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PREPARATION AND EVALUATION OF FENOFIBRATE IMMEDIATE-RELEASE MULTIPARTICULATES (PELLETS) USING FLUIDIZATION TECHNOLOGY

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Abstract:

Fenofibrate is a poorly water-soluble BCS Class II drug with dissolution-rate–limited oral bioavailability, necessitating formulation strategies that enhance its immediate-release performance. The present study aimed to develop and characterize immediate-release fenofibrate multiparticulate pellets using fluidized bed (Wurster) coating technology. Pellets were prepared by layering fenofibrate onto microcrystalline cellulose cores using hydrophilic polymers and surfactants, followed by systematic evaluation of physical, micromeritic, and pharmaceutical properties. Four formulations (F1–F4) were developed and comparatively characterized for particle size distribution, surface morphology, flow properties, drug content uniformity, friability, hardness, wettability, and moisture content. All formulations exhibited acceptable pellet quality; however, formulation F2 demonstrated superior performance, characterized by narrow size distribution, smooth and spherical morphology, excellent flow behavior, uniform drug content, low friability, optimal mechanical strength, rapid wettability, and minimal residual moisture. The results confirm that controlled formulation design combined with optimized fluidized bed processing is an effective approach for developing immediate-release fenofibrate pellets with reproducible quality and enhanced performance.

Keywords: *Fenofibrate; Immediate-release pellets; Fluidized bed coating; Multiparticulate drug delivery; Wurster technology; Dissolution enhancement*

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INTRODUCTION:

Fenofibrate is a widely prescribed hypolipidemic agent belonging to the fibric acid derivative class, primarily used in the management of hypertriglyceridemia, hypercholesterolemia, and mixed dyslipidemia. By activating peroxisome proliferator-activated receptor alpha (PPAR-α), fenofibrate effectively reduces triglyceride levels, increases high-density lipoprotein cholesterol, and improves overall lipid profiles, thereby lowering the risk of cardiovascular complications.[1-15] Despite its established therapeutic efficacy, fenofibrate presents significant formulation challenges due to its extremely low aqueous solubility and dissolution-rate–limited absorption, which result in variable oral bioavailability and delayed onset of action.

Fenofibrate is categorized as a poorly water-soluble drug with dissolution being the rate-limiting step for its gastrointestinal absorption. Conventional oral dosage forms such as tablets and capsules often fail to provide rapid and reproducible drug release, leading to inconsistent plasma drug levels and reduced therapeutic performance. To overcome these limitations, immediate-release formulations with enhanced surface area and rapid dissolution characteristics are essential. Improving the dissolution behavior of fenofibrate is therefore a critical formulation objective to ensure predictable absorption and improved bioavailability.[16-25]

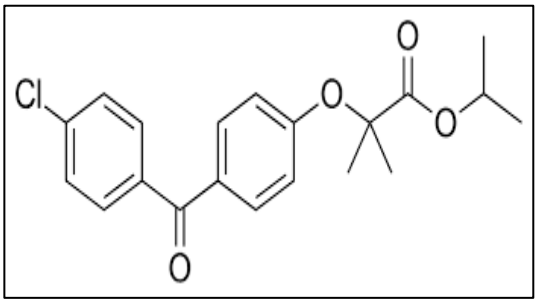

Figure 1: Chemical structure of Fenofibrate

Multiparticulate drug delivery systems, particularly pellet-based formulations, have gained considerable attention as an effective approach for enhancing dissolution and drug release performance of poorly soluble drugs. Pellets offer several advantages over single-unit dosage forms, including uniform drug distribution, reduced risk of dose dumping, improved flow properties, and flexible formulation design. The large surface area of multiparticulates promotes faster wetting and dissolution, making them especially suitable for immediate-release applications. Additionally, pellet-based systems allow for better control over drug loading and release behavior, while maintaining excellent content uniformity.[26-30]

Fluidization technology, particularly fluidized bed processing, is a well-established and industrially scalable technique for the preparation of pharmaceutical pellets. This technology enables simultaneous particle movement, efficient heat and mass transfer, and uniform coating or layering of drug substances onto inert cores. Fluidized bed systems provide precise control over critical process parameters such as inlet air temperature, spray rate, atomization pressure, and fluidization airflow, which directly influence pellet size, morphology, drug distribution, and release characteristics. The versatility and reproducibility of fluidization technology make it a preferred choice for manufacturing multiparticulate dosage forms.

