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Development of Immediate-Release Solid Dispersion Tablets of Bempedoic Acid with Enhanced Dissolution Performance and Stability

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ABSTRACT: Bempedoic acid, a recently introduced ATP-citrate lyase inhibitor, exhibits poor aqueous solubility, limiting its dissolution rate and oral bioavailability. The present study investigates the development of a poloxamer-based solid dispersion system, focusing on improving dissolution performance and elucidating the underlying physicochemical transformations.

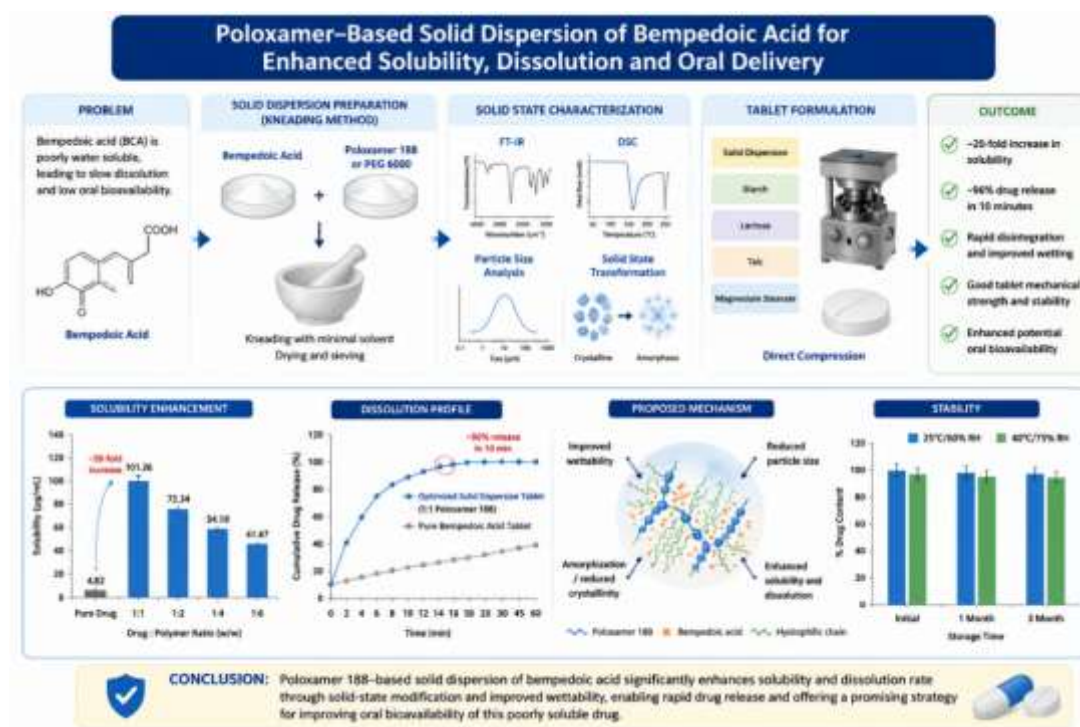
Solid dispersions were prepared using Poloxamer 188 and polyethylene glycol (PEG 6000) via the kneading method at varying drug-to-polymer ratios. Preformulation and solid-state characterization, including FT-IR and differential scanning calorimetry, confirmed drug integrity and suggested partial modulation of crystallinity in the optimized system. Among the prepared formulations, the 1:1 drug–polymer ratio exhibited the highest solubility enhancement, achieving approximately a 20-fold increase compared to the pure drug.

The optimized solid dispersion was further formulated into immediate-release tablets and evaluated for micromeritic, mechanical, and performance characteristics. The tablets demonstrated acceptable hardness, low friability, rapid disintegration, and significantly reduced wetting time. In vitro dissolution studies revealed rapid drug release, with approximately 96% release achieved within 10 minutes, indicating a marked improvement over the untreated drug.

The enhanced dissolution behavior is attributed to improved wettability, reduced particle size, and possible partial amorphization induced by the hydrophilic carrier system. Stability studies confirmed the robustness of the formulation with no significant changes in drug content or release profile.

Overall, this study demonstrates that poloxamer-mediated solid dispersion is an effective and scalable strategy for enhancing the dissolution characteristics of bempedoic acid, providing a promising platform for improving its oral delivery.

GRAPHICAL ABSTRACT



Highlights

- Solid dispersion of bempedoic acid was successfully developed using Poloxamer 188 and PEG 6000.
- Optimized formulation (1:1 ratio) achieved ~20-fold enhancement in aqueous solubility.
- Significant improvement in dissolution rate with ~96% drug release within 10 minutes.
- Enhanced performance attributed to improved wettability and possible solid-state modification.
- Formulated tablets exhibited rapid disintegration, acceptable mechanical strength, and stability.
- Study demonstrates an effective and scalable approach for improving oral delivery of poorly soluble drugs.

Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Credits Author Contributions:

- Ketul Patel: Investigation, Methodology, Writing – Original Draft
- Mital Patani: Supervision, Writing – Review & Editing
- Bhavna Nangha: Validation
- Poorva Maske: Data Collection, Formal Analysis

- Joseph Kassi: Formal Analysis
- Sushma Patil: Methodology, Data Collection
- Siddhi Upadhyay: Visualization, Validation

INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of global mortality, with elevated low-density lipoprotein cholesterol (LDL-C) playing a central role in atherosclerosis and related complications [1–8]. Although statins are widely used as first-line therapy, their clinical utility is often limited by intolerance and insufficient lipid control, necessitating alternative therapeutic strategies [9–13]. Bempedoic acid (BCA), a novel adenosine triphosphate-citrate lyase (ACL) inhibitor, has demonstrated significant reductions in LDL-C and improved cardiovascular outcomes, particularly in statin-intolerant patients [9–15].

Despite its therapeutic potential, BCA is classified as a Biopharmaceutical Classification System (BCS) Class II drug, characterized by poor aqueous solubility, which limits its dissolution rate and oral bioavailability [16–21]. Since dissolution is the rate-limiting step for such compounds, effective solubility enhancement strategies are essential to ensure optimal therapeutic performance [22–27].

Various formulation approaches have been investigated, including particle size reduction, complexation, lipid-based systems, and solid dispersion techniques [28–31]. Among these, solid dispersion is widely recognized for its ability to enhance dissolution through improved wettability, reduced crystallinity, increased surface area, and amorphous transformation [32–37]. Hydrophilic carriers such as Poloxamer 188 and polyethylene glycol (PEG 6000) further improve drug solubilization and stability through surfactant and matrix-forming properties [38–41].

Therefore, the present study focuses on the development and evaluation of solid dispersion-based tablets of bempedoic acid to enhance solubility, dissolution, and potential oral bioavailability.

3. MATERIALS AND METHODS

3.1 Materials

Bempedoic acid was obtained as a gift sample from a reputed pharmaceutical manufacturer. Poloxamer 188 and polyethylene glycol (PEG 6000) were selected as hydrophilic carriers due to their established roles in enhancing solubility and stabilizing amorphous drug forms [33–36]. Excipients, including lactose (diluent), starch (disintegrant), talc (glidant), and magnesium stearate (lubricant), were of pharmaceutical grade and used as received. All solvents, including methanol and isopropyl alcohol, were of analytical grade. Phosphate buffer (pH 7.4) was prepared according to Indian Pharmacopeia (IP) specifications.

3.2 Instruments and Equipment

Analytical and processing instruments were employed to ensure accurate characterization and reproducibility of results. An electronic analytical balance (Cyber Lab, USA) was used for precise weighing. UV–visible spectrophotometric analysis was performed using a Shimadzu UV-1800 spectrophotometer. Dissolution studies were conducted using a USP Type II dissolution apparatus (Electrolab, India). FT-IR spectroscopy (Shimadzu FTIR-8400) and differential scanning calorimetry (DSC) were used for solid-state characterization [35,37]. Particle size analysis was carried out using a Malvern particle size analyzer. Tablet properties were evaluated using a Monsanto hardness tester, Roche friabilator, and standard disintegration apparatus.

3.3 Preformulation Studies

3.3.1 Organoleptic Properties

Bempedoic acid was evaluated for physical appearance, color, odor, and nature by visual inspection.

3.3.2 Melting Point Determination

The melting point was determined using the capillary method with a digital melting-point apparatus. The observed values were compared with the reported standard ranges.

3.3.3 Solubility Study

Solubility studies were conducted by adding an excess of the drug to various solvents (water, ethanol, acetone, chloroform, DMSO, DMF, and phosphate buffer, pH 7.4). The mixtures were equilibrated for 24 h at room temperature, filtered, and analyzed spectrophotometrically. Solubility enhancement studies are critical for BCS Class II drugs where dissolution is rate-limiting [19–23].

3.3.4 Determination of $\lambda_{\max}$ and Calibration Curve

A stock solution of bempedoic acid was prepared in methanol and diluted to obtain concentrations ranging from 2–10 $\mu\text{g/mL}$. The solution was scanned between 200–400 nm to determine $\lambda_{\max}$. The calibration curve was constructed in phosphate buffer (pH 7.4) by plotting absorbance versus concentration to ensure linearity for quantitative analysis.

3.3.5 FT-IR Analysis

FT-IR spectroscopy was performed using the KBr pellet method over the range of 4000–400 cm^{-1} to identify functional groups and detect possible drug–polymer interactions [35,38].

3.3.6 Differential Scanning Calorimetry (DSC)

DSC analysis was conducted to evaluate thermal behavior and detect potential solid-state modifications, such as amorphization or drug–polymer interactions, that influence dissolution performance [36,39].

3.3.7 Particle Size Analysis

Particle size distribution of the pure drug was determined using optical microscopy and laser diffraction, as particle size significantly influences the dissolution rate and bioavailability [31,32].

3.4 Preparation of Solid Dispersions

Solid dispersions were prepared using the kneading method, a widely reported technique for enhancing solubility of poorly water-soluble drugs [34,35]. Bempedoic acid and hydrophilic carriers (Poloxamer 188 and PEG 6000) were mixed in different drug-to-polymer ratios (1:1 to 1:6). The mixture was triturated with a minimal amount of isopropyl alcohol to form a homogeneous paste and kneaded for 30 min. The mass was dried at 40°C, pulverized, sieved through a #30 sieve, and stored in a desiccator until further evaluation.

