Correlation and Regression Analysis between Agronomic and Quality Attributes of Apple (*Malus × domestica* Borkh.) cv. Anna

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Authors' contributions

This work was carried out in collaboration among all authors. Authors MLJ and GSR designed the study and wrote the protocol. Authors SB and JSS managed the literature searches, performed the statistical analysis. Authors RKJ, RM and SK managed the analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

Aim: To assessed the relationships between fruit yield and various growth, yield, fruit quality attributes and leaf nutrient content of apple cultivar "Anna" using Pearson correlation coefficients (r) and coefficients of determination (r²).

Place and Duration of Study: A field experiment was conducted during two consecutive year 2020-21 and 2021-22 at Horticulture Farm (PFDC), Department of Horticulture, CCS Haryana Agricultural University, Hisar, Haryana.

Study Design and Methodology: The 19 treatments in study consists various nutrients and organic substances sources with replicated thrice and laid out in randomized block design. Various plant growth, yield and quality attributes and leaf nutrient content were recorded with the using standard producers.

Results: The Significant positive correlations were observed between yield and attributes such as plant height, plant spread, leaf area, trunk girth and days taken for flowering after spray. Among these attributes the days taken for flowering after spray (r = 0.992) had the strongest positive correlation with fruit yield. Regression equations were derived to predict yield based on these agronomic and quality attributes. The results indicated that number of flower buds, flowering duration and fruit set play significant role in determining yield, and the corresponding equations offer a framework for predicting yield outcomes. Additionally, fruit quality attributes such as total soluble solids, titratable acidity, total sugars, total phenol content, total anthocyanin content and total carbohydrate content were positively correlated with fruit yield. The strongest correlation was with total carbohydrate content (r = 0.921). Leaf nutrient variables, including nitrogen, zinc, boron, iron and manganese, exhibited weaker correlations with yield, suggesting that while important for overall plant health, they have less direct influence on yield outcomes.

Conclusion: Overall, this analysis highlights the complex interplay between growth, yield and fruit quality attributes in determining the yield of apple cultivar "Anna".

1. INTRODUCTION

Apple (*Malus × domestica* Borkh.) is one of the most widely cultivated and economically significant fruit crop in the world. Its cultivation has a diverse range of climates and soil types, making it a vital component of agricultural systems in many countries [1]. It was regarded as a crop for temperate regions in the past but its cultivation is now increasing in sub-tropical and tropical climates. "Anna" is a cultivar of domesticated apples that is suitable for cultivation in warm climate [2]. Among the many "Anna" apple has gained prominence due to its adaptability and desirable fruit characteristics, such as firmness, sweetness and color. Despite its advantages, optimizing yield in cv. Anna remains a challenge that requires a deeper understanding of the factors influencing its productivity [3]. Yield is a multifaceted attribute influenced by a complex interplay of growth characteristics, fruit quality parameters and nutrient availability [4]. In apple cultivation, growth attributes such as plant height, spread, leaf area and trunk girth are significantly affecting overall productivity. However, their direct impact on yield can vary and their interactions with other variables are not always well understood. Similarly, yield attributes including flowering dynamics, fruit set, fruit size and fruit weight play crucial roles in determining the final fruit yield [5]. The relationships between these attributes and yield are often intricate and influenced by various physiological and environmental factors. Recent research has highlighted the significance of fruit quality parameters in yield determination. Total soluble solids (TSS), titratable acidity (TA), total sugars (TS), total phenol content (TPC), total anthocyanin content (TAC) and total carbohydrate content (TCC) are critical indicators of fruit quality that also correlate with fruit yield. High levels of these quality attributes often reflect improved fruit development and maturity, which can contribute to higher yields. Leaf nutrient content is another important factor influencing apple fruit yield. Nutrients such as nitrogen (N), zinc (Zn), boron (B), iron (Fe) and manganese (Mn) are essential for various physiological processes in apple tree. Nitrogen, for instance, is crucial for vegetative growth and overall plant vigor, while micronutrients like zinc and boron play roles in enzyme function and fruit development [6, 7]. Understanding how these nutrients impact yield can provide valuable

insights into nutrient management practices that enhance productivity.

The objective of this study is to investigate the relationships between yield and various growth, yield and quality parameters, and leaf nutrient content in apple cv. Anna. The use of Pearson correlation coefficients and linear regression analysis in this research aims to elucidate how these factors interact to influence yield. Specifically, the study seeks to, assess the strength and direction of correlations between yield and various growth and yield attributes, fruit quality parameters, and leaf nutrients. This will help identify which variables are most strongly associated with yield and provide insights into their relative importance. Use linear regression analysis to derive equations that describe the relationships between yield and significant attributes. These models will offer practical tools for predicting yield based on specific growth, yield and quality parameters. Explore the complex interactions between different attributes and their combined effects on yield. This includes examining how growth attributes interact with fruit quality parameters and nutrient content to impact overall productivity.

