Immplementation in Pharmaceutical Development: A Comprehensive Framework for Robust Solid Dosage Formulation of Metformin Hydrochloride

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Abstract

Fast dissolving tablets (FDTs) of Metformin hydrochloride were developed using the direct compression technique. The formulations incorporated superdisintegrants such as croscarmellose sodium (4%) and sodium starch glycolate (8%). The hardness of formulations F1–F6 ranged from 4.5±0.08 to 3.7±0.10 kg/cm², while disintegration time varied between 61.5±0.54 and 24.5±1.04 seconds. All batches complied with pharmacopeial limits for friability and weight variation.

An increase in superdisintegrant concentration resulted in reduced hardness and faster disintegration. Among all formulations, F6 demonstrated superior performance with the shortest disintegration time (24.5±1.04 seconds), attributed to the effect and mechanism of the superdisintegrants used. In vitro drug release studies showed a release range of 97.40±2.46% to 99.54±1.12%.

Evaluation results indicated that formulations containing natural superdisintegrants exhibited improved hardness, disintegration time, wetting time, and drug release compared to those with synthetic agents. Formulation F6 showed optimal characteristics, including hardness of 3.7±0.10 kg/cm², friability of 0.44±0.01%, wetting time of 17.1±0.76 seconds, dispersion time of 16.3±0.8 seconds, and drug content of 100±1.2%. It achieved maximum drug release (99.54±1.12%) and met all criteria for an effective fast dissolving tablet. Overall, F6 was identified as the best formulation due to its rapid disintegration and wetting, along with adequate mechanical strength.

Keywords

Fast Dissolving Tablets, Super Disintegrates, Disintegration Time, Hardness, Wetting Time, Friability, Weight Variation, Drug Release.

Introduction

Fast dissolving drug delivery systems (FDDS) were introduced in the late 1970s to address the needs of paediatric and geriatric patients who experience difficulty in swallowing conventional dosage forms. As reported by Kuchekar and Arumugam (2001), these formulations are designed to disintegrate or dissolve rapidly in saliva, typically within 60 seconds, without the need for water. Over time, several terminology variants have emerged, including mouth melting tablets (MMTs), mouth dissolving tablets (MDTs), orally disintegrating tablets (ODTs), fast disintegrating tablets (FDTs), and immediate-release tablets. These dosage forms, as described by Chaudhary et al. (2007), offer improved patient compliance due to their ease of administration. Market analyses suggest that nearly half of patients prefer FDTs over conventional tablets.

MDTs are commonly formulated using superdisintegrants such as crospovidone, sodium starch glycolate, and croscarmellose sodium, which facilitate rapid tablet breakup. According to Chang et al. (2000), such systems may enhance drug bioavailability through pre-gastric absorption in the oral cavity and reduce first-pass metabolism compared to traditional dosage forms.

Metformin hydrochloride, chemically known as 1,1-dimethylbiguanide hydrochloride, is a widely prescribed oral hypoglycemic agent used in the management of type 2 diabetes mellitus, particularly in overweight and obese patients. Its therapeutic action is primarily attributed to the inhibition of hepatic glucose production and the improvement of peripheral insulin sensitivity, while maintaining a favorable safety profile. Due to its cost-effectiveness, minimal risk of weight gain, and potential cardiovascular benefits, it is recommended as a first-line treatment. Recent studies have also indicated possible benefits of metformin in certain cancer conditions.

Metformin is classified as a BCS Class III drug, characterized by high aqueous solubility and low membrane permeability. The conventional immediate-release dosage typically ranges from 250–500 mg administered two to three times daily, with a maximum daily dose of up to 3 g. Such high dosing often results in large tablet sizes, which can reduce patient compliance, especially among elderly individuals with swallowing difficulties. Although splitting or chewing tablets is sometimes practiced, the inherently bitter taste of metformin can lead to poor patient acceptability.

To address these limitations, orally disintegrating tablets (ODTs) of metformin have been developed, offering rapid disintegration in the oral cavity and eliminating the need for water, thereby improving patient convenience and compliance. From a manufacturing perspective, direct compression and dry granulation techniques are generally preferred over wet granulation due to the elimination of additional drying steps and reduced process complexity. Wet granulation often involves challenges such as granule adhesion to equipment surfaces and structural instability during drying. To overcome these issues, a continuous granulation approach known as moisture-activated dry granulation (MADG), as described by Ullah et al., has been developed, offering improved process efficiency and product quality.

Fast Dissolving Tablet (FDT):

Fast dissolving/disintegrating tablets (FDDTs) have been recognized as a suitable dosage form for patients who experience difficulty in swallowing, particularly paediatric and geriatric populations (Vikas et al., 2007). These formulations are also referred to by various terms such as fast melting, fast dispersing, rapid dissolve, quick melt, or fast dissolving tablets. The European Pharmacopoeia defines orodispersible tablets as solid dosage forms intended to be placed in the oral cavity, where they rapidly disperse prior to swallowing.

According to Chawdory et al. (2012), fast dissolving tablets were developed to overcome limitations associated with conventional solid dosage forms, particularly swallowing difficulties. These tablets are designed to disintegrate or dissolve in saliva within a short time frame, typically ranging from 5 to 60 seconds. As reported by Reddy et al. (2002), such formulations improve patient compliance and acceptability, and may also enhance biopharmaceutical performance, including improved bioavailability, therapeutic efficacy, convenience, and overall safety compared to traditional dosage forms.

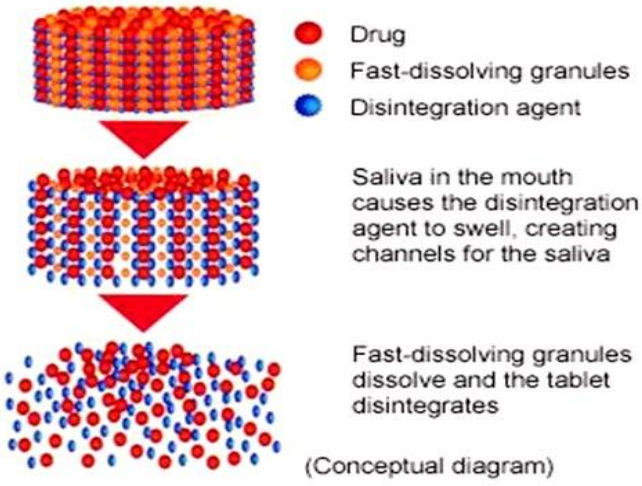

Fig. 1: Mechanism of action of superdisintegrants

Superdisintegrants:

Play a crucial role in the formulation of fast dissolving tablets prepared by direct compression, as they facilitate rapid tablet disintegration and breakup (Nautiyal et al., 2014). The presence of auxiliary excipients such as effervescent agents and water-soluble materials can further accelerate the disintegration process. With increasing demand for faster disintegrating dosage forms, there is a need to develop highly efficient superdisintegrants that are effective even at low concentrations and exhibit superior intragranular performance.