3.5 Preparation of Tablets

The optimized solid dispersion, equivalent to 20 mg of bempedoic acid, was blended with excipients and compressed using a rotary tablet compression machine by direct compression. This method was selected due to its simplicity and suitability for solid dispersion systems [33,34].

3.6 Evaluation of Powder Blend (Pre-compression Parameters)

3.6.1 Angle of Repose

The funnel method was used to determine the flow properties. The angle of repose (θ) was calculated as follows:

$$\tan \theta = \frac{h}{r}$$

where h is the height and r is the radius of the powder cone, respectively.

3.6.2 Bulk Density

The bulk density was determined by measuring the initial volume of the powder in a graduated cylinder.

$$\text{Bulk Density} = \frac{M}{V_0}$$

3.6.3 Tapped Density

The tapped density was calculated after tapping the cylinder until a constant volume was reached:

$$\text{Tapped Density} = \frac{M}{V_f}$$

3.6.4 Carr's Index and Hausner Ratio

The compressibility index and Hausner ratio were calculated to assess flowability.

$$\text{Carr's Index} = \frac{\text{TD} - \text{BD}}{\text{BD}} \times 100$$
$$\text{Hausner Ratio} = \frac{\text{TD}}{\text{BD}}$$

3.7 Post-compression Evaluation of Tablets

3.7.1 Weight Variation

Twenty tablets were weighed individually, and the mean $\pm$ SD was calculated.

3.7.2 Hardness

Tablet hardness was measured using a Monsanto hardness tester ($n = 5$).

3.7.3 Friability

Friability was determined using a Roche friabilator at 25 rpm for 100 revolutions.

$$F = \frac{W_i - W_f}{W_i} \times 100$$

3.7.4 Drug Content

The powdered tablet equivalent to 30 mg of the drug was dissolved in phosphate buffer (pH 7.4), filtered, diluted, and analyzed at 258 nm.

3.7.5 Disintegration Time

The disintegration time was determined using a standard disintegration apparatus in distilled water at $37 \pm 0.5^\circ\text{C}$.

3.7.6 Wetting Time

The tablet was placed on folded tissue paper in a Petri dish containing 6 mL of water, and the wetting time was recorded.

3.8 In-vitro Dissolution Study

Dissolution studies were performed using USP Type II apparatus at $37 \pm 0.5^\circ\text{C}$ and 50 rpm in 900 mL phosphate buffer (pH 7.4). Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically. Dissolution testing is essential for evaluating the performance of solid dispersion systems and predicting in vivo behavior [35–38].

3.9 Stability Study

The optimized formulation was subjected to short-term stability studies under room temperature conditions. Samples were analyzed at specified intervals for drug content, hardness, and dissolution behavior to assess formulation stability.

4. RESULTS

4.1 Preformulation Studies of Bempedoic Acid

Preformulation studies were conducted to establish the physicochemical characteristics of bempedoic acid and generate essential data for formulation development. These studies included organoleptic evaluation, melting point determination, solubility analysis, UV spectroscopic characterization, Fourier-transform infrared (FT-IR) analysis, and differential scanning calorimetry.

4.1.1 Organoleptic Properties

Bempedoic acid was observed as a white, crystalline powder with a characteristic odor and solid state at room temperature. The absence of discoloration or aggregation indicates good physical stability of the active pharmaceutical ingredient (API). These observations are consistent with the reported pharmacopeial specifications, confirming the authenticity and purity of the drug sample.

4.1.2 Melting Point Determination

The observed melting point of bempedoic acid was $150\text{--}152^\circ\text{C}$, which falls within the reported standard range of $147\text{--}152^\circ\text{C}$. The narrow melting range indicates the high purity of the drug and the absence of significant impurities. This result confirms the crystalline nature of the API and validates its suitability for further formulation development.

4.1.3 Solubility Studies

Solubility analysis revealed that bempedoic acid exhibits extremely poor aqueous solubility (0.010 ± 0.01 mg/mL), confirming its hydrophobic nature. In contrast, significantly higher solubility was observed in organic solvents such as ethanol (4.34 ± 0.05 mg/mL), DMSO (24.59 ± 0.15 mg/mL), and DMF (20.67 ± 0.097 mg/mL) than in water. The marked difference in solubility between aqueous and organic media suggests that dissolution is likely the rate-limiting step in oral absorption. The poor aqueous solubility of bempedoic acid categorizes it as a poorly water-soluble drug, supporting the need for solubility enhancement strategies, such as solid dispersion systems. The significantly improved solubility in polar aprotic solvents further indicates the drug compatibility with hydrophilic carriers. These findings strongly support the use of solid dispersion as an appropriate approach to enhance dissolution behavior and potential oral bioavailability.

4.1.4 Determination of $\lambda_{\max}$

The UV absorption spectrum of bempedoic acid in methanol showed a distinct maximum absorbance ($\lambda_{\max}$) at 258 nm, as represented in Figure 1, consistent with values reported in the literature. The sharp, well-defined peak confirmed the suitability of UV spectrophotometry for quantitative analysis of the drug.

