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Statistical Quality Control Methods and MANOVA: Evaluating Pharmaceutical Quality at Blue Nile Pharmaceutical Company in Sudan (2017-2019)

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ABSTRACT

This study evaluates the quality of products manufactured by Blue Nile Pharmaceutical Company in Sudan from 2017 to 2019 using Statistical Quality Control (SQC) tools and Multivariate Analysis of Variance (MANOVA). Samples were collected through a systematic random edge sampling method, focusing on critical quality attributes, including friability, hardness, and chemical composition across various rates and batches. The analysis demonstrated that most quality attributes were stable and met established specifications; however, concerns were identified regarding friability and hardness. MANOVA results ($P < 0.05$) revealed statistically significant differences based on test type and dosage, while no significant differences were observed between batches, indicating consistent production quality with potential variations influenced by dose and test type. This study provides a comprehensive approach to pharmaceutical quality control by effectively integrating SQC and MANOVA, enabling precise identification of process variations. The findings underscore the necessity of stringent quality control systems and regulatory frameworks to ensure product consistency and reliability in emerging markets. This approach can be adapted by pharmaceutical industries in similar contexts to enhance production quality and mitigate operational risks

Keywords: MANOVA, Pharmaceutical Quality, Quality Assurance, Six Sigma, Statistical Quality Control (SQC)

1 INTRODUCTION

Pharmaceutical quality is a cornerstone of public health, especially in developing countries where robust quality control systems are often lacking. Pharmaceutical companies, including Blue Nile Pharmaceutical Company in Sudan, face significant production challenges in maintaining consistent product quality. Although important chemicals are produced locally, variability in manufacturing processes raises concerns about the efficacy, safety, and reliability of these products. This statement is particularly important given Sudan's economic reforms and the increasing global emphasis on pharmaceutical quality standards. The review examines methods for the quantitative analysis of Glimepiride, with an emphasis on advances in HPLC and spectroscopy. It addresses challenges in

pharmaceutical research and highlights future developments such as rapid non-destructive methods. In contrast to theoretical approaches, this work combines mathematical analysis with practical applications to improve production efficiency [1]. The analysis employs an enhanced MANOVA method to control interdependent variables and reveal complex relationships. In contrast to that theory-based focus, your study applies MANOVA to practical pharmacological data, differentiating between theoretical and real-world applications by addressing Glimepiride formulations, well-being, and stability [2]. The research emphasizes Wilk's lambda in chemistry, while your work utilizes MANOVA to analyze the quality of Glimepiride, focusing on its breakdown, degradation, and stability. This approach combines statistical tools with quality assurance techniques [3]. Application of MANOVA has also been seen in pig production studies in Nigeria and environmental genetic analysis. However**,** your research specifically targets Glimepiride. quality in Sudan, employing MANOVA and quality measures to assess key drugs and improve local industry standards [4]. The QbD concept optimizes Glimepiride synthesis and its ADME properties. In contrast, your research emphasizes monitoring the quality of Glimepiride in Sudan, exploring key characteristics using MANOVA and trait monitoring strategies [5]. The review also discusses regulatory challenges and best practices to ensure safety and effectiveness. Meanwhile, your research focuses on Glimepiride quality control in Sudan, using MANOVA and quality measures to address local industry gaps and improve efficiency [6]. Lean and Six Sigma methodologies are known to increase productivity and quality in the pharmaceutical industry. In contrast, your research examines Glimepiride storage quality and addresses regional manufacturing challenges in ensuring product consistency, stability, and precision [7]. Lean Six Sigma improves the quality of clinical research. Similarly, your study uses MANOVA and control charts to tackle medical challenges in Sudan, offering practical solutions for local industry reform [8]. This study employs MANOVA and quality control charts to address pharmaceutical quality challenges in Sudan, identify key factors to enhance pharmaceutical trust, and align local practices with global standards. The assessment increases public confidence in local pharmaceuticals and strengthens the competitiveness of Sudanese industry by leveraging advanced statistical tools to ensure quality and protect public health. Utilized a robust meta-analytic approach combining fixed-effect and random-effect models based on study heterogeneity. Heterogeneity was assessed using Cochran's Q and I^2 statistics, while publication bias was evaluated to ensure data reliability. This method provided a comprehensive understanding of Glimepiride's pharmacokinetics and pharmacodynamics, contributing to evidence-based clinical recommendations with strong regional relevance [9].

2 MATERIAL AND METHODS

Several researchers have applied statistical methods to assess product quality in various industries, including pharmaceuticals [7]. Statistical Quality Control (SQC) is a widely used methodology that monitors product quality throughout the manufacturing process. In this study, we employed SQC methods and MANOVA (Multivariate Analysis of Variance) to evaluate the quality attributes of pharmaceutical products at the Blue Nile Pharmaceutical Company.

2.1 Control charts are fundamental tools in SQC

This study specifically used X-bar and R-charts to evaluate the stability of key quality characteristics, such as analysis**,** Assay, dissolution, disintegration, weight variations, friability and hardness.

