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FORMULATION AND EVALUATION OF PARACETAMOL TABLETS BY WET GRANULATION METHOD

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ABSTRACT

The objective of this research work was to formulate and comprehensively evaluate paracetamol (acetaminophen) tablets utilizing the wet granulation methodology with varying binder concentrations. Tablets represent the most widely prescribed solid oral dosage form owing to their dosing accuracy, physical stability, and ease of manufacturing. In this study, starch paste was explored as a binder at three differing concentrations (1% w/w, 2% w/w, and 3% w/w for formulations F1, F2, and F3 respectively). Pure drug blend and granules were characterized via standard Preformulation assays including bulk/tapped density, Carr's index, Hausner ratio, and angle of repose. Post-compression metrics evaluated included weight variation, thickness, diameter, mechanical hardness, friability, disintegration profile, and *in-vitro* dissolution patterns. Results indicated that increasing binder concentrations significantly enhanced tablet hardness and restricted friability while concomitantly prolonging disintegration times. Formulation F1 (1% w/w starch paste) achieved a near-complete immediate-release profile with 99.9% dissolution efficacy within 90 minutes meeting all official compendial requirements.

Keywords: Paracetamol, Preformulation, Wet granulation, Disintegration and Dissolution

1.INTRODUCTION

Oral solid dosage forms, particularly compressed tablets, comprise the largest segment of multi-source pharmaceutical configurations globally due to manufacturing throughput advantages, chemical stability, packaging efficiency, and precise patient dosing adherence [1, 2, 5]. Modern multi-component tablet matrices consist of targeted active pharmaceutical ingredients (APIs) alongside selected inert functional excipients including binders, diluents, and lubricants [3]. Paracetamol (Acetaminophen; N-(4-hydroxyphenyl) acetamide) serves as a gold-standard therapeutic agent displaying distinct analgesic and antipyretic pharmacodynamics, widely indicated for mild-to-moderate physical pain control and core body temperature management [4]. Due to its universal clinical administration, developing reliable, economically scalable manufacturing pathways that assure batch-to-batch biological performance is a continuous mandate.

Among prevailing industrial tablet unit operations, wet granulation remains a primary manufacturing technique for high-dose drugs like paracetamol. This process converts fine powder components into multi-particulate granular aggregates, significantly improving material bulk flow kinetics, enhancing operational punch compressibility, and preventing component segregation to guarantee systematic dose uniformity [6]. Successful product performance hinges on extensive Preformulation evaluations (e.g., density metrics, angle of repose) [7] and structural post-compression parameters (e.g., friability, weight consistency, disintegration rates, and dissolution profiles) [8]. This study systematically optimizes starch paste binder variants to meet stringent Indian Pharmacopoeia (IP) standards [9, 12].

DRUG PROFILE

The primary physical, chemical, and biological clearance constraints governing the model drug entity are detailed in table 1.

2. AIM & OBJECTIVES

The aim of this work is to formulate and evaluate the Paracetamol tablet by using wet granulation method. To Study the

Preformulation of Paracetamol tablet. To Formulate the Paracetamol tablet by using wet granulation technique. To Evaluate the Paracetamol tablets.

3. COMPOSITION & PROCEDURE FOR THE FORMULATION OF THE TABLET

The formulation matrix utilizes microcrystalline cellulose (MCC) as a compressible filler and binder, lactose as a hydrophilic diluent, and maize starch as an internal disintegrant and binder paste. Purified talc and magnesium stearate were used to control lubrication and glidant performance during ejection cycles.

Steps involved in the formulation of Tablets

The wet granulated blends were manufactured through a multi-stage operational pathway

Dry Sifting: Paracetamol API, microcrystalline cellulose, and lactose were passed through a #40 mesh screen to eliminate aggregates.

Liquid Wetting Phase: Prepared starch paste solution (1%, 2%, 3% w/w variations) was added to the dry powder blend to form a cohesive damp mass.

Wet Sieve Reduction: The damp mass was immediately pushed through a #12 sieve screen to form wet aggregates.

Thermal Desiccation Phase: Aggregates were transferred to a hot air oven controlled at 60°C to achieve moisture equilibrium.

Granular Calibration Sifting: Dried structures were calibrated through a #16 sieve, using a #44 sieve line to limit fines.

