RESEARCH PAPER

Development and Evaluation of Pediatric Dual-Layer Chewable Tablets Containing Paracetamol and Zinc

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ABSTRACT

The present study aimed to develop and evaluate a pediatric dual-layer chewable tablet containing paracetamol and zinc sulphate to provide effective fever and pain management along with nutritional and immune support in children. Pediatric patients often experience difficulties swallowing conventional tablets, making chewable dosage forms a more convenient and acceptable alternative. The dual-layer design was selected to accommodate both active ingredients within a single dosage unit while maintaining formulation stability and improving patient compliance.

Preformulation studies were conducted to assess the physicochemical properties of the active pharmaceutical ingredients and their compatibility with selected excipients. Fourier-transform infrared spectroscopy confirmed the absence of significant drug–excipient interactions. Powder blends were evaluated for flow and compression characteristics and demonstrated satisfactory bulk density, compressibility, and flowability suitable for direct compression. The tablets were formulated using microcrystalline cellulose, mannitol, crospovidone, aspartame, vanilla flavour, talc, and magnesium stearate.

The prepared tablets were subjected to post-compression evaluation, including weight variation, thickness, hardness, friability, drug content uniformity, and dissolution testing. All quality parameters complied with pharmacopeial requirements. The optimized formulation exhibited adequate mechanical strength, excellent chewability, and acceptable organoleptic properties. In vitro dissolution studies revealed rapid drug release, with paracetamol and zinc sulphate releasing 94.6% and 97.1%, respectively, within 30 minutes. Accelerated stability studies conducted for three months demonstrated no significant changes in physical characteristics, drug content, or dissolution profile.

The developed dual-layer chewable tablet represents a promising pediatric dosage form that combines therapeutic efficacy, improved palatability, enhanced patient compliance, and nutritional support in a single convenient formulation.

Keywords: Pediatric formulation, Dual-layer tablet, Chewable tablet, Paracetamol, Zinc sulphate, Direct compression.
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INTRODUCTION

This section introduces the need for pediatric-friendly dosage forms, especially chewable tablets, for ease of administration. It highlights the common issue of fever and mild infections in children, and how a combination of Paracetamol (an antipyretic and analgesic) with Zinc (an immunity booster) can be effective. The rationale for a dual-layer design is to separate active ingredients for better stability and controlled release. Pediatric patients often face difficulty in swallowing conventional solid dosage forms, making chewable tablets a patient-friendly alternative. Paracetamol is a widely used analgesic and antipyretic, while Zinc plays an important role in boosting immunity and overall growth in children.

A dual-layer chewable tablet allows the incorporation of both drugs in a single unit, ensuring dose convenience, improved compliance, and better therapeutic outcome. Microcrystalline cellulose (MCC) is selected as an

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excipient due to its excellent flow, compressibility, and taste-masking properties, making it suitable for pediatric formulations. Pre-formulation studies are carried out to ensure drug–excipient compatibility, stability, and suitability for tablet formulation.

MATERIALS AND METHODS

Materials
Paracetamol and Zinc Sulphate were used as active pharmaceutical ingredients (APIs). Microcrystalline Cellulose (MCC) was employed as a directly compressible diluent and binder. Mannitol was incorporated as a sweetening and bulking agent to improve chewability and mouthfeel. Crospovidone was used as a superdisintegrant. Aspartame and vanilla flavor were added to enhance palatability, while talc and magnesium stearate served as glidant and lubricant, respectively. All materials used in the study were of pharmaceutical grade.

Preformulation Studies

Organoleptic Evaluation
Paracetamol and Zinc Sulphate were examined for color, odor, texture, and appearance. Organoleptic evaluation was performed visually and manually to assess suitability for formulation development.

Melting Point Determination
The melting point of Paracetamol was determined using the capillary method. A small quantity of drug was filled into a capillary tube and heated gradually until complete melting occurred. The observed melting temperature was recorded and compared with pharmacopeial specifications.

Solubility Study
The solubility of Paracetamol and Zinc Sulphate was investigated in distilled water and other suitable solvents. Excess quantities of the drug were added to solvents and shaken until equilibrium was achieved. Solubility behavior was recorded visually.

FTIR Compatibility Study
Drug–excipient compatibility studies were conducted using FTIR spectroscopy. Potassium bromide pellets were prepared by mixing drug samples with spectroscopic-grade KBr. The spectra were recorded in the range of 4000–400 cm^{-1}. Characteristic peaks of pure drugs and physical mixtures were compared to identify potential interactions.

