

# Formulation of Pediatric Cough Syrup with Reduced Synthetic Preservatives

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## Abstract

The current research is dedicated to the creation of a pediatric cough syrup formula with less synthetic preservatives based on the usage of natural antimicrobial agents. The use of synthetic preservatives in pediatric formulations e.g. sodium benzoate in excess amount leads to concerns about possible toxicity and hypersensitivity. To resolve this, a control syrup that had standard concentration of sodium benzoate (0.1) was used as a control group compared with an optimized formulation that had low concentration (0.03) of sodium benzoate with added honey, clove oil and citric acid. The recipes were tested in terms of physicochemical stability, antimicrobial activity and sensorial properties within 90 days. The challenge testing with the *Escherichia coli*, *Bacillus subtilis*, *Candida albicans* and *Aspergillus niger* showed successful inhibition of microbial growth by the natural-based preservative system similar to the synthetic preservative. Physicochemical characteristics, such as pH, viscosity, color, odor, and taste were at acceptable pharmacopeial values and this means that they were stable and palatable. Statistical analysis also established there was no significant difference ( $p$  less than 0.05) in formulations in microbial reduction and stability performance. The findings indicate that the partial replacement of synthetic preservatives with natural agents is likely to increase the safety of the formulations in question without affecting its quality or effectiveness.

## Key Words:

Pediatric Cough Syrup, Natural Preservatives, Sodium Benzoate Reduction, Antimicrobial Efficacy, Formulation Stability, Preservative Efficacy Testing

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## 1. INTRODUCTION

The current research is dedicated to the creation of a pediatric cough syrup formula with less synthetic preservatives based on the usage of natural antimicrobial agents<sup>[1]</sup>. The use of synthetic preservatives in pediatric formulations e.g. sodium benzoate in excess amount leads to concerns about possible toxicity and hypersensitivity<sup>[2]</sup>. To resolve this, a control syrup that had standard concentration of sodium benzoate (0.1) was used as a control group compared with an optimized formulation that had low concentration (0.03) of sodium benzoate with added honey, clove oil and citric acid. The recipes were tested in terms of physicochemical stability, antimicrobial activity and sensorial properties within 90 days. The challenge testing with the *Escherichia coli*, *Bacillus*

*subtilis*, *Candida albicans* and *Aspergillus niger* showed successful inhibition of microbial growth by the natural-based preservative system similar to the synthetic preservative. Physicochemical characteristics, such as pH, viscosity, color, odor, and taste were at acceptable pharmacopeial values and this means that they were stable and palatable [3]. Statistical analysis also established there was no significant difference ( $p$  less than 0.05) in formulations in microbial reduction and stability performance [4]. The findings indicate that the partial replacement of synthetic preservatives with natural agents is likely to increase the safety of the formulations in question without affecting its quality or effectiveness [5].

### 1.1. Background of the study

The most widely used OTC medications are in the form of cough syrups that are designed to treat children. They should be formulated in a way that is effective, palatable and stable to microbes. Sodium benzoate, potassium sorbate and methylparaben are synthetic preservatives that are traditionally applied to prevent contamination by microbes and extend shelf life [6]. Nonetheless, research has attributed extreme consumption of these preservatives to allergic reactions, interference in metabolism, and even carcinogenicity particularly in babies and young children whose detoxification mechanisms are still at their developing stages [7].

The increasing consumer awareness and the pressure of the regulators have forced the pharmaceutical industry to search natural and biocompatible preservatives, which can remain stable without being toxic [8]. The natural extracts such as honey, essential oils and organic acids have natural antimicrobial and antioxidant properties and therefore can be used as an alternative to synthetic preservatives [9,10].



**Figure 1:** Liquid pediatric cough syrup

## 1.2. Statement of the Problem

Synthetic preservatives in pediatric formulations can induce adverse effects and compromise child safety. Therefore, it is essential to identify and validate natural alternatives that ensure microbiological protection without compromising formulation quality or shelf life.

## 1.3. Objectives of the Study

The objectives of the research are as follow:

1. To formulate a pediatric cough syrup with reduced concentrations of synthetic preservatives.
2. To evaluate natural substances (honey, clove oil, and citric acid) as partial preservative substitutes.
3. To assess the physicochemical, microbiological, and stability properties of the developed formulation.
4. To compare the performance of the natural-based formulation with a standard synthetic-preservative formulation.