Lubrication & Tooling Compression: Dried granules were blended with magnesium stearate and talc in a tumbling mixer for 5 minutes. The lubricated mass was then compressed on a single-punch tableting press using 9 mm round punches to target a nominal tablet weight of 250 mg.

4.PREFORMULATION.

Micromeritic Characterization

Prior to compression, raw paracetamol powder and the intermediate granulated matrices were analyzed across defined mathematical characterization models to assess bulk quality parameters:

$$\text{Bulk Density (Bd)} = \text{Mass (M)} / \text{Bulk Volume } (V_0)$$

$$\text{Tapped Density (Dt)} = \text{Mass (M)} / \text{Tapped Volume } (V_t)$$

$$\text{Carr's Index (\%)} = [(Dt\ \ Bd) / Dt] \times 100$$

$$\text{Hausner Ratio} = \text{Tapped Density (Dt)} / \text{Bulk Density (Bd)}$$

$$\text{Angle of Repose } (\theta) = \tan^{-1}(h / r)$$

5. POST-COMPRESSION

Manufacturing Quality Control Test

Weight Variation test

Mass uniformity was assessed by weighing twenty individual tablet units selected at random from each formulation batch. In compliance with pharmacopoeial specifications, the maximum allowable percentage deviation for tablets weighing between 130 mg and 324 mg is established at ±7.5%.

The weight variation test was performed on twenty tablets from each formulation. The average tablet weights were 254.00 ± 5.88 mg (F1), 256.60 ± 4.84 mg (F2), and 256.85 ± 4.58 mg (F3) (mean ± SD, n = 20). All tablets complied with the IP/USP weight variation requirements, as none exceeded the permissible deviation of ±5% from the average weight. These findings indicate satisfactory weight uniformity and consistency of the compression process

Physical Evaluation of Tablet Formulations (Thickness, Diameter, and Hardness)

Thickness parameters were recorded using digital calipers across 10 sample units. Tablet hardness was evaluated using a Monsanto tester, and friability were calculated by using Roche model friabilator.

The physical properties of the compressed tablets were evaluated by measuring thickness, diameter, and hardness. The average thickness of formulations F1, F2, and F3 was **3.988 ± 0.004 mm**, **3.990 ± 0.006 mm**, and **3.989 ± 0.003 mm**, respectively. The tablet diameter remained nearly constant at approximately **9.01 mm** for all formulations, indicating uniform die filling and consistent compression.

Table 1: Drug Profile of Pure Paracetamol API

Official IUPAC Identity	N-(4-hydroxyphenyl) acetamide
Empirical Formula	$C_8H_9NO_2$
Molecular Weight Balance	151.165 g/mol
Melting Point Range	168°C to 172°C
Organoleptic Identification	White crystalline powder, completely odorless, displaying a characteristic bitter taste profile
Solubility Constants	Soluble in water at elevated temperatures, readily soluble in organic media
Systemic Vol. of Distribution	0.95 L/kg (with uniform tissue partition indices)
Plasma Protein Binding Split	10% to 25% under normal clinical limits
Primary Hepatic Clearance	First-order metabolism driven by Phase II glucuronidation and sulfation pathways
Elimination Half-Life ($t_{1/2}$)	Approximately 2.5 Hours
Excretion Clearance Pathway	Renal pathways via urine elimination

Table 2: Master Formula Composition per Target Tablet Unit (250 mg)

S. No.	EXCIPIENT / INGREDIENT COMPONENT	F1	F2	F3
1	Paracetamol	125.0 mg	125.0 mg	125.0 mg
2	Microcrystalline Cellulose (MCC)	45.0 mg	51.0 mg	60.0 mg
3	Maize Starch Paste (w/ w)	1.0 %	2.0 %	3.0 %
4	Magnesium Stearate	2.5 mg	2.5 mg	2.5 mg
5	Purified Talc Screened	2.5 mg	2.5 mg	2.5 mg
6	Lactose Monohydrate	75.0 mg	69.0 mg	60.0 mg
	Total	**250.0 mg**	**250.0 mg**	**250.0 mg**

