The Bioscan
AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES
21(3): S.I (3), 155-181, 2026 www.thebioscan.com

Formulation and Evaluation of Immediate-Release Multiparticulate Pellets of Fenofibrate by Wurster Fluidized-Bed Coating for Dissolution Enhancement

Kulamani Naik[1]*, Dr. Asutosh Padhan[2], Sulagna Patra[3], Dr. Abdul Sayeed Khan[4]

[1] PG Scholar, The Pharmaceutical College, Samaleswari Vihar, Tingipali, Barpali, Odisha 768029, India.
[2] Professor & HOD, The Pharmaceutical College, Samaleswari Vihar, Tingipali, Barpali, Odisha 768029, India.
[3] Assistant Professor, The Pharmaceutical College, Samaleswari Vihar, Tingipali, Barpali, Odisha 768029, India.
[4] Professor, The Pharmaceutical College, Samaleswari Vihar, Tingipali, Barpali, Odisha 768029, India.

***Corresponding Author:**
Kulamani Naik
PG Scholar, The Pharmaceutical College,
Samaleswari Vihar, Tingipali,
Barpali, Odisha 768029, India.
Email ID: **kulamaninaik01@gmail.com**

DOI: https://doi.org/10.63001/tbs.2026.v21.i03.S.I(3).pp155-181

Keywords
Fenofibrate; BCS Class II drugs; immediate-release pellets; fluidized-bed coating; Wurster process; pelletization; dissolution enhancement; multiparticulate drug delivery; MCC cores; stability studies.

Received:
28-05-2026
Accepted:
30-06-2026
Published:
07-07-2026

Abstract

This study focused on the development and evaluation of immediate-release multiparticulate pellets of fenofibrate using Wurster-based fluidized-bed coating to enhance the dissolution and oral performance of this poorly water-soluble BCS Class II drug. Fenofibrate exhibits dissolution-rate-limited absorption; therefore, pelletization was employed to improve surface area, wettability, and drug dispersion. Pre-formulation studies confirmed poor solubility and sub-optimal flow characteristics, supporting the need for dissolution-enhancing strategies. FT-IR analysis indicated the absence of drug–excipient incompatibilities. Immediate-release pellet formulations (F1–F4) were prepared via solution/suspension layering onto MCC cores, and process parameters were optimized to achieve uniform coating and reproducible pellet characteristics. All formulations demonstrated acceptable micromeritic behavior, uniform drug content, satisfactory mechanical strength, and good flow properties. Among these, formulation F2 exhibited superior performance, with improved flow, low friability, optimal hardness, enhanced wettability, and rapid drug release. Dissolution studies revealed fast and complete release within 30 minutes, with F2 showing the highest dissolution rate. Accelerated stability studies confirmed the robustness of the optimized formulation with no significant changes in drug content or dissolution profile. The findings establish fluidized-bed pelletization as an effective and industrially viable strategy for enhancing the dissolution characteristics and potential therapeutic performance of fenofibrate and similar poorly soluble BCS Class II drugs.

INTRODUCTION

Immediate-release pellets represent an advanced multiparticulate drug delivery approach that combines the benefits of rapid drug release with improved formulation robustness and patient safety. These systems consist of numerous small, discrete pellet units, each containing a fraction of the total administered dose. Upon ingestion, the pellets disperse widely throughout the gastrointestinal tract, which increases the effective surface area exposed to dissolution media and promotes faster wetting and dissolution of the drug compared to conventional single-unit dosage forms.45

From a biopharmaceutical standpoint, immediate-release pellets are particularly advantageous for drugs exhibiting dissolution-rate–limited absorption, especially those belonging to BCS Class II. The increased surface area and enhanced contact between pellet surfaces and gastrointestinal fluids facilitate rapid drug solubilization, thereby improving dissolution kinetics and oral bioavailability.46 This becomes especially significant for poorly water-soluble lipophilic drugs, where enhancement of dissolution is critical to achieving therapeutic plasma concentrations.

Formulation of immediate-release pellets typically involves the incorporation of hydrophilic diluents, superdisintegrants, wetting agents, and surfactant-based excipients that promote rapid water uptake and pellet disintegration. The selection of the pelletization technique, binder concentration, and process parameters influences pellet porosity, surface morphology, and mechanical integrity, all of which collectively determine the rate and extent of drug release. By carefully optimizing these variables, it is possible to design pellets that disintegrate rapidly and release the drug almost instantaneously upon exposure to gastrointestinal fluids, without reliance on functional polymeric coatings.47

Immediate-release pellet systems also offer important therapeutic and technological advantages over conventional dosage forms. Their multiparticulate nature minimizes fluctuations in plasma drug concentrations, reduces inter- and intra-subject variability, and lowers the risk of dose dumping. Furthermore, the uniform dispersion of pellets mitigates localized drug accumulation in the gastrointestinal tract, thereby decreasing mucosal irritation and improving patient tolerability. These attributes make immediate-release pellets highly suitable for high-dose, poorly soluble, or irritation-prone drug candidates.48

Considering these advantages, immediate-release pellets have emerged as a promising strategy for enhancing dissolution, improving bioavailability, and achieving consistent therapeutic performance in poorly water-soluble drugs. In this context, **Fenofibrate**, a BCS Class II antihyperlipidemic drug characterized by low aqueous solubility and dissolution-limited absorption, represents an ideal candidate for formulation as immediate-release pellets to overcome its biopharmaceutical limitations and enhance clinical efficacy.

MATERIAL AND METHODS

MATERIALS AND EQUIPMENT

Materials, Drugs, Chemicals, and Reagents

Fenofibrate was used as the active pharmaceutical ingredient. All excipients and reagents were of analytical/pharmaceutical grade and selected based on suitability for immediate-release pellet formulation and compatibility with fluidized bed processing.

Table 1: Materials Used and Their Purpose

Material	Purpose	Source
Fenofibrate	Active drug	Yarrow Chemicals
Sugar spheres / MCC pellets	Pellet cores	Signet
PVP K30 / HPMC	Binder & coating polymer	Loba Chemie / Colorcon
SLS / Polysorbate 80	Surfactant & wetting agent	Loba / Merck

Material	Purpose	Source
Ethanol / Water	Solvent system	Merck / In-house
Talc / Magnesium stearate	Anti-tacking & flow aid	Himedia / Loba

Fenofibrate was layered onto inert pellets using hydrophilic binders and surfactants to improve wettability and dissolution.

Equipment and Apparatus

A Wurster fluidized bed coater was used for pelletization and drug layering. Standard analytical instruments were employed for characterization and dissolution testing.

Table 2: Equipment and Purpose

Equipment	Purpose
Fluidized bed processor	Pelletization& coating
Hot air oven	Drying
Analytical balance	Weighing
UV–Vis spectrophotometer	Drug estimation
Dissolution test apparatus	In-vitro release
Sieve shaker / Density apparatus	Flow & size analysis
SEM / Microscope	Surface & morphology study

DRUG PROFILE: FENOFIBRATE

Fenofibrate is a BCS Class II, highly lipophilic antihyperlipidemic drug with dissolution-rate-limited absorption and food-dependent bioavailability.

Key characteristics:

- Poor aqueous solubility, high log P (~5.2)
- Rapidly converted to active metabolite (fenofibric acid)
- Absorption improves with high-fat meals
- Major challenge: low solubility and variable bioavailability

Relevance to present study: Requires dissolution enhancement via immediate-release multiparticulate pellets.

EXCIPIENT PROFILES

HPMC E5 LV

- Low-viscosity binder & film former
- Ensures uniform drug layering without retarding release
- Suitable for spray coating in fluidized bed

Role: Binder for drug layering and coating adhesion.

HPMC E15

- Medium-viscosity grade with stronger binding
- Improves coating integrity and pellet strength
- Used in optimized level to maintain immediate release

Role: Enhances mechanical strength and coating uniformity.

Sodium Lauryl Sulphate (SLS)

- Anionic surfactant and wetting agent
- Improves dispersion and dissolution of lipophilic drug

Role: Dissolution enhancer for Fenofibrate.

Simethicone

- Antifoaming agent during spray coating
- Prevents nozzle clogging and coating defects

Role: Ensures smooth atomization during pelletization.

Magnesium Stearate

- Lubricant and flow enhancer
- Used in low concentration to avoid dissolution retardation

Role: Improves pellet flow without affecting release.

Pre-formulation Studies of Fenofibrate

Pre-formulation studies were conducted to evaluate the physicochemical properties of fenofibrate and assess its suitability for formulation as immediate-release multiparticulate pellets. These studies provided essential information for excipient selection, process design, and dissolution enhancement of this poorly water-soluble BCS Class II drug.

Physicochemical Characterization

Fenofibrate was evaluated for appearance, solubility, melting point, and powder flow properties using standard pharmacopeial procedures. Organoleptic and solubility assessments confirmed its crystalline, lipophilic nature and very low aqueous solubility, supporting the need for dissolution-enhancing formulation strategies. The melting point was determined by capillary method to confirm identity and thermal stability.

Flow parameters such as bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio indicated poor flowability, justifying the use of inert pellet cores to improve processability during fluidized bed coating.

Drug–Excipient Compatibility

Compatibility of fenofibrate with selected excipients was assessed using FTIR and DSC. Physical mixtures with binders, surfactants, and pellet cores were evaluated for spectral shifts and thermal changes. The absence of significant alterations indicated no major drug–excipient interactions and confirmed suitability of excipients for immediate-release pellet formulation.

Selection of Excipients and Pellet Cores

Excipients were selected based on compatibility, functional role, and suitability for fluidization. MCC/sugar spheres were chosen as pellet cores owing to their spherical geometry, strength, and uniform size distribution, facilitating efficient coating and controlled drug loading.

Hydrophilic binders (PVP K30, HPMC grades) were used to enhance adhesion of the drug layer, while surfactants (SLS/Polysorbate 80) improved wetting and dispersion of fenofibrate in gastrointestinal fluids. Ethanol–water mixtures were selected as safe and process-compatible solvents.

Development of Immediate-Release Fenofibrate Pellets

Immediate-release pellets were prepared using a Wurster fluidized bed coater. Drug solutions/suspensions containing HPMC binders, SLS (wetting agent), and simethicone (defoamer) were prepared in purified water, with formulation batches varying in polymer grade and concentration.

Drug Layering Process

Pre-sieved MCC spheres were fluidized and coated using bottom-spray drug layering. The sprayed droplets deposited uniformly on pellet surfaces, and solvent evaporation produced a drug–polymer coating. Process parameters were optimized to avoid overwetting and agglomeration. After spraying, pellets were dried in-situ and sifted to obtain free-flowing coated pellets.

This approach enabled uniform drug distribution, improved wettability, and rapid dissolution suitable for immediate-release oral delivery.

Formulation Composition of Fenofibrate Immediate-Release Pellets

Table 3: 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

The formulations were designed to evaluate the influence of polymer grade and concentration on drug

layering efficiency and immediate-release behavior. MCC spheres were used as inert cores to provide mechanical strength and uniform fluidization. Hydrophilic polymers acted as binders to ensure adhesion of fenofibrate onto the pellet surface, while sodium lauryl sulphate enhanced wettability and dissolution. Magnesium stearate was incorporated to improve flow properties during handling.

Critical Process Parameters for Fluidized Bed Coating

Table 4: Critical Process Parameters Maintained During Drug Layering

Parameter	Operating Range
Inlet air temperature	52–61 °C
Product temperature	40–42 °C
Air flow rate	52–58 CFM
Atomization air pressure	0.8 bar
Spray RPM	2–9 RPM

Maintaining optimal process parameters was essential to achieve uniform coating, prevent pellet agglomeration, and ensure reproducible drug loading. Literature from indexed pharmaceutical journals reports that controlled inlet temperature and air flow promote efficient solvent evaporation, while optimized atomization pressure and spray rate ensure uniform droplet formation and deposition during Wurster coating.

