

Formulation and Evaluation of a Palatable Pediatric Oral Suspension of Cefixime Trihydrate Using Guar Gum, Poloxamer 407 and Sucralose

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Abstract

Background: Oral liquid dosage forms permit flexible, weight-based dosing in children, but poor palatability and unsuitable dosage strength can reduce adherence and therapeutic success. Cefixime trihydrate is poorly water-soluble and bitter, so a stable, readily redispersible and palatable suspension is required.

Objective: To formulate and evaluate a pediatric oral suspension of cefixime trihydrate using guar gum as the suspending agent, poloxamer 407 as the wetting and solubilizing agent, and sucralose as the sweetener.

Methods: Nine suspensions (F1–F9; 2.0% w/v cefixime trihydrate, equivalent to about 100 mg per 5 mL) were prepared in a three-level, two-factor design in which guar gum and poloxamer 407 were each varied at 0.5%, 1.0% and 1.5% w/v. The batches were evaluated for appearance, pH, rheology, sedimentation volume, redispersibility, particle size, drug content, palatability and in-vitro release. Drug–excipient compatibility was assessed by Fourier-transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC). The selected batch was compared with a marketed suspension and stored for three months at $40 \pm 2^\circ\text{C}/75 \pm 5\% \text{RH}$, $25 \pm 2^\circ\text{C}/60 \pm 5\% \text{RH}$ and $2-8^\circ\text{C}$.

Results: All batches had pH values of 4.45–4.56 and drug contents of 96.2–99.4%. Viscosity at 50 rpm increased from 186–238 cP at 0.5% guar gum to 758–868 cP at 1.5%, and all batches showed shear-thinning flow. F5 (1.0% guar gum and 1.0% poloxamer 407) was selected as the balanced formulation: viscosity 462 cP, sedimentation volume 0.94 at 14 days, redispersion in two inversions, mean particle size $21.8 \mu\text{m}$, drug content 99.4%, and mean palatability score 7.7 on a nine-point scale. F5 released 96.8% of the drug in 45 min, against 97.3% for the marketed product (f1 2.9, f2 78.6). Release followed first-order kinetics ($r^2 = 0.9958$) with a Korsmeyer–Peppas exponent of 0.42. FTIR and DSC showed no evidence of incompatibility. After three months of accelerated storage, F5 remained uniform and retained 98.4% of its initial drug content.

Conclusion: A combination of 1.0% w/v guar gum and 1.0% w/v poloxamer 407 produced a physically stable, readily redispersible and palatable cefixime suspension whose in-vitro release resembled that of a marketed product. Longer stability studies, microbial-limit and preservative-efficacy testing, and scale-up validation are needed before any clinical use.

Keywords: Cefixime Trihydrate; Guar Gum; Palatability; Pediatric Suspension; Poloxamer 407; Sucralose; Stability.

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Introduction

Child-appropriate medicines should allow accurate dosing, easy administration and acceptable sensory properties. Large tablets, unsuitable dose strengths and poor palatability are recognized barriers to treatment in children, and liquid or dispersible forms are therefore needed for many age groups.

Taste, aftertaste, smell and mouthfeel all influence acceptability, and evidence on whether solid or liquid forms give better adherence in children

remains limited. [1][2] Cefixime is an oral third-generation cephalosporin. Its prescribing information describes safety and effectiveness in patients aged six months and older, while data below six months are insufficient. [3]

Cefixime trihydrate is only slightly soluble in water and has a distinctly bitter taste, so a pediatric liquid must control sedimentation and caking, keep the dose uniform from the top to the bottom of the

bottle, and remain acceptable to taste. Guar gum is a hydrophilic galactomannan that hydrates rapidly and raises viscosity, and it has wide pharmaceutical applications. [4] Poloxamer 407 is a non-ionic block copolymer used as a wetting, solubilizing and rheology-modifying excipient. [5] Sucralose is an intense sweetener that can provide sweetness at a very low concentration, which limits the sugar load of a pediatric liquid. The balance between the viscosity needed to hold particles in suspension and the viscosity that still allows pouring, redispersion and drug release is central to such a product.

This study therefore aimed to prepare and evaluate a cefixime trihydrate pediatric suspension in which guar gum and poloxamer 407 were varied systematically, to select a balanced formulation on

the basis of physical stability, dose uniformity, palatability and in-vitro release, and to compare its release with a marketed suspension.

Materials and Methods

Materials: Cefixime trihydrate was the active ingredient. Guar gum, poloxamer 407, sucralose, sodium benzoate, citric acid, sodium citrate, flavour, potassium dihydrogen phosphate, sodium hydroxide, hydrochloric acid, methanol and potassium bromide were of pharmacopoeial or analytical grade, and purified water was prepared in the laboratory. A marketed cefixime pediatric suspension was used as the dissolution comparator (Table 1).