2. MATERIALS AND METHODS

2.1 Description of the Study Area

The experiment was carried out at Horticulture Farm (PFDC), Department of Horticulture, CCS Haryana Agricultural University, Hisar, Haryana on "Anna" apple during two consecutive years *i.e.* 2020–21 and 2021–22. The experiment site is situated at 215.2 m above mean sea level with coordinates of 29° 10′ N latitude and 75° 46′ E longitude. The soil of the study area belongs to the order Entisol a series of sandy loam soils with a pH range of 6.5 to 7.2 with high organic matter and good water holding capacity.

2.2 Experimental Design and Treatment Details

The low chill apple cultivar 'Anna' was used during the experimentation. The treatments in the trial comprised various nutrients and organic substances sources and consists nineteen treatments with replicated thrice and laid out in randomized block design *viz.*, T_0 – Control, T_1- 1% Urea (N) + 2% Humic acid, T_2- 1.5% Urea (N) + 3% Humic acid, T_3- 2.0% Urea (N) + 4% Humic acid, T_4- 200 ppm Boron + 2% Humic acid, T_5- 300 ppm Boron + 3% Humic acid, T_6-

400 ppm Boron + 4% Humic acid, T_7- 200 ppm Zinc + 2% Humic acid, T_8- 400 ppm Zinc + 3% Humic acid, T_9- 600 ppm Zinc + 4% Humic acid, T_{10}- 1.0% Urea (N) + 5% Cow urine, T_{11} -1.5% Urea (N) + 10% Cow urine, T_{12} -2.0% Urea (N) + 15% Cow urine, T_{13} -200 ppm Boron + 5% Cow urine, T_{14} -300 ppm Boron + 10% Cow urine, T_{15}- 400 ppm Boron + 15% Cow urine, T_{16}- 200 ppm Zinc + 5% Cow urine, T_{17}- 400 ppm Zinc + 10% Cow urine and T_{18}- 600 ppm Zinc + 15% Cow urine. The foliar application of nitrogen, zinc and boron with the source of urea, borax and zinc monohydrate, respectively, whereas, humic acid and cow urine were applied directly in liquid form. Foliar spray was done three times at last week of November, 2nd week of February and 3rd week of March in each year during the investigation.

2.3 Evaluation of Various Fruit Attributes

The growth parameters i.e., plant height (m), spread (m), leaf area (cm) and trunk girth (cm) were measured during 3rd week of November and 4th week of June. Whereas, the flowering parameters i.e., days taken for flowering, number of flower bud, flowering duration (days) and fruit set (%) were observed during the period of February to April and fruit parameters, *viz.*, fruit diameter (cm), weight (g), number of fruits and yield (kg/ plant) were recorded after harvesting from last week of June to 2nd week of July. Fruit firmness was measured with the help of Effegi hand-held penetrometer (Facchini, Alfonsine, Italy) driving an Effegi probe with a convex tip into whole fruit and expressed in kg per cm^2. Total soluble solids of the fruit juice were estimated with the use of Erma- Hand refractometer and expressed in °Brix. Titratable acidity was analysed based on neutralization (NaOH 0.1 N) to pH 8.1 using phenolphthalein (1–2 drops) as an indicator and values were expressed as per cent malic acid [8]. Total sugars content (%) of fruit juice was determined as per the Lane and Eynon method [8]. The total phenol content (TPC) was quantified according to the Folin Ciocalteu method and expressed in mg GAE per g FW [9] and total anthocyanin content (TAC) in fruits analysed using UV–visible spectrophotometer Cary 300 UV/Vis spectrophotometer and note in mg per 100g. Total carbohydrate content (TCC) was determined calorimetrically by using phenol sulphuric acid reagent and expressed in mg per g [10]. The starch-iodine chart was used to determine fruit maturity, with a starch index ranging from 1 (immature) to 9 (over mature) [11]. Total nitrogen (%) in leaves was calculated

using Micro- Kjeldhal's as proposed by Jackson [12], and the results were expressed as a percentage of nitrogen by dry weight. A sequential emission spectrometer with an inductively coupled plasma (ICP Perkin-Elmer model Optima 2000 DV, Boston, MA, USA) was used to measure the micronutrients (B, Zn, Fe, and Mn). The wavelengths of the chosen elements were identified [13].

2.4 Data Analysis

The Pearson correlation coefficient (r) was used to calculate the straightforward association between yield and various agronomic and quality parameters. The MS-Office Excel software was utilized to compute the simple correlation matrix as described by Snedecor and Cochran [14]. Simple linear regression (SLR) is one of the statistical methods which attempts to model the relationship between one interpretive variable (independent) and a response variable (dependent) by fitting a linear equation into the observed data [15]. The model for SLR is:

$$Y = \beta_o + \beta_1 X + \epsilon$$

Where, *Y* is the dependent variable; *X* is the independent variable; β_0 is an intercept (the value of Y when X=0); β_1 is the slope of the regression line (the change in Y for a one-unit change in X); ϵ is the error term and used SPSS ver. 15 (Cary, NC., USA) to calculate the simple linear regression.