The development of immediate-release fenofibrate pellets using fluidization technology represents a rational strategy to enhance dissolution rate and ensure rapid drug availability. By layering fenofibrate onto suitable starter cores and optimizing formulation and process variables, it is possible to produce pellets with uniform size distribution, smooth surface morphology, and improved drug-release profiles. Systematic evaluation of these pellets for physicochemical properties, mechanical strength, drug content uniformity, and in vitro dissolution behavior is essential to establish their suitability as an immediate-release dosage form.[31-36]

Therefore, the present research focuses on the preparation and evaluation of fenofibrate immediate-release multiparticulates using fluidization technology. The study aims to develop a robust, scalable, and efficient pellet-based delivery system capable of overcoming the biopharmaceutical limitations of fenofibrate. Successful formulation of such multiparticulates has the potential to improve therapeutic performance, ensure consistent drug release, and contribute to the advancement of immediate-release drug delivery strategies for poorly soluble compounds.

MATERIALS AND METHODS:

MATERIALS:

Fenofibrate was used as the active pharmaceutical ingredient and was procured from Yarrow Chemicals Pvt. Ltd. Inert starter cores, including sugar spheres or microcrystalline cellulose (MCC) pellets, were obtained from Signet Entrepreneurs and employed as the substrate for pelletization. Polyvinylpyrrolidone (PVP K30) and hydroxypropyl methylcellulose (HPMC), sourced from Loba Chemie and Colorcon respectively, were utilized as binders and film-forming agents during the drug-layering process.

Sodium lauryl sulfate and polysorbate 80, procured from Loba Chemie and Merck, were incorporated as surfactants to improve wettability and dissolution of fenofibrate. Ethanol (Merck) and purified water were used as solvents and vehicles for the preparation of drug-layering solutions. Talc (HiMedia) was employed as an anti-tacking agent, while magnesium stearate (Loba Chemie) was used as a flow enhancer to improve pellet handling and processing. All chemicals and excipients used in the study were of analytical or pharmaceutical grade and were selected to ensure compatibility with immediate-release pellet formulation and fluidized bed processing requirements.

METHODOLOGY:

Preformulation Studies of Fenofibrate

Preformulation investigations were undertaken to obtain critical information on the physicochemical properties of fenofibrate and to assess its suitability for development as an immediate-release multiparticulate system. These studies provided a scientific basis for rational selection of excipients and optimization of processing conditions, which is particularly important for poorly water-soluble BCS Class II drugs where dissolution enhancement governs oral absorption.[37-40]

Physicochemical Characterization of Fenofibrate

The physicochemical characteristics of fenofibrate were evaluated to understand parameters that could influence formulation behavior, processing performance, and in vitro drug release. Standard pharmacopeial and literature-reported methods were employed to assess properties such as appearance, solubility, melting behavior, and powder flow characteristics, all of which are relevant for fluidized bed pelletization.[41-44]

Fenofibrate was visually examined for color, odor, and physical form to confirm its organoleptic properties. Solubility studies were conducted in purified water, acidic media, and selected organic solvents to confirm its poor aqueous solubility and dissolution-rate-limited nature. These findings supported the need for formulation approaches aimed at improving wettability and dissolution.

The melting point of fenofibrate was determined using the capillary method to confirm drug identity and assess thermal stability. In addition, powder flow properties including bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio were evaluated to assess handling and flow behavior. The poor intrinsic flow properties of fenofibrate further justified the use of pelletization on inert cores to improve processability and uniformity during fluidized bed coating.[45-47]

Drug–Excipient Compatibility Studies

Compatibility studies were performed to ensure chemical and physical stability of fenofibrate in the presence of selected excipients. Such studies are essential in multiparticulate formulation development, as drug–excipient interactions may adversely affect stability, drug release, and overall product quality.

Physical mixtures of fenofibrate with commonly used excipients, including binders, surfactants, and pellet cores, were prepared in appropriate ratios and analyzed using Fourier Transform Infrared (FTIR) spectroscopy. The infrared spectra of the pure drug and physical mixtures were compared to identify any significant peak shifts, disappearance, or formation of new peaks that could indicate chemical interaction.

Differential Scanning Calorimetry (DSC) was additionally employed to evaluate thermal behavior and detect any changes in melting characteristics that might suggest interaction or partial amorphization. The absence of significant changes in both spectral and thermal profiles confirmed the compatibility of fenofibrate with the selected excipients, supporting their suitability for immediate-release pellet formulation.[48-52]

Selection of Excipients and Pellet Cores

Excipients and pellet cores were selected based on preformulation findings, literature support, regulatory acceptance, and suitability for fluidized bed processing. The excipients were chosen to facilitate efficient drug layering, enhance wettability, promote rapid drug release, and ensure reproducible pellet quality.

