Original Research Article

Evaluation of the effect of excipient content on the physical properties of *Parkia speciosa* Hassk. tablets through regression analysis

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ABSTRACT

Parkia speciosa Hassk. boasts numerous health benefits, yet its raw consumption may be inconvenient or unpalatable for many. To date, limited research has explored the development of *Parkia speciosa* Hassk. chewable tablets. This study uses regression analysis to analyse the impact of compaction pressure and excipient compositions on the physical characteristics of these tablets. Various compositions of microcrystalline cellulose (MCC, MicroceLac® 100, Lot No.: L103155221) excipient and dried *Parkia speciosa* Hassk. powder underwent direct compaction at four compaction pressures (22.61, 37.68, 52.75, and 67.82 MPa), with friability and tensile strength measured to assess breakage resistance. The regression analyses were performed using the built-in regression analysis tools available in Microsoft Excel (Version 16.73 (23051401)). Both compaction variables significantly influenced tablet mechanical strength (p-values ≤ 0.05). Higher pressure and increased MCC excipient reduced friability, enhancing breakage resistance. The 44.11% MCC excipient formulation, compacted at 67.82 MPa, demonstrated the lowest friability and high tensile strength. The friability and tensile strength models demonstrate a strong to good fit to the data, with an R-squared value of 86.48% and 63.77%, respectively. The coefficients' findings confirm the hypothesis, indicating that increased excipient composition and compaction pressure decrease friability and enhance tensile strength. This study's findings and predictive model are useful for expedited development and optimization of *Parkia speciosa* Hassk tablet formulation.

Keywords: *Parkia speciosa* Hassk. tablet, microcrystalline cellulose, friability, compaction pressure, regression analysis

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1.0 Introduction

The development of pharmaceutical formulations seeks to harness the therapeutic potential of natural substances and enhance their accessibility and palatability for widespread consumer acceptance. One such natural ingredient, *Parkia speciosa* Hassk., is renowned for its manifold health benefits but presents a unique challenge due to its unappealing raw form, characterized by unpleasant taste and smell (1-3). Developing chewable tablets that effectively deliver the active constituents of *Parkia speciosa* Hassk. poses a key challenge, yet these tablets present advantages such as ease of administration, enhanced consumer compliance, and improved bioavailability (4).

The evaluation of tablet characteristics encompasses critical parameters such as friability and tensile strength. These metrics serve as quantitative indicators of the tablets' propensity to break under stress and their ability to withstand mechanical forces during handling and transportation. The compaction pressure, exerted during the tablet manufacturing process, is a key determinant of tablet hardness and structural integrity. The mechanical strength and breakage resistance of chewable tablets are critical attributes influencing their overall performance and consumer acceptability (5-9).

Tablet excipients, often constituting a substantial portion of the total tablet mass, exert a significant influence on various mechanical properties, such as tensile strength, fracture energy, friability, and dissolution time, which are interconnected and necessitate a meticulous approach to tablet formulation (10). Binders, disintegrants, and lubricants, among other excipients, play crucial roles in shaping these properties, requiring careful consideration of their selection and concentration to achieve tablets that are robust, durable, and effective. Striking the right balance between these mechanical characteristics poses a challenging task for pharmaceutical formulators, yet it is indispensable for ensuring the quality and efficacy of tablet medications (11,12). Moreover, the choice of excipients, particularly microcrystalline cellulose (MCC), further influences the tablet's mechanical properties, with MCC's binder and disintegrant properties significantly impacting cohesion and resistance to breakage (13,14).

This study aims to establish the statistical significance of compaction pressure and MCC composition as predictors of mechanical strength through regression analysis. The findings are anticipated to contribute valuable insights into the formulation of optimized chewable tablets, ensuring that *Parkia speciosa* Hassk. can be consumed conveniently without compromising on mechanical integrity, thus paving the way for improved therapeutic outcomes and consumer satisfaction.

2.0 Materials and Methods

2.1 Materials

Materials used in this study were: *Parkia speciosa* Hassk. (a local farmer in Nilai, Negeri Sembilan, Malaysia), MCC (MicroceLac® 100, Lot No.: L103155221, MEGGLE Pharma in Wasserburg, Germany), and mint powder (Baker & Flavourist. Kuala Lumpur, Malaysia). All materials were used as received.

