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Quality By Design (Qbd) Based Manufacturing Process Optimization For Robust Manufacturing Of Ibuprofen Tablets

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ABSTRACT

The pharmaceutical industry continues to face challenges in the seamless manufacturing of ibuprofen tablets, despite decades of commercial production. Key issues include the drug's inherent properties—such as its low melting point (70°C), which causes sticking during compression—as well as solubility and in vitro release challenges due to its BCS Class II classification. Additionally, modifying API properties and approved formulations involves significant regulatory and cost constraints under SUPAC Level 2 changes. While Quality by Design (QbD) approaches have primarily focused on Critical Material Attributes (CMAs) and formulation-based Design of Experiments (DOE), understanding the impact of process variability on Critical Process Parameters (CPPs) remains crucial for ensuring consistent product quality.

The integration of Artificial Intelligence and Machine Learning (AIML) in Pharma 4.0 offers transformative potential by enabling predictive analytics, real-time monitoring, and automated decision-making for CPP optimization. Key benefits include precise process control, predictive deviation management, and continuous improvement through data-driven insights. A structured approach involving statistical analysis, machine learning, and process rationalization is essential to minimize variability and align with quality attributes. By leveraging AIML, pharmaceutical manufacturers can enhance efficiency, reduce downtime, and ensure consistent production of high-quality ibuprofen tablets, paving the way for advanced, data-driven pharmaceutical manufacturing**.**

Objective: Identify the optimal Critical Process Parameters (CPPs) for the manufacture of ibuprofen tablets (600mg).

Determine the point of control within the specification and control limits to ensure process capability and reliability.

Methods: PubMed and Embase databases have been searched, and related studies are compiled and summarized.

Results: A designed experiment evaluated critical process parameters (CPPs)—granulation time (3–12 min), drying temperature (45–60°C), compaction force (6–18 kN), and compression speed (10–25 RPM) on tablet quality. Physical, disintegration, and dissolution tests were conducted. Statistical analysis (Jupiter Notebook) revealed correlations between CPPs and critical quality attributes (CQAs), particularly disintegration time (DT) and dissolution %.

Conclusion: This study established key correlations between critical process parameters (CPPs) and quality attributes: compression speed/force and granulation/drying times significantly affect disintegration time (DT), while DT shows an inverse relationship with dissolution%. Regression analysis revealed limitations in predictive modeling, emphasizing the need for comprehensive CPP evaluation combined with physical testing. The identified CPP control ranges (9 min granulation, 50°C drying, 14 kN compaction, 16 RPM speed) enable targeted optimization of DT and dissolution%, ensuring therapeutic efficacy. These findings provide a science-based framework for quality-by-design in tablet manufacturing, though continued validation through physical testing remains essential for robust quality assurance.

Keywords: *Ibuprofen, Critical Process Parameters (CPPs), Pharma 4.0, Artificial Intelligence (AI), Machine Learning (ML), Process Variability, Quality by Design (QbD), Predictive Analytics.*

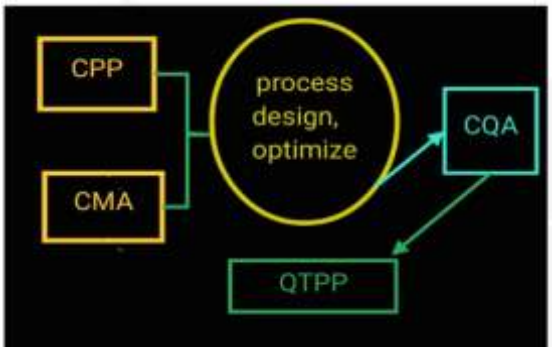
1. INTRODUCTION

Understanding QBD concept: Product quality in pharmaceutical manufacturing is fundamentally governed by critical material attributes (CMAs) and critical process parameters (CPPs), which directly influence critical quality attributes (CQAs). Systematic control and monitoring of these factors enables reduction in process variability, leading to enhanced product quality, mitigated risks, and improved production efficiency. A comprehensive risk management framework facilitates this process through identification, evaluation, and control of potential risks categorized by their severity and impact.

The pharmaceutical industry benefits significantly from combining design space methodologies with robust quality management systems. This integration supports adaptive regulatory compliance while fostering ongoing process enhancements that deliver mutual advantages for both healthcare providers and manufacturers. Our research employs Quality by Design (QbD) principles to formulate a rapidly dispersible tablet, aiming to improve both therapeutic outcomes and manufacturing consistency.

For our model BCS Class II drug candidate, we first established a detailed quality target product profile (QTPP), followed by thorough risk assessment to pinpoint essential CQAs. Preliminary investigations included comprehensive physicochemical analysis and compatibility testing with standard pharmaceutical excipients. The experimental design specifically targeted CMAs and CPPs, with subsequent design space development ensuring all potential failure modes maintained acceptable risk thresholds after control strategy implementation.

This approach enables real-time quality assurance through in-process monitoring and control. The study demonstrates how QbD methodology, when integrated with systematic risk assessment and quality management practices, effectively incorporates quality throughout the manufacturing process from development to production.



Preamble: Foundations of Process Robustness in Pharmaceutical Manufacturing

The pharmaceutical industry increasingly emphasizes deepening process understanding, driven by manufacturers' strong motivation to cultivate resilient processes. Well-understood and robust processes offer a heightened sense of predictability regarding yields, cycle times, and waste levels. Moreover, they enable manufacturers to maintain lower inventories of final products, assuming the manufacturing process's reliability.

Regulatory frameworks, particularly ICH Q8 guidelines, highlight the importance of evaluating process robustness as part of comprehensive risk management strategies. Developing robust manufacturing systems delivers significant advantages: patients gain access to consistently effective medications, regulatory bodies benefit from more predictable quality assurance, and companies achieve sustainable production efficiencies.

However, true process robustness requires more than just compliance with end-product specifications. It must be intentionally designed into products from their earliest development phases, with ongoing performance monitoring during technology transfer, commercialization, and full-scale production. This lifecycle approach allows for timely process adjustments to maintain consistent quality standards.

Process robustness refers to a process's ability to maintain acceptable quality and performance despite input variations. It's influenced by both formulation and process design and encompasses factors such as raw material composition and manufacturing parameters.

Before understanding Process Robustness, we must first understand the definitions of a few common words in this topic. Glossary definitions clarify key terms, aiding in effectively implementing robustness strategies.

Robustness: The ability of a system, process, or product to maintain stable and consistent performance despite variations or uncertainties in external conditions, input parameters, or operating environments.

Design Space: The design space refers to the defined spectrum of process parameters that have been validated to ensure quality. Design space denotes the multidimensional combination and the interaction of variables that are input (e.g., material characteristics and process parameters) that have been demonstrated to ensure quality.

Manufacturing Science:

Manufacturing Science is an interdisciplinary field focused on the study, analysis, and application of principles and methods involved in the design, development, optimization, and control of manufacturing processes and systems. It combines knowledge from multiple disciplines, including materials science, mechanical engineering, electrical engineering, chemical engineering, and computer science, to enhance and innovate manufacturing techniques and technologies.

2. THE NORMAL OPERATING RANGE

Normal Operating Range (NOR) refers to the range of values within which a process or system functions under standard conditions while meeting performance, quality, and safety requirements. It defines the acceptable variation in key parameters that ensure consistent and reliable operation. Deviations from the NOR may signal potential issues, requiring corrective action to maintain process stability and product integrity. Monitoring and controlling the NOR is essential for optimizing manufacturing efficiency and minimizing variability.

Process Analytical Technologies (PAT)

Process Analytical Technologies (PAT) refers to a system of tools, strategies, and methodologies used in the manufacturing industry to monitor and control manufacturing processes in real-time. PAT uses analytical techniques, sensors, and data analysis tools to understand and optimize a production process's critical parameters and attributes.

Proven Acceptable Range (PAR)

A characterized range at which a process parameter may be operated. The PAR represents the boundaries within which parameter variations or attributes are considered acceptable without compromising product quality or safety.

Critical Process Parameter (CPP)

A Critical Process Parameter is a process input that directly and significantly influences a Critical Quality Attribute when varied beyond a limited range.

Critical Quality Attribute (CQA)

A Critical Quality Attribute (CQA) is a measurable physical, chemical, biological, or microbiological property or characteristic of a product that ensures its safety, efficacy, and quality. These attributes are critical because they directly affect the product's performance, efficacy, or safety and must be controlled within predefined limits to ensure the product meets its intended quality standards. CQAs are identified and defined during the development and manufacturing process of pharmaceuticals, biologics, medical devices, and other regulated products to ensure consistency and compliance with regulatory requirements.

Quality:

Quality can be defined as the degree to which a product or service meets or exceeds customer expectations and requirements or the degree to which a set of inherent properties of a product, system, or process fulfills requirements. It encompasses various attributes such as reliability, durability, performance, safety, and consistency. Quality is not just about the absence of defects but also about meeting customer needs and delivering value. It involves continuous improvement efforts to enhance processes and outcomes to achieve higher levels of satisfaction and excellence.

Quality System:

A formalized system that documents the structure, responsibilities, and procedures required for effective quality management.

Requirements: Needs or expectations that are stated, generally implied, or obligatory by the patients or their surrogates (e.g., health care professionals, regulators, and legislators).

Repeatability

Repeatability refers to obtaining consistent and similar results when the same experiment or process is repeated multiple times by the same operator, using the same equipment and procedures, under the same conditions. It measures the precision and consistency of measurements or outcomes within a single set of conditions or parameters.

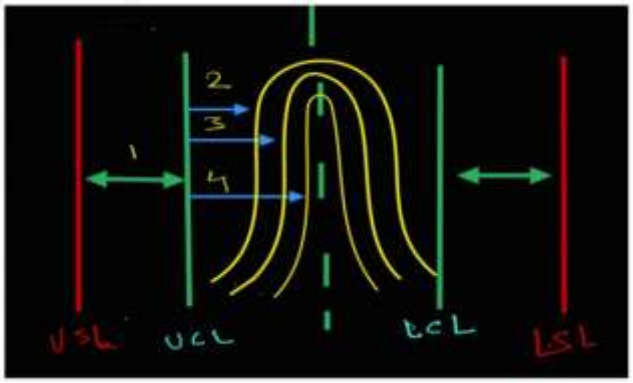
Reproducibility

Reproducibility refers to the ability to achieve consistent and similar results when an experiment or process is repeated under similar conditions by different operators or in different settings. It indicates the reliability and consistency of experimental

or observational findings.

3. DEVELOPING A ROBUST PROCESS- 8 STEPS PROCESS

Adopting a systematic, team-based approach to development enhances process comprehension and ensures the creation of a robust process. Despite the absence of explicit guidance on robust process development, this section aims to outline a systematic method and identify which parameters qualify as CPPs.



- Define control limit and get all attributes within the control limit.
- Further set operating ranges stringent to narrows process spread.
- Continue stage 2 to get more control on operating parameters.
- Set point of control with which operating parameters will reproduce the results and common variations will not impact on process consistency and performance.

Steps for Developing a Robust Process:

Step 1. Team Formation: To establish a comprehensive process, assemble a team of technical specialists from research and development, technology transfer, manufacturing, statistical sciences, and relevant fields. At the initial stage, preferably prior to optimization and scaling.

Led by experts with extensive understanding of the product, production techniques, analytical methodologies, and statistical tools, promotes collaboration and assures early consensus on technical decisions.

Step 2. Process Definition: A standard process consists of multiple unit operations. Prior to advancing with the development of a comprehensive process, delineate the process parameters and attributes. Create process flow diagrams or flowcharts that offer adequate detail to comprehend the principal function of each stage.

Identify prospective product attributes and reach consensus on Critical Quality Attributes (CQAs). Including assay, dissolution, degradation, uniformity absence of microbial proliferation, and appearance. Establishing process parameters necessitates the evaluation of factors including materials, processes, machinery, personnel, measurement, and environment. Tools like as Fishbone or Ishikawa diagrams can assist in documenting these criteria. Documenting results is a crucial component of this process, and thorough records must capture all developmental findings.

Step 3: Prioritizing Experiments: Developing a robust process requires an extensive understanding of the process and its parameters.

However, examining every conceivable correlation between process parameters and qualities isn't practical nor essential. The team should utilize a structured analytical approach, such as a prioritizing matrix, to identify and rank process parameters and attributes for future examination. In contrast to more statistically-oriented methods, a prioritization matrix primarily depends on the process expertise and technical proficiency of the participating team members, although data from structured experiments may also be used.

Step 4: Analyze Measurement Capability: All measurements are subject to variability. Therefore, the process analysis cannot be meaningful unless the measuring instrument used to collect data is both repeatable and reproducible, accurate precise. MSA measurement system Analysis should be performed to assess the measurement system's capability for both parameters and attributes.

Step 5: Identify Functional Relationship between Parameters and Attributes: The next step is to identify the functional relationships between parameters and attributes and to gather information on potential sources of variability.

Including computational approaches, simulations (small-scale unit ops), or experimental approaches. Where experimental approaches are needed, one-factor-at-a-time experiments can be used but are least preferred. Design of Experiments (DOE)

is the recommended approach because of its ability to find and quantify the interaction effects of different parameters.