Table 1: Materials used in the study

Material	Role in the study	Grade
Cefixime trihydrate	Active ingredient	IP
Guar gum	Suspending agent	IP
Poloxamer 407	Wetting and solubilizing agent	BP
Sucralose	Sweetener	BP
Sodium benzoate	Preservative	USP-NF
Citric acid / sodium citrate	Buffer system (target pH about 4.5)	IP / BP
Potassium dihydrogen phosphate, NaOH, HCl	Buffer and media preparation	AR
Methanol; KBr	Assay co-solvent; FTIR discs	AR / spectroscopic
Marketed cefixime suspension	Dissolution comparator	Commercial product

Analytical Method and Validation: Cefixime was quantified by UV spectrophotometry (double-beam instrument) at the absorption maximum of 288 nm in phosphate buffer pH 7.2. A 1000 µg/mL stock solution was prepared in a small volume of methanol made up with buffer, and standards of 5, 10, 20, 30 and 40 µg/mL were measured in triplicate. The method was validated for linearity, accuracy (recovery at 80%, 100% and 120%), repeatability and intermediate precision, limits of detection (3.3σ/S) and quantitation (10σ/S), specificity against placebo, and robustness (±2 nm in wavelength), following the principles of the ICH Q2 guideline for analytical procedures. [6][7]

Drug–excipient compatibility: Cefixime and 1:1 w/w physical mixtures with guar gum, poloxamer 407 and sucralose were examined by FTIR (KBr

discs, 4000–400 cm⁻¹, 4 cm⁻¹ resolution). Retention of the diagnostic cefixime bands without marked shifts, loss or new bands was taken to indicate compatibility. DSC was performed on 3–5 mg samples in sealed aluminium pans, heated from 30°C to about 300°C at 10°C/min under nitrogen (50 mL/min).

Formulation design and preparation: Nine batches (F1–F9) were prepared in a three-level, two-factor design in which guar gum and poloxamer 407 were each used at 0.5%, 1.0% and 1.5% w/v. The other components were constant in all batches (Table 2). Citrate buffer was added to a target pH of about 4.5, flavour was added in sufficient quantity, and purified water was added to 100 mL.

Table 2: Composition of cefixime suspension batches F1–F9 (per 100 mL)

Batch	Cefixime trihydrate (g)	Guar gum (g)	Poloxamer 407 (g)	Sucralose (g)	Sodium benzoate (g)
F1	2	0.5	0.5	0.1	0.15
F2	2	0.5	1	0.1	0.15
F3	2	0.5	1.5	0.1	0.15
F4	2	1	0.5	0.1	0.15
F5	2	1	1	0.1	0.15
F6	2	1	1.5	0.1	0.15
F7	2	1.5	0.5	0.1	0.15
F8	2	1.5	1	0.1	0.15
F9	2	1.5	1.5	0.1	0.15

Guar gum was sprinkled slowly into freshly boiled and cooled purified water with continuous stirring and allowed to hydrate into a lump-free mucilage. Poloxamer 407 was dissolved separately in cold water. The weighed cefixime trihydrate was levigated with the poloxamer solution to wet the particles and form a smooth slurry, which was added to the guar gum mucilage and mixed with an overhead stirrer. Sodium benzoate, citrate buffer, sucralose solution and flavour were then added, the pH was adjusted, the volume was made up, and the suspension was transferred to amber glass bottles.

Evaluation of the Suspensions: Appearance, pourability and phase separation were assessed visually, and pH was measured in triplicate at 25°C. Apparent viscosity was measured at $25 \pm 1^\circ\text{C}$ with a Brookfield-type rotational viscometer at 10, 20, 50 and 100 rpm ($n = 3$). Sedimentation volume was calculated as $F = V_u/V_o$, the ratio of the final sediment volume to the original suspension volume, in a 100 mL stoppered cylinder for up to 14 days. Redispersibility was recorded as the number of gentle inversions needed to restore a uniform dispersion ($n = 3$). Particle size was measured by optical microscopy with a calibrated eyepiece micrometer on at least 100 particles. Drug content was determined as a percentage of label claim after extraction with methanol and phosphate buffer pH 7.2, sonication, filtration and dilution, with an acceptance range of 90–110%. Dose uniformity of the selected batch was assessed using samples from the upper, middle and lower thirds of the container.