Flow Property Evaluation
Powder blends were characterized using bulk density, tapped density, Carr's compressibility index, Hausner ratio, and angle of repose.

Bulk Density
Bulk density was determined by transferring a known quantity of powder into a graduated cylinder and measuring the volume occupied.

Bulk Density = Mass / Bulk Volume

Tapped Density
The cylinder containing the powder was tapped repeatedly until constant volume was obtained.

Tapped Density = Mass / Tapped Volume

Carr's Compressibility Index
Carr's Index (%) = [(Tapped Density – Bulk Density) / Tapped Density] × 100

Hausner Ratio
Hausner Ratio = Tapped Density / Bulk Density

Angle of Repose
The fixed funnel method was employed. The height and radius of the powder cone were measured and used to calculate the angle of repose.

$\tan \theta = h/r$

Particle Size Analysis
Particle size distribution was evaluated using sieve analysis. The powder was passed through a series of standard sieves and retained fractions were recorded.

Moisture Content (LOD)
Loss on drying was determined using a hot air oven. Samples were weighed before and after drying until constant weight was achieved.

Formulation of Dual-Layer Chewable Tablets

Preparation of Zinc Layer
Zinc Sulphate, MCC, mannitol, aspartame, and flavoring agents were weighed accurately and passed through suitable sieves. The ingredients were blended uniformly and lubricated using talc and magnesium stearate.

Preparation of Paracetamol Layer
Paracetamol, MCC, crospovidone, and other excipients were blended separately and lubricated appropriately.

Compression of Dual-Layer Tablets
The zinc layer blend was first introduced into the die cavity and subjected to light pre-compression. Subsequently, the Paracetamol layer blend was added over the zinc layer and final compression was performed using a rotary tablet compression machine.

Post-Compression Evaluation

General Appearance
Prepared tablets were examined visually for color uniformity, surface texture, layer separation, and physical defects.

Weight Variation Test
Twenty tablets were selected randomly and weighed individually. The average weight and percentage deviation were calculated according to pharmacopeial requirements.

Thickness Measurement
Tablet thickness was measured using a digital vernier caliper.

Hardness Test
Tablet hardness was determined using a Monsanto hardness tester. Six tablets from each batch were tested

and the average value was recorded.

Friability Test
Friability was evaluated using a Roche friabilator operated at 25 rpm for 4 minutes. The percentage weight loss was calculated.

Friability (%) = [(Initial Weight – Final Weight) / Initial Weight] × 100

Drug Content Uniformity
Accurately weighed powdered tablets equivalent to the required dose were dissolved, filtered, and analyzed using UV spectrophotometry at the predetermined wavelength.

In-Vitro Dissolution Study
Dissolution testing was performed using USP Type II (Paddle) apparatus containing 900 mL phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C and stirred at 50 rpm. Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically.

Stability Studies
The optimized formulation was stored under accelerated conditions (40 ± 2°C/75 ± 5% RH) for three months according to ICH guidelines. Samples were evaluated periodically for physical appearance, hardness, friability, drug content, and dissolution characteristics.

Statistical Analysis
All experiments were performed in triplicate. Data were expressed as Mean ± Standard Deviation. Statistical significance was assessed using one-way ANOVA followed by appropriate post hoc testing. A p-value less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Organoleptic Evaluation
Paracetamol and Zinc Sulphate appeared as white, odorless powders with acceptable physical characteristics. Their appearance and texture were suitable for the preparation of pediatric chewable tablets. No unusual color or odor was observed that could affect patient acceptability.

Table 1: Organoleptic Characteristics of Paracetamol and Zinc Sulphate

Parameter	Paracetamol	Zinc Sulphate
Color	White crystalline powder	White crystalline powder
Odor	Odorless	Odorless
Appearance	Fine powder	Fine powder
Taste	Slightly bitter	Astringent

Both APIs exhibited acceptable organoleptic characteristics suitable for pediatric chewable tablet formulation.

Melting Point Determination
The observed melting point of Paracetamol (169.4 ± 0.8°C) was within the reported pharmacopeial range. This confirms the purity and identity of the drug and indicates its suitability for formulation development.

Table 2: Melting Point Determination of Paracetamol

Drug	Observed Melting Point (°C)	Reported Melting Point (°C)
Paracetamol	169.4 ± 0.8	168–172

The observed melting point was within pharmacopeial limits, confirming purity of the drug.