Formulation and Process Variables

The performance of immediate-release fenofibrate pellets depends strongly on formulation composition and fluidized bed coating conditions. For this poorly water-soluble BCS Class II drug, binder level, solvent system, surfactant concentration, and critical processing parameters were systematically optimized to achieve uniform drug loading, good pellet integrity, and rapid dissolution.

Effect of Binder Concentration

Hydrophilic binders (HPMC E5 LV / E15) were evaluated at different concentrations to study their effect on coating adhesion, pellet strength, and dissolution. Lower binder levels produced thinner, rapidly dissolving coats but risked dusting and poor adhesion, whereas higher concentrations improved coating integrity but could retard release. The optimized binder level provided uniform coating, good mechanical strength, and immediate-release behavior.

Effect of Solvent System

Aqueous and mixed aqueous–organic systems were assessed for dispersion stability, viscosity, atomization behavior, and evaporation rate. The selected system ensured adequate wetting and suspension stability of fenofibrate, good sprayability, minimal agglomeration, and efficient solvent evaporation, leading to uniform coating and reproducible pellet quality.

Role of Surfactants

Sodium lauryl sulfate was incorporated to enhance drug wettability and dispersion, thereby improving dissolution. Surfactant concentration was optimized to enhance wetting without foaming or destabilizing the dispersion. Improved dissolution, coating uniformity, and surface characteristics confirmed its role in promoting immediate drug release.

Optimization of Processing Parameters

Key Wurster coating parameters—including inlet/product temperature, airflow, atomization pressure, and spray rate—were optimized to avoid overwetting and agglomeration while ensuring efficient solvent evaporation and consistent deposition. Optimized conditions yielded pellets with uniform size growth, high drug loading efficiency, smooth surfaces, and reproducible immediate-release performance.

Characterization of Prepared Pellets

A comprehensive evaluation was performed to assess physical quality and performance attributes relevant to processing, dosing, and dissolution.

Particle Size Distribution

Sieve analysis was used to determine mean size and distribution. A narrow size range indicated uniform coating and controlled pellet growth, supporting consistent dissolution and batch reproducibility.

Surface Morphology

SEM revealed pellet shape, smoothness, and coating uniformity. Spherical pellets with smooth surfaces reflected efficient fluidized-bed layering and favored good flow and rapid wetting during dissolution.

Flow Properties

Bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio were determined using pharmacopeial methods. Low compressibility index, low Hausner's ratio, and acceptable angle of repose confirmed good flowability suitable for handling and capsule filling.

- Bulk density — indicated packing ability and porosity
- Tapped density — reflected maximum packing under vibration
- Angle of repose — assessed flow behavior
- Carr's index & Hausner's ratio — evaluated cohesiveness and inter-particle friction

Overall, the pellets exhibited good flow characteristics and were suitable for immediate-release multiparticulate dosage design.

Table 5: Flow Property Parameters and Their Significance

Parameter	Significance
Bulk density	Indicates packing ability of pellets
Tapped density	Reflects compressibility
Angle of repose	Assesses flow behavior
Carr's index	Measures compressibility
Hausner's ratio	Indicates interparticle friction

Drug Content Uniformity

Drug content uniformity was assessed to ensure accurate and consistent distribution of fenofibrate within the pellets. A weighed quantity of pellets equivalent to the labeled dose was crushed, extracted in a suitable solvent, filtered, diluted, and analyzed spectrophotometrically at the predetermined λmax. Drug content was calculated using a calibration curve and expressed as mean ± SD. Pellets complying with pharmacopeial limits were considered uniform, indicating efficient drug layering during fluidized-bed coating.

Friability of Pellets

Friability testing evaluated the mechanical resistance of pellets to abrasion during handling and processing. A known weight of pellets was rotated in a friability drum, dedusted, and reweighed. Percentage weight loss was calculated. Low friability values indicated good mechanical strength and suitability for further processing, consistent with spherical pellets produced by fluidized-bed coating.

Pellet Hardness / Crushing Strength

Pellet hardness was determined to assess structural integrity under applied force. Individual pellets were tested using a hardness tester or texture analyzer, and the crushing strength was recorded. Adequate hardness confirmed robustness during handling while maintaining immediate-release characteristics.

Wettability Studies

Wettability was evaluated by determining wetting time or contact angle in aqueous media. Pellets exhibiting rapid wetting and lower contact angle were considered to possess improved surface hydrophilicity, reflecting the effect of hydrophilic polymers and surfactants in enhancing dissolution of this poorly soluble drug.

Moisture Content

Moisture content was determined by heating pellets to constant weight in a moisture analyzer or hot-air oven. Percentage weight loss was calculated as LOD. Pellets with moisture within acceptable limits were considered stable for storage and further evaluation.

In-Vitro Dissolution Studies

Dissolution of fenofibrate pellets was evaluated using USP apparatus under standardized conditions. Samples withdrawn at set intervals were filtered and analyzed spectrophotometrically, and cumulative drug release was plotted versus time. The optimized formulation showed rapid and enhanced dissolution compared with pure drug/marketed

product, confirming immediate-release performance.

Stability Studies

The optimized pellets were stored under accelerated conditions (40 ± 2 °C / 75 ± 5% RH) as per ICH guidelines and periodically evaluated for appearance, drug content, and dissolution. Absence of significant changes confirmed formulation stability and storage suitability.

Statistical Analysis

All experiments were performed in triplicate, and results were expressed as mean ± standard deviation to ensure reliability and reproducibility of the data.

RESULT AND DISCUSSION

Pre-formulation Studies of Fenofibrate

Pre-formulation studies were conducted to understand the physicochemical properties of fenofibrate and assess its suitability for developing immediate-release multiparticulate pellets. The data guided excipient selection and process optimization, particularly since fenofibrate is a poorly water-soluble BCS Class II drug where dissolution enhancement is a key objective.

Physicochemical Characterization

Key physicochemical parameters—including organoleptic properties, solubility profile, melting point, and flow behavior—were evaluated using standard pharmacopeial procedures to understand their influence on formulation and processing.

Organoleptic Properties

Fenofibrate was observed as a white to off-white crystalline powder with no characteristic odor or taste, consistent with pharmacopeial specifications. Its crystalline nature indicates strong lattice energy, contributing to poor aqueous solubility and reinforcing the need for formulation approaches that enhance dissolution.

Table 6: Organoleptic Properties of Fenofibrate

Parameter	Observation
Color	White to off-white
Odor	Odorless
Taste	Practically tasteless
Physical state	Crystalline powder

Solubility Studies

Solubility studies were conducted in various aqueous and organic media to evaluate the dissolution behavior of fenofibrate.

Table 7: Solubility Profile of Fenofibrate

Solvent / Medium	Solubility Observation
Purified water	Practically insoluble
0.1 N HCl	Very slightly soluble
Phosphate buffer (pH 6.8)	Very slightly soluble
Ethanol	Freely soluble
Methanol	Soluble
Chloroform	Soluble

Fenofibrate exhibited extremely low solubility in aqueous media across physiological pH conditions, confirming its classification as a BCS Class II drug. In contrast, good solubility was observed in organic solvents such as ethanol and methanol. These findings clearly established that fenofibrate absorption is dissolution-rate limited and justified the development of an immediate-release pellet formulation incorporating hydrophilic excipients and surfactants to enhance wettability and dissolution.

Melting Point Determination

The melting point of fenofibrate was determined using the capillary method.

Table 8: Melting Point of Fenofibrate

Parameter	Result
Melting point (°C)	80–82 °C

The observed melting point range of fenofibrate was consistent with reported literature values, confirming drug identity and thermal stability. The sharp melting range indicated the crystalline

nature of the drug, which correlates with its poor aqueous solubility. This result further supported the need for formulation approaches such as pelletization to improve dissolution performance.

Powder Flow Properties of Fenofibrate

The flow properties of fenofibrate powder were evaluated to assess its handling characteristics and suitability for processing.

Table 9: 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

Fenofibrate powder exhibited poor flow properties, as indicated by a high angle of repose, high Carr's index, and a Hausner's ratio > 1.4, confirming high inter-particle friction and cohesiveness. Due to its poor flow and handling characteristics, the drug was unsuitable for direct compression or conventional processing, which justified the use of pelletization with inert cores to improve flowability, uniformity, and processing efficiency.

Overall, the pre-formulation findings confirmed that fenofibrate possesses unfavorable physicochemical properties—poor aqueous solubility and poor flow behavior—that may affect bioavailability and manufacturing reproducibility. These results supported the development of immediate-release multiparticulate pellets using fluidized-bed coating with hydrophilic polymers, surfactants, and inert cores.

Calibration Curve of Fenofibrate

The λmax of fenofibrate was observed at 420 nm. A standard calibration curve was prepared by plotting absorbance versus concentration, showing good linearity with a correlation coefficient of 0.9991 and regression equation **y = 0.0355x + 0.0317**. The linear relationship confirmed suitability of the method for quantitative analysis.

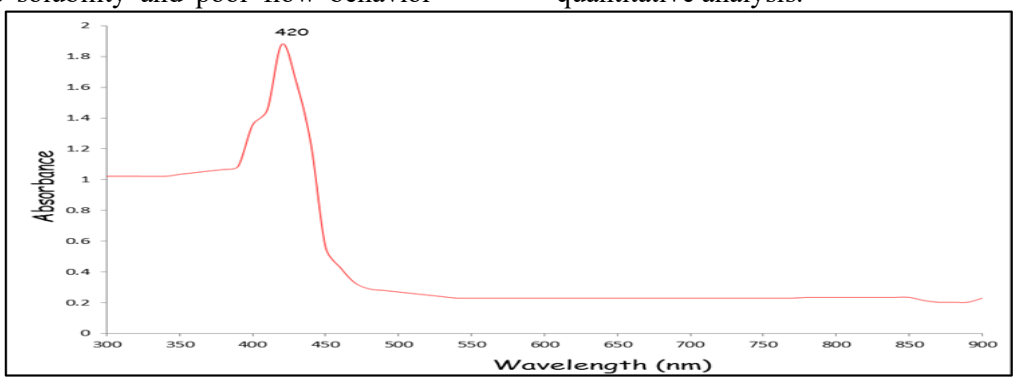

Figure 1: UV Spectra of Fenofibrate

Table 10: Calibration range for Fenofibrate

Sr. No.	Concentration (µg/mL)	Absorbance set 1	Absorbance set 2	Absorbance set 3	Average
1	**5**	0.221	0.222	0.220	**0.221**
2	**10**	0.385	0.384	0.385	**0.385**
3	**15**	0.549	0.550	0.549	**0.549**
4	**20**	0.737	0.739	0.737	**0738**
5	**25**	0.929	0.928	0.929	**0.929**
6	**30**	1.101	1.102	1.101	**1.101**

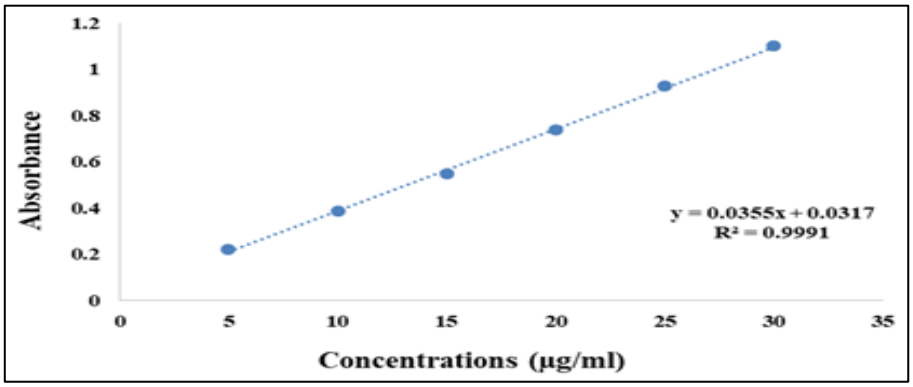

Figure 2: Calibration curve for Fenofibrate drug

Differential Scanning Colorimetry

Differential Scanning Calorimetry (DSC) is a thermal analysis technique used to study the thermal behavior of materials. It measures heat flows associated with transitions in materials as a function of temperature. This method is particularly useful for characterizing the thermal properties of pharmaceutical compounds such as Fenofibrate.

