and allowed for evaluation of spray angle, droplet size, and actuation force. The choice of dark glass protected the sensitive ingredients, particularly the essential oil, from light degradation during testing.

All raw materials used in the study were of pharmaceutical or food-grade quality and were stored under controlled laboratory conditions in compliance with standard storage guidelines. No preservatives or flavoring agents were added to ensure that the product's performance was assessed in its pure, functional form.

2.3. Research methods

The methodological framework of this research was built around practical and accessible techniques, commonly used in pharmaceutical technology laboratories for evaluating liquid dosage forms. Given the nature of the product a non-sterile, locally acting throat spray priority was given to methods that emphasize physical characterization, technological behavior, and user experience, rather than chemical quantification or microbiological assays.

At the initial stage of development, solubility and compatibility tests were conducted to determine whether eucalyptus essential oil could be effectively dispersed in water using polysorbate-80 as a solubilizing agent. Various ratios of oil to surfactant were tested, and each mixture was diluted with purified water, stirred thoroughly, and observed over time for clarity, turbidity, or phase separation. Similarly, the compatibility of licorice extract with each auxiliary substance was evaluated by preparing binary mixtures and monitoring them visually under consistent lighting for signs of flocculation or sedimentation after standing for up to 72 hours.

The pH of all raw materials and finished formulations was measured using a digital pH meter, previously calibrated with standard buffer solutions of pH 4.00 and 7.00. Each sample was measured at room temperature, and the electrode was carefully rinsed with distilled water between readings to avoid cross-contamination. This parameter was considered particularly important, as it directly affects mucosal tolerability and formulation stability.

Viscosity, a critical determinant of both sprayability and retention time on the throat mucosa, was evaluated using a manual capillary flow method. Samples were allowed to flow through a narrow glass capillary tube, and the time required for 10 milliliters of solution to pass through was recorded with a stopwatch. Relative viscosity was calculated by comparing flow time to that of water, which served as the baseline reference.

To assess spray performance, the formulations were transferred into standard amber glass bottles equipped with manual pump sprayers. Spray angle and droplet dispersion were evaluated by spraying the contents onto vertically positioned sheets of white paper from a fixed distance of 10 centimeters. The resulting spray patterns were examined for symmetry and coverage. Additionally, the amount of liquid dispensed per actuation was measured gravimetrically by weighing the bottles before and after 10 consecutive sprays.

Stability testing was performed by storing the selected formulations at both room temperature (22–25 °C) and under accelerated conditions (40 ± 2 °C) for a period of 30 days. During this period, the formulations were monitored at predefined intervals (Day 0, 7, 14, and 30) for changes in pH, viscosity, and visual appearance. Any observable signs of sedimentation, color shift, or phase instability were carefully documented.

Finally, sensory and usability assessments were carried out with the help of a small panel of volunteers. Each participant used the spray under controlled conditions and provided feedback on taste, throat feel, ease of actuation, and overall acceptability. This subjective evaluation provided crucial insight into patient-centered factors that influence the product’s suitability for repeated use.

All measurements were performed in triplicate where possible to ensure reproducibility. The methods used in this study, though simple, were sufficient to provide a thorough and meaningful technological characterization of the throat spray formulations.

Conclusions to chapter 2

1. The selected active substances licorice extract and eucalyptus essential oil were justified based on their documented soothing, anti-inflammatory, and antiseptic properties, making them suitable for oromucosal application in a throat spray format.

2. The chosen auxiliary components glycerin and polysorbate-80 ensured appropriate viscosity, physical stability, and user comfort, contributing to the technological feasibility of the formulation.

3. The applied research methods, including solubility testing, pH measurement, viscosity estimation, sprayability evaluation, and stability observation, were simple yet adequate for the objectives of pharmaceutical technological research, especially under laboratory conditions.

4. The methodological approach used in this study was consistent with the standards of experimental development in pharmaceutical sciences and demonstrated high practical value, reproducibility, and relevance for dosage form optimization.

CHAPTER 3

DEVELOPMENT OF THE COMPOSITION AND EXPERIMENTAL STUDY OF THE THROAT SPRAY

3.1. Study of the physical and technological properties of active and auxiliary substances

3.1.1 Measurement of pH of individual aqueous solutions

To evaluate the acid–base characteristics of the primary ingredients, 1% aqueous solutions of the selected raw materials were prepared: licorice extract, eucalyptus essential oil (pre-emulsified), glycerin, and polysorbate-80. Each solution was freshly made using purified water and mixed for 3–5 minutes to ensure uniformity. The pH was measured at 25 °C using a calibrated digital pH meter (Hanna Instruments, HI 2211 model), previously standardized with pH 4.00 and 7.00 buffers.

Licorice extract was observed to produce a slightly alkaline solution, consistent with the presence of glycyrrhizic acid salts, while eucalyptus essential oil required pre-mixing with polysorbate-80 in a 1:3 ratio before aqueous dilution, due to its hydrophobic nature. Glycerin and polysorbate-80 were fully miscible with water.

Table 3.1

pH of individual aqueous solutions

Substance	Concentration	pH (25 °C)	Visual appearance
Licorice extract (aqueous)	1%	7.6	Brown, slightly opaque
Eucalyptus oil + Polysorbate-80 (1:3)	1% oil equivalent	6.2	Slightly turbid, aromatic
Glycerin	1%	6.4	Colorless, clear
Polysorbate-80	1%	5.9	Colorless, slightly viscous

The measured pH values indicate that all excipients fall within an acceptable range for mucosal application (typically pH 5.5–7.5), with the licorice solution being the most alkaline. The eucalyptus oil mixture showed slightly acidic properties, likely due to terpene content interacting with water.

3.1.2. Solubility screening of eucalyptus oil in aqueous systems

Since eucalyptus essential oil is a lipophilic compound, its incorporation into an aqueous throat spray requires an appropriate solubilization strategy. To address this, we conducted a series of small-scale solubility tests using polysorbate-80 as a non-ionic surfactant, preparing a range of mixtures with different oil-to-solubilizer ratios. The goal was to determine the minimum concentration of polysorbate-80 required to form a clear or visually acceptable dispersion of eucalyptus oil in water.

Each test sample was prepared in a 10 mL volumetric flask by mixing eucalyptus oil and polysorbate-80 in specific ratios (1:1, 1:2, 1:3, 1:4), followed by gradual addition of distilled water under magnetic stirring at room temperature. After mixing, samples were visually evaluated for clarity, turbidity, and separation at 1 and 24 hours.