Solubility Study
Paracetamol showed slight solubility in water and good solubility in methanol and phosphate buffer, while Zinc Sulphate was freely soluble in water. The solubility profile suggests that both drugs can provide adequate dissolution and release from the chewable tablet formulation.

Table 3: Solubility Profile of Paracetamol and Zinc Sulphate in Different Solvents

Solvent	Paracetamol	Zinc Sulphate
Distilled Water	Slightly soluble	Freely soluble
Methanol	Soluble	Soluble
Ethanol	Sparingly soluble	Slightly soluble
Phosphate Buffer pH 6.8	Soluble	Soluble

FTIR Compatibility Study
FTIR spectra of the pure drugs and physical mixtures showed no significant shifts or disappearance of characteristic peaks. This indicates the absence of chemical interactions between the drugs and excipients, confirming compatibility within the formulation.

Table 4: FTIR Spectral Analysis of Pure Drug and Drug–Excipient Physical Mixture

Functional Group	Pure Drug Peak (cm^{-1})	Physical Mixture Peak (cm^{-1})
O–H Stretching	3324	3321
N–H Stretching	3162	3160
C=O Stretching	1651	1650
Aromatic C=C	1563	1560

No significant shift in characteristic peaks was observed, indicating compatibility between drug and excipients.

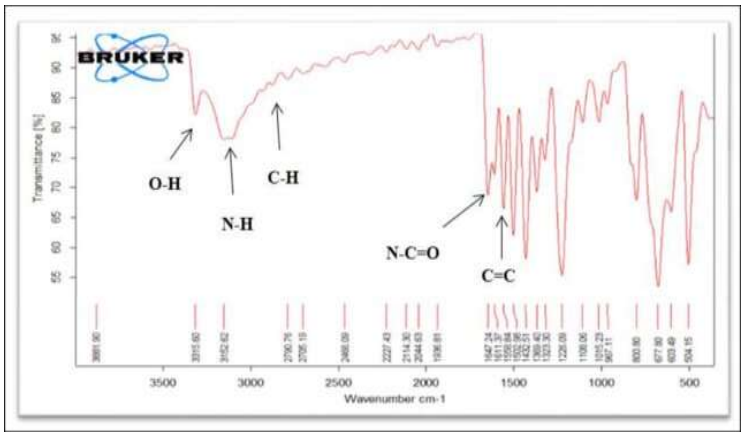

Figure 1: FTIR Spectrum of Pure Paracetamol

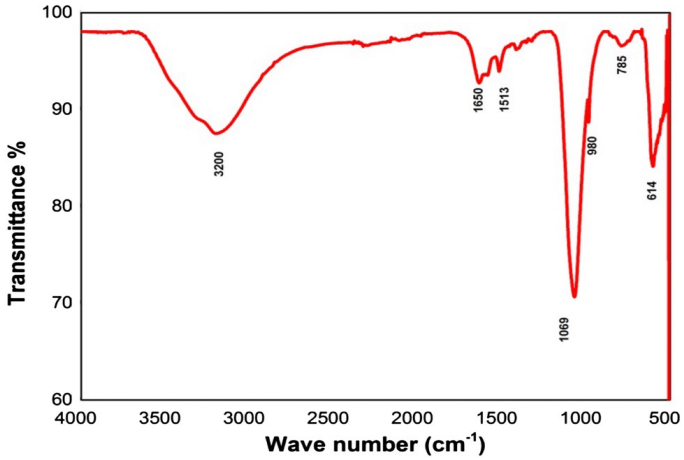

Figure 2: FTIR Spectrum of Pure Zinc Sulphate

Flow Property Evaluation

The powder blends exhibited acceptable bulk density, tapped density, Carr's index, Hausner ratio, and angle of repose values. These results indicate good flowability and compressibility, which are essential for uniform die filling and successful tablet compression.

Table 5: Pre-Compression Flow Properties of Zinc and Paracetamol Powder Blends

Parameter	Zinc Layer Blend	Paracetamol Layer Blend
Bulk Density (g/cm³)	0.46 ± 0.01	0.48 ± 0.02
Tapped Density (g/cm³)	0.53 ± 0.02	0.56 ± 0.01
Carr's Index (%)	13.20 ± 0.54	14.28 ± 0.67
Hausner Ratio	1.15 ± 0.02	1.17 ± 0.01
Angle of Repose (°)	27.4 ± 1.1	28.6 ± 1.3

The results indicated good flowability and compressibility of both blends.