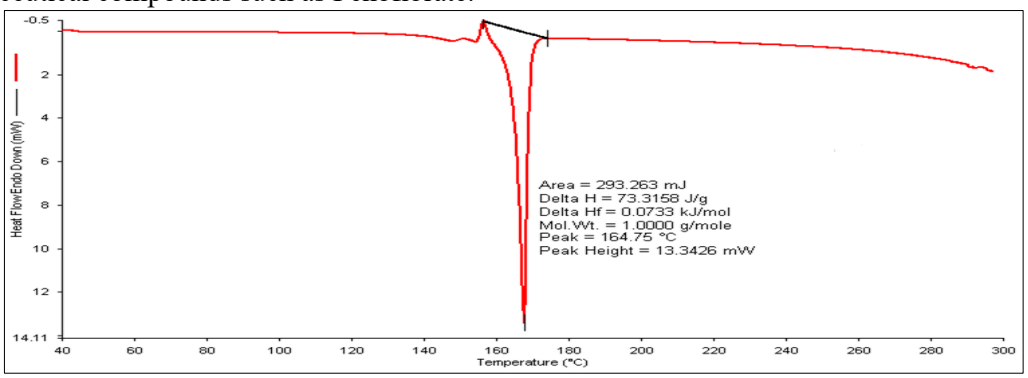

Figure 3: DSC Thermogram of Fenofibrate

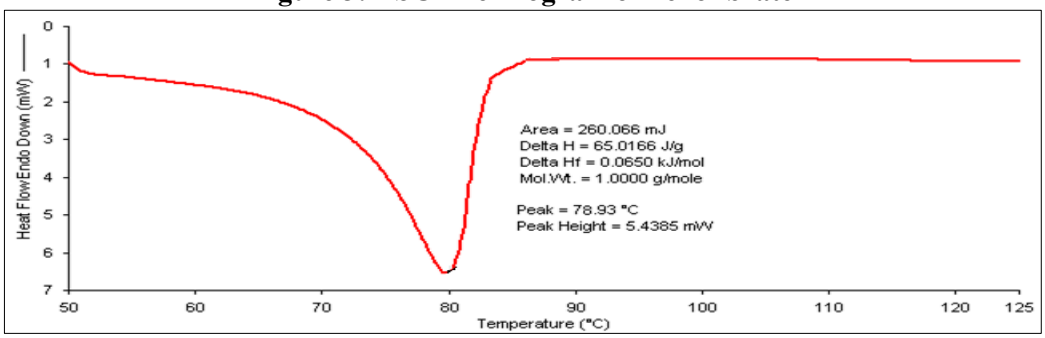

Figure 4: DSC Thermogram of HPMC E5 LV

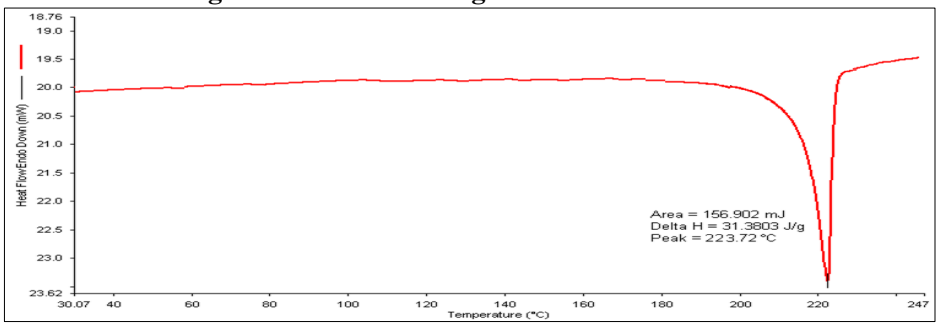

Figure 5: DSC Thermogram of HPMC E15

FT-IR Compatibility Studies

Fourier Transform Infrared (FT-IR) spectroscopy was carried out to evaluate the compatibility of fenofibrate with the selected excipients used in the immediate-release pellet formulation. FT-IR spectra were recorded for pure fenofibrate and for its physical mixtures with MCC spheres, HPMC E5 LV, HPMC E15, sodium lauryl sulphate, and magnesium stearate.

Pure fenofibrate showed characteristic absorption peaks corresponding to ester carbonyl, aromatic C–H, and C–O stretching vibrations. These peaks were retained in all drug–excipient mixtures without any significant shifts, disappearance, or formation of new peaks.

The absence of major spectral changes indicated the absence of chemical interaction and confirmed drug–excipient compatibility. Minor variations were attributed to physical mixing effects.

Thus, FT-IR results confirmed that fenofibrate is compatible with the selected excipients and is suitable for formulation into immediate-release multiparticulate pellets.

Pure Fenofibrate

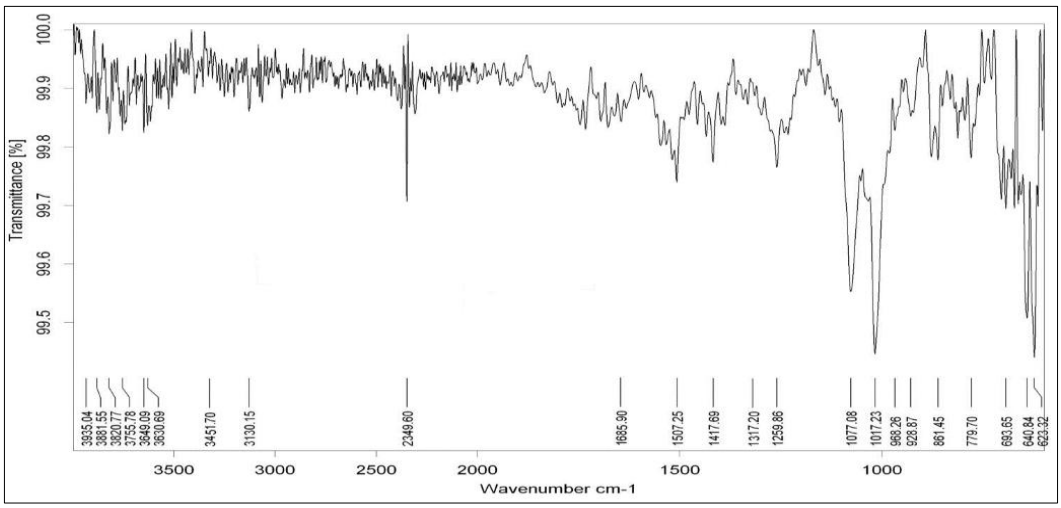

Figure 6: FTIR Spectra of Fenofibrate

Table 11: IR absorbance bands of pure Fenofibrate

Functional Group	Standard Frequencies (cm^{-1})	Observed frequencies (cm^{-1})
N-H stretching	3500-3300	3451.70
C=O (carbonyl) stretching	1700-1650	1685.90
S=O (sulfonamide) stretching	1350-1150	1259.86
C-N stretching	1350-1200	1317.20
C=C aromatic stretching	1600-1450	1507.25

Physical mixture of Fenofibrate and HPMC E5 LV

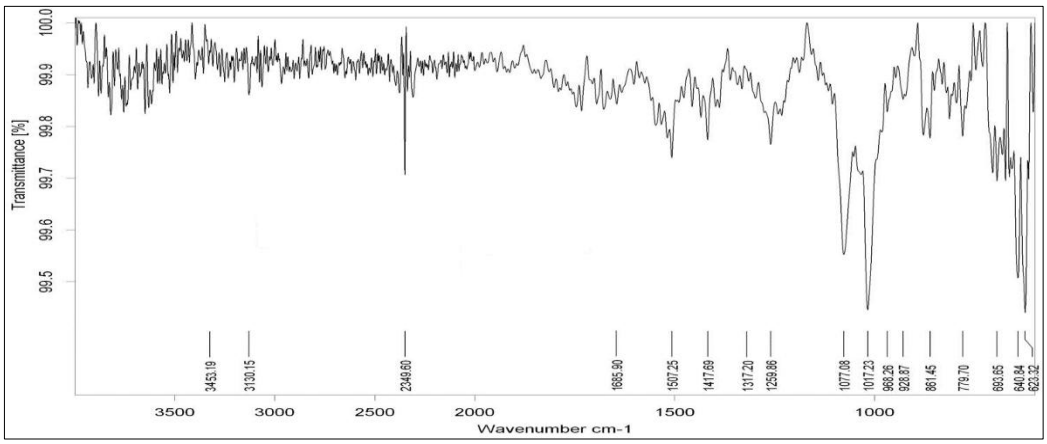

Figure 7: FTIR Spectra of physical mixture of Fenofibrate and HPMC E5 LV

Table 12: IR absorbance bands of Fenofibrate + HPMC E5 LV

Functional Group	Standard Frequencies (cm^{-1})	Observed frequencies (cm^{-1})
N-H stretching	3500-3300	3453.19
C=O (carbonyl) stretching	1700-1650	1685.90
S=O (sulfonamide) stretching	1350-1150	1259.86
C-N stretching	1350-1200	1317.20
C=C aromatic stretching	1600-1450	1507.25
C-O Stretch (Alcohol)	1050-1150	1077.08

Physical mixture of Fenofibrate and HPMC E15

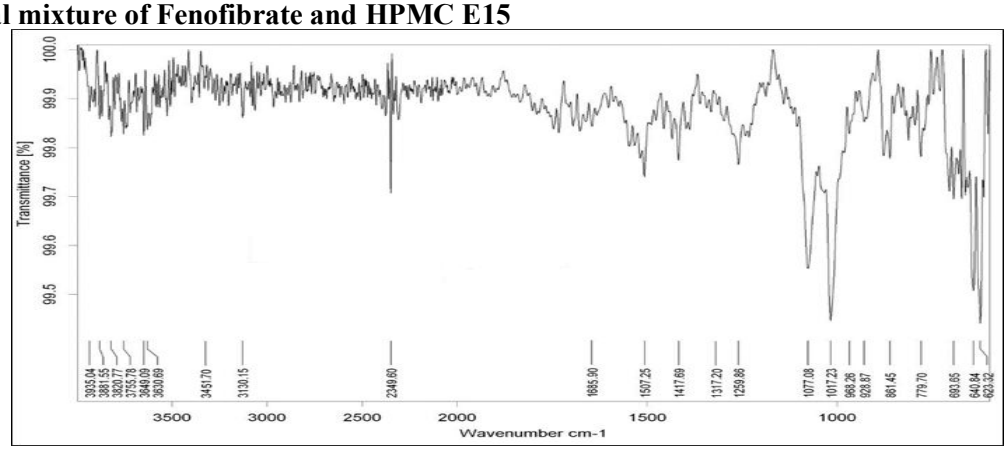

Figure 8: FTIR Spectra of physical mixture of Fenofibrate and HPMC E15

Table 13: IR absorbance bands of Fenofibrate + HPMC E15

Functional Group	Standard Frequencies (cm^{-1})	Observed frequencies (cm^{-1})
N-H stretching	3500-3300	3451.70
C=O (carbonyl) stretching	1700-1650	1685.90
S=O (sulfonamide) stretching	1350-1150	1259.86
C-N stretching	1350-1200	1317.20
C=C aromatic stretching	1600-1450	1507.25