Step 6: Assessing Measurement Capability: Understanding the variability inherent in measurements is crucial. Hence, analyzing a process requires reliable data collection instruments that are both repeatable and reproducible. Conducting a Gage Repeatability and Reproducibility (R&R) study or similar analysis is essential to evaluate the measurement system's capability for parameters and attributes. Measurement tools and techniques must exhibit suitable precision across the range of interest for each parameter and attribute.

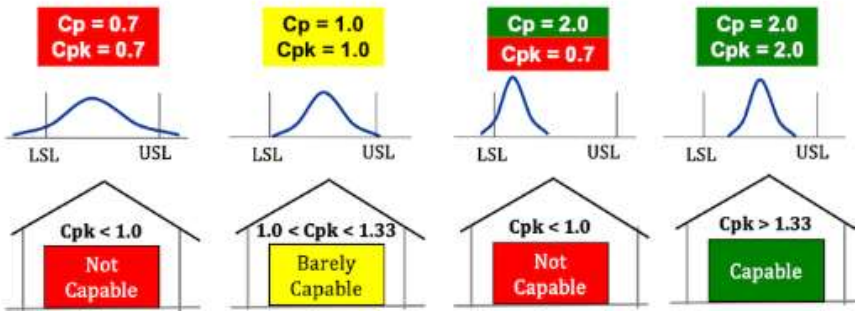
Step 7: Establishing Functional Relationships between Parameters and Attributes: The subsequent step entails identifying the functional interactions between parameters and attributes while identifying potential sources of variability. These correlations can be identified using many means, including programming languages, simulations (such as small-scale unit operations), or experimental procedures. While one-factor-at-a-time studies may be employed when required, design of studies (DOE) is favored for its capacity to reveal and measure interaction effects among several parameters. Well-designed experiments can improve scientific understanding while reducing resource expenditure due to the following reasons Multiple factors can be manipulated simultaneously.

1. Pre-planning experiments reduce the need for additional trials.
2. Fewer studies are necessary.
3. Each study encompasses a broader scope.

The design of experiments usually involves two steps: first, testing to find the main components, and then using response surface methods to better understand how key factors and features relate to each other. Table C presents a statistical Design of Experiments (DOE) illustration for the analysis of a direct compression tablet.

Step 8: Validating Critical Quality Attributes (CQAs) and Critical Process Parameters (CPPs): Once achieving sufficient process understanding, it becomes possible to validate the previously established Critical Quality Attributes (CQAs) from step 2. In the case study of direct compression tablets, essential quality parameters encompassed dissolve, assay, tablet uniformity, and stability. Critical Process Parameters (CPPs), characterized as process inputs that directly affect Critical Quality Attributes (CQAs), are generally found through the functional linkages established in Step 5. In the case study of direct compression tablets, tablet press speed and compression pressure were recognized as critical process parameters affecting dissolution. These functional correlations facilitate the application of optimization methodologies to determine optimal process set points or operational ranges for press speed and compaction pressure.

4. KEY INDICATORS OF PHARMACEUTICAL PROCESS ROBUSTNESS



Process Capability Indices (Cpk, Cp):

CP = process capability CPK = Process Performance.

CPK value is always equal or less than CP value.

Cpk > 1 means process confirms the specification.

Cpk < 1 means process does not confirm the specification.

Cpk = 1 means process just conforms the specification.

Cp = CPK means process is centered

Control Chart Analysis: Observe critical quality attributes (CQAs) and critical process parameters (CPPs) over time to detect trends, shifts, or atypical variations that may indicate a deficiency in robustness.

Consistency of Critical Quality Attributes (CQAs): ensure that CQAs, including potency, purity, dissolution rate, and stability, are uniform throughout various batches and manufacturing cycles.

Reproducibility and Repeatability: Analyze the capacity to generate identical outcomes under uniform conditions and to consistently repeat the procedure across several cycles or batches.

Process Yield and Efficiency: Evaluate the uniformity of yield and overall efficiency. Significant variances may suggest concern regarding robustness.

Deviation and Non-Conformance Rate: Monitor the incidence and severity of deviations and non-conformances. A diminished rate typically signifies a more resilient process.

Change Control Impact: Evaluate the influence of process modifications (e.g., alterations in raw materials and equipment upgrades) on product quality and performance.

Factors Influencing the Compaction and tablet quality attributes.

Material Properties:

1. Crystal habit
2. Particle size and distribution
3. Polymorphism and amorphism
4. Moisture content
5. Salt form

Process Parameters:

1. Tableting speed
2. Dwell time (time under compression)
3. Lag time (time between compression cycles)
4. Mechanism of compaction (e.g., direct compression, granulation)
5. Pre- and main-compression force profile

Lubrication and Excipients:

1. Solid state of lubricants (e.g., powder, liquid)
2. Concentration of lubricants
3. Co-processing of excipients or drugs

Granulation and Vibration:

1. Granulation methods (e.g., wet, dry, fluidized bed)
2. Ultrasonic vibration (to enhance compaction)

These factors interact with each other, making compaction a complex process. Understanding their effects is crucial for achieving consistent product quality, uniformity, and stability.

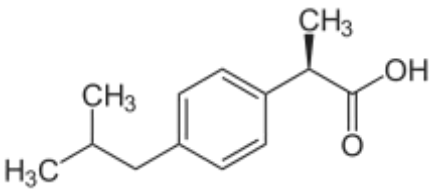
Materials and methods

Materials

Ibuprofen properties:

Drug profile Ibuprofen: IUPAC name: Ibuprofen; 15687-27-1; 2-(4-Isobutylphenyl) propionic acid. Compound CID: 3672

Chemical formula: MF: C13H18O2



Structure of Ibuprofen

Molecular weight: 206.28g/mol

Melting point: 75^0c to 78^0c

The hypothesis that tablet dissolution can be influenced by the physical properties and quantity of ibuprofen was tested in this study. Ibuprofen bought from suppliers was assessed: supplier A. The following parameters identified as significant in this study were selected: Fourier Transform Infrared (FTIR) spectroscopy, particle size distribution (particularly mean particle diameter), and particle shape, and crystal form, melting point.

Factor 1: particle size distribution: Particle size (PS) and particle size distribution: (PSD) are critical parameters in the pharmaceutical industry. The PS and PSD of active pharmaceutical ingredients (APIs) and excipients can significantly influence key properties of the final formulation, including dissolution rate, appearance, and stability.

In this study, the particle size of Ibuprofen A was analyzed using a light scattering technique performed on a Mastersizer 2000 instrument from Malvern. The standard parameter is 85 percentile d (0.15) NLT 30 micron, Median particle size d (4.3)55 to 85 micron, 15 percentile d (0.85) NMT 150 micron and results is 38 micron, 71 micron, 109 micron respectively.

Factor 2: Drug-excipients Compatibility study by FTIR Spectroscopy: To study the compatibility of formulation excipients with Ibuprofen, solid admixtures were prepared by mixing the drug with each formulation excipient separately. The pellet was scanned from 200 to 400-1 in FTIR. the change in the obtained peaks of pure drug, the solid mixtures were characterized using FTIR analysis.

Factor 3: Bulk and tapped density:

Batches	B1	B2	B3	B4
Ingredient (Per tablet)				
Ibuprofen 70 microns (mg)	600	600	600	600
Hypromellose (mg)	12	12	12	12
Croscarmellose Sodium (mg)	13.5	13.5	13.5	13.5
Lactose Monohydrate (mg)	50	50	50	50
Microcrystalline cellulose (PH 101) (mg)	40	40	40	40
Maize starch Pregelatinised (mg)	30	30	30	30
Anhydrous Colloidal Silica (CAB-O-SIL M5P) (mg)	11	11	11	11
Magnesium stearate (mg)	13.5	13.5	13.5	13.5
Purified water	q.s.	q.s.	q.s.	q.s.

- 10 g of Ibuprofen powder was placed in a 100 mL measuring cylinder.
- The initial volume occupied by the powder was recorded as V_o.

- Tapped Volume (V_a and Vb):
  - The cylinder was subjected to 200 taps, and the volume was recorded as V_a.
  - Further tapping (750 taps) was performed, and the volume was recorded as Vb.
  - Since the difference between V_a and Vb was less than 2%, Vb was taken as the final tapped volume.
- **Hausner Ratio (HR):** Hausner Ratio=$\frac{\rho \text{tapped}}{\rho \text{bulk}} \times 100$

Tabletting

Table: Formulation Table of Batches.

In the granulation process, the raw materials (RM) were initially sifted through a 14-mesh sieve (#) to ensure uniform particle size distribution. Specifically, 779.4 g of sifted ibuprofen and 58.5 g of pregelatinized maize starch (also sifted through a 14# sieve) were loaded into a high-shear mixer (HSM). The mixing was conducted at a slow impeller speed, with the duration being a variable parameter set at either 3, 5, or 7 minutes to evaluate its impact on granule formation. This step was critical in achieving a homogeneous blend before further processing, and the varying mixing times were investigated to determine the optimal conditions for granule consistency and quality in the formulation.

Binder preparation: The binder solution was prepared by first measuring 200 mL of purified water per kilogram of formulation and transferring it into a clean stainless steel vessel. The water was heated and maintained within a controlled temperature range of 35–40°C, with 35°C set as the target. Under continuous mechanical stirring, 13.6 grams of hypromellose was slowly added to ensure even dispersion and prevent clumping. The mixture was agitated at a speed between 650 and 800 RPM until a smooth, uniform solution formed, typically requiring around 25 minutes of stirring. Precise measurements were recorded, including the actual amount of purified water used (_____ kg) and the exact mixing duration (_____ minutes), to maintain consistency and reproducibility in the granulation process.

Binder Addition and Kneading Granulation Process: The prepared binder solution from Step 3.3.3 was transferred into the High-Shear Mixer (HSM) containing the pre-mixed powders from Step 3.3.2. The binder was added gradually while mixing at a slow impeller speed (52 ±5 RPM) over 9 to 15 minutes, ensuring even distribution. The temperature of the binder solution was maintained at 35°C (range: 32–38°C) to optimize binding efficiency. The actual binder addition time was recorded as _____ minutes (within 9–15 min).

Following binder addition, the wet mass was granulated by switching the impeller to high speed and operating the chopper intermittently at high speed for 3 minutes or until optimal granule formation was achieved (monitored via amperage load). The kneading time was studied at four different durations to evaluate its impact on granule characteristics. The total granulation time (sum of binder addition and kneading phases) was documented as _____ minutes. This step was critical in achieving a uniformly granulated mass with desired flow and compaction properties.

Drying: Load wet granules into FBE bowl. Set inlet temp: 50–55°C, outlet temp: ≤50°C (product temp ~42°C). Perform intermittent raking if needed. Check LOD (≤1.5% w/w) at exhaust temp 27°C (target: 0.5–1.0%).

Sizing: Mill dried granules through 2.0 mm screen at 700–900 RPM, collect in octagonal blender.

Lubrication Blending: Blend granules for 10 min in octagonal blender. Add sifted magnesium stearate, blend 3 min at 12 RPM. Record actual RPM.

Tablet Compression Specifications: Physical Characteristics:

Shape & Color: Oblong, biconvex, white cores

Dimensions:

Length: 17.00 ± 0.20 mm (16.80–17.20 mm)

Width: 8.50 ± 0.20 mm (8.30–8.70 mm)

Thickness: 6.80 ± 0.50 mm (6.30–7.30 mm

Weight & Uniformity

Weight of 20 tablets: 15.405 g ± 3% (14.942–15.867 g)

Individual tablet weight: 770.25 mg ± 5% (731.74–808.76 mg)

Mechanical Properties

Hardness: 100–140 N (avg. of 20 tablets)

Friability: ≤1.0% w/w

Disintegration Time: ≤15 minutes

Coating Process and Parameter Optimization: The coating suspension was prepared in two stages. First, 8.360 kg of hypromellose was gradually added to 75.000 L of purified water under continuous stirring (400–1500 RPM) for at least 30 minutes. Separately, a dispersion containing 0.623 kg titanium dioxide, 1.247 kg talc, and 1.475 kg propylene glycol was prepared in 25.440 L purified water, with each ingredient added sequentially only after achieving homogeneity (mixing time ≥15 min, 400–1500 RPM). The two solutions were then combined and stirred until uniform, with the final weight verified.

