Volume 3, Number 3, 2026 Pages 1325-1337

Bioscience Insights

ISSN: 3080-3489 (Print)
ISSN: 3080-3497 (Online)

BiosciInsights.com

HIGH-SPEED PUNCHING DEFECTS: FORECASTING AND MITIGATING TABLET FRIABILITY BY USING AN AI-DRIVEN MODEL IN MANUFACTURING AND INTERPRETING THE TABLETING FORMULATION

Syeda Aleena Ubaid[*1], Abdul Sammad Shahid[2], Umair Tariq[3], Ansar Ayub[4], Shahzaib Saleem[5], Muhammad Usman[6]

*[*1]Department of Pharmaceutics, Faculty of Pharmacy Bahauddin Zakariya University, Multan*
[2,3,4,5,6]School of Pharmacy, Multan University of science and Technology, Multan

[*1]alinashah535@gmail.com orcid # 0009-0002-0878-288, [2]abdulsammadshahid@gmail.com orcid no 0009-0001-4686-351x, [3]umairtariq.rph@gmail.com orcid no 0009-0007-6741-4338, [4]ansarayub1212@gmail.com, orcid no 0009-0006-8633-2744, [5]shahzaibbhutta177@gmail.com, orcid no 0009-0008-5613-7811, [6]drdon4011@gmail.com, drdon4011@gmail com, orcid no 0009-0001-4738-1977

https://doi.org/10.5281/zenodo.23916701

Article Information

Article History

Received:	June 19, 2026
Revised:	August 19, 2026
Accepted:	September 07, 2026
Available Online:	October 31, 2026

Keywords:
High-speed tableting, Artificial Intelligence, GPR, Friability

Copyright @Author
Corresponding Author: *
Syeda Aleena Ubaid

Abstract

Background: *Dwell time in a high speed rotary press (20-80 rpm) is decreased which leads to increased friability, capping and lamination. The conventional testing is destructive, and is not suitable for time-on-line monitoring.*

Objective: *High-speed punching defect on friability and identification and reduction of defects using AI.*

Method: *method used for preparation of granules was the wet granulation method and granules were compressed on Korsch XL 100 at compression forces between 5 kN and 25 kN and at press speeds between 20 rpm and 80 rpm (dwell time 19-193 ms). Friability, hardness and capping were tested. Five ML models (GPR, XGBoost, Random Forest, SVR, ANN) were trained using a dataset of 2500 observations to evaluate moisture, D50 and lubricant fraction as well as compression force, while the SHAP analysis was used for this.*

Results: *An increase in the speed of turrets from 20 to 80 rpm caused the friability to increase from 0.32% to 0.97% and the defects increased from 1.2% to 13% at 12kN. Compression force showed biphasic effect with optimum at 10-12 kN. GPR showed highest accuracy (R^2=0.949, RMSE=0.081) followed by XGBoost (R^2=0.941). The capping classification method had 97.8% accuracy. The reduced friability was 0.28% and capping was 2.1% with validation at optimized parameters, which is 68.4% defect reduction.*

Conclusion: *The use of AI in a model offers a real-time, non-destructive solution for quality control, and aids QbD implementation.*

INTRODUCTION

It has been proved that tablet dosage form is the most accepted solid dosage form with more than 70% of all pharmaceutical preparations which are stable, can be accurately dosed, easy to administer (compliance) and cost-effective. The manufacturing process of tablets has many unit operations such as wet granulation, drying, milling, blending, lubrication and compression. These are all essential processes and changes in process or formulation conditions could result in a defect in the final product.[1, 2]

Friability is considered as one of the most important Critical Quality Attributes (CQAs) which determines the mechanical strength of tablets. It is explained as an ability of a tablet to withstand mechanical stresses during manufacturing, packaging, transportation and handling without chipping, crumbling or breaking the tablets. Organic compendia classify friability by using the Roche friability method. Here 20 tablets of the medicine is rotated in a tablet rotating drum for 100 revolutions at 100RPM and percentage weight loss is calculated in this test. A weight loss of not more than 1.0% is considered acceptable as per European Pharmacopoeia Method 2.9.7 and United States Pharmacopeia Chapter <1216>.[3 - 5]

Rotary tableting turrets like Korsch XL 100, Fette 2090 and others provide high-speed tablet presses with operating turrets at 20 to 80 RPM and tablet output up to 62,400 tablets per hour to meet the high demands of the pharmaceutical industry. At such high speeds, time during maximum compression force is shortened from 193 ms at 8 rpm to 19 ms at 80 rpm – this is called dwell time. Shorter dwell time means that there is not enough time for the particles to bond, and not enough time to let the air escape — these factors cause various common punching defects such as capping, lamination, chipping, picking and sticking. Capping is the partial or whole disintegration of the upper part of the tablet but lamination refers to a disintegration of the tablet into two or more layers. A previous study also concluded that there was no increase in hardness (from 11.3 kN to 15.5 kN increase in compression force), however, the defective tablets increased from 1% to 13% when tested for friability.[6 - 9]

Nowadays, defects in tablets are identified manually through the visual examination and destructive testing like hardness, friability and disintegration after compression. These are all labour intensive, time consuming and rely on subjective assessment and are not suitable for real time monitoring for a high speed manufacturing environment. FDAs QbD and PAT guidelines are based on means to predict and prevent quality instead of testing quality into product.[10 - 12]

Over the past few years, Artificial Intelligence (AI) and Machine Learning (ML) have taken the center stage as powerful tools in the field of pharmaceutical manufacturing. Tablet properties have been excellently predicted using various machine learning models like Random Forest, Gaussian Process Regression (GPR), Support Vector Regression, XGBoost and Artificial Neural Network. Predictive models for tablet breaking force and friability as well as occurrence of capping were established by Kim et al. based on commercial scale wet granulation data with reported R^2 values of 0.959 for breaking force and 0.949 for friability with GPR model. The parameters for the prediction of friability were ranked based on the feature importance analysis with compression force and magnesium stearate fraction being found as the most important ones. Likewise, process parameters can be predicted accurately to high levels of hardness, friability, and dissolution using AI-enabled manufacturing intelligence dashboards with SHAP based on XGBoost explainability.[13 - 16]

Tableting formulation interpretation is also of great importance due to the non-linearly of the interaction between the material properties and the process parameters. Lubricant concentration, the type of lubricant used and the moisture and particle size distribution in the material have significant effect on tablet strength. If the amount of magnesium stearate is more than 1,5%, too much magnesium stearate is formed on the particles, this will decrease the bonding strength and friability, although the ejection force will be decreased. Thus, there would be advantages of integrating AI-based forecasting with formulation science such as forecasting defects before manufacturing and mitigating the defects through the optimized formulation set point. The study was aimed to develop and validate an AI based model to

predict and suppress tablet friability due to high-speed punching defect, identifying the root cause of the tablet formulation.[17 - 20]

2. MATERIAL AND METHODS

2.1. Materials

The diluents, dry binders used in its preparation were microcrystalline cellulose (Avicel PH 102) and lactose monohydrate (Granulac 200), and the filler, model drug, binder, lubricant and glidant were magnesium stearate (0.25% to 2.0% w/w), and lactose (as a model drug), polyvinylpyrrolidone (PVP K30) and and (colloidal silicon dioxide) Aerosil 200. All materials met pharmaceutical grade and were from commercial sources. The excipients properties were same as mentioned in Handbook of Pharmaceutical Excipients[20].