2.1.1 X-bar chart

The X-bar chart monitors the mean of the process and is calculated as follows:
The middle line denoted by ($\bar{\bar{X}}$), which represents the average of the samples, and is calculated as follows:

$$\bar{\bar{X}} = \frac{\sum_{j=1}^{N} \bar{X}_j}{N} \quad (1)$$

where $\bar{\bar{X}}$ is the average sample mean, $\bar{X}$ is the average vocabulary of sample, N is the number of samples, and $j = 1, 2, \dots, N$.

The Upper Limit of control:

It is denoted by ($USC_{\bar{X}}$) and calculated by [10] as follows:

$$USC_{\bar{X}} = \bar{\bar{X}} + A_2\bar{R} \quad (2)$$

where $\bar{R}$ is average for all ranges, A_2 is factor depends on the size of the sample taken.

The Lower Limit of control:

It is denoted by ($LSC_{\bar{X}}$) and calculated as follows [11]:

$$LSC_{\bar{X}} = \bar{\bar{X}} - A_2\bar{R} \quad (3)$$

where $\bar{\bar{X}}$, $\bar{R}$, and A_2 are defined in this section.

*2.1.2 **R chart***

Monitors the mean of the process. It is used to study changes in the range of samples around their mean and denoted by (R). The range chart is drawn in the same way as the mean, and the range chart consists of:

Middle line ($\bar{R}$): It is the mean of the samples and is calculated from the relationship:

$$CL = \bar{R} = \frac{\sum_{j=i}^{N} R_j}{N} \quad (4)$$

where $\bar{R}$ is the average range of all samples, N is the number of samples, R_j is the sample range j.

$$R_j = X_L - X_S \quad (5)$$

where X_L is the largest reading of vocabulary in the sample, X_S: is the smallest reading of vocabulary in the sample.

The upper limit of control is calculated as follows:

$$UCL_R = D_4\bar{R} \quad (6)$$

The lower limit control, calculated as follows:

$$LCL_R = D_3\bar{R} \quad (7)$$

where D_3, D_4 are the Factors depend on the size of the sample taken [12].

2.2 Control Charts for Standard Deviation (*S*.chart)

The standard deviation of each sample is examined to determine the presence of an anomalous sample outside the expected range of the limits of the standard deviations in the production process. Control chart for standard deviation consists of:
The middle line: It is denoted by $\bar{S}$:

$$\bar{S} = \frac{\sum_{j=1}^{N} S_j}{N} \quad (8)$$

where $\bar{S}$ is the mean values of the standard deviations of the sample, N is the Number of samples, S_j is the sample standard deviation.

The upper limit of control:

$$\text{UCL} = \text{B}_4\bar{\text{S}} \quad (9)$$

The lower limit control:

$$\text{LCL} = \text{B}_3\bar{\text{S}} \quad (10)$$

where $\bar{S}$ is defined in equation (8), B_3, B_4: is the factors depend on the size of the sample taken [11].

2.3 Process Capability Analysis

In many cases, the process may be stable, but it does not meet the required specifications, so we resort to an analysis of the process capability.

2.3.1 Capability Indicators

It is a set of important metrics known as ability indicators, and it is used routinely in quality control and improvement programs in most organizations [12].

Process Capability indicators (C_P)

It is the allowable variation ratio for the actual variation and is calculated mathematically as follows:

$$C_P = \frac{USL - LSL}{6\sigma} \tag{11}$$

where USL is the upper specifications limit, LSL is the lower specifications limit, and σ is the true standard deviation of the process output.

In real reality, the value of the standard deviation of the process output is often unknown, so it is estimated from the sample data to validate the indicator formula as follows:

$$C_p = \frac{USL - LSL}{6\hat{\sigma}} \tag{12}$$

where $\hat{\sigma}$ is the standard deviation of the process output.

2.3.2 Capability Ratio Indicators (C_r)

It is the actual dispersion ratio of the process outputs to the permissible range and measures the process utilization percentage to the permissible specification.

Range, the relationship between the power index C_P and the ratio of the estimated C_r reverse ratio and calculated by the following formula:

$$\bar{\bar{X}} = \frac{\sum_{j=1}^{N} \bar{X}_j}{N} \tag{13}$$

$$C_r = \left(\frac{1}{C_P}\right) * 100 = \left(\frac{6\sigma}{USL-LSL}\right) * 100 \tag{14}$$

2.3.3 Capability Indicators in the Case of One-sided Specifications (C_{PU}, C_{PL})

It is one of the indicators that are used in the case of the specification for a one-way product or service by specifying either a lower or an upper value for the process output and it gives the first defect to C_P and is calculated in the following two formulas:

$$C_{PL} = \frac{\mu - LSL}{3\sigma} \quad , \quad C_{PU} = \frac{USL - \mu}{3\sigma} \tag{15}$$

where μ is the mean of the population data.