Table 3: Comparative Physical Powder Flow & Micromeritic Matrix

S. No.	PHYSICAL FLOW CHARACTERIZATION ASSAY TEST	PURE RAW PARACETAMOL API	OPTIMIZED PROCESSED GRANULES
1	Bulk Density Limit (*Bd*)	0.452 g/mL	0.556 g/mL
2	Tapped Density Limit (*Dt*)	0.565 g/mL	0.657 g/mL
3	Angle of Repose Measurement (θ)	34.05° (Poor Flow Regimes)	27.02° (Excellent Flow Trajectories)
4	Hausner Cohesiveness Coeff. (*HR*)	1.28	1.18
5	Carr's Compressibility Percentage (*CI %*)	18.98 %	12.12 %

Table 4: Particle Size Sieve Analysis Profile (% Retention Distribution Splitting)

MESH IDENTIFICATION	INTERNAL NOMINAL APERTURE SIZE	PURE PARACETAMOL DISTRIBUTION	INTERMEDIATE PROCESSED GRANULES
Sieve #20	0.850 mm	0.00 %	8.00 %
Sieve #30	0.600 mm	17.84 %	18.05 %
Sieve #40	0.425 mm	5.20 %	32.65 %
Sieve #60	0.250 mm	17.67 %	25.43 %
Sieve #80	0.180 mm	23.08 %	12.23 %
Sieve #100	0.150 mm	25.68 %	2.00 %
Pan Bottom	Fines Pass-through limit	10.03 %	1.50 %

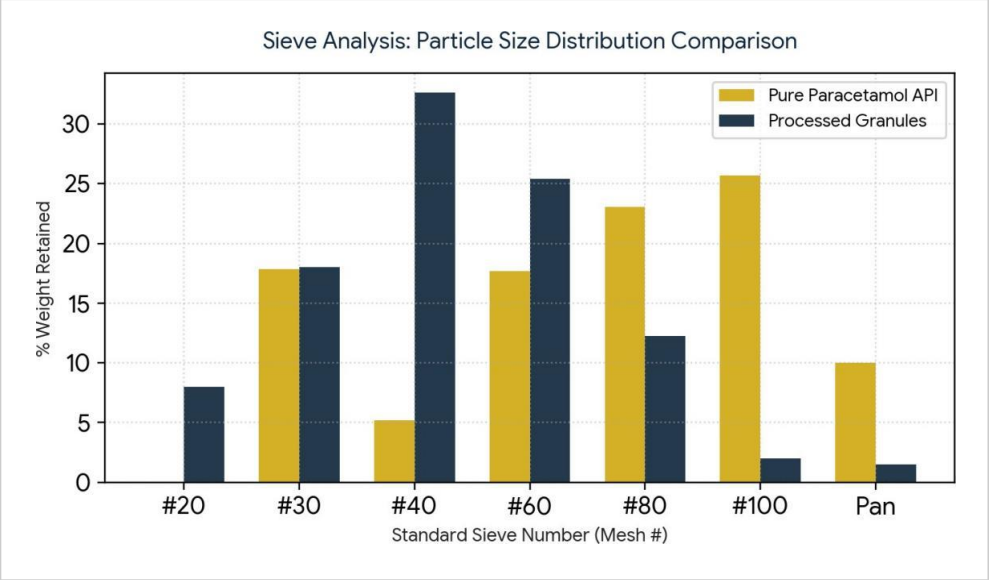

Figure 1: Laser-calibrated sieve size retention histogram displaying the structural conversion of fines into uniform, intermediate flow- stable granules.

Table 5: Weight Uniformity Test

S. No.	F1	F2	F3	S. No.	F1	F2	F3
1	255 mg	251 mg	254 mg	11	244 mg	256 mg	256 mg
2	250 mg	254 mg	253 mg	12	249 mg	257 mg	252 mg
3	251 mg	263 mg	268 mg	13	262 mg	252 mg	252 mg
4	253 mg	251 mg	255 mg	14	252 mg	255 mg	258 mg
5	264 mg	264 mg	260 mg	15	259 mg	256 mg	251 mg
6	253 mg	262 mg	256 mg	16	251 mg	266 mg	262 mg
7	251 mg	255 mg	266 mg	17	252 mg	260 mg	256 mg
8	255 mg	258 mg	255 mg	18	250 mg	255 mg	259 mg
9	266 mg	257 mg	252 mg	19	262 mg	248 mg	254 mg
10	249 mg	253 mg	258 mg	20	251 mg	263 mg	253 mg