2.2 Freeze-drying Parkia speciosa Hassk. seeds

Approximately 1.2 kg of *Parkia speciosa* Hassk seeds were freeze-dried at -112°C for 117 hours until they reached a constant weight with about 5% moisture content. The dried seeds were then ground into

powder using a mixer grinder (model MX-AC210S, Panasonic, Japan), sieved with a 0.6 mm mesh, and stored in amber bottles with silica gels at 25°C.

2.3 Blending and compaction

Three formulations containing 500mg *Parkia speciosa* Hassk. powder in an excipient consisting of low, medium and high concentrations of MCC (14.07%, 29.41%, or 44.11%), magnesium stearate (0.25%), and mint leaves powder (0.5%) were prepared by thoroughly dry mixed using the tumble blending technique to ensure uniform distribution. This process did not involve granulation because each tablet was individually prepared to ensure a homogenous mixture. The mixture was transferred to a cylindrical tablet die with a diameter of 13 mm. Then, the mixtures were compressed using a universal testing machine at varying pressures of 22.61 MPa, 37.68 MPa, 52.75 MPa, and 67.82 MPa (14). This process involved applying pressure to compact the mixtures into solid tablets within the die cavity. After compression, the tablets were ejected from the tablet press, ensuring proper release without any damage or deformation. These tablets were then subjected to friability and tensile strength tests.

2.4 Determination of friability

Each *Parkia speciosa* Hassk tablet was carefully weighed before undergoing the friability test. The apparatus subjected the tablets to continuous rotation at a speed of 25 rpm for 4 minutes. During the rotation, the tablets experienced repeated impacts and collisions within the apparatus, simulating the mechanical stresses encountered during handling, transportation, and packaging. After completing the test, the tablets were removed from the apparatus, and any loose fragments or debris were carefully collected. The tablets were then reweighed, and the percentage weight loss, representing the friability, was calculated using the formula [1]:

$$\frac{Initial\ Weight - Final\ Weight}{Initial\ weight} \times 100$$

2.5 Determination of tensile strength

The strength of the *Parkia speciosa* Hassk tablet was measured by applying a compressive stress, known as the Indirect Tensile test or the Brazilian test (15). The tablets were carefully positioned between two platens of the universal testing machine (model 5566, Instron, Canton MA, USA), aligning the tablet edges with the loading points. Compressive stress was applied to the tablet at a constant rate of 0.0116mm/s (16) through the upper and lower platens until the tablet fractured. During the test, the force applied, and the corresponding displacement were recorded. From these measurements, the tensile strength of the tablets was calculated using the following formula [2]:

$$Tensile\ Strength\ (\sigma) = \frac{2P}{\pi dt}$$

Where:
σ represents the tensile strength of the tablet.
P is the maximum load or force applied during the test.
d is the diameter of the tablet.
t is the thickness of the tablet.

2.6 Statistical analysis

Data analysis was performed using Microsoft Excel version 16.7. The data utilized regression analysis to assess two models: the friability model and the tensile strength model. The goodness-of-fit of the models was determined using measures such as R-squared, adjusted R-squared, and p-values.

3.0 Results

3.1 Tablet friability and tensile strength

Friability, a critical characteristic of tablet quality, is influenced by various factors, including material properties, mechanical strength, and internal structure (17). A negative relationship between friability and compaction pressure was observed, indicating that as the compaction pressure increased, the tablets became less prone to friability (Figure 1). The highest friability value of 0.97% was observed for the tablet formulation containing 14.07% MCC and compacted at 22.61 MPa. Conversely, the lowest friability value of 0.26% was obtained for the tablet formulation containing 44.11% MCC and compacted at 67.82 MPa. These findings suggest that increasing the compaction pressure and MCC concentration can improve the tablet's resistance to friability.

Considering tensile strength as an indispensable parameter (18-20), our study has elucidated that augmenting compaction pressure and MCC concentration leads to a substantial improvement in the tensile strength of the tablets (21). Figure 2 shows in terms of tensile strength, a positive relationship was identified, implying that higher compaction pressures led to increased tensile strength of the tablets. The highest tensile strength value of 0.39460 MPa was achieved for the tablet comprising 44.11% MCC and compacted at 52.75 MPa. On the other hand, the lowest tensile strength value of 0.12489 MPa was observed for the tablet formulation consisting of 29.41% MCC and compacted at 37.68 MPa. These findings suggest that increasing the compaction pressure and MCC concentration can enhance the tensile strength of the tablets.