2.3.4 Estimated Capability Indicators for Decentralized Operations (C_{PK})

It is an indicator that avoids the second defect from the defects of the capability indicators, as the process may be able, but it is not decentralized, because the mean of its output is closer to one of the specifications (upper or lower). To determine the effect of the process's concentration on the ability of the process, the C_{PK} indicator is calculated, which is calculated by the following formula:

$$C_{PK} = min\left[C_{PU} = \frac{USL - \mu}{3\sigma} \ , \qquad C_{PL} = \frac{\mu - LSL}{3\sigma}\right] \tag{16}$$

$$C_{PK} = \frac{min\{USL - \mu \ , \ \mu - LSL\}}{3\sigma} = \frac{d - \{\mu - m\}}{3\sigma} \tag{17}$$

$$m = \frac{USL - LSL}{2} \ , \ d = \frac{USL - LSL}{2} \tag{18}$$

where K is the defined as one of the index indicators C_{PK} and measures the distance of the centre of the process from the target value (half the distance between the two specifications), also

$$K = \frac{|USL + LSL, 2 - \mu|}{\frac{USL - LSL}{2}} \tag{19}$$

2.3.5 Capability Indicator (C_{Pm})

It is a better scale than the C_{PK} capability scale, which is used to measure the capability of the non-decentralized operations. It is calculated by the following formula:

$$C_{PM} = \frac{USL - LSL}{\sqrt[6]{\sigma^{2(\mu - T)^2}}} = \frac{USL - LSL}{\sqrt[6]{\frac{\sum(X_i - T)^2}{N}}} \tag{20}$$

where T is the target value, which is half the distance between the specifications,

$$T = \frac{USL - LSL}{2} \tag{21}$$

Capability indicator (C_{PMK})

It is an indicator close to C_{PMK} known as the third generation and calculated as follows [12]:

$$C_{PMK} = \frac{min\{USL - \mu \ , \mu - LSL\}}{\sqrt[3]{\sigma^2 + (\mu - T)^2}} \tag{22}$$

$$C_{PmK} = \frac{d - |\mu - m|}{\sqrt[3]{\sigma^2 + (\mu - T)^2}} \tag{23}$$

2.4 Multivariate Analyses of Variance (MANOVA)

MANOVA extends univariate ANOVA to multiple dependent variables, testing the same hypothesis. Based on the number of independent variables it determines the direction(s) of the analysis.

Assumption:

1. Independence of observation.
2. Homogeneity of variance, covariance matrices.
3. Levene's Univariate tests (similar process as in ANOVA).
4. Box's M-test for covariance matrices [13].

The hypothesis is:

$$H_0: \Sigma_1 = \Sigma_2 = \cdots = \Sigma_g = \Sigma$$

H_1: At least two of the covariance matrices are not equal, where Σ_g is the covariance matrix for the e-th population $e = 1,2, \ldots, g$, and Σ: is the presumed common covariance matrix.

$$\wedge \prod_e \left(\frac{|S_e|}{|S_{pooled}|} \right)^{\frac{(n_e - 1)}{2}} \tag{24}$$

where n_e is the sample size for the eth group, S_e is the eth group sample covariance matrix, and S_{Pooled} is the pooled sample covariance matrix.

Box's test is based on his χ^2 approximation to the sample distribution of $-2\ ln \wedge$

$$\mathrm{M} = -2\ ln \wedge \tag{25}$$

where M is the Box's M statistics [14].

Normality

Check histograms and Kolmogorov-Smirnov test.
Normality and independence (Multivariate normality)

- All dependent variables should be normally distributed.
- Any linear combination of the dependent variables should be also normally distributed.

Multicollinearity of dependent variables.
Sensitivity to outliers.
The correlation matrix is an identity matrix [15].

2.4.1 Multivariate Analysis of Variance Model (MANOVA)

MANOVA model for dependent variables can be expressed by:

$$y_{ijk} = \mu + \alpha_i + \beta_j + x_{ij} + \varepsilon_{ijk} \quad (26)$$

$$for\ all\ i = 1,2,\dots,a \quad j = 1,2,\dots,b \quad k = 1,2,\dots,n$$

where α_i is the effect of the i −th level of A, P is the variables in y_{ijk}, β_j is the effect of the j −th level of B, and y_{ij} is the AB interaction effect.

The Hypothesis of MANOVA:

H_0: $\mu_1 = \mu_2 = \cdots = \mu_k$

H_1: at least two μ's are unequal

where

$$(H_0) = \begin{pmatrix} \mu_{11} \\ \mu_{12} \\ . \\ . \\ . \\ \mu_{1p} \end{pmatrix} = \begin{pmatrix} \mu_{21} \\ \mu_{22} \\ . \\ . \\ . \\ \mu_{2p} \end{pmatrix} = \cdots = \begin{pmatrix} \mu_{k1} \\ \mu_{k2} \\ . \\ . \\ . \\ \mu_{kp} \end{pmatrix} \quad (27)$$

For the Two-way MANOVA model with balanced data, the total sum of squares and products matrix is partitioned as;

$$T = H_A + H_B + H_{AB} + E \quad (28)$$

where T is the total sum of squares and cross products, H is between sum of squares and cross products, and E within sum of squares and cross products (residual). Then,

$$E = T - H_A - H_B - H_{AB} \quad (29)$$

Pillai's Trace

More robust and preferred when sample size decreases, unequal groups, or homogeneity of covariance's is violated.

$$\mathrm{v} = \sum_{\mathrm{i}=1}^{\mathrm{k}} \frac{1}{1+\lambda_{\mathrm{i}}} \quad (30)$$

where k is the number of nonzero eigenvalues of HE^{-1}, λ_i: is the i −th eigenvalue.
Pillai's test statistic is an extension of Roy's statistic.

$$\theta = \frac{\lambda_i}{1+\lambda_i} \quad (31)$$

Wilk's Lambda

Often referred to as the multivariate $F - tset$ and preferred when basic requirements (sample size, no violations, approximately equal sized groups are met). Wilk's Lambda has the virtue of being convenient and related to the likelihood ratio criterion.

$$\wedge = \frac{|E|}{|E+H|} \tag{32}$$

where ∧ Wilk's "we reject $H_0\ if\ \wedge \leq \wedge_{\alpha,P,vH,vE}$", P is the number of variables (dimension), vH is the degree of freedom for hypothesis, vE is the degrees of freedom for error.