The consistency of the observed $\lambda_{\max}$ with standard values further confirmed drug identity and validated the analytical method for subsequent dissolution and drug content studies.

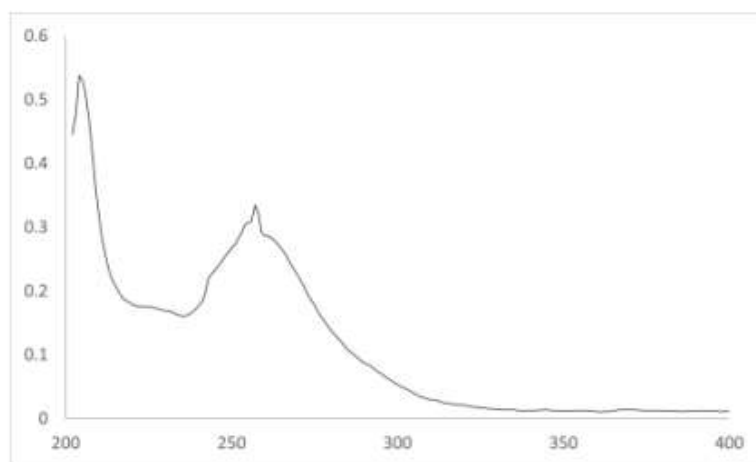


Figure 1 Wavelength max ($\lambda_{\max}$) of Bempedoic Acid

4.1.5 Calibration Curve

As shown in Figure 2, the calibration curve constructed in the concentration range of 2–10 $\mu\text{g/mL}$ demonstrated excellent linearity between the concentration and absorbance at 258 nm. The regression analysis showed a high correlation coefficient (R^2 close to 1), indicating the strong linearity and reliability of the developed analytical method. The validated calibration curve was subsequently used for quantification in the solubility and dissolution studies.

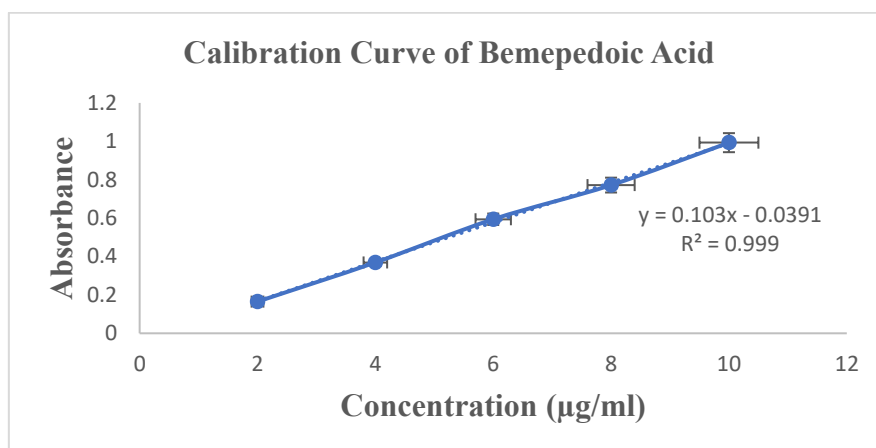


Figure 2 Calibration Curve of Bempedoic Acid

4.1.6 FT-IR Analysis

FT-IR spectroscopy confirmed the structural integrity of bempedoic acid. Characteristic absorption peaks corresponding to

- C=O stretching ($\sim 1720\text{ cm}^{-1}$)
- O–H stretching ($\sim 2500\text{--}3300\text{ cm}^{-1}$)

- C–O stretching ($\sim 1178\text{ cm}^{-1}$)
- C–H stretching ($\sim 2878\text{ cm}^{-1}$)

were observed without significant deviations from the standard reference values. The presence of all characteristic functional group peaks confirmed the drug identity and chemical purity.

No unexpected peaks or major shifts were observed, indicating the absence of degradation or structural modification during preformulation processing, as shown in Figure 3.

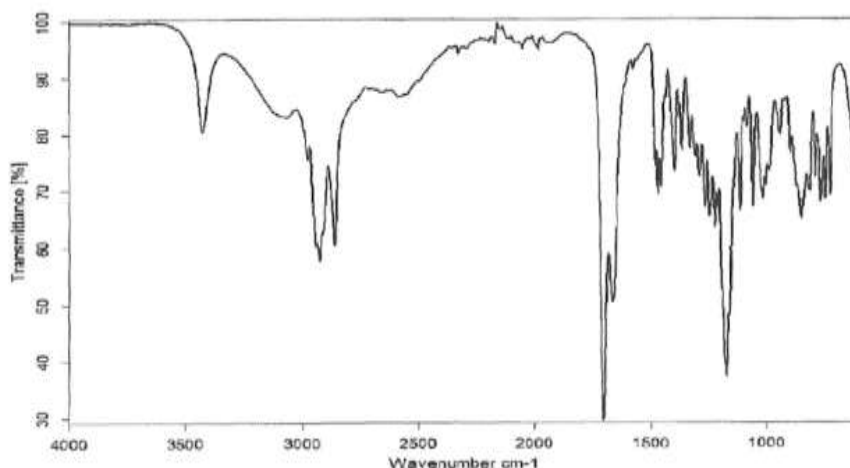


Figure 3 FTIR of Bempedoic Acid

4.1.7 Differential Scanning Calorimetry (DSC)

The DSC thermogram of pure bempedoic acid, represented in Figure 5, exhibited a sharp endothermic peak corresponding to its melting point, confirming its crystalline nature. The sharpness of the peak indicates a high purity and uniform crystal structure.