Palatability:

Palatability of the selected batch was evaluated by ten consenting adult volunteers after Institutional Ethics Committee approval and written informed consent. A swirl-and-expectorate (taste-and-spit) procedure was used so that the product was not swallowed, and no children were used as taste subjects. Sweetness, absence of bitterness or aftertaste, mouthfeel, colour and appearance, and overall acceptability were scored on a nine-point hedonic scale (9 = like extremely; 1 = dislike extremely). As a supporting measure, the amount of drug released into simulated salivary fluid (pH 6.8) within 60 seconds was determined.

In-vitro dissolution and release kinetics:

Dissolution was performed using USP apparatus II (paddle) with 900 mL of phosphate buffer pH 7.2 at $37 \pm 0.5^\circ\text{C}$ and 50 rpm ($n = 6$). Samples of 5 mL were withdrawn at 5, 10, 15, 20, 30, 45 and 60 min,

replaced with fresh medium, and analysed at 288 nm. The profile of the selected batch was compared with that of the marketed suspension using the difference factor (f_1) and similarity factor (f_2), where f_2 values of 50–100 are generally taken to indicate similar profiles. [8][9][10]

The release data of the selected batch were fitted to zero-order, first-order, Higuchi and Korsmeyer–Peppas models, and the release exponent (n) was used to characterise the release mechanism.

Stability study: The selected batch was filled in amber glass bottles and stored at $40 \pm 2^\circ\text{C}/75 \pm 5\%$ RH (accelerated), $25 \pm 2^\circ\text{C}/60 \pm 5\%$ RH and $2\text{--}8^\circ\text{C}$ for three months, in line with the storage conditions described in ICH Q1A(R2). [11] Samples were examined at 0, 1, 2 and 3 months for appearance, pH, viscosity, sedimentation volume, redispersibility, drug content and release at 45 min.

Statistical Analysis: Results are expressed as mean $\pm$ standard deviation for the number of replicates stated in each table. Differences among batches in viscosity were analysed by one-way analysis of variance, with $p < 0.05$ taken as significant. Other batch comparisons are presented descriptively, and no inferential test was applied to the stability data.

Results

Preformulation: Cefixime trihydrate was a white to pale-yellow, fine, free-flowing crystalline powder with a faint odour and a distinctly bitter taste. Its melting point was $220.6 \pm 0.9^\circ\text{C}$ with decomposition ($n = 3$), consistent with the reference range of about $218\text{--}225^\circ\text{C}$. Equilibrium solubility at $25 \pm 1^\circ\text{C}$ was 0.42 ± 0.03 mg/mL in purified water, 0.68 ± 0.05 mg/mL in 0.1 N hydrochloric acid, 3.85 ± 0.12 mg/mL in phosphate buffer pH 7.2 and 12.40 ± 0.34 mg/mL in methanol ($n = 3$). The low aqueous solubility supported the choice of a suspension, and the higher solubility in phosphate buffer pH 7.2 supported its use as the dissolution medium.

Analytical method validation: The absorbance of cefixime was linear over $5\text{--}40$ $\mu\text{g/mL}$ ($y = 0.0248x + 0.0052$; $r^2 = 0.9996$) (Figure 1). Mean recovery was 99.7% (99.2%, 100.4% and 99.6% at the 80%, 100% and 120% levels), intra-day and inter-day precision were 0.62% and 0.94% RSD, and the limits of detection and quantitation were 0.68 and 2.06 $\mu\text{g/mL}$. No placebo interference was seen at 288 nm, and a ± 2 nm change in wavelength gave 0.85% RSD (Table 3).

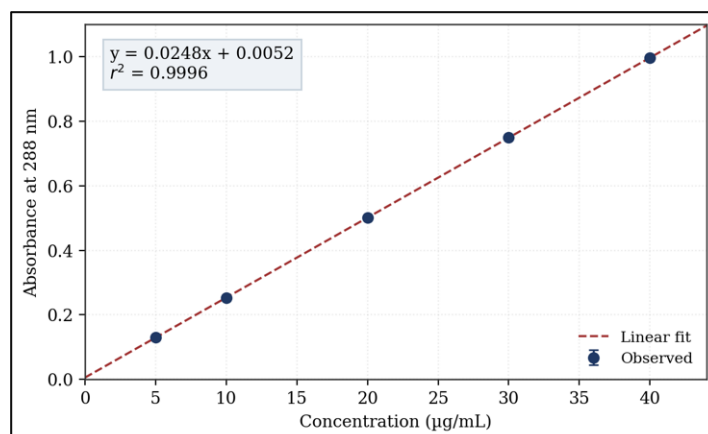


Figure 1: Calibration curve of cefixime trihydrate at 288 nm in phosphate buffer pH 7.2 (mean $\pm$ SD, n = 3)