Inert starter cores such as sugar spheres or microcrystalline cellulose (MCC) pellets were selected due to their spherical geometry, narrow size distribution, and high mechanical strength. These characteristics are critical for uniform fluidization, efficient coating, and minimization of attrition during processing. Use of inert cores also allows precise control over drug loading and pellet size.

Hydrophilic binders such as polyvinylpyrrolidone (PVP K30) and hypromellose (HPMC) were selected to promote adhesion of fenofibrate onto the pellet surface during solution or suspension layering. These polymers are widely reported for their film-forming ability, compatibility, and suitability for immediate-release formulations. Surfactants such as sodium lauryl sulphate or polysorbate 80 were incorporated to improve drug wettability and dispersion in gastrointestinal fluids, which is particularly important for BCS Class II drugs. Ethanol and purified water were selected as

solvents based on safety, solubility considerations, and compatibility with fluidized bed coating.[53-56]

Development of Immediate-Release Fenofibrate Pellets

Immediate-release fenofibrate pellets were developed using fluidization technology in a Wurster-type fluidized bed coater. The formulation approach involved preparation of drug-containing solutions or suspensions using hydrophilic polymers, followed by drug layering onto MCC starter cores. This strategy was adopted to improve wettability, achieve uniform drug distribution, and ensure rapid drug release suitable for immediate oral administration.[57-60]

Preparation of Drug Solution or Suspension

Drug solutions or suspensions were prepared carefully to ensure homogeneity, appropriate viscosity for spraying, and uniform drug dispersion. Purified water was primarily used as the solvent system due to its safety and suitability for fluidized bed processing.

For each formulation batch, purified water was transferred into a suitable vessel and stirred continuously using a mechanical stirrer. Selected grades of hypromellose (E5 LV and/or E15) were gradually added under continuous stirring until a clear and uniform polymeric solution was obtained. The polymer composition and concentration were varied among formulations to study their influence on coating efficiency, pellet integrity, and drug release behavior.

Sodium lauryl sulphate was incorporated as a surfactant to enhance wettability and dispersion of fenofibrate, while simethicone was added as a defoaming agent to prevent foam formation during spraying. Fenofibrate was slowly added under continuous stirring to obtain a uniform dispersion. The prepared dispersion was filtered through an ASTM #40 mesh filter to remove agglomerates and ensure smooth atomization during coating. The same preparation procedure was followed for all formulations, with variations only in polymer type and concentration.[61-63]

Drug Layering Using Wurster Fluidized Bed Coater

Drug layering was performed using a bottom-spray Wurster fluidized bed configuration to ensure efficient particle circulation and uniform coating. Pre-sieved MCC spheres were loaded into the product container and fluidized using controlled inlet air until stable fluidization was achieved.

The prepared drug solution or suspension was sprayed through the Wurster nozzle onto the fluidized pellets. Atomized droplets adhered to the pellet surface, and rapid solvent evaporation resulted in deposition of the drug–polymer layer. Critical process parameters such as inlet air temperature, product temperature, air flow rate, atomization pressure, and spray rate were carefully controlled to prevent overwetting, agglomeration, or spray drying.

After completion of spraying, the coated pellets were dried in the same equipment by maintaining fluidization at elevated product temperature for approximately 30 minutes. The dried pellets were then sifted to remove agglomerates. The same layering and drying procedure was applied for all formulations.[64-65]

Formulation Design of Fenofibrate Immediate-Release Pellets

The formulations were designed to evaluate the effect of polymer grade and concentration on drug layering efficiency and immediate-release performance. MCC spheres served as inert cores to provide mechanical strength and uniform fluidization. Hydrophilic polymers acted as binders to ensure effective adhesion of fenofibrate, while sodium lauryl sulphate enhanced wettability and dissolution. Magnesium stearate was incorporated to improve flow properties during handling and further processing.[66-68]

Table 1: Composition of Immediate-Release Fenofibrate Pellets (F1–F4)

S. No.	Ingredient	F-1	F-2	F-3	F-4
1	MCC spheres (#50/60)	12.66	12.58	13.33	12.92
2	Fenofibrate	66.67	68.31	67.50	66.84
3	HPMC E5 LV	13.29	13.20	–	15.00
4	HPMC E15	1.33	–	13.41	3.98
5	Sodium lauryl sulphate	5.46	5.38	5.00	5.21
6	Simethicone	0.21	0.14	0.33	0.35
7	Magnesium stearate	0.38	0.38	0.42	0.38
8	Purified water	QS	QS	QS	QS

CHARACTERIZATION OF PREPARED PELLETS[52-72]

The prepared fenofibrate immediate-release pellets were systematically characterized to assess their physical, micromeritic, and pharmaceutical quality attributes. Evaluation of pellet characteristics is essential in multiparticulate systems, as parameters such as size uniformity, surface morphology, flow behavior, and drug content directly influence processing performance, dosage accuracy, and in-vitro drug release.

