Research Article

Formulation and Evaluation of Ceritinib Suspension Using Different Suspending Agents and A Bioenhancer

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ABSTRACT

Poor aqueous solubility of drugs is a major challenge in pharmaceutical formulation, particularly for BCS Ⅳ Class-IV drugs such as Ceritinib, which exhibit low solubility and low permeability. This study aimed to formulate and evaluate an oral suspension of Ceritinib using different suspending agents and a bioenhancer to "improve solubility, stability, and dissolution behavior". Various formulations were prepared using different concentrations of suspending agents along with suitable excipients such as surfactants and stabilizers. The prepared suspensions were evaluated for organoleptic properties, viscosity, sedimentation volume, redispersibility. Viscosity was determined using a Brookfield viscometer to evaluate flow properties and physical stability. In vitro dissolution studies were carried out to examine the drug release profile. Among all the prepared formulations, the optimized one showed good physical stability, suitable viscosity, easy redispersion, and a higher dissolution rate compared to the others. The results indicate that the use of appropriate suspending agents and bioenhancers significantly improves the formulation performance. Therefore, the formulated suspension may enhance drug solubility and provide better therapeutic effectiveness.

Keywords: Pediatric oral suspension, Microcrystalline cellulose, Sedimentation volume, Dissolution studies.

INTRODUCTION

Non-small cell lung cancer is one of the most common types of lung cancer and is primarily associated with environmental risk factors, particularly tobacco exposure, although genetic predisposition also plays a role. The exception to this is exposure to radon.[1]

NSCLC originates in the epithelial cells lining the respiratory tract and may arise in central bronchi or peripheral lung tissues. The are three main types include squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. Common symptoms include fatigue, unexplained weight loss, dyspnoea, wheezing and persistent cough. Primary lung cancer in children is extremely rare. However, when lung malignancies occur in paediatric patients, treatment typically involves a combination of therapies such as chemotherapy, radiotherapy, and immunotherapy. [2]

Ceritinib is a drug that blocks anaplastic lymphoma kinase (ALK) and is classified as a BCS Class IV drug, which means it has low solubility and poor permeability. It is currently available as hard gelatin capsules, which may not be suitable for certain populations, especially paediatric patients, due to swallowing difficulties and lack of dose flexibility. The development of paediatric formulations is essential to improve patient compliance. The evaluation parameters such as sedimentation volume, redispersibility, viscosity and filtration through Whatman filter paper can be used to assess suspension stability. [3]

Suspension:[3]

A pharmaceutical suspension is a system made up of two phases, where very small insoluble drug particles are evenly distributed in a liquid medium. The dispersed phase contains internal solid particles, usually in the size range of 0.5-50 micrometres, which remain uniformly spread throughout the suspending liquid with the help of one or more suspending agents. In most cases, the liquid medium is water-based, although for some non-oral formulations, oily or other organic liquid may be used.

Advantages:

- Improve patient compliance.
- The onset and duration of the drug's action can be adjusted.
- Oral suspension help reduce or hide the bitter taste of drugs. (for Example: chloramphenicol).
- Pharmaceutical oral suspension can improve the chemical stability of certain drug. Example: penicillin G
- Use of co-solvents can be avoided.
- Easy to swallow for elderly patients.
- The dose can be easily adjusted, especially for paediatric and geriatric patients.
- Suspensions make it possible to give higher drug concentrations compared to some other dosage forms.

- In general, drug absorption follows this order: solutions show the fastest effect, followed by suspensions, capsule, compressed tablet, and coated tablet

Limitation:

- Issues with physical stability such as settling and compact formulation, may occur.
- These formulations are bulky and require careful handling and transportation.
- Their preparation can be challenging.
- Accurate and uniform dosing is difficult unless suspension is provided in unit dose form.
- Aqueous suspensions may support microbial growth if not properly preserved.

Applications:

- ❖ Contrast media used for diagnostic purposes is also given in the form of suspension (for example: Barium sulphate for examination of alimentary canal).
- ❖ For drugs that are unstable in aqueous solution, insoluble derivatives or non-aqueous suspensions may be used.
- ❖ Drugs which have low solubility can be formulated in suspension.
- ❖ Suspensions are a good option for children and elderly patients, especially for giving drug that do not dissolve well.
- ❖ They can be administrated through different routes, such as oral, parenteral and topical.
- ❖ They help in reducing or masking the unpleasant bitter taste of certain drug. **(**for example: Chloramphenicol palmitate suspension).
- ❖ Many vaccines used for immunization are prepared in the form of suspensions (for example: cholera vaccine).
- ❖ Suspension can improve stability of drugs and help protect them from degradation (for example: oxytetracycline suspension).