These agents primarily function through mechanisms such as swelling and enhanced water uptake. Upon contact with saliva, superdisintegrants absorb water and expand, generating outward (radial) pressure that promotes tablet rupture. This swelling action significantly increases the volume of granules and facilitates rapid disintegration of the dosage form.

Metformin HCl:

Metformin hydrochloride is a widely prescribed oral antihyperglycemic agent used in the management of type 2 diabetes mellitus. It helps improve glucose tolerance by reducing both fasting and postprandial blood glucose levels. Due to its effectiveness, safety profile, and additional benefits such as reduced risk of cardiovascular complications, it is commonly considered a first-line therapy, particularly in overweight or obese patients when lifestyle modifications alone are insufficient.

Metformin is also used in combination with other antidiabetic agents, including sulfonylureas, in cases where glycemic control is not adequately achieved with monotherapy. Additionally, emerging evidence suggests its potential role in reducing certain diabetes-related complications, including cardiovascular disorders and some forms of cancer.

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Table 1 : Characteristicts of Metformin Hydrochloride

Parameters	**Properties**
Colour	White
Nature	Crystalline Powder (solid); hygroscopic
Odor	Odorless
Taste	Tasteless
M.P.	224°C
pH	pH of 1% aqueous solution of Metformin hydrochloride is 6.68
Λmax	290 nm
Dissociation constant (pKa)	12.4
Specific Rotation	15.3 to 17.0°
Loss on Drying	Not more than 0.5 % (drying 1 g in an oven at 105°C)
Storage temperature	At Room Temperature; in closed container (light protected)
Refractive index	1.392-1.396
Clearance	Excreted unchanged by kidney
Solubility	Freely soluble in Water; • Slightly soluble in methanol; • Insoluble in acetone, chloroform, dichloromethane, ether;
Route of Administration	Oral (200-800 mg / day)
Dosage Form	Tablet
Bioavailability	50-60%
Protein Binding	Metformin HCl negligibly bound to plasma proteins
Half-life	6.2 hours

THE BIOPHARMACEUTICS CLASSIFICATION SYSTEM (BCS):

The Biopharmaceutics Classification System (BCS) is commonly applied during the early development of immediate-release oral dosage forms. It classifies drugs into four categories based on the key factors that influence their absorption, namely aqueous solubility, dissolution rate, and intestinal permeability, which collectively determine the rate and extent of drug absorption from the gastrointestinal tract.

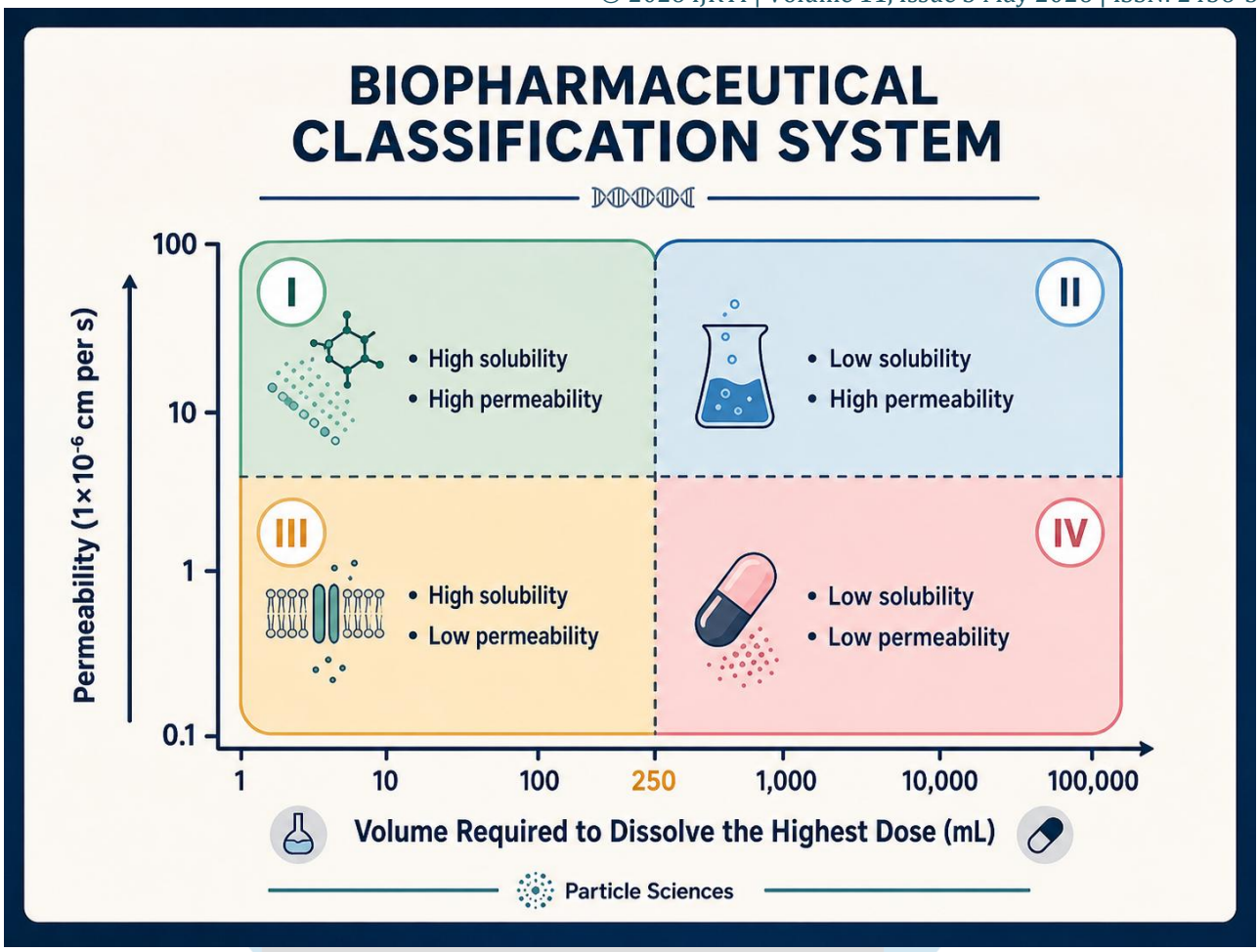

Figure 2 : Biopharmaceutical Classification

Polymer Profile Croscarmellose Sodium (Croscarmellose Sodium):

Croscarmellose sodium is a cross-linked derivative of sodium carboxymethylcellulose (Na-CMC) widely used as a disintegrating agent in pharmaceutical formulations. The cross-linking process renders it insoluble while maintaining its hydrophilic nature, allowing it to rapidly absorb water. Due to its high swelling capacity and effective wicking properties, it promotes quick tablet disintegration. It is also recognized as a safe and approved pharmaceutical excipient for use in drug products.