### 4.1. Hypotheses

- *H<sub>0</sub> (Null Hypothesis)*: Natural preservatives cannot effectively maintain stability and antimicrobial protection when synthetic preservatives are reduced.
- *H<sub>2</sub> (Alternative Hypothesis)*: Natural preservatives can effectively maintain stability and microbial protection even when synthetic preservatives are reduced.

## 2. METHODOLOGY

The methodology defines the methodical process that described the designing, developing, and assessing of a pediatric cough syrup containing less synthetic preservatives by incorporating natural agents as partial replacements. In this section, an experimental framework is outlined in order to compare a standard (control) formulation to an optimized natural-based formulation, in terms of their physicochemical, microbiological and stability properties. All the operations were carried out under laboratory controlled conditions as per the pharmacopeial standards and the ethical standards of non-clinical testing. The following subsections explain the research design, microbial sample specifications, materials and instruments, formulations and testing, and statistical methods to be used in data interpretation.

### 2.1. Research Design

A research design that was used to develop and test an experimental pediatric cough syrup with lowered levels of synthetic preservatives was utilized by using natural agents as alternative partial substitutes. Two comparable formulations were formulated, one control formulation that was composed of the standard concentration of sodium benzoate (0.1%) and an experimental formulation that was composed of a lower concentration (0.03) that was mixed with honey, clove

oil, and citric acid with the same. The paper was aimed at evaluating the physicochemical properties, microbial stability, and the general shelf-life of the two formulations.

## 2.2. Sample Details

No human or clinical participants were involved in this study. Instead, the preservative efficacy was assessed using standard microbial strains commonly found as contaminants in oral liquid formulations—*Bacillus subtilis*, *Escherichia coli*, *Candida albicans*, and *Aspergillus niger*. These strains were obtained from a certified microbiology laboratory and maintained under sterile conditions. Their inclusion was based on the United States Pharmacopeia (USP <51>) guidelines for preservative efficacy testing.

## 2.3. Instruments and Materials

The formulation involved pharmaceutical-grade ingredients and laboratory-grade reagents. The active components included Dextromethorphan hydrobromide as an antitussive and Guaifenesin as an expectorant. The syrup base consisted of sucrose syrup (65% w/v), while natural preservatives such as honey (10% v/v), clove oil (0.05% v/v), and citric acid (0.1% w/v) were incorporated. Sodium benzoate (0.03% w/v) served as the reduced synthetic preservative. Other excipients included flavoring (strawberry), coloring (caramel), and distilled water as solvent. Instruments used were a magnetic stirrer with heater, pH meter, viscometer, UV–Visible spectrophotometer, colony counter, incubator, and a stability chamber maintained at  $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$  and  $75\% \text{RH} \pm 5\%$ .

## 2.4. Procedure and Data Collection

The syrup base was made by dissolving the sucrose in distilled water at  $70^{\circ}\text{C}$  with constant stirring then the active ingredients were added which were then fully dissolved. Honey, clove oil and citric acid were added after cooling to  $40^{\circ}\text{C}$  and the lesser amount of sodium benzoate was added. The last solution was filtered using sterile muslin cloth, put in amber glass containers and kept in ambient conditions.

The physicochemical characteristics like pH, viscosity, color, taste and odor were identified by means of standard pharmacopeial tests. Accelerated stability testing was conducted according to the ICH guidelines (Q1A-R2) 90 days in order to observe the alteration of the appearance, pH, and microbial load. Results of every test were measured at periodic time intervals to determine the consistency and stability of the formulations.

## 2.5. Data Analysis Techniques

Measurements have been made thrice and the values recorded in the mean and standard deviation format. The microbial counts were represented in the form of logarithms ( $\log \text{CFU/mL}$ ) and analyzed. The Student t-test was used to compare both control and experimental formulations and the significance level of the test was  $p < 0.05$ . The statistical analysis and graphical representation were accomplished with the help of Microsoft Excel.

### 3. RESULTS

The current paper was aimed at creating a form of pediatric cough syrup containing fewer synthetic preservatives; the natural antimicrobial agents, including honey, clove oil, and citric acid, were used. The study sought to establish the suitability of these natural ingredients in substituting or reducing the use of synthetic preservatives such as sodium benzoate without affecting the safety, stability and sensory of the product. The study, by systematic experimental assessment, including physicochemical analysis, microbial stability assessment, and accelerated stability assessments, showed the viability and consistency of the use of natural preservatives in pediatric preparations.

