RESEARCH ARTICLE

An Innovative Approach Towards Taste Masking: Formulation and Evaluation of Clarithromycin Suspension for Pediatrics

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ABSTRACT

This research addresses the critical need for palatable pediatric formulations of Clarithromycin, a widely used antibiotic, by developing a taste-masked liquid suspension. The study aims to identify effective taste-masking techniques to create a stable, ready-to-use formulation that conceals the bitter taste of Clarithromycin, improving its acceptability among pediatric patients. Given the challenges with administering solid dosage forms and granules to children, the research focuses on developing a more user-friendly alternative. Various taste-masking agents and techniques were investigated to ensure optimal taste-masking without compromising the drug's stability, safety, or efficacy, with Carbopol 974P explored as a key agent. Utilizing the Box-Behnken design, the formulation was optimized, and stability studies assessed its shelf life and effectiveness under different storage conditions. By developing a liquid suspension, this research aims to enhance adherence and treatment outcomes in pediatric patients by providing a more acceptable and user-friendly medication.

Keywords: Palatable Pediatric Formulation, Taste Masked liquid Suspension, Carbopol 974P, Box Behnken Design.

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INTRODUCTION

Even though administering different dose forms orally is the easiest and simplest method, swallowing solid dosage forms presents a significant obstacle for pediatric patients since many young patients are unwilling and unable to swallow, which results in low compliance among patients.[1] It is simple to get around this by using a liquid formulation. However, the majority of medications have an unpleasant taste or irritate the oral mucous membranes, which might impair compliance among patients.[2] Drugs having a bitter taste can impact patient compliance, which represents a key limitation in the effectiveness of the therapy.[3] A particular approach for increasing patient acceptability is to mask the bitter or unpleasant taste of medications.[4] In human beings, there are a total of twenty-five intact bitter receptor genes, twenty-one of which have ligands identified. Nevertheless, recent evidence suggests that bitterness is not experienced in a single, unified sense, and the assumption that bitterness is just an indicator of harmful substances to avoid is an over simplification.[5]

According to one estimate, more than half of patients neglect to administer their prescriptions as recommended simply because they dislike the taste.[6] This denotes the necessity to mask the bitter taste of drugs and to achieve this goal, several ways have been used. Taste masking is the technique of diminishing or removing the sense of disagreeable tastes caused by specific drugs so that they are more palatable to patients. Multiple methods have been disclosed to mask the bitter taste of the medication[7] such as the application of additives such as sweeteners, Flavors, and amino acids.[8] The use of local anaesthetic drugs such as phenol and phenolic derivatives to anesthetize the taste buds, the use of traditional granulation technique, the use of polymeric dispersion for coating of the bitter drug.[9] Preparing a complex of unpleasant API with ion exchange resins to produce a resonate and then utilizing that resonate[10] use of various methods including freeze-drying[11-13] usage of β-cyclodextrin to produce a complex with bitter-tasting drug.[14,15] To make the medication more palatable, different emulsion forms are prepared and additional excipients such as starch, gelatin, liposomes, lecithin, surfactants, polymeric membrane, or salts and are added to mask the unpleasant aftertaste.[16-18]

A second-generation highly bitter macrolide antibiotic called Clarithromycin (CLA) is employed to treat a variety of diseases in adults and children.[19] It is a powder made of white crystals. When susceptible bacteria cause infections of the respiratory system in young people, such as pneumonia, bronchitis, and sinusitis, Clarithromycin is frequently used as a treatment. Treatment with Clarithromycin has been shown to have great overall clinical effectiveness and good bacteriological elimination. However, because of Clarithromycin's strong bitterness, several methods have been used to hide it in pharmaceutical products. Since children have trouble swallowing solid dose forms and the medication has an unpleasant taste, the only commercially available preparations of Clarithromycin are film-coated, extended-release tablets and granules for suspension.[20,21]

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Table 1: Formulation steps of Clarithromycin Suspension

Step	Action	Description
Step 1: Preparation of Carbopol Suspension	1. Choose Carbopol for its thickening and suspending properties. 2. Accurately weigh Carbopol to ensure correct proportion. 3. Use distilled water as a solvent to minimize impurities. 4. Continuously stir on a magnetic stirrer for one hour to hydrate Carbopol fully, forming a gel-like matrix. Allow the suspension to settle undisturbed to further hydrate Carbopol, ensuring uniform dispersion.	Carbopol is selected and weighed accurately before being dissolved in distilled water with continuous stirring for an hour. Allowing the suspension to settle after stirring facilitates further hydration and uniform dispersion.
Step 2: Preparation of Sodium Alginate Suspension	1. Choose Sodium Alginate for its gelling and thickening properties. 2. Gradually add Sodium Alginate to distilled water under continuous stirring to prevent clumping. 3. Stir for 1-2 hours for complete dissolution and dispersion, ensuring uniformity. 4. Sodium alginate serves as a suspending agent to maintain a uniform distribution of drug particles.	Sodium Alginate is gradually added to distilled water while stirring continuously to prevent clumping. Stirring continues for 1-2 hours to ensure complete dissolution and dispersion.
Step 3: Preparation of Sucrose Syrup	1. Heat a mixture of sucrose and water for dissolution. 2. Stir continuously during heating to ensure uniform mixing and prevent localized overheating.	Sucrose syrup is prepared by heating a mixture of sucrose and water, with continuous stirring to ensure complete dissolution and uniform mixing.
Step 4: Preparation of Drug Solution	1. Dissolve Clarithromycin in propylene glycol solvent to enhance solubility. 2. Accurately measure the drug to ensure the desired dose. Stir continuously for 1-2 hours for complete dissolution, forming a clear solution.	Clarithromycin is dissolved in propylene glycol with continuous stirring for 1-2 hours to ensure complete dissolution and formation of a clear solution.
Step 5: Formulation of Suspension	1. Add Carbopol suspension, sodium alginate suspension, drug solution, and sucrose syrup under continuous stirring. 2. Slow addition of each component to prevent phase separation. Incorporate sodium benzoate, flavor, and colorant for stability and appeal. Vigorously stir for 30-45 minutes.	The suspension is formulated by sequentially adding components under continuous stirring, ensuring thorough mixing and uniform distribution of particles and excipients. Vigorous stirring for 30-45 minutes ensures complete homogenization.