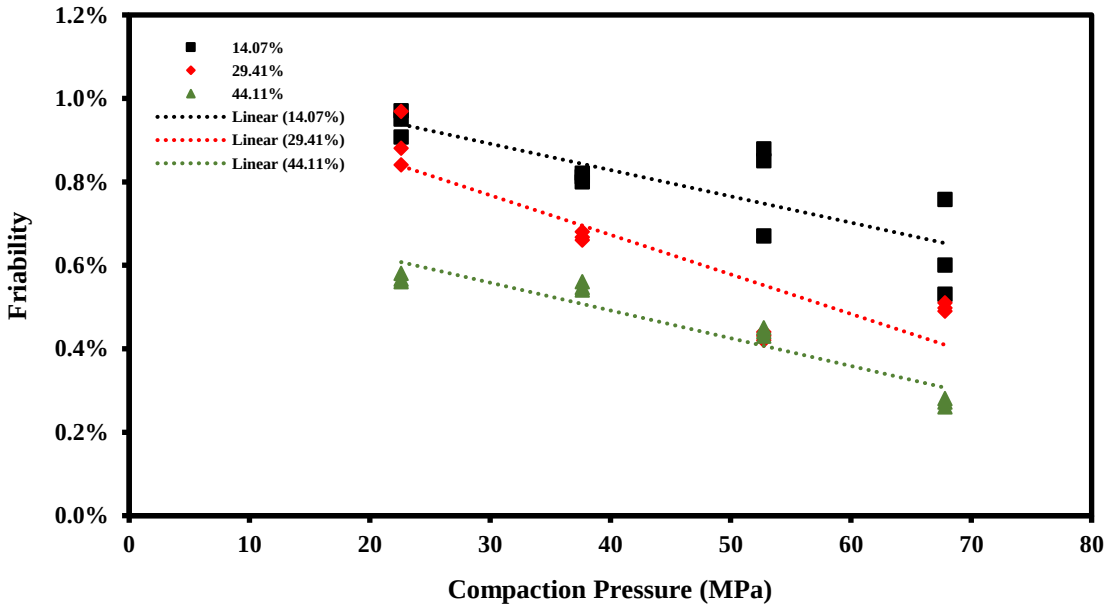

Figure 1: Friability of various *Parkia speciosa* Hassk tablet formulations

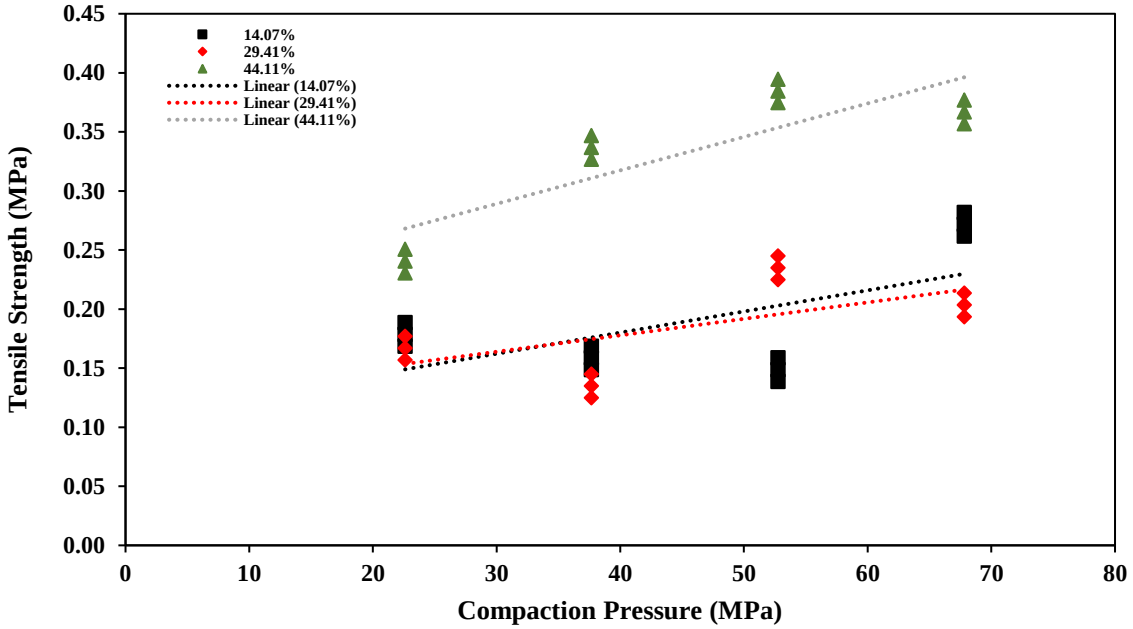

Figure 2: Tensile strength of various *Parkia speciosa* Hassk tablet formulations