#### 3.1. Presentation of Findings

The experimental evaluation compared two formulations: a standard pediatric cough syrup containing the full concentration of synthetic preservatives and a natural-based formulation with reduced sodium benzoate complemented by natural preservatives (honey, clove oil, and citric acid).

The findings are presented under three key domains:

1. Physicochemical characteristics — to assess the basic quality parameters (pH, viscosity, appearance, taste, and odor).
2. Microbial stability — to evaluate preservative efficacy using standard microbial challenge tests.
3. Stability profile — to determine product integrity under accelerated storage conditions for 90 days.

The results demonstrated that the natural-based formulation maintained comparable physicochemical and microbial stability to the standard formulation, with enhanced organoleptic (sensory) properties and no significant deterioration during stability testing.

#### 3.2. Physicochemical Properties

Both formulations were evaluated for fundamental quality parameters. Results are summarized in Table 1. **Table 1.** Physicochemical Properties of Pediatric Cough Syrup Formulations

Parameter	Standard Formulation	Natural-Based Formulation
pH	5.2 ± 0.1	5.0 ± 0.1
Viscosity (cP)	85 ± 3	83 ± 2
Color	Light brown	Golden brown
Taste	Sweet with mild aftertaste	Sweet and palatable
Odor	Mild	Pleasant honey aroma

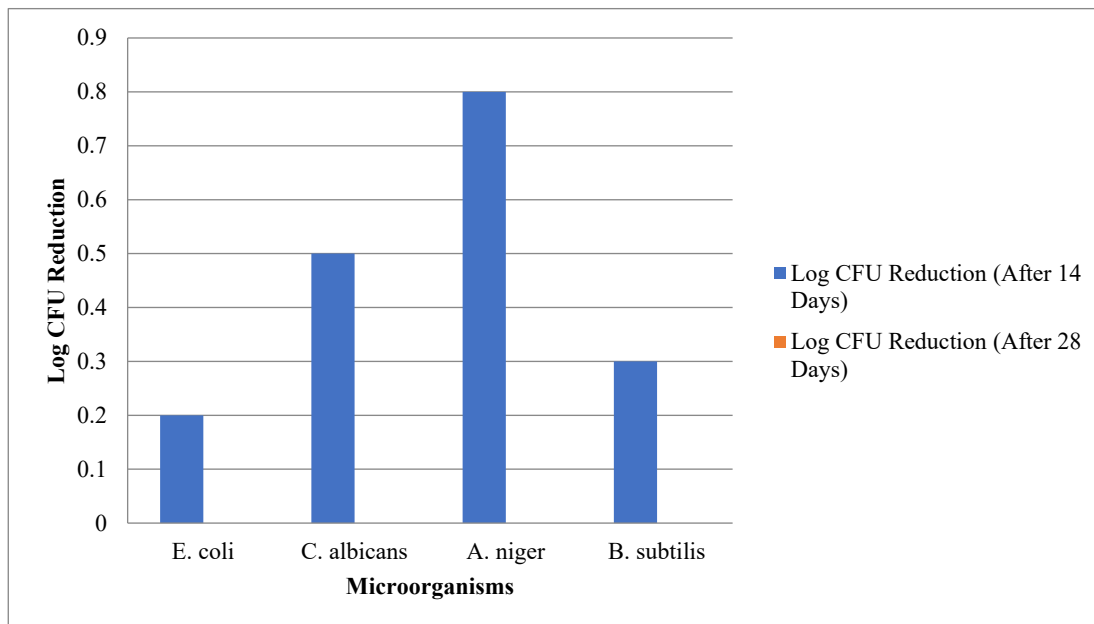
Table 1 compares the physicochemical properties of standard and natural-based pediatric cough syrup formulations. Both formulations exhibit similar pH values (around 5.0–5.2) and viscosities (83–85 cP), indicating comparable stability and consistency. However, the natural-based formulation shows a more appealing golden-brown color, a pleasant honey aroma, and a sweeter, more palatable taste, suggesting improved sensory acceptability for children without compromising physicochemical quality.