The goal of this research is to improve patient acceptability and efficacy by forming a liquid suspension of Clarithromycin that is palatable to children.[22,23] The study also demonstrates that the bitterness masking method for Clarithromycin may be inexpensively and quickly used throughout the pharmaceutical industry without requiring specific equipment.[24] The current study focuses on using Carbopol 974P absorption to mask the bitter taste of Clarithromycin.[25,26] The mechanism is forming an ionic link with high molecular weight polyacrylic acid, the amine macrolide removes the drug from the solution phase and forms an ion-free suspension. The macrolide-Carbopol complexes were made into a taste-masked liquid solution using a straightforward agitation technique.[27]

MATERIALS AND METHOD

Materials

Clarithromycin was received as a gift sample from Ajanta Pharma Limited, Mumbai, India. Carbopol 974P was obtained as a gift sample from Lubrizol. Sucrose was obtained from Sisco Research
Laboratories Pvt. Ltd. (SRL), Sodium Benzoate was procured from Sisco Research Laboratories Pvt. Ltd. (SRL), Sodium Alginate was obtained from Analab Fine Chemicals, Mumbai, Propylene glycol was procured from Analab Fine Chemicals, Mumbai. Raspberry Flavour was obtained from Research Lab Fine Chem Industries. All other ingredients were of Laboratory grade.

Table 2: Variables in Box Behnken Design

Independent Variables	Levels		
Ingredients	Low(-1)	Medium(0)	High(+1)
Carbopol 974P	0.5%	1%	1.5%
Sodium Alginate	3%	4%	5%
Sodium Benzoate	0.25%	0.075%	0.125%

Method of Preparation

Clarithromycin liquid Suspension is prepared by simply stirring on a magnetic stirrer[26]

Characterization of Clarithromycin

Fourier Transform-Infrared Spectroscopy Study of Clarithromycin and Taste Masked Suspension

FTIR analysis was employed to identify the drug and compare its formulation, focusing on distinctive peak identification for functional group characterization and impurity detection. The study utilized Bruker Alpha E Opus Software to scan samples across the spectral range of 4000-

Table 3: Responses for variable batches of Formulation

Runs	Independent Variables			Dependent Variables	
	A: Sodium Alginate (gm)	B: Carbopol 974P (gm)	C: Sodium Benzoate (gm)	Viscosity (cp)	DC (%)
1	0.6	0.3	0.0375	400.1	84.52
2	1	0.2	0.025	400.9	84.52
3	0.6	0.1	0.0375	296.1	96.03
4	0.6	0.2	0.025	300.4	97.04
5	0.6	0.2	0.05	297.2	88.56
6	0.8	0.3	0.025	310.3	97.04
7	1	0.1	0.0375	320.9	82.50
8	0.8	0.1	0.05	320.10	89.17
9	1	0.3	0.0375	420.10	98.20
10	0.8	0.1	0.025	298.1	93.00
11	0.8	0.2	0.0375	410.10	94.01
12	1	0.2	0.05	410.15	84.52
13	0.8	0.3	0.05	310.5	95.02

400 cm^{-1}, capturing and recording characteristic peaks essential for a rigorous comparative assessment. By aligning observed wave numbers with a reference spectrum, the method facilitated a comprehensive evaluation of the drug's API and its formulated state.

Differential Scanning Calorimetry

The DSC technique was employed as a thermal analysis tool to measure changes in the physical properties of a sample concerning temperature over time, using a Shimadzu instrument. As reported, the DSC thermogram of 1 mg Clarithromycin was obtained, revealing its characteristic melting point range of 217^0C to 230^0C.

Development of Clarithromycin Suspension

Use of Box-Behnken Design to Achieve Optimized Batch of Suspension[28]

In this research, a taste-masked oral suspension of Clarithromycin was optimized using a Box-Behnken design, focusing on the concentrations of Sodium Benzoate, Carbopol 974P, and Sodium Alginate. These were chosen as independent variables for their impact on the suspension's rheological characteristics, stability, and flavour masking. Carbopol 974P and Sodium Alginate are used for taste masking and as viscosity enhancers, respectively, aiding in prolonged oral cavity residency. Sodium Benzoate acts as a preservative due to its antibacterial properties. The study focused on viscosity and drug content as dependent variables, both crucial for the suspension's pharmaceutical quality and patient acceptance.

The concentration variables of these three polymers are mentioned below in Table No.2 from the trial batches and inputted in the Design Expert Software to get an optimized batch.

Evaluations of Taste Masked Clarithromycin Suspension

Fourier Transform of Clarithromycin Suspension

FTIR analysis was employed to identify clarithromycin in both its active pharmaceutical ingredient (API) and formulation stages. This analytical method involves examining characteristic peaks across the spectrum from 4000 to 400 cm^{-1}. By comparing these peaks with a reference spectrum, functional groups were determined and impurities detected. This approach facilitated a comprehensive comparison between the API and its formulation, ensuring consistency and quality throughout the manufacturing process.