Table 3: Validation of the UV spectrophotometric method

Parameter	Result	Acceptance criterion
Linearity range	5–40 $\mu\text{g/mL}$	Linear
Correlation coefficient (r^2)	0.9996	≥ 0.999
Accuracy (mean recovery)	99.70%	98–102%
Repeatability (intra-day, % RSD)	0.62	≤ 2
Intermediate precision (inter-day, % RSD)	0.94	≤ 2
LOD / LOQ	0.68 / 2.06 $\mu\text{g/mL}$	Reported
Specificity	No placebo interference at 288 nm	No interference
Robustness (± 2 nm, % RSD)	0.85	≤ 2

Compatibility: The diagnostic bands of cefixime were retained in all three binary mixtures: the β -lactam carbonyl at about 1770 cm^{-1} , the carboxylic acid carbonyl at 1710 cm^{-1} , the amide I band at 1662 cm^{-1} , the C=N band at 1600 cm^{-1} , the amide II band at 1530 cm^{-1} and the C–N/C–O band at 1250 cm^{-1} . Broadening in the N–H/O–H region near 3310 cm^{-1} was attributed to physical hydrogen bonding, and no new band appeared. In the DSC thermograms, pure cefixime trihydrate showed a dehydration endotherm at about 112°C and a melting endotherm at 221.4°C, whereas the 1:1 mixture showed endotherms at about 108°C and 219.6°C, a shift of less than 2°C without a new thermal event. Together, these findings indicate no evidence of chemical interaction under the conditions studied.

Physicochemical properties of the batches: All nine suspensions were uniform on preparation, and pH ranged narrowly from 4.45 to 4.56, indicating effective buffering. F1–F3, with 0.5% guar gum, were thin and showed rapid settling; F4–F6 (1.0%) were smooth and easily pourable; F7–F9 (1.5%) were distinctly viscous, and F9 was difficult to pour. Viscosity at 50 rpm rose from 186–238 cP at 0.5% guar gum to 418–496 cP at 1.0% and 758–868 cP at 1.5%, with a smaller but consistent increase when poloxamer 407 was raised at each guar gum level (Table 4, Figure 2). Differences among batches were significant by one-way analysis of variance ($p < 0.05$). Apparent viscosity fell as spindle speed rose from 50 to 100 rpm in every batch, which indicates pseudoplastic (shear-thinning) flow.

Table 4: pH, viscosity, sedimentation and redispersibility of batches F1–F9 (mean $\pm$ SD, n = 3)

Batch	Guar gum (%)	Poloxamer 407 (%)	pH	Viscosity at 50 rpm (cP)	Viscosity at 100 rpm (cP)	F at 14 days	Inversions
F1	0.5	0.5	4.52 $\pm$ 0.03	186 $\pm$ 6	139 $\pm$ 5	0.71 $\pm$ 0.02	8 $\pm$ 1
F2	0.5	1	4.48 $\pm$ 0.02	212 $\pm$ 7	158 $\pm$ 6	0.74 $\pm$ 0.02	7 $\pm$ 1
F3	0.5	1.5	4.45 $\pm$ 0.03	238 $\pm$ 8	178 $\pm$ 6	0.78 $\pm$ 0.02	6 $\pm$ 1
F4	1	0.5	4.54 $\pm$ 0.02	418 $\pm$ 11	312 $\pm$ 9	0.88 $\pm$ 0.02	4 $\pm$ 1
F5	1	1	4.52 $\pm$ 0.02	462 $\pm$ 12	345 $\pm$ 10	0.94 $\pm$ 0.01	2 $\pm$ 0
F6	1	1.5	4.49 $\pm$ 0.03	496 $\pm$ 13	370 $\pm$ 11	0.95 $\pm$ 0.01	3 $\pm$ 1
F7	1.5	0.5	4.56 $\pm$ 0.03	758 $\pm$ 18	566 $\pm$ 15	0.96 $\pm$ 0.01	3 $\pm$ 1
F8	1.5	1	4.53 $\pm$ 0.02	812 $\pm$ 21	606 $\pm$ 17	0.97 $\pm$ 0.01	3 $\pm$ 1
F9	1.5	1.5	4.50 $\pm$ 0.02	868 $\pm$ 23	648 $\pm$ 19	0.98 $\pm$ 0.01	4 $\pm$ 1