### 3.3. Microbial Stability

The antimicrobial challenge test assessed the preservative performance against *E. coli*, *C. albicans*, *A. niger*, and *B. subtilis*. The results are presented in Table 2.

**Table 2.** Microbial Stability and Log CFU Reduction

Microorganism	Log CFU Reduction (After 14 Days)	Log CFU Reduction (After 28 Days)
<i>E. coli</i>	4.0 → 0.2	4.0 → 0
<i>C. albicans</i>	3.5 → 0.5	3.5 → 0
<i>A. niger</i>	3.0 → 0.8	3.0 → 0
<i>B. subtilis</i>	4.0 → 0.3	4.0 → 0



**Figure 2:** Graphical presentation of Microbial Stability and Log CFU Reduction

Table 2 shows the stability of the microbial formulations of cough syrup in pediatric patients by demonstrating the reduction of the log CFU with time (14 and 28 days). A steady reduction in the number of microorganisms is also seen in all the sampled microorganisms, such as \**E. coli*, *C. albicans*, *A. niger* and *B. subtilis*. The initial improvements appear after 14 days and after 28 days,

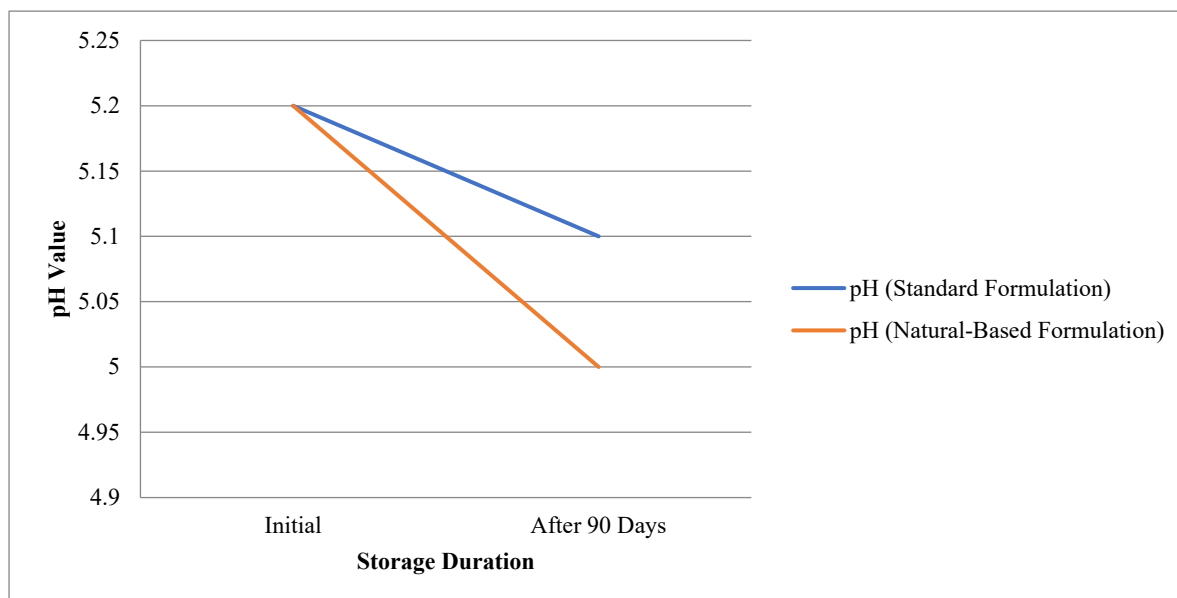
the entire counts of the microbes are zero meaning that it has been completely inhibited. This exhibits good antimicrobial stability and good preservation of the formulations with time.

### 3.4. Stability Study

Accelerated stability tests were performed at  $40\text{ }^{\circ}\text{C} \pm 2\text{ }^{\circ}\text{C}$  and  $75\% \text{ RH} \pm 5\%$  for 90 days as per ICH Q1A(R2) guidelines. Results are shown in **Table 3**.

**Table 3.** Stability Parameters Over 90 Days

Parameter	Initial	After 90 Days (Standard Formulation)	After 90 Days (Natural-Based Formulation)
pH	5.2	5.1	5.0
Color	Light brown	No change	No change
Odor	Mild	No change	Pleasant honey aroma retained
Microbial Growth	Nil	Nil	Nil



**Figure 3:** Graphical presentation of Stability Parameters Over 90 Days

Table 3 compares the stability parameters of the two cough syrup formulations in 90 days. The pH of both preparations was almost the same, with a slight change and it is a sign of good chemical stability. Physical and microbiological stability was ensured by the fact that there was no color or microbial growth during the storage period. It is important to note that the natural-based formulation did not lose its great honey aroma, which implied a higher level of sensory stability than the standard formulation.