Table 3.2

Solubility screening of eucalyptus oil in aqueous systems

Eucalyptus oil : Polysorbate-80	**Appearance after 1 hour**	**Appearance after 24 hours**	**Interpretation**
1:1	Milky, phase separation seen	Oil layer visible	Unsuitable
1:2	Opaque emulsion	Mild sedimentation	Borderline
1:3	Translucent, uniform	No separation	Acceptable for formulation
1:4	Clear, low turbidity	No change	Optimal but excessive surfactant

From the observations, the 1:3 ratio of eucalyptus oil to polysorbate-80 achieved a stable translucent mixture without visible phase separation for at least 24 hours. Increasing the polysorbate content further (1:4) produced a clearer

solution but is not preferred due to potential irritation or soapy taste when used in oral formulations.

Based on these results, the 1:3 ratio was selected for future formulation trials as it provides sufficient solubilization with acceptable sensory characteristics.

3.1.3. Visual and organoleptic evaluation of raw materials

Understanding the visual and sensory characteristics of raw materials is essential for the formulation of an acceptable throat spray. This evaluation helps anticipate possible issues related to color, odor, and overall mouthfeel, which directly influence patient compliance.

Each excipient was examined under ambient light for clarity, color, and consistency, while odor and taste (where applicable) were assessed subjectively by the formulator. Organoleptic impressions were noted without masking agents, as this represents the baseline upon which taste corrections might be planned.

Table 3.3

Evaluation of raw materials

Substance	Appearance	Odor	Taste / Mouthfeel
Licorice extract	Dark brown, opaque	Characteristic, sweet	Sweet–bitter, slightly astringent
Eucalyptus oil	Pale yellow, oily liquid	Strong, camphor-like	Irritating, pungent
Glycerin	Colorless, viscous	Odorless	Sweet, smooth, lubricating
Polysorbate-80	Yellowish, viscous	Slightly fatty/soapy	Slightly bitter, oily aftertaste
Water (reference)	Clear, colorless	Neutral	Neutral

Licorice extract, despite its natural origin, has a pleasant sweet note but also introduces bitterness and astringency, which may linger. This must be balanced in the final composition. Eucalyptus oil provides a pronounced medicinal aroma and strong taste; its irritating effect on the throat was noted in undiluted form, suggesting a need for careful dosing. Glycerin was found to be soothing and is expected to improve mouthfeel and throat lubrication, aligning with the product's

goal of soothing action. Polysorbate-80, while essential for emulsification, introduced a slightly unpleasant oily bitterness, necessitating dosage control to avoid sensory side effects.

The combined organoleptic profile suggests that careful balancing of licorice and eucalyptus, along with possible flavor correction, will be necessary in the final spray to ensure acceptability for users.

3.1.4. Viscosity estimation of glycerin–water mixtures

The viscosity of a throat spray influences not only the sprayability but also the retention time on the mucosa and overall sensory feel. Glycerin, a key excipient in the formulation, serves both as a humectant and a viscosity modifier. To determine the optimal concentration for desirable viscosity without impairing spray performance, a series of aqueous glycerin mixtures were prepared and tested.

Five different concentrations of glycerin in water (5%, 10%, 15%, 20%, and 30% w/w) were prepared. The dynamic viscosity was measured at 25 °C using the simple time-flow method, which involved recording the time it took for 10 mL of solution to pass through a narrow glass capillary tube (internal diameter 2 mm, 10 cm long). Each measurement was repeated 3 times and averaged. Water was used as the baseline (1.0 cP).

Table 3.4

Viscosity estimation

Glycerin concentration (%)	**Time to flow (s)**	**Relative viscosity (approx.)**	**Observation during flow**
0 (pure water)	10.2	1.0	Flows easily, low resistance
5%	11.8	~1.2	Slightly more viscous
10%	13.4	~1.4	Smooth, uniform flow
15%	17.9	~1.75	Slight drag, still acceptable
20%	23.8	~2.3	Noticeable resistance
30%	37.5	~3.7	Thick flow, not suitable for spray

5–15% glycerin yielded mixtures with low to moderate viscosity, suitable for pump sprays. At 20%, the viscosity was on the higher side but might still be acceptable if enhanced throat adhesion is needed. 30% glycerin resulted in excessive thickness, which may hinder sprayability and cause nozzle clogging or uneven dispersion.

Based on these results, a 10–15% glycerin concentration range was selected for formulation trials, offering a balance between sprayability and mucosal retention without compromising user comfort.

3.1.5. Compatibility pre-test of licorice extract with auxiliary substances

Before proceeding to full-scale formulation development, a preliminary compatibility assessment was conducted by mixing licorice extract with each of the auxiliary components: glycerin, polysorbate-80, and the eucalyptus oil–polysorbate solution (1:3), to evaluate physical stability. The aim was to detect any immediate or delayed incompatibility, such as precipitation, flocculation, phase separation, or turbidity, which may impair the final product's uniformity or appearance.

Three binary mixtures were prepared in glass test tubes:

A: Licorice extract + Glycerin (1:1)

B: Licorice extract + Polysorbate-80 (1:1)

C: Licorice extract + Eucalyptus oil pre-emulsified in Polysorbate-80 (1:3)

Each test tube was mixed gently and left to stand at room temperature (22–25 °C). Observations were recorded at 0, 3, 24, and 72 hours under ambient light.

Table 3.5

Compatibility pre-test

Mixture	**Initial Appearance**	**24h Observation**	**72h Observation**	**Compatibility Conclusion**
A: Licorice + Glycerin	Homogeneous, brown	No change	No sedimentation	Compatible
B: Licorice + Polysorbate	Slightly turbid	Light haze	Mild dark floccules	Borderline – monitor
C: Licorice + EO/P-80 (1:3)	Uniform, light brown	No separation	Minor ring at meniscus	Acceptable with mild caution

Glycerin and licorice showed excellent miscibility with no visible changes over 3 days - fully compatible. The licorice–polysorbate mixture showed slight flocculation over time. While not immediately disqualifying, the proportion of polysorbate-80 should be kept minimal. The complete eucalyptus–licorice mixture (with solubilizer) remained visually acceptable, confirming the viability of the essential oil system in a licorice-containing base.

Thus, no immediate physical incompatibility was detected that would prevent formulation development. However, monitoring long-term clarity and sedimentation will be essential during stability testing, especially for mixtures with higher surfactant content.

3.2. Development of spray base formulations and preliminary evaluation

3.2.1. Preparation of formulations with varying glycerin and polysorbate-80 content

Based on the physicochemical properties established in the previous section, five pilot formulations (F1–F5) of the throat spray were prepared. Each formulation contained a fixed dose of licorice extract (5% w/w) and eucalyptus essential oil (0.5% w/w), with glycerin and polysorbate-80 varied to optimize viscosity, stability, and dispersion. Purified water was used as the vehicle, and all components were blended under magnetic stirring at 500 rpm for 15 minutes at room temperature.

The eucalyptus essential oil was first mixed with polysorbate-80 (1:3 ratio) to form a uniform pre-emulsion, which was then added to the aqueous phase containing licorice extract and glycerin. Final volumes were adjusted with water, and the solutions were transferred into amber glass bottles with pump sprayers for subsequent evaluation.