Sr. no	Ingredients	Quantity per Tablet	Category
1.	Coating		
2.	Hypromellose	3.67	Film former
3.	Titanium dioxide (E-171)	0.27	Opacifier
4.	Talc	0.55	Glident
5.	Propylene glycol	0.65	Plasticizer
		778	1 % wait gain

Coating was performed under controlled conditions:

Pan speed: 1–7 RPM

Spray rate: 300–600 g/min

Inlet/outlet temperature: 55–65°C (inlet), ≤42°C (outlet)

Air pressure: 6–8 kg/cm² (total), 1–4 kg/cm² (atomizing)

Continuous spray & stirring: For process optimization, batches were prepared with:

Granulation times: 3min, 6min, 9min, 12 min

Drying temperatures: 45°C, 50°C, 55°C, 60°C

Compaction forces: 6N, 10N, 14N, 18 N

Compression speeds: 10RPM, 15RPM, 20RPM, and 25 RPM

	Specs	B1	B2	B3	B4
Granulation time	--	3 min	6 min	9 min	12 min
PSD	40# -60# :30 % 60#- 80 # 60 # 80# above :10 #	complies	complies	complies	complies
Bulk density	0.5 to 0.6 g/ml	0.55	0.6	0.58	0.54
Tapped density	0.6 to 0.7 g/ml	0.66	0.7	0.68	0.7
Carr's index	good to fair	1.20	1.17	1.17	1.30
Compressibility index	good to fair	16.67	14.29	14.71	22.86
Wt AVG	750 - 780	774	772	778	770
Hardness AVG	90 -140 N	104	100	98	109
DT	NMT 15 min	5	5.5	6	10

Physical parameters observed satisfactory

	Specs	B1	B2	B3	B4
Drying temp	--	45	50	55	60
PSD	40# -60# :30 % 60#- 80 # 60 # 80# above :10 #	complies	complies	complies	complies
Bulk density	0.5 to 0.6 g/ml	0.55	0.58	0.5	0.58
Tapped density	0.6 to 0.7 g/ml	0.69	0.68	0.68	0.68
Carr's index	good to fair	1.25	1.17	1.36	1.17
Compressibility index	good to fair	20.29	14.71	26.47	14.71
Wt AVG	750 - 780	770	774	775	770
Hardness AVG	90 -140 N	100	99	105	100
DT	NMT 15 min	5	5	9	10

Physical parameters observed satisfactory

compaction force RPM KN	Specs	B1	B2	B3	B4
	--	6	10	14	18
PSD	40# -60# :30 % 60#- 80 # 60 # 80# above :10 #	complies	complies	complies	complies
Bulk density	0.5 to 0.6 g/ml	0.6	0.55	0.55	0.6
Tapped density	0.6 to 0.7 g/ml	0.7	0.66	0.69	0.72
Carr's index	good to fair	1.17	1.20	1.25	1.20
Compressibility index	good to fair	14.29	16.67	20.29	16.67
Wt AVG	750 - 780	772	770	774	772
Hardness AVG	90 -140 N	97	105	98	103
DT	NMT 15 min	7	8	12	13
Hardness AVG	90 -140 N	97	105	98	103
DT	NMT 15 min	12	12	13	19

Physical parameters observed satisfactory

compaction force RPM	Specs	B1	B2	B3	B4
	--	10	15	20	25
PSD	40# -60# :30 % 60#- 80 # 60 #	complies	complies	complies	complies

	80# above :10 #				
Bulk density	0.5 to 0.6 g/ml	0.54	0.62	0.52	0.58
Tapped density	0.6 to 0.7 g/ml	0.68	0.7	0.68	0.7
Carr's index	good to fair	1.26	1.13	1.31	1.21
Compressibility index	good to fair	20.59	11.43	23.53	17.14
Wt AVG	750 - 780	772	770	774	772
Hardness AVG	90 -140 N	97	105	98	103
DT	NMT 15 min	7	8	12	13
Hardness AVG	90 -140 N	97	105	98	103
DT	NMT 15 min	7	8	12	13

Evaluation Parameter

Dissolution Parameter:

Medium	900 mL (Phosphate Buffer pH 7.2)
Apparatus	Paddle
RPM	50 rpm.
Temperature	37 ± 0.5 ºC

Dissolution medium (pH 7.2 phosphate buffer dissolution):

Weight 6.805 g of potassium dihydrogen phosphate and 1.388 g of sodium hydroxide. Dissolve and dilute to 750 mL with purified water. Adjust the pH to 7.2 ± 0.05 with sodium hydroxide or phosphoric acid as needed. Dilute up to 1000 mL with purified water.

Higher volumes can be prepared according the described procedure maintaining the proportions described for 1 liter.

Standard solution:

For Ibuprofen 600 mg tablets:

Exactly weigh around 66.66 mg of standard Ibuprofen WS and transfer quantitatively to a 100 ml volumetric flask. Add 50 mL of dissolution medium, sonicate for 15 minutes, temper and bring up to volume with the same dissolution medium.

Evaluation:

Measure the absorbance at the maximum of 266 nm of the test and standard solutions in a, using the dissolution medium as a blank.

Calculations:

$$D = \quad D = \frac{At \times Wst \times R}{Ast \times \overline{C\ N}}$$

D: Quantity of dissolved ibuprofen as a percentage of the nominal quantity.

At: Absorbance of the test solution.

Ast: Absorbance of the standard solution.

Wst: Weight of the Working standard ibuprofen in the reference solution, in mg.

R: Working standard ibuprofen content as %.

CN: Nominal ibuprofen content (600 for Ibuprofen 600 mg film-coated tablets)

Acceptance Criteria: 80 (Q) % in 30 min

Result and Discussions: **Observation table dissolution results**

sample type	sample	DT min	Dissolution %		
			15 min	20min	30 min
core tab	Tablet-1	8	101.9	101.8	102
	Tablet-2	9	102.3	102.8	102.9
	Tablet-3	8	101.3	101.5	101.9
	Tablet-4	8	101.3	101.5	101.6
	Tablet-5	5	101.7	101.8	102.1
	Tablet-6	6	101.8	101.9	102.8
coated tab	Tablet-1	18	99.6	102.1	102.4
	Tablet-2	15	71.3	90.2	102.2
	Tablet-3	16	98.3	102.1	101.7
	Tablet-4	20	68.2	87.1	102.5
	Tablet-5	18	82.7	94.9	99.8
	Tablet-6	17	61.7	80.8	101
		correl	-0.70543	-0.62792	-0.35871

	DT min	Disso %
min	5	101.3
max	9	102.9
min	15	61.7
max	20	102.1
	correl	-0.26956

sample	DT	disso 15 min
coated tab	18	74.1
coated tab	18	71.2
coated tab	18	85.9
coated tab	18	64.7
coated tab	18	86.3
coated tab	18	74.1
coated tab	12	106.3
coated tab	12	101.8
coated tab	12	105.8
coated tab	12	103.7
coated tab	12	104.7

coated tab	12	102.3
	correl	-0.9282818

5. DISSOLUTION TEST CALCULATION

CALCULATION SHEET DISSOLUTION BY UV

Product Name & Srength :		**Ibuprofen 600 MG Tablets (FML)**						Label Claim	600
Batch No:	IBU600/24/08							Factor	1.000
Mfgr	QP	Mfg dt		Exp dt				Potency	99.72
							conc mg/ml	WS Expt dt	
Std1	66.35	100	1	1	1	1	0.6616	Balance :	QP/ADL/I-016/23
Std2	66.22	100	1	1	1	1	0.6604	Dissolution	QP/ADL/E-019/23
Spl Conc	600	900	1	1	1	1	0.6667	Apparatus	Paddle
Injections	**Standard Abs**							RPM	50
Std-1_1	1.132							Volume	900ml
Std-2-1	1.130	CC(Std1/Std2)	1.00					UV ID	QP/ADL/I-007/22
Std-2-2	1.130							Medium	Phos Buff Ph-7.2
Std-2-3	1.130							ƛ (nm)	266
Std-2-4	1.129							Cuvette	1 Cm
Std-2-5	1.130							Condition	Initial Coated
Avg	1.1298							Packing	Polybag
SD	0.0004							Limit	NLT 85 %
%RSD	0.0396								
Bkt-std	1.129		**Sample details :**						
Avg	1.13								
SD	0.00								
%RSD	0.05								

Sample ID	Tab wt (mg)	**15 MIN**	**20 MIN**	**30 MIN**
Tablet-1	771.28	1.162	1.161	1.164
Tablet-2	763.78	1.167	1.173	1.174
Tablet-3	774.28	1.156	1.158	1.163
Tablet-4	765.49	1.156	1.158	1.160
Tablet-5	773.15	1.160	1.162	1.165
Tablet-6	775.47	1.161	1.163	1.173
Tablet-7	777.83	1.171	1.169	1.172
Tablet-8	774.02	1.166	1.169	1.172
Tablet-9	774.03	1.165	1.170	1.173
Tablet-10	766.98	1.152	1.154	1.162
Tablet-11	777.91	1.150	1.154	1.157
Tablet-12	777.65	1.153	1.154	1.157

Sample ID	Observation								
Tablet-1		101.90	101.8	102.0	3.4	3.4	3.4	3.4	3.4
Tablet-2		102.30	102.8	102.9	3.5	3.5	3.5	3.5	3.5
Tablet-3		101.30	101.5	101.9	3.4	3.4	3.4	3.4	3.4
Tablet-4		101.30	101.5	101.6	3.4	3.4	3.4	3.4	3.4
Tablet-5		101.70	101.8	102.1	3.4	3.4	3.4	3.4	3.4
Tablet-6		101.80	101.9	102.8	3.4	3.4	3.5	3.4	3.4
Tablet-7		102.70	102.5	102.8	3.5	3.5	3.5	3.5	3.5
Tablet-8		102.20	102.5	102.8	3.5	3.5	3.5	3.5	3.5
Tablet-9		102.10	102.5	102.9	3.5	3.5	3.5	3.5	3.5
Tablet-10		101.00	101.2	101.8	3.4	3.4	3.4	3.4	3.4
Tablet-11		100.80	101.2	101.4	3.4	3.4	3.4	3.4	3.4
Tablet-12		101.10	101.2	101.4	3.4	3.4	3.4	3.4	3.4
	Min	**100.8**	**101.2**	**101.4**	**3.4**	**3.4**	**3.4**	**3.4**	**3.4**
	Max	**102.7**	**102.8**	**102.9**	**3.5**	**3.5**	**3.5**	**3.5**	**3.5**
	Avg	**101.7**	**101.9**	**102.2**	**3.4**	**3.4**	**3.4**	**3.4**	**3.4**
	SD	**0.6**	**0.6**	**0.6**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**
	%RSD	**0.6**	**0.6**	**0.6**	**1.5**	**1.5**	**1.5**	**1.5**	**1.5**
Analysed By :		**Rajendra khodade**					**Checked By :**	Sanjay rangdhol	
Date :		**18-08-2024**					**Date :**	**18-08-2024**	

CALCULATION SHEET DISSOLUTION BY UV

Product Name & Srength :		**Ibuprofen 600 MG Tablets (FML)**							Label Claim	600
Batch No:									Factor	1.000
Mfgr	QP	Mfg dt		Exp dt					Potency	99.06
								conc mg/ml	WS Expt dt	
Std1	66.22	100	1	1	1	1		0.6560	Balance :	QP/ADL/I-016/23
Std2	66.23	100	1	1	1	1		0.6561	Dissolution	QP/ADL/E-019/23
Spl Conc	600	900	1	1	1	1		0.6667	Apparatus	Paddle
Injections	**Standard Abs**								RPM	50
Std-1_1	1.132								Volume	900ml
Std-2-1	1.130	CC(Std1/Std2)	1.00						UV ID	QP/ADL/I-007/22
Std-2-2	1.130								Medium	Phos Buff Ph-7.2
Std-2-3	1.130								λ (nm)	266
Std-2-4	1.129								Cuvette	1 Cm
Std-2-5	1.130								Condition	Initial Coated
Avg	1.1298								Packing	Polybag
SD	0.0004								Limit	NLT 85 %
%RSD	0.0396									
Bkt-std	1.103		**Sample details :**							
Avg	1.13									
SD	0.01									
%RSD	0.97									

Sample ID	Tab wt (mg)	**15 MIN**	**20 MIN**	**30 MIN**					
Tablet-1	769.12	1.143	1.179	1.189					
Tablet-2	774.39	0.819	1.044	1.192					
Tablet-3	775.02	1.128	1.179	1.180					
Tablet-4	784.79	0.783	1.008	1.196					
Tablet-5	786.66	0.950	1.098	1.162					
Tablet-6	777.42	0.708	0.935	1.180					
Sample ID	Observation								
Tablet-1		99.60	102.1	102.4	3.4	3.4	3.5	3.4	3.4
Tablet-2		71.30	90.2	102.2	3.0	3.0	2.9	3.0	3.0
Tablet-3		98.30	102.1	101.7	3.4	3.4	3.3	3.4	3.4
Tablet-4		68.20	87.1	102.5	3.0	3.0	3.0	3.0	3.0
Tablet-5		82.70	94.9	99.8	3.1	3.1	3.2	3.1	3.1
Tablet-6		61.70	80.8	101.0	2.7	2.7	2.7	2.7	2.7
	Min	**61.7**	**80.8**	**99.8**	**2.7**	**2.7**	**2.7**	**2.7**	**2.7**
	Max	**99.6**	**102.1**	**102.5**	**3.4**	**3.4**	**3.5**	**3.4**	**3.4**
	Avg	**80.3**	**92.9**	**101.6**	**3.1**	**3.1**	**3.1**	**3.1**	**3.1**
	SD	**16.0**	**8.5**	**1.0**	**0.3**	**0.3**	**0.3**	**0.3**	**0.3**
	%RSD	**19.9**	**9.1**	**1.0**	**8.7**	**8.7**	**9.4**	**8.7**	**8.7**
Analysed By :		**Rajendra khodade**					**Checked By :**	**Sanjay rangdhol**	
Date :		**19-08-2024**					**Date :**	**19-08-2024**	