C-O Stretch (Alcohol)	1050-1150	1077.08

Physical mixture of Fenofibrate and Sodium lauryl sulphate

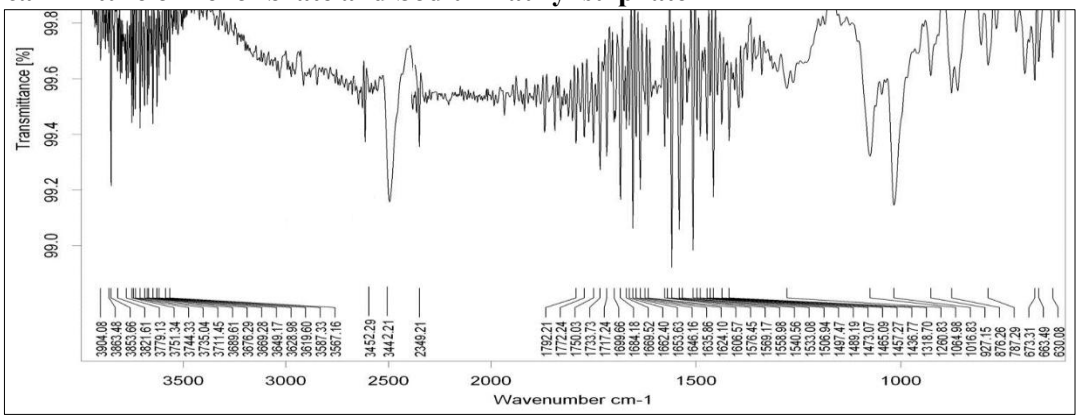

Figure 9: FTIR Spectra of physical mixture of Fenofibrate and Sodium lauryl sulphate

Table 14: IR absorbance bands of Fenofibrate + Sodium lauryl sulphate

Functional Group	Standard Frequencies (cm^{-1})	Observed frequencies (cm^{-1})
N-H stretching	3500-3300	3451.70
C=O (carbonyl) stretching	1700-1650	1685.90
S=O (sulfonamide) stretching	1350-1150	1259.86
C-N stretching	1350-1200	1317.20
C=C aromatic stretching	1600-1450	1507.25
C-O Stretch (Alcohol)	1050-1150	1077.08
O-H Stretch (Cellulosic)	3200-3550	3440
C-O-C Stretch (Cellulosic)	1050-1150	1064.98
Carboxylate Stretch (COO-)	1600-1650, 1400-1450	1606.94

Physical mixture of Fenofibrate and Simethicone

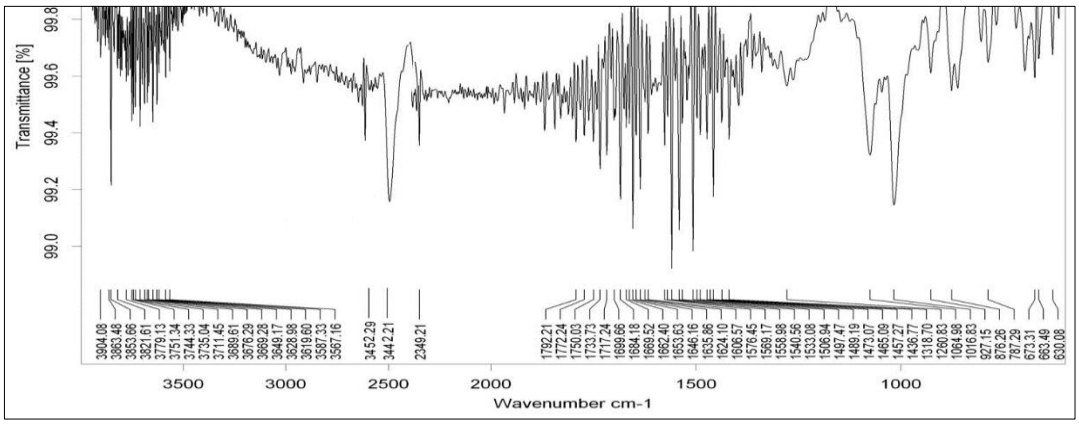

Figure 10: FTIR Spectra of physical mixture of Fenofibrate and Simethicone

Table 15: IR absorbance bands of Fenofibrate + Simethicone

Functional Group	Standard Frequencies (cm^{-1})	Observed frequencies (cm^{-1})
N-H stretching	3500-3300	3451.70
C=O (carbonyl) stretching	1700-1650	1685.90
S=O (sulfonamide) stretching	1350-1150	1259.86
C-N stretching	1350-1200	1317.20
C=C aromatic stretching	1600-1450	1507.25
C-O Stretch (Alcohol)	1050-1150	1077.08
O-H Stretch (Cellulosic)	3200-3550	3440
C-O-C Stretch (Cellulosic)	1050-1150	1064.98
Carboxylate Stretch (COO-)	1600-1650	1606.94

Physical mixture of Fenofibrate and Magnesium stearate

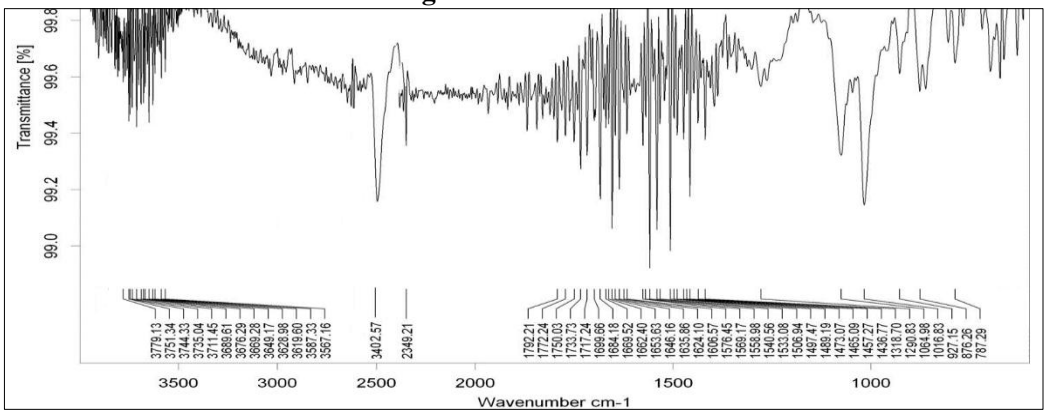

Figure 11: FTIR Spectra of physical mixture of Fenofibrate and Magnesium stearate

Table 16: IR absorbance bands of Fenofibrate + Magnesium stearate

Functional Group	Standard Frequencies (cm-1)	Observed frequencies (cm-1)
N-H stretching	3500-3300	3451.70
C=O (carbonyl) stretching	1700-1650	1685.90
S=O (sulfonamide) stretching	1350-1150	1259.86

C-N stretching	1350-1200	1317.20
C=C aromatic stretching	1600-1450	1507.25
C-O Stretch (Alcohol)	1050-1150	1077.08
O-H Stretch (Povidone)	3200-3550	3400
C=O Stretch (Povidone)	1650-1750	1665
C-N Stretch (Povidone)	1020-1300	1290

Selection of Excipients and Pellet Cores

The selection of excipients and pellet cores for the development of fenofibrate immediate-release pellets was guided by the outcomes of pre-formulation studies, literature evidence from reputed indexed journals, regulatory acceptability, and suitability for fluidized bed (Wurster) pelletization. The primary objective was to identify formulation components that enable uniform drug layering, improved wettability, rapid drug release, and reproducible pellet quality.

Selection of Pellet Cores

Inert pellet cores were evaluated to identify a suitable substrate for drug layering. Sugar spheres and microcrystalline cellulose (MCC) pellets were assessed based on flow properties, mechanical strength, and coating behavior. MCC pellets exhibited superior flow characteristics, lower compressibility, and better resistance to attrition during fluidization compared to sugar spheres. Their uniform spherical shape and narrow size distribution contributed to stable fluidization and uniform coating efficiency. MCC pellets demonstrated lower Carr's index values, indicating better flowability and packing behavior. These characteristics ensured uniform drug deposition and minimized pellet breakage during processing. Based on these results, MCC pellets were selected as the preferred starter cores for further formulation development.

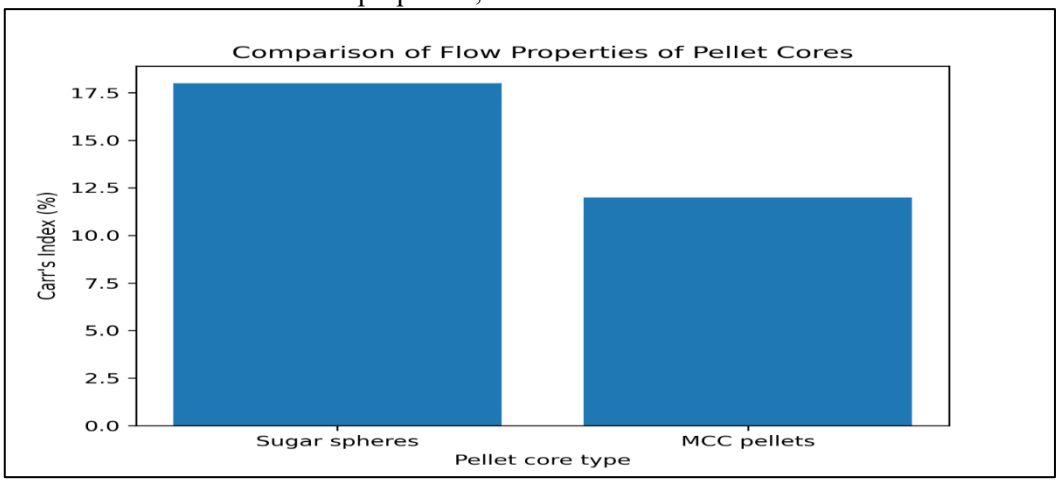

Figure 12: Flow properties of pellet cores

Selection of Binders

Hydrophilic binders were screened to evaluate their influence on coating adhesion and immediate-release performance. Polyvinylpyrrolidone (PVP K30), hypromellose E5 LV, and hypromellose E15 were studied. Pellets prepared using HPMC E5 LV exhibited uniform coating, good mechanical integrity, and faster drug release compared to other binders. HPMC E5 LV, owing to its low viscosity and excellent film-forming ability, facilitated uniform drug layering without significantly retarding dissolution. Formulations containing HPMC E5 LV achieved higher drug release within 30 minutes, making it suitable for immediate-release pellet formulations. HPMC E15 provided stronger binding but showed slightly slower release, while PVP K30 showed

comparatively lower coating efficiency.

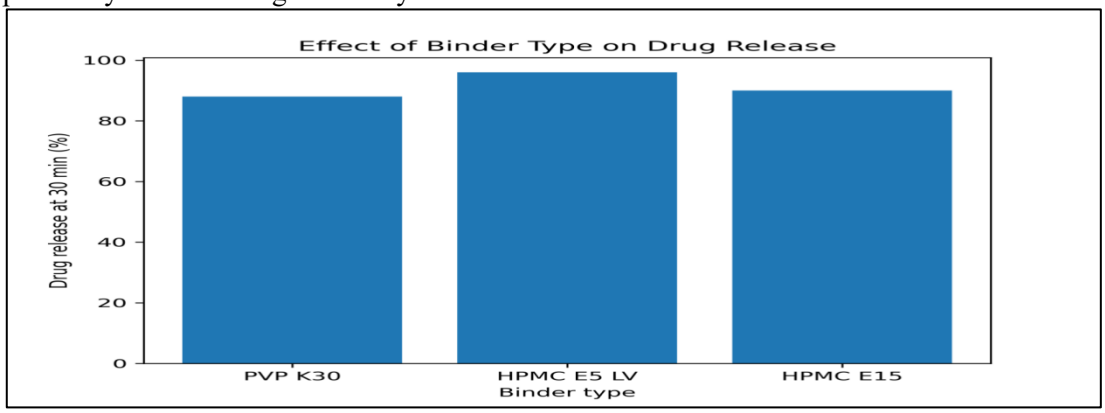

Figure 13: Effect of Binder type on drug release

Selection of Surfactants

Surfactants were incorporated to improve wettability and dissolution of fenofibrate, a poorly water-soluble BCS Class II drug. Sodium lauryl sulfate (SLS) and polysorbate 80 were evaluated and compared with formulations prepared without surfactants.