Table 2: Characteristics of Croscarmellose Sodium

Parameters	**Properties**
pH	5.0 – 7.0
Heavy Metals, NMT%	10
Sodium glycolate NMT%	0.5
Degree of Substitution	0.60 – 0.85
Loss on Drying	Not more than 10 %
Storage temperature	At Room Temperature; in closed container (light protected)
Content of water soluble material	Upto 10.0 %
Settling Volume (ml)	10.0 - 30.0

Lubricating Agent Profile*:*

Magnesium Stearate: Magnesium stearate is safe for human as a filling agent / lubricant (prevents ingredients from sticking to manufacturing equipments during compression of chemical powder into tablets / capsules. It has two equivalents of stearate and one magnesium cation. It consists mainly of magnesium stearate (C17H35CO2)2Mg with variable proportions of magnesium palmitate (C17H31CO2)2Mg and magnesium oleate.rewrite this paragraph and remove plagiarism

Parameters	**Properties**
Color	White
Nature	Light, Unctuous and free from grittiness
Odor	Faint odor of stearic acid
Taste	Slightly acidic
M.P.	69-70°C
Loss on Drying	Not more than 6 %
Storage temperature	At Room Temperature; in closed container (light protected)
Use	Lubricant

Sodium Starch Glycolate*:*

Sodium starch glycolate is a modified starch derivative obtained as the sodium salt of the carboxymethyl ether of starch, with a high molecular weight typically exceeding 500,000. It is widely used as a superdisintegrant in pharmaceutical formulations. The material is produced through chemical modification of starch involving carboxymethylation to increase its hydrophilic nature, followed by cross-linking to limit solubility while maintaining rapid swelling properties.

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Parameters	**Properties**
Color	White or Off white
Nature	Free flowing powder grittiness
Odor	Odorless
Solubility	Insoluble in water • Insoluble in organic solvents
Shape of granules	Oval / Spherical (30-100 μm)
Storage temperature	At Room Temperature; in closed container (light protected)
Use	Super disintegrating agent

Purified Talc:

Talc (USP) is a hydrated magnesium silicate with the chemical composition (H2Mg3(SiO3)4), corresponding approximately to 4.8% water, 31.7% magnesium oxide, and 63.5% silicon dioxide. It is a naturally occurring mineral formed through hydrothermal processes and regional metamorphism of magnesium-rich rocks such as dolomite, pyroxenite, amphibolite, serpentine, dunite, and chlorite.

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Parameters	Properties
Color	White or graying-white powder
Nature	Free flowing powder free from grittiness (soft soapy feel)
Taste	Tasteless
Odor	Odorless
Specific gravity	2.2 to 2.8
Solubility	Insoluble in water • Insoluble in dilute acids and alkali hydroxides
Shape of granules	Spherical
Storage temperature	At Room Temperature; in closed container (light protected)
Use	Lubricant; absorbs excess moisture

Micro Crystalline Cellulose (MCC):

Microcrystalline cellulose (MCC) is a white, fine to granular, odorless powder with a typical particle size of 15–40 μm, containing between 97% and 100.5% cellulose. It is a naturally derived, highly crystalline form of cellulose composed of aggregated crystallites. MCC is chemically inert, stable, and insoluble in water, making it a safe and widely used pharmaceutical excipient. Structurally, it is a natural polymer made up of glucose units linked through β-(1→4) glycosidic bonds..

Lactose:

Lactose is a disaccharide chemically described as O-β-D-galactopyranosyl-(1→4)-α-D-glucopyranose monohydrate. Spray-dried lactose (e.g., Lactopress) is produced by spray drying a suspension of fine α-lactose monohydrate crystals in a saturated lactose solution. The resulting material typically consists of about 85% crystalline α-lactose monohydrate and 15% amorphous lactose. This form exhibits good flow properties, low hygroscopicity, and enhances tablet characteristics such as compressibility, uniformity of weight, disintegration, and solubility.

Parameters	Properties
Color	White
Nature	Crystalline
Taste	Sweet
Odor	Odorless
Shape of granules	Spherical
Storage temperature	At Room Temperature; in closed container (light protected)

Mannitol*:*

Mannitol is a widely used excipient as well as an active pharmaceutical ingredient, valued for its low hygroscopicity, high stability, and chemical inertness across different particle sizes. In its pyrogen-free form, it is also suitable for use in parenteral formulations. Fast dissolving tablets (FDTs) are designed to be placed on the tongue or oral mucosa, where they rapidly absorb saliva, leading to quick hydration, disintegration, and initiation of drug release.

The primary aim of fast dissolving drug delivery systems is to ensure rapid dissolution in the oral cavity while providing a pleasant mouthfeel. The overall goal of such formulations is to enhance patient compliance without compromising therapeutic effectiveness. Therefore, the present study was undertaken with the following objectives:

Development of fast dissolving tablets of Metformin hydrochloride
Masking of taste of the bitter drug for the incorporation into fast dissolving dosage form.
Use of direct compression technology for development of fast dissolving dosage forms
Quality assessments / evaluation of formulated fast dissolving tablets of Metformin hydrochloride
In-vitro release of drug from FDT formulation of Metformin hydrochloride
Stability studies of the FDT formulations of Metformin hydrochloride
To enhance the bioavailability of the FDT of Metformin HCl
To conduct the bioavailability study (In vitro study) and evaluate bioavailability enhancement of drug.
To develop a stable tablet / formulation and evaluate its stability according to ICH guidelines.