3. RESULTS AND DISCUSSION

3.1 Relationship in Fruit Yield with Growth and Yield Attributes

Pearson correlation coefficients (r) and coefficients of determination (r²) were calculated to assess the relationships between subjective dependent variables (Yield) and independent variables (growth and yield attributes) of apple cv. Anna (Table 1). Significant correlations were observed between yield (kg tree⁻¹) and growth and yield attributes. The strongest positive correlation was found between yield and days taken for flowering after spray (0.992). While, variables such as number of flower buds (0.968), flowering duration (0.982), fruit set (0.961), fruit diameter (0.941), fruit weight (0.983), number of fruits (0.975) and fruit firmness (0.902) exhibited highly positive correlations with yield. Plant spread (0.160), plant height (0.204), leaf area (0.255) and trunk girth (0.271) showed low positive correlations with fruit yield.

The coefficients of determination (r²) for relationships between various growth and yield attributes range from 0.026 to 0.983, indicating low to high level of explanation for the variation by yield. Linear regression equations were derived for variables showing significant correlations with yield. The relationship between yield (Y) and days taken for flowering after spray (DTF) was described by the equation *i.e.*, Y = -0.1672x + 22.984, for number of flower bud by Y = 0.073x - 5.7371, for flowering duration by Y = 0.2119x + 3.1955, for fruit set by Y = 0.6389x - 1.3035, for fruit diameter by Y = 3.0641x - 7.9688, for fruit weight by Y = 0.1013x - 7.0411, number of fruits by Y = 0.3401x - 10.267, and for fruit firmness by Y = 0.9549x - 0.5578. Overall, the findings highlighted the complex interplay between growth and yield attributes and yield in apple cv. Anna, underscoring the importance of these attributes in determining fruit yield. The analysis of the relationships between yield and various growth and yield attributes in apple cv. Anna reveals a nuanced and multifaceted interaction among these variables. The Pearson correlation coefficients (r) indicated that several growth and yield attributes have significant correlations with yield, though the strength of these correlations varies. The low positive correlations observed between yield and attributes such as plant height, plant spread, leaf area and trunk girth suggested that these factors contribute to yield but lower in direct manner. These attributes, while important for overall plant vigor, might influence yield through more complex mechanisms, possibly interacting with other environmental and physiological factors that were not captured in this analysis.

The strongest positive correlation was found between yield and the number of days taken for flowering after spray highlighted the critical role of timely flowering in maximizing yield. This strong relationship suggested that optimizing the timing of flowering through management practices could be a significant strategy for improving yield in apple cultivar "Anna". Similarly, the number of flower buds, flowering duration, fruit set, fruit diameter, fruit weight, number of fruits and fruit firmness exhibited highly positive correlated with yield, showed their importance in the determination of overall yield. The wide range of coefficients of determination (r²) indicated varying levels of explanation for the variation in yield by the different attributes. However, the r² value for the relationship between yield and days taken for flowering after spray suggested that nearly 98.3% of the variation in yield can be

determined by this single attribute showed its major role. While, the lower r² values for other attributes imply that while these factors are important, they might not independently explain a significant portion of the yield variation. The linear regression equations derived for each variable provide a mathematical framework to predict yield based on specific growth and yield attributes. These equations suggest potential avenues for targeted interventions in apple orchard management. The equation Y = -0.1672x + 22.984 for days taken for flowering after spray can be used to forecast yield changes based on variations in this critical period. Similarly, the equations for other variables offer valuable predictive insights that could be used to fine-tune agronomic practices aimed at maximizing yield. Similar findings were reported by Sarkar et al. [16] and Fotirić Akšić et al. [17] in apple and Mahmoud et al. [18] in both Hollywood plum and apple.