Particle Size and Size Distribution

Particle size and size distribution were determined to evaluate pellet uniformity and suitability for further processing. Sieve analysis was performed using a series of standard sieves, and the percentage weight retained on each sieve was calculated. A narrow size distribution was considered desirable, indicating uniform drug layering and controlled pellet growth during fluidized bed processing.

Surface Morphology

Surface morphology of the pellets was examined to assess shape, smoothness, and coating uniformity. Scanning Electron Microscopy (SEM) was used to visualize pellet surfaces at different magnifications. Spherical pellets with smooth and uniform surfaces were considered indicative of efficient fluidized bed coating and favorable dissolution behavior.

Flow Properties

Flow properties were evaluated to determine the handling characteristics of the pellets during processing and capsule filling. Parameters such as bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio were measured using standard methods. Pellets exhibiting low compressibility and good flow indices were considered suitable for multiparticulate dosage forms.

Bulk and Tapped Density

Bulk density was determined by measuring the volume occupied by a known weight of pellets without external force, while tapped density was measured after subjecting the pellets to mechanical tapping. These parameters provided insight into pellet packing ability and compressibility, which are important for uniform dosing and capsule filling.

Angle of Repose

The angle of repose was measured using the fixed funnel method to evaluate pellet flowability. Pellets forming a conical heap with a lower angle of repose were considered to possess good flow properties and reduced inter-particle friction.

Carr's Index and Hausner's Ratio

Carr's index and Hausner's ratio were calculated from bulk and tapped density values to assess compressibility and flow behavior. Lower Carr's index values and Hausner's ratios close to unity indicated good flowability and minimal cohesiveness of the pellets.

Drug Content Uniformity

Drug content uniformity was evaluated to ensure consistent distribution of fenofibrate within the pellets. A weighed quantity of pellets was crushed, and the drug was extracted using a suitable solvent. The solution was analyzed using a UV–Visible spectrophotometer, and drug content was calculated from a calibration curve. Pellets within acceptable limits were considered uniform and suitable for further evaluation.

Friability

Friability testing was conducted to assess the mechanical resistance of pellets to abrasion during handling and processing. A known weight of pellets was subjected to controlled agitation, and percentage weight loss was calculated. Pellets showing minimal weight loss were considered mechanically stable.

Pellet Hardness (Crushing Strength)

Pellet hardness was measured to evaluate resistance to breakage under applied force. Individual pellets were subjected to compression using a hardness tester, and the force required for fracture was recorded. Adequate hardness was considered essential to maintain pellet integrity without compromising immediate-release behavior.

Wettability Studies

Wettability was assessed to evaluate the interaction of pellets with aqueous media, which is critical for poorly water-soluble drugs like fenofibrate. Wetting time or contact angle measurements were used to assess surface hydrophilicity. Rapid wetting indicated improved wettability and enhanced dissolution potential.

Moisture Content (Loss on Drying)

Moisture content was determined to evaluate residual water present in the pellets after drying. Loss on drying was measured by heating a known weight of pellets until constant weight was achieved. Pellets with moisture content within acceptable limits were considered stable and suitable for storage and further studies.

RESULTS AND DISCUSSION:

Pre-Formulation Studies of Fenofibrate

Pre-formulation studies were conducted to evaluate the physicochemical properties of fenofibrate and to assess its suitability for development as

immediate-release multiparticulate pellets. As fenofibrate is a poorly water-soluble BCS Class II drug, understanding its solid-state characteristics, solubility behavior, and thermal properties was essential for rational excipient selection and formulation design aimed at enhancing dissolution performance.

Physicochemical Characterization

Fenofibrate was evaluated for organoleptic properties, solubility in different media, and melting point using standard pharmacopeial methods. The drug appeared as a white to off-white, odorless, crystalline powder. Solubility studies demonstrated extremely low solubility in aqueous media across physiological pH conditions, confirming dissolution-rate-limited absorption. In contrast, good solubility was observed in organic solvents. The melting point determination confirmed drug identity and crystalline nature, further supporting the need for formulation strategies to improve dissolution.