Materials And Methods

Table 3: Active Pharmaceutical Ingredient

Name of Drug
Metformin HCl

Table 4: List of Chemicals

Name of Chemical
Croscarmellose Sodium
Magnesium stearate
Sodium starch glycolate
Purified Talc
Micro Crystalline Cellulose
Lactose
Mannitol

Pre-Formulation Studies

Identification and Characterisation of Metformin hydrochloride*:*

The drug was characterized through various physicochemical evaluations, including determination of its melting point and spectroscopic analyses such as UV and IR studies of pure metformin hydrochloride.

Physical Characterisation:

The physical properties of metformin hydrochloride—such as its appearance, color, and odor—were evaluated. The observed features were then documented and compared with those described in standard literature..

Identification of Metformin hydrochloride:

Dissolve 25 mg of the sample in 5 ml of water and add 1.5 ml of 5 M sodium hydroxide solution. Then, while continuously shaking, add 1 ml of 1-naphthol solution followed by 0.5 ml of diluted sodium hypochlorite dropwise. An orange-red color develops, which gradually intensifies over time.

In another test, dissolve 10 mg of the sample in 10 ml of water. Prepare a reagent mixture by combining equal volumes of 10% w/v sodium nitroprusside solution, 10% w/v potassium ferricyanide solution, and 10% w/v sodium hydroxide solution. Add 10 ml of this mixture to the prepared sample solution and allow it to stand for 20 minutes. A crimson color appears within approximately 3 minutes.

Melting point :

The melting point of the drug was determined using the capillary tube method, either with an oil bath or a melting point apparatus. This method involves noting the temperature range over which the sample transitions from solid to liquid. The melting point of metformin hydrochloride was measured using the glass capillary technique (Table 5).

Table 5: Melting Point of Metformin hydrochloride

S. No.	Reported	Observed
1.	222°C to 226°C	224°C

Solubility Analysis *:*

Solubility is a key factor in preformulation studies due to its impact on drug performance:

1. It plays a major role in determining the dissolution rate of the drug.
2. The bioavailability of a drug, especially after oral administration, is closely related to its dissolution behavior.
3. Characteristics such as particle size, shape, and surface area can influence dissolution, making solubility evaluation essential during preformulation.

Method:

Weighed quantity of drug was added to the suitable volume of solvent and solubility checked.

UV Spectroscopy*:*

UV spectrophotometric analysis of metformin hydrochloride was performed to determine its maximum absorbance in artificial saliva (pH 6.8) and 0.1 N HCl. The prepared solution was scanned over a wavelength range of 200–400 nm using a UV spectrophotometer (Systronics Model 2202), and the corresponding spectrum was recorded (Fig. 2).

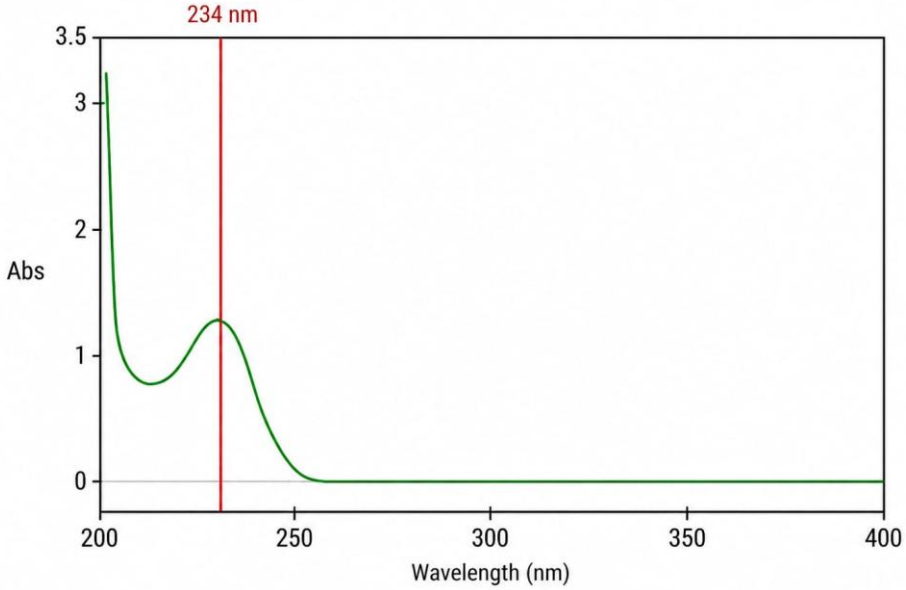

Fig. 2 : UV spectrum of metformin hydrochloride at 234 nm

Partition Coefficient*:*

The partition coefficient of metformin hydrochloride was determined using an n-octanol/water system. An accurately weighed 10 mg sample of the drug was placed in a glass vial containing 5 ml of n-octanol, followed by the addition of 5 ml of water. The mixture was agitated using a vortex mechanical shaker and then allowed to stand until the two phases separated completely. After suitable dilution, the aqueous phase was analyzed for drug content using a UV spectrophotometer (Systronics Double Beam Spectrophotometer, Model 2202) against a reagent blank (Table 6). The partition coefficient (P) was subsequently calculated using the appropriate equation.

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P o/w = (C org / C aq)P w/o = (C aq / C org)

Where,

Corg = Concentration of drug in organic phase.

Caq = Concentration of drug in aqueous phase.

Co/w = Partition coefficient of drug in oil in water system.

Cw/o = Partition coefficient of drug in water in oil system

Table 6 : Partition Coefficient of Metformin hydrochloride.

S. No.	Medium	Partition Coefficient
1.	O/DW	5.1

Note: DW: Distilled water; O: Octanol

Solubility Study:

Solubility refers to the ability of two or more substances to interact and form a uniform molecular solution. The solubility of the drug was evaluated using different common solvents. A measured quantity of the drug (10 mg) was added to 10 ml of each solvent and observed at room temperature (Table 7).

Table 7: Solubility of

S. No.	Solvent	Solubility
1.	Distilled water	Freely soluble
2.	Alcohol	Slightly soluble
3.	Methanol	Slightly soluble
4.	Acetone	Insoluble
5.	Chloroform	Insoluble
6.	Dichloromethane	Insoluble
7.	Ether	Insoluble

IR Spectroscopy:

The IR spectrum of metformin hydrochloride was obtained by the KBr pellet technique. The sample was blended with IR-grade potassium bromide in a 1:100 ratio and compressed into a pellet using an 8-ton pressure press. The pellet was then scanned in the 4000–400 cm^{-1} range using an FTIR spectrophotometer (Shimadzu 8400S), and the spectrum obtained is presented in Fig. 3.