3.2 Relationship in Fruit Yield with Fruit Quality and Leaf Nutrients

The relationships between yield and various fruit quality and leaf nutrient variables of apple cultivar "Anna" were evaluated through Pearson correlation coefficients (r), coefficients of determination (r²) and linear regression analysis as presented in Table 2. Significant positive correlations were observed between yield and total soluble solids (TSS), titratable acidity (TA), total sugar (TS), total phenol content (TPC), total
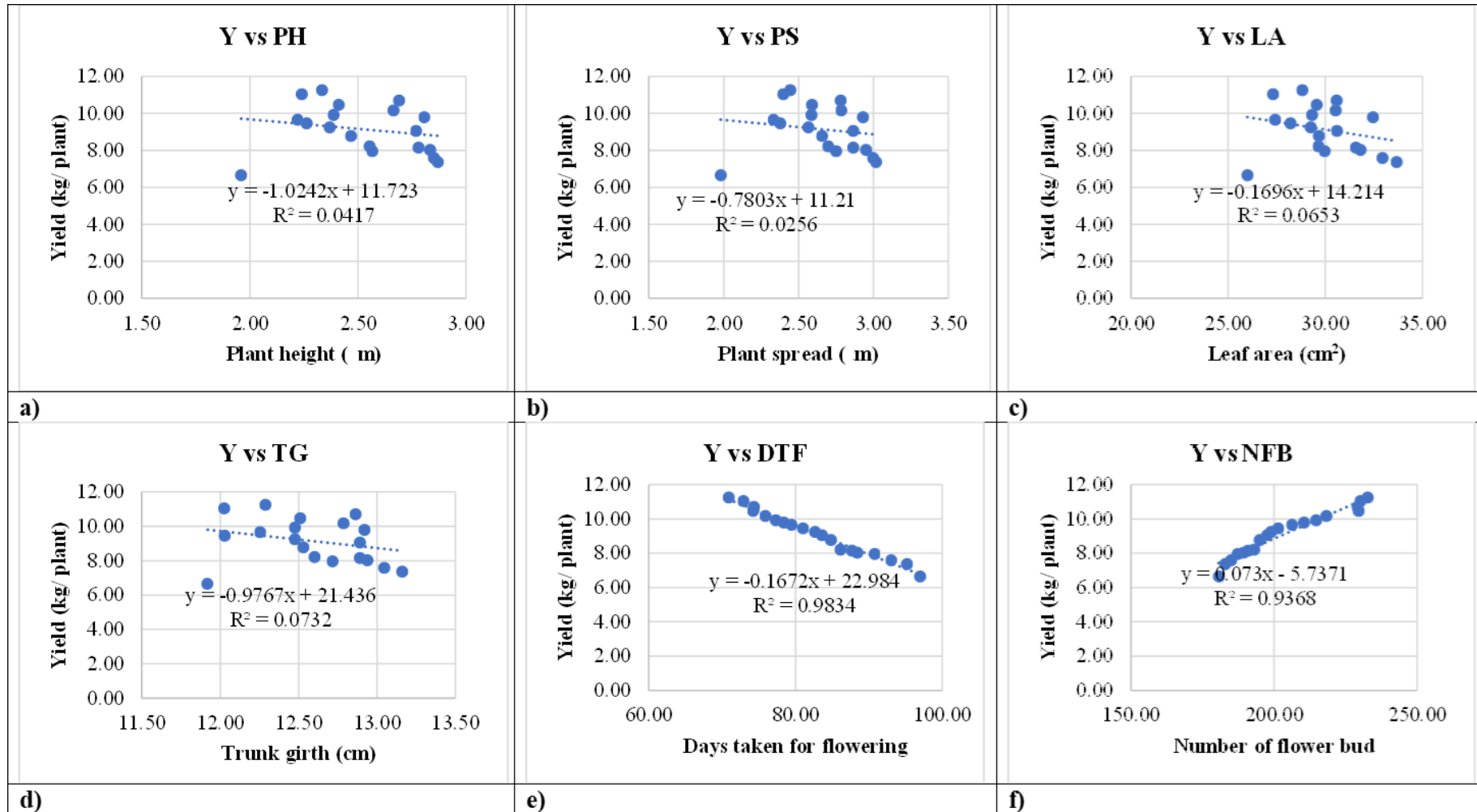
anthocyanin content (TAC) and total carbohydrate content (TCC). These attributes showed high correlation coefficients ranging from 0.775 to 0.921, with coefficients of determination (r²) between 0.600 and 0.848. The yield was showed strongest significant positive correlation with total carbohydrate content with the value of r = 0.921 and r² = 0.848 and regression equation Y = 0.2159x - 22.143.
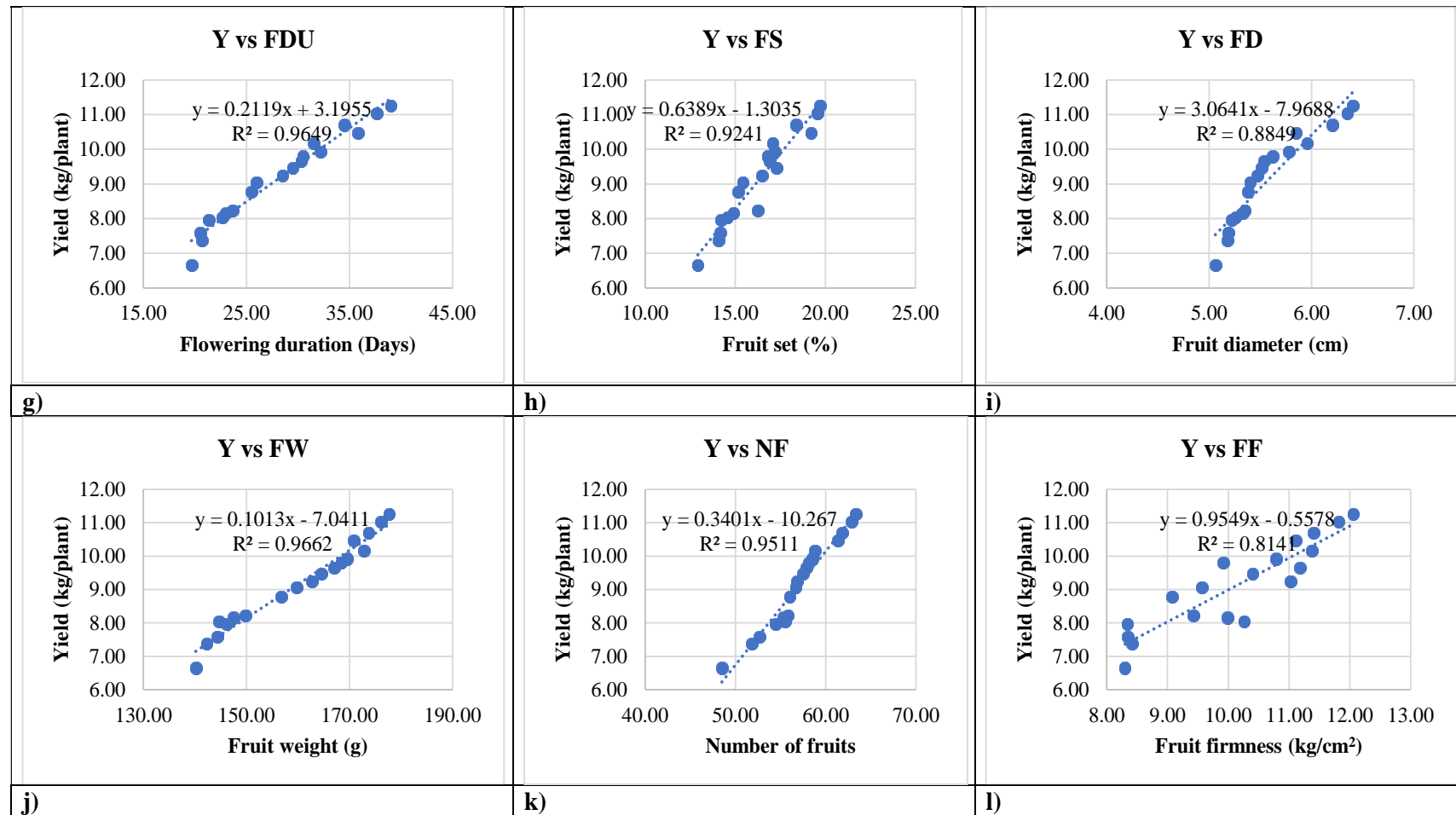
While, the correlations between yield and leaf nutrient content variables *viz.*, nitrogen (N), zinc (Zn), boron (B), iron (Fe) and manganese (Mn) were weaker during the experimentation. Nitrogen showed a moderate positive correlation with yield (r = 0.442, r² = 0.195), whereas zinc exhibited a very weak correlation (r = 0.049, r² = 0.002). Boron, iron, and manganese showed moderate to weak correlations with yield, with r values ranging from 0.495 to 0.757 and r² values from 0.245 to 0.573. Linear regression equations for the significant variables were computed to described their relationship with yield. While, the total soluble solids (TSS) and yield relationship was described by the equation Y = 2.06x - 12.645 showed a strong positive association. These results indicate that fruit quality attributes such as total soluble solids, titratable acidity, total sugars, total phenol content, total anthocyanin content and total carbohydrate content are strongly associated with yield in apple cv. Anna, while the impact of leaf nutrients on yield appears to be less pronounced.