3.2 Influence of excipient composition and compaction pressure on mechanical strength

In the friability model, the P-value for the constant term (Y) is extremely small, indicating a highly significant relationship between friability and the other variables. The P-values for the independent variables "X_1" and "X_2" are <0.05 suggesting that both excipient composition and compaction pressure have a significant impact on friability (Table 1). On the other hand, in the tensile model, the P-value for the dependent variable "Y" is relatively large and exceeds the conventional significance level of 0.05, indicating that there is no significant relationship between the independent variables and tensile strength. However, it is important to note that the P-values for the independent variables "X_1" and "X_2" are both very small, suggesting that both excipient composition and compaction pressure have a significant influence on tensile strength.

Based on the provided P-values, we can accept the hypothesis for the friability model as there is strong evidence of a significant relationship between excipient composition, compaction pressure, and friability. However, for the tensile model, the hypothesis is not fully supported as the P-value for the dependent variable (tensile strength) suggests no significant relationship, although the individual effects of the independent variables are significant.

Table 1: P-values of each component for the two models

	Friability Model	Tensile Strength Model
Y	4.67E-24	0.827
X_1	2.69E-12	1.76E-7
X_2	2.71E-11	5.23E-4

3.3 Friability model and tensile strength model

The results of the friability and tensile strength models indicate the quality of the regression analysis and provide insights into the relationships between the Friability Model and the Tensile Strength Model (Table 2).

The friability model demonstrates a strong fit to the data, with an R-squared value of 86.48%. This means that approximately 86.48% of the variation in the friability can be explained by the independent variables included in the model. The adjusted R-squared value of 85.66% considers the number of predictors in the model and provides a more reliable measure of the model's goodness of fit. These high R-squared values indicate that the model effectively captures the relationship between the independent variables and friability.

Similarly, the tensile strength model shows a good fit, although relatively lower than the friability model, with an R-squared value of 63.77%. This indicates that approximately 63.77% of the variation in the tensile strength can be explained by the independent variables in the model. The adjusted R-squared value of 61.58% accounts for the number of predictors and provides a more conservative estimate of the model's fit. Despite being lower than the friability model, the R-squared values still suggest a reasonable degree of explanatory power for the tensile strength model.

The standard error measures the average distance between the observed data points and the predicted values of the model. In the friability model, the standard error is 0.0008, indicating a relatively low level of dispersion between the observed and predicted values. For the tensile strength model, the standard error is 0.0527, suggesting a slightly higher level of dispersion. However, without additional context or comparison to other models, it is difficult to determine the significance of these standard error values. The significance of 0.0000 for both models indicates that both models are statistically significant. This means that the independent variables collectively have a significant impact on the dependent variable in each model.

3.4 Coefficient of models

The coefficients of models are denoted in two equations as follows:

$$Friability = -0.0113X_1 - 0.0001X_2 + 0.0129$$

$$Tensile\ strength = 0.4716X_1 + 0.0020X_2 + 0.0072$$

Where:
X_1 *represents the diluent content*
X_2 *is the compaction pressure*

Based on the friability equation, the coefficient for X_1 is -0.0113, indicating that there is a negative relationship between X_1 and friability. As the value of X_1 increases, the predicted friability value decreases. Similarly, the coefficient for X_2 is -0.0001, indicating a negative relationship between X_2 and friability. Changes in X_2 lead to corresponding changes in the predicted friability value, albeit to a lesser extent compared to X_1.

Table 2: Model Summary and ANOVA output

Metrics	Friability Model	Tensile Strength Model
R-squared	86.48%	63.77%
Adjusted R-squared	85.66%	61.58%
Standard Error	0.0008	0.0520
Significance	0.0000	0.0000

This supports the hypothesis that an increase in excipient composition and compaction pressure will lead to a decrease in friability.