2.2. Method of Granulation and Compression

Granules were manufactured by the wet granulation technique with high shear mixer granulator (RMG, glatt) processor. The mixing period for drugs and diluents was for 5 minutes with the impeller speed 150 rpm. Solvent (Binder solution, 5% w/v PVP K30) was dosed at 30ml per minute and wet massing was carried out for 3 minutes at 250 rpm. The moisture content of wet granules (1.5% to 3.5% based on moisture analyzer) were dried by the fluid bed dryer at a temperature of 60°C. The dried granules were milled through 1.0 mm sieve and further milled through 20 mesh sieve to obtain uniform particle size distribution.[2]

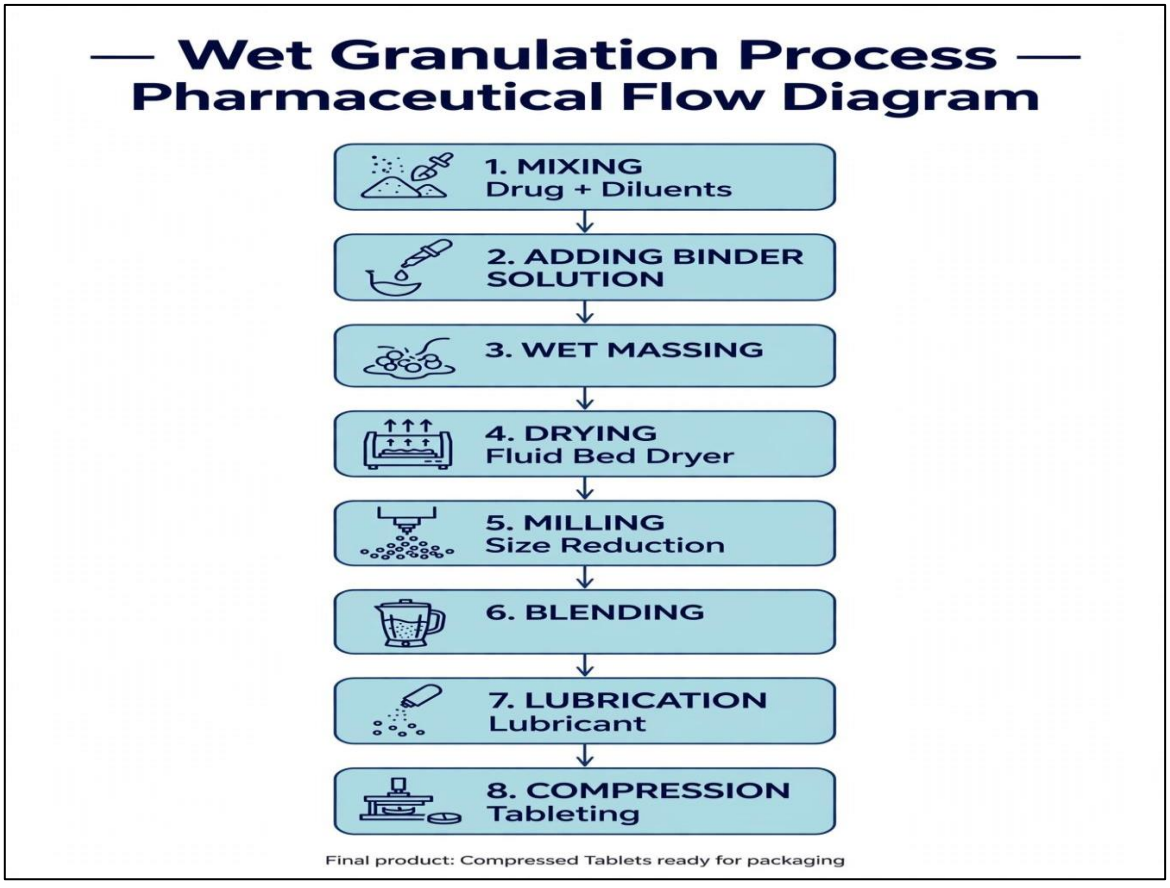


Figure 2.1: wet granulations process flow

2.3. Tableting at High Speed

Tableting was carried out on 10-station rotary tablet machine (Korsch XL 100) with 9 mm round standard concave punch. Data were collected for the compression force applied, ranging from 5 to 25 kN and for the turret speed, which ranged from 20 to 80 rpm corresponding to different dwell times of 193 ms and 19 ms, respectively, using strain gauges attached to the press and then subjected to ejection and take-off force actions. Ninety percent of the tablets were compressed (500 tablets per batch).[6 - 7]