Table 1. Pearson correlation coefficient (r), coefficient of determination (r²), linear regression equation (y) and significance of the relationship (p) between subjective dependent (yield) and independent variables (growth and yield attributes) of apple cv. Anna

Variable	r =	r² =	y =	p <
Y vs PH	0.204	0.042	-1.0242x + 11.723	0.01
Y vs PS	0.160	0.026	-0.7803x + 11.21	0.01
Y vs LA	0.255	0.065	-0.1696x + 14.214	0.01
Y vs TG	0.271	0.073	-0.9767x + 21.436	0.01
Y vs DTF	0.992	0.983	-0.1672x + 22.984	0.01
Y vs NFB	0.968	0.937	0.073x - 5.7371	0.01
Y vs FDU	0.982	0.965	0.2119x + 3.1955	0.01
Y vs FS	0.961	0.924	0.6389x - 1.3035	0.01
Y vs FD	0.941	0.885	3.0641x - 7.9688	0.01
Y vs FW	0.983	0.966	0.1013x - 7.0411	0.01
Y vs NF	0.975	0.951	0.3401x - 10.267	0.01
Y vs FF	0.902	0.814	0.9549x - 0.5578	0.01

Note: PH, Plant height; PS, Plant spread; LA, Leaf area; TG, Trunk girth; DTF, Days taken for flowering after spray; NFB, Number of flower bud, FD, Flowering duration; FS, Fruit set, FD, Fruit diameter; FW, Fruit weight; NF, Number of fruits; FF, Fruit firmness and Y, Yield

Y vs PH

$y = -1.0242x + 11.723$
$R^2 = 0.0417$

Y vs PS

$y = -0.7803x + 11.21$
$R^2 = 0.0256$

Y vs LA

$y = -0.1696x + 14.214$
$R^2 = 0.0653$

a)

b)

c)

Y vs TG

$y = -0.9767x + 21.436$
$R^2 = 0.0732$

Y vs DTF

$y = -0.1672x + 22.984$
$R^2 = 0.9834$

Y vs NFB

$y = 0.073x - 5.7371$
$R^2 = 0.9368$

d)

e)

f)

Fig. 1a-l. Scatter plots and linear gression lines showing the relationship between subjective yield and a) PH, Plant height; b) PS, Plant spread; c) LA, Leaf area; d) TG, Trunk girth; e) DTF, Days taken for flowering after spray; f) NFB, Number of flower bud, g) FD, Flowering duration; h) FS, Fruit set; i) FD, Fruit diameter; j) FW, Fruit weight; k) NF, Number of fruits; l) FF, Fruit firmness for apple cv. Anna