Table 2: Physicochemical Properties of Fenofibrate

Parameter	Observation / Result
Color	White to off-white
Odor	Odorless
Taste	Practically tasteless
Physical state	Crystalline powder
Solubility in purified water	Practically insoluble
Solubility in 0.1 N HCl	Very slightly soluble
Solubility in phosphate buffer (pH 6.8)	Very slightly soluble
Solubility in ethanol	Freely soluble
Solubility in methanol	Soluble
Solubility in chloroform	Soluble
Melting point	80–82 °C

Flow Properties of Fenofibrate Powder

The flow characteristics of fenofibrate powder were evaluated to assess its suitability for processing. As summarized in Table 7.4, fenofibrate exhibited poor flow behavior, evidenced by a high angle of repose (41.8°), elevated Carr's index (31.1%), and Hausner's ratio exceeding 1.4. These results indicate significant inter-particle friction and cohesiveness, rendering the drug unsuitable for direct processing. The poor flowability further justified the selection of pelletization using inert cores to improve handling, uniformity, and process reproducibility.

Table 3: Flow Properties of Fenofibrate Powder

Parameter	Result
Bulk density (g/cm³)	0.31 ± 0.02
Tapped density (g/cm³)	0.45 ± 0.03
Angle of repose (°)	41.8 ± 1.2
Carr's index (%)	31.1 ± 1.5
Hausner's ratio	1.45 ± 0.04

Calibration Curve of Fenofibrate

Fenofibrate showed maximum absorbance (λmax) at 420 nm. A linear calibration curve was obtained over the concentration range of 5–30 µg/mL, with a correlation coefficient (R^2) of 0.9991. The regression equation was found to be $y = 0.0355x + 0.0317$, confirming the suitability of the UV spectrophotometric method for quantitative estimation of fenofibrate in subsequent studies.

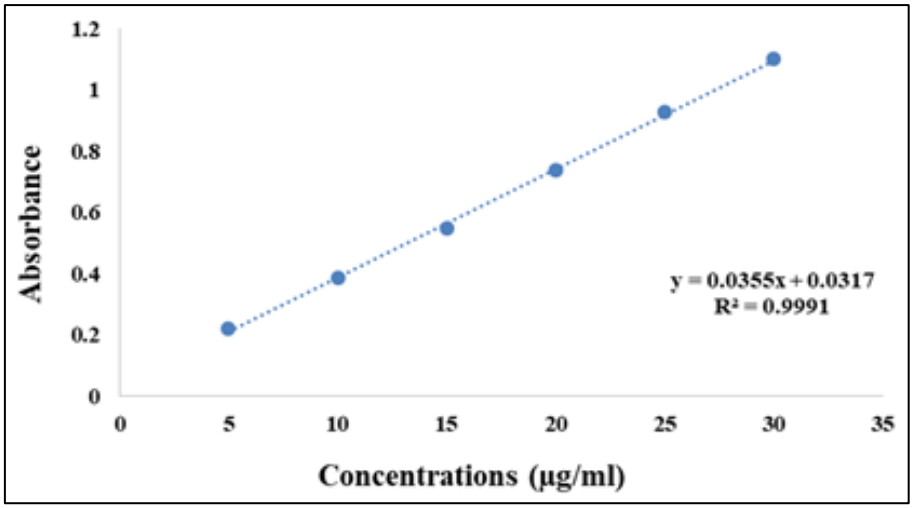

Figure 2: Calibration curve for Fenofibrate drug

Differential Scanning Calorimetry (DSC)

DSC analysis of fenofibrate exhibited a sharp endothermic peak corresponding to its melting point, confirming its crystalline nature. DSC thermograms of HPMC E5 LV and HPMC E15 showed characteristic thermal transitions without interference. The absence of additional or shifted peaks suggested thermal compatibility of fenofibrate with the selected polymers.

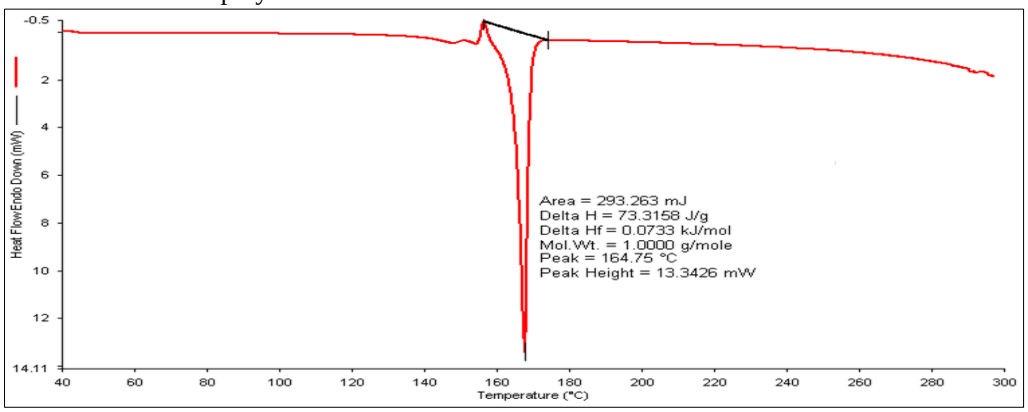

Figure 3: DSC Thermogram of Fenofibrate

Fourier Transform Infrared (FT-IR) Spectroscopy

FT-IR analysis was performed to evaluate drug–excipient compatibility. Fenofibrate exhibited characteristic absorption peaks corresponding to its functional groups. FT-IR spectra of physical mixtures containing fenofibrate and selected excipients showed retention of all major characteristic peaks without significant shifts or disappearance. These findings indicate the absence of chemical interactions, confirming compatibility of fenofibrate with formulation excipients and suitability for immediate-release pellet development.