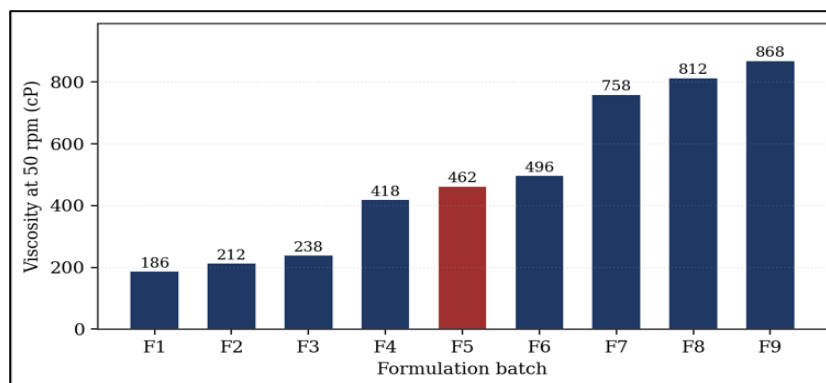


Figure 2: Apparent viscosity of batches F1–F9 at 50 rpm and 25°C (mean $\pm$ SD, n = 3). F5 is shown in dark blue

Sedimentation volume at 14 days increased with guar gum concentration, from 0.71–0.78 in F1–F3 to 0.88–0.95 in F4–F6 and 0.96–0.98 in F7–F9, and only F5–F9 reached the target of $F \geq 0.90$. Redispersibility, however, followed a different pattern (Figure 3). The low-viscosity batches F1–

F3 formed compact sediments that needed 6–8 inversions, whereas the highly viscous F7–F9 settled very little but were harder to homogenise and pour, with F9 requiring four inversions. F5 gave a loose, fluffy sediment and redispersed completely in two inversions.

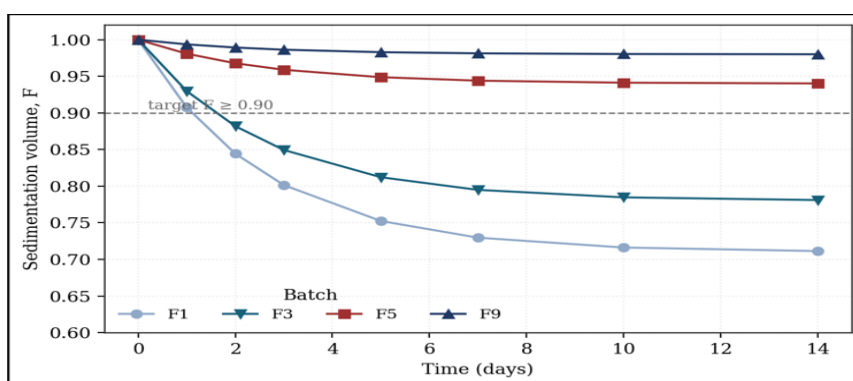


Figure 3: Sedimentation volume (F) as a function of storage time for representative batches F1, F3, F5 and F9. The dashed line marks the target of $F \geq 0.90$

Particle size, drug content and palatability:

Mean particle size ranged from 18.4 to 27.8 μm and decreased as the poloxamer 407 concentration increased at each guar gum level, which is consistent with better wetting and dispersion of the hydrophobic drug particles; the batches with 0.5% poloxamer showed some agglomerates (Table 5). Drug content was 96.2–99.4% of label claim in all

batches, within the 90–110% range, and F5 had the highest value ($99.4 \pm 0.6\%$).

In F5, the upper, middle and lower thirds of the container contained $99.6 \pm 0.7\%$, $99.4 \pm 0.6\%$ and $98.9 \pm 0.8\%$ of label claim (overall $99.3 \pm 0.7\%$, RSD 0.74%).

Table 5: Particle size, drug content and release of batches F1–F9 (mean $\pm$ SD)

Batch	Mean particle size (μm)	Drug content (% label claim)	Release at 15 min (%)	Release at 45 min (%)	t_{50} (min)
F1	27.8 ± 1.4	96.2 ± 1.8	60.4 ± 2.1	88.4 ± 1.9	11.6
F2	22.4 ± 1.1	97.4 ± 1.5	62.9 ± 2.0	91.2 ± 1.8	10.9
F3	19.2 ± 0.9	98.1 ± 1.3	65.2 ± 1.9	93.6 ± 1.7	10.3
F4	27.2 ± 1.3	98.6 ± 1.1	64.6 ± 2.0	92.8 ± 1.8	10.5
F5	21.8 ± 1.0	99.4 ± 0.6	68.3 ± 1.8	96.8 ± 0.9	9.6
F6	18.9 ± 0.9	99.1 ± 0.8	66.9 ± 1.7	95.4 ± 1.2	9.9
F7	26.6 ± 1.2	97.8 ± 1.0	58.7 ± 2.2	86.2 ± 2.0	12.2
F8	21.2 ± 1.0	98.4 ± 0.9	60.9 ± 2.1	88.6 ± 1.9	11.5
F9	18.4 ± 0.8	98.0 ± 1.2	55.8 ± 2.3	82.4 ± 2.1	13.1

Ten adult volunteers rated the palatability of F5 (Table 6). Sweetness scored 7.8 ± 0.6 , absence of bitterness or aftertaste 7.4 ± 0.7 , mouthfeel 7.6 ± 0.5 , colour and appearance 7.9 ± 0.6 and overall acceptability 7.7 ± 0.6 . Only $4.2 \pm 0.4\%$ of the dose was released into simulated salivary fluid within 60 seconds, which supports the sensory findings.