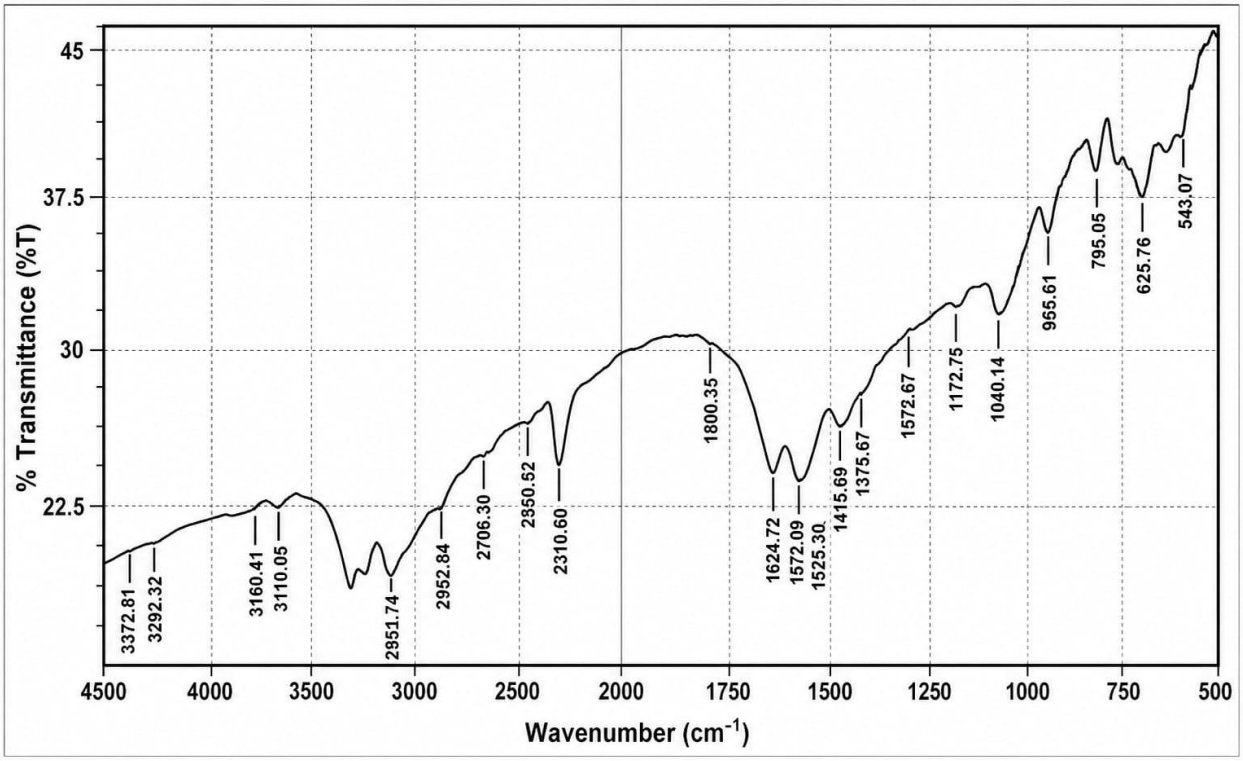

Fig. 3: FT-IR Spectrum of metformin hydrochloride

Drug Excipient Compatibility Screening:

Compatibility between the drug and excipients was assessed through physical observation. Samples containing the pure drug and polymer were stored in glass vials at 40 ± 2°C and 75 ± 5% relative humidity for one month. Mixtures of the drug and polymer in specified proportions were prepared and monitored weekly for any visible changes, such as color variation or formation of lumps.

Selection of Excipients :

Excipients play a vital role in the development of drug delivery systems, significantly influencing their performance and overall quality. In the formulation of fast dissolving tablets of Metformin HCl, various excipients were used for specific functions. Lactose served as the diluent, microcrystalline cellulose (MCC) was used as a binder, and magnesium stearate acted as a lubricant. Mannitol was included as an additive, while sodium starch glycolate and croscarmellose sodium were employed as superdisintegrants to promote rapid tablet disintegration.

Preparation of Standard Curve :

A stock solution of metformin hydrochloride (1000 µg/ml) was prepared by dissolving 100 mg of the drug in 100 ml of 0.1 N HCl. From this stock, a series of dilutions were made to obtain concentrations of 1, 2, 3, 4, 5, and 10 µg/ml. The absorbance of these solutions was then measured at 266 nm using a UV spectrophotometer (Tables 8–9; Fig. 4–5).

Table 8: Standard curve of Metformin hydrochloride in Distilled water

S.No	Conc. (µg/ml)	Absorbance
1.	0	0
2.	1	0.012
3.	2	0.021
4.	3	0.034
5.	4	0.043
6.	5	0.055
7.	6	0.067
8.	7	0.078
9.	8	0.087
10.	9	0.096
11.	10	0.108