Table 3.6

Compatibility pre-test

Component	F1	F2	F3	F4	F5
Licorice extract (%)	5.0	5.0	5.0	5.0	5.0
Eucalyptus oil (%)	0.5	0.5	0.5	0.5	0.5
Polysorbate-80 (%)	1.5	2.0	2.0	2.5	2.5
Glycerin (%)	5.0	10.0	15.0	15.0	20.0
Purified water (%)	qs to 100	qs to 100	qs to 100	qs to 100	qs to 100

Each formulation was visually uniform at the time of preparation, with F1 and F2 showing slight turbidity, and F3–F5 appearing increasingly viscous and more translucent. All sprays were labeled and stored for further physical testing under controlled ambient conditions.

3.2.2. Macroscopic appearance and color stability

The prepared formulations (F1–F5) were stored at room temperature (22–25 °C) in tightly closed amber glass bottles for visual evaluation over 7 days. The primary parameters assessed were clarity, color changes, presence of sediment or oil droplets, and phase stability (i.e., absence of layer formation or creaming).

Table 3.7

Macroscopic appearance and color stability

Formulation	Initial Appearance	Day 1	Day 3	Day 7	Stability Conclusion
F1	Slight turbidity, yellowish	Increased turbidity, faint ring	Sediment at bottom	Phase separation observed	Unstable
F2	Slightly hazy, pale amber	Stable	No visible change	Slight bottom haze	Acceptable for short term
F3	Translucent, amber	Stable	Stable	Slight darkening in tone	Good visual stability
F4	Viscous, honey-colored	Stable	Stable	No changes	Excellent stability
F5	More viscous, slightly darker	Stable	Slight surface film appeared	Increased viscosity observed	Acceptable with caution

Observations were recorded at 0 hours, 24 hours, 72 hours, and 7 days under identical lighting conditions, and minor changes were documented in a comparative table.

F1, with the lowest polysorbate-80 content (1.5%), failed to maintain oil dispersion, showing visible separation and turbidity over time. F2 was visually acceptable, but beginning to show sedimentation by Day 7, suggesting borderline emulsification capacity. F3 and F4, with balanced glycerin and adequate solubilizer, maintained visual clarity and physical stability throughout the observation period. F5, though stable, showed increased viscosity and a slight oily film, possibly due to saturation of surfactant at higher glycerin content.

Based on these results, F3 and F4 were selected as candidates for continued evaluation, demonstrating the best balance of clarity, stability, and viscosity.

3.2.3. Homogeneity and clarity evaluation of formulation

In addition to long-term macroscopic observations, each formulation was subjected to a targeted homogeneity and clarity test at Day 3 to assess the internal consistency and potential for phase instability. Homogeneity was assessed by visual inspection under transmitted light, using a black-and-white background, while clarity was ranked on a 5-point scale: 5 – perfectly clear; 4 – slightly opalescent; 3 – visible turbidity; 2 – slight sedimentation; 1 – visible separation or oil droplets.

Table 3.8

Homogeneity and clarity evaluation

Formulation	**Top–Bottom Uniformity**	**Clarity Score**	**Notable Visual Notes**
F1	Non-uniform	2	Clear upper phase, sedimented bottom
F2	Slightly inconsistent	3	Faint haze, small suspended particles
F3	Uniform	4	Translucent, slight amber hue
F4	Uniform	5	Very clear, slightly viscous
F5	Uniform	4	Increased viscosity, faint oily sheen

A pipette was used to draw samples from both the top and bottom of each formulation to check for any non-uniformity in color, viscosity, or particulate distribution.

F1 was rejected due to poor uniformity and low clarity, indicating unstable oil dispersion. F2 showed borderline results, with light suspended particles, possibly plant residues or surfactant–extract complexes. F3, F4, and F5 all exhibited uniformity and acceptable clarity, with F4 scoring the highest due to excellent dispersion and appearance.

These findings confirmed the previous selection of F3 and F4 for further sprayability and performance testing. While F5 remained acceptable, its viscosity may limit performance in manual spray systems.

3.2.4. Measurement of initial pH and viscosity of the formulations

To evaluate the physicochemical suitability of the prepared throat spray compositions, each formulation (F1–F5) was tested for initial pH and viscosity. These parameters are critical for ensuring mucosal compatibility, spray performance, and physical stability.

Table 3.9

pH and viscosity of the formulations

Formulation	pH (25 °C)	Flow Time (s)	Estimated Relative Viscosity (cP)	Sensory Note on Flow
F1	6.5	11.8	~1.2	Free-flowing, watery
F2	6.4	13.5	~1.4	Slightly thicker
F3	6.3	16.6	~1.7	Smooth, light resistance
F4	6.2	21.8	~2.1	Moderately viscous
F5	6.1	29.5	~2.9	Thick, delayed drip

pH was measured using a calibrated digital pH meter (Hanna HI 2211), with each sample equilibrated to 25 °C prior to testing. The meter was calibrated with standard buffer solutions (pH 4.00 and 7.00) before each use.

Due to the absence of a rotational viscometer, viscosity was assessed via the time-flow method: 10 mL of each sample was allowed to flow through a narrow glass capillary (2 mm diameter, 10 cm length), and the average time (triplicate) was recorded. Relative viscosity was expressed by comparison to water (defined as 1.0 cP = 10.2 s).

All formulations had a pH within the physiologically acceptable range (6.1–6.5) for oropharyngeal application. Viscosity increased proportionally with glycerin content, as expected, with F1–F3 remaining in the ideal sprayable range (≤1.7 cP). F4 showed moderate viscosity, which may enhance mucosal adhesion, while F5 approached the upper threshold for easy spray actuation.

The combination of pH neutrality and moderate viscosity in F3 and F4 confirmed their technical suitability for continued evaluation.

3.2.5. Selection of optimal formulations based on clarity and handling

Following the preliminary tests on appearance, homogeneity, pH, and viscosity, a comparative analysis was performed to select the most promising spray base formulations. The criteria included: clarity and physical stability over time, ease of handling and uniformity, physiological pH compatibility, sprayable viscosity range (<2.5 cP), absence of separation, sedimentation, or excessive turbidity.

Based on the compiled results, the formulations were scored across four main parameters using a semi-quantitative 5-point scale (5 = excellent, 1 = poor).

Table 3.10

Selection of optimal formulations based on clarity and handling

Formulation	Clarity & Stability	Viscosity Suitability	pH Suitability	Overall Handling	Total Score
F1	2	5	5	2	**14**
F2	3	4	5	3	**15**
F3	4	5	5	5	**19**
F4	5	4	5	4	**18**
F5	4	3	5	3	**15**

F3 achieved the highest overall score, showing excellent sprayability, clarity, and handling, with a slightly translucent amber appearance. F4 was also selected for further testing due to its outstanding physical stability and viscosity balance, though slightly thicker. F1 and F2 were rejected due to instability and handling concerns. F5, although physically stable, was not preferred due to its excessive viscosity for a throat spray format.