The thermal profile further supports the drug's suitability for solid-dispersion formulation, in which conversion from the crystalline to the partially amorphous form may improve dissolution. DSC graph complies with standard data which further confirms the drug identity and purity

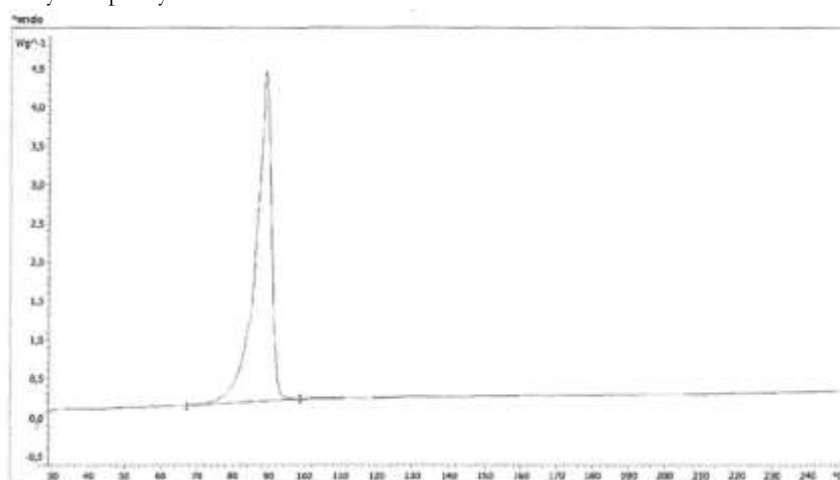


Figure 4 Differential Scanning Calorimetry of Bempedoic Acid

4.2 Particle Size Analysis of Bemepedicoic Acid (API)

Particle size analysis of pure bemepedicoic acid was performed to understand its baseline physical characteristics prior to formulation development. Figure 5 shows that microscopic and laser diffraction analyses confirmed that the drug exists as crystalline particles with a relatively large size distribution, which is consistent with its poor aqueous solubility profile.

The relatively coarse particle size of the API may contribute to the reduced surface area and slower dissolution rate. These findings further justify the selection of solid dispersion technology as a strategy to reduce the effective particle size and enhance the dissolution behavior through improved wettability and possible amorphization.

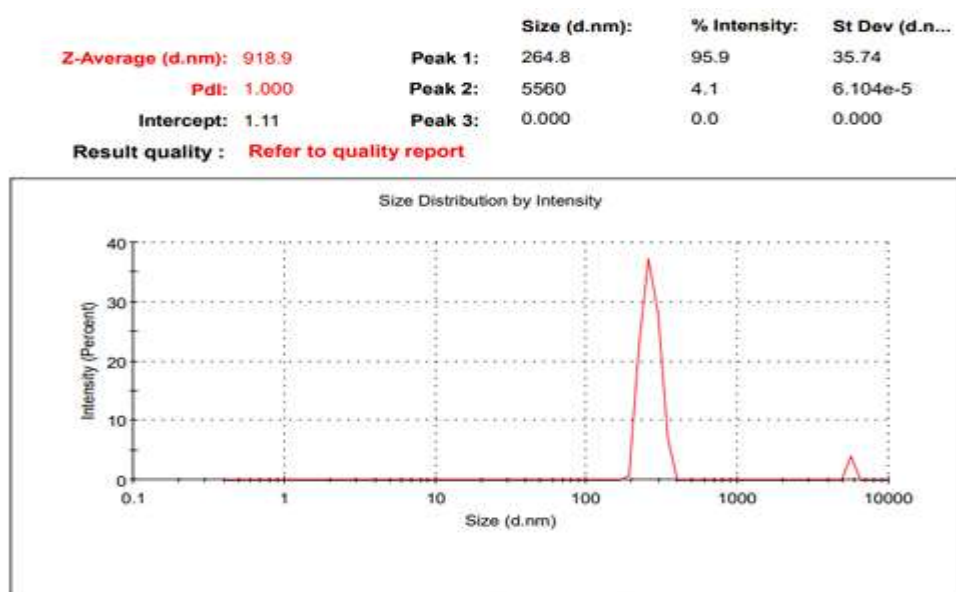


Figure 5 Particle Size Study

4.3 Preparation and Screening of Solid Dispersion Batches

Preliminary solid dispersions (BASD 1–BASD 6) were prepared using Bemepedicoic acid and Poloxamer 188 in different drug-to-polymer ratios (1:1 to 1:6) using the kneading method represented in Table 1.