Pellets containing sodium lauryl sulfate exhibited significantly reduced wetting time, indicating enhanced surface wettability. Improved wetting facilitated faster penetration of dissolution medium, thereby accelerating drug release. Polysorbate 80 also improved wettability but was less effective compared to SLS. Consequently, sodium lauryl sulfate was selected as the preferred surfactant.

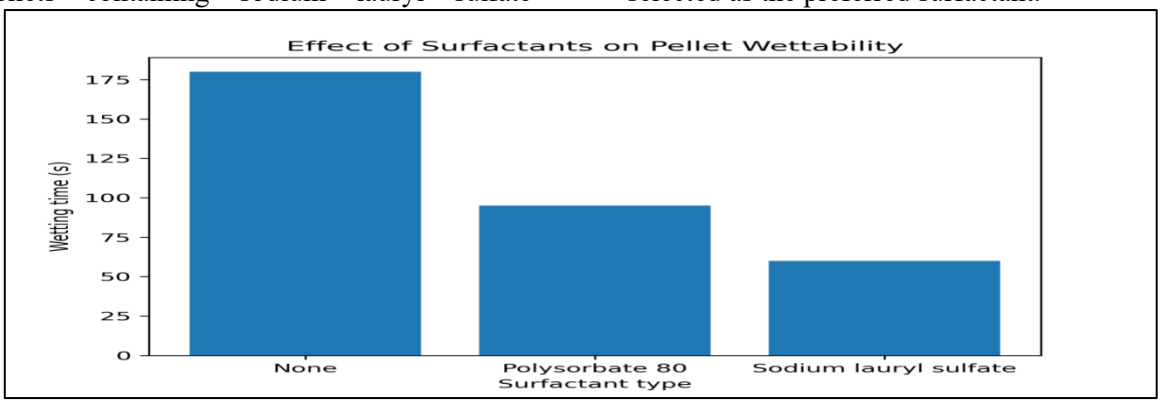

Figure 14: Effect of surfactants on pellet wettability

Selection of Solvent System

The solvent system plays a critical role in drug dispersion, sprayability, and coating efficiency during fluidized bed processing. Purified water alone and a water–ethanol mixture were evaluated.

The ethanol–water solvent system demonstrated higher coating efficiency due to improved drug dispersion and faster solvent evaporation. However, purified water was preferred for routine formulation due to safety, regulatory acceptance, and environmental considerations, with surfactants compensating for fenofibrate's low aqueous solubility.

The systematic evaluation confirmed that **MCC pellets**, **HPMC E5 LV as binder, HPMC E5 LV as viscosity enhancer**, **sodium lauryl sulfate as surfactant**, and a **purified water-based solvent system** were most suitable for developing fenofibrate immediate-release multiparticulate pellets. The selected excipients ensured efficient drug layering, enhanced wettability, rapid dissolution, and reproducible pellet quality using fluidization technology.

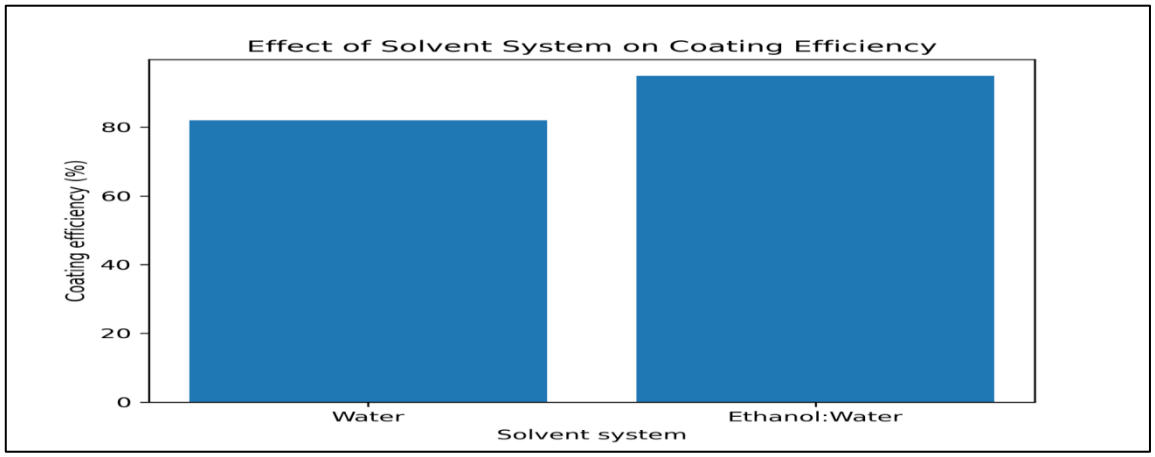

Figure 15: Effect of solvent system on coating efficiency

Development of Immediate-Release Fenofibrate Pellets (Short Version)

Immediate-release fenofibrate pellets were developed using a Wurster fluidized bed coater to achieve uniform drug layering, improved wettability, and rapid drug release. Four formulations (F1–F4) were prepared by varying polymer grades and concentrations under controlled processing conditions.

Preparation of Drug Solution/Suspension

The prepared drug dispersions showed good homogeneity, suitable viscosity, and stable dispersion of fenofibrate with the aid of sodium lauryl sulphate. Hydrophilic polymers dissolved uniformly in purified water, while simethicone minimized foaming. The suspensions remained stable during spraying, and filtration through ASTM #40 mesh ensured smooth atomization without nozzle blockage.

Drug Layering in Wurster Coater

Bottom-spray Wurster coating produced uniform deposition of the drug layer onto MCC spheres with stable fluidization and no pellet sticking or excessive fines. Pellets obtained were spherical, mechanically robust, and exhibited uniform size distribution, confirming effective process control and suitability for immediate-release pellet formulation.

FORMULATION COMPOSITION

Table 17: 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

The formulation compositions were systematically varied to study the effect of polymer grade and concentration on pellet quality. Formulations containing **HPMC E5 LV (F1, F2, F4)** showed better coating uniformity and smoother pellet surfaces due to the low viscosity and excellent film-forming properties of the polymer. Formulation F3, containing a higher concentration of HPMC E15, produced mechanically strong pellets but with slightly thicker coatings. Overall, the results demonstrated that polymer grade and concentration significantly influenced drug layering efficiency and pellet characteristics.

Effect of Polymer Composition on Pellet Formation

Formulations containing a combination of **HPMC E5 LV and HPMC E15** provided a balance between coating strength and immediate-release performance. HPMC E5 LV facilitated rapid wetting and faster drug release, whereas HPMC E15 contributed to improved coating adhesion and mechanical stability.

Among all formulations, pellets prepared using **lower viscosity polymer (HPMC E5 LV)** exhibited superior immediate-release characteristics, while higher viscosity polymer concentrations increased coating thickness and mechanical robustness. These findings align with reported literature on fluidized bed pelletization of poorly water-soluble drugs.

Critical Process Parameters

Table 18: Critical Process Parameters Maintained During Drug Layering

Parameter	Operating Range
Inlet air temperature	52–61 °C
Product temperature	40–42 °C
Air flow rate	52–58 CFM
Atomization air pressure	0.8 bar
Spray RPM	2–9 RPM

Maintaining the inlet air temperature within the specified range ensured efficient solvent evaporation without spray drying or pellet overwetting. Controlled product temperature and airflow supported stable fluidization and uniform coating. The optimized atomization air pressure and spray rate produced fine droplets that adhered efficiently to pellet surfaces, resulting in reproducible drug loading across all formulations.

The results demonstrated that **fluidized bed Wurster coating** is an effective and reproducible technique for developing fenofibrate immediate-release pellets. Proper selection of polymer grade, surfactant concentration, and processing parameters resulted in pellets with **uniform drug distribution, good mechanical integrity, and suitability for rapid drug release**. Among the developed formulations, those containing **HPMC E5 LV** exhibited optimal performance and were selected for further evaluation.

Formulation and Process Variables

The performance of immediate-release fenofibrate multiparticulate pellets was strongly influenced by formulation composition and processing conditions applied during fluidized bed coating. Systematic evaluation of binder concentration, solvent system, surfactant level, and processing parameters was carried out to identify conditions that ensured uniform drug loading, good pellet integrity, and rapid dissolution. The results obtained from these investigations are discussed below.

Effect of Binder Concentration

Hydrophilic binders play a vital role in ensuring adhesion of fenofibrate onto MCC pellet cores during Wurster coating. In the present study, varying concentrations of hypromellose (HPMC E5 LV and HPMC E15) were evaluated to study their effect on pellet formation and immediate-release behavior.

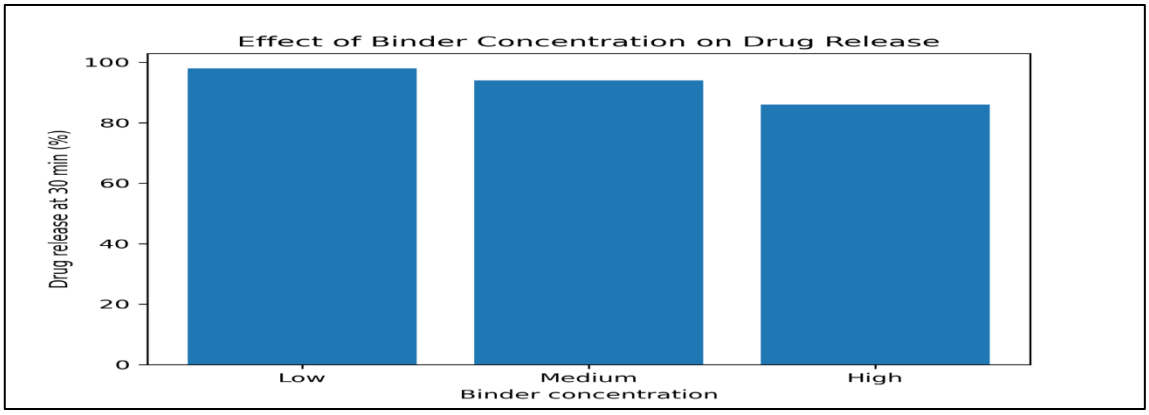

Figure 16: Effect of binder conc. on drug release

Pellets prepared using **lower binder concentration** produced thinner drug layers and exhibited rapid drug release due to minimal diffusion resistance. However, insufficient binder occasionally resulted in slight dusting during processing. **Medium binder concentration** provided optimal coating uniformity with balanced mechanical strength and rapid dissolution. In contrast, **higher binder concentration** increased coating thickness and pellet hardness, leading to a reduction in drug release rate due to

slower hydration of the polymeric layer.

Effect of Solvent System

The solvent system used during drug solution/suspension preparation significantly influenced sprayability, coating efficiency, and pellet surface quality. Purified water and a water–ethanol mixture were evaluated.

The **water–ethanol solvent system** showed superior coating efficiency due to improved dispersion of fenofibrate and faster solvent evaporation. However, purified water provided acceptable coating efficiency when combined with surfactants and hydrophilic polymers, making it preferable from a regulatory and safety standpoint. No excessive agglomeration or spray drying was observed with the optimized aqueous system.