These findings narrowed the focus to F3 and F4, which will undergo further evaluation in the next experimental section, including spray performance testing.

3.3. Evaluation of sprayability and dose uniformity

3.3.1. Spray pattern assessment

An effective throat spray should produce a uniform, cone-shaped dispersion that evenly coats the oropharyngeal mucosa without generating large droplets or causing discomfort. To evaluate this, a qualitative spray pattern test was performed for the selected formulations (F3 and F4).

Manual pump spray bottles (10 mL, standard nozzle diameter ~0.6 mm) were filled with each test solution. Each formulation was sprayed once onto a vertically placed sheet of white absorbent paper from a fixed distance of 10 cm. The spray angle, symmetry, and spot uniformity were documented. Measurements were made by drawing lines from the center of the pattern to its widest edges, forming an approximate spray cone.

Table 3.11

Spray pattern

Formulation	Spray Angle (°)	Center Spot Diameter (cm)	Spray Shape Quality	Edge Diffusion	Subjective Mist Quality
F3	~48°	3.5 cm	Symmetrical cone	Smooth	Fine mist, even coverage
F4	~42°	3.2 cm	Slightly narrower	Mildly irregular	Soft mist, slightly denser

F3 produced a wider spray cone and more diffuse mist, ideal for broad mucosal coverage. The spray was fine and evenly distributed, suggesting good

atomization at its viscosity. F4, with higher viscosity, had a slightly narrower angle and denser central zone, indicating slower droplet formation and slightly heavier deposition. Both formulations were functionally sprayable, but F3 demonstrated superior dispersion geometry, making it preferable for comfortable and effective throat application.

3.3.2. Dose per actuation test

Precise and reproducible dosing per spray is essential for ensuring the correct amount of active substance is delivered to the throat. To evaluate the dose uniformity, we measured the volume of liquid delivered per actuation of the manual pump for both F3 and F4.

Each spray bottle was weighed empty (W_0), then filled with 10.00 mL of test formulation and weighed again (W_1). The spray was actuated 10 times, allowing full pump depressions. The bottle was then weighed again (W_2), and the difference ($W_1 - W_2$) was used to calculate the total delivered volume, assuming density ≈ 1.00 g/mL. The result was divided by the number of sprays to obtain the average volume per actuation. The test was repeated three times for each formulation to assess repeatability.

Table 3.12

Dose per actuation test

Formulation	Total Volume Delivered (10 sprays)	Avg. Volume per Spray (mL)	Relative Standard Deviation (RSD, %)
F3	1.52 mL, 1.49 mL, 1.51 mL	0.151 mL	0.99%
F4	1.43 mL, 1.44 mL, 1.40 mL	0.143 mL	1.41%

Both formulations demonstrated consistent delivery, with RSD values well below 2%, which is acceptable for non-metered manual pump systems. F3 delivered a slightly higher dose per spray, in line with its lower viscosity and broader spray pattern. F4, being more viscous, exhibited slightly lower volume per actuation, but remained within an acceptable range for local mucosal application. These findings confirm that both formulations can deliver accurate and

reproducible spray doses, with F3 again showing a slight advantage in mist quality and dose output.

3.3.3. Spray reproducibility across batches

To assess the batch-to-batch consistency of spray delivery, we prepared three independent samples of each formulation (F3 and F4) using the same method and equipment. Each batch was tested for: dose per spray (as in previous test), spray pattern uniformity, subjective handling and spray feel, this step simulates small-scale manufacturing variability, ensuring that the formulation remains stable and functional even with slight procedural variations.

Each formulation (F3 and F4) was prepared fresh on three different days. The same raw materials, stirring speed (500 rpm), and ambient temperature (22–25 °C) were maintained. Each batch was filled into identical 10 mL spray bottles and evaluated for 10-spray output and pattern quality.

Table 3.13

Spray reproducibility

Formulation	Batch No.	Avg. Dose per Spray (mL)	Spray Pattern (Qualitative)	Handling Consistency
F3	B1	0.152 mL	Fine mist, symmetrical	Excellent
	B2	0.149 mL	Fine mist, symmetrical	Excellent
	B3	0.151 mL	Even cone, mild edge softening	Very good
F4	B1	0.144 mL	Slightly denser center	Good
	B2	0.141 mL	Narrower cone, heavier mist	Good
	B3	0.142 mL	Consistent, denser feel	Acceptable

F3 showed excellent reproducibility, with spray output varying less than ±2% across batches and consistent spray geometry. F4 was also reproducible, but the spray was slightly denser and narrower due to higher viscosity, causing a less

diffuse mist. No clogging, foaming, or leakage was observed in any batch, confirming the suitability of formulation and container choice.

This consistency confirms that both F3 and F4 formulations are robust and scalable, with F3 again slightly favored for its superior handling and reproducibility.

3.3.4. Subjective nozzle feedback and actuation force observations

An important practical aspect of throat spray usability is the user experience during spraying. This includes the actuation force, smoothness of spray, and any mechanical resistance, leakage, or clogging. These factors were assessed subjectively for both F3 and F4 using a standardized bottle and nozzle under consistent manual force.

Each formulation was filled into a 10 mL amber glass spray bottle with the same type of mechanical atomizer pump. A trained operator (same person for all trials) performed five actuations per sample and noted: ease of pressing the pump, resistance or stiffness, return speed of the nozzle, any observable dripping, clogging, or back-pressure, a qualitative 5-point scale was used (5 = excellent, 1 = poor).

Table 3.14

Nozzle feedback and actuation force

Formulation	Actuation Force	Smoothness of Spray	Nozzle Return Speed	Dripping / Backflow	User Feedback Summary
F3	5 (Very light)	5 (Very smooth)	5 (Quick and clean)	None observed	“Easy to spray, clean break”
F4	4 (Moderate)	4 (Slight resistance)	4 (Slight lag)	Minimal film noted	“Slightly heavy, thicker mist”

F3 was consistently smooth and light to actuate, with no post-spray dripping and instant nozzle rebound. The user described it as “comfortable and responsive.” F4, due to its higher viscosity, required noticeably more finger pressure, and the spray felt denser, with a slight residual film forming around the nozzle after

repeated use. Neither formulation clogged or foamed, and no container leakage occurred. These results highlight F3's superior ergonomic performance, especially important for older patients or frequent use. While F4 remains acceptable, it may be better suited for niche use cases where prolonged throat coating is desirable.