Properties and characteristics of Wilk's

- In order for the determinants to be positive, it is necessary that,vE ≥ P.
- For any MANOVA model, the degrees of freedom vH & vE are always the same.
- The parameters P & vH can be interchanged. The distribution of $\bigwedge_{\mathrm{P,vH,vE}}$ is the same as that of $\bigwedge_{\mathrm{vH,P,vE,vH-P}}$.
- This Wilk's$\wedge = \frac{|\mathrm{E}|}{|\mathrm{E+H}|}$ can be expressed in terms of the eigenvalues [15].

$$\lambda_1, \lambda_2, \ldots, \lambda_{\mathrm{k}} \text{ of } \mathrm{E}^{-1}\mathrm{H}$$

$$\wedge = \prod_{i=1}^{k} \frac{1}{1+\lambda_i} \tag{33}$$

- The range of $\Lambda\ is\ 0 \leq \wedge \leq 1$ [15].

Roy's

Most appropriate when dependent variables are strongly interrelated on one dimension. Strongly affected by violations of assumptions.

$$\theta = \frac{\lambda_1}{1+\lambda_1} \tag{34}$$

we reject $H_0 : \mu_1 = \mu_2 = \cdots = \mu_k\ \ if\ \theta \geq\ \theta_{\alpha,k,m,N}$

where k is min(P, vH),m is $\min\frac{1}{2}(|\mathrm{vH} - \mathrm{P}| - 1)$, N is $\min\frac{1}{2}(\mathrm{vE} - \mathrm{P} - 1)$, and λ_1: is the largest eigenvalues.

Hotelling's $\mathbf{T^2}$

Similar to Wilk's more robust and preferred when sample size decreases, unequal groups, or homogeneity of covariance's is violated. Also known as Hotelling's generalized T^2 – statistic [13] is given as

$$\mathrm{T} = \sum_{\mathrm{i=1}}^{\mathrm{k}} \lambda_{\mathrm{i}} \tag{35}$$

3 RESULTS AND DISCUSSION

This section presents the findings of the quality control charts and process capability analysis of the pharmaceutical tablets (Amax) evaluated in this study. The focus is on various quality parameters, including assay, dissolution, disintegration, weight variation, hardness, and friability.

3.1 Quality Control Charts

3.1.1 Dissolution of the Active Substance

- **X-bar chart of Amax 1mg, 2mg, 3mg, 4mg Dissolution**
  Figure 1(a) shows six data points exceeding the upper control limit, indicating system instability and invalidity of the reactive component. The operations manager must analyze the root cause and implement corrective actions to restore stable and efficiency in production.
- **R chart of the Amax 1mg, 2mg, 3mg, 4mg Dissolution**
  Figure 1(b) presents an R-chart for monitoring the dissolution of the active ingredient in widely used diabetes medications. Examination of this chart shows that the simulation process is statistically stable, with all data points within the established control limits, indicating that the process is under statistical control.
- **S chart of the Amax 1mg, 2mg, 3mg, 4mg Dissolution**
  In Figure 1(c), Sample 27 exceeds the upper control limit, indicating that the method is out of control. The operations manager must investigate the cause and implement corrective actions to ensure that quality standards are met.

3.1.2 Disintegration of the Active Substance

- **X-Bar chart of Amax 1mg, 2mg, 3mg, 4mg Disintegration**
  Figure 1(d) shows two examples exceeding the upper limit (1-7) and three examples below the lower limit (10-11-22) for the disintegration of the active ingredient. This indicates that the process is out of control and requires immediate corrective action to restore stability.
- **R Chart of Amax 1mg, 2mg, 3mg, 4mg Disintegration**

Figure 1(e) shows the R - Chart for controlling the Disintegration of active substance for high diabetes tablets. The chart indicates that the process is under control.