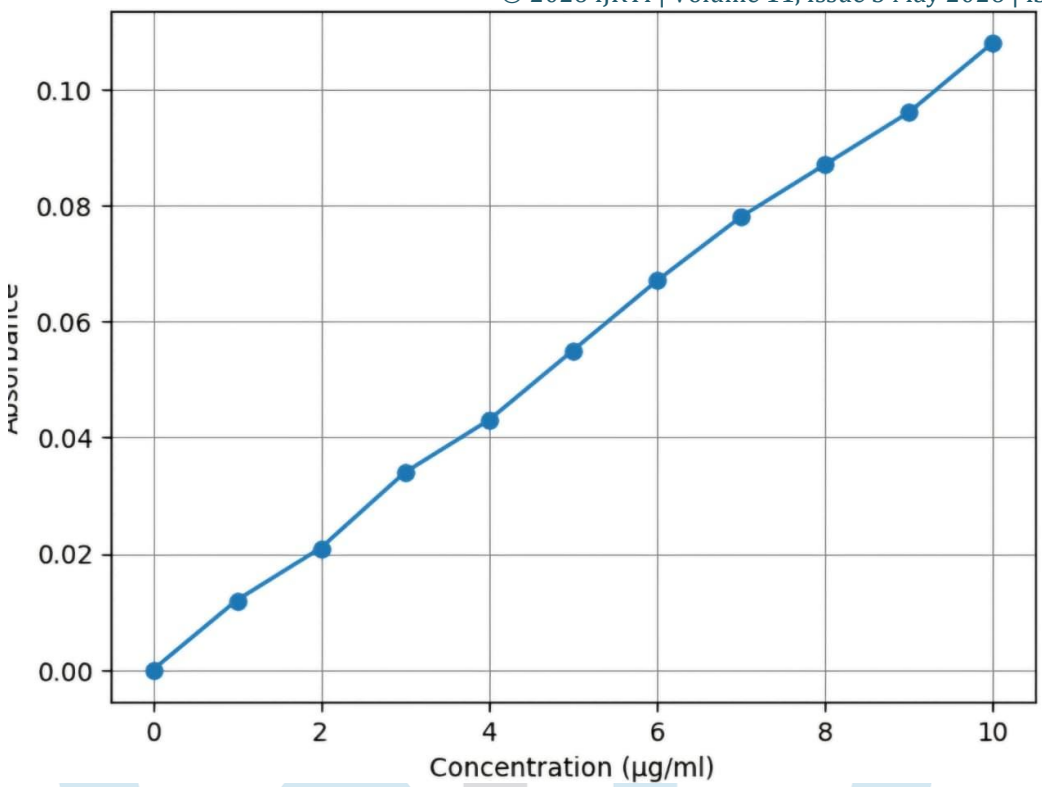

Fig. 4: Standard curve of Metformin hydrochloride in Distilled water.

Table 9: Standard curve of Metformin hydrochloride in 0.1N HCl

0	**Conc (µg/ml)**	**Absorbance**
1.	0	0
2.	1	0.04
3.	2	0.07
4.	3	0.1
5.	4	0.12
6.	5	0.15
7.	6	0.18
8.	7	0.21
9.	8	0.24
10.	9	0.27
11.	10	0.30

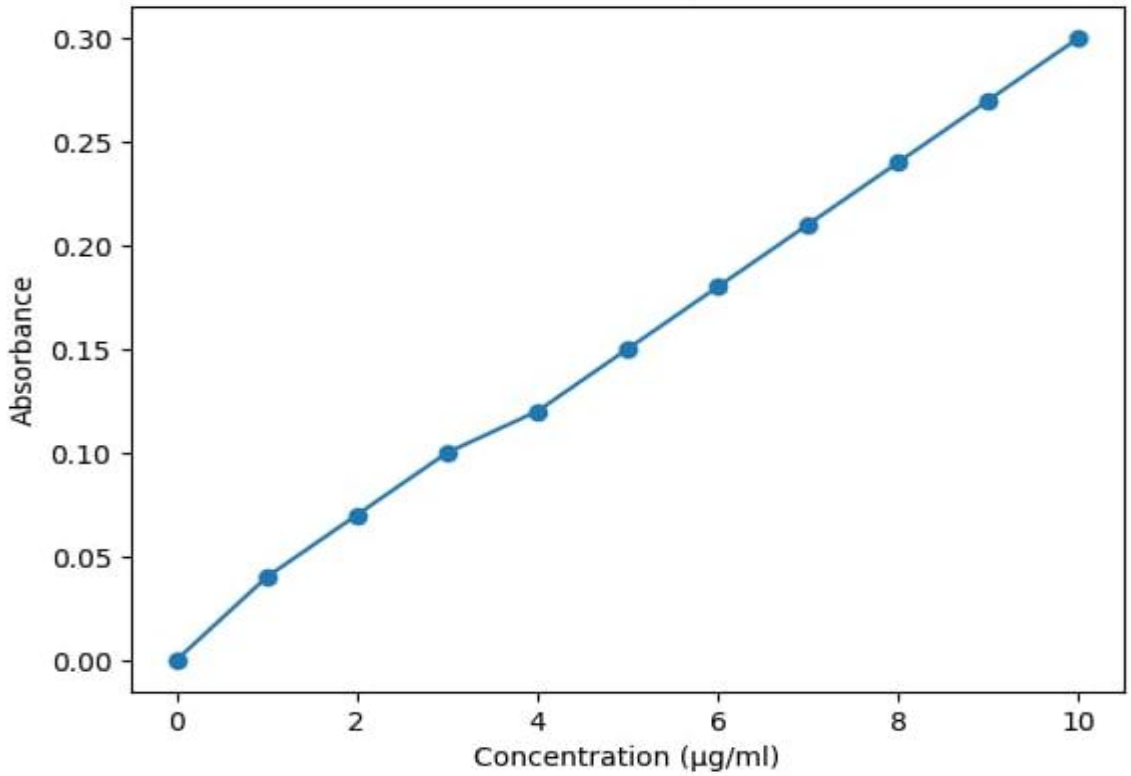

Fig 5 : Standard curve of Metformin hydrochloride in 0.1N HCl

Formulation of FDT of Metformin HCl :

To ensure uniform blending, the drug and excipients were first passed through a sieve. Fast dissolving tablets containing 200 mg of metformin hydrochloride were then prepared using the direct compression method. Various formulations were developed using superdisintegrants such as croscarmellose sodium. After thorough mixing of all ingredients, talc and magnesium stearate were incorporated as lubricants. The final blend was compressed into tablets using a tablet compression machine fitted with an 8 mm punch (Table 10).

Table 10: Formulation of Metformin hydrochloride Fast Dissolving Tablets

S.No	Ingredients Name	Formulation (µg)					
		F1	F2	F3	F4	F5	F6
1	Metformin hydrochloride	100	100	100	100	100	100
2	Cross carmellose sodium	8	16	0	0	0	0
3	Sodium starch glycolate	0	0	8	16	0	0
4	Isaphagula	0	0	0	0	8	16
5	Magnesium stearate	20	20	20	20	20	20
6	Purified Talc	20	20	20	20	20	20
7	Mannitol	20	20	20	20	20	20
8	Spray dried Lactose	32	24	32	24	32	24
Total		200	200	200	200	200	200

The powder Blend was evaluated for flow properties as follows:

Bulk Density*:*

Bulk density was determined by dividing the mass of the powder by its bulk volume (cm^3). Approximately 50 cm^3 of the powder sample, previously passed through a standard sieve (No. 20), was carefully transferred into a 100 ml graduated cylinder. For tapped density measurement, the cylinder was tapped by dropping it from a height of about one inch onto a hard wooden surface at two-second intervals for 100 taps. The tapped density for each formulation was then calculated by dividing the weight of the sample (g) by the final tapped volume (cm^3) of the powder (Table 11 and Fig. 6). The values were calculated using the appropriate formula:

$$\mathbf{Df = M/Vp}$$

Where ,

Df = Bulk density

M = Weight of the sample in grams

Vp = final volumes of granules in cm3

Table 11: Bulk density of Metformin HCl

Physical Parameter	Formulation (µg)						
	F1	F2	F3	F4	F5	F6	
Bulk density	0.69±0.4	0.83±0.3	0.76±0.2	0.72±0.1	0.87±0.2	0.69±0.2	