Determination of Sedimentation Volume (F)

The sedimentation volume was calculated to assess the suspensions' physical stability. A 50 ml graduated cylinder was filled with 20 ml of each solution and inverted three times to distribute the suspension. The initial sediment volume (Vo) was measured after three minutes. The cylinder was left undisturbed for two weeks, and the ultimate sediment volume (Vu) was measured on the seventh day. Sedimentation volume (F) was calculated as

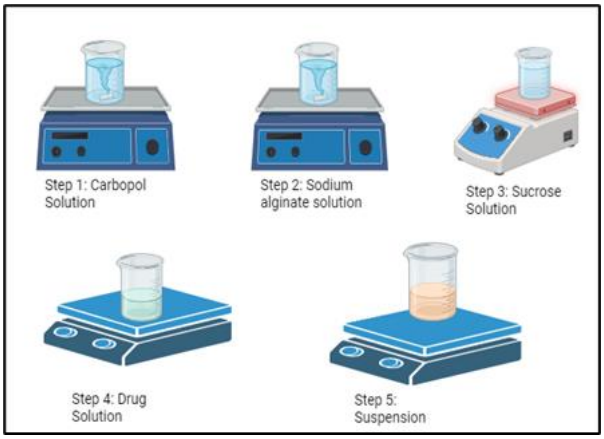

Figure 1: Steps of Preparation of Clarithromycin Suspension

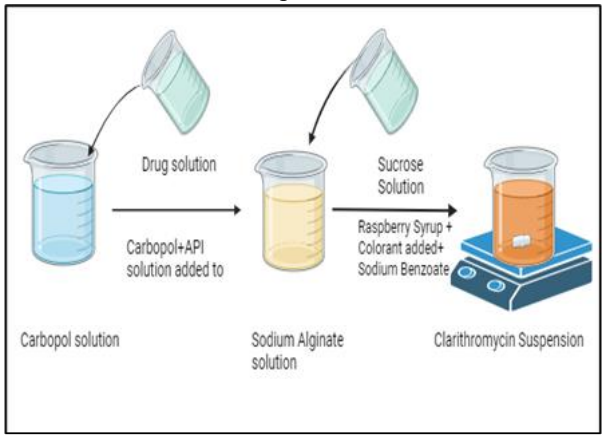

Figure 2: Order of Addition of all Excipients

Table 4: Stability Study for Optimized Batch (CLA 9)

Conditions	Time Period	Physical Parameters		Chemical Parameters	
(25 ± 2°C/45 % RH ± 5% RH)	Days	Color	Viscosity (cp)	Drug Content (%)	pH
(25 ± 2°C/45% RH ± 5% RH)	10 days	No Change	420±0.03	98.20±2	5.5±0.1
(25 ± 2°C/45% RH ± 5% RH)	20 days	No Change	420±0.03	98.20±2	5.5±0.3
(25 ± 2°C/45% RH ± 5% RH)	30 days	No Change	418±0.04	98.18±1	5.5±0.1
(25 ± 2°C/45% RH ± 5% RH)	40 days	No Change	418±0.06	98.18±2	5.4±0.2
(25 ± 2°C/45% RH ± 5% RH)	50 days	No Change	418±0.05	98.18±1	5.4±0.2

Table 5: Rating Scale of Taste Evaluation

Parameters	Very Poor	Poor	Average	Good	Excellent
Taste			2	4	
Appearance				3	3
Aroma				2	4
Mouthfeel	1	2	2	1	
Sweetness	2	1	1	2	

F = Vu/Vo. F values range from 0 to 1, with 1 indicating an ideal suspension. Dispersibility was examined by inverting the cylinder until no sediment remained at the bottom. The results and commentary display the sedimentation volume findings

Determination of Viscosity

One important suspension characteristic is viscosity. The Brookfield DV-E Viscometer was used to test the viscosity. A glass beaker with a capacity of 25 ml has been filled with 20 ml of suspension. A stand is placed above the beaker to ensure that the viscometer's bob is fully submerged in the solution. The viscometer was operated at various RPMs once the switch was switched on. The viscosity of the suspension was measured using spindle number six.

Determination of pH

The suspension's pH was determined using a Digital pH meter.

Determination of Drug Content

The drug content of the liquid oral suspension was determined using centrifugation and UV spectrophotometry. After diluting the suspension sample with a 1.2 pH buffer and sonication for 30 minutes, the sample was centrifuged to remove insoluble components. The clear supernatant was then analysed using a UV spectrophotometer. The drug concentration was calculated