The evaluation of the relationships between yield and various fruit quality attributes, along with leaf nutrient content in apple cultivar "Anna" provides valuable insights into the factors most closely associated with yield outcomes. The analysis reveals that fruit quality attributes such as total soluble solids (TSS), titratable acidity (TA), total sugars (TS), total phenol content (TPC), total anthocyanin content (TAC) and total carbohydrate content (TCC) exhibit strong positive correlations with yield, with correlation coefficients ranging from 0.775 to 0.921. These findings suggested that higher levels of these quality attributes are generally associated with increased yield, reinforcing the notion that the biochemical composition of the fruit plays a critical role in yield determination.

The particularly strong correlation observed between yield and total carbohydrate content (TCC), with an r value of 0.921 and an r² value of 0.848, underscores the significant role that carbohydrates may play in the development and maturation of fruits. The linear regression equation derived for this relationship (Y = 0.2159x - 22.143) further highlights the predictive capacity of TCC in relation to yield, suggesting that carbohydrate accumulation in the fruit is a important attribute of yield in apple cv. Anna. This finding is consistent with the understanding that carbohydrates serve as essential energy sources and structural components during fruit growth, and their abundance likely supports higher fruit productivity [19]. Whereas, the correlations between yield and leaf nutrient content variables such as nitrogen (N), zinc (Zn), boron (B), iron (Fe) and manganese (Mn) were