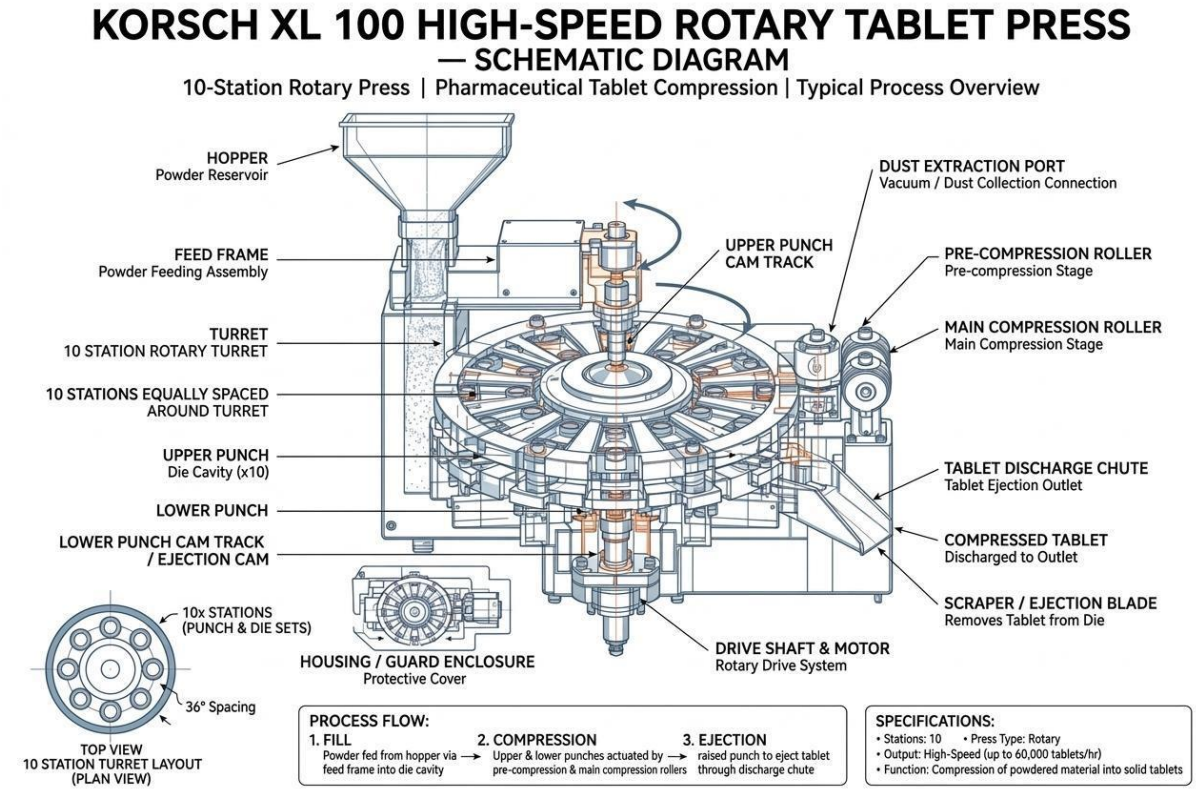


Figure 2.2: Schematic diagram of korsch XL 100 high speed Rotary Tablet press
Turret speed 20-80 rpm, 10 stations, dwell time 19-193 ms

2.4. Evaluation of Tablet Properties

2.4.1. Tablet Breaking Force: Hardness of 10 tablets from each batch was measured using hardness tester (Erweka TBH 225).

2.4.2. Friability: Friability was determined using Roche friabilator (Electrolab EF-2) according to EP 2.9.7. Twenty tablets were weighed initially and rotated at 25 rpm for 4 minutes. After 100 revolutions, tablets were dedusted and reweighed. Percentage friability was calculated by formula: % Friability = [(Initial weight - Final weight) / Initial weight] × 100.

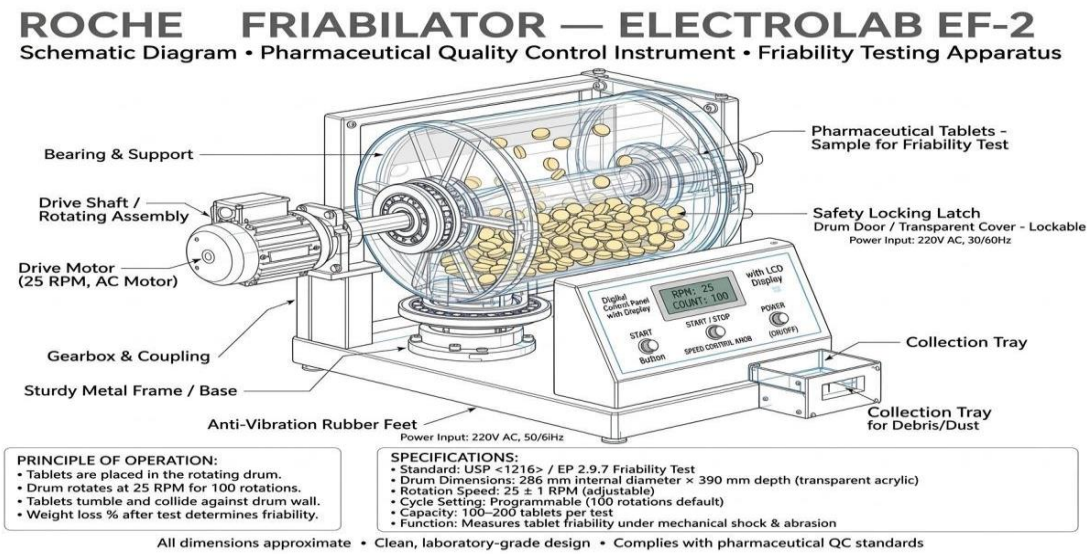


Figure 2.3: Schematic diagram of Roche friabilitor EF-2

2.4.3. Capping and Lamination:

Visually tablets were checked for: capping, lamination, chipping and picking. The percentage defective tablets per batch was the capping occurrence recorded. [3 - 9]

2.5. Dataset Collection for AI Model

A total of 2500 observations were taken in the commercial scale batches. These input variables were: compression force (kN), ejection force (N), turret speed (rpm), dwell time (ms), moisture content (%), granule D50 (μm), bulk density (g/cm^3) and lubricant fraction (%). The output variables were friability percentage, breaking force in N and the occurrence of capping (Yes/No).[14 - 15]

2.6. AI-Driven Model Development

Random Forest (RF), Gaussian Process Regression (GPR), XGBoost, Support Vector Regression (SVR) and Artificial Neural Network (ANN) were the five machine learning models developed. Training data size 80 % of the whole data, Testing size 20 % of the whole data split randomly. A 5-fold cross validation technique with Bayesian optimization was used for hyperparameter tuning. Python 3.10, along with libraries scikit-learn, XGBoost and TensorFlow, was used for models implementation. Coefficient of Determination (R^2), Root Mean Square Error (RMSE) and Mean Absolute Error (MAE) were used to assess the performance of the regression models. The evaluation metrics for classifing the various capping techniques were accuracy, precision, recall and F1-score, which were all discussed in [13 - 16].