3.3.5. Evaluation of minimum usable volume per bottle

In practical use, residual product loss within a spray bottle known as "dead volume" reduces dosing efficiency. It is important to estimate how much of the formulation remains inaccessible due to nozzle geometry or pump limitations. This test helps optimize fill volume and reduce waste.

Identical 10 mL spray bottles with mechanical pumps were filled with 10.00 mL of either F3 or F4. The spray was actuated repeatedly (manually, full depression) until no more liquid was discharged. The bottle was then inverted and shaken to release trapped liquid, and residual volume was measured by removing the pump and weighing the remaining liquid. The test was repeated for three bottles per formulation.

Table 3.15

Minimum usable volume per bottle

Formulation	Initial Volume (mL)	Final Residual Volume (mL)	Usable Volume (%)	Observations
F3	10.00	0.58 ± 0.04	94.2%	No pooling, clean emptying
F4	10.00	0.82 ± 0.06	91.8%	Slight film inside bottle, viscous lag

F3 allowed extraction of over 94% of the initial content, with only minimal loss inside the nozzle or bottle shoulder. F4, being more viscous, left a higher dead volume, possibly due to adhesion to internal surfaces and slower flow near the end of dispensing. Both values are acceptable for non-metered throat sprays, but F3 provides greater dose efficiency and better economic use. This confirms that F3 not only sprays better and more consistently but also minimizes residual waste, reinforcing its status as the leading formulation candidate.

3.4. pH and viscosity stability under accelerated storage

3.4.1. Storage of selected formulation(s) at room and elevated temperature

To assess stability over time, formulations F3 and F4 were stored under two controlled conditions: room temperature (RT): 22–25 °C, ambient humidity, elevated temperature (ET): 40 ± 2 °C, simulating accelerated aging.

The goal was to observe changes in physical appearance, pH, and viscosity over 30 days. Storage was done in tightly sealed amber glass bottles (10 mL), placed upright and protected from light. Samples were withdrawn at Day 0, 7, 14, and 30.

Table 3.16

Stability over time

Storage Conditions	Sample Code	Storage Time	Observations
RT (22–25 °C)	F3-RT	0–30 days	Stable, clear, no sediment
RT (22–25 °C)	F4-RT	0–30 days	Slight thickening at Day 30
ET (40 ± 2 °C)	F3-ET	0–30 days	Mild darkening, still uniform
ET (40 ± 2 °C)	F4-ET	0–30 days	Increased viscosity, slight turbidity

F3 remained stable under both conditions, with only minor color deepening at elevated temperature, no phase separation or precipitation. F4 showed viscosity increase, particularly under elevated storage, which may affect sprayability over time. No microbial growth, foaming, or gas formation was observed (visual inspection only, no microbiological testing used). This setup established the foundation for the next key steps: quantitative tracking of pH and viscosity, which will be presented in detail in the following tables.

3.4.2. Weekly measurement of pH

The pH stability of throat spray formulations is critical to ensure mucosal compatibility, chemical integrity of actives, and user comfort. During the 30-day storage period under room temperature (RT) and elevated temperature (ET, 40 ± 2 °C), the pH of formulations F3 and F4 was measured on Day 0, 7, 14, and 30 using a calibrated digital pH meter (Hanna Instruments, accuracy ±0.01).

Table 3.17

pH stability

Day	**F3 – RT (22–25 °C)**	**F3 – ET (40 °C)**	**F4 – RT (22–25 °C)**	**F4 – ET (40 °C)**
0	6.3	6.3	6.2	6.2
7	6.3	6.2	6.2	6.1
14	6.2	6.1	6.2	6.0
30	6.2	6.0	6.1	5.9

F3 maintained excellent pH stability at room temperature, with only a minor 0.3 unit decrease under elevated conditions by Day 30. F4 showed a slightly greater pH drift, dropping to 5.9 under heat, though still within the acceptable physiological range (5.5–7.0). No signs of hydrolysis or strong acidification were detected. These results confirm that both formulations retain their chemical stability over short-term accelerated storage, with F3 showing better pH resilience under thermal stress.

3.4.3. Viscosity estimation every 2 weeks

The viscosity stability of throat spray formulations was evaluated at Day 0, 14, and 30 under both room temperature (RT) and elevated temperature (ET, 40 ± 2 °C). Changes in viscosity may indicate glycerin evaporation, polymer thickening, or phase changes-all of which can impact spray performance.

10 mL samples of F3 and F4 were measured using the capillary time-flow method, as previously described. The flow time for 10 mL through a glass tube (2 mm diameter) was recorded three times and averaged. Viscosity is expressed relative to water, using Day 0 as baseline.

Table 3.18

Viscosity estimation

Day	F3 – RT (sec)	F3 – ET (sec)	F4 – RT (sec)	F4 – ET (sec)
0	16.6 (1.7 cP)	16.6 (1.7 cP)	21.8 (2.1 cP)	21.8 (2.1 cP)
14	16.7 (1.7 cP)	17.4 (1.8 cP)	23.1 (2.2 cP)	25.5 (2.5 cP)
30	17.0 (1.7 cP)	18.2 (1.9 cP)	24.6 (2.4 cP)	28.7 (2.8 cP)

F3 remained stable, with only a 0.2 cP increase at 40 °C over 30 days, well within operational tolerances. F4 showed gradual thickening, especially under thermal stress, reaching 2.8 cP, which could begin to impair fine mist formation. These results align with earlier findings: F3 is more robust, with viscosity resilience under both typical and accelerated conditions.

3.4.4. Visual stability evaluation (appearance, color, separation)

To complement quantitative data, the formulations were subjected to visual inspections throughout the 30-day storage period. The aim was to detect color changes, turbidity, sedimentation, or phase separation, which are common indicators of physical instability in emulsion-based or extract-containing solutions.

Samples of F3 and F4 stored at RT (22–25 °C) and ET (40 ± 2 °C) were observed visually on Day 0, 14, and 30. Evaluations were conducted under daylight-equivalent light against black and white backgrounds. Observations focused on clarity, sediment formation, surface oil separation, and color shift.

Table 3.19

Visual stability

Day	F3 – RT	F3 – ET	F4 – RT	F4 – ET
0	Clear amber, uniform	Clear amber, uniform	Light brown, uniform	Light brown, uniform
14	Slightly deeper tone	Amber, minor darkening	Slightly darker	Increased opacity, hazy base
30	Slight amber shift	Mild surface ring formed	No visible sediment	Slight sedimentation noted

F3 maintained excellent visual stability. At 40 °C, a minor surface ring (oil trace) was noted by Day 30, but no phase separation occurred. F4, by contrast,

showed signs of reduced clarity and early sedimentation under elevated temperature likely due to extract–surfactant interaction and increased viscosity. No microbial growth, gas formation, or foul odor was detected in either sample. Overall, F3 retained its uniform appearance, reinforcing its status as the more stable and visually acceptable formulation over time.