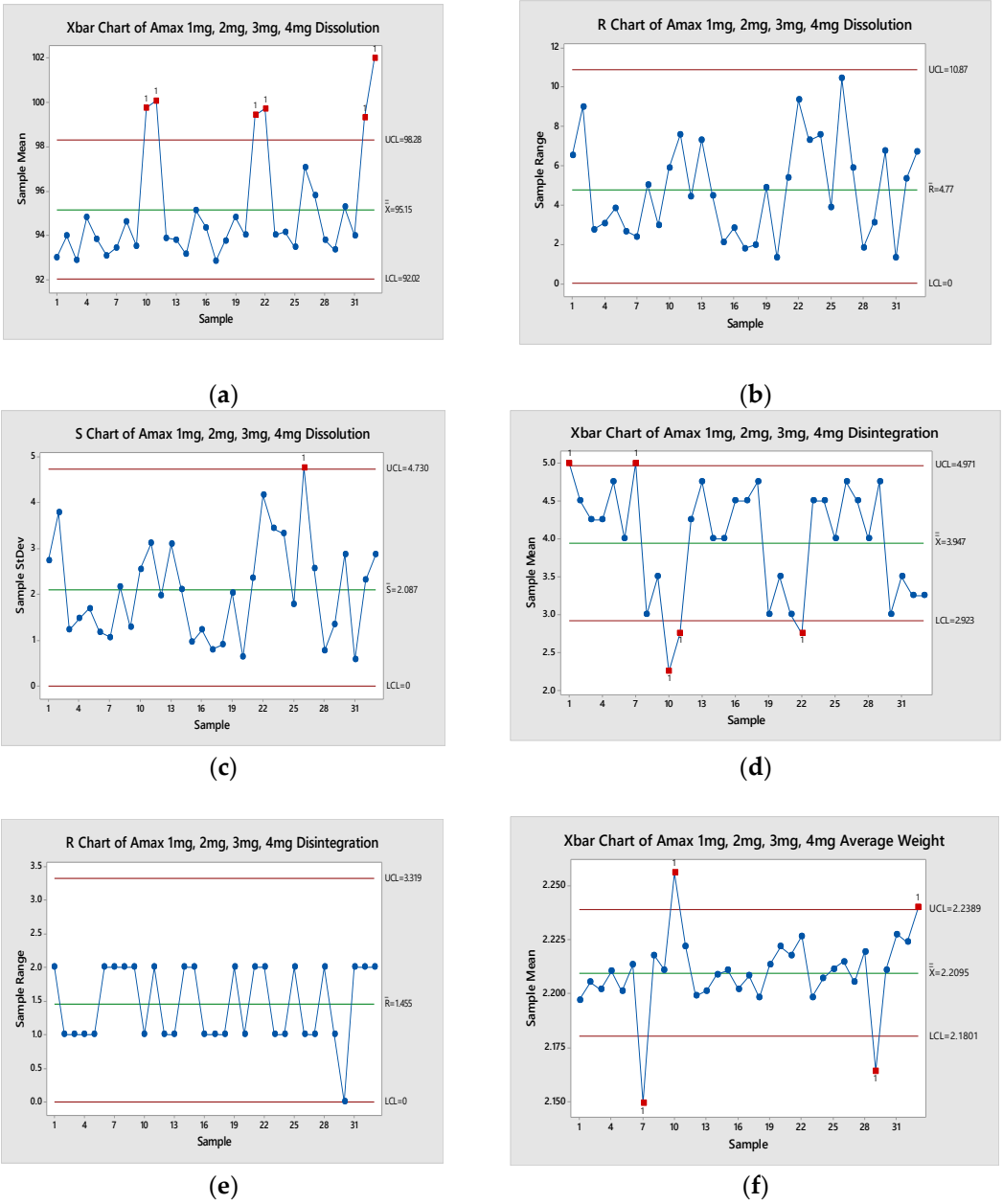


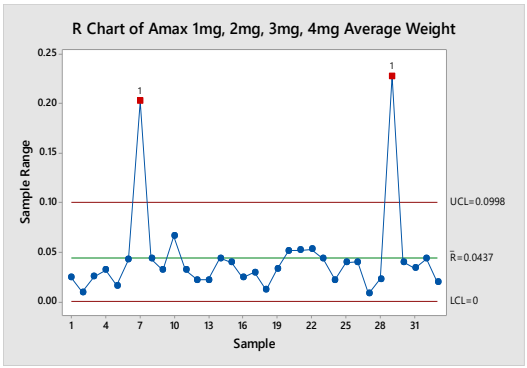
Figure 1: The Amax 1mg, 2mg, 3mg, 4mg for: (a) X-bar Dissolution; (b) R-chart Dissolution; (c) S-chart Dissolution; (d) X-bar Disintegration; (e) R-chart Disintegration; (f) X-bar Weight.

3.1.3 Weight Variation of the Active Substance

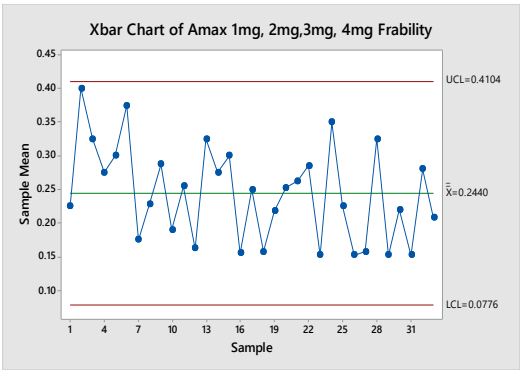
- **X-Bar of Amax 1mg, 2mg, 3mg, 4mg Average Weight**

  Figure 1(f) shows two samples exceeding the upper limit (10-33) and two falling below the lower limit (7-29) for the average weight of the high diabetes tablets. This indicates that the operation is out of control, and immediate corrective actions are needed to meet the standards.