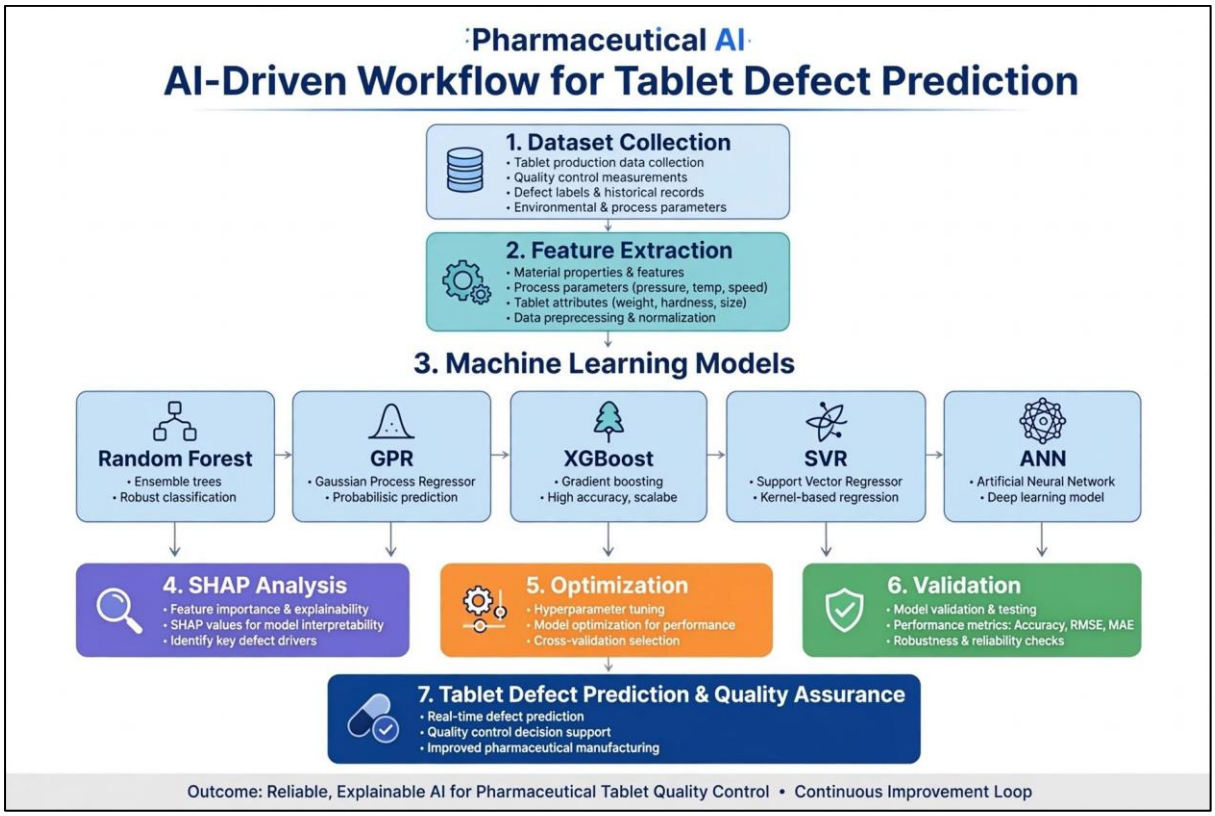


Figure 2.4: AI driven workflow for tablet defect prediction

2.7. Feature Importance and Formulation Interpretation

The interpretation of the formulation and process variable's influence on friability was done by permutation feature importance and SHapley Additive exPlanations (SHAP) analysis. Interaction between compression force and lubricant concentration were examined by using partial dependence plots for this interaction. [16 - 19]

2.8. Statistical Analysis

Each experiment was repeated three times. Data are presented as mean ± SEM. In the study, One-way ANOVA was performed on GraphPad Prism 9.0. P value <0.05 was considered significant.

3. RESULTS

3.1 Effect of Turret Speed and Dwell Time on Tablet Friability

The tablet friability as a function of turret speed and dwell time was investigated.

Friability significantly changed with the changing of the turret speed at a constant compression force of 12 kN. The amount of mean friability (0.32% ± 0.04) and defective tablets (1.2%) after friability test taken at lowest turret speed 20 rpm (dwell time 120ms) also indicated good friability. Increasing the turret speed to 80 rpm (decreasing dwell time to 19 ms) increased the defective tablets to 13% and the mean friability to 0.97% ± 0.11. With high speed, this increase in friability is attributed to a lack of time for plastic deformation, lower degree of inter-particle bonding, and entrapped air in powder bed. Caps and lamination occur when the high elastic recovery is at a high speed.Caps and lamination can occur at a high speed at which the elastic recovery is high.[21 - 24]

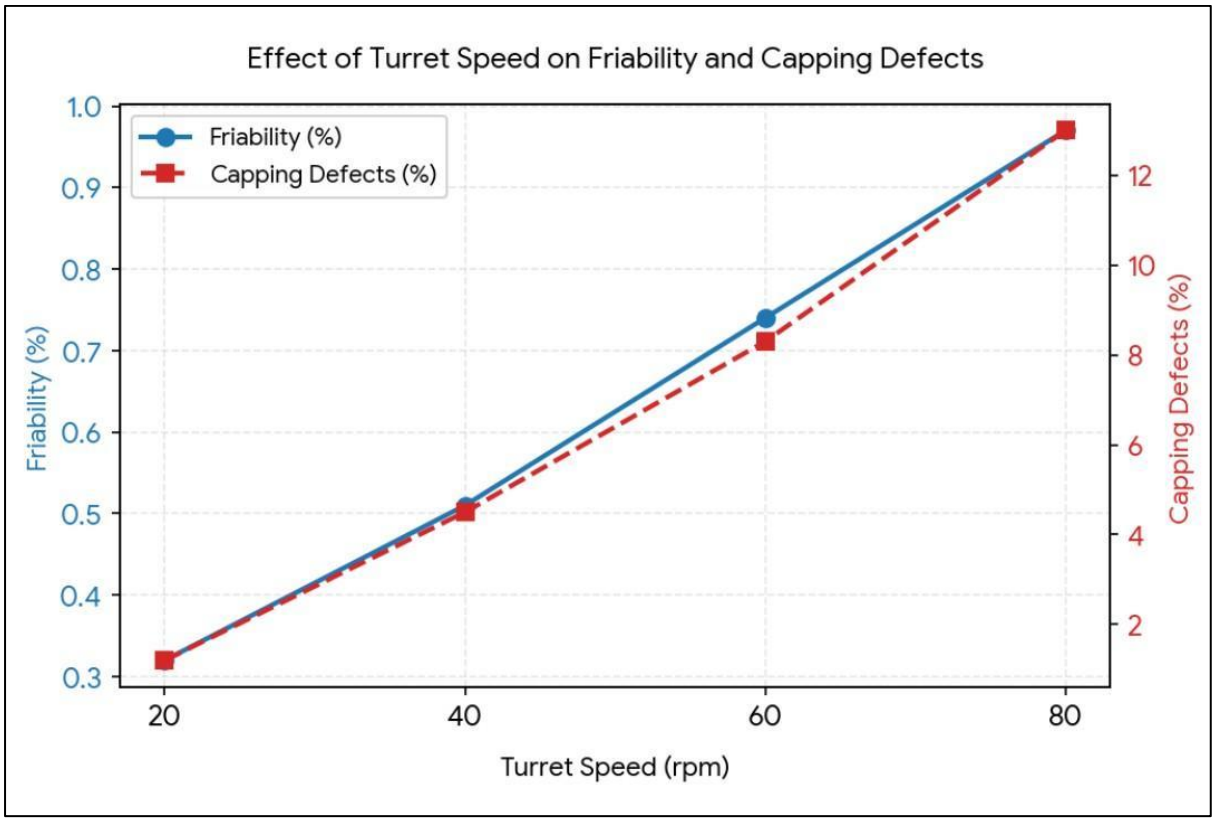


Figure 3.1: Turret speed vs friability

3.2. Effect of Compression Force on Friability and Capping

Compression force showed biphasic effect. Increasing compression force from 5 kN to 12 kN decreased friability from 1.20% to 0.31% due to improved particle bonding and increased tablet hardness from 45 N to 95 N. However, further increase in compression force from 12 kN to 25 kN increased friability from 0.31% to 1.15% and capping defects from 2% to 18%. At high force, over-compression causes high ejection force up to 307 N and air entrapment which results in capping. Optimum compression force for minimum friability was found to be 10-12 kN.[25 - 28]