3.4.5. Summary comparison between storage conditions

To consolidate the findings of the accelerated stability study, a comparative analysis of F3 and F4 under room temperature (RT) and elevated temperature (ET) conditions was conducted across all tested parameters: pH, viscosity, and visual appearance. This summary helps identify the formulation with superior stability under both standard and stress conditions.

Table 3.20

Comparison between storage conditions

Parameter	F3 – RT	F3 – ET	F4 – RT	F4 – ET
pH drift	−0.1 unit	−0.3 units	−0.1 unit	−0.3 units
Viscosity change	+0.1 cP	+0.2 cP	+0.3 cP	+0.7 cP
Visual stability	Stable, clear	Minor ring, no phase	Slight thickening	Haze, sedimentation
Overall assessment	Excellent	Good	Good	Borderline

F3 demonstrated better resilience to thermal stress across all parameters. Changes in pH and viscosity were minimal, and no significant visual degradation occurred. F4, although acceptable at room temperature, showed pronounced thickening and early signs of physical instability at elevated temperature by Day 30. These findings confirm that F3 offers superior short-term physical and physicochemical stability, making it the preferred candidate for final sensory testing and potential scale-up.

3.5. Sensory evaluation and optimal formulation selection

3.5.1. Sensory assessment of taste and aftertaste

A critical step in developing a throat spray for direct oropharyngeal application is the evaluation of its organoleptic profile, especially taste, aftertaste, and mouthfeel. These factors determine patient acceptability and compliance, particularly for repeated use.

A panel of 5 untrained volunteers (aged 22–28) was asked to self-administer one spray of each test formulation (F3 and F4) under supervision. The sprays were applied to the back of the throat without swallowing for 30 seconds, followed by qualitative assessment. The following attributes were rated on a 5-point hedonic scale: sweetness (5 = very sweet, 1 = none), bitterness (5 = very bitter, 1 = none), astringency (5 = very dry/puckering, 1 = none), aftertaste duration (5 = long-lasting, 1 = very short). Overall palatability (5 = very pleasant, 1 = unpleasant).

Table 3.21

Assessment of taste and aftertaste

Attribute	F3 (Mean ± SD)	F4 (Mean ± SD)	Comments
Sweetness	3.8 ± 0.4	4.2 ± 0.3	F4 felt slightly thicker and sweeter
Bitterness	2.1 ± 0.6	2.4 ± 0.5	Licorice masked oil bitterness well
Astringency	2.6 ± 0.5	2.8 ± 0.4	Mild due to licorice; acceptable
Aftertaste duration	3.2 ± 0.7	3.6 ± 0.6	Slightly longer for more viscous F4
Overall palatability	4.4 ± 0.5	4.2 ± 0.6	Both well tolerated; F3 slightly fresher

Both formulations were rated highly acceptable, with no major aversive effects. F4, being more viscous, was perceived as sweeter and longer-lasting, but also slightly heavier. F3 was described as fresher and easier to swallow, with a cleaner aftertaste, suggesting it may be preferred for users seeking light, soothing sprays. This panel confirmed that both prototypes are sensorially acceptable, but

F3 provided a better overall mouthfeel with less coating sensation, aligning with its superior spray performance.

3.5.2. Throat comfort and coating effect

Beyond taste, a throat spray must deliver a soothing sensation and mucosal coverage to fulfill its therapeutic function. This key point evaluates the subjective throat feel, including cooling, burning, coating, and soothing effects experienced immediately after application.

The same panel of 5 volunteers from the previous key point participated in this assessment. Each participant used one spray of F3 and F4 on separate days. They were asked to describe: throat coating (1 = none, 5 = thick film), soothing sensation (1 = none, 5 = strong relief), irritation or burning (1 = none, 5 = very irritating), cooling effect (1 = none, 5 = strong, pleasant). Ratings were based on 2–3 minutes of observation post-application.

Table 3.22

Throat comfort and coating effect

Attribute	F3 (Mean ± SD)	F4 (Mean ± SD)	Comments
Throat coating	3.2 ± 0.6	4.1 ± 0.5	F4 formed a noticeably thicker film
Soothing sensation	4.4 ± 0.5	4.2 ± 0.4	Both gave relief; F3 felt lighter
Irritation/ Burning	1.4 ± 0.5	1.6 ± 0.4	Minor tingling in both, no discomfort
Cooling effect	3.6 ± 0.7	3.3 ± 0.6	F3 felt fresher due to spray dispersion

F4 offered greater throat coating, likely due to its higher viscosity, which may prolong contact time, but at the cost of a slightly heavier feel. F3 was perceived as more refreshing and lighter, with a better cooling effect and less residue, making it suitable for frequent use. Both had low irritation levels, confirming that eucalyptus oil concentration (0.5%) was tolerable in the current emulsified form. Overall, both sprays fulfilled their intended soothing role, but the

light, refreshing action of F3 was more favorable in terms of comfort and daily usability.

3.5.3. Spray usability score (ease of use and delivery feel)

In addition to taste and comfort, user interaction with the device, including how easily the spray can be applied and how it feels during actuation, is essential for compliance and acceptance. This assessment focused on: ease of pressing the nozzle, targeting accuracy, perceived spray force and mist, clean exit and lack of dripping.

Each panelist rated both F3 and F4 using the same 10 mL pump-action spray bottle. Participants were instructed to spray into their open mouth, simulating real-world use. Feedback was collected immediately after application.

Table 3.23

Spray usability

Usability Parameter	**F3 (Mean ± SD)**	**F4 (Mean ± SD)**	**Panelist Feedback Highlights**
Ease of pressing	4.8 ± 0.4	4.2 ± 0.5	F3 “sprayed effortlessly”; F4 “slightly stiff”
Targeting and aim	4.6 ± 0.5	4.4 ± 0.5	Both easy to aim; F3 finer cone
Spray force / mist feel	4.5 ± 0.5	3.9 ± 0.6	F3 had softer, more pleasant mist
Exit cleanliness	4.7 ± 0.3	4.1 ± 0.4	F4 left a “slight residue” on nozzle
Overall usability score	**4.7**	**4.2**	F3 “felt smoother and cleaner to apply”

F3 was easier to use, especially for individuals with reduced hand strength, and produced a fine, clean spray with no backflow or leakage. F4 required more force to actuate, and the denser formulation occasionally left residue around the nozzle, which may be unpleasant for users. Both allowed accurate targeting of the throat area, but the superior misting characteristics of F3 contributed to a more pleasant delivery experience. The results favor F3 as the more user-friendly option, particularly for frequent daytime use or by elderly patients or children.

3.5.4. Panel preference comparison (blind ranking)

To obtain an unbiased evaluation, a blind ranking test was conducted to determine the overall user preference between the two formulations. Neither the formulation codes (F3 or F4) nor composition details were revealed to the participants.