Table 6: Result of Weight Uniformity Test

Parameter	F1	F2	F3
Number of tablets tested	20	20	20
Average weight (mg)	254.00 ± 5.88	256.60 ± 4.84	256.85 ± 4.58
%RSD	2.31	1.89	1.78
IP/USP Limit	±5%	±5%	±5%
Result	Pass	Pass	Pass

Table 7: Thickness, Diameter, and Hardness

F1			F2			F3		
THICK (MM)	DIA (MM)	HARDNESS (N)	THICK (MM)	DIA (MM)	HARDNESS (N)	THICK (MM)	DIA (MM)	HARDNESS (N)
3.99	9.01	8.0	3.99	9.01	10.0	3.99	9.01	14.0
3.99	9.01	8.0	3.99	9.01	11.0	3.99	9.01	15.0
3.98	9.00	8.5	3.99	9.01	10.0	3.99	9.01	14.0
3.99	9.01	8.0	4.00	9.00	10.0	3.99	9.01	15.0
3.99	9.01	8.0	3.99	9.01	12.0	3.99	9.01	14.0
3.99	9.01	8.0	3.98	9.01	10.0	3.99	9.01	14.0
3.98	9.00	8.5	3.99	9.01	10.0	3.98	9.00	14.0
3.99	9.01	8.0	3.99	9.01	10.0	3.99	9.01	14.0
3.99	9.01	8.0	3.99	9.01	15.0	3.99	9.01	14.0
3.99	9.01	8.0	3.99	9.01	10.0	3.99	9.01	16.0

Table 8: Mean for Thickness, Diameter, and Hardness

Parameter	F1	F2	F3
Thickness (mm)	**3.988 ± 0.004**	**3.990 ± 0.006**	**3.989 ± 0.003**
Diameter (mm)	**9.008 ± 0.004**	**9.009 ± 0.003**	**9.009 ± 0.003**
Hardness (N)	**8.10 ± 0.21**	**10.80 ± 1.62**	**14.40 ± 0.84**

The hardness values increased from **8.10 ± 0.21 N** for F1 to **10.80 ± 1.62 N** for F2 and **14.40 ± 0.84 N** for F3. This progressive increase in hardness suggests improved mechanical strength of the tablets, which may be attributed to the formulation composition and compression characteristics. Despite the increase in hardness, the tablets maintained uniform dimensions, indicating a reproducible manufacturing process.Overall, all formulations exhibited acceptable physical characteristics with consistent thickness, diameter, and hardness

suitable for further evaluation.

Friability test

Table 9: Friability test

Formulation	**% Friability**	**COMPENDIAL QUALITY ACCEPTANCE LEVEL**
F1	0.78 % Loss	PASSED (Conforms to < 1.00% Limit)
F2	0.54 % Loss	PASSED (Conforms to < 1.00% Limit)
F3	0.43 % Loss	PASSED (Conforms to < 1.00% Limit)

The friability test was performed to evaluate the mechanical strength of the formulated tablets. According to pharmacopeial specifications, tablet weight loss after friability testing should not exceed 1.0%. The percentage friability of formulations F1, F2, and F3 was found to be 0.78%, 0.54%, and 0.43%, respectively. All formulations complied with the official limit, indicating adequate resistance to abrasion and mechanical stress during handling, packaging, transportation, and storage. Among the three formulations, F3 exhibited the lowest friability (0.43%), suggesting superior mechanical strength, followed by F2 (0.54%) and F1 (0.78%). The decrease in friability from F1 to F3 may be attributed to improved tablet integrity resulting from the formulation composition. All formulations successfully passed the friability test, with F3 showing the best mechanical strength due to its lowest percentage weight loss.

Disintegration Test

Disintegration trials were conducted in an IP-standard basket-rack assembly filled with simulated gastric fluid (0.1 N HCl, pH 1.2) maintained at 37 ± 0.5°C.