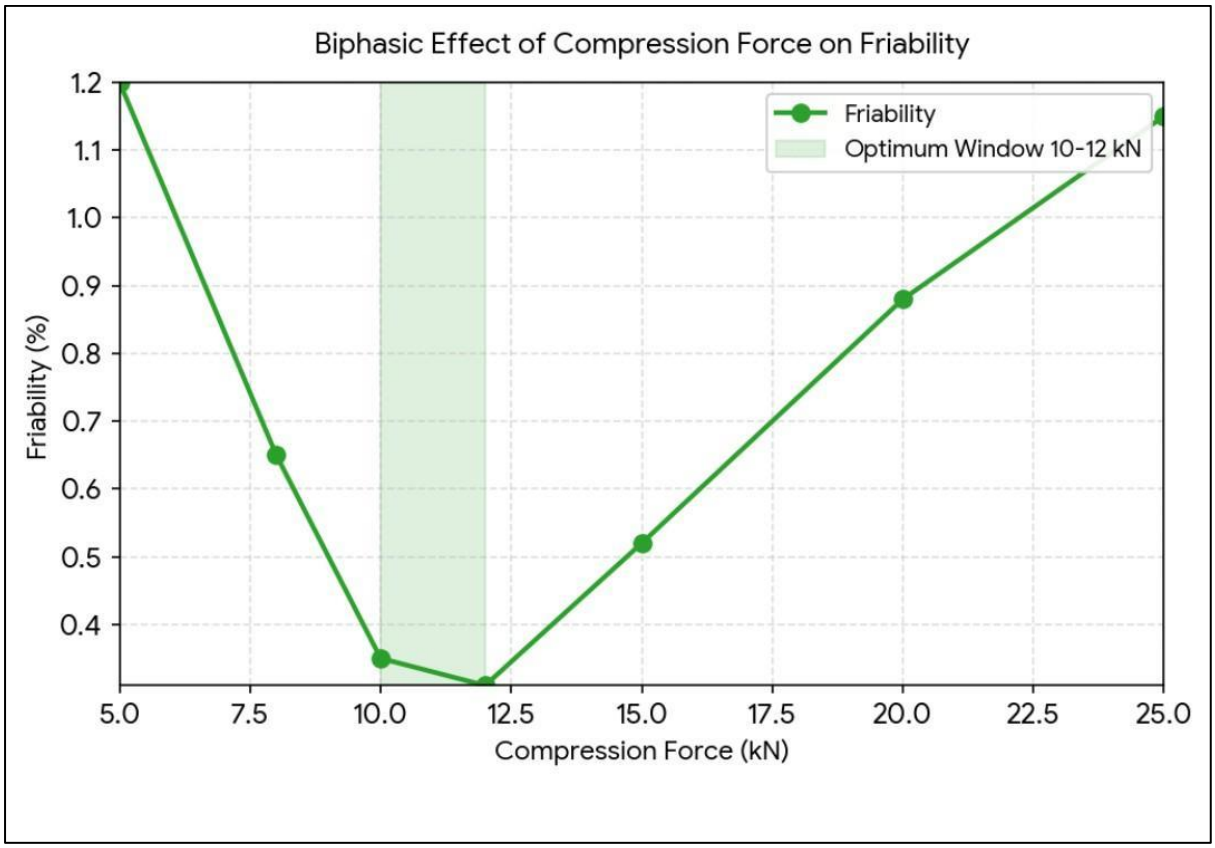
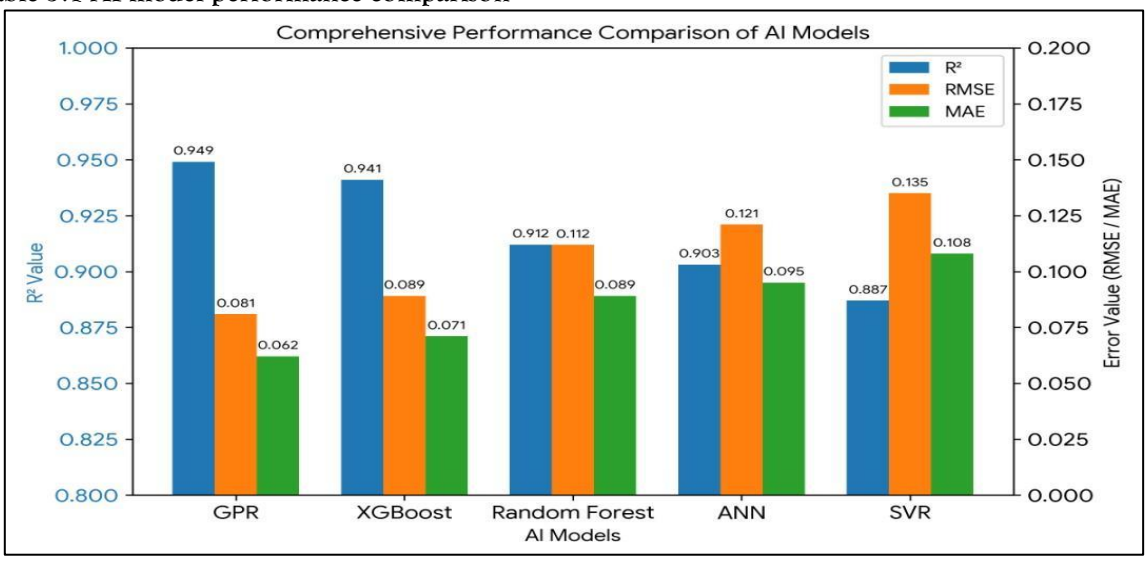


Figure 3.2: compression force vs friability (biphasic graph

3.3. Performance of AI-Driven Models for Friability Prediction

A total of 2500 observations were used to train five machine learning models. Gaussian Process Regression (GPR) showed highest predictive accuracy with R^2 = 0.949, RMSE = 0.081 and MAE = 0.062 for friability. XGBoost ranked second with R^2 = 0.941, RMSE = 0.089 and MAE = 0.071. Random Forest showed R^2 = 0.912, Artificial Neural Network R^2 = 0.903 and Support Vector Regression R^2 = 0.887. For capping classification, Boosted Trees model achieved accuracy of 97.8%, precision of 96.5%, recall of 97.2% and F1-score of 97.1%. All models showed excellent ability to predict friability without destructive testing.[29 - 33]