Each panelist received two anonymized samples (coded A and B) containing F3 and F4 in identical bottles. After using both samples, participants were asked to rank them from 1 (preferred) to 2 (less preferred) based on overall experience, including taste, comfort, ease of use, and after-feel. They were also asked to briefly explain their choice.

Table 3.24

Preference comparison

Panelist	**Preferred Sample**	**Reason Given**
1	A (F3)	"Lighter feel, no residue, fresher taste"
2	A (F3)	"Easier to spray, pleasant cooling"
3	B (F4)	"Coats better, feels like it stays longer"
4	A (F3)	"Smooth spray, no bitterness"
5	A (F3)	"Clean mouthfeel, more comfortable to use"

4 out of 5 participants preferred Formulation F3 over F4. The primary reasons for F3's preference were its lighter sensation, cleaner finish, and better spraying behavior. The only preference for F4 was attributed to its enhanced throat coating, which may be advantageous for users with persistent dryness or irritation.

This blind ranking confirmed that F3 offers superior overall user satisfaction, balancing performance, comfort, and ease of application. These outcomes, combined with its physicochemical and sprayability advantages, support its selection as the final optimized formulation.

3.5.5. Justification of final formula choice and conclusion of experimental development

Based on the comprehensive experimental results, covering physicochemical stability, spray performance, and sensory acceptability, Formulation F3 has been selected as the optimal composition of the throat spray for further development and potential scale-up.

Key Rationale for Selection of F3:

Superior Sprayability - F3 demonstrated the widest and most uniform spray cone, with smooth actuation, consistent droplet distribution, and minimal mechanical resistance.

Physicochemical Stability - It showed minimal changes in pH and viscosity under both room and accelerated storage conditions. No signs of sedimentation, phase separation, or color degradation were observed over 30 days.

Sensory Superiority - F3 provided a lighter, fresher feel, with lower coating intensity and better mouth comfort. It was rated more pleasant by 80% of the panel in a blind test.

Handling and Usability - F3 had the lowest dead volume, required less force for actuation, and left no nozzle residue, enhancing user convenience.

Acceptable Organoleptic Profile - Sweetness was balanced, bitterness was masked effectively by licorice, and no throat irritation occurred at the tested eucalyptus oil concentration.

Conclusions to chapter 3

1. A series of experimental studies was carried out to develop and evaluate throat spray formulations containing licorice extract and eucalyptus essential oil, focusing on physicochemical properties, sprayability, and user acceptability.

2. Among the tested variants, Formulation F3 demonstrated optimal characteristics, including pH stability, suitable viscosity, fine mist dispersion, and favorable organoleptic properties, making it the most technologically and functionally appropriate option.

3. The selected formulation remained stable under accelerated storage conditions, with minimal changes in viscosity or pH, and showed no signs of phase separation or degradation, confirming its physical robustness.

4. Sensory and usability evaluations confirmed that F3 was preferred by the majority of testers due to its light feel, soothing throat effect, and ease of application, supporting its suitability for further development as a mucosal spray.

CONCLUSIONS

1. A throat spray with licorice extract and eucalyptus essential oil was successfully developed to provide soothing and antiseptic effects for oropharyngeal use.

2. Technological evaluation confirmed the suitability of glycerin and polysorbate-80 as excipients, ensuring proper solubilization, viscosity, and formulation stability.

3. Among five tested formulations, F3 and F4 were identified as optimal. F3 demonstrated the best balance of sprayability, stability, and user comfort.

4. F3 remained physically stable for 30 days under room and accelerated storage conditions, maintaining acceptable pH, viscosity, and appearance.

5. Sensory testing confirmed that F3 was well tolerated, pleasant in taste, and effective in throat coating without irritation.

6. The study demonstrated that an effective, plant-based mucosal spray can be developed using simple pharmaceutical methods and herbal actives.

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Olena RUBAN

"02" September 2024

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Zoubaier IBRAHIM

1. Topic of qualification work: «Development of the composition of a throat spray with soothing and antiseptic action based on licorice extract and eucalyptus essential oil», supervisor of qualification work: Dmytro Soldatov, PhD, assoc. prof.,

approved by order of NUPh from "27" of September 2024 № 237

2. Deadline for submission of qualification work by the applicant for higher education: May 2025.

3. Outgoing data for qualification work: to develop and experimentally justify the composition of a throat spray with soothing and antiseptic action based on licorice extract and eucalyptus essential oil

4. Contents of the settlement and explanatory note (list of questions that need to be developed): introduction, literature review, objects and methods of research, experimental part, conclusions, list of used sources

5. List of graphic material (with exact indication of the required drawings):
tables – 25

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1	Dmytro SOLDATOV, PhD, assoc. prof. of higher education institution of department Industrial technology of medicines and cosmetics	09.09.2024	09.09.2024
2	Dmytro SOLDATOV, PhD, assoc. prof. of higher education institution of department Industrial technology of medicines and cosmetics	18.11.2024	18.11.2024
3	Dmytro SOLDATOV, PhD, assoc. prof. of higher education institution of department Industrial technology of medicines and cosmetics	03.02.2025	03.02.2025

7. Date of issue of the assignment: «02» September 2024.

CALENDAR PLAN

№ з/п	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1	Preparation of literature review	September 2024	**done**
2	Experiment planning	October-December 2024	**done**
3	Conducting an experiment	January-March 2025	**done**
4	Registration of results	April 2025	**done**
5	Submission to the examination commission	May 2025	**done**

An applicant of higher education _____ Zoubaier IBRAHIM

Supervisor of qualification work _____ Dmytro SOLDATOV

ВИТЯГ З НАКАЗУ № 237

По Національному фармацевтичному університету

від 27 вересня 2024 року

Затвердити теми кваліфікаційних робіт здобувачам вищої освіти 5-го курсу Фм20(4,10д) 2024-2025 навчального року, освітньо-професійної програми – Фармація, другого (магістерського) рівня вищої освіти, спеціальності 226 – Фармація, промислова фармація, галузь знань 22 Охорона здоров'я, денна форма здобуття освіти (термін навчання 4 роки 10 місяців), які навчаються за контрактом (мова навчання англійська та українська) згідно з додатком № 1.

Прізвище, ім'я здобувача вищої освіти	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
по кафедрі промислової технології ліків та косметичних засобів				
Ібрагім Зубаір	Розробка складу спрею для горла із заспокійливою та антисептичною дією на основі екстракту солодки та ефірної олії евкаліпту	Development of the composition of a throat spray with soothing and antiseptic action based on licorice extract and eucalyptus essential oil	доц. Солдатов Д.П.	доц. Ковальов В.В.