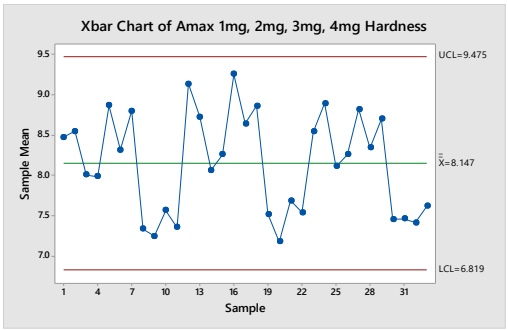
- **R Chart of Average Weight**
  The R-chart shows that two sample points exceed the upper control limit (7-29) for the average active ingredient with sugar a weight of the mouthpiece (Figure 2(a)). This reversal indicates that the process has completed control and needs corrective action to restore stability.



(**a**)



(**b**)



(**c**)

Figure 2: The Amax 1mg, 2mg, 3mg, 4mg for: (a) R-chart Average Weight; (b) X-bar Friability; (c) X-bar Hardness.

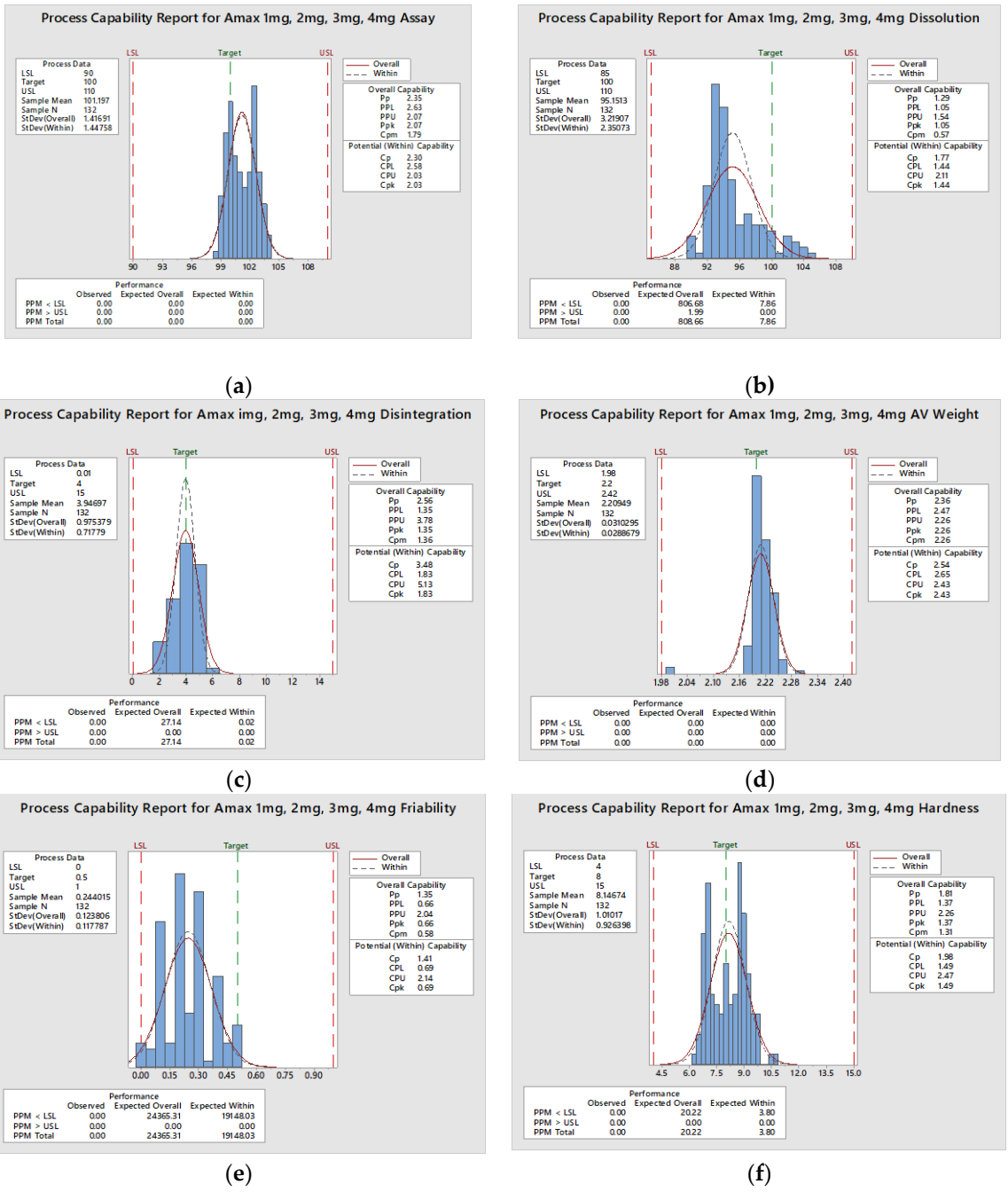


Figure 3: Process Capability Report for Amax 1mg, 2mg, 3mg, 4mg based on: (a) Assay; (b) Dissolution; (c) Disintegration; (d) Average Weight; (e) Friability; (f) Hardness.

3.1.4 Friability and Hardness of the Active Substance

- **Friability of the Active Substance**
  Figure 2(b) shows the X-bar chart for controlling the friability of the active substance in high diabetes tablets. The chart indicates that the process is under control.