CALCULATION SHEET DISSOLUTION BY UV

Product Name & Srength :		**Ibuprofen 600 MG Tablets (FML)**							Label Claim	600
Batch No:									Factor	1.000
Mfgr	QP	Mfg dt		Exp dt					Potency	99.72
								conc mg/ml	WS Expt dt	
Std1	66.22	100	1	1	1	1		0.6604	Balance :	QP/ADL/I-016/23
Std2	66.23	100	1	1	1	1		0.6605	Dissolution	QP/ADL/E-019/23
Spl Conc	600	900	1	1	1	1		0.6667	Apparatus	Paddle
Injections	**Standard Abs**								RPM	50
Std-1_1	1.110								Volume	900ml
Std-2-1	1.111	CC(Std1/Std2)	1.00						UV ID	QP/ADL/I-007/22
Std-2-2	1.110								Medium	Phos Buff Ph-7.2
Std-2-3	1.111								λ (nm)	266
Std-2-4	1.110								Cuvette	1 Cm
Std-2-5	1.111								Condition	Initial Coated
Avg	1.1106								Packing	Polybag
SD	0.0005								Limit	NLT 85 %
%RSD	0.0493									
Bkt-std	1.103		**Sample details :**							
Avg	1.11									
SD	0.00									
%RSD	0.28									

Sample ID	Tab wt (mg)	**DT 18**	**DT 12**						
Tablet-1		0.831	1.196						
Tablet-2		0.798	1.145						
Tablet-3		0.963	1.188						
Tablet-4		0.725	1.168						
Tablet-5		0.967	1.176						
Tablet-6		0.831	1.151						
Sample ID	Observation								
Tablet-1		74.10	106.3	2.0	2.0	2.0	2.1	2.0	2.0
Tablet-2		71.20	101.8	1.9	1.9	1.9	1.9	1.9	1.9
Tablet-3		85.90	105.8	2.2	2.2	2.2	2.2	2.2	2.2
Tablet-4		64.70	103.7	1.9	1.9	1.9	2.0	1.9	1.9
Tablet-5		86.30	104.7	2.2	2.2	2.2	2.2	2.2	2.2
Tablet-6		74.10	102.3	1.9	1.9	1.9	2.0	1.9	1.9
	Min	**64.7**	**101.8**	**1.9**	**1.9**	**1.9**	**1.9**	**1.9**	**1.9**
	Max	**86.3**	**106.3**	**2.2**	**2.2**	**2.2**	**2.2**	**2.2**	**2.2**
	Avg	**76.1**	**104.1**	**2.0**	**2.0**	**2.0**	**2.1**	**2.0**	**2.0**
	SD	**8.5**	**1.8**	**0.2**	**0.2**	**0.2**	**0.1**	**0.2**	**0.2**
	%RSD	**11.2**	**1.8**	**7.5**	**7.5**	**7.5**	**5.7**	**7.5**	**7.5**
Analysed By :		**Rajendra khodade**					**Checked By :**	**Sanjay rangdhol**	
Date :		**19-08-2024**					**Date :**	**19-08-2024**	

Observation table DT

Granulation time	DT observed in min											
3	4.5	4	6.5	6	4.5	5	6.5	6	5	4	6	5
6	5	5	6.5	4.5	5	7	6.5	6	7	4	7	6
9	5	6	6.5	6	5	6.5	7	6	7	6	6	7
12	10	9.5	11	12.5	8	10	9.5	11	10.4	12	7.5	10

Drying temp ^{0}c	DT observed in min											
45	4.5	5	6.5	6	6	5.5	4.5	4	5	5.5	6.5	4
50	6.5	6	5	6.5	4.5	4	4	5	4	5	5	5
55	9	10.5	8	8	10	9.5	10.4	12	7.5	9.5	10	11
60	11	10.5	9	12	10.5	12	11	10	9	9	11	11.5

Compaction force KN	DT observed in min											
6	12	11.5	12	13	12.5	14	13	12.5	14	12	13	12
10	13	12.5	14	13	12	11.5	12	11	12	13.5	14	11
14	14	12.5	13	14.5	13	14	12.5	13	13	12.5	13	12
18	20.5	19	21	20.5	19	18	18.5	19.5	20	18	21	20.5

Compression speed RPM	DT observed in min											
10	6.5	8	9	7	9	6.5	6	7	7.5	8	7	8
15	8.8	7.5	8	7.5	6	8	9	8.5	9.5	8.5	9	8.5
20	11.5	12	11	13.5	12	11.5	13	14.5	12	11.5	14	11
25	14	12	13.5	12	11.5	13	14	12.5	13	15	13.5	12

Dissolution test graph

Sample Table Report

08/21/2024 02:34:59 PM

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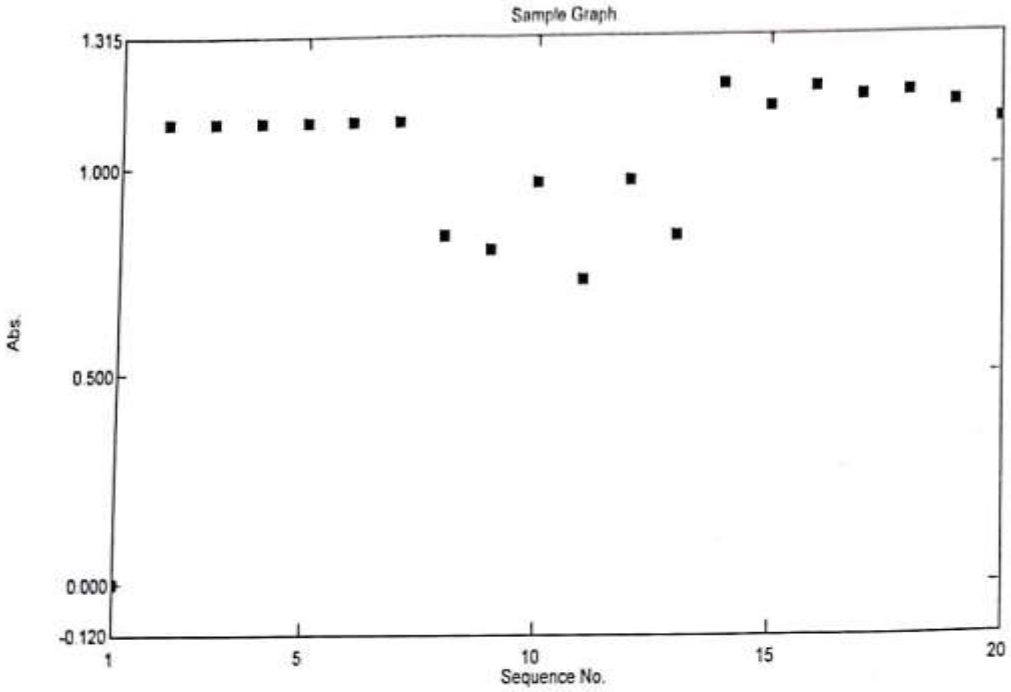

Sample Table

	Sample ID	Type	Ex	WL266.0	Comments
1	Blank	Unknown		-0.000	
2	Std 1_1	Unknown		1.110	
3	Std 2_1	Unknown		1.111	
4	Std 2_2	Unknown		1.110	
5	Std 2_3	Unknown		1.111	
6	Std 2_4	Unknown		1.110	
7	Std 2_5	Unknown		1.111	
8	DT 1 SPL_1	Unknown		0.831	Coated Tablets DT 18
9	DT 1 SPL_2	Unknown		0.798	
10	DT 1 SPL_3	Unknown		0.963	
11	DT 1 SPL_4	Unknown		0.725	
12	DT 1 SPL_5	Unknown		0.967	
13	DT 1 SPL_6	Unknown		0.831	
14	DT 2 SPL_1	Unknown		1.196	Coated Tablets DT 12
15	DT 2 SPL_2	Unknown		1.145	
16	DT 2 SPL_3	Unknown		1.188	
17	DT 2 SPL_4	Unknown		1.168	
18	DT 2 SPL_5	Unknown		1.176	

Sample Table Report

08/18/2024 02:41:13 PM

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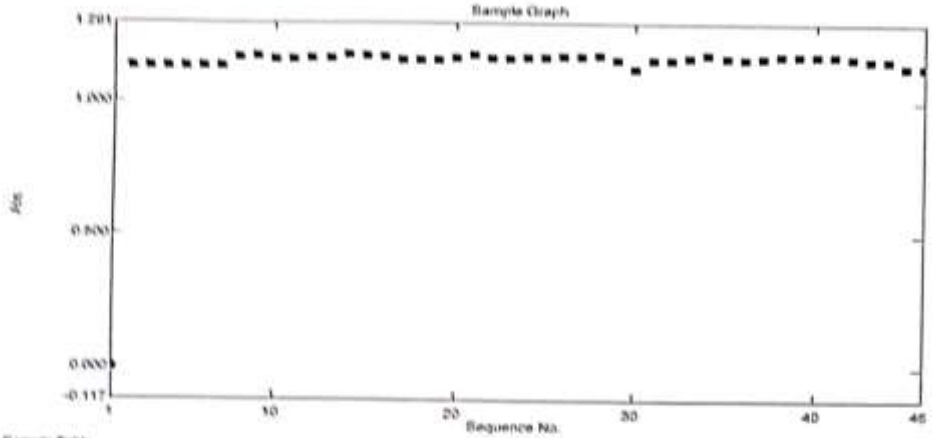

Sample Table

	Sample ID	Type	Ex	WL266.0	Comments
37	30 MIN SPL_5	Unknown		1.165	
38	30 MIN SPL_6	Unknown		1.173	
39	30 MIN SPL_7	Unknown		1.172	
40	30 MIN SPL_8	Unknown		1.172	
41	30 MIN SPL_9	Unknown		1.173	
42	30 MIN SPL_10	Unknown		1.162	
43	30 MIN SPL_11	Unknown		1.157	
44	30 MIN SPL_12	Unknown		1.157	
45	BKT STD_1	Unknown		1.129	
46	BKT STD_2	Unknown		1.129	
47					

Sample Table Report

08/18/2024 02:41:13 PM

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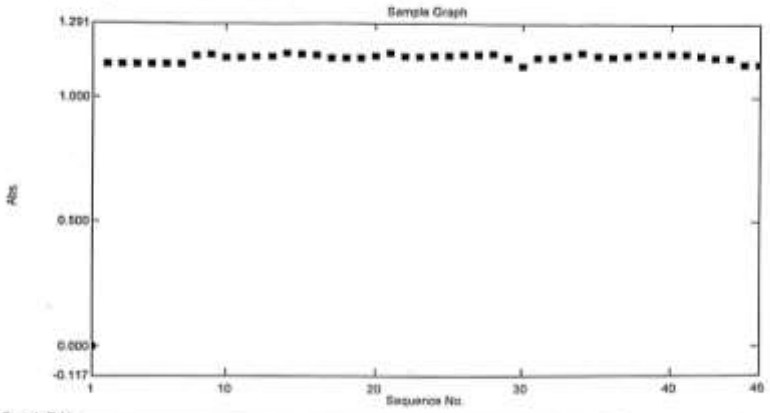

Sample Table

	Sample ID	Type	Ex	WL266.0	Comments
19	15 MIN SPL_12	Unknown		1.153	
20	20 MIN SPL_1	Unknown		1.161	Batch no : IBU600/24/08
21	20 MIN SPL_2	Unknown		1.173	
22	20 MIN SPL_3	Unknown		1.158	
23	20 MIN SPL_4	Unknown		1.158	
24	20 MIN SPL_5	Unknown		1.162	
25	20 MIN SPL_6	Unknown		1.165	
26	20 MIN SPL_7	Unknown		1.169	
27	20 MIN SPL_8	Unknown		1.169	
28	20 MIN SPL_9	Unknown		1.170	
29	20 MIN SPL_10	Unknown		1.154	
30	20 MIN SPL_11	Unknown		1.121	
31	20 MIN SPL_11 REP	Unknown		1.154	
32	20 MIN SPL_12	Unknown		1.154	
33	30 MIN SPL_1	Unknown		1.164	Batch no : IBU600/24/08
34	30 MIN SPL_2	Unknown		1.174	
35	30 MIN SPL_3	Unknown		1.163	
36	30 MIN SPL_4	Unknown		1.160	

Sample Table Report

09/18/2024 02:41:13 PM

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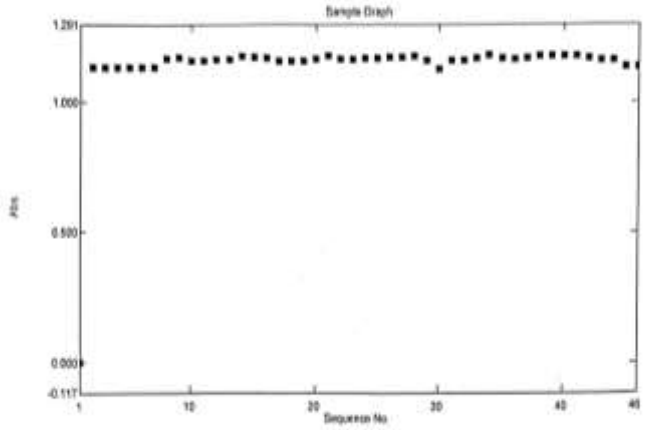