Drug profile

Ceritinib (brand name: Zykadia) is a medicine used to treat a type of lung cancer called non-small cell lung cancer. It appears as a white to off-white, odourless substance with a slightly metallic taste. The drug has very low solubility in water and is classified under the BCS Ⅳ class drug as having poor solubility and low permeability. Ceritinib acts by inhibiting the anaplastic lymphoma kinase (ALK)protein, which involved in the growth of certain cancer cells. By inhibiting this protein and related signaling pathway, it helps stop the multiplication of cancer cells. After oral administration, the drug reaches its highest concentration in the blood within 4 to 6 hours. It spreads widely throughout the body and strongly binds to blood proteins. Ceritinib is mainly processed in the liver by CYP3Aenzymes, and most of the drug is eliminated through feces, with only a small amount excreted in urine. It has a long half-life of about 41 hours, allowing it to remain in the body for an extended period.

MATERIALS AND METHODS

Material:

Ceritinib was kindly supplied as a sample by Natco Pharma Ltd., Switzerland. Poloxamer 188 was procured from Simson Pharma Ltd., Mumbai. Vitamin E was procured from Fairchem organics., Ahmedabad. Microcrystalline Cellulose was obtained from Chemfield cellulose Pvt. Ltd., Maharashtra. Sodium lauryl sulfate was obtained from Alpha Chemical Pvt. Ltd., Mumbai. Propylene glycol, Citric acid was obtained from Nice chemical (P)Ltd. Edappally, Kochi

Method:

Preformulation Studies

Preformulation studies were performed to evaluate the basic characteristics of the drug. The color, odor, and taste were observed and recorded using standard terms to maintain clarity and avoid confusion. Solubility was checked by adding excess drug to distilled water and shaking until equilibrium was reached. The pH was measured to assess the drug stability and nature. Bulk and tapped densities were determined to study powder behavior. Flowability of the powder was evaluate using Carr's index, While the angle of repose, determined by the funnel method, was used to further assess its flow characteristics.

Development of ceritinib oral suspension:

Table 1: Formulation Table of Ceritinib Suspension

Sl.NO	Ingredients	F1	F2	F3	F4
1	Ceritinib	1.5g	1.5g	1.5g	1.5g
2	Poloxamer 188	--	--	1g	1g
3	Vitamin E	--	--	1g	1g
4	Microcrystalline cellulose	2g	1.5g	1g	0.5g
5	Pectin	2g	1.5g	1g	0.5g
6	Propyl paraben	0.4g	0.4g	0.4g	0.4g
7	Sodium lauryl sulfate	1.2g	1.2g	1.2g	1.2g
8	Simethicone	0.01g	0.01g	0.01g	0.01g
9	Citric acid	0.4g	0.4g	0.4g	0.4g
10	Sucrose	20g	20g	20g	20g
11	Water	Q. S	Q. S	Q. S	Q. S

The insoluble components are first grouping with the vehicle and a wetting agent to form a smooth paste. Any soluble ingredients are dissolved separately in a small amount of the vehicle and then mixed with this paste to produce a slurry.

The slurry obtained is transferred to a graduated cylinder, and the mortar is rinsed with additional portions of the vehicle to ensure complete transfer. The mixture is then observed to check whether the particles are properly flocculated before suspension. The pH is adjusted to the drug's isoelectric point to achieve optimal formulation. Finally, more vehicle is added to make up to the suspension to the required volume.

EVALUATION OF ORAL SUSPENSION[10,11,15]

1. Physical appearance

The prepared suspension was observed visually to assess its color, uniformity, clarity, and presence of aggregates or foreign particles to ensure acceptable physical appearance and overall formulation quality.

2. Determination of pH

The digital pH meter was set up using buffer solutions with pH 4.0 and pH 7.0.

3. Viscosity measurement:

The viscosity of each ceritinib suspension was determined using a Brookfield viscometer operated at 50 rpm. A 50mL sample was tested, the spindle was immersed to the mark, and reading recorded after stabilization to determine formulation viscosity.