Particle Size Analysis

The average particle size was found to be 154.3 ± 6.2 µm, indicating a uniform particle size distribution. Proper particle size contributes to improved flow properties, blending efficiency, and content uniformity.

Table 6: Particle Size Distribution of the Powder Blend by Sieve Analysis

Sieve No.	Average Retention (%)
#40	8.4
#60	18.7
#80	41.5
#100	21.8
Pan	9.6

Average Particle Size

154.3 ± 6.2 µm

Moisture Content (Loss on Drying)

The moisture content of both blends was below 2%, indicating minimal moisture uptake. Low moisture content helps maintain powder stability, prevents degradation, and supports efficient compression.

Table 7: Moisture Content (Loss on Drying) of Powder Blends

Sample	LOD (%)
Paracetamol Blend	1.12 ± 0.09
Zinc Blend	1.35 ± 0.11

Moisture content remained below 2%, indicating suitability for direct compression.

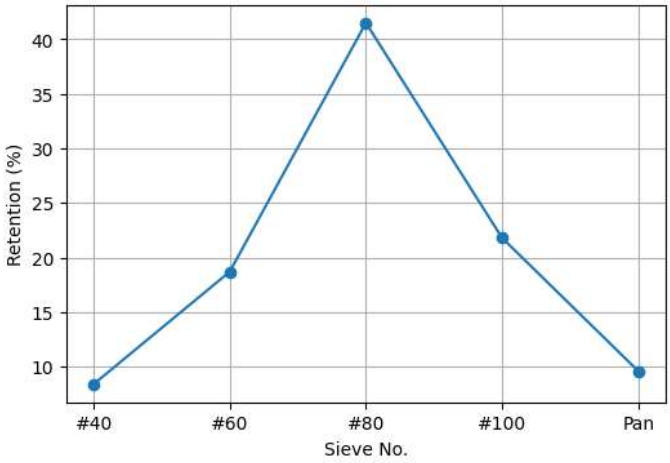

Figure 3: Particle Size Distribution Curve of Powder Blend

Formulation Composition

Optimized Formulation (F4)

The optimized formulation contained appropriate quantities of Paracetamol, Zinc Sulphate, MCC, mannitol, and other excipients. The selected composition ensured good compressibility, palatability, and mechanical strength while maintaining the desired therapeutic dose.

Table 8: Composition of Optimized Dual-Layer Chewable Tablet Formulation (F4)

Ingredient	Zinc Layer (mg)	Paracetamol Layer (mg)
Zinc Sulphate	20	-
Paracetamol	-	250
MCC	70	80
Mannitol	45	25
Crospovidone	-	15
Aspartame	5	5
Vanilla Flavor	3	3
Talc	3	3
Magnesium Stearate	2	2
Total Weight	148	383

Total Tablet Weight = 531 mg

Post Compression Evaluation

General Appearance

The prepared dual-layer chewable tablets were uniform in color and shape with smooth surfaces. No defects such as capping, chipping, cracking, or layer separation were observed, indicating successful tablet compression.

Weight Variation Test

The average tablet weight was 531.1 ± 2.3 mg, and individual tablets showed minimal variation. The results complied with pharmacopeial limits, indicating uniform distribution of the formulation blend during compression.

Table 9: Weight Variation of Optimized Dual-Layer Chewable Tablets

Tablet No.	Weight (mg)
1	529
2	532
3	535
4	530
5	528
6	533
7	531
8	529

9	534
10	530

Average Weight

531.1 ± 2.3 mg
All tablets complied with IP specifications.

Thickness
The tablets exhibited an average thickness of 5.42 ± 0.12 mm. Uniform thickness reflects consistent compression force and ensures reproducibility of the manufacturing process.

Hardness
The average hardness value of 4.82 ± 0.25 kg/cm² indicated adequate mechanical strength. The tablets were sufficiently hard to withstand handling while remaining easy to chew for pediatric patients. The hardness was adequate for chewable tablets while maintaining patient acceptability.

Friability
The friability value of 0.54 ± 0.06% was below the acceptable limit of 1%. This demonstrates that the tablets possess good resistance to abrasion and mechanical stress during packaging and transportation. Friability remained below 1%, indicating good mechanical strength.

Drug Content Uniformity
Drug content values of 99.12 ± 0.78% for Paracetamol and 98.46 ± 0.85% for Zinc Sulphate were within acceptable limits. This confirms uniform distribution of both active ingredients throughout the tablet batch.