Sample Table

	Sample ID	Type	Ex	WL266.0	Comments
1	Blank	Unknown		0.000	
2	Standard 1	Unknown		1.132	
3	Standard 2_1	Unknown		1.130	
4	Standard 2_2	Unknown		1.130	
5	Standard 2_3	Unknown		1.130	
6	Standard 2_4	Unknown		1.129	
7	Standard 2_5	Unknown		1.130	
8	15 MIN SPL_1	Unknown		1.102	Batch no: IDU0003400
9	15 MIN SPL_2	Unknown		1.107	
10	15 MIN SPL_3	Unknown		1.106	
11	15 MIN SPL_4	Unknown		1.106	
12	15 MIN SPL_5	Unknown		1.100	
13	15 MIN SPL_6	Unknown		1.101	
14	15 MIN SPL_7	Unknown		1.171	
15	15 MIN SPL_8	Unknown		1.168	
16	15 MIN SPL_9	Unknown		1.165	
17	15 MIN SPL_10	Unknown		1.152	
18	15 MIN SPL_11	Unknown		1.150	

Sample Table Report

09/21/2024 02:38:46 PM

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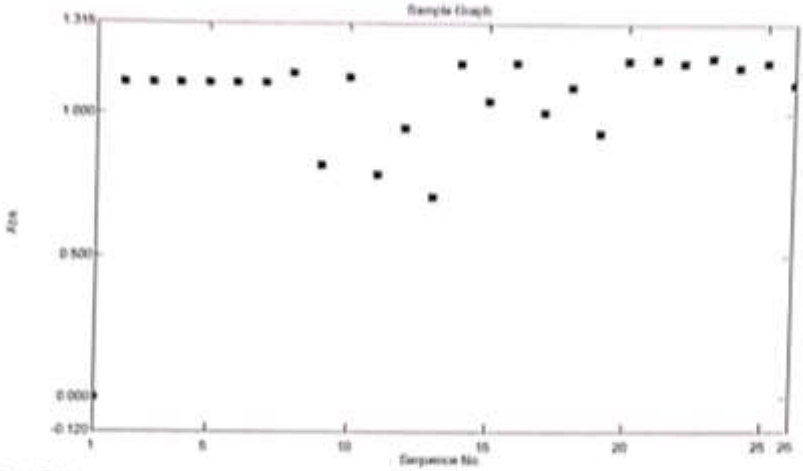

Sample Table

	Sample ID	Type	Ex	WL266.0	Comments
19	20min spl_6	Unknown		0.935	
20	30min spl_1	Unknown		1.089	
21	30min spl_2	Unknown		1.092	
22	30min spl_3	Unknown		1.100	
23	30min spl_4	Unknown		1.100	
24	30min spl_5	Unknown		1.102	
25	30min spl_6	Unknown		1.100	
26	DKT STD	Unknown		1.103	
27					

Sample Table Report

08/21/2024 02:34:46 PM

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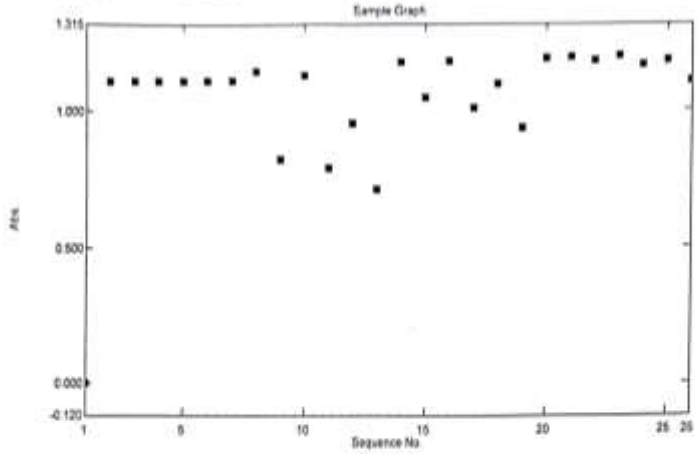

Sample Table

	Sample ID	Type	Ex	WL266.0	Comments
1	Blank	Unknown		-0.000	
2	Std 1	Unknown		1.109	
3	Std 2_1	Unknown		1.109	
4	Std 2_2	Unknown		1.110	
5	Std 2_3	Unknown		1.110	
6	Std 2_4	Unknown		1.110	
7	Std 2_5	Unknown		1.110	
8	15 min spl_1	Unknown		1.143	
9	15 min spl_2	Unknown		0.819	
10	15 min spl_3	Unknown		1.126	
11	15 min spl_4	Unknown		0.783	
12	15 min spl_5	Unknown		0.950	
13	15 min spl_6	Unknown		0.708	
14	20 min spl_1	Unknown		1.179	
15	20 min spl_2	Unknown		1.044	
16	20 min spl_3	Unknown		1.179	
17	20min spl_4	Unknown		1.038	
18	20min spl_5	Unknown		1.098	

Sample Table Report

08/21/2024 02:34:59 PM

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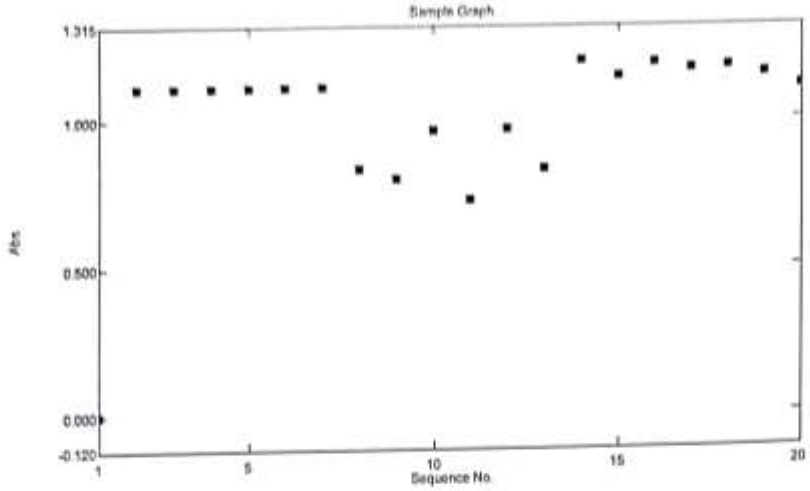

Sample Table

	Sample ID	Type	Ex	WL266.0	Comments
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20	BKT STD	Unknown		1.108	
21					

Report :