The rationale for varying the polymer concentration was to evaluate its influence on micromeritic behavior, solubility enhancement, drug content, and yield. Poloxamer 188 was selected for its amphiphilic nature, surfactant properties, and ability to improve the wettability of hydrophobic drugs, as previously described.

Table 1 Preliminary Trial batch of Bemepedicoic Acid Solid Dispersion

Code	Solid Dispersion	Drug: Polymer
BASD 1	Bemepedicoic Acid: Poloxamer 188	1:1
BASD 2	Bemepedicoic Acid: Poloxamer 188	1:2
BASD 3	Bemepedicoic Acid: Poloxamer 188	1:3
BASD 4	Bemepedicoic Acid: Poloxamer 188	1:4
BASD 5	Bemepedicoic Acid: Poloxamer 188	1:5
BASD 6	Bemepedicoic Acid: Poloxamer 188	1:6

4.4 Micromeritic Properties of Solid Dispersions

Micromeritic evaluation demonstrated that all prepared batches exhibited acceptable flow properties. The angle of repose ranged from approximately 20° to 28°, indicating good-to-excellent flowability. Carr's index values were below 10% for all formulations, and Hausner ratio values were close to unity (1.01–1.12), confirming minimal interparticulate friction and good compressibility.

BASD 1 and BASD 5 batches exhibited comparatively lower angles of repose (~20°), indicating enhanced flow properties relative to batches with higher polymer content. This improvement is likely due to the surfactant action of poloxamer 188, which decreases interparticle cohesion. Table 2 summarizes these findings. Overall, the micromeritic data confirm that the prepared solid dispersions are well-suited for tablet production via direct compression.

Table 2 Micromeritic properties of Bemepedolic Acid Solid Dispersion

Formulation Code	BD (g/cm ²)	TD (g/cm ²)	Θ	CR (%)	HR
BASD 1	0.475±0.04	0.511±0.09	20.27±0.07	7.65±0.05	1.061
BASD 2	0.467±0.06	0.517±0.04	25.52±0.05	6.68±0.04	1.121
BASD 3	0.413±0.04	0.433±0.05	28.38±0.04	7.70±0.12	1.085
BASD 4	0.452±0.02	0.522±0.06	28.45±0.05	8.45±0.26	1.014
BASD 5	0.471±0.07	0.475±0.03	20.54±0.09	6.40±0.04	1.072
BASD 6	0.435±0.09	0.420±0.04	28.36±0.04	7.39±0.05	1.082

4.5 Solubility Enhancement and Physicochemical Evaluation

A marked improvement in aqueous solubility was observed for all solid dispersion batches compared to pure bemepedolic acid (0.010 mg/mL). The solubility increased significantly, reaching a maximum of 0.226 mg/mL in BASD 1, representing more than a 20-fold enhancement.

Interestingly, increasing the polymer ratio beyond 1:1 did not enhance the solubility proportionally. Instead, a slight reduction in solubility was observed at higher polymer ratios (BASD 2–BASD 6). This phenomenon may be attributed to the following reasons:

- Possible formation of a viscous diffusion layer at higher polymer concentration
- Reduced effective drug release due to excessive carrier matrix
- Saturation of drug–polymer interaction sites

The drug content in all formulations ranged between 95% and 99%, reflecting uniform distribution of the drug within the polymer matrix. The percentage yield varied from approximately 90% to 97%, indicating the kneading process was efficient with minimal material loss, as detailed in Table 3.

Table 3 Properties of Bemepedolic Acid Solid Dispersion

Formulation Code	Solubility (mg/ml)	% Content	% Yield
BASD 1	0.226±1.67	97.63±1.67	90.67±1.67
BASD 2	0.199±1.26	97.46±1.34	95.45±1.49
BASD 3	0.198±1.34	98.37±1.45	93.57±1.45
BASD 4	0.209±1.79	95.52±1.27	96.78±1.34
BASD 5	0.197±1.45	98.80±1.67	94.58±1.26
BASD 6	0.209±1.24	96.46±1.46	95.12±1.78

4.6 Selection of Optimized Batch

Based on a comparative evaluation of solubility, drug content, yield, and micromeritic parameters, BASD 1 (Drug:Poloxamer 188, 1:1 ratio) was selected as the optimized formulation.

The selection was justified as follows:

- Highest solubility enhancement (0.226 mg/mL)
- Acceptable drug content (97.63%)
- Satisfactory production yield (90.67%)
- Excellent flow properties

The results indicate that a lower polymer concentration (1:1 ratio) is sufficient to effectively enhance drug solubility without excessive carrier loading. This suggests optimal drug–polymer interactions at balanced ratios.

4.7 Preparation of Tablets of Solid Dispersions

The optimized solid dispersion (BASD 1) equivalent to 20 mg of bempedoic acid was formulated into tablets using the direct compression method. Lactose was used as a diluent, starch as a disintegrant, talc as a glidant, and magnesium stearate as a lubricant. The total tablet weight was approximately 300 mg. The selected excipient combination was designed to ensure adequate flowability, compressibility, rapid disintegration, and mechanical strength while maintaining the enhanced dissolution characteristics imparted by the solid dispersion.