Hardness of the Active Substance

Figure 2(c) shows the X-bar chart for controlling the hardness of the active substance in high diabetes tablets. The chart indicates that the process is under control.

3.2 Process Capability Analysis

The process capability was evaluated using CP,Cpk and Cpm indices to determine the extent to which the production process meets specified quality standards.

3.2.1 Assay of Active Substance

Figure 3(a) shows that the Cp value is 2.30, indicating sufficient potency in the diabetic compounds. However, the target of 101.197 differs from the expected 100, suggesting a lack of focus. The Cpk value of 2.03, exceeding the benchmark of 1, shows the process is capable. Additionally, the Cpm value of 1.79 indicates that the process is centered and reliable.

3.2.2 Dissolution of the Active Substance

Figure 3(b) shows that the Cp value of 1.77 indicates sufficient potential to meet required data, but the process is not centered. The Cpk value of 1.44 confirms the process meets specifications, while the Cpm value of 0.57 suggests a concentration limitation. This highlights the need for flexibility to improve focus while maintaining quality standards.

3.2.3 Disintegration of the Active Substance

The process capability index (Cp) for the disintegration of the active ingredient in high-diabetes tablets is 3.48, indicating strong capability to meet specifications. However, the target value of 4 differs from the process mean of 3.947, suggesting a lack of centering. The adjusted Cpk value of 1.83 confirms the process's ability to produce within specification limits, while the Cpm value of 1.36 highlights the need for centering improvements (Figure 3(c)). These results validate the process's robustness and the importance of improving centering for optimal performance.

3.2.4 Weight Variation of the Active Substance

Figure 3(d) shows that the process capacity index (Cp) for the average weight of the high-diabetes tablets is 2.54, indicating the process is well-centered and capable of meeting demand. The adjusted Cpk value of 2.43 confirms production within specification limits, while the Cpm value of 2.26 supports process stability and adherence to quality standards.

3.2.5 Friability of the Active Substance

Figure 3(e) shows that the Cp for the friability of high-diabetes tablets is 1.41, indicating sufficient capacity to meet specifications. However, the process is not centered, with a Cpk of 0.69 and a Cpm of 0.58, highlighting the need for system improvements to ensure quality compliance.

3.2.6 Hardness of the Active Substance

Figure 3(f) shows that the process capability index (Cp = 1.98) confirms sufficient capacity for the hardness of the active ingredient in high-diabetes tablets. However, the target value (8) differs from the mean (8.14674), indicating a lack of centering. The adjusted index (Cpk = 1.49) and performance index (Cpm = 1.31) confirm the process's capability and alignment with quality standards.

4 MULTIVARIATE ANALYSIS OF VARIANCE (MANOVA)

This section summarizes the MANOVA findings on factors affecting Glimepiride tablet quality attributes, including dosage, dissolution, weight variation, hardness, friability, and assay.

4.1 Assumptions for MANOVA

Before conducting the MANOVA, several assumptions were tested to ensure the validity of the results.

- **Normality**

The Shapiro-Wilk test confirmed multivariate normality for dissolution, weight variation, hardness, and assay (p-values > 0.05). Figure 4 shows no significant deviation from normality, confirming the assumption is met.

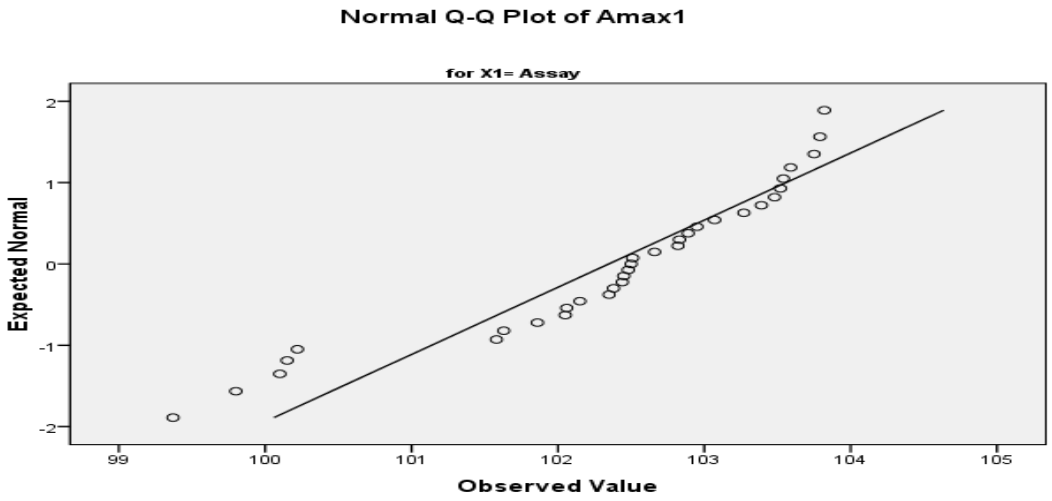


Figure 4: Normal Q-Q Plot of Amax1

- **Absence of Multicollinearity**

The Variance Inflation Factor (VIF) for each dependent variable was less than 10, indicating no issues with multicollinearity between the variables. Therefore, this assumption is also satisfied (Table 1).