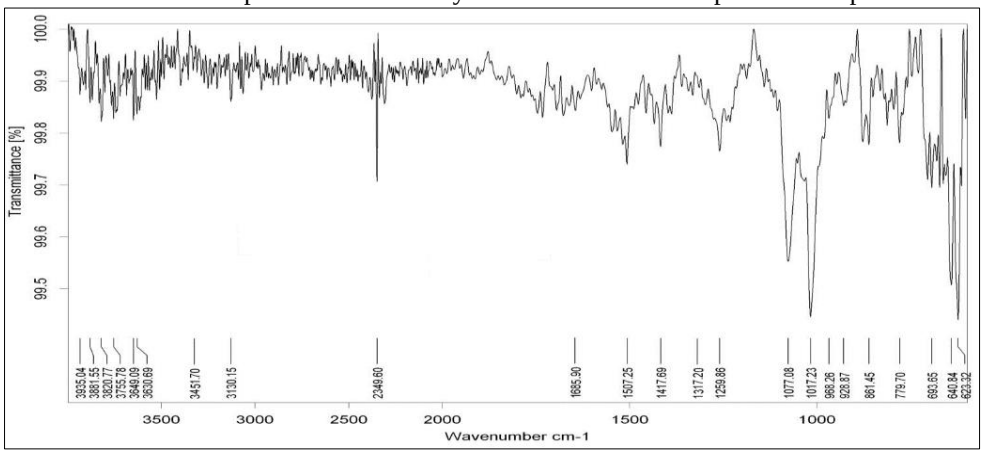

Figure 4: FTIR Spectra of Fenofibrate

Selection of Excipients and Pellet Cores
The selection of excipients and pellet cores for fenofibrate immediate-release pellets was based on pre-formulation findings, literature support, regulatory acceptability, and suitability for fluidized bed processing. The objective was to achieve uniform drug layering, enhanced wettability, rapid drug release, and reproducible pellet quality.

Pellet Core Selection
Sugar spheres and microcrystalline cellulose (MCC) pellets were evaluated as starter cores. MCC pellets demonstrated superior flow properties, lower compressibility, and better resistance to attrition compared to sugar spheres. Their uniform spherical shape and narrow size distribution enabled stable fluidization and consistent coating. Based on these advantages, MCC pellets were selected as the preferred cores.

Binder Selection
Hydrophilic binders including PVP K30, HPMC E5 LV, and HPMC E15 were screened. Pellets formulated with HPMC E5 LV showed uniform coating, good mechanical integrity, and faster drug release due to its low viscosity and efficient film-forming ability. HPMC E15 provided stronger binding but slightly slower release, while PVP K30 showed comparatively lower coating efficiency. HPMC E5 LV was therefore selected for immediate-release formulation.

Surfactant Selection
To enhance wettability of fenofibrate, sodium lauryl sulfate (SLS) and polysorbate 80 were evaluated. Pellets containing SLS exhibited significantly reduced wetting time and faster drug release compared to polysorbate 80 and surfactant-free formulations. SLS was selected as the optimal surfactant.

Solvent System Selection
Purified water and a water–ethanol mixture were assessed as coating solvents. Although the ethanol–water system improved coating efficiency, purified water was selected due to its safety, regulatory acceptance, and environmental compatibility, with surfactant incorporation effectively overcoming solubility limitations.

Overall, MCC pellets as cores, HPMC E5 LV as binder, sodium lauryl sulfate as surfactant, and a purified water-based solvent system were identified as optimal components for developing fenofibrate immediate-release multiparticulate pellets using fluidization technology.

DEVELOPMENT OF IMMEDIATE-RELEASE FENOFIBRATE PELLETS

Immediate-release fenofibrate pellets were successfully developed using a Wurster fluidized bed coating process. Four formulations (F1–F4) were prepared by varying polymer grade and concentration to evaluate their impact on pellet quality and drug-release performance. Uniform drug layering, improved wettability, and rapid drug release were achieved under controlled processing conditions.