4. Sedimentation volume:

The Sedimentation volume of 50 ml suspension was measured in a 100 ml cylinder at 1,2,3 and 7 days, then weekly interval for 12 weeks. Triplicate reading was taken, and sedimentation volume was calculated accordingly,

$$F=H_u/H_o$$

5. Redispersibility

A measured amount (50ml) of each suspension was placed in calibrated tubes and kept at room temperature for different time period (5,15,25 days). At each time point, one tube was taken out and shaken well to mix any settled particles. The samples were then checked for any sediment or deposits, and the observations were noted.

6. Flow rate

The time required for a 10mL suspension sample to pass through a 10mL pipette was measured, and the flow rate was then calculated using the equation below.

$$F = Volume\ of\ pipette\ (ml)/Flow\ time\ (sec)$$

7. *In-vitro* dissolution test

HPLC analysis of the suspension measures how much drug dissolves over time. The suspension is placed in a dissolution medium at 37 °C with constant stirring. Samples are taken at set time intervals and filtered or centrifuged to remove undissolved particles. The clear liquid is diluted with the mobile phase if needed. A standard drug solution is prepared to create a calibration curve. The sample is then injected into the HPLC system, where the peak area indicates drug concentration. Using the calibration curve, the amount drug released is calculated and used to evaluate the suspension performance and drug release.

RESULTS AND DISCUSSION

Preformulation Studies

Table 2: Evaluation parameter of pre-formulation studies

Test parameter	Batch F1
Colour	White-off
Odour	Odourless
Ph	6(neutral)
Bulk density	0.5172g/cm^3
Tapped density	0.6818g/cm^3
Carr's index	24.141%
Angle of Repose	35.75
Water	Partially insoluble
Alcohol	Partially soluble

Determination of lambda (λmax) of ceritinib:

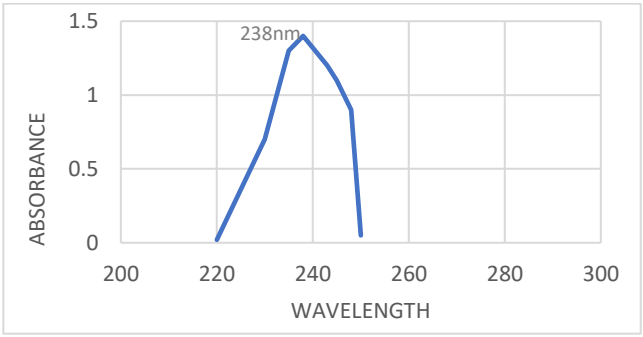

Figure 1: Lambda max for Ceritinib drug (238nm)

The maximum absorption wavelength (λmax) of ceritinib was identified by scanning a suitable drug concentration in phosphate buffer (pH 6.5) over the range of 200–400 nm using a UV spectrophotometer. The highest absorption was observed at 238 nm.

Standard curve of Ceritinib:

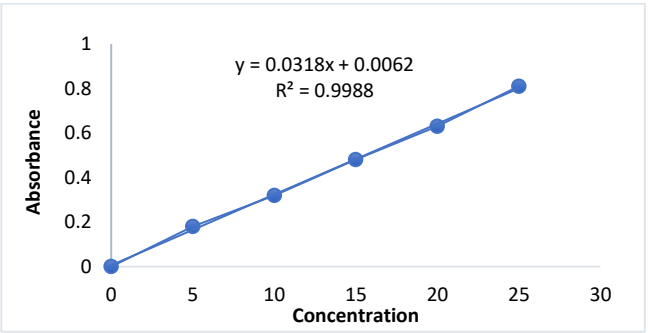

Figure 2: Calibration curve for Ceritinib drug. (pH 6.5) at 238 nm

The calibration curve of Ceritinib was developed using phosphate buffer (pH 6.5) over a concentration range of 5–25 µg/mL. The absorbance values was measured at 238 nm using a UV spectrophotometer. A linear relationship

between concentration and absorbance was observed, and it confirms that the drug obeys Beer–Lambert's law as Figure 2 illustrates. The calibration curve's slope was found to be 0.0325, and 0.9999 was the regression coefficient (R2)

EVALUATION OF SUSPENSION

1. Physical appearance

The formulation showed a uniform, smooth, and milky white appearance throughout the preparation. No visible lumps, aggregates, or coarse particles were observed in the suspension. Also, the sediment was minimal and could be easily redispersed by shaking, indicating that the suspension possessed acceptable physical stability

pH

The pH of the suspension formulations was found to range between 6.0 and 6.4. This pH range is considered suitable for pharmaceutical suspensions and ensures the stability of the formulation without causing irritation.