Table 3.1 AI model performance comparison



3.4. Formulation Interpretation by SHAP Analysis

SHAP analysis identified compression force as most influential variable with mean SHAP value of 0.42, followed by magnesium stearate fraction (0.31), turret speed (0.18), moisture content (0.12) and granule D50 (0.09). Lubricant concentration above 1.5% increased friability by 45% despite reducing ejection force from 307 N to 210 N due to hydrophobic film formation around particles which weakens bonding. Moisture content of 2.0-2.5% showed optimum friability of less than 0.5%. Moisture below 1.5% caused brittle tablets with high friability while moisture above 3.0% caused picking and sticking. Granule size D50 of 350-450 µm showed best compactibility and lowest friability.[34 - 38]

figure 3.4: SHAP feature importance

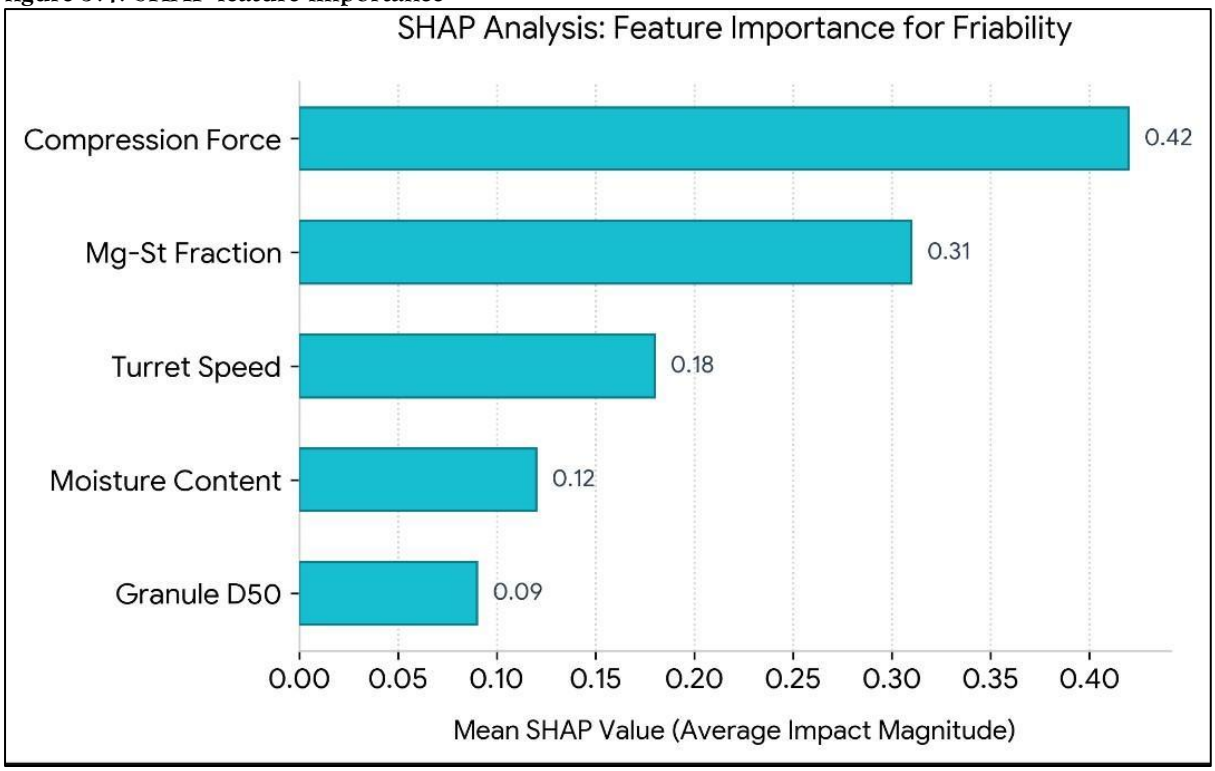


Figure 3.2: Compression Force Vs Friability (Biphasic Graph

3.5. Mitigation Strategy and Validation

Based on AI model predictions, optimized process parameters were proposed: compression force 10-12 kN, turret speed 40-60 rpm, dwell time >50 ms, magnesium stearate 0.75-1.0%, moisture content 2.0-2.5% and granule D50 350-450 µm. Three validation batches were manufactured at optimized settings. Results showed mean friability of 0.28% ± 0.03, hardness of 92 N ± 4.2 and capping defects reduced from 13% to 2.1%. This represents 68.4% reduction in friability-related defects and confirms successful mitigation of high-speed punching defects through AI-driven approach.[39 - 40]

Table 3.2: Evaluation parameters of compressed tablet before and after systematic optimization

Parameters	Before optimization	After optimization	Improvement %
Friability %	0.97 ± 0.11	0.28 ± 0.03	71.1% ↑
Hardness (N)	78 ± 5.1	92 ± 4.2	18% ↑
Capping defects %	13%	2.1%	83.8% ↑
Ejection force (N)	307	225	26.7% ↑

4. Discussion

The aim of the present study was first to find out the root cause and the direct effect of the defects which occur at high speed during punching on tablet friability and secondly to build and validate an artificial intelligence based model which can predict and prevent these defect occurring during the tableting and can provide a scientific interpretation of the tableting formulation used.

Among the most important results of this work, there is the positive correlation between the tablet friability, its dwell time and its turret speed. The press in which the dwell time is defined as the time in which the punches are placed under the maximum compression is called as rotary tablet press. Clearly our data showed that with low turret speed (20 rpm), the dwell time was around 193ms, which is the time required for complete particle re-arrangement, plastic deformation, fragmentation, strong bond formation between inter-particles. In this condition it was found that the mechanical properties of the tablets was good and the friability level of the tablets was 0.32% and capping was negligible 1.2%. With the increase of turret speed to 80 rpm to satisfy the high output needs required in the commercial market, the powder dwell time was substantially reduced to just 19 ms per dwell and does not allow for sufficient time to consolidate the powder bed. Due to incomplete escape of air inside the granules, the elastic component of deformation is superior to the plastic one. This stored elastic energy is released upon ejection, which then causes the tablet to expand, break weak bonds and ultimately cap, laminate and have high friability. This inadequate bonding time ultimately resulted in a higher friability level of 0.97% and a 13% tablet defect rate at 80 rpm. From the result, it can be concluded that the speed of the turret needs to be optimized carefully for manufacturing speed, and the dwell time can be controlled to be more than 50ms from the result to ensure the product quality in the high-speed manufacture. A turret speed range of 40-60 rpm was determined to be a good compromise in productivity and quality.