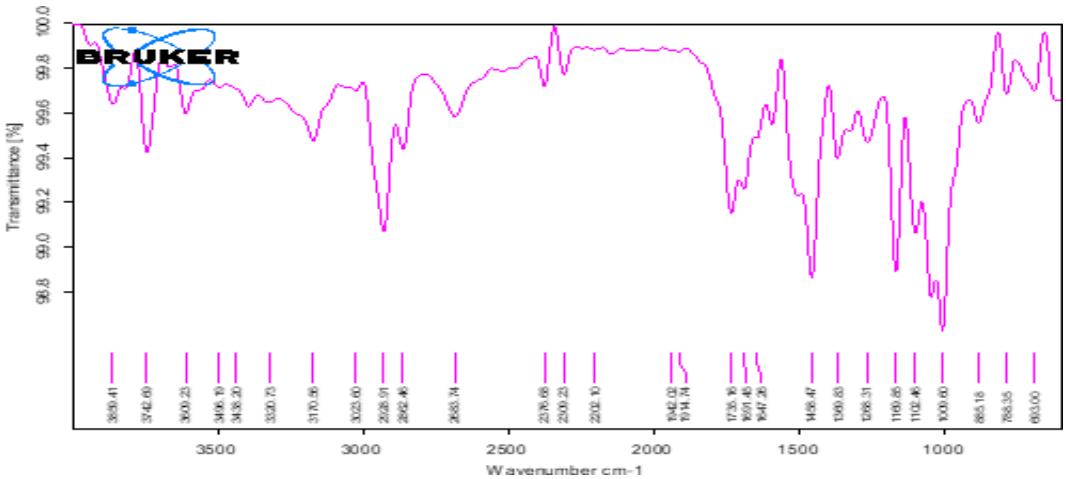

Figure 3: Fourier Transform-Infrared Spectroscopy of Clarithromycin

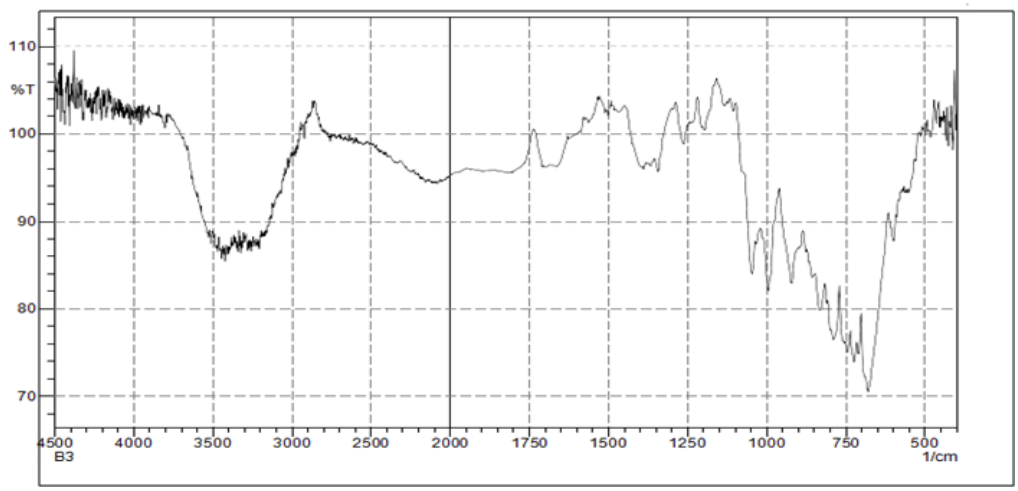

Figure 4: Fourier Transform Infrared Spectroscopy of Taste Masked Clarithromycin Suspension

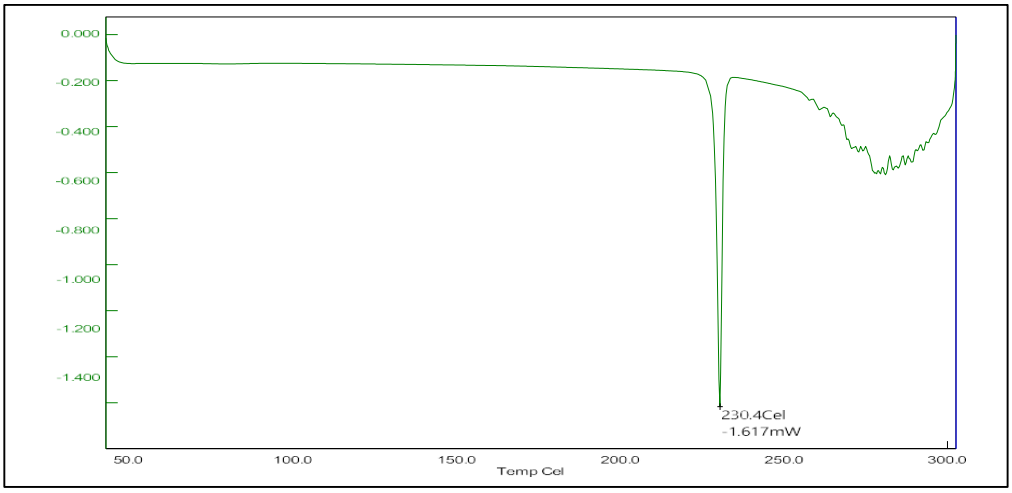

Figure 5: Differential Scanning Calorimetry (DSC) of Clarithromycin

by comparing the absorbance of the sample to a calibration curve built from standard solutions with known drug concentrations.

Determination of Texture

The qualities of suspension were ascertained using texture analysis. This test performed an analysis of spreadability and strength. The Brookfield Texture Analyzer CT3 was used to examine the suspension's texture.

Determination of Zeta Potential

The zeta potential was measured by Malvern zeta sizer. Before the measurement, the suspension was diluted with distilled water.

Freeze-Thaw Cycle

A freeze-thaw cycling study was conducted to evaluate the stability of an oral formulation of Clarithromycin under temperature conditions of -10°C and 25°C for two days for each condition for the same formulation, focusing on an optimized batch. This investigation involved subjecting the formulation to alternating freezing and thawing cycles to simulate potential storage and transportation conditions.[29]

Antimicrobial Study

The antibacterial activity was evaluated using the Zone Inhibition Method (Kirby Bauer method). MHA plates were inoculated with 100 µl of S. aureus culture (1.5 x 10^8 CFU/mL, 0.5 McFarland Unit). Discs containing 10 µl of various concentrations (0 to 100 mg/ml) were placed on the plates. A solvent-loaded disc served as the vehicle control, and a Ciprofloxacin disc (10 µg) was the positive control. Plates were incubated at 37°C for 24 hours. The clear inhibition zones around the discs were measured and recorded.

Stability Studies

The stability of the oral formulation of Clarithromycin was determined at Room Temperature at 25.8^{0}C /43RH for 50 days. Regular assessment was done for changes in physical parameters like color and sedimentation.