Viscosity

The viscosity of different Ceritinib suspension formulations (F1–F4), ranging from 540 to 650 cP, which significantly affect stability and flow properties. Formulations F1 (550 cP) and F3 (540 cP) have lower viscosity, which may lead to faster sedimentation and reduced stability. In contrast, F2 (630 cP) and F4 (650 cP) exhibit higher viscosity, helping to minimize particle settling and improve stability. However, very high viscosity can reduce pourability. Among all, F4 provides the best balance between stability and flow, making it the most suitable formulation.

Sedimentation volume:

Figure 3: sedimentation volume of suspension (F1, F2, F3, F4)

Sedimentation volume is an key factor used to assess0 the stability of suspension formulations. The sedimentation volume values of formulations F1 to F4 ranged from 1.5 to 1.66 as shown in Table. Among the formulations**,** F4 and F2 exhibit higher values, suggesting better suspension characteristics such as improved dispersion or viscosity. F1 shows moderate performance, while F3 has the lowest value, indicating comparatively lower stability. Overall, F2 and F4 are more suitable formulations, whereas F3 is less suitable. However, all values appear within an acceptable range for suspension systems.

Redispersibility

Redispersibility studies conducted over three days showed that all formulations (F1–F4) could be easily re-dispersed, indicating good suspension stability. Formulation containing Poloxamer (F1, F2) required slightly more shaking (about 2–5 times) compared to those without poloxamer (F3, F4) which needed around 2–4 shakings. A small increase in number of shaking from Day 1 to Day 3 suggests slight sediment compaction over time, however the sediments remained loose and no caking was observed. The use of appropriate suspending agents played a key role in maintaining uniform dispersion and preventing the formulation of hard sediment. Overall, all formulations demonstrated acceptable stability, with poloxamer containing formulations showing marginally better performance during extended storage

Flow rate

The flow rate of the prepared ceritinib suspensions was evaluated to determine their pourability and viscosity. The results showed clear differences among the formulations, mainly due to variations in the concentration of the suspending agent and the presence of poloxamer. Formulation F1 and F2, which do not contain poloxamer, exhibit lower flow rates (0.443 mL/s and 0.856 mL/s), indicating higher viscosity and less ease of flow. In contrast, formulations F3 and F4, containing poloxamer, showed higher flow rates of 0.993 mL/s and 1.276 mL/s reflecting, improved flowability and reduced resistance. Furthermore, in the poloxamer containing formulations, a decrease in the concentration of the suspending agent led to an increase in flow rate, lower viscosity and pourability.

***In vitro* dissolution studies:**

The dissolution study of ceritinib oral suspension was performed using USP Apparatus Ⅱ under simulated gastric conditions (0.1N HCl, 37°C, 50 rpm). Samples were analyzed by HPLC, and the standard showed 99.7% potency, confirming method reliability. The bioenhancer-containing formulation exhibited high drug release (95.9% -97.5%, average of ~96.6%) with very low (%RSD ~0.11), indicating excellent uniformity. In contrast, the formulation without bioenhancer showed lower drug release (74.8%–77.9% average of ~76.45%) and higher variability. These results demonstrate that the addition of a bioenhancer significantly improves dissolution, consistency, and the overall potential bioavailability of the optimized ceritinib suspension.

CONCLUSION

This study was conducted to develop and assess an oral suspension of ceritinib, aiming to address its low water solubility and poor permeability, as it is classified as a BCS Class IV drug. The goal was to improve its dissolution, stability, and therapeutic performance by incorporating suitable suspending agents and bioenhancers. The prepared formulations were evaluated for physicochemical

properties including appearance, pH, viscosity, sedimentation volume, ease of redispersibility, flow rate, and *in-vitro* dissolution studies.

The finding indicates that all formulations exhibited satisfactory physical properties and stability. The pH values were within the suitable range for oral administration and viscosity ensured both good pourability and suspension stability. Sedimentation studies indicated slow settling of particles and easy redispersibility. The optimized formulation showed better performance compared to others, with sedimentation volume, redispersibility, viscosity, and drug release profile. The presence of Poloxamer 188 enhanced drug solubility while, Vitamin E acted as a bioenhancer and antioxidant, improving absorption.