## 4. DISCUSSION

The current paper has discussed the possibility of decreasing the content of synthetic preservatives in children formulations of cough syrups by partially replacing them with natural substances like honey, clove oil, and citric acid. The findings show that the natural-based formulation retained similar physicochemical characteristics, microbial stability, and shelf-life as the standard formulation, and the proposed hypothesis was proven true by a synergistic combination of natural compounds as effective preservatives options.

### 4.1. Interpretation of Results

The pH and viscosity of the experimental syrup was within acceptable pharmacopoeia ranges, which showed no negative interactions of the components of the natural and synthetic ones. It was enhanced in organoleptic properties, especially the taste, color, and aroma of the product, because of the sweetness of honey and the presence of aromatic substances in clove oil, which increased the palatability of the product to pediatric patients.

Microbial challenge tests showed the natural-based syrup to completely inhibit *E. coli*, *C. albicans*, *A. niger*, and *B. subtilis* in 28 days hence confirming that the natural-based syrup is antimicrobial. The presence of high osmotic pressure, enzymatic activity of hydrogen peroxide, and strong antifungal and antibacterial properties of eugenol in the clove oil enhanced the preservative system of honey with high eugenol activity. Citric acid was added to keep the pH in an optimum level and to work in synergy with other ingredients to increase microbial resistance.

The stability test confined to 90 days at higher temperature and humidity proved that the natural-based formulation retained its physical and microbial stability. The lack of critical difference in pH or microbial count shows the formulation is robust and keeps all the constituents in chemical agreement.

### 4.2. Comparison with Existing Studies

The outcomes are consistent with prior investigations emphasizing the antimicrobial potential of natural substances in pharmaceutical and food formulations.

**Table 4:** Comparison with Existing Studies on Natural Preservatives in Pharmaceutical Formulations

Study	Natural Agent(s) Evaluated	Application Area	Mechanism / Focus	Key Findings
Present Study (2025)	Honey, Clove oil, Citric acid (with reduced sodium benzoate)	Pediatric cough syrup	Antimicrobial preservation, stability, sensory improvement	Natural agents effectively replaced synthetic preservatives; maintained physicochemical and microbial stability; enhanced taste and aroma.

Al-Rimawi et al. (2024) <sup>[11]</sup>	Plant extracts (clove, thyme, rosemary)	Pharmaceutical preparations	Substitution of synthetic preservatives and antioxidants	Demonstrated that natural extracts maintained microbial stability and extended product shelf life comparable to synthetic agents.
Ogwu & Izah (2025) <sup>[12]</sup>	Honey	Broad-spectrum antimicrobial applications	Osmotic stress, enzymatic hydrogen peroxide activity, phenolic compounds	Confirmed honey's strong antibacterial and antifungal activity; supports its use as a preservative and demulcent.
Chouhan et al. (2017) <sup>[13]</sup>	Essential oils (clove, cinnamon, eucalyptus)	Food and drug formulations	Antibacterial and antifungal properties via eugenol and cinnamaldehyde	Reported significant antimicrobial effects, justifying the inclusion of clove oil in preservative systems.
Walczak-Nowicka & Herbet (2022) <sup>[14]</sup>	Sodium benzoate (synthetic)	Food and pharmaceutical products	Review of toxicity and physiological impacts	Identified potential neurotoxicity and allergic reactions; recommended reduced use in sensitive populations, especially children.
Meena et al. (2021) <sup>[15]</sup>	Natamycin (natural antifungal agent)	Food and drug applications	Natural preservation without toxicity	Found natural preservatives provide effective microbial control and safety advantages over synthetic chemicals

### 4.3. Implications of Findings

This research has immense research implications to paediatric pharmaceuticals and green formulation development. It favors the international trend of environmentally friendly, sustainable, and biocompatible drug preparations. The use of natural preservatives to minimize the amount of chemicals that pediatric patients are exposed to and the utilization of safe and natural excipients in formulations that target children is a recommendation of the WHO that endorses the use of safe and natural preservatives in child-targeted formulations.