Taste Evaluation

To evaluate the taste masking effectiveness and overall palatability of the formulated Clarithromycin suspension, a 1 to 5 scaling method was used (1 = Very Poor, 2 = Poor, 3 = Average, 4 = Good, 5 = Excellent). Six adult volunteers, who provided consent, participated in the study. Each was given a consistent dose of the taste-masked suspension and rated its taste, appearance, aroma, mouthfeel, and sweetness using the scale.[30]

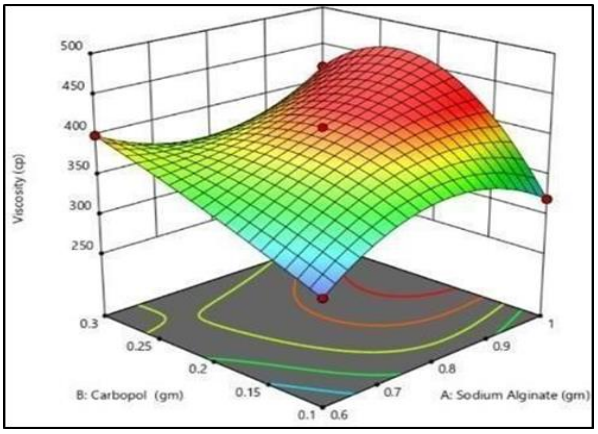

Figure 6: Effect of Carbopol and Sodium Alginate on Viscosity of Taste Masked Clarithromycin Suspension

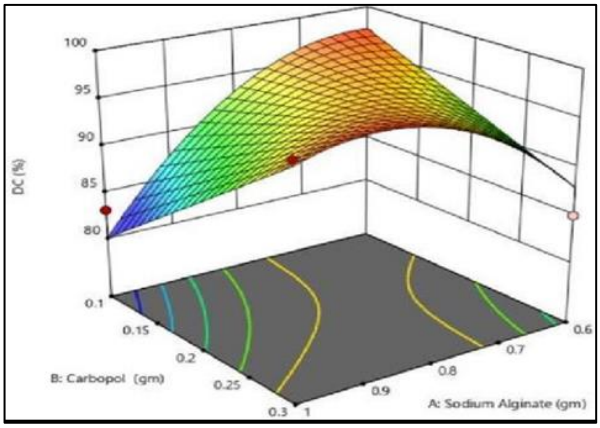

Figure 7: Effect of Carbopol and Sodium Alginate on Drug Content of Taste Masked Clarithromycin Suspension

RESULTS

Fourier Transform-Infrared Spectroscopy (FTIR) of Clarithromycin and Formulation

FTIR analyses of Clarithromycin in pure form and as a suspension formulation were conducted, revealing distinctive peaks characteristic of its functional groups. In

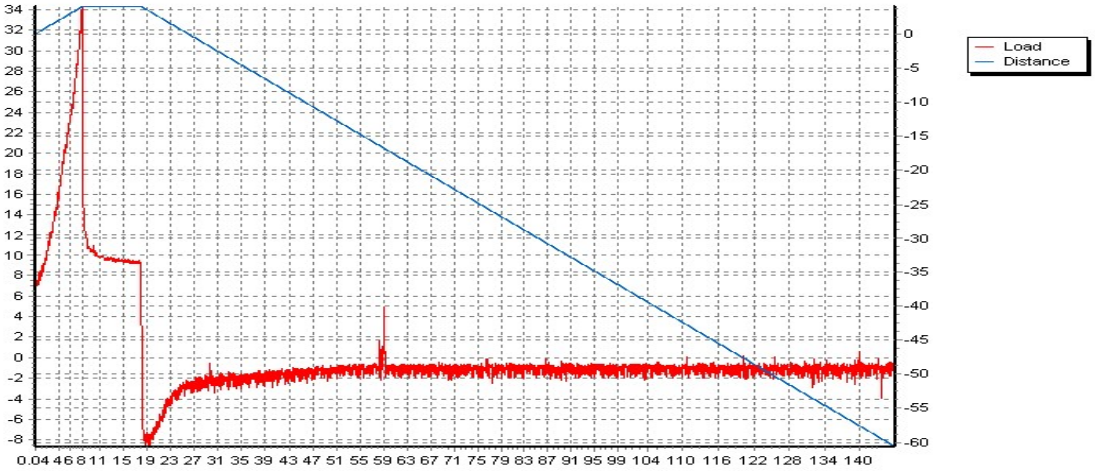

Figure 8: Texture Analysis of Taste Masked Clarithromycin Suspension

the pure form, peaks corresponding to ether (C-O-C stretching at 1002 cm^{-1}, 1102 cm^{-1}, 1169 cm^{-1}), alkyl CH_2 bending (1268 cm^{-1}), N-CH_3 stretching (1428 cm^{-1}), ketone and lactone C=O stretching (1691 cm^{-1}, 1735 cm^{-1}), alkane stretching (2928 cm^{-1}, 2859 cm^{-1}), and hydrogen-bonded hydroxyl groups (3496 cm^{-1}) confirmed the presence of ether, hydroxyl, carbonyl, ketone, and tertiary amine groups, verifying the drug's identity and purity. In contrast, the FTIR spectrum of the Clarithromycin suspension formulation exhibited peaks indicative of hydrogen-bonded OH (3450 cm^{-1}), alkane stretching (2780-3000 cm^{-1}, prominent at 3030.17 cm^{-1}), lactone carbonyl (1731 cm^{-1}), ketone carbonyl (1692 cm^{-1}), N-CH_3 (1422 cm^{-1}), and CH_2 bending (1340-1400 cm^{-1}). Minor shifts in peak positions suggested interactions with excipients, without altering the drug's fundamental functional groups. These analyses underscored the formulation's structural integrity, confirming the preservation of Clarithromycin's efficacy and purity in its suspended state, crucial for maintaining therapeutic effectiveness.