4.8 Pre-compression Evaluation of Powder Blend

The powder blend exhibited an angle of repose of 26.71°, indicating good flow properties that were suitable for direct compression. The bulk and tapped densities were 0.472 g/mL and 0.566 g/mL, respectively. The compressibility index (15.1%) and Hausner ratio (1.184) suggested fair-to-good flowability. These values fell within the acceptable pharmacopeial limits, confirming that the blend possessed adequate packing ability and compressibility for tablet manufacturing without flow-related processing issues. The satisfactory pre-compression parameters demonstrated that the incorporation of solid dispersion did not adversely affect the powder handling characteristics.

4.9 Post-compression Evaluation of Tablets

The formulated (F1–F6) and marketed tablets were evaluated for weight variation, drug content, hardness, friability, disintegration time (DT), and wetting time.

4.9.1 Weight Uniformity

All formulations showed a uniform weight distribution (186–203 mg), indicating consistent die filling and compression performance. The variation was within the acceptable pharmacopeial limits.

4.9.2 Drug Content

Among the formulations, F3 showed the highest drug content (90.55%), which was comparable to and slightly superior to that of the marketed formulation (84.23%). The lower drug content in F1 and F5 may indicate non-uniform dispersion or processing variation. The high drug content in F3 confirmed the uniform distribution of the solid dispersion within the tablet matrix.

4.9.3 Hardness and Friability

Tablet hardness ranged between 3.5 and 3.9 kg/cm², indicating adequate mechanical strength to withstand the handling. The friability values for all batches were below 1%, demonstrating good resistance to abrasion and compliance with pharmacopeial standards. The mechanical strength of the tablets confirmed that the incorporation of poloxamer-based solid dispersions did not compromise compressibility.

4.9.4 Disintegration Time and Wetting Time

F4 showed the fastest disintegration (2.36 min), whereas F3 demonstrated a rapid wetting time (43 s) compared to the marketed tablet (61 s). The reduced wetting time of the formulated tablets may be attributed to the improved hydrophilicity imparted by Poloxamer 188. The enhanced wetting and disintegration properties are expected to contribute to an improved dissolution performance.

Table 4 Post-Compression Evaluation of Marketed & Formulated Tablet

Parameters	F1	F2	F3	F4	F5	F6	Marketed Tablet
Weight Uniformity (mg)	196	194	186	203	197	190	180
Drug content (%)	62.35	78.99	90.55	73.58	67.96	75.74	84.23
DT (min)	3.15	2.41	2.64	2.36	3.36	3.25	3.22
Friability (%)	0.52	0.66	0.62	0.55	0.64	0.58	0.6
Hardness (kg/cm ²)	3.7	3.5	3.6	3.7	3.9	3.6	3.14
Wetting time (sec)	57	53	43	57	52	46	61

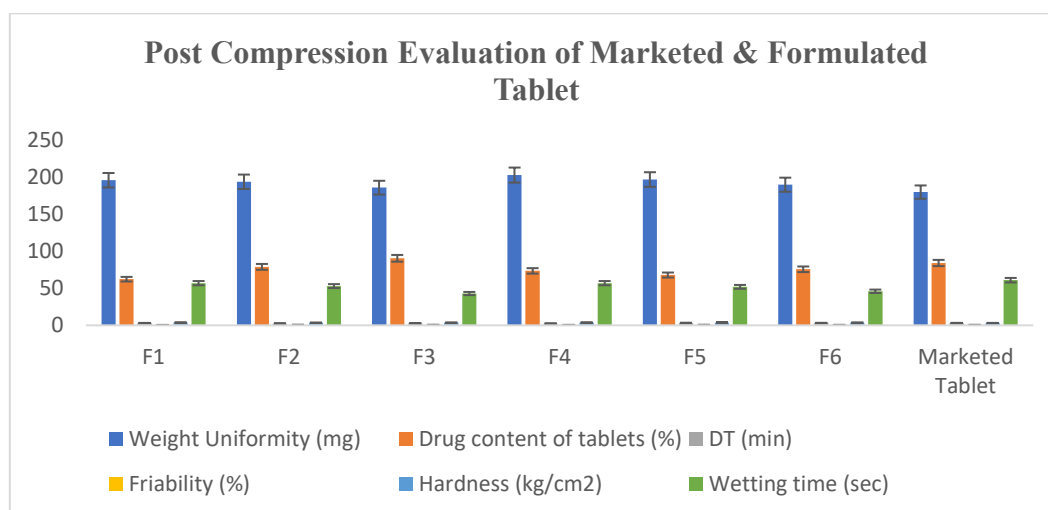


Figure 6 Post-Compression Evaluation of Marketed & Formulated Tablet

4.10 In-Vitro Drug Release Study

Dissolution studies revealed rapid and enhanced drug release from the optimized formulation. Approximately 45.78% drug release was observed within 2 min, which increased progressively to 96.58% within 10 min.

This rapid-release profile indicates a significant improvement over the pure drug and demonstrates the effectiveness of the solid dispersion approach.