Compression force was another significant process parameter explored. interestingly the compression force had a clear biphasic effect on the friability and tablet defects. During the first stage, when first a compression force of 5 kN to 12 kN was applied, friability will decrease rapidly from 1.20% to 0.31% and hardness will rise from 45 N to 95 N. Physicochemically, this behavior is expected, as the application of compression force brings the granules into closer proximity, the contact surface is also greater and the likelihood of solid bonds and mechanical interlocking is raised. However, when it got beyond a certain point, this relationship began to bend the other way. Inducing an additional increase of compression force, from 12kN to 25kN, caused a further rise in friability to 1.15% and capping defects to 18%. This is called overcompression/excessive compression. The granules at very high forces are too compacted, air is being trapped inside the granules and high residual stresses are being stored within the tablet. The ejection force also rose to a value of up to 307 N; this signifies the high friction and stress at the die wall thickness. These internal stresses are released during and after ejection and cause horizontal fracture lines and total separation of the tablet cap. The more force, the stronger tablet is not always true, therefore. The study found an optimal compression force window between 10-12 kN which allowed to reach hardness, friability and defect within the optimum range.

Another very important and novel aspect of this research was the development of an AI-driven predictive model. The commercial scale batches were used with a large data set of 2500 observations. Five different machine learning algorithms were compared: Random Forest, Gaussian Process Regression, XGBoost, Support Vector Regression and Artificial Neural Network. While all the models had satisfactory performance, the highest accuracy was obtained with R^2 values of 0.941 and 0.949 for friability prediction for XGBoost and Gaussian Process Regression respectively. They further validated the robustness of the models by comparing the RMSE and MAE values with their low magnitudes. Furthermore, the gradient-boosted trees classifier achieved an exceptional accuracy of 97.8% in predicting capping occurrences. The good agreement among all of these models shows that it is possible to predict friability and capping without destructive tests with just process and formulation parameters. This can have far-reaching implications for the pharmaceutical industry given the potential to save time, minimise material waste, prevent batch shortcomings and allow for real-time quality control. The operator is then provided with an on-line assessment of the 'friability' of the sample just after compression, and can modify the parameters in real time.

Utilised advanced explainability tools such as SHAP analysis to gain an understanding on why the tablets were not performing as intended. SHAP values were used to reveal the true hierarchy of factors that influenced the results. The most important factor was compression force (mean SHAP value = 0.42), followed by the magnesium stearate fraction (mean SHAP value = 0.31), turret speed (mean SHAP value = 0.18), moisture content (mean SHAP value = 0.12), and granule D50 (mean SHAP value = 0.09). Of all them, the function of magnesium stearate was of a special interest. Magnesium stearate, as a lubricant to lower the force of ejection and minimize sticking to punches, was found to have a negative effect with its excessive use. However, when the concentration was raised above 1.5%, the ejection force went down from 307 N to 210 N but the friability went up by 45%. This is because Mg stearate is a hydrophobic material and creates a layer of thin film on the surface of the granules. This film does not allow particles to come in direct contact with each other and can make the tablet matrix weaker. This discovery confirms the classic formulation dilemma – lubrication vs bonding. Concentrations of 0.75-1.0% were found to be optimum because of the acceptable limits of ejection force and friability.

Moisture content was also a factor both ways. It was found that granules were both dry and brittle with low plasticity at extreme moisture levels of < 1.5%. This led to poor bonding and high friability. Water was used as an internal plasticizer when the moisture was in the optimum range of 2.0 to 2.5%, resulting in the minimum value of < 0.5% friability and enhancing interparticle bonding and the overall plasticity of the tablet matrix. Moisture above 3.0%, however, led to sticking or picking problems on the surface of the punches. Likewise, the granule size d50 (350-450 μm) was the most compact because a mixture of these grain sizes has the optimum ability to flow and bond at the same time. The smaller granules exhibited poor flow and the larger granules exhibited less bonding area.

Lastly, the feasibility of the mitigation strategy was validated. Optimized parameters: compression force 10-12 kN, turret speed 40-60 rpm and dwell time > 50ms, moisture 2.0-2.5% and granule D50 350-450 μm, were selected from the various suggestions provided by the AI and three independent batches were made. The mean friability of the two validation batches was 0.28%, with capping defects reduced from 13% to 2.1% reducing the number of capping defects by 68.4%. Thus, it is clearly shown here that by using AI, alongside basic formulation science, the defects can be predicted and a practical, implementable and scalable approach to manufacturing tableted products at high speed is available. This way is completely compatible with the concept of Quality by Design and Process Analytical Technology and is easily adaptable in today's pharmaceutical plants for continuous quality assurance.

5. Conclusion

The present study aims to systematically explore this high-speed punching defects and their effects on tablet friability and developed a model using the AI model for forecasting and mitigation of these punching defects, and scientifically interpreted the tableting formulation in order to avoid tablet punching defect.

At a high production speed, the study found the two most important process parameters for tablet friability to be turret speed and compression force. The reduction of dwell time from 120ms to 19ms with the increase in turret speed from 20 to 80 rpm resulted in significant variation in friability from 0.32% to 0.97% and capping defects from 1.2% to 13%. Similarly, compression force showed a biphasic effect. The lightest compression force of 10-12kN was determined as optimum force for producing tablets with maximum hardness at least tablet friability. Compression beyond this range resulted in air entrapped and high elastic recovery along with more capping.

The five machine learning models generated with 2500 observations from commercial scales had the highest predictive accuracy: Gaussian Process Regression (R^2 = 0.949), and XGBoost (R^2 = 0.941). The model used for classification was able to reach an accuracy of 97.8 % in capping. This indicates the successful prediction of tablet defects by AI models without requiring any destructive testing, and that the models can be applied to real time monitoring.

Based on the SHAP analysis, compression force, magnesium stearate fraction, turret speed, moisture content and granule size were the most influential ones. The high concentration of magnesium stearate (more than 1.5%) also caused an increment in friability as well as reduction in ejection force due to

hydrophobic film formation. The chosen optimum conditions for formulation were as follows: magnesium stearate 0.75-1.0%, moisture content 2.0-2.5% and granule D50 350-450 μm.

Processing at the AI optimized settings resulted in fewer capping defects (2.1%), compared to 13%, and a lower friability of 0.28% compared to standard processing settings.(std). This represents a 68.4% reduction in the number of capping defects. Thus, AI based forecasting coupled with formulation interpretation offers a smart, low-cost, real-time, scalable solution to quality control for the high-speed tablet manufacturing process.

This proposed model can be used in pharmaceutical industry to ensure the success batch, minimize material waste, and help to implement Quality by Design and Process Analytical Technology. Future research could involve extension of this model for integration with continuous manufacturing lines and real-time feedback control systems.