Table 10: Disintegration test (Minutes)

TABLET NO	**F1**	**F2**	**F3**
Tablet Unit #1	2.00 Minutes	3.70 Minutes	10.00 Minutes
Tablet Unit #2	2.10 Minutes	3.10 Minutes	9.00 Minutes
Tablet Unit #3	2.50 Minutes	3.00 Minutes	10.00 Minutes
Tablet Unit #4	2.00 Minutes	3.60 Minutes	9.80 Minutes
Tablet Unit #5	2.00 Minutes	3.30 Minutes	9.00 Minutes
Tablet Unit #6	2.10 Minutes	3.60 Minutes	9.00 Minutes
Mean Disintegration time	2.12 Minutes	3.38 Minutes	9.30 Minutes

The disintegration time of the tablet formulations was evaluated using six tablets from each batch. The mean disintegration times were 2.12 ± 0.20 min, 3.38 ± 0.30 min, and 9.30 ± 0.52 min for formulations F1, F2, and F3, respectively. An increase in disintegration time was observed from F1 to F3, which may be attributed to the increase in tablet hardness and formulation composition. Nevertheless, all formulations disintegrated within the pharmacopeial limit for conventional uncoated tablets, indicating satisfactory disintegration behavior suitable for further dissolution studies.

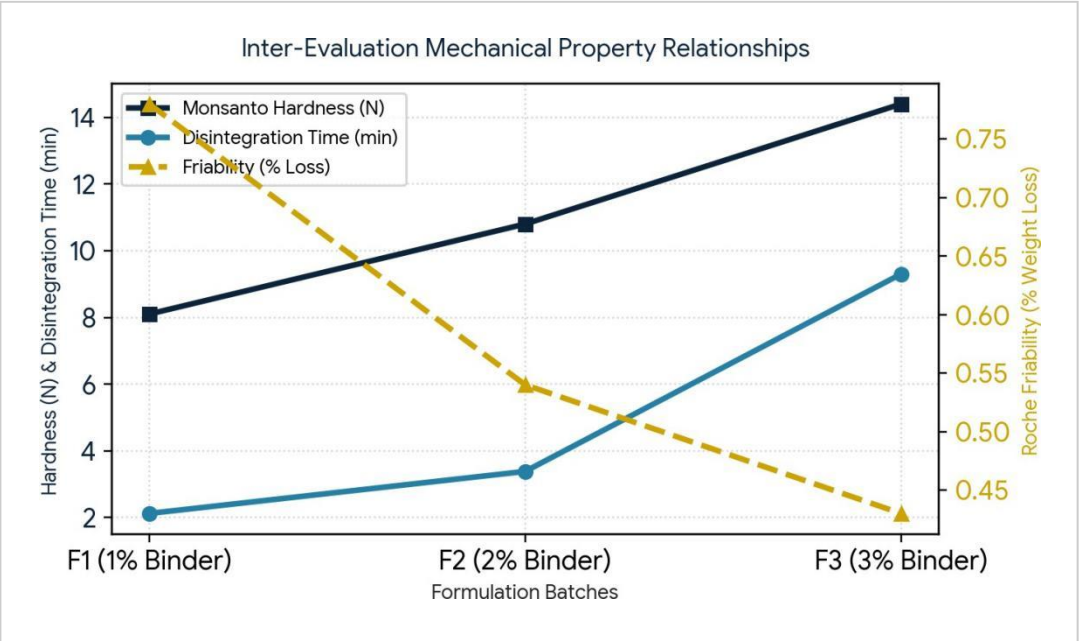

Figure 2: Multivariable physical evaluation diagram showing the trade-off between mechanical hardness, reduced friability, and disintegration delays.

In-Vitro Dissolution test

Dissolution profiles were established using a USP Apparatus II (paddle configuration) operated at 50 rpm in 900 mL of phosphate buffer solution (pH 5.8) maintained at 37 ± 0.5°C.

Table 11: In-Vitro Drug Release Test

Time in mins	F1	F2	F3
0 Minutes	0.0 %	0.0 %	0.0 %
5 Minutes	6.0 %	4.0 %	5.5 %
10 Minutes	10.0 %	12.0 %	14.0 %
15 Minutes	24.0 %	22.0 %	19.8 %
30 Minutes	45.0 %	31.8 %	29.7 %
45 Minutes	67.0 %	43.9 %	35.6 %
60 Minutes	79.2 %	54.3 %	45.9 %
75 Minutes	89.6 %	65.9 %	59.8 %
90 Minutes	96.9 %	78.3 %	67.4 %
120 Minutes	--	90.6 %	78.9 %