The enhanced dissolution may be attributed to the following:

- Improved wettability due to Poloxamer 188
- Reduced effective particle size
- Increased surface area

- Possible partial amorphous transformation
- Prevention of drug agglomeration

The drug exhibited nearly complete release within 10 minutes, demonstrating immediate-release properties that could potentially improve oral absorption, as illustrated in Figure 7.

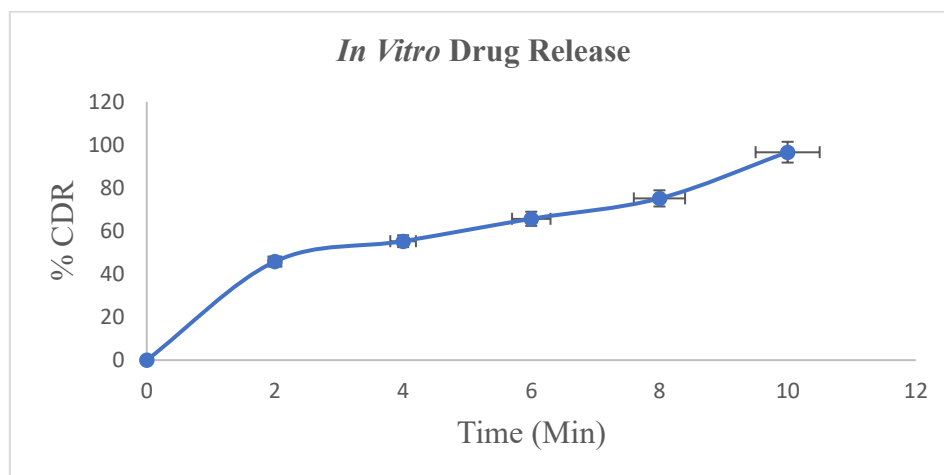


Figure 7: In Vitro Drug Release

4.11 Stability Study

Stability evaluation of the optimized formulation at room temperature for 30 days demonstrated no significant change in hardness (3.6 kg/cm²), wetting time (43 sec), drug content (90.55% to 90.45%), or dissolution profile (96.58% to 96.30%). The minimal variation confirmed the formulation's physicochemical stability and indicated the absence of drug degradation or recrystallization during the study period. The stability findings further support the robustness of the solid dispersion system and its suitability for pharmaceutical applications.

5. DISCUSSION

Bempedoic acid, a BCS Class II drug, exhibits poor aqueous solubility, making dissolution the rate-limiting step for its oral absorption [16–21]. In the present study, solid dispersion with hydrophilic carriers significantly improved solubility and dissolution behavior, consistent with previously reported approaches for poorly soluble drugs [32–37].

The optimized formulation (1:1 drug–Poloxamer 188 ratio) demonstrated approximately 20-fold enhancement in solubility and rapid drug release (~96% within 10 min). This improvement can be attributed to enhanced wettability, increased surface area, and possible partial reduction in crystallinity, which are well-established mechanisms of solid dispersion systems [33–37]. The amphiphilic nature of Poloxamer 188 further contributes to micellar solubilization and improved drug dispersion within the dissolution medium [32,38].

Interestingly, increasing polymer concentration beyond the optimal ratio did not enhance solubility, indicating a non-linear relationship between carrier concentration and drug release. This may be due to the formation of a viscous diffusion layer that hinders drug release, a phenomenon previously reported in polymer-based systems [34–36].

The successful formulation of tablets with acceptable mechanical properties, rapid disintegration, and reduced wetting time confirms the suitability of the developed system for immediate-release applications. Stability studies further demonstrated minimal variation in drug content and dissolution, indicating formulation robustness.

However, the study is limited by the absence of advanced solid-state characterization techniques, such as PXRD, and in vivo evaluation, which are essential to confirm amorphous transformation and to establish a correlation with bioavailability [24,40,41].

6. CONCLUSION

The present study demonstrated that solid dispersion with Poloxamer 188 is an effective strategy to enhance the solubility and dissolution performance of bempedoic acid, a poorly water-soluble drug. The optimized formulation (1:1 drug–polymer ratio) achieved a significant (~20-fold) increase in solubility and rapid drug release (~96% within 10 minutes), indicating substantial improvement in dissolution behavior.

The enhanced performance can be attributed to improved wettability, increased surface area, and possible partial reduction in crystallinity induced by the hydrophilic carrier system. Furthermore, the successful development of immediate-release tablets with acceptable mechanical properties and stability highlights the practical applicability and scalability of the formulation approach.

Overall, the findings suggest that polymer-based solid dispersion is a promising platform for improving the oral delivery and therapeutic performance of bempedoic acid.

7. FUTURE SCOPE

Future studies should focus on advanced solid-state characterization techniques such as powder X-ray diffraction (PXRD) and scanning electron microscopy (SEM) to confirm the extent of amorphous transformation and morphological changes. Additionally, in vivo pharmacokinetic studies are required to establish a correlation between enhanced dissolution and bioavailability.

Further optimization using design of experiments (DoE) and exploration of alternative preparation techniques, such as spray drying or hot-melt extrusion, may provide deeper insights into formulation performance. Investigation of long-term stability under accelerated conditions and evaluation in biorelevant media are also recommended to ensure clinical applicability.

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