Table 1: Multicollinearity

Variables	VIF	Tolerance
X_1	1.000	1.000
X_2	1.000	1.000

4.2 Hypotheses Tested

The MANOVA was performed to assess the effects of two independent factors, type of tests (X_1) and batch type (X_2), on the dependent variables: dissolution, weight variation, hardness, friability, and assay across different dosages (1 mg to 4 mg). The following hypotheses were tested:

- **H_0**: There is no significant effect of the independent factors on the quality attributes of Amax tablets.
- **H_1**: There is a significant effect of at least one independent factor on the quality

➢ **Pillai's Trace Test**

Table 2 showed the results of the overall significance test of the model indicate that the type of tests performed (X_1) had a significant effect on the doses of the active substance (Pillai's Trace, **$p < 0.001$),** while the type of batches (X_2) did not have a significant effect (**$p = 0.489$**).

Table 2: Pillai's Trace Test

Independent variables	Statistic test Pillai's Trace	F	P. Value
X_1	0.000	31.160	0.000
X_2	0.039	0.933	0.489

➢ **Wilk's Lambda Test**

Table 3 showed the Wilk's Lambda test shows that the type of test (X_1) significantly affects the doses of the active substance ($p < 0.001$), while the type of batches (X_2) is not significant ($p = 0.488$).

Table 3: Wilk's Lambda Test

Independent variables	Statistic test Wilk's Lambda	F	P. Value
X_1	0.000	398.645	0.000
X_2	0.961	0.934	0.488

➢ **Hotelling's Trace Tests**

Hotelling's Trace and Roy's Largest Root tests confirmed the significant results for the type of tests (X_1) but not for the type of batches (X_2) as shown in Table 4.

Table 4: Hotelling's Trace Tests

Independent variables	Statistic test Hotelling's Trace	F	P. Value
X_1	0.000	0.00016	0.000
X_2	0.040	0.936	0.487

- **Roy's Largest Root Tests**
  Roy's Largest Root tests confirmed the significant results for the type of tests (X_1) but not for the type of batches (X_2) as shown in Table 5.

Table 5: Roy's Largest Root Tests

Independent variables	Statistic test Roy's Largest Root	F	P. Value
X_1	0.000	0.00067	0.000
X_2	0.037	1.724	0.146

4.3 Univariate Results

Univariate analysis was conducted to further explore the effect of each independent variable on individual dependent variables.

4.3.1 Type of Tests (X_1)

The type of tests (X_1) had a significant effect on the doses of the active substance for all Amax tablet doses (1 mg, 2 mg, 3 mg, and 4 mg) as shown in Table 6**.**

Table 6: Type of Tests

Dependent Variable	F-Value	F
Amax 1 mg (Y_1)	48100	0.000
Amax 2 mg (Y_2)	33090	0.000
Amax 3 mg (Y_3)	37810	0.000
Amax 4 mg (Y_4)	47320	0.000

4.3.2 Type of Batches (X_2)

The type of batches (X_2) did not show a significant effect on any dose of the active substance as shown in Table 7.

Table 7: Type of Batches

Dependent Variable	F-Value	F
Amax 1 mg (Y_1)	0.043	0.958
Amax 2 mg (Y_2)	1.508	0.224
Amax 3 mg (Y_3)	0.134	0.874
Amax 4 mg (Y_4)	0.344	0.709

*4.3.3 **Interaction Effect***

The interaction between the type of tests (X_1) and the type of batches (X_2) was not significant for any of the dependent variables as shown in Table 8.

Table 8: Interaction Effect

Independent variables	Statistic test	F	P. Value
Reciprocal influence ($X_1 * X_2$)	Pillai's Trace	0.746	0.875
Reciprocal influence (X1*X2)	Wilk's Lambda	0.748	0.873

5 CONCLUSION

The main objective of this study was to evaluate the diabetes medication (Glimepiride) produced by Blue Nile Pharmaceutical Company in Sudan using advanced statistical controls, particularly Statistical Quality Control (SQC) and Multivariate Analysis of Variance (MANOVA). This study demonstrates the application of these sophisticated techniques to assess the fundamental properties of the drugs (2019). Key findings of the study show that while dynamic testing results for all doses were stable, some characteristics indicated control issues, even though other parameters like range and standard deviation remained consistent. Hardness and friability were within acceptable limits. The production capacity analyses (Cpm, Cpk, and Cp) confirmed that production met required quality specifications. Statistically significant differences were found between test types and active substance doses, but no differences were observed between batch types, nor was there an interaction between test type and batch type.

This study provides a robust statistical framework for quality assurance in the Sudanese pharmaceutical industry, emphasizing the importance of quality control measures. It integrates SQC and MANOVA to monitor and enhance production processes. However, the study is limited by the scope, as only one manufacturer was investigated. Further research should include more manufacturers and drug types. It also suggests adopting more comprehensive testing protocols in the future.

In conclusion, the study advocates for the use of advanced statistical tools in pharmaceutical quality control. It recommends that pharmaceutical companies in Sudan and other developing countries adopt similar auditing methods to ensure product safety and effectiveness, which would enhance the competitiveness of the Sudanese pharmaceutical industry. Future research could explore the broader use of SQC and MANOVA, incorporating methods like real-time machine learning monitoring and studying the impact of external factors on product development and policy.

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