DT core vs DT coated

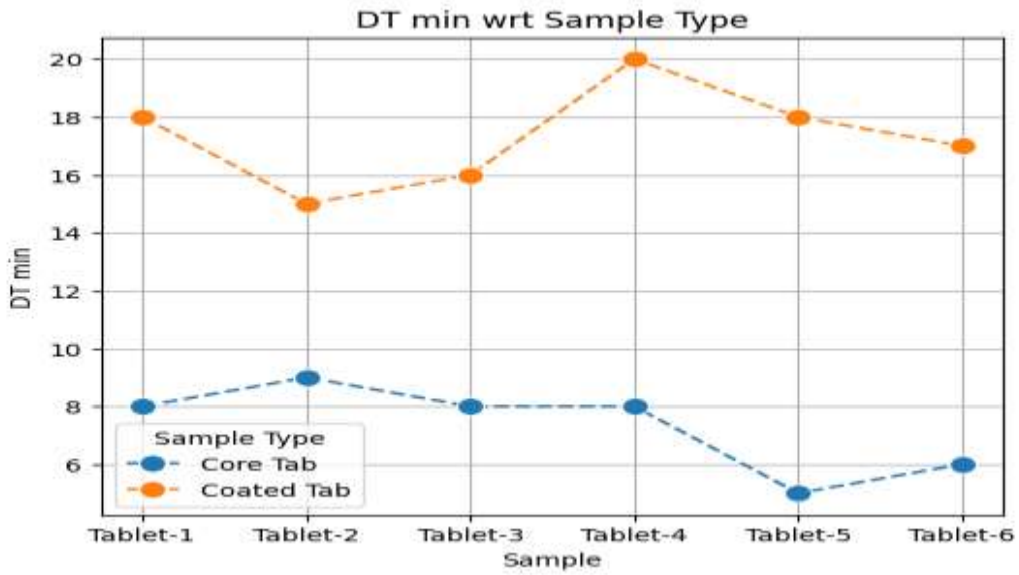


Figure. DT Core vs DT coated

-High DT values for coated tablets as compared to core tabs

DT min vs Dissolution% at time intervals

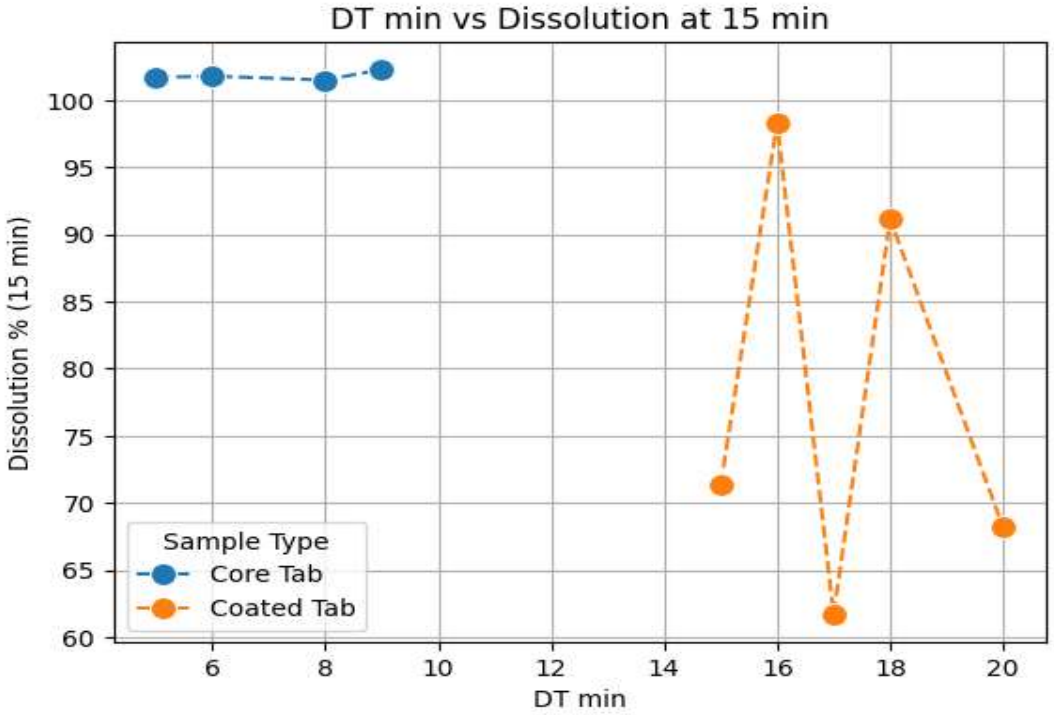


Figure. DT min vs Dissolution% at time intervals

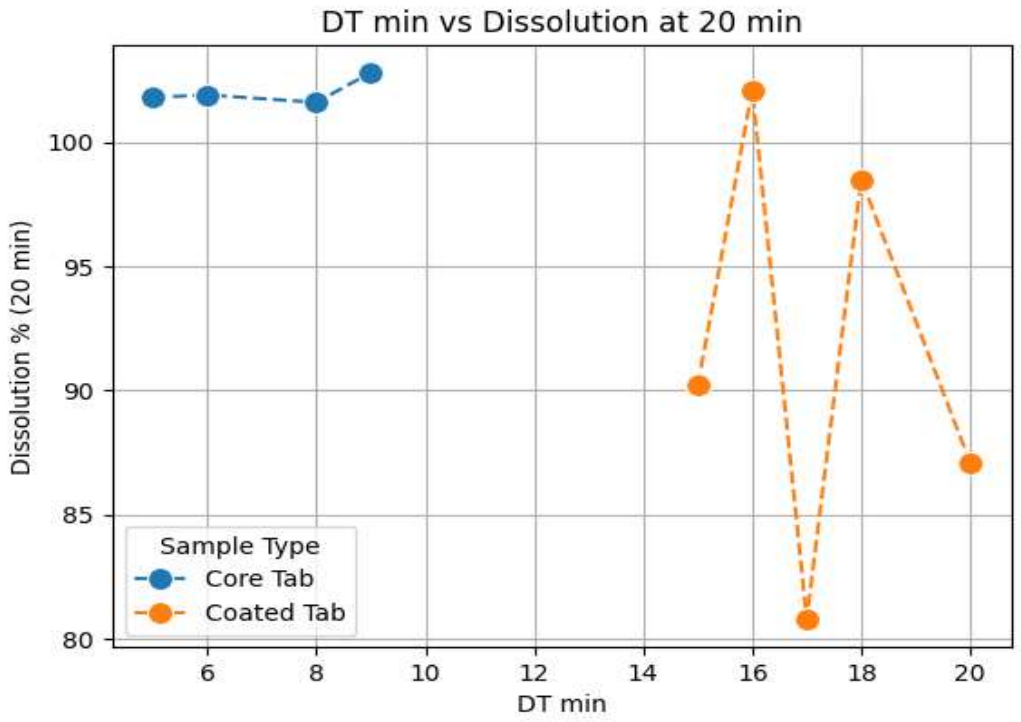


Figure. DT min vs Dissolution% at time intervals

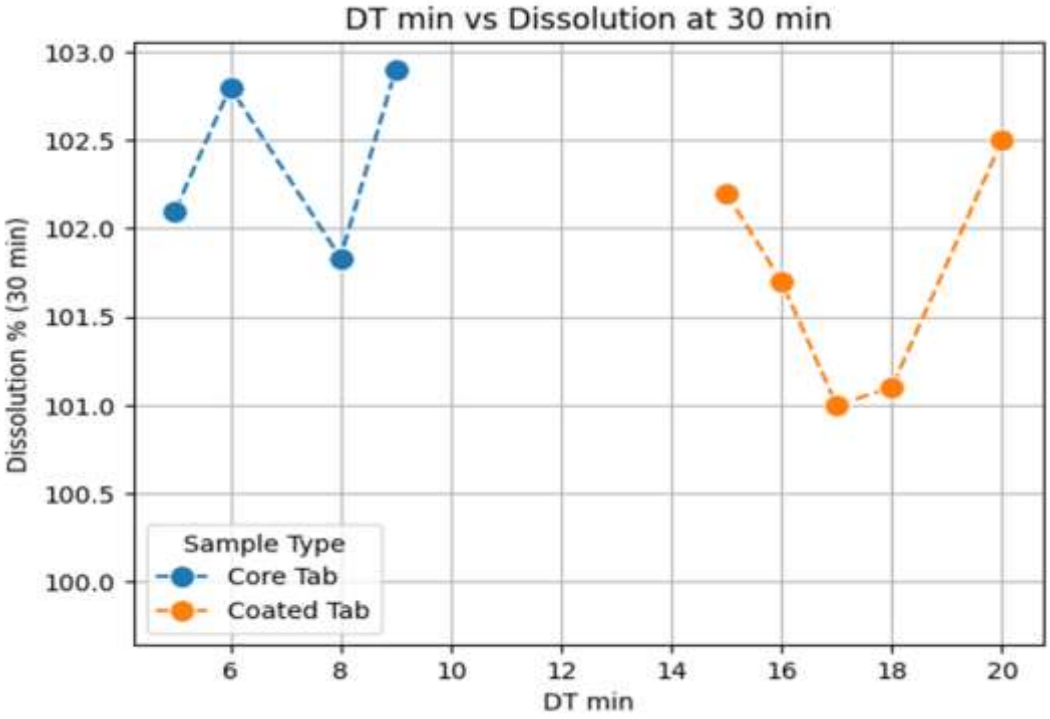


Figure. DT min vs Dissolution% at time intervals

Correlation Matrix of Core Tablets

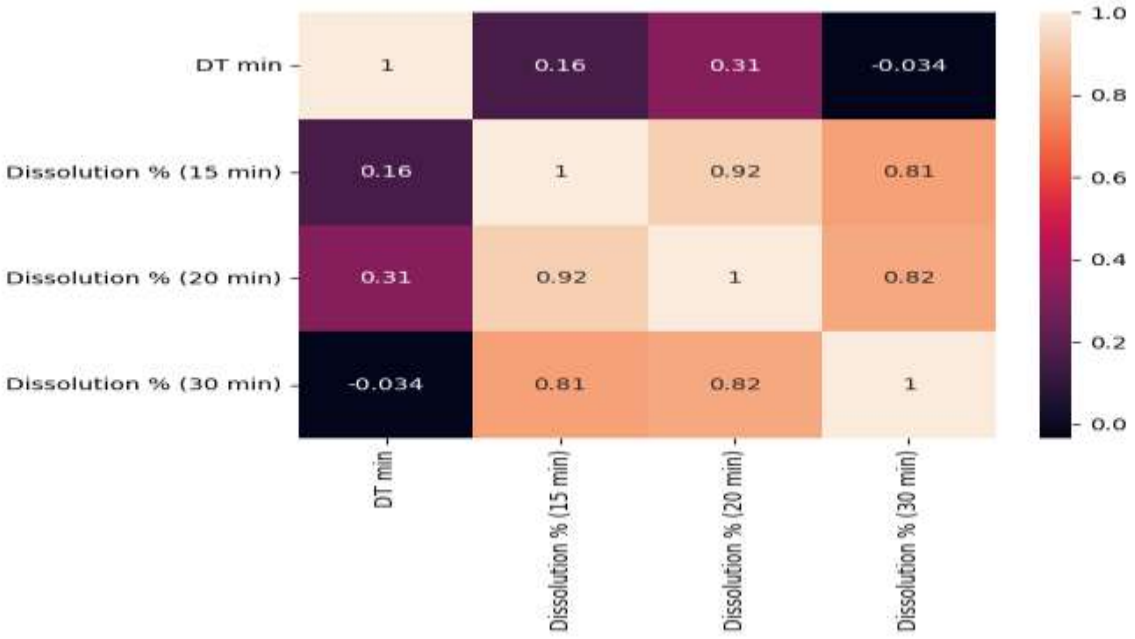


Figure Correlation Matrix of Core Tablets

WRT DT: weak positive at 15 min, moderate positive ate 20 min, very weak negative at 30 min

Correlation Matrix for coated Tablets

WRT DT: weak negative at 15 min, weak negative at 20 min and very weak positive 30 min.

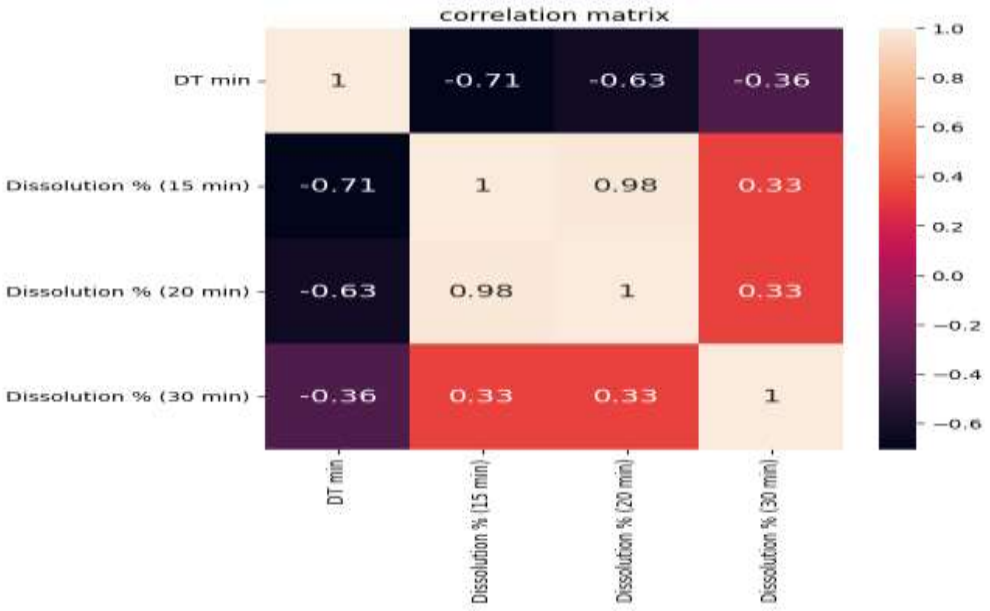


Figure Correlation Matrix of Coated Tablets

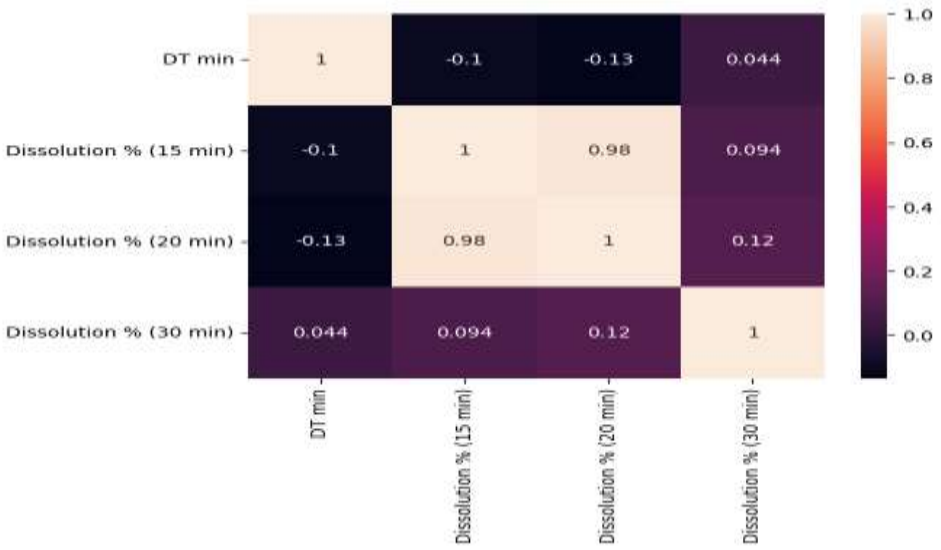
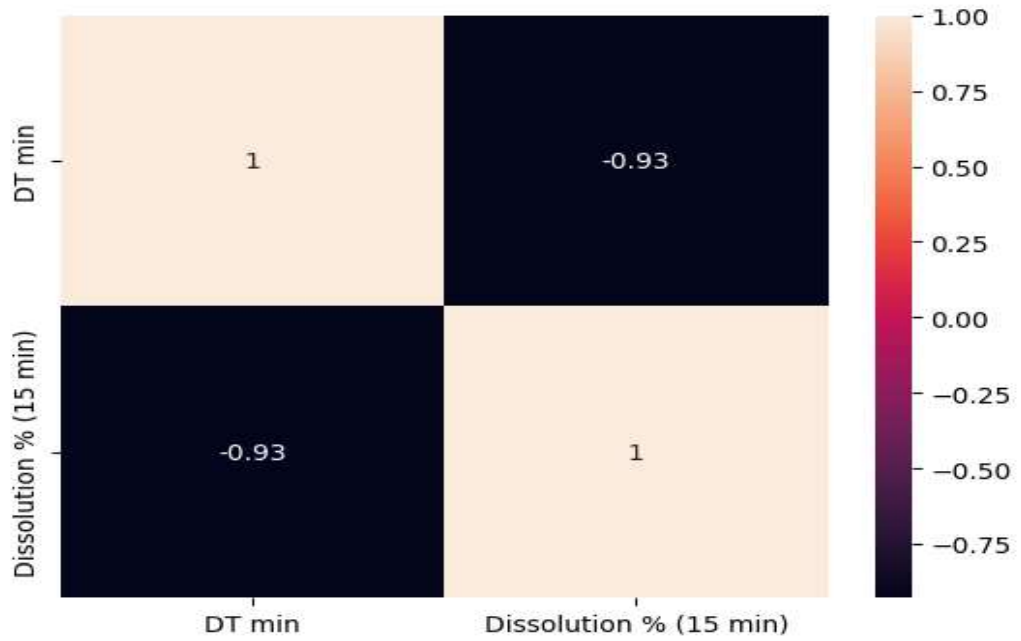


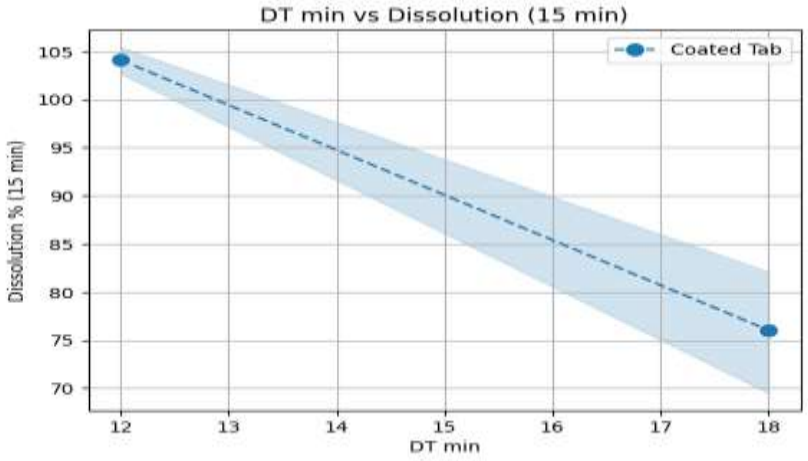
Figure Correlation Matrix of combined (core and coated) Tablets

Combined (core and coated tabs) Correlation:

Around moderate negative if both core and coated are taken into consideration Means:



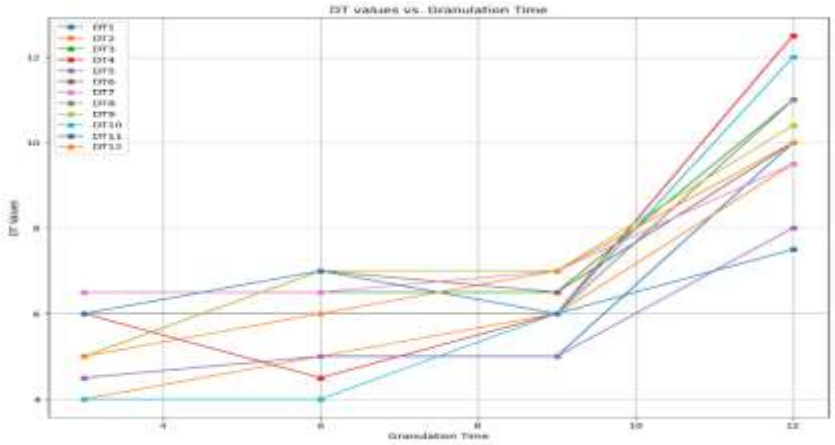
Coated Tablets



Correlation:

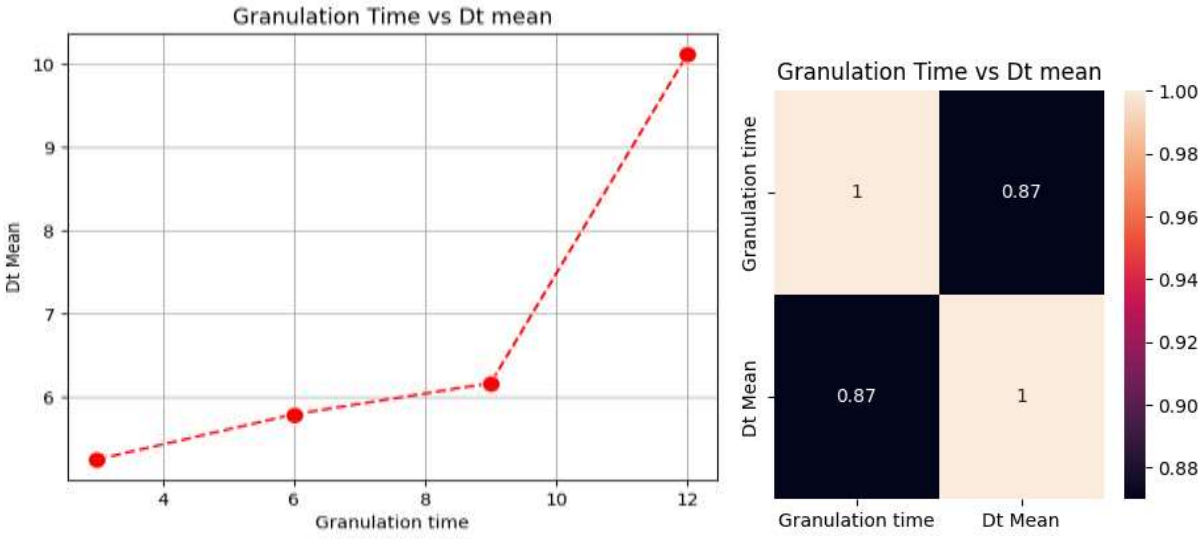
Strong negative for dt values 18 and 12 WRT diss at 15 min

Granulation Time:



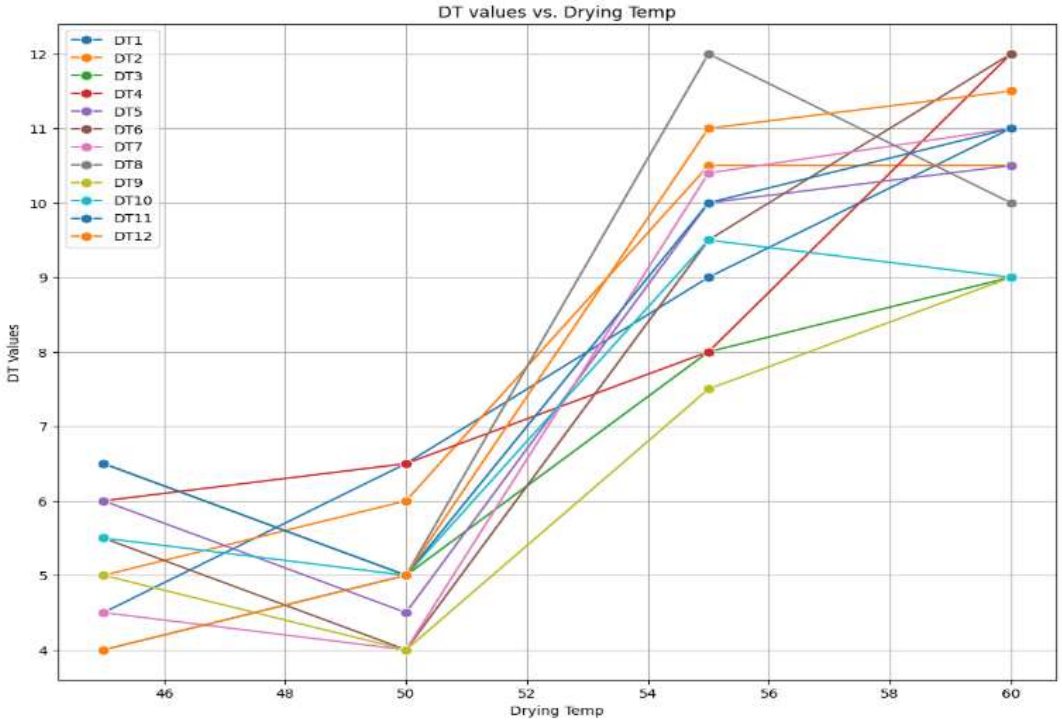
Corr Matrix: time vs dt mean:

Strong +ve more change in dt values if granulation time increases



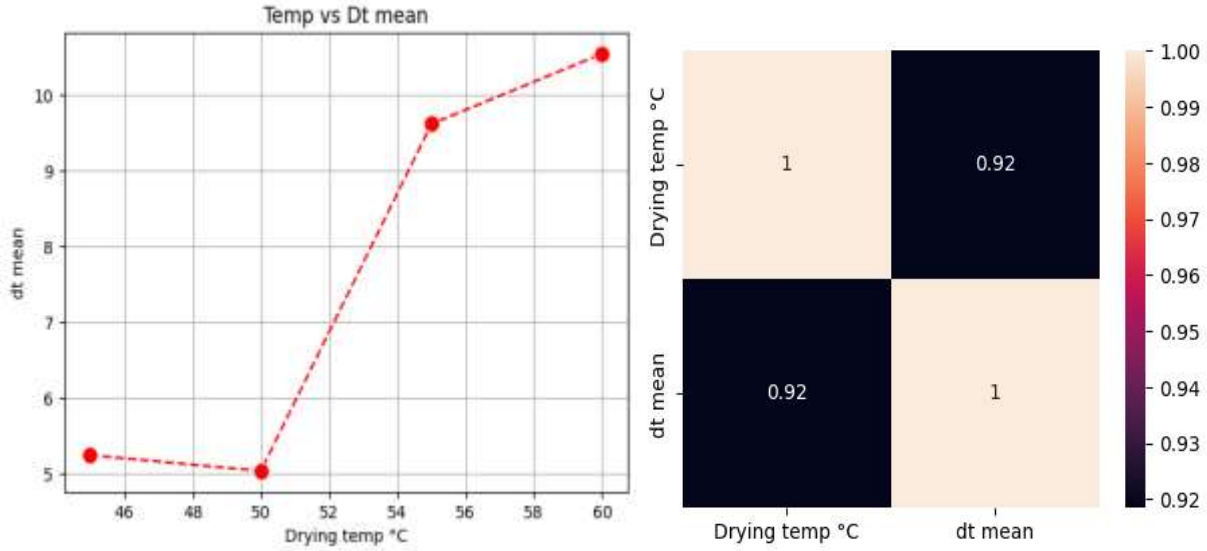
Sample Type	DT min	Dissolution % (15 min)	Dissolution % (20 min)	Dissolution % (30 min)
Coated Tab	17.333333	80.300000	92.866667	101.600000
Core Tab	7.333333	101.716667	101.883333	102.216667

Drying Temperature:



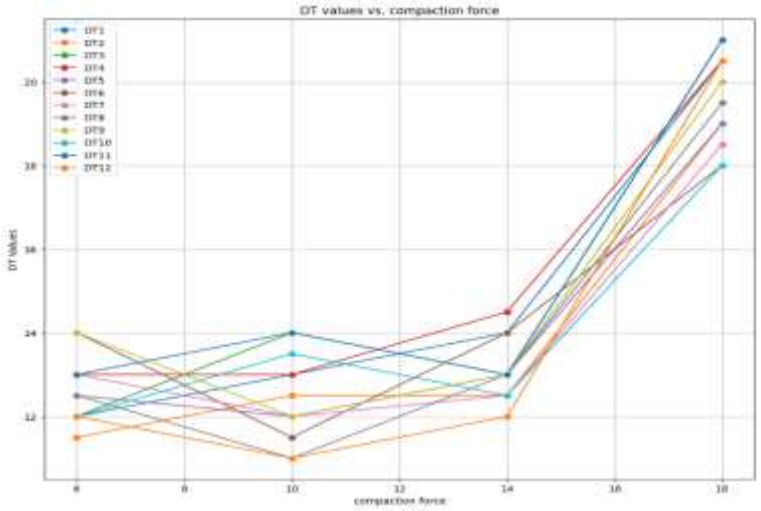
Correlation Matrix: temp vs Dt mean

Strong +ve

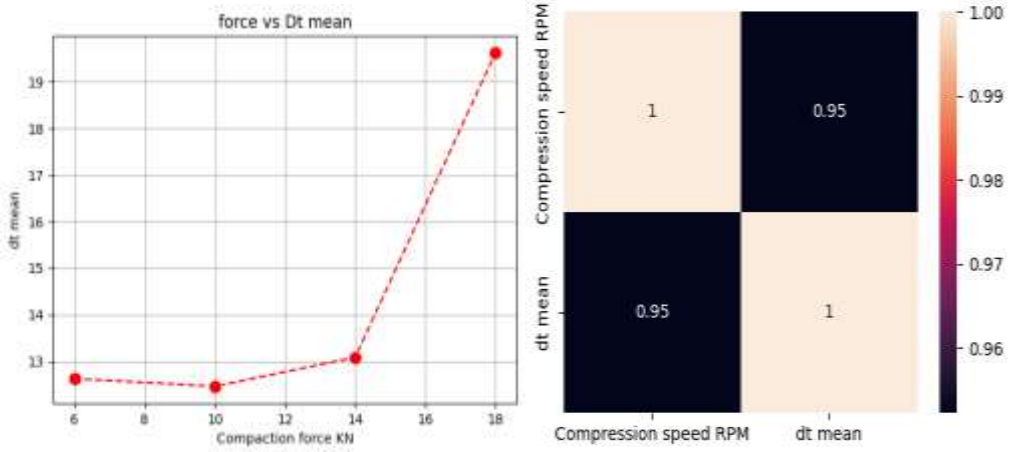


More changes in dt values 50^0 c of temp

Compaction Force:



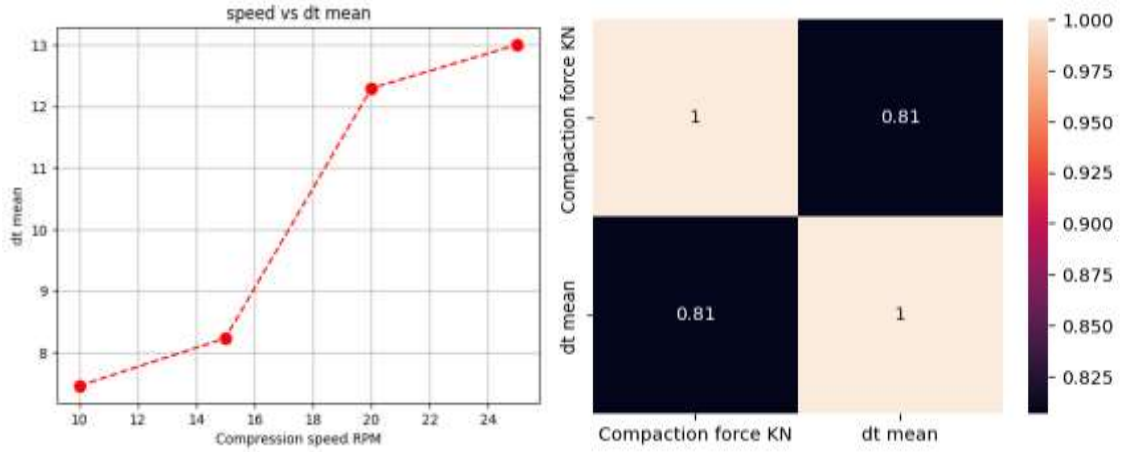
Corr matrix: strong +ve force vs dt mean