Table 6: Palatability of batch F5 on a nine-point hedonic scale (mean $\pm$ SD, n = 10 adult volunteers)

Attribute	Mean score $\pm$ SD	Descriptor
Sweetness	7.8 ± 0.6	Like very much
Absence of bitterness / aftertaste	7.4 ± 0.7	Like moderately
Mouthfeel / texture	7.6 ± 0.5	Like very much
Colour and appearance	7.9 ± 0.6	Like very much
Overall acceptability	7.7 ± 0.6	Like very much

Selection of the lead formulation: When all batches were checked against the acceptance criteria (pH 3.5–6.0, $F \geq 0.90$, redispersion within three inversions, assay 90–110%, and at least 85% release at 45 min), F5, F6 and F8 met all the numerical limits (Table 7); all batches complied with the pH and assay criteria. F8 was considered unsuitable for convenient pediatric dosing because

it was very viscous, and F6 gave marginally lower drug content and slower release than F5 and needed one more inversion.

F5 was therefore selected as the balanced lead formulation and carried forward for comparative dissolution, kinetic and stability studies.

Table 7: Evaluation of batches against the acceptance criteria

Batch	$F \geq 0.90$	Redispersion ≤ 3 inversions	Release $\geq 85\%$ at 45 min	Meets all numerical criteria
F1	No (0.71)	No (8)	Yes	No
F2	No (0.74)	No (7)	Yes	No
F3	No (0.78)	No (6)	Yes	No
F4	No (0.88)	No (4)	Yes	No
F5	Yes (0.94)	Yes (2)	Yes	Yes
F6	Yes (0.95)	Yes (3)	Yes	Yes
F7	Yes (0.96)	Yes (3)	No (86.2)	No
F8	Yes (0.97)	Yes (3)	Yes	Yes (too viscous)
F9	Yes (0.98)	No (4)	No (82.4)	No

Comparative dissolution and release kinetics:

The F5 and marketed profiles were close throughout the test (Table 8, Figure 4). F5 released 68.3% at 15 min and 96.8% at 45 min, against 71.4% and 97.3% for the marketed product, and the largest mean difference was 3.4 percentage points

(at 10 min). From the mean values in Table 8, the difference factor f_1 was 2.9 and the similarity factor f_2 was 78.6, so the profiles are similar by the usual f_2 criterion of 50–100 under the stated test conditions.

Table 8: In-vitro release of F5 and the marketed suspension (mean $\pm$ SD, n = 6)

Time (min)	F5 released (%)	Marketed released (%)	Difference
5	32.4 ± 1.4	35.1 ± 1.6	-2.7
10	51.8 ± 1.6	55.2 ± 1.7	-3.4
15	68.3 ± 1.8	71.4 ± 1.5	-3.1
20	79.5 ± 1.5	82.6 ± 1.4	-3.1
30	90.2 ± 1.2	92.4 ± 1.1	-2.2
45	96.8 ± 0.9	97.3 ± 0.8	-0.5
60	98.1 ± 0.7	98.6 ± 0.6	-0.5

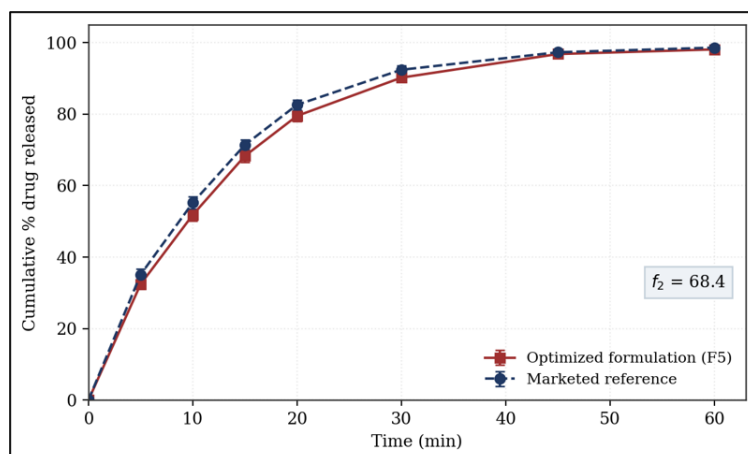


Figure 4: Comparative in-vitro release profiles of F5 and the marketed cefixime suspension in phosphate buffer pH 7.2 (USP apparatus II, 50 rpm, $37 \pm 0.5^\circ\text{C}$; mean $\pm$ SD, $n = 6$)