significant weaker. Nitrogen, which is essential for vegetative growth and overall plant vigor, showed a moderate positive correlation with yield (r = 0.442, r² = 0.195). However, the relatively low r² value indicated that while nitrogen content is related to yield, it does not explain a large portion of the variation in yield on its own. The weak correlation observed for zinc (r = 0.049, r² = 0.002) suggested that it has minimal direct impact on yield at least within the context of this study.
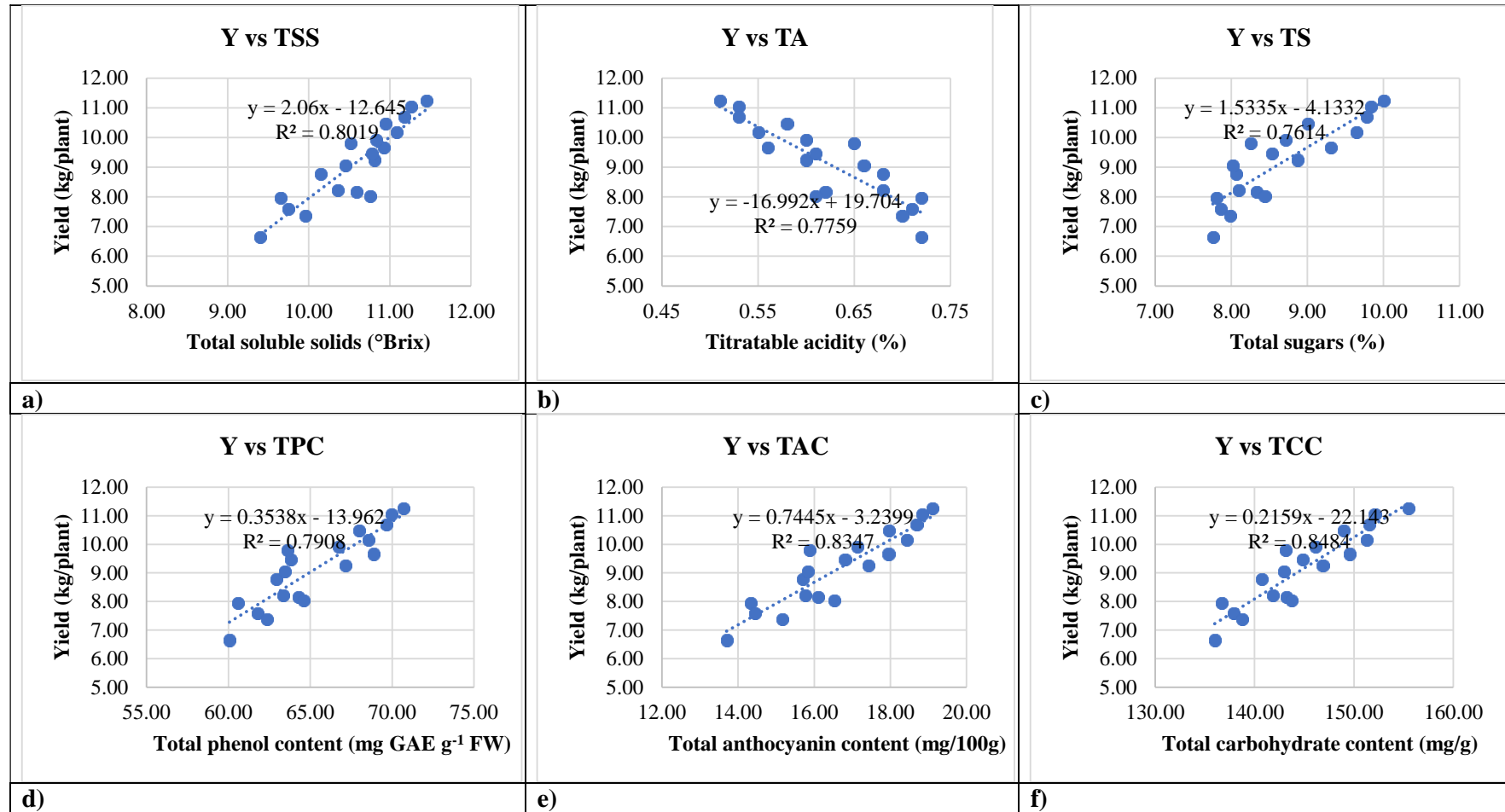
Boron, iron and manganese exhibited moderate to weak correlations with yield, with r values ranging from 0.495 to 0.757 and r² values from 0.245 to 0.573. These results indicated that while these nutrients are important for various physiological processes, their direct influence on yield is less pronounced compared to the fruit quality attributes examined. This could be due to the fact that these micronutrients, while crucial for specific metabolic functions, may not directly translate to higher fruit yield but rather contribute to overall plant health and resilience. The linear regression equations derived for the significant variables provide practical tools for predicting yield based on specific fruit quality and nutrient parameters. For example, the equation describing the relationship between TSS and yield (Y = 2.06x - 12.645) reflects the strong positive association between sweetness (as indicated by TSS) and yield, suggesting that enhancing sugar accumulation in the fruit could be a viable strategy for increasing yield. Similar findings were reported by Hou et al. [20] in apple, Ramezanpour and Farajpour [21] in banana, Razi et al. [22] and Peng et al. [23] in mango.
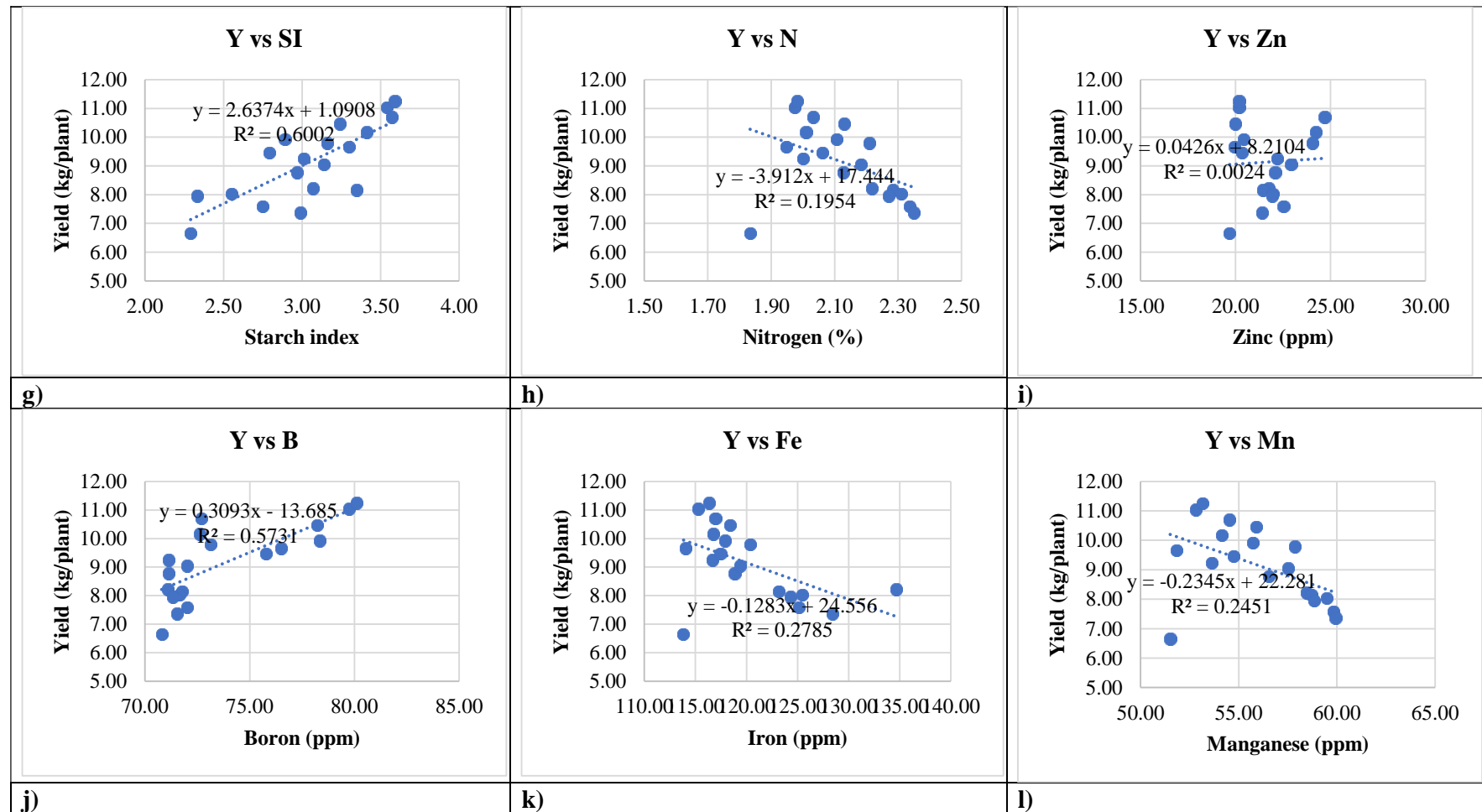
Table 2. Pearson correlation coefficient (r), coefficient of determination (r²), linear regression equation (y) and significance of the relationship (p) between subjective dependent (yield) and independent variables (fruit quality and leaf nutrients) of apple cv. Anna