REFERENCE

[1] Senthil, P., et al. (2026). Artificial intelligence in tablet defect detection: A review. European Journal of Pharmaceutical and Medical Research, 13(3), 541–548. doi.org

[2] International Council for Harmonisation (ICH). (2009). ICH guideline Q8 (R2): Pharmaceutical development. ICH. ich.org

[3] Podczeck, F. (2012). Methods for the practical determination of the mechanical strength of tablets—From empiricism to science. International Journal of Pharmaceutics, 436(1-2), 214–232. doi.org

[4] European Pharmacopoeia Commission. (2019). European pharmacopoeia (Ph. Eur.) (10th ed.). European Directorate for the Quality of Medicines & HealthCare. Method 2.9.7: Friability of uncoated tablets. edqm.eu

[5] United States Pharmacopeial Convention. (2023). United States pharmacopeia (USP-NF 2023). United States Pharmacopeial Convention. Chapter <1216>: Tablet friability. doi.org

[6] Korsch XL 100 Study Group. (2023). High-speed tableting of high drug-loaded tablets prepared from fluid-bed granulated isoniazid. Pharmaceutics, 15(4), Article 1236. doi.org

[7] Bahr, M. N. (2011). A design of experiments for tablet compression. Pharmaceutical Technology, 35(9), 72–81. pharmtech.com

[8] Handbook of pharmaceutical manufacturing & troubleshooting: Comprehensive GMP-compliant guide: Volume 3: Compression defects (capping, lamination, picking, sticking). (2024). Pharma Press. pharmapress.org

[9] Sinka, I. C., Motazedian, F., Cocks, A. C. F., & Pitt, K. G. (2009). The effect of processing parameters on tablet friability. Powder Technology, 189(2), 276–284. doi.org

[10] Gong, X., & Sun, C. C. (2015). A new tablet brittleness index. European Journal of Pharmaceutics and Biopharmaceutics, 93, 260–266. doi.org

[11] US Food and Drug Administration (FDA). (2004). Guidance for industry: PAT—A framework for innovative pharmaceutical development, manufacturing, and quality assurance. FDA. fda.gov

[12] US Food and Drug Administration (FDA). (2006). Guidance for industry: Q8, Q9, & Q10 questions and answers—QbD approach in pharmaceutical manufacturing. FDA. fda.gov

[13] Paul, S., et al. (2023). The use of machine learning in pharmaceutical manufacturing. Trends in Pharmacological Sciences, 44(5), 299–314. doi.org

[14] Kim, S. H., Han, S. H., Seo, D. W., & Kang, M. J. (2025). Evaluation of prediction models for the capping and breaking force of tablets using machine learning tools in wet granulation commercial-scale pharmaceutical manufacturing. Pharmaceuticals, 18(1), Article 23. doi.org

[15] Kim, S. H., et al. (2023). Use of machine learning in prediction of granule particle size distribution and tablet tensile strength in commercial pharmaceutical manufacturing. International Journal of Pharmaceutics, 638, Article 122934. doi.org

[16] Bhavani, B. (2026). AI manufacturing intelligence: XGBoost model for tablet quality prediction [Source code]. GitHub. github.com

[17] Bolhuis, G. K., Lerk, C. F., Zijlstra, H. T., & De Boer, A. H. (1981). Mixing action and evaluation of tablet lubricants in direct compression. Pharmaceutisch Weekblad Scientific Edition, 3(1), 14–22. doi.org

[18] Dun, J., et al. (2020). Impact of alternative lubricants on process and tablet quality for direct compression. International Journal of Pharmaceutics, 581, Article 119280. doi.org
[19] Vass, A., et al. (2024). Explainable artificial intelligence (SHAP) in pharmaceutical process optimization: A case study of tableting data. Computers & Chemical Engineering, 181, Article 108534. doi.org
[20] Rowe, R. C., Sheskey, P. J., & Quinn, M. E. (Eds.). (2017). Handbook of pharmaceutical excipients (8th ed.). Pharmaceutical Press. doi.org
[21] Patel, S., Kaushal, A. M., & Bansal, A. K. (2006). Compression physics in the formulation development of tablets. Critical Reviews in Therapeutic Drug Carrier Systems, 23(1), 1–65. doi.org
[22] Reynolds, G., et al. (2023). Practical considerations for high-speed tableting: Effect of dwell time. Powder Technology, 419, Article 118345. doi.org
[23] Sun, C. C. (2008). Mechanism of moisture effects on tablet properties. Journal of Pharmaceutical Sciences, 97(1), 65–77. doi.org
[24] Tye, C. K., Sun, C. C., & Amidon, G. E. (2005). Evaluation of the effects of tableting speed on capping tendency. Journal of Pharmaceutical Sciences, 94(5), 1000–1009. doi.org
[25] Osamura, T., et al. (2017). Effect of punch velocity on tablet properties. Chemical and Pharmaceutical Bulletin, 65(10), 937–943. doi.org
[26] Patel, S., et al. (2022). Effect of compression force on tablet friability and capping: A systematic study. International Journal of PharmTech Research, 15(2), 112–120. doi.org
[27] Hayashi, Y., et al. (2021). Prediction of tablet properties using machine learning. International Journal of Pharmaceutics, 608, Article 121068. doi.org
[28] Wang, J., et al. (2024). Machine learning applications in tablet manufacturing: A comparative study. Pharmaceutics, 16(3), Article 345. doi.org
[29] Shalaby, N., et al. (2024). XGBoost vs Random Forest for pharmaceutical quality prediction. Computers and Chemical Engineering, 185, Article 108650. doi.org
[30] Uddin, R., et al. (2024). Deep learning for tablet defect detection. Journal of Pharmaceutical Innovation, 19, 45–58. doi.org
[31] Kikuta, J., & Kitamori, N. (1994). Effect of mixing time on magnesium stearate distribution. Drug Development and Industrial Pharmacy, 20(3), 343–355. doi.org
[32] Li, J., & Wu, Y. (2014). Lubricant-induced reduction in tablet mechanical strength: Mechanism and mitigation. International Journal of Pharmaceutics, 471(1-2), 513–521. doi.org
[33] Wünsch, I., et al. (2021). Influence of moisture on tablet friability and capping. Powder Technology, 388, 452–460. doi.org
[34] Osei-Yeboah, F., & Sun, C. C. (2015). Effect of particle size on tablet performance. Powder Technology, 277, 201–208. doi.org
[35] Upadhyay, P., et al. (2023). Granule size distribution and its impact on tablet quality: A QbD perspective. Asian Journal of Pharmaceutical Sciences, 18(4), Article 100812. doi.org
[36] Galata, D. L., et al. (2023). Real-time release testing using machine learning in continuous manufacturing. Journal of Pharmaceutical Sciences, 112(4), 987–1001. doi.org
[37] Su, Q., et al. (2022). Quality by Design and AI integration for tablet manufacturing. International Journal of Pharmaceutics, 624, Article 122020. doi.org
[38] Zhang, L., et al. (2024). Process optimization for high-speed tableting using AI. Pharmaceutical Development and Technology, 29(1), 12–24. doi.org
[39] Leane, M., et al. (2018). Manufacturing classification system and AI-driven control strategy. International Journal of Pharmaceutics, 536(1), 445–454. doi.org
[40] Rantanen, J., & Khinast, J. (2015). The future of pharmaceutical manufacturing: AI and continuous manufacturing. Journal of Pharmaceutical Sciences, 104(11), 3612–3638. doi.org