Release from F5 was best described by the first-order model ($r^2 = 0.9958$; $k = 0.0721 \text{ min}^{-1}$), followed by Korsmeyer–Peppas ($r^2 = 0.9906$) and Higuchi ($r^2 = 0.9832$), while the zero-order fit was poor ($r^2 = 0.9124$) (Table 9). The Korsmeyer–Peppas exponent of 0.42 is below 0.45, which is characteristic of Fickian, diffusion-controlled release.

Table 9: Kinetic modelling of the release data of F5

Model	r^2	Constant	Interpretation
Zero-order	0.9124	$K_0 = 1.62 \text{ \%/min}$	Poor fit
First-order	0.9958	$K_1 = 0.0721 \text{ min}^{-1}$	Best fit
Higuchi	0.9832	$K_H = 14.86 \text{ \%/min}^{0.5}$	Good fit; diffusion contribution
Korsmeyer–Peppas	0.9906	$n = 0.42$	Fickian diffusion

Stability: F5 stayed uniform and was easily redispersed at every time point, with no caking, phase separation, colour change or visible microbial growth. Under accelerated storage, pH changed from 4.52 to 4.47, viscosity from 462 to

451 cP, sedimentation volume from 0.94 to 0.93, drug content from 99.4% to 98.4%, and release at 45 min from 96.8% to 95.8%; the number of inversions needed rose from two to three at month 3 (Table 10).

Table 10: Stability of F5 at $40 \pm 2^\circ\text{C}$ / $75 \pm 5\% \text{ RH}$

Parameter	0 month	1 month	2 months	3 months
Appearance	Uniform	Uniform	Uniform	Uniform
pH	4.52	4.51	4.49	4.47
Viscosity (cP)	462	458	455	451
Sedimentation volume (F)	0.94	0.94	0.93	0.93
Redispersibility (inversions)	2	2	2	3
Drug content (%)	99.4	99.1	98.8	98.4
Release at 45 min (%)	96.8	96.5	96.2	95.8

Discussion

The results show that guar gum concentration was the main determinant of the mechanical and physical behaviour of the suspension. Raising guar gum from 0.5% to 1.5% increased viscosity roughly four-fold, improved sedimentation volume and slowed drug release. This is consistent with the ability of guar gum to hydrate into highly viscous dispersions, [4] and with Stokes' law, because a more viscous continuous phase lowers the settling velocity of the dispersed particles.

Low guar gum levels gave thin systems whose sediments packed closely and needed six to eight inversions to redisperse, whereas 1.5% guar gum

gave very viscous systems that were difficult to pour and released the drug more slowly. The optimum therefore lay at the intermediate level.

Poloxamer 407 played a complementary role. Its non-ionic surfactant character, micellization and rheological effects are well documented, [5] and in this study, higher poloxamer concentrations reduced mean particle size and generally favoured release at a given guar gum level, which is consistent with better wetting of the hydrophobic drug particles. The highest poloxamer level did not give the best overall product, however: F5 (1.0%) showed the highest drug content, the shortest t_{50} and the lowest redispersion effort, and F6 (1.5%)

was marginally poorer on these measures. The study design does not allow a formal interaction between the two excipients to be estimated, so the intermediate optimum should be read as an empirical balance within the range tested.

F5 formed a loose sediment ($F = 0.94$) that redispersed in two inversions, and its shear-thinning behaviour is advantageous for a pediatric liquid because viscosity is high at rest, which limits settling, and falls during shaking and pouring, which eases dosing. The narrow pH range of 4.45–4.56 across all batches shows that the citrate buffer controlled the vehicle reliably. Dose uniformity across the top, middle and bottom of the container (RSD 0.74%) is important for a weight-based pediatric dose.

The release of F5 closely matched that of the marketed suspension, and the first-order fit with a Fickian exponent suggests a conventional immediate-release suspension in which dissolution at the particle surface, aided by poloxamer wetting, is followed by diffusion through the viscous vehicle. An f_2 value above 50 indicates similar in-vitro profiles under the test conditions; [9][10] it does not establish bioequivalence, clinical equivalence or interchangeability, which would require in-vivo evidence.

Palatability is a central determinant of acceptance of pediatric medicines. [1] The mean overall score of 7.7 and the small amount of drug released in simulated saliva support the taste-masking effect of the vehicle and sweetener. The panel, however, consisted of ten adults using a taste-and-spit procedure, so the result cannot be extrapolated directly to children, whose taste perception differs and who would need a separately approved acceptability study.