Variable	r =	r² =	y =	p <
Y vs TSS	0.896	0.802	2.06x - 12.645	0.01
Y vs TA	0.881	0.776	-16.992x + 19.704	0.01
Y vs TS	0.873	0.761	1.5335x - 4.1332	0.01
Y vs TPC	0.889	0.791	0.3538x - 13.962	0.01
Y vs TAC	0.914	0.835	0.7445x - 3.2399	0.01
Y vs TCC	0.921	0.848	0.2159x - 22.143	0.01
Y vs SI	0.775	0.600	2.6374x + 1.0908	0.01
Y vs N	0.442	0.195	-3.912x + 17.444	0.01
Y vs Zn	0.049	0.002	0.0426x + 8.2104	0.01
Y vs B	0.757	0.573	0.3093x - 13.685	0.01
Y vs Fe	0.528	0.279	-0.1283x + 24.556	0.01
Y vs Mn	0.495	0.245	-0.2345x + 22.281	0.01

Note: TSS, Total soluble solids; TA, Titratable acidity; TS, Total sugar; TPC, Total phenol content; TAC, Total anthocyanin content; TCC, Total carbohydrate content; SI, Starch index, N, Nitrogen; Zn, Zinc; B, Boron; Fe, Iron; Mn, Manganese and Y, Yield.

Y vs TSS

$y = 2.06x - 12.645$
$R^2 = 0.8019$

Total soluble solids (°Brix)

Yield (kg/plant)

a)

Y vs TA

$y = -16.992x + 19.704$
$R^2 = 0.7759$

Titratable acidity (%)

Yield (kg/plant)

b)

Y vs TS

$y = 1.5335x - 4.1332$
$R^2 = 0.7614$

Total sugars (%)

Yield (kg/plant)

c)

Y vs TPC

$y = 0.3538x - 13.962$
$R^2 = 0.7908$

Total phenol content (mg GAE g^{-1} FW)

Yield (kg/plant)

d)

Y vs TAC

$y = 0.7445x - 3.2399$
$R^2 = 0.8347$

Total anthocyanin content (mg/100g)

Yield (kg/plant)

e)

Y vs TCC

$y = 0.2159x - 22.143$
$R^2 = 0.8484$

Total carbohydrate content (mg/g)

Yield (kg/plant)

f)

Fig. 2a-l. Scatter plots and linear egression lines showing the relationship between subjective yield and a) TSS, Total soluble solids; b) TA, Titratable acidity; c) TS, Total sugar; d) TPC, Total phenol content; e) TAC, Total anthocyanin content; f) TCC, Total carbohydrate content; g) SI, Starch index; h) N, Nitrogen; i) Zn, Zinc; j) B, Boron; k) Fe, Iron; l) Mn, Manganese for apple cv. Anna

4. CONCLUSION

The investigation on apple cv. "Anna" revealed intricate relationships between fruit yield and several plant growth, yield attributes, fruit quality and leaf nutrient variables. The correlation showed significant relationship and varying from low to high positive levels. Notably, variables such as days taken for flowering after spray, number of flower buds, flowering duration and various fruit characteristics exhibited strong correlations with yield, underscoring their pivotal roles in fruit production. The coefficients of determination provided insights into the extent to which these attributes explain yield variability, emphasizing the predominant influence of timely flowering and fruit-related factors. The derived linear regression equations offer predictive models that could guide orchard management strategies aimed at optimizing yield. Overall, this study contributes valuable insights into the complex interplay of factors influencing apple yield, prominence way for targeted interventions to maximize productivity while maintaining fruit quality and sustainability in orchard management practices.

5. FUTURE RECOMMENDATION

To enhance the robustness and applicability of the findings in the study "Correlation and Regression Analysis between Agronomic and Quality Attributes of Apple (*Malus × domestica* Borkh.) cv. Anna," future research should expand the geographical scope to diverse regions and climates, include additional growth and quality variables such as fruit size, color, and disease resistance, and employ advanced statistical methods like multivariate analysis or machine learning to capture complex relationships. Long-term studies across multiple seasons are recommended to observe trends and sustainability, while more detailed nutrient analysis should focus on the indirect effects of micronutrients on yield. Additionally, considering environmental factors such as pest management, soil health, and irrigation practices would provide a more comprehensive understanding of factors influencing apple yield and help develop integrated cultivation strategies.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declares that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during writing or editing of manuscripts.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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