Preparation of Drug Solution/Suspension
All drug solutions or suspensions showed good homogeneity, suitable viscosity for spraying, and stability throughout the coating process. Hydrophilic polymers formed clear solutions in purified water, while sodium lauryl sulphate improved fenofibrate dispersion and simethicone effectively minimized foaming. Filtration ensured smooth atomization without nozzle blockage, confirming the suitability of the selected solvent system and excipients.

Drug Layering by Wurster Coating
Bottom-spray Wurster coating produced uniformly coated pellets with stable fluidization and minimal agglomeration. Efficient solvent evaporation resulted in smooth drug–polymer layers and reproducible drug loading. The pellets exhibited spherical shape, narrow size distribution, and good mechanical integrity across all formulations.

Effect of Formulation Composition
Formulation composition significantly influenced pellet characteristics. Pellets containing HPMC E5 LV showed superior coating uniformity and smoother surfaces due to the polymer's low viscosity and film-forming ability. Higher concentrations of HPMC E15 produced mechanically stronger pellets but with slightly thicker coatings. A combination of HPMC E5 LV and HPMC E15 provided an optimal balance between mechanical strength and immediate-release performance.

Critical Process Parameters
Maintaining inlet air temperature (52–61 °C), product temperature (40–42 °C), airflow (52–58 CFM), atomization pressure (0.8 bar), and spray rate (2–9 RPM) ensured efficient solvent evaporation, stable fluidization, and uniform coating. Optimized conditions prevented overwetting, spray drying, and pellet agglomeration, resulting in consistent pellet quality.

Effect of Binder Concentration
Binder concentration played a key role in pellet formation and drug release. Lower binder levels produced thinner coatings and faster drug release but occasionally caused minor dusting.

Intermediate concentrations achieved optimal coating integrity with rapid dissolution, while higher binder concentrations increased coating thickness and reduced drug release due to slower polymer hydration.

Effect of Solvent System
A water–ethanol system enhanced coating efficiency due to improved drug dispersion and faster evaporation. However, purified water provided satisfactory coating performance when combined with surfactants and hydrophilic polymers and was preferred due to safety and regulatory considerations.

Role of Surfactants
Sodium lauryl sulphate significantly improved pellet wettability and dissolution. Increasing surfactant concentration reduced wetting time, enhancing immediate-release performance. An optimized surfactant level improved dissolution without causing foaming or dispersion instability.

Optimization of Processing Parameters
Optimized fluidized bed parameters ensured uniform size growth, minimal agglomeration, and consistent drug loading. Deviations in inlet air temperature or spray conditions led to coating defects or agglomeration, highlighting the importance of precise process control.

CHARACTERIZATION OF FENOFIBRATE IMMEDIATE-RELEASE PELLETS
The prepared fenofibrate immediate-release pellets (F1–F4) were comprehensively characterized to evaluate their physical, micromeritic, and pharmaceutical quality attributes, which are critical for multiparticulate dosage forms. The results of comparative characterization are summarized in Table 7.14 and were used to identify the optimized formulation based on overall pellet quality and immediate-release performance.

Comparative Evaluation of Pellet Properties
All formulations produced pellets within an appropriate size range with mean diameters between approximately 828–862 µm. Formulations F1, F2, and F4 exhibited narrow size distributions, indicating controlled pellet growth and uniform drug layering, whereas F3 showed a slightly broader distribution, likely due to higher polymer viscosity. Surface morphology analysis revealed smooth and spherical pellets for F1, F2, and F4, while F3 exhibited relatively rough surfaces, suggesting thicker polymeric coatings.

Table 4: Comparative Characterization of Fenofibrate Immediate-Release Pellets (F1–F4)

Parameter	F1	F2	F3	F4
Mean pellet size (µm)	835 ± 22	828 ± 19	862 ± 25	840 ± 21
Size distribution	Narrow	Narrow	Slightly broader	Narrow
Surface morphology	Smooth, spherical	Smooth, spherical	Slightly rough	Smooth
Bulk density (g/cm³)	0.58 ± 0.02	0.60 ± 0.01	0.55 ± 0.02	0.59 ± 0.02
Tapped density (g/cm³)	0.66 ± 0.02	0.68 ± 0.02	0.64 ± 0.03	0.67 ± 0.02
Angle of repose (°)	24.8 ± 1.1	23.6 ± 1.0	27.9 ± 1.3	24.2 ± 1.1
Carr's index (%)	12.1 ± 0.8	11.8 ± 0.7	14.1 ± 1.0	12.0 ± 0.9
Hausner's ratio	1.14 ± 0.02	1.13 ± 0.02	1.16 ± 0.03	1.14 ± 0.02
Drug content (%)	99.1 ± 0.9	99.4 ± 0.6	98.6 ± 1.1	99.0 ± 0.8
Friability (%)	0.42	0.38	0.51	0.40
Pellet hardness (N)	5.8 ± 0.4	6.1 ± 0.3	6.6 ± 0.5	6.0 ± 0.4
Wetting time (s)	62 ± 4	55 ± 3	78 ± 5	60 ± 4
Moisture content (%)	1.9 ± 0.2	1.7 ± 0.1	2.2 ± 0.2	1.8 ± 0.2