Overall, the developed Ceritinib suspension demonstrated improved dissolution and stability, suggesting its potential to enhance bioavailability and therapeutic effectiveness

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REFERENCES

1. Walkwe S Update in non-small cell lung cancer, Clinical journal of oncology nursing. 2008;12(4):50-56. doi:10.1188/08.
2. Goldstraw P, Ball D, Jett JR, LeChevallier T, Lim e non-small cell lung cancer, The lancet. 2011;378(9804)1727_40 doi:10.1016/S0140.
3. Sahu Y, Jadon AS, Jain P, Thakur BS An Overview on Recent Advances in Pharmaceutical Suspension, International Journal of Medical Sciences and Pharma Research. 2021 Mar 15;7(1): 1-3.doi:10.22270.
4. Nousheen L, Rajasekaran S, Qureshi MS. Solubility enhancement of lornoxicam with poloxamer 188 by solvent evaporation method. International Journal of Health Sciences. 2022;5(1):8186-95.
5. Gaikwad SS, Morales JO, Lande NB, Laddha UD, Kshirsagar SJ. Exploring paediatric oral suspension development: Challenges, requirements, and formulation advancements. International journal of pharmaceutics. 2024 May 25; 657:124169.
6. Strickley RG. Paediatric oral formulations: an updated review of commercially available paediatric oral formulations since 2007. Journal of Pharmaceutical Sciences. 2019 Apr 1;108(4):1335-65.
7. Baratta F, Zingarelli C, Fanton F, Lamy E, Di Lascio G, Brusa P. Metronidazole Suspension for Paediatric Use in Developing Countries: Formulation, Quality, and Stability. Pharmaceutics. 2025 Jun 17;17(6):787-94.
8. Navid F, Christensen R, Minkin P, Stewart CF, Furman WL, Baker S. Stability of sunitinib in oral suspension. Annals of Pharmacotherapy. 2008 Jul;42(7-8):962-6.
9. Patel HR, Patel RP, Patel MM. Poloxamers: A pharmaceutical excipient with therapeutic behaviours. Int. J. Pharm Tech Res. 2009 Apr;1(2):299-303.
10. Gaikwad SS, Morales JO, Lande NB, Catalán-Figueroa J, Laddha UD, Kshirsagar SJ. Exploring paediatric oral suspension development: Challenges, requirements, and formulation advancements. International journal of pharmaceutics. 2024 May 25; 657:124169.
11. Wang H, Tan P, Barona D, Li G, Hoe S, Lechuga-Ballesteros D, Nobes DS, Vehring R. Characterization of the suspension stability of pharmaceuticals using a shadow graphic imaging method. International Journal of Pharmaceutics. 2018 Sep 5;548(1):128-38.
12. Almeida M, Magalhães M, Veiga F, Figueiras A. Poloxamers, poloxamines and polymeric micelles: Definition, structure and therapeutic applications in cancer. Journal of Polymer Research. 2018 Jan;25(1):31-6.
13. Moghimi SM, Hunter AC. Poloxamers and poloxamines in nanoparticle engineering and experimental medicine. Trends in biotechnology. 2000 Oct 1;18(10):412-20.
14. Almeida M, Magalhães M, Veiga F, Figueiras A. Poloxamers, poloxamines and polymeric micelles: Definition, structure and therapeutic applications in cancer. Journal of Polymer Research. 2018 Jan;25(1):31-8.
15. Jangde R, Daharwal SJ, Sahu RK, Singh J. Formulation development and evaluation of suspension of Gatifloxacin using suspending agent. Pharmacology Online. 2011; 2:1161-70.
16. Larsson M, Hill A, Duffy J. Suspension stability; why particle size, zeta potential and rheology are important. Annu. Trans. Nord. Rheol. Soc. 2012 Jan;20(6):55-62.
17. Rajora A, Nagpal K. Suspensions: Theory, formulation Considerations, flocculated and deflocculated suspensions, and evaluation of suspension stability. In Advances in Pharmaceutical Product Development 2025 Mar 19 (pp. 199-218). Singapore: Springer Nature Singapore.
18. Sai V, T Praveen S, V Gunadeep N, Asma Sultana, MCK Phani Sai, K Bhumika, U Prakash, K Deepika B Sravanthi S: Formulation and evaluation of paracetamol suspension by using natural suspending agent International Journal of Pharmacy and Pharmaceutical Science 2024; 6(2): 19-26.
19. Kuchekar A, Kulkarni A, Kole S, Pawar S, Gawade A, An Innovative Approach Towards Taste Masking: Formulation and Evaluation of Clarithromycin Suspension for Paediatrics. International Journal of Pharmaceutical Quality Assurance. 2024;15(4):2566-75.
20. C. K. Dhanapal, R. Manavalan, N. Chandra, A. Chenthilnathan Formulation development of paediatric rifampicin oral suspension, 2012;4 (3):845-853.