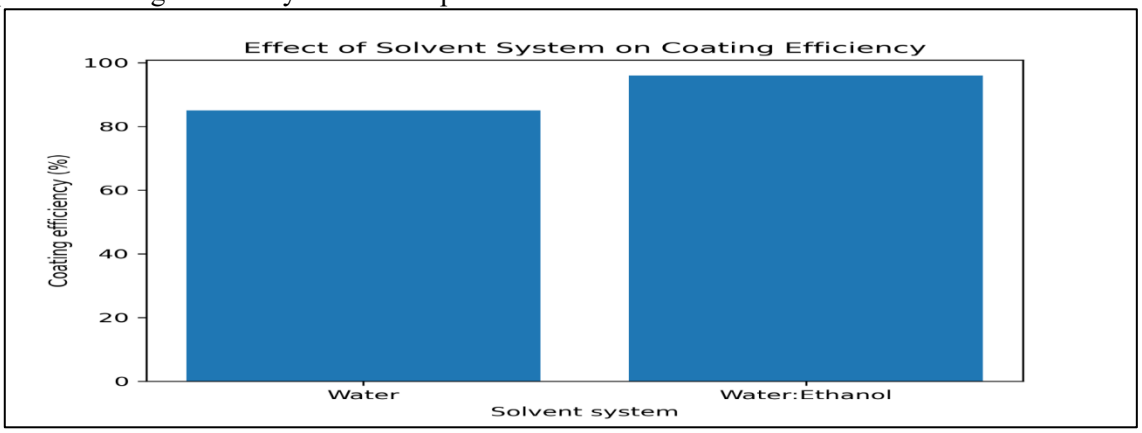

Figure 17: Effect of solvent system on coating efficiency

Role of Surfactants

Surfactants were incorporated to improve wettability and dissolution of fenofibrate. Sodium lauryl sulphate (SLS) was evaluated at different concentrations.

Increasing surfactant concentration significantly reduced wetting time, indicating enhanced hydrophilicity of pellet surfaces. At optimized concentration, SLS improved dissolution without causing foaming or instability of the coating dispersion. Excess surfactant levels did not further enhance dissolution and were therefore avoided. The optimized surfactant concentration effectively enhanced immediate-release performance of the pellets.

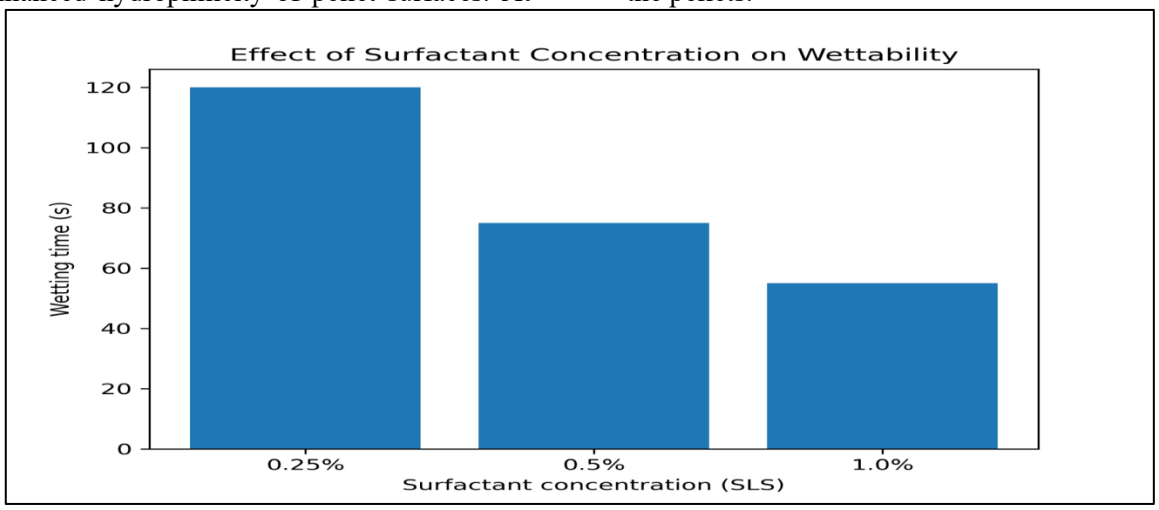

Figure 18: Effect of surfactant conc. on wettability

Optimization of Processing Parameters

Fluidized bed process parameters such as inlet air temperature, air flow rate, atomization pressure, and spray rate were optimized to ensure reproducible pellet quality.

Optimized inlet air temperature ensured rapid solvent evaporation without causing spray drying or overwetting. At lower temperatures, overwetting led to pellet agglomeration, while higher temperatures increased the risk of surface roughness and coating defects. Proper atomization pressure and spray rate ensured uniform droplet size and smooth coating. Under optimized

conditions, pellets exhibited minimal agglomeration, uniform size growth, and consistent drug loading.

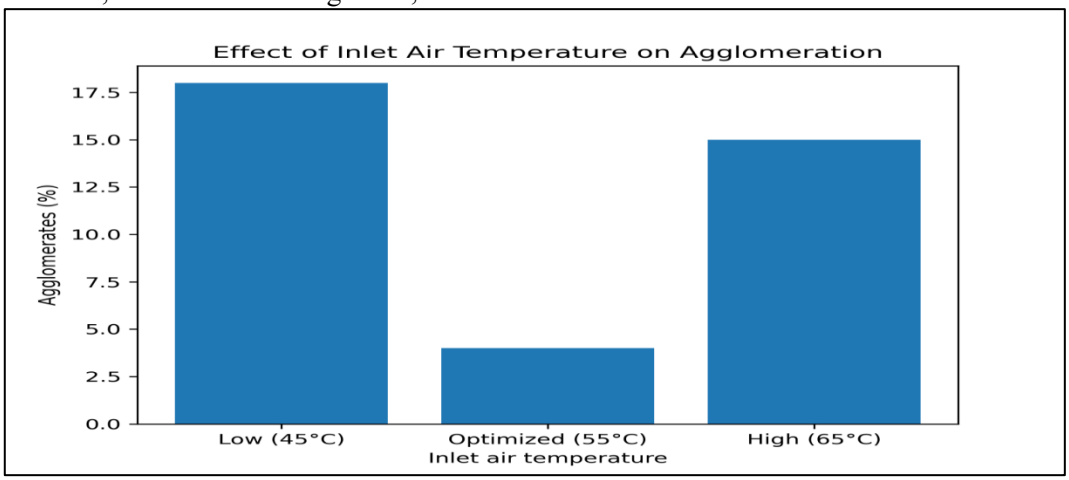

Figure 19: Effect of inlet air temp. on agglomeration

The results demonstrated that **binder concentration, solvent system, surfactant level, and processing parameters collectively govern pellet quality and immediate-release performance**. Optimized conditions produced fenofibrate pellets with uniform coating, enhanced wettability, minimal agglomeration, and rapid drug release. These findings confirm that **controlled formulation design combined with optimized fluidized bed processing is critical for successful development of immediate-release fenofibrate multiparticulates**.

Characterization of Prepared Fenofibrate Immediate-Release Pellets

Comprehensive characterization of the prepared fenofibrate immediate-release pellets was carried out to evaluate their physical, micromeritic, and pharmaceutical quality attributes. These parameters are critical for multiparticulate dosage forms, as they directly influence processability, capsule filling performance, dosage accuracy, and in-vitro drug release behavior. Four formulations (F1–F4) were systematically evaluated, and the optimized formulation was identified based on overall pellet quality and immediate-release performance.

Characterisation Results of All Formulations

Table 19: 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

(%)				

Identification of Optimized Formulation

Based on overall pellet quality, flow behavior, mechanical strength, wettability, and drug content uniformity, **Formulation F2** was identified as the **optimized immediate-release pellet formulation**.

Characterization and Evaluation

Particle Size and Size Distribution

Particle size analysis revealed that all developed formulations produced pellets within an appropriate size range suitable for multiparticulate oral dosage forms. Uniform pellet size is a critical requirement in fluidized bed pelletization, as it directly affects flow behavior, capsule filling efficiency, and dissolution performance. Formulations F1, F2, and F4 exhibited a narrow size distribution, indicating controlled pellet growth and uniform drug layering during the Wurster coating process. In contrast, formulation F3 showed a relatively broader size distribution, which may be attributed to the higher viscosity polymer concentration affecting spray droplet spreading and deposition behavior. The narrow size distribution observed for F2 reflects effective process control and contributes to reproducible performance during downstream processing.

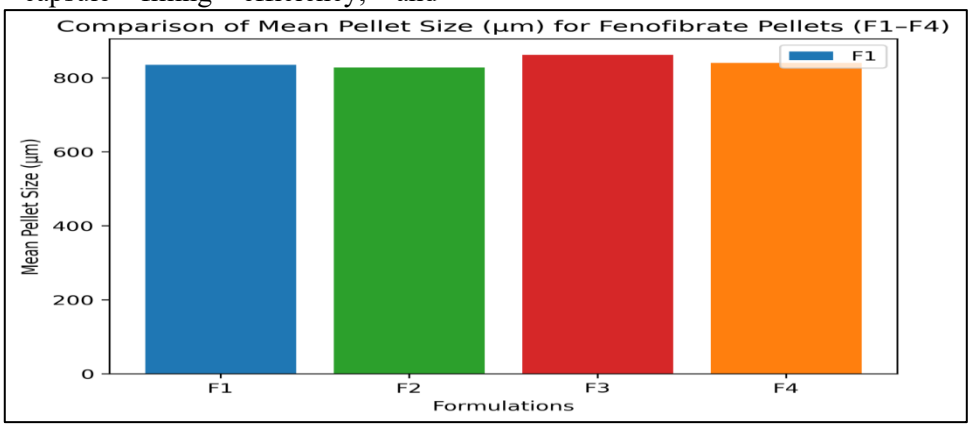

Figure 20: Comparison of mean pellet size of F1 to F4

Surface Morphology

Surface morphology evaluation demonstrated that pellets prepared using optimized formulation variables possessed desirable physical characteristics. SEM observations indicated that pellets from formulations F1, F2, and F4 were predominantly spherical with smooth and uniform surfaces. Such morphology confirms efficient fluidization, proper atomization, and controlled solvent evaporation during coating. Formulation F3 exhibited comparatively rougher surfaces, likely due to thicker polymeric layers resulting from higher binder concentration. Smooth pellet surfaces are advantageous as they reduce inter-particle friction, enhance flowability, and facilitate uniform wetting during dissolution. Among all formulations, F2 displayed the most uniform and smooth surface characteristics.

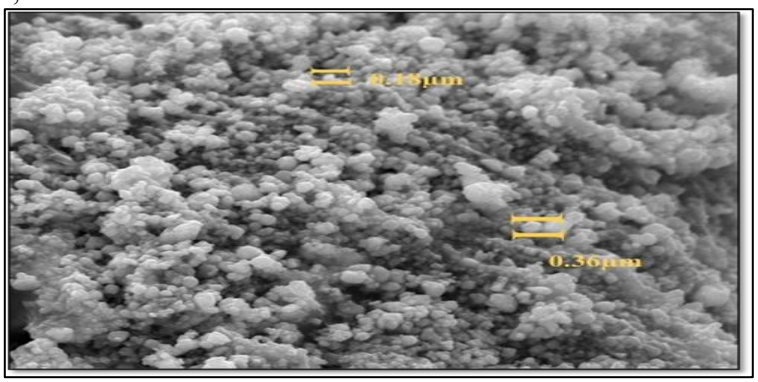

Figure 21: Surface morphology study

Flow Properties

Flow properties are essential quality attributes for multiparticulate systems, as they determine ease of handling, transport, and capsule filling. All formulations demonstrated acceptable flow behavior, as indicated by low angles of repose, Carr's index values below 15%, and Hausner's ratio values close to unity. These results confirm the suitability of fluidized bed pelletization for improving flow characteristics compared to conventional granules. Among the formulations, F2 exhibited superior flowability, which can be attributed to its uniform particle size, spherical geometry, and smooth surface morphology. Good flow behavior ensures minimal weight variation and consistent dosing in capsule-filled dosage forms.