Flow property evaluation demonstrated acceptable flow behavior for all formulations, with angles of repose below 30°, Carr's index values below 15%, and Hausner's ratios close to unity. Among the formulations, F2 showed superior flowability, attributed to its uniform size distribution and smooth surface characteristics. Bulk and tapped density measurements further confirmed efficient packing and low compressibility, with F2 showing the most favorable density profile.

Drug content uniformity across all formulations was within pharmacopeial limits, indicating reproducible drug deposition during fluidized bed coating. Formulation F2 exhibited the least variability, reflecting consistent and uniform drug layering. Friability values for all formulations were well below acceptable limits, confirming adequate mechanical strength, with F2 showing the lowest friability. Pellet hardness results indicated sufficient mechanical integrity for all batches; however, F3 exhibited higher hardness due to increased polymer content, which could potentially retard drug release.

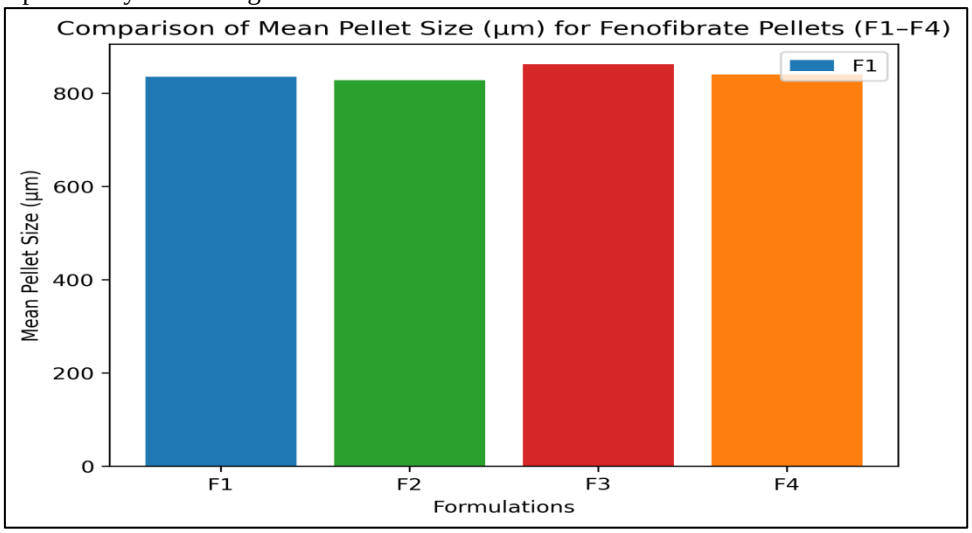

Figure 5: Comparison of mean pellet size of F1 to F4

Wettability studies highlighted the influence of formulation variables on hydration behavior. Formulation F2 demonstrated the shortest wetting time, indicating enhanced surface hydrophilicity and favorable conditions for rapid dissolution. Moisture content analysis showed that all formulations had residual moisture within acceptable limits, with F2 exhibiting the lowest moisture content, suggesting efficient drying and improved stability.

Identification of Optimized Formulation

Based on overall pellet quality, including size uniformity, surface morphology, flow properties, mechanical strength, wettability, moisture content, and drug content uniformity, formulation F2 was identified as the optimized immediate-release fenofibrate pellet formulation.

CONCLUSION:

Immediate-release fenofibrate pellets were successfully developed using fluidization technology, demonstrating the feasibility of multiparticulate systems for improving the performance of poorly water-soluble drugs. Comprehensive characterization confirmed that formulation variables, particularly polymer grade and concentration, significantly influenced pellet quality, mechanical integrity, wettability, and flow behavior. Among the evaluated formulations, F2 exhibited the most desirable balance between uniform drug distribution, excellent flow properties, sufficient mechanical strength, rapid wetting, and low moisture content. These attributes make F2 suitable for immediate-release oral delivery and further in-vitro and in-vivo evaluation. Overall, the study highlights fluidized bed pelletization as a robust and scalable platform for developing immediate-release formulations of BCS Class II drugs such as fenofibrate.

CONFLICT OF INTEREST:

The authors declare that there is no conflict of interest regarding the publication of this research.

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