Differential Scanning Calorimetry (DSC)

DSC thermogram of Clarithromycin is shown in Figure 5. The result shows the melting point at 230.4°C. The reported melting point of Clarithromycin is 217 °C to 230 °C. This consistency in the melting point confirms the purity and authenticity of the Clarithromycin sample, indicating that the drug has not degraded and retains its expected thermal properties.

Experimental Runs with Input Independent Variable with Result of Output Response

A Box-Behnken Design (BBD) was used to optimize the concentrations of Carbopol 974P (taste masking and suspending agent), Sodium Alginate (viscosity enhancer), and Sodium Benzoate (preservative) across 13 batches, with the 9th batch coded as CLA 9 was identified as the optimized formulation. The independent variables were the concentrations of these agents, while the dependent variables were viscosity and drug content. Design Expert software and ANOVA confirmed the statistical significance of these factors. Graphic tools identified data abnormalities and evaluated each factor's impact. Key findings included a highly stable and homogeneous sedimentation volume with

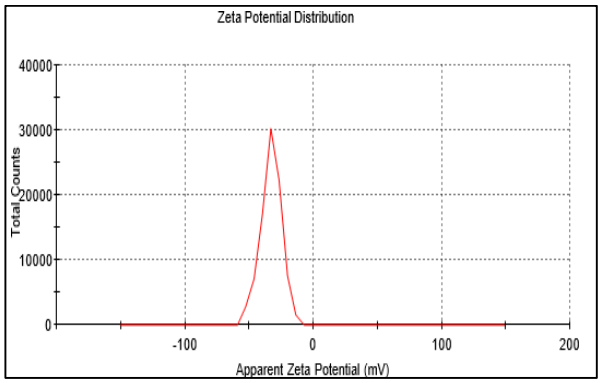

Figure 9: Zeta Potential of Taste Masked Clarithromycin Suspension

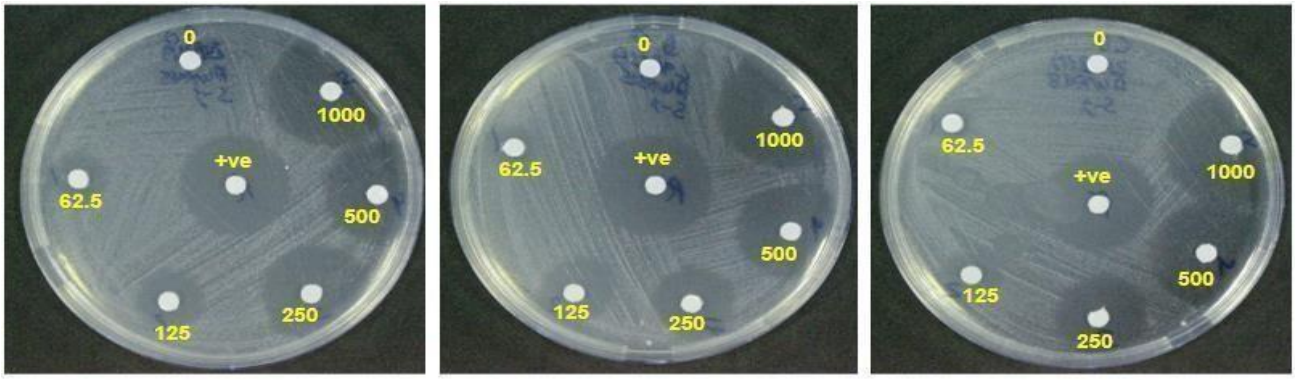

Figure 10: Antibacterial Zone Inhibition Test

minimal particle settling, essential for reliable dosage and patient compliance. Table No. 3 gives clear data regarding Independent Variables and Dependent Variables.

Results of Optimized Batch of Clarithromycin Suspension: Viscosity and Drug Content Optimization

A systematic exploration of Sodium Alginate (A), Carbopol 974P (B), and Sodium Benzoate (C) optimized both viscosity and drug content in the oral liquid suspension. The ninth experimental run, with 1 gm of Sodium Alginate, 0.3 gm of Carbopol 974P, and 0.0375 gm of Sodium Benzoate, was identified as optimal. This formulation achieved a viscosity of 420.10 cp, ensuring suitable flow properties and stability, and a drug content of 98.20%, indicating high drug incorporation and uniformity. Sodium Alginate contributed to the thickening and stabilizing properties, Carbopol 974P enhanced the viscosity and gel formation, while Sodium Benzoate acted as a preservative, ensuring formulation stability. These results highlight its potential for further development and commercialization.

ANOVA Data for Dependent Variable Viscosity

The ANOVA analysis reveals compelling and statistically significant insights into the formulation's viscosity. Sodium Alginate significantly contributes to thickening and stability by increasing the consistency and cohesiveness of the formulation. On the other hand, Carbopol 974P plays a crucial role in enhancing viscosity and gel formation, providing a smoother and more uniform texture. The model's R^2 value falls within the ideal range, indicating a strong and accurate correlation between these variables and viscosity, effectively explaining most of the observed variation. This high R^2 value underscores the model's reliability in predicting viscosity changes based on the concentrations of Sodium Alginate and Carbopol 974P. Overall, this statistically significant model proves to be a good fit for predicting viscosity, demonstrating its robustness and suitability for formulation optimization. Figure 6 shows the effect of Carbopol 974P and Sodium Alginate on Viscosity.