Table 10: Drug Content Uniformity of Paracetamol and Zinc Sulphate in Optimized Tablets

Drug	Drug Content (%)
Paracetamol	99.12 ± 0.78
Zinc Sulphate	98.46 ± 0.85

Drug content was within pharmacopeial limits (95–105%).

In-Vitro Dissolution Study
The formulation showed rapid drug release, with Paracetamol and Zinc Sulphate releasing 94.6% and 97.1%, respectively, within 30 minutes. This dissolution behavior is desirable for achieving a quick therapeutic effect in pediatric patients.

Paracetamol Release Profile

Table 11: In-vitro Dissolution Profile of Paracetamol from Dual-Layer Chewable Tablets

Time (min)	% Drug Release
5	28.4 ± 1.2
10	48.7 ± 1.6
15	66.5 ± 1.4
20	82.3 ± 1.8
30	94.6 ± 1.2

Zinc Sulphate Release Profile

Table 12: In-vitro Dissolution Profile of Zinc Sulphate from Dual-Layer Chewable Tablets

Time (min)	% Drug Release
5	32.5 ± 1.4
10	56.7 ± 1.8
15	74.2 ± 1.5
20	88.4 ± 1.3
30	97.1 ± 1.0

Both drugs exhibited rapid release suitable for pediatric chewable formulations.

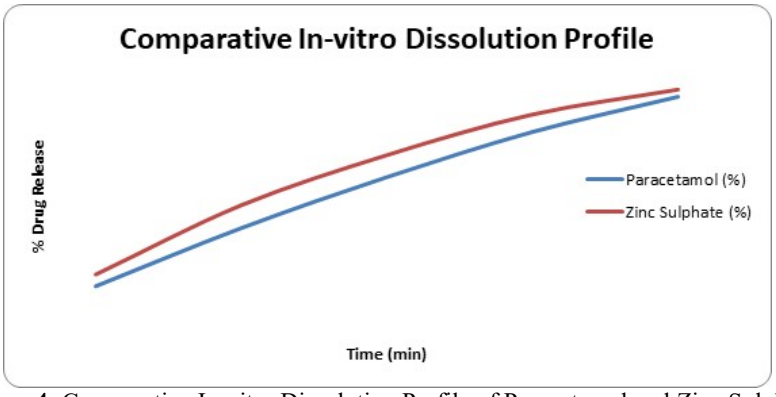

Figure 4: Comparative In-vitro Dissolution Profile of Paracetamol and Zinc Sulphate

Stability Study (40°C ± 2°C / 75% RH ± 5%)

Three-Month Accelerated Stability Results

The optimized formulation remained physically and chemically stable under accelerated storage conditions for three months. Only minor changes in hardness, friability, drug content, and dissolution were observed, indicating excellent stability.

Table 13: Accelerated Stability Study Results of Optimized Formulation (F4)

Parameter	Initial	1 Month	2 Months	3 Months
Hardness (kg/cm²)	4.82	4.79	4.76	4.72
Friability (%)	0.54	0.57	0.58	0.61
Paracetamol Content (%)	99.12	98.95	98.67	98.31
Zinc Content (%)	98.46	98.22	97.94	97.71
Drug Release at 30 min (%)	94.6	94.2	93.8	93.3

No significant changes were observed during storage ($p > 0.05$), confirming formulation stability.

Statistical Analysis

All values were expressed as Mean ± Standard Deviation ($n = 3$). One-way ANOVA revealed no statistically significant difference among stability study results during the storage period ($p > 0.05$), demonstrating robustness of the optimized pediatric dual-layer chewable tablet formulation.

CONCLUSION

The present investigation successfully developed and evaluated a pediatric dual-layer chewable tablet containing paracetamol and zinc sulphate using a direct compression technique. Preformulation studies confirmed the suitability and compatibility of the selected ingredients, while the powder blends exhibited satisfactory flow and compression properties. The optimized formulation demonstrated acceptable hardness, friability, thickness, weight uniformity, and drug content, meeting established pharmacopeial standards. Rapid and consistent drug release was achieved, ensuring prompt therapeutic action and effective zinc supplementation. Furthermore, the tablets exhibited good palatability, chewability, and stability under accelerated storage conditions. The dual-layer chewable tablet offers a convenient, patient-friendly, and effective dosage form for children, improving treatment adherence while simultaneously providing antipyretic, analgesic, and nutritional benefits.

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