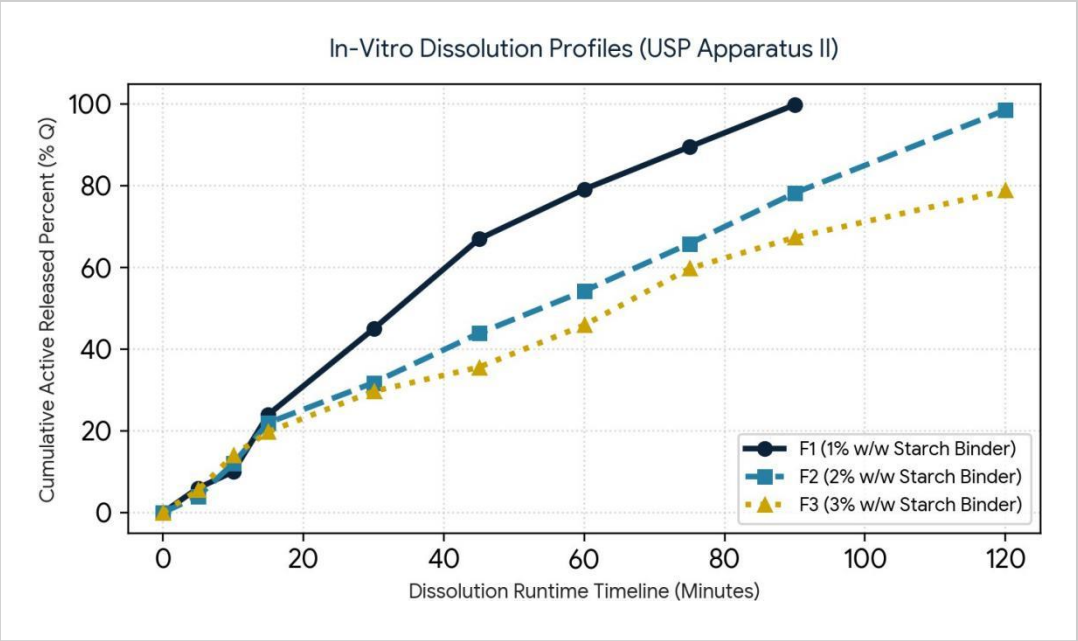

Figure 3: Comparative multi-batch in-vitro dissolution profile highlighting immediate active release behavior from the F1 formulation matrix.

6. SUMMARY

Analyzing the Preformulation metrics confirms that raw paracetamol API has poor powder flow properties, as indicated by a Carr's index of 18.98% and an angle of repose of 34.05°. Transforming this material into structured multi-particulate granules improved flow behavior, lowering the angle of repose to 27.02° and the Carr's index to 12.12%. This shift indicates an optimal flow regime for uniform die filling on high-speed tableting equipment. This improvement is confirmed by the analytical sieve partition data (Figure 1), which illustrates a significant reduction in fine particles. This reduction minimizes air entrapment and decreases the risk of tablet defects like capping or lamination.

Post-compression evaluation results demonstrate consistent quality parameters. The individual weight variation logs show tight standard errors well within compendial boundaries. Mechanical testing indicates that increasing the concentration of the starch paste binder expands the solid polymer bridge network within the matrix. This structural reinforcement increased crushing hardness from 8.1 N in the F1 batch to 14.4 N in the F3 batch. This enhanced matrix structure helped lower Roche friability weight loss to 0.43% for F3, demonstrating strong physical durability against handling stress.

However, as illustrated in the multivariable performance summary (Figure 2), this increased mechanical density reduces structural porosity, which delays liquid infiltration into the tablet core. As a result, the mean disintegration timeline increased from 2.12 minutes for F1 to 9.30 minutes for F3. This disintegration lag directly influences the dissolution profile curves shown in Figure 3. Formulation F1 achieved rapid and complete drug release (99.9% active release) within 90 minutes. In contrast, batches F2 and F3 showed delayed release rates, yielding only 78.3% and 67.4% release at the same milestone. These findings show that the F1 configuration provides an optimal balance between physical durability and immediate drug release performance.

7. CONCLUSION

Paracetamol tablets were successfully formulated using the wet granulation method. Binder concentration significantly influenced tablet hardness, disintegration, and drug release rates. The lower binder concentration batch (F1) achieved immediate disintegration and the highest complete drug release profile, proving to be the most optimal configuration for immediate-release solid dosage forms.

CONFLICT OF INTEREST STATEMENT

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

ETHICAL STATEMENT

This article is a review and does not contain any studies with human participants or animals performed by the authors. Therefore, ethical approval and informed consent were not required.

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