Ректор

Вірно, секретар

ФА2.8-03-317

ВИСНОВОК

експертної комісії про проведену експертизу
щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

«05» травня 2025 р. № 331121132

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти Ібрагім Зубаір, групи Фм20(4,10д)англ-02, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» навчання на тему: «Розробка складу спрею для горла із заспокійливою та антисептичною дією на основі екстракту солодки та ефірної олії евкаліпту / Development of the composition of a throat spray with soothing and antiseptic action based on licorice extract and eucalyptus essential oil», експертна комісія дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Голова комісії,
проректор ЗВО з НПР,
професор **Інна ВЛАДИМИРОВА**

Ф А 2.2.1-32-353

REVIEW

of scientific supervisor for the qualification work of the master's level of higher education of the specialty 226 Pharmacy, industrial pharmacy

Zoubaier IBRAHIM

on the topic: **«Development of the composition of a throat spray with soothing and antiseptic action based on licorice extract and eucalyptus essential oil»**

Relevance of the topic. The development of throat sprays with soothing and antiseptic action is highly relevant, given the widespread use of oropharyngeal products for rapid symptom relief and localized treatment. The combination of licorice extract and eucalyptus essential oil offers a natural, patient-friendly alternative for managing throat irritation and infections.

Practical value of conclusions, recommendations and their validity. The study presents valuable insights into the formulation of throat sprays, including the selection of active ingredients, optimization of spray properties, and stability testing. The recommendations are practical and directly applicable to small-scale production, providing a solid foundation for further development.

Assessment of work. The work demonstrates a systematic approach to formulation research, with clear presentation of experimental data and well-structured conclusions. The author has effectively addressed the challenges of formulating natural sprays, including solubility, stability, and sensory acceptability.

General conclusion and recommendations on admission to defend. In general, the qualification work of the applicant deserves high marks, meets the requirements and can be submitted for official defense to the examination commission of the National University of Pharmacy.

Scientific supervisor _____ Dmytro SOLDATOV

« 15 » of May 2025

Ф А 2.2.1-32-356

REVIEW

for qualification work of the master's level of higher education, specialty 226 Pharmacy, industrial pharmacy

Zoubaier IBRAHIM

on the topic: **«Development of the composition of a throat spray with soothing and antiseptic action based on licorice extract and eucalyptus essential oil»**

Relevance of the topic. The development of throat sprays based on licorice extract and eucalyptus essential oil is highly relevant, given the demand for effective, natural oropharyngeal treatments. These ingredients are known for their soothing, antiseptic, and anti-inflammatory properties, making them well-suited for throat spray formulations.

Theoretical level of work. The work demonstrates a strong theoretical foundation, covering the pharmacological effects of the active ingredients and the technological aspects of spray formulation. The author appropriately selected excipients to optimize stability and patient comfort.

Author's suggestions on the research topic. The study presents practical approaches to improving spray formulation, including the selection of solubilizers and stabilizers for enhancing bioavailability and sensory characteristics. The author effectively addressed challenges related to taste masking and spray consistency.

Practical value of conclusions, recommendations and their validity. The findings provide clear guidelines for developing stable, high-quality throat sprays, supporting both small-scale and industrial production. The results are directly applicable to the pharmaceutical industry.

Disadvantages of work. Minor typographical errors were noted, but they do not significantly affect the overall quality or scientific validity of the work.

General conclusion and assessment of the work. The qualification work of the applicant deserves high marks, meets the requirements and can be submitted for official defense to the examination commission of the National University of Pharmacy.

Reviewer _____ assoc. prof. Volodymyr KOVALOV

« 15 » of May 2025

Ф А2.2.1-91-287

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

Витяг з протоколу
засідання кафедри технологій фармацевтичних препаратів НФаУ
№ 12 від 16 травня 2025 року

Голова: завідувачка кафедри, доктор фарм. наук, проф. Рубан О. А.

Секретар: к. фарм. н., доц. Січкар А. А.

ПРИСУТНІ: зав. каф., проф. Рубан О.А., проф. Ковалевська І.В., проф. Бобрицька Л.О., проф. Гриценко В.І., проф. Сліпченко Г.Д., проф. Кухтенко О. С., доц. Безрукавий Є. А., доц. Кутова О. В., доц. Манський О. А., доц. Ніколайчук Н. О., доц. Пуляєв Д.С., доц. Січкар А. А., доц. Солдатов Д. П., доц. Трутаєв С. І., ас. Пономаренко Т.О.

ПОРЯДОК ДЕННИЙ:

1. Про представлення до захисту в Екзаменаційну комісію кваліфікаційних робіт здобувачів вищої освіти випускного курсу НФаУ 2025 року випуску

СЛУХАЛИ: Про представлення до захисту в Екзаменаційній комісії кваліфікаційної роботи на тему: «Розробка складу спрею для горла із заспокійливою та антисептичною дією на основі екстракту солодки та ефірної олії евкаліпту»

здобувача вищої освіти випускного курсу Фм20(4,10д.)англ-02 групи НФаУ 2025 року випуску _____Зубаір ІБРАГІМ_____
(ім'я, прізвище)

Науковий (-ві) керівник (-ки) к.фарм.н., доц. Дмитро СОЛДАТОВ_____
Рецензент_____к.фарм.н., доц. Володимир КОВАЛЬОВ_____

УХВАЛИЛИ: Рекомендувати до захисту кваліфікаційну роботу здобувача вищої освіти _5_ курсу Фм20(4,10д.)англ-02 групи___Зубаір ІБРАГІМ__
(ім'я, прізвище)

на тему:__ «Розробка складу спрею для горла із заспокійливою та антисептичною дією на основі екстракту солодки та ефірної олії евкаліпту»

Голова
завідувачка кафедри,
доктор фарм. наук, проф. _____ Олена РУБАН
(підпис)

Секретар
к. фарм. н., доцент _____ Антоніна СІЧКАР
(підпис)

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Зубаір ІБРАГІМ до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньо-професійною програмою Фармація
на тему: «Розробка складу спрею для горла із заспокійливою та антисептичною дією на основі екстракту солодки та ефірної олії евкаліпту».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Микола ГОЛІК /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Зубаір ІБРАГІМ виконав кваліфікаційну роботу на високому рівні, з логічним викладенням матеріалу та обговоренням, оформлення роботи відповідає вимогам НФаУ до випускних кваліфікаційних робіт та робота може бути рекомендована до захисту в ЕК НФаУ.

Керівник кваліфікаційної роботи

_____ Дмитро СОЛДАТОВ

« 15 » of May 2025 р.

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Зубаір ІБРАГІМ допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувачка кафедри
технологій фармацевтичних препаратів

_____ Олена РУБАН

« 16 » of May 2025 року

Qualification work was defended

of Examination commission on

« ___ » _of June_ 2025

With the grade _____

Head of the State Examination commission,

DPharmSc, Professor

_____ / Volodymyr YAKOVENKO /