The coefficient for X_1 is 0.4716, indicating a positive relationship between X_1 and tensile strength. As the value of X_1 increases, the predicted tensile strength value also increases. Similarly, the coefficient for X_2 is 0.0020, indicating a positive relationship between X_2 and tensile strength. Changes in X_2 lead to corresponding changes in the predicted tensile strength value, although to a lesser extent compared to X_1. This aligns with the hypothesis that an increase in excipient composition and compaction pressure will lead to an enhancement of tensile strength.

4.0 Discussion

Pharmaceutical factories typically employ three main methods for tablet production: direct compression, tabletting after dry granulation, and tabletting after wet granulation (22). Notably, direct compression is gaining popularity among drug manufacturers due to its cost-effectiveness and seamless production continuity (23). In the realm of direct compaction tablets, excipients play a significant role, constituting a substantial portion of the formulation. Recently, MCC can be considered the most widely used diluent in direct compression and wet granulated tablet-making procedures (13).

The post-compression properties of excipients wield considerable influence over the overall quality of the tablets. Extensive research has been conducted to unravel the intricate effects of excipients on various tablet qualities. In line with this, our recent investigation has uncovered that manipulating compaction pressure and MCC concentration plays a pivotal role in enhancing a tablet's resistance to friability. Notably, MCC has emerged as a key player, showcasing not only the hardest tablet but also exhibiting the lowest friability and the shortest disintegration time—a trifecta of tablet properties highly sought after in pharmaceutical formulations (24). The optimal concentration of MCC and compaction pressure must be balanced to achieve the desired tablet hardness while minimizing brittleness and friability (12, 25).

Our findings underscore the significant influence of compaction pressure and MCC excipient concentration on both friability and tensile strength. Interestingly, our study revealed that the highest friability was observed at the lowest and highest MCC concentrations, while the highest tensile strength was achieved at the highest MCC concentration. At the lowest MCC concentration, there is insufficient binding material, resulting in a weak tablet structure and higher friability. Conversely, at the highest MCC concentration, the tablets become excessively brittle due to strong binding properties, leading to higher friability. Both extremes in MCC concentration thus adversely affect the tablet's durability. The highest tensile strength observed at the highest MCC concentration can be attributed to the strong binding properties of MCC, which enhance cohesion and structural integrity (26, 27). These characteristics collectively contribute to the overall quality and mechanical strength of the tablets, providing a plausible justification for the study findings.

As we delve deeper into the statistical aspects of our investigation, the regression models developed for both friability and tensile strength yield valuable insights into the intricate relationships between the variables. The models exhibit robust fits, supported by high R-squared values and significant F-values. These results not only affirm the validity of the models but also underscore the substantial impact of

the chosen independent variables in elucidating variations in friability and tensile strength. Examining the coefficients in the regression equations, our findings validate the comparative hypothesis. An increase in excipient composition and compaction pressure correlates with a decrease in friability and a concurrent enhancement of tensile strength, aligning with our initial predictions.

While our study provides a comprehensive understanding of the interplay between compaction parameters and tablet properties, it opens avenues for further exploration. Future investigations may delve into additional factors and optimize excipient concentrations to fine-tune *Parkia speciosa* Hassk. tablet characteristics, ultimately contributing to the advancement of pharmaceutical tablet manufacturing processes. This holistic approach ensures a more nuanced comprehension of tablet behavior and paves the way for continued improvements in drug delivery systems.

5.0 Conclusion

The study highlights the substantial influence of compaction pressure and MCC excipient concentration on tablet friability and tensile strength of *Parkia speciosa* Hassk. tablet. While the friability model shows a strong correlation between excipient composition, compaction pressure, and friability, the tensile strength model remains partially validated, indicating a lack of a clear relationship. To fully validate the tensile strength hypothesis, future research should explore additional factors such as the type of binders and disintegrants, particle size variations, and moisture content. Further investigation into the effects of tablet shape, size, and environmental conditions like storage and transportation could provide deeper insights. Additionally, examining compression speed and interactions among excipients could refine the understanding of tensile strength in tablet formulations. These findings highlight the need for balanced excipient concentration and compaction pressure in developing robust formulations, ultimately aiming to enhance mechanical properties and improve therapeutic outcomes and patient compliance.

Authorship contribution statement

FB: Data analysis, Methodology, Formal analysis, Writing–original draft. **MSA & MZMN**: Supervision, Visualization, Methodology, Writing – review & editing.

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Conflict of Interest

The authors declared that they have no conflict of interest to disclose.

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