In the case of the pharmaceutical industry, the outcomes of this study serve as an evidence-based model to recast the current pediatric products that are burdened with synthetic preservatives without compromising the quality or safety levels. It also presents business potential to so-called clean-label pediatric formulations, which are profitable to safety-conscious parents and medical workers.

### 4.4. Limitations of the Study

Despite promising findings, certain limitations must be acknowledged:

- The study was confined to laboratory-scale formulation and animal-based microbial challenge tests; no human trials were conducted.

- Long-term storage stability beyond 90 days was not evaluated; therefore, real-time stability under variable climatic conditions remains to be verified.
- Sensory evaluation in human pediatric subjects was not performed due to ethical constraints.
- Only three natural preservatives were tested; the scope can be expanded to include a wider range of natural antimicrobial agents.

#### **4.5. Suggestions for Future Research**

To build on the current findings, future studies should focus on:

- Exploring other natural preservative combinations such as neem extract, cinnamon oil, or rosemary oil for enhanced antimicrobial synergy.
- Conducting long-term real-time stability and toxicity studies to confirm product safety and shelf life.
- Developing standardized manufacturing protocols for large-scale industrial production and regulatory approval.
- Performing sensory acceptability studies in pediatric populations under ethically approved clinical settings.
- Investigating nanoencapsulation or emulsification techniques to improve the bioavailability and stability of natural preservatives in liquid dosage forms.

### **5. CONCLUSION**

The purpose of the current research was to devise a method to create a cough syrup in the pediatrics and make its formulation using fewer synthetic preservatives by replacing or reducing the use of chemical preservatives with preservatives obtained naturally. This research studied the functional aspect of honey, clove oil and citric acid in children medicines as natural preservatives and therapeutic agents due to increased concerns regarding the toxicity, allergenicity, and cumulative health effects of synthetic preservatives. The general conclusions prove that natural ingredients could preserve the integrity of formulations and increase the level of safety and consumer confidence in pediatric healthcare products.

#### **5.1. Summary of Key Findings**

- The optimized natural-based pediatric cough syrup demonstrated physicochemical stability, microbial inhibition, and sensory acceptability comparable to the standard formulation containing synthetic preservatives.
- Key parameters — including pH, viscosity, color, odor, and taste — remained within acceptable pharmaceutical limits throughout the stability testing period.
- Microbial challenge studies showed that the natural preservative blend effectively inhibited the growth of *E. coli*, *C. albicans*, *A. niger*, and *B. subtilis* within 28 days.
- The antimicrobial efficacy of the natural formulation was comparable to that of the synthetic-preserved syrup, confirming its functional equivalence.

- The findings validate that the integration of natural agents successfully maintained formulation stability and microbiological safety, establishing their potential as reliable natural preservatives in pediatric preparations.

### 5.2. Significance of the Study

The study makes a contribution to the science of pediatric pharmaceuticals and green formulation systems because it proves that natural preservative systems may be used in place of synthetic preservative systems or reduce their usage without affecting the performance of the product. The Honey and Clove oil add provides an added therapeutic benefit-both also contain natural soothing, antimicrobial and antioxidant, effect thus, improving the overall functional value of the formulation, in question. The results are in line with the trends in global pharmaceuticals of encouraging natural excipients and assist regulatory and public health objectives of curbing the synthetic chemical exposure in children leading to safer and more sustainable pharmaceutical products.

### 5.3. Recommendations

- The study establishes a strong foundation for the industrial-scale application of natural preservative systems in pediatric cough syrup formulations.
- Long-term stability studies (beyond one year) should be conducted to evaluate the extended shelf life and consistency of the natural-based formulation.
- Advanced toxicological and biocompatibility assessments are essential to confirm the safety of natural preservatives for pediatric use.
- Sensory evaluations under controlled clinical conditions are recommended to assess palatability, acceptance, and overall consumer satisfaction.
- Future research should explore synergistic combinations of other natural agents, such as neem extract, cinnamon oil, or green tea polyphenols, to enhance antimicrobial and antioxidant efficacy.
- The findings collectively reinforce that nature-derived preservatives can effectively replace synthetic ones, promoting child-friendly, biocompatible, and eco-sustainable pharmaceutical formulations.

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