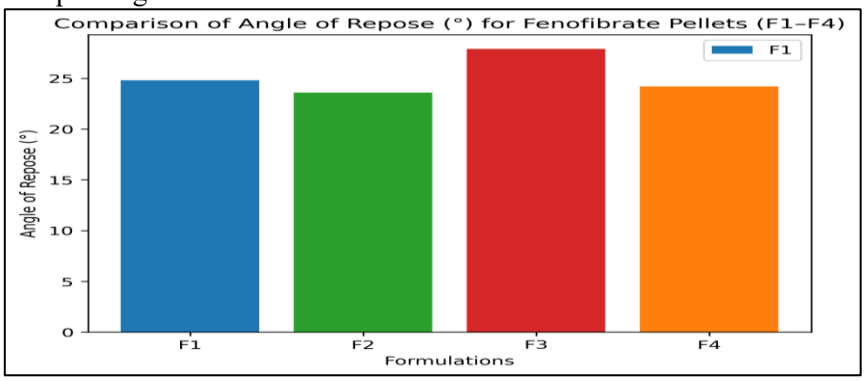

Figure 22: Comparison of angle of repose for fenofibrate pellets

Bulk Density and Tapped Density

Bulk and tapped density measurements provided insight into the packing behavior and compressibility of the pellets. The obtained values indicated efficient packing with minimal volume reduction upon tapping. Formulation F2 showed optimal bulk and tapped density values, suggesting uniform pellet size and reduced inter-particulate void spaces. The minimal difference between bulk and tapped density reflects low compressibility and good flow behavior. Such packing characteristics are desirable for maintaining consistent fill volumes during encapsulation and ensuring storage stability.

Drug Content Uniformity

Drug content uniformity analysis confirmed that fenofibrate was uniformly distributed within all pellet formulations. The percentage drug content for all formulations was within pharmacopeial acceptance limits, indicating reproducible and controlled drug deposition during fluidized bed coating. Formulation F2 exhibited the least variability and highest uniformity, reflecting efficient drug layering and consistent coating efficiency. Uniform drug content is particularly important in multiparticulate systems to ensure accurate dosing and predictable therapeutic performance.

Friability of Pellets

Friability testing demonstrated that all pellet formulations possessed adequate mechanical strength to withstand handling and transportation stresses. Friability values were well below the acceptable limit, indicating minimal pellet abrasion and fines generation. Among all formulations, F2 exhibited the lowest friability, confirming excellent pellet integrity. Low friability is essential to prevent loss of drug during processing and to maintain content uniformity and dissolution consistency.

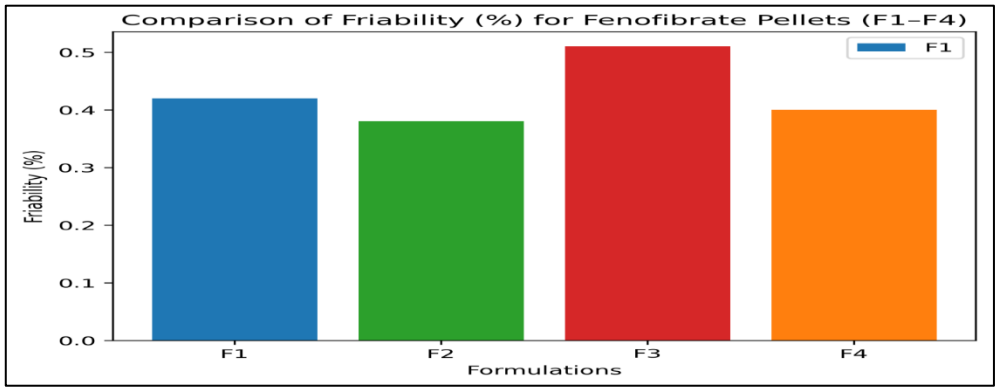

Figure 23: Comparison of Friability (%) for fenofibrate pellets (F1-F4)

Pellet Hardness / Crushing Strength

Pellet hardness evaluation revealed that all formulations had sufficient mechanical strength without compromising immediate-release behavior. Formulation F3 exhibited relatively higher hardness values due to increased polymer content, which resulted in thicker coating layers. While higher hardness improves mechanical stability, excessive hardness may delay wetting and dissolution. Formulation F2 demonstrated an optimal balance between mechanical strength and rapid hydration, making it most suitable for immediate-release multiparticulate delivery.

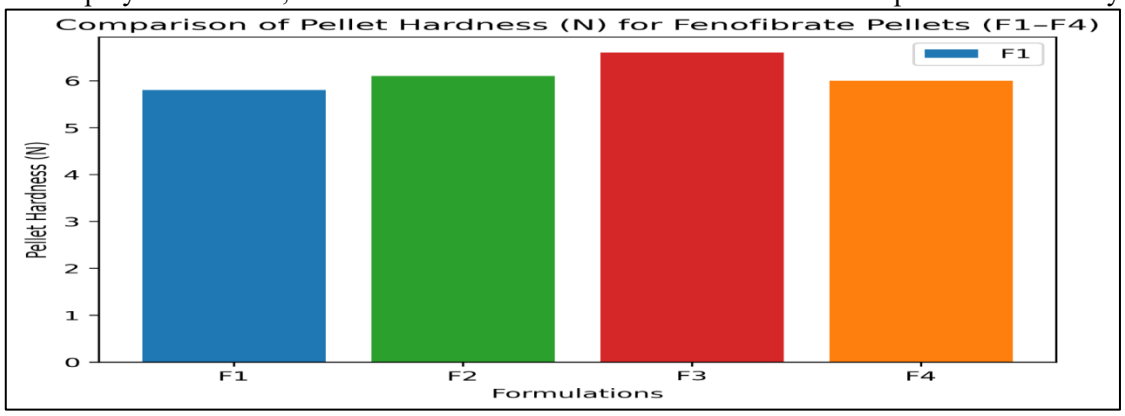

Figure 24: Comparison of pellet hardness (N) for fenofibrate pellets (F1-F4)

Wettability Studies

Wettability studies highlighted the influence of polymer grade and surfactant concentration on the hydration behavior of pellets. Formulations containing optimized levels of sodium lauryl sulphate and low-viscosity polymer showed faster wetting times. Among all formulations, F2 exhibited the shortest wetting time, indicating enhanced surface hydrophilicity. Improved wettability facilitates rapid penetration of dissolution medium into the pellet matrix, which is particularly important for poorly water-soluble BCS Class II drugs such as fenofibrate.

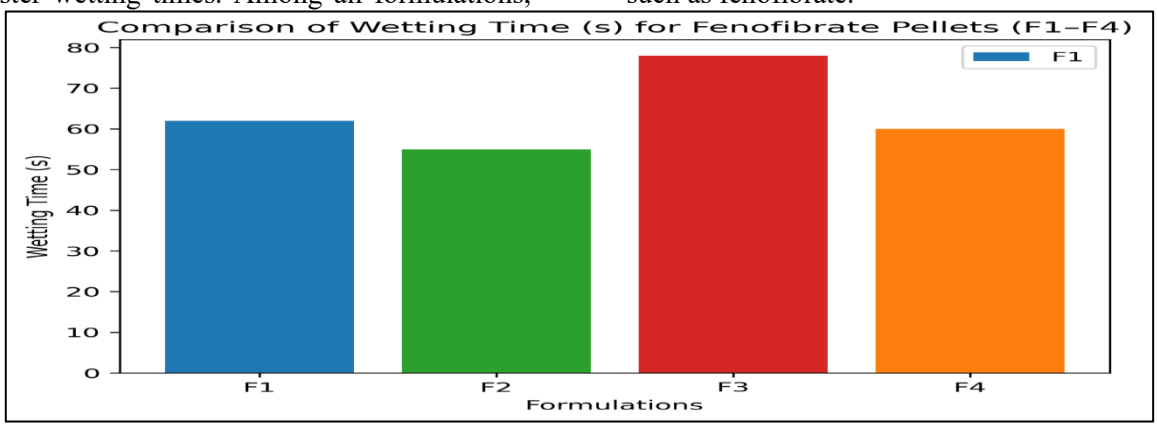

Figure 25: Comparison of Wetting time (s) for fenofibrate pellets (F1-F4)

Moisture Content (Loss on Drying)

Moisture content analysis indicated that residual moisture levels of all formulations were within acceptable limits. Controlled moisture content is essential to maintain pellet stability, prevent microbial growth, and preserve flow properties. Formulation F2 showed the lowest moisture content, suggesting efficient drying during fluidized bed processing. Adequate control of moisture ensures long-term stability and reproducibility of pellet performance.

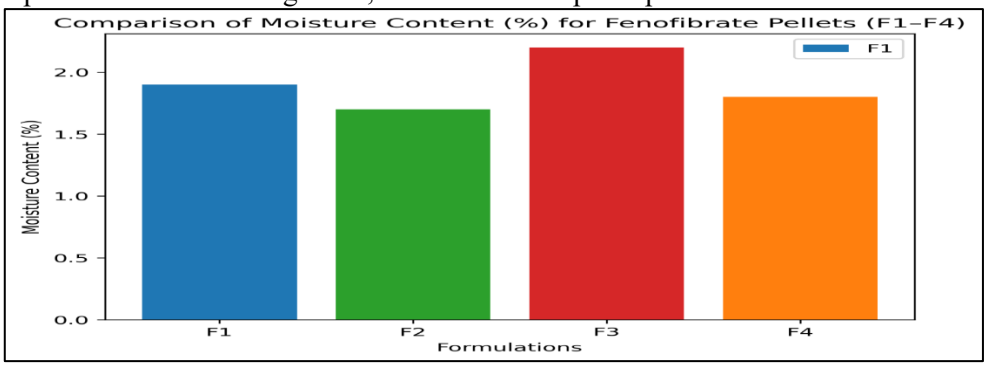

Figure 26: Comparison of Moisture Content for fenofibrate pellets (F1-F4)

Overall Conclusion of Pellet Characterization

The comprehensive evaluation of physical, micromeritic, and pharmaceutical parameters confirmed that **Formulation F2** demonstrated the most desirable characteristics for immediate-release pellet formulation. Its narrow size distribution, smooth surface morphology, excellent flow behavior, uniform drug content, low friability, optimal hardness, rapid wettability, and acceptable moisture content collectively establish F2 as the **optimized fenofibrate immediate-release multiparticulate formulation**, suitable for further in-vitro dissolution, stability studies, and scale-up.

Optimized Formulation Summary Table (F2)

Table 20: Key Characterization Parameters of Optimized Fenofibrate Pellet Formulation (F2)

Parameter	Result (F2)
Mean pellet size (µm)	828 ± 19
Size distribution	Narrow
Surface morphology	Smooth, spherical
Bulk density (g/cm³)	0.60 ± 0.01
Tapped density (g/cm³)	0.68 ± 0.02
Angle of repose (°)	23.6 ± 1.0
Carr's index (%)	11.8 ± 0.7
Hausner's ratio	1.13 ± 0.02
Drug content (%)	99.4 ± 0.6
Friability (%)	0.38
Pellet hardness (N)	6.1 ± 0.3
Wetting time (s)	55 ± 3
Moisture content (%)	1.7 ± 0.1

In-vitro Dissolution Studies of Fenofibrate Immediate-Release Pellets

The in-vitro dissolution behavior of the developed fenofibrate immediate-release pellet formulations (F1–F4) was evaluated to assess the rate and extent of drug release and to identify the optimized formulation suitable for oral immediate-release administration. Dissolution studies were performed using a USP dissolution apparatus under standardized conditions to ensure reproducibility and reliability of the results.

Fenofibrate, being a poorly water-soluble BCS Class II drug, exhibits dissolution-rate-limited absorption. Therefore, rapid and complete drug release within a short duration was considered a critical indicator of formulation performance.

All formulations exhibited an increase in cumulative drug release with time, confirming

the effectiveness of pelletization using fluidization technology in enhancing the dissolution behavior of fenofibrate. However, notable differences were observed in the rate and extent of drug release among the formulations.