Tapped Density:

Tapped density was determined by dividing the mass of the powder by its tapped volume (cm^3). About 50 cm^3 of the powder sample, previously passed through sieve No. 20, was carefully transferred into a 100 ml graduated cylinder. The cylinder was then tapped by dropping it from a height of approximately one inch onto a hard wooden surface at intervals of two seconds for three taps. The tapped density of each formulation was calculated by dividing the weight of the sample (g) by the final volume occupied by the granules in the cylinder (cm^3) (Table 12). The values were obtained using the appropriate formula.

$$\mathbf{Dt = M/Vp}$$

Where Dt = Tapped density

M = Weight of the sample in grams

Vp = final volumes of granules in cm3

Table 12: Tapped density of Metformin HCl

Physical Parameter	Formulation (µg)						
	F1	F2	F3	F4	F5	F6	
Bulk density	0.82±0.6	0.93±0.4	0.89±0.6	0.91±0.5	0.93±0.3	0.96±0.5	

Compressibility Index:

It is measurement of free flowing powders and determined by the following formula (Table 13):

$$\frac{\text{Tapped density} - \text{Bulk Density}}{\text{Tapped density}} \times 100$$

% Compressibility = Tapped density

Physical Parameter	Formulation						
	F1	F2	F3	F4	F5	F6	
% Compressibility	15.66%	14.54%	12.18%	13.64%	15.52%	16.56%	

Haussner's Ratio:

Haussner's ratio is an indirect index of ease of powder flow and is calculated by the following formula (Table 14)

Haussner's ratio = Dt / Df

Where,

Dt = tapped density

Df = bulk density

Table 14: Haussner's ratio of Metformin HCl formulations

Physical Parameter	Formulation						
	F1	F2	F3	F4	F5	F6	
Haussner's ratio	1.15	1.17	1.14	1.13	1.18	1.20	

Angle of Repose:

The angle of repose of the granules for each formulation was measured using the funnel method. The powder was allowed to flow through a funnel onto a flat, horizontal surface, forming a conical heap. The height (H) of the pile and the radius (R) of its base were recorded (Table 15; Fig. 10). These values were then used to calculate the angle of repose using the appropriate equation.

:

Tan0 = H/R

0 = tan-1(H/R)

Table 15: Angle of Repose of formulations

Physical Parameter	**Formulation**						
	F1	F2	F3	F4	F5	F6	
Angle of repose (degree)	22.55°C	25.97°C	20.57°C	21.35°C	22.20°C	24.15°C	

Flow Rate:

The flow rate of a powder is defined as the rate at which a given quantity passes through a funnel of specified diameter. For each formulation, a known weight of granules was carefully introduced into a funnel with an 8 mm orifice. The time required for the entire sample to pass through the opening was recorded using a stopwatch. The flow rate was then calculated using the appropriate formula (Table 16).

Flow rate = Time (in seconds)

Table 16: Flow rate of Metformin HCl formulations

Physical Parameter	**Formulation**						
	F1	F2	F3	F4	F5	F6	
Flow rate	Good	Fair	Good	Good	Good	Good	

Evaluation of Tablets

Tablet Thickness:

Tablet diameter and thickness are important parameters for ensuring uniformity in tablet size. These dimensions were measured using a Vernier caliper (Table 17).

Table 17: Tablet Thickness of various formulation of Metformin HCl

Physical Parameter	Formulation						
	F1	F2	F3	F4	F5	F6	
Thickness	3.2±0.07	3.3±0.03	3.5±0.02	3.3±0.09	3.5±0.05	3.5±0.06	

Tablet Hardness:

Tablet hardness reflects its ability to withstand mechanical stress during storage, transportation, and handling. The hardness of each formulation was measured using a Monsanto hardness tester, and the results are presented in Table 18.

Table 18: Tablet hardness of various formulation of Metformin HCl

Physical Parameter	Formulation						
	F1	F2	F3	F4	F5	F6	
Hardness (kg/c.m2)	4.5±0.08	4.4±0.07	4.41±0.01	4.2±0.08	4.1±0.09	3.8±0.10	

Friability:

Friability is used to evaluate the mechanical strength of tablets. The test was carried out according to standard operating procedures using a Roche friabilator. Twenty tablets were accurately weighed and placed in the instrument, which rotates at 25 rpm, allowing the tablets to fall from a height of about six inches during each revolution. After 4 minutes, the tablets were reweighed, and the percentage weight loss was calculated (Table 19).

Table 19: Friability of various formulation of Metformin HCl

Physical Parameter	Formulation						
	F1	F2	F3	F4	F5	F6	
Friability (%)	0.65±0.01	0.61±0.01	0.57±0.08	0.52±0.012	0.47±0.01	0.44±0.01	

Weight Variation:

For the USP weight variation test, twenty tablets were individually weighed and the average weight was calculated. The weight of each tablet was then compared with this average to assess uniformity. This test serves as a quality control measure and may also involve sampling tablets at regular intervals during the manufacturing process (Table 20).

Table 20: Weight variations of various formulation of Metformin HCl

Physical Parameter	Formulation						
	F1	F2	F3	F4	F5	F6	
Weight Variation (%)	99.8±1.1	99.5±1.04	99.3±1.3	100.3±0.8	100.2±0.8	100.5±1.0	

Tensile Strength:

The tensile strength of the tablets was determined using the appropriate mathematical expression, and the results are presented in Table 21.

$$T = 2Fc/d.t$$

Where Fc = Crushing strength

d = diameter

t = thickness of tablet

Physical Parameter	**Formulation**						
	F1	F2	F3	F4	F5	F6	
Tensile Strength	0.192	0.211	0.181	0.203	0.172	0.186	

In-vitro Disintegration Time:

The disintegration time of each formulation was evaluated using a tablet disintegration test apparatus. Six tablets were placed in the tubes of the device, one in each tube. The test was carried out using pH 6.8 phosphate buffer maintained at 37 ± 2°C, and the time required for complete disintegration of the tablets was recorded according to standard procedures (Table 22).