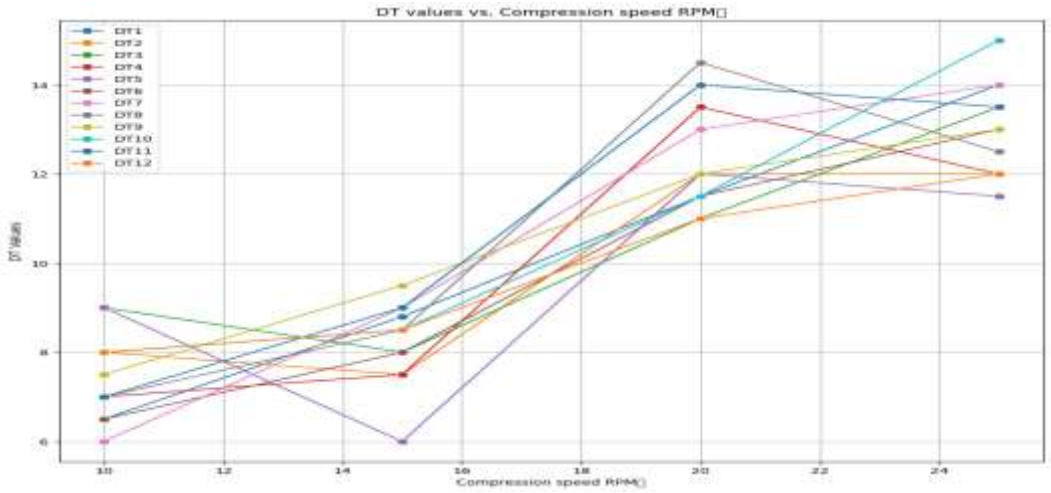


More fluctuation in dt values if force increases beyond 12 KN force

Corr matrix: strong +ve speed VS DT mean

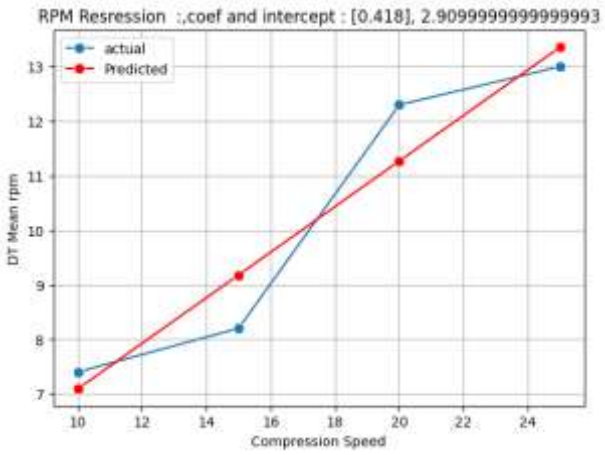
More changes in dt values mid 20 rpm

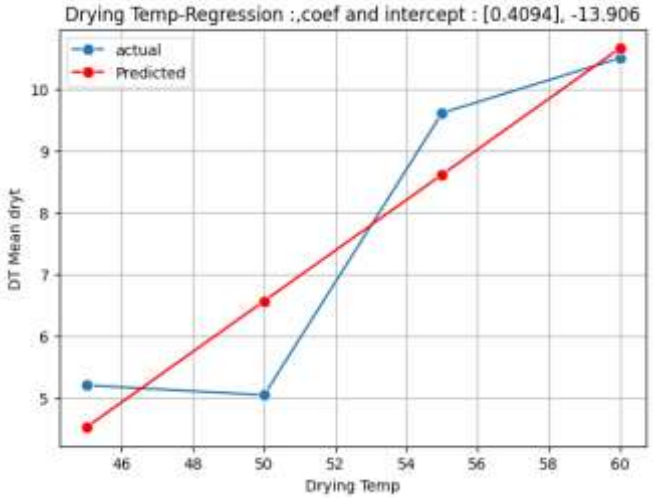


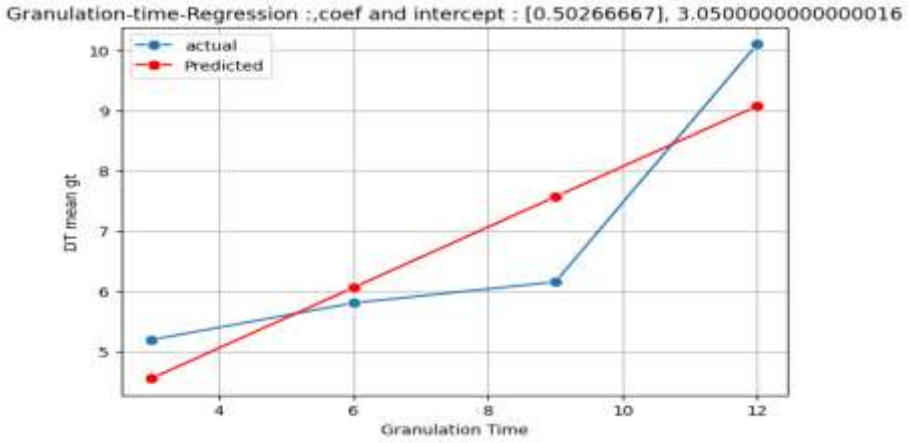


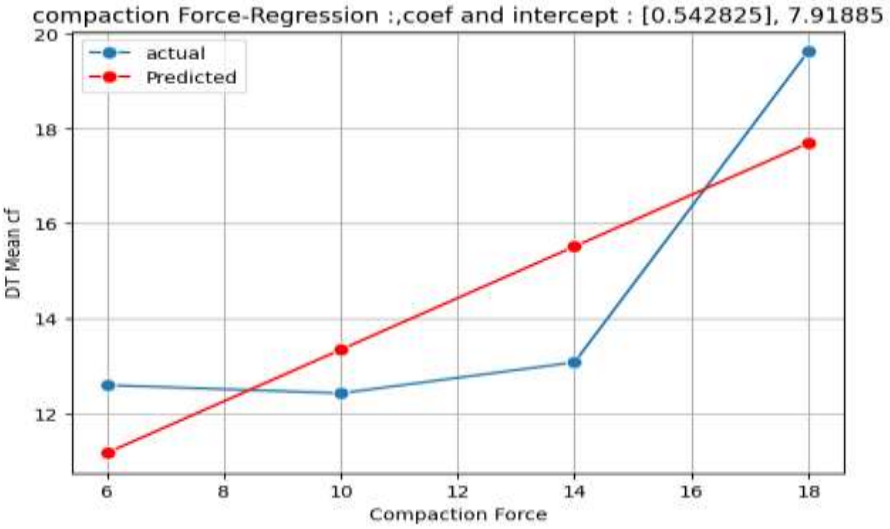
RPM Speed

Regression analysis









	Granulation Time	DT mean gt	Drying Temp	DT Mean dryt	Compaction Force	DT Mean cf	Compression Speed	DT Mean rpm
0	3	5.20	45	5.20	6	12.600	10	7.4
1	6	5.81	50	5.04	10	12.430	15	8.2
2	9	6.16	55	9.61	14	13.080	20	12.3
3	12	10.11	60	10.50	18	19.621	25	13.0

First column is variable and next is its dT mean (from data provided)

Ex: col 1-granulation temp, col2 ->its mean; col3-Drying temp, col4 ->its mean

DT values and therefore DT mean are different for each variable therefore separate reg analysis can be performed for each variable and not multiple regression

If multiple regression performed then regression coef and intercepts may contain errors

Corr matrix:

	Granulation Time	DT mean gt	Drying Temp	DT Mean dryt	Compaction Force	DT Mean cf	Compression Speed	DT Mean rpm
Granulation Time	1.000000	0.873438	1.000000	0.919815	1.000000	0.807874	1.000000	0.952216
DT mean gt	0.873438	1.000000	0.873438	0.764550	0.873438	0.989334	0.873438	0.759048
Drying Temp	1.000000	0.873438	1.000000	0.919815	1.000000	0.807874	1.000000	0.952216
DT Mean dryt	0.919815	0.764550	0.919815	1.000000	0.919815	0.730699	0.919815	0.990144
Compaction Force	1.000000	0.873438	1.000000	0.919815	1.000000	0.807874	1.000000	0.952216
DT Mean cf	0.807874	0.989334	0.807874	0.730699	0.807874	1.000000	0.807874	0.705988
Compression Speed	1.000000	0.873438	1.000000	0.919815	1.000000	0.807874	1.000000	0.952216
DT Mean rpm	0.952216	0.759048	0.952216	0.990144	0.952216	0.705988	0.952216	1.000000

	Granulation Time	Drying Temp	Compaction Force	Compression Speed	DT
Granulation Time	1.000000	1.000000	1.000000	1.000000	0.951176
Drying Temp	1.000000	1.000000	1.000000	1.000000	0.951176
Compaction Force	1.000000	1.000000	1.000000	1.000000	0.951176
Compression Speed	1.000000	1.000000	1.000000	1.000000	0.951176
DT	0.951176	0.951176	0.951176	0.951176	1.000000

[(Granulation Time *0.078) + (Drying Temp *0.13) + (Compaction Force * 0.104) + (Compression Speed0.1302)] -1.18

Multi variant regression analysis may contain error.

6. INFERENCE

1. DT core tablets vs coated tablets: Coated tablets exhibit significantly higher DT values compared to core tablets which is common phenomenon due to the coating polymer.

Controlling factor for the % increase in DT of the coated tablets are coating process parameter specially temperature need to control to keep DT increase in check.

2. DT vs Dissolution % at Time Intervals: The dissolution percentage of coated tablets shows volatility in relation to DT, indicating that small changes in DT can lead to significant fluctuations in dissolution performance, particularly at earlier time intervals.

3. Correlation Analysis:

Core Tablets: A weak positive correlation exists between DT and dissolution % at 15 minutes, which becomes moderately positive at 20 minutes and slightly negative at 30 minutes (negligible). This implies that DT has a variable impact on dissolution depending on the time point.

Coated Tablets: The correlation is weakly negative at 15 and 20 minutes, and only slightly positive at 30 minutes. This suggests that for coated tablets, higher DT values slightly decrease dissolution efficiency early on but have minimal effect over longer periods.

Combined Tablets: When core and coated tablets are considered together, there is a moderate negative correlation between DT and dissolution %, indicating that higher DT values generally reduce dissolution effectiveness.

Granulation Time: A strong positive correlation exists between granulation time and DT, meaning longer granulation times lead to higher DT values, which could impact the disintegration and dissolution processes.

Drying Temperature: There is a strong positive correlation between drying temperature and DT values, suggesting that as drying temperature increases, DT values rise, particularly at mid-range temperatures. This can be crucial for optimizing the drying process.

Compaction Force: Compaction force shows a strong positive correlation with DT, with significant fluctuations observed when force exceeds 12 units. This indicates that over-compression may lead to increased DT, potentially hindering tablet

disintegration.

RPM Speed: A strong positive correlation exists between RPM speed and DT, with notable changes in DT values at mid-range RPMs.

7. RECOMMENDATIONS

1. Optimize Coating Processes: Consider fine-tuning the coating thickness or material to achieve a more consistent dissolution profile. This may reduce the volatility observed in dissolution percentages.

2. Granulation Time Adjustment: Optimize granulation times to balance DT values, ensuring they remain within an acceptable range that supports the desired dissolution rate. Avoid excessively long granulation times that could increase DT unnecessarily.

3. Temperature Control: Carefully monitor and control drying temperatures, especially in the mid-range, to maintain consistent DT values. Adjust drying protocols to minimize the impact of temperature fluctuations on DT.

4. Compaction Force Calibration: Re-evaluate the compaction process to prevent applying excessive force that could lead to increased DT and reduced dissolution efficiency. Aim to maintain compaction force within a range that supports optimal tablet disintegration.

5. RPM Speed Regulation: Adjust RPM speeds during production to control DT values effectively. Fine-tuning RPM settings can help maintain the desired balance between production efficiency and tablet quality.

6. Regression: Though multiple regression model predicts some values behavior of the DT can be concluded by actual testing of the parameters. Multivariate analysis can be implemented and hypothesis testing can be used to predict the exact behavior of the CPPs for required CQAs. Out of all applicable factors 4 critical were selected other factors and interdependence of the factors and its outcome for mist fix CPP can be studied.

7. Further Testing: Further additional trials can be conducted to study and explore the impact of these variables on long-term quality attributes leading to stability and bioavailability.

This will help refine the manufacturing process and fixing the point of control based on scientific studies to produce tablets with consistent performance.

8. CONCLUSION

Key relationships influencing tablet performance:

1. **Compression speed and compaction force** showed a strong positive correlation with **Disintegration Time (DT)**, meaning higher values lead to longer DT.
2. **Granulation time and drying time** also had a strong positive correlation with DT, indicating extended processing times increase DT.
3. A **moderate to strong negative correlation** was observed between **DT and Dissolution %**, suggesting that faster disintegration improves drug release.

These findings highlight opportunities for process optimization, such as adjusting compression parameters, granulation, and drying times to achieve desired DT and dissolution profiles, ultimately ensuring drug bioavailability.

To enhance reliability, future work should:

- Combine predictive models with mechanistic or machine learning approaches,
- Validate findings through physical testing, and
- Implement continuous CQA monitoring.

Pharmaceutical manufacturers can achieve more robust, efficient, and compliant tablet production processes.

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