ANOVA Data for Dependent Variable Drug Content

The ANOVA analysis provides compelling and statistically significant insights into the formulation's drug content. Sodium Alginate significantly contributes to thickening and stability, while Carbopol 974P plays a crucial role in enhancing viscosity and gel formation. The model's R^2 value falls within the ideal range, indicating a strong correlation between these variables and drug content, effectively explaining most of the observed variation. This high R^2 value underscores the model's reliability in predicting drug content based on the concentrations of Sodium Alginate and Carbopol 974P. Overall, this statistically significant model proves to be a good fit for predicting drug content, demonstrating its robustness and suitability for formulation optimization. Figure 7 depicts the effect of Carbopol 974P and sodium Alginate on Drug Content.

Evaluations

Sedimentation Volume

Through careful examination, it was found to be 0.95 and the optimized batch's (CLA 9) sedimentation volume was close to 1, which indicates outstanding stability and homogeneity. This indicates that there is little particle settling, as both Carbopol 974P and Sodium Alginate are strong viscosity enhancers that don't allow the suspension to sediment. This emphasizes the formulation's strong suspension qualities which are crucial for reliable dosage administration and patient acceptance. The formulation's effectiveness in reducing sedimentation-related problems is highlighted by the observed low sedimentation volume, which confirms its applicability for practical use.

Viscosity

The optimized batch's (CLA 9) viscosity of 420 cps, maintained consistently, is ideal for ensuring the formulation's desired thickness and flow characteristics, crucial for safe and effective pediatric administration. This viscosity level, supported by Sodium Alginate and Carbopol 974P, ensures the suspension remains easy to handle, prevents particle settling, and maintains uniform drug distribution. These polymers enhance the suspension's stability and consistency, facilitating precise dosing and improving patient compliance.

pH

The pH of the optimized batch was found to be 5.5 which is similar to that of the marketed formulation of Clarithromycin which is between 4.9 to 5.5. The pH of the optimized Clarithromycin suspension, at 5.5, is ideal for pediatric use, aligning with the marketed formulation's range of 4.9 to 5.5. This pH ensures the drug's stability, preventing degradation and maintaining its efficacy. It also enhances the effectiveness of taste-masking agents like Sodium Alginate and Carbopol 974P, improving palatability. Additionally, the pH is gentle on mucous membranes, minimizing irritation and gastrointestinal discomfort.

Drug Content

The optimized batch showed a remarkable drug content of 98.20%. This high drug content is attributed to the synergistic effects of Sodium Alginate and Carbopol 974P. Sodium Alginate forms a gel matrix that encapsulates the drug, ensuring even distribution and sustained release, enhancing stability and bioavailability. Carbopol 974P, with its high viscosity and gelling properties, stabilizes the suspension, preventing drug particle aggregation and ensuring consistent drug concentration. These polymers maintain the suspension's integrity and homogeneity, maximizing drug content and therapeutic effectiveness.

Texture Analysis

As illustrated in Figure 8. The optimized formulation exhibits pseudoplastic flow behaviour with shear-thinning

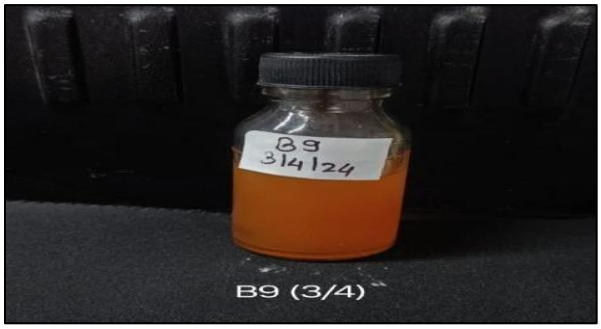

Figure 11: Formulated Clarithromycin Suspension

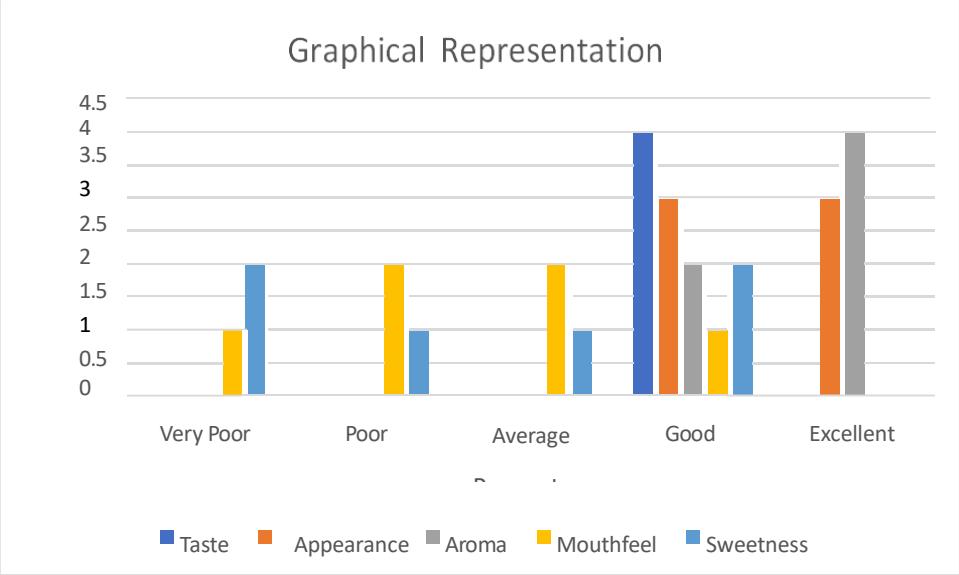

Figure 12: Ratings of Taste Masked Clarithromycin Suspension by Volunteers

properties. In this system, the relationship between shear rate and viscosity is nonlinear. At rest or low shear, long-chain molecules are disarranged and entangled, resulting in high viscosity. These molecules align under higher shear stress, such as agitation, decreasing viscosity, and enhancing flowability. This is due to the reorientation of molecular chains, facilitating particle movement and reducing flow resistance. The pseudoplastic behaviour indicates the formulation's ability to adapt to varying shear rates, making it suitable for applications requiring controlled flow properties.