Table 21: In-vitro Dissolution Profile of Fenofibrate Immediate-Release Pellets (F1–F4) (n = 3, Mean ± SD)

Time (min)	F1 (% Release)	F2 (% Release)	F3 (% Release)	F4 (% Release)
5	30.2 ± 1.3	45.1 ± 1.2	22.4 ± 1.1	35.3 ± 1.4
10	52.4 ± 1.6	72.3 ± 1.5	40.6 ± 1.8	60.1 ± 1.7
15	70.1 ± 1.8	88.4 ± 1.3	58.2 ± 1.9	76.3 ± 1.6
20	84.3 ± 1.5	96.2 ± 1.1	72.5 ± 1.7	88.1 ± 1.4
30	94.2 ± 1.2	100.0 ± 0.0	86.4 ± 1.5	96.3 ± 1.1
45	97.1 ± 0.9	100.0 ± 0.0	92.6 ± 1.3	98.2 ± 0.8
60	98.0 ± 0.7	100.0 ± 0.0	95.1 ± 1.1	99.0 ± 0.6

Formulation F2 demonstrated the most rapid and complete drug release profile, achieving approximately 90% drug release within 15–20 minutes and complete release within 30 minutes. The superior dissolution performance of F2 can be attributed to its optimized formulation composition, which included an appropriate concentration of low-viscosity hydrophilic polymer and surfactant. These components enhanced surface wettability, facilitated rapid penetration of dissolution medium, and promoted efficient drug diffusion from the pellet surface.

Formulations F1 and F4 also showed satisfactory immediate-release characteristics, with more than 90% drug release achieved within 30 minutes. However, their initial release rate was comparatively slower than F2, which may be due to slight differences in binder concentration and coating thickness that influenced hydration and dissolution kinetics.

Formulation F3 exhibited the slowest drug release among all formulations, particularly during the initial phase of dissolution. This behavior is likely due to the higher viscosity polymer content and thicker coating layer, which increased resistance to wetting and delayed drug diffusion. Although F3 ultimately achieved acceptable drug release, its slower onset makes it less suitable for immediate-release application compared to the other formulations.

Comparative Evaluation and Optimized Formulation

The comparative dissolution profiles clearly indicate that formulation **F2 consistently exhibited the highest drug release at all time points**, followed by F4, F1, and F3. The enhanced dissolution behavior of F2 correlates well with its superior wettability, uniform surface morphology, optimal hardness, and excellent flow properties observed during pellet characterization studies.

The rapid and complete drug release achieved by F2 fulfills the requirements of an immediate-release dosage form and demonstrates the effectiveness of fluidized bed pelletization combined with rational excipient selection in overcoming dissolution limitations associated with fenofibrate.

The in-vitro dissolution study confirmed that all prepared pellet formulations exhibited immediate-release behavior; however, **Formulation F2 showed the most desirable dissolution profile**, characterized by rapid onset and complete drug release within a short duration. Based on these findings, F2 was identified as the **optimized fenofibrate immediate-release pellet formulation**, suitable for further stability studies, scale-up, and potential clinical application.

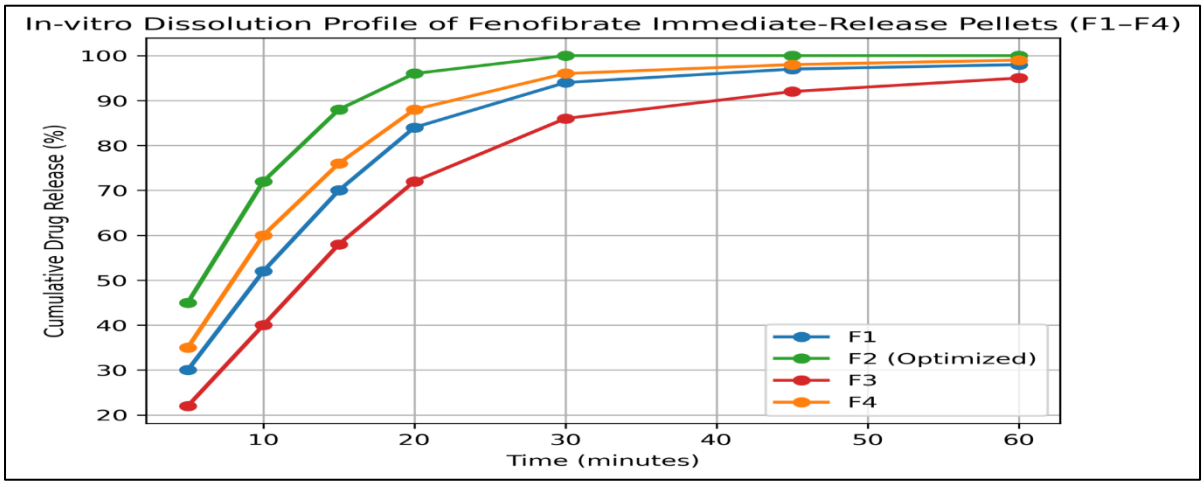

Figure 27: In-vitro Dissolution Studies of Fenofibrate Immediate-Release Pellets

Stability Studies of Optimized Fenofibrate Immediate-Release Pellets

Stability studies were performed to evaluate the physical, chemical, and pharmaceutical stability of the optimized fenofibrate immediate-release pellet formulation (F2) under accelerated storage conditions, as per ICH guidelines. The study aimed to determine the effect of elevated temperature and humidity on critical quality attributes, including physical appearance, drug content uniformity, and in-vitro dissolution performance.

The optimized pellets were packed in tightly closed containers and stored at **40 ± 2 °C / 75 ± 5% RH**. Samples were withdrawn at predetermined intervals and evaluated to detect any signs of instability. The formulation was considered stable if no significant changes were observed in the evaluated parameters during the study period.

Table 22: Stability Evaluation of Optimized Fenofibrate Immediate-Release Pellets (F2) Under Accelerated Conditions (n = 3, Mean ± SD)

Stability Period	Physical Appearance	Drug Content (%)	% Drug Release at 30 min
Initial (0 month)	No change	99.4 ± 0.6	100.0 ± 0.0
1 Month	No change	99.1 ± 0.7	99.6 ± 0.5
2 Months	No change	98.9 ± 0.8	99.2 ± 0.6
3 Months	No change	98.7 ± 0.9	98.9 ± 0.7

The consolidated stability data clearly demonstrate that the optimized fenofibrate immediate-release pellet formulation (F2) remained **physically intact**, **chemically stable**, and **pharmaceutically effective** under accelerated storage conditions. The absence of significant changes in appearance, drug content, and dissolution behavior confirms the robustness of the formulation and supports its suitability for further development, long-term storage studies, and potential scale-up.

SUMMARY AND CONCLUSION

SUMMARY

This study aimed to develop and evaluate immediate-release multiparticulate pellets of fenofibrate using fluidization technology to improve dissolution and oral performance of this poorly water-soluble BCS Class II drug. Fenofibrate exhibits dissolution-rate-limited absorption; therefore, pelletization via Wurster fluidized-bed coating was selected to enhance surface area, wettability, and drug dispersion.

Pre-formulation studies confirmed poor solubility and flow properties, supporting the need for dissolution-enhancing strategies. FT-IR compatibility results indicated no drug–excipient interactions. Immediate-release pellets (F1–F4) were prepared by solution/suspension layering onto MCC spheres, with formulation and process parameters optimized for uniform coating and reproducible pellet formation.

All formulations showed acceptable micromeritic properties, good flow, uniform drug content, and adequate mechanical strength. Among them, Formulation F2 exhibited the best overall performance, with superior flow characteristics, low friability, optimal hardness, enhanced wettability, and

controlled moisture content. Dissolution studies confirmed rapid and complete drug release, with F2 showing the fastest release within 30 minutes.

Accelerated stability studies demonstrated that the optimized formulation remained stable with no significant change in drug content or dissolution profile, confirming formulation robustness.

CONCLUSION

The work successfully established fluidized-bed pelletization as an effective strategy for developing immediate-release fenofibrate pellets and overcoming dissolution limitations of poorly soluble drugs. The Wurster coating technique enabled uniform drug layering, controlled processing, and reproducible pellet quality.

Optimized formulation F2 showed desirable physical properties, excellent content uniformity, rapid dissolution, and good stability under accelerated conditions, indicating suitability for further development and potential scale-up.

Overall, the study demonstrates that fluidized-bed-based pelletization is a practical and industrially viable approach for improving dissolution and therapeutic performance of BCS Class II drugs such as fenofibrate.

REFERENCES

1. Food and Drug Administration. Guidance for industry: Waiver of in vivo bioavailability and bioequivalence studies for immediate-release solid oral dosage forms based on a Biopharmaceutics Classification System (BCS). Rockville (MD): US Food and Drug Administration; 2000. Available from: https://www.fda.gov
2. Amidon GL, Lennernäs H, Shah VP, Crison JR. A theoretical basis for a biopharmaceutics drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. **Pharm Res.** 1995;12(3):413–420.
3. Wu CY, Benet LZ. Predicting drug disposition via application of BCS: transport/absorption/elimination interplay and development of a Biopharmaceutics Drug Disposition Classification System. **Pharm Res.** 2005;22(1):11–23.
4. Broccatelli F, Cruciani G, Benet LZ, Oprea TI. BDDCS class prediction for new molecular entities. **Mol Pharm.** 2012;9(3):570–580.
5. Chen ML, Amidon GL, Benet LZ, Lennernäs H, Yu LX. The BCS, BDDCS, and regulatory guidances. **Pharm Res.** 2011;28(7):1774–1778.
6. Yan Y, Faustino PJ, Volpe DA, Lyon RC, Yu LX. Biopharmaceutics classification of selected beta-blockers: solubility and permeability class membership. **Mol Pharm.** 2007;4(4):608–614.
7. Chen ML, Yu L. The use of drug metabolism for prediction of intestinal permeability. **Mol Pharm.** 2009;6(1):74–81.
8. Benet LZ, Larregieu CA. The FDA should eliminate ambiguities in the current BCS biowaiver guidance and make public the drugs for which BCS biowaivers have been granted. **Clin Pharmacol Ther.** 2010;88(3):405–407.
9. European Medicines Agency. Guideline on the investigation of bioequivalence. London: EMA; 2010. Available from: https://www.ema.europa.eu
10. Lennernäs H. Human jejunal effective permeability and its correlation with preclinical drug absorption models. **J Pharm Pharmacol.** 1997;49(7):627–638.
11. World Health Organization. Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability. **WHO Tech Rep Ser.**2006;937:347–390.
12. Shugarts S, Benet LZ. The role of transporters in the pharmacokinetics of orally administered drugs. **Pharm Res.** 2009;26(9):2039–2054.
13. Benet LZ. The drug transporter–metabolism alliance: uncovering and defining the interplay. **Mol Pharm.** 2009;6(6):1631–1643.
14. Benet LZ. Predicting drug disposition via application of a biopharmaceutics drug disposition classification system. **Basic Clin PharmacolToxicol.** 2010;106(3):162–167.
15. Lau YY, Okochi H, Huang Y, Benet LZ. Multiple transporters affect the disposition of atorvastatin and its two active hydroxy metabolites. **J Pharmacol Exp Ther.** 2006;316(2):762–771.

16. He YJ, Zhang W, Chen Y, Guo D, Tu JH, Xu LY, et al. Rifampicin alters atorvastatin plasma concentration based on SLCO1B1 521T>C polymorphism. **Clin Chim Acta.** 2009;405(1–2):49–52.
17. Zhang HX, Huang Y, Frassetto LA, Benet LZ. Elucidating rifampin's inducing and inhibiting effects on glyburide pharmacokinetics. **Clin Pharmacol Ther.** 2009;85(1):78–85.
18. Wu CY, Benet LZ. Disposition of tacrolimus in isolated perfused rat liver. **Drug MetabDispos.** 2003;31(10):1292–1295.
19. Sconce EA, Khan TI, Wynn HA, Avery P, Monkhouse L, King BP, et al. Impact of CYP2C9 and VKORC1 polymorphisms on warfarin dose requirements. **Blood.** 2005;106(7):2329–2333.
20. Frymoyer A, Shugarts S, Browne M, Wu AH, Frassetto L, Benet LZ. Effect of rifampin on warfarin pharmacokinetics. **Clin Pharmacol Ther.** 2010;88(4):540–547.