The stability data indicate that F5 retained its physical and chemical characteristics over three months, with a 1.0% fall in drug content under accelerated conditions and smaller falls at 25°C and 2–8°C. Because the study lasted only three months, did not include variability estimates or inferential comparison for the stability data, and did not include microbial-limit or preservative-efficacy tests, it supports short-term stability only and cannot assign a commercial shelf life. The UV method measures total absorbance at 288 nm and is not a stability-indicating method, so degradation products that absorb at this wavelength could be missed. A stability-indicating chromatographic method should be used in further work.

This study is a dosage-form development study. It does not provide evidence of clinical efficacy or safety in children, and it does not support any change in the antimicrobial stewardship principles that govern when cefixime should be prescribed.

Conclusion

A palatable cefixime trihydrate pediatric suspension was prepared using guar gum, poloxamer 407 and sucralose. Guar gum mainly controlled viscosity, sedimentation and release, and poloxamer 407 mainly influenced particle dispersion and release. F5, containing 1.0% w/v of each polymer, gave the best balance of viscosity (462 cP), sedimentation volume (0.94), redispersibility (two inversions), dose uniformity, palatability (7.7/9) and 45-min release (96.8%), with an in-vitro release profile similar to that of a marketed suspension. F5 remained acceptable over three months of storage under accelerated, room-temperature and refrigerated conditions. It should be regarded as a promising development candidate; long-term stability, microbial-limit and preservative-efficacy testing, stability-indicating assay, container-closure studies, scale-up reproducibility and an appropriately approved pediatric acceptability study are required before any clinical or commercial claim is made.

References

1. Zajicek A, Fossler MJ, Barrett JS, Worthington JH, Ternik R, Charkoftaki G, et al. A report from the Pediatric Formulations Task Force: perspectives on the state of child-friendly oral dosage forms. *AAPS J.* 2013;15(4):1072-1081. doi:10.1208/s12248-013-9511-5.
2. Lajoinie A, Janiaud P, Henin E, Gleize JC, Berlion C, Nguyen KA, et al. Assessing the effects of solid versus liquid dosage forms of oral medications on adherence and acceptability in children (protocol). *Cochrane Database Syst Rev.* 2017;(9):CD012783. doi:10.1002/14651858.CD012783.
3. National Library of Medicine. DailyMed: Cefixime capsule [Internet]. Bethesda (MD): National Library of Medicine; [cited 2026 Oct 10]. Available from: <https://dailymed.nlm.nih.gov/dailymed/drugInf.o.cfm?setid=9cdb156f-7a99-413e-b49a-ffa9af9e93fe>.
4. Thombare N, Jha U, Mishra S, Siddiqui MZ. Guar gum as a promising starting material for diverse applications: a review. *Int J Biol Macromol.* 2016;88:361-372. doi:10.1016/j.ijbiomac.2016.04.001.
5. Dumortier G, Grossiord JL, Agnely F, Chaumeil JC. A review of poloxamer 407 pharmaceutical and pharmacological characteristics. *Pharm Res.* 2006;23(12):2709-2728. doi:10.1007/s11095-006-9104-4.
6. ICH. ICH harmonised guideline Q2(R2): validation of analytical procedures. Geneva: ICH; 2023 (corrected 2025). Available from: [https://database.ich.org/sites/default/files/ICH_Q2\(R2\)_Guideline_2023_1130_ErrorCorrection_2025.pdf](https://database.ich.org/sites/default/files/ICH_Q2(R2)_Guideline_2023_1130_ErrorCorrection_2025.pdf)

7. US Food and Drug Administration. Q2(R2) validation of analytical procedures: guidance for industry. Silver Spring (MD): FDA; 2024. Available from: <https://www.fda.gov/media/161201/download>
8. Moore JW, Flanner HH. Mathematical comparison of dissolution profiles. *Pharm Technol.* 1996;20(6):64-74.
9. Shah VP, Tsong Y, Sathe P, Liu JP. In vitro dissolution profile comparison - statistics and analysis of the similarity factor, *f2*. *Pharm Res.* 1998;15(6):889-896. doi:10.1023/A:1011976615750.
10. Lourenço FR, Ghisleni DDM, Yamamoto RN, Pinto TJA. Comparison of dissolution profile of extended-release oral dosage forms: two one-sided equivalence test. *Braz J Pharm Sci.* 2013;49(2):367-371. doi:10.1590/S1984-82502013000200019.
11. ICH. ICH Q1A(R2): Stability testing of new drug substances and products. Geneva: ICH; 2003.