Table 22: In-vitro Disintegration Time of various formulations

Physical Parameter	**Formulation**						
	F1	F2	F3	F4	F5	F6	
Disintegration time (in sec.)	61.5± 0.54	54.5 ± 1.04	47.1 ± 0.74	40.3 ± 1.03	30.8 ± 1.16	24.5 ± 1.04	

In-vitro Dispersion Time:

The dispersion time of the tablets was determined by placing each tablet in 10 ml of pH 6.8 phosphate buffer, maintained at 37 ± 0.5°C to simulate salivary conditions. The time required for complete dispersion of the tablet was recorded following standard operating procedures (Table 23).

Physical Parameter	Formulation					
	F1	F2	F3	F4	F5	F6
Disintegration time (in sec.)	42.5 ±0.80	38.2 ± 1.03	31.8± 1.1	27.1 ± 08	24.5 ± 0.57	15.7 ± 0.9

Wetting Time:

A circular piece of tissue paper (8 cm in diameter), folded twice, was placed in a Petri dish (9 cm internal diameter) containing 10 ml of pH 6.8 buffer solution to simulate saliva. A tablet was then carefully placed on the tissue paper, and the time required for complete wetting was recorded. For each formulation, three tablets were selected randomly, and the average wetting time was calculated in accordance with standard procedures (Table 24).

Table 24: Wetting time of various formulations

Physical Parameter	Formulation					
	F1	F2	F3	F4	F5	F6
Wetting Time (in sec.)	60.4 ± 1.16	60.2 ± 1.13	38.1 ± 1.2	33.6 ± 1.1	25.6 ± 1.03	17.1 ± 0.74

Water Absorption Ratio:

A circular tissue paper (8 cm in diameter), folded twice, was placed in a Petri dish of 9 cm diameter containing 10 ml of water. A tablet was carefully positioned on the paper, and the time required for complete wetting was recorded according to standard operating procedures (Table 25). The water absorption ratio was then calculated using the appropriate formula.

:

$$R = 100 \times Wa - Wb / Wb$$

Where

Wb = Weight of tablet before water absorption

Wa = Weight of tablet after water absorption

Table 25: Water absorption ratio of various formulations

Physical Parameter	Formulation					
	F1	F2	F3	F4	F5	F6
Water Absorption Ratio	56.53 %	68.44 %	57.64 %	63.96 %	70.28 %	72.8 %

Because of its higher swelling and water penetration capabilities, formulation F6 had the highest water absorption ratio of all the formulations.

Uniformity of Content:

For each formulation, five tablets were weighed individually and reduced to a fine powder. An amount of the powder equivalent to 10 mg of metformin hydrochloride was taken, dissolved in 10 ml of distilled water, and the volume was adjusted to 100 ml with pH 6.8 phosphate buffer. A 1 ml aliquot of this solution was then further diluted to 100 ml using the same buffer. The final solution was measured at 233 nm using a UV spectrophotometer, employing pH 6.8 buffer as the blank (Table 26).

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Table 26: % Drug Content of Different formulations

Physical Parameter	Formulation					
	F1	F2	F3	F4	F5	F6
% Drug Content	99.6±0.8	99.8±0.9	99.1±1.1	100.3±1.0	100.6±0.5	100.2±1.2

Results and Discussion

Metformin hydrochloride ($C_4H_{11}N_5 \cdot HCl$) is a white, crystalline, hygroscopic, and odorless powder with a melting point of approximately 224°C and a λmax of 290 nm. It is widely used as an oral antihyperglycemic agent for the management of non-insulin-dependent diabetes mellitus (NIDDM), where it reduces both fasting and postprandial blood glucose levels. The drug is freely soluble in water, slightly soluble in methanol, and insoluble in organic solvents such as acetone, chloroform, dichloromethane, and ether. It shows negligible plasma protein binding and is excreted unchanged via the kidneys. Metformin exhibits an oral bioavailability of about 50–60%, is typically administered in doses ranging from 200–800 mg/day, and has a half-life of approximately 6.2 hours.

The present study aimed to develop fast dissolving tablets (FDTs) of metformin hydrochloride using the direct compression method. Superdisintegrants such as croscarmellose sodium (4%) and sodium starch glycolate (8%) were incorporated into the formulations. The powder blends were evaluated for flow properties, including bulk density, tapped density, compressibility index, Hausner's ratio, angle of repose, and flow rate, all of which indicated satisfactory flow behavior.

The prepared tablets were further evaluated for various quality parameters. All formulations met the required preformulation and post-compression criteria. The hardness of formulations F1 to F6 ranged from 4.5±0.08 to 3.7±0.10 kg/cm². Among these, formulation F6 demonstrated optimal performance, exhibiting a hardness of 3.7±0.10 kg/cm², disintegration time of 24.5±1.04 seconds, friability of 0.44±0.01%, wetting time of 17.1±0.76 seconds, dispersion time of 16.3±0.8 seconds, and drug content of 100±1.2%, thus meeting the requirements for an ideal fast dissolving tablet.

The disintegration time across all formulations ranged from 61.5±0.54 to 24.5±1.04 seconds. It was observed that increasing the concentration of superdisintegrants led to a reduction in both hardness and disintegration time. Formulation F6 showed the most favorable characteristics, with the shortest disintegration time, likely due to the effective action and mechanism of the superdisintegrants used. In vitro drug release studies revealed a release profile ranging from 97.40±2.46% to 99.54±1.12%, with formulation F6 exhibiting the highest drug release.

Conclusion :

This study presents a comprehensive quantitative evaluation of the relationships among AI-enabled business analytics capability, smart manufacturing integration, and supply chain resilience within data-driven manufacturing and supply chain systems. Through a rigorous experimental and statistical methodology, analytics capability is identified as a key organizational resource that significantly influences both manufacturing integration and resilience. Organizations with well-developed analytical capabilities exhibited improved operational integration, characterized by enhanced coordination, synchronization, and alignment of data-driven decision-making across manufacturing activities.

In addition, analytics capability demonstrated a strong positive association with supply chain resilience, indicating that organizations with advanced analytical systems are better prepared to maintain stability and continuity during disruptions. The findings also reveal that smart manufacturing integration serves as an important mediating factor, partially transmitting the impact of analytics capability on resilience outcomes. This emphasizes the need to effectively integrate analytical tools within coordinated operational frameworks to maximize resilience benefits.

The reliability of the results is supported by robust statistical validation, including assessments of reliability, validity, and collinearity, which strengthen the credibility of the study. The behavior of control variables aligns with existing literature, further confirming the consistency of the findings. Overall, the study provides valuable empirical insight into how analytics capability and manufacturing integration collectively influence resilience, offering an integrated framework that explains resilience as a system-level outcome driven by both analytical proficiency and operational alignment.

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