Zeta Potential

The optimized batch's Zeta potential was -32.8 mV, as shown in Figure 9. Compared to the marketed Clarithromycin suspension (-14.8 mV), it is more stable. Zeta potential values between -30 mV and -60 mV are ideal for suspensions, providing strong electrostatic repulsion to prevent particle aggregation and ensure stability. The optimized suspension's Zeta potential of -32.8 mV indicates robust stability, minimizing particle aggregation, and enhancing uniformity and effectiveness.

Freeze-Thaw Cycle

The freeze-thaw cycling study conducted on the 9th batch of Clarithromycin oral formulation reaffirmed its stability under simulated temperature conditions of -10°C and 25°C. No visual changes indicative of formulation degradation was observed. This is because of agents like Carbopol 974P and Sodium Alginate that form a protective envelope or covering around the drug, reducing the risk of degradation and phase separation during freeze-thaw cycles. Carbopol 974P provides a stable, viscous gel structure, while Sodium Alginate enhances the formulation's ability to withstand mechanical stresses.

Antimicrobial Study

In the study, substance amounts measured in micrograms per disc across plates A, B, and C showed consistent positive control values of 22 µg/disc for plates A and B and 21 µg/disc for plate C. The negative control registered 0 µg/disc across all plates. As substance concentration increased from 62.5 µg/disc to 1000 µg/disc, variations were observed. Plates A and B exhibited gradual increases from 13 µg/disc to 22 µg/disc, while plate C showed slight deviations, particularly at 250 µg/disc (19 µg/disc vs. 20 µg/disc in other plates). All plates reached 22 µg/disc at 1000 µg/disc. Overall, the Clarithromycin suspension demonstrated effective antimicrobial activity comparable to the positive control, indicating its potential as an antimicrobial agent. Figure 10, shows the zone inhibition of Clarithromycin.

Stability Study

Stability was monitored visually for Color, Viscosity, Drug Content, and pH for fifty days of stability at Room temperature trial for the optimized batch. A visual evaluation of color changes was conducted as illustrated in Figure 11, and Table 4 noting any variations that would point to deterioration. These findings aided our assessment of the formulation's stability over time.

Taste Evaluation

The taste masking effectiveness and overall palatability of the Clarithromycin suspension were evaluated using a 1-5 scale. Most participants rated the taste as good (4/5), though none rated it excellent, indicating room for improvement. Appearance was rated as good by 3 participants and excellent by 3. Aroma received mixed reviews: 2 rated it as good and 4 as excellent. Mouthfeel had varied responses: 1 very poor, 2 poor, 2 average, and 1 good. Sweetness was mostly rated poor, with only 2 participants rating it as good. Below is Table 5 which depicts individual ratings for each parameter and also a graphical representation mentioned in Figure 12 which makes a clear comprehension in a statistical format.

The effective taste masking of the Clarithromycin suspension is attributed to Carbopol 974P and Sodium Alginate, which increase viscosity and reduce the drug's bitter taste, resulting in most participants rating the taste as good (4/5). Mixed reviews for appearance, aroma, mouthfeel, and sweetness indicate areas for improvement: consistency in appearance and aroma, better texture for

mouthfeel, and enhanced sweetness for overall palatability. While the formulation has strengths, optimizing taste masking and adjusting sweetness levels could further improve patient acceptance.

CONCLUSIONS

In conclusion, this project successfully developed and evaluated a taste-masked formulation of Clarithromycin tailored for pediatric use. By employing Carbopol 974 P polymer, the bitter taste of Clarithromycin was effectively masked, enhancing palatability and potentially improving patient compliance. The optimization process, utilizing the Box-Behnken design, identified optimal conditions for formulation preparation, ensuring both taste masking and stability. Comprehensive evaluations provided insights into formulation properties, guiding further refinement efforts. The use of oral liquid suspensions addressed challenges associated with solid dosage forms, offering a more palatable and easily administrable alternative for pediatric patients. Overall, this project underscores the significance of taste masking in pediatric formulations and demonstrates the efficacy of Carbopol 974 P polymer in enhancing medication acceptability.

DISCUSSION

This study successfully addressed the critical need for palatable pediatric formulations of Clarithromycin by developing a taste-masked liquid suspension. Utilizing Carbopol 974P, the formulation effectively improved the aroma and appearance of the suspension, enhancing its acceptability among pediatric patients. Carbopol 974P played a crucial role by encapsulating the drug particles, thereby preventing their interaction with taste receptors to some extent. However, further efforts are needed to achieve complete taste masking.

The optimization process, guided by the Box-Behnken design, identified optimal conditions for stability, ensuring a robust and effective formulation. Comprehensive stability tests, including sedimentation volume analysis, freeze-thaw cycle assessment, and pH measurement, provided valuable insights into the formulation's physical and chemical properties, confirming its robustness and stability. The use of oral liquid suspensions overcomes the challenges associated with administering solid dosage forms to children, offering a more palatable and easily administrable alternative. This improved palatability is expected to significantly enhance patient adherence and therapeutic outcomes. The findings of this study highlight the importance of effective taste masking in pediatric formulations.

By demonstrating the efficacy of Carbopol 974P in enhancing the aroma and appearance of Clarithromycin suspension, the research underscores its potential to improve medication compliance and treatment success in pediatric populations. Despite these successes, further optimization is required to fully mask the bitter taste.

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