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The Role of K-Humate and Iron Oxide Nanoparticles for Nutrient Accumulation Under Salinity Stress Condition in Cotton (*Gossypium hirsutum* L.)

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Abstract

Salinity stress poses a significant challenge to cotton (*Gossypium hirsitum* L.) production, particularly during early growth stages. The present study investigates the effects of iron oxide nanoparticles (Fe (II, III) oxide NPs), K-humate, and their combination on nutrient accumulation in cotton plants under saline conditions. Cotton seedlings were subjected to both saline and non-saline environments, with treatments applied to assess their impact on nutrient uptake in the stem and root sections. Principal Component Analysis (PCA) was employed to evaluate nutrient variability across different treatments. Results showed that Fe (II, III) oxide NPs and K-humate enhanced nutrient balance under saline conditions by promoting nutrient uptake and mitigating salinity-induced nutrient imbalances, particularly for potassium (K), sodium (Na), phosphorus (P), and iron (Fe). The combined treatment of iron oxide nanoparticles (Fe (II, III) oxide NPs) and K-humate demonstrated a synergistic effect, improving nutrient interactions and it may contribute to plant resilience. These findings suggest that the use of nanomaterials, particularly in combination with organic compounds like K-humate, holds potential for enhancing cotton tolerance to salinity stress due to alleviating nutrient imbalances caused by salinity stress.

Keywords: Cotton, salinity stress, K-humate, iron oxide nanoparticles, nutrient accumulation

1. Introduction

Saline stress represents a significant challenge to cotton production, primarily due to the crop's moderate salt tolerance, with a salinity threshold of approximately 7.7 dS m^{-1} (Han, 2023; Rahman, 2023). Notwithstanding this tolerance, cotton plants suffer considerable yield losses when subjected to salinity, particularly during crucial growth phases such as germination and seedling development (Guo et al. 2020). The physiological impacts of salinity stress include osmotic stress, ion toxicity and impaired nutrient uptake, which collectively impede plant growth and development (Ergin et al. 2021). The available evidence suggests that cotton is particularly susceptible to saline conditions during the germination and early seedling stages, where growth inhibition is most pronounced (Wang et al. 2020; Rahman, 2023).

The physiological responses of cotton to saline stress are characterised by intricate mechanisms, including the regulation of ion homeostasis and the expression of specific genes associated with salt tolerance. For example, studies have demonstrated that the expression of genes involved in Na^+ transport is markedly altered in saline conditions, thereby impairing the plant's capacity to maintain ionic equilibrium (Wang et al. 2019; Su et al. 2020). Furthermore, the function of microRNAs in regulating salt stress responses has been emphasised, with specific miRNAs identified as crucial regulators of reactive oxygen species (ROS) metabolism, which is vital for maintaining cellular integrity under stress conditions (Ma, 2023). Moreover, the utilisation of exogenous compounds, such as melatonin, has been demonstrated to facilitate seed germination and osmotic regulation in the presence of salt stress, thereby offering promising avenues for the alleviation of the detrimental effects of salinity (Wang et al. 2021; Gören, 2024).

Furthermore, the interaction between salinity and other abiotic stresses, such as drought and alkaline conditions, intensifies the adverse effects on cotton growth. The combined effects of saline and alkaline stress have been demonstrated to be more deleterious than the effects of either stressor alone, resulting in greater reductions in biomass and overall plant health (Ibrahim et al. 2018). The physiological markers, such as shoot potassium content, have been proposed as indicators for the screening of cotton genotypes for osmotic and salt tolerance, underscoring the significance of genetic diversity in the development of resilient cotton varieties.

Salinity stress represents a significant environmental challenge that has a deleterious impact on plant growth and productivity, particularly in crops such as cotton. The physiological impacts of salinity include osmotic stress, ion toxicity, and nutrient imbalances, which collectively impede plant development and yield (Zhang, 2023). Salinity results in elevated concentrations of sodium (Na+) and chloride (Cl-) ions in the soil, which can impede the uptake of essential nutrients such as potassium (K+), nitrogen (N), and phosphorus (P) (García-Caparrós et al., 2016). This imbalance in nutrients can result in stunted growth, reduced photosynthetic rates and, ultimately, lower yields (Sakamoto et al. 2021).

Recent studies have investigated the potential of various nanomaterials, including khumate and iron nanoparticles (Fe (II,III) oxide NPs), to alleviate the adverse effects of salinity stress on plants. Khumate, a natural organic compound derived from humic substances, has been demonstrated to facilitate enhanced nutrient uptake and improve soil structure, which can be advantageous in saline conditions (Asl et al. 2019; Öztürk Erdem, 2024). The application of khumate may assist in maintaining a favourable K^+/Na^+ ratio, thereby promoting enhanced physiological responses in plants subjected to salinity stress (Asl et al. 2019).

In contrast, iron nanoparticles have been demonstrated to enhance salt tolerance in a range of plant species, including cotton. The interaction of Fe (II,III) oxide NPs with plant systems has been demonstrated to enhance antioxidant enzyme activities, which play a pivotal role in mitigating oxidative stress caused by salinity (Aazami et al. 2021). For example, the application of iron nanoparticles has been linked to increased chlorophyll content and enhanced photosynthetic efficiency, which are essential for sustaining growth under saline conditions (Mozafari et al. 2018). Furthermore, Fe (II,III) oxide NPs can facilitate improved ion regulation within plant cells, thereby reducing the toxic effects of excessive Na^+ accumulation (Aazami et al. 2021).

In conclusion, the utilisation of khumate and iron nanoparticles represents a promising avenue for the alleviation of salinity stress in cotton, thereby enhancing plant health and productivity. These materials facilitate not only the uptake of nutrients and ion regulation but also the overall physiological resilience of plants in adverse conditions. Future research should prioritise the elucidation of the specific mechanisms by which these nanomaterials exert their beneficial effects, as well as the optimisation of their application rates and methods for maximum efficacy. The aim of this study is to investigate the effects of FeO_3 NPs, K-humate, and the combination of FeO_3 NPs + K-humate on nutrient accumulation in cotton plants under salinity stress. Specifically, the study focuses on how these treatments influence the nutrient balance in the stem and root sections of cotton seedlings during the seedling stage. The findings aim to provide insights into potential mechanisms that enhance plant growth and development under saline conditions, contributing to sustainable strategies for improving cotton tolerance to salinity stress.

2. Materials and Methods

In order to evaluate the effects of salinity stress and the role of microparticles on plant growth, a two-factor randomised plot experiment was conducted using *Gossypium hirsitum* L.(Carisma) as the plant material. The objective of the experiment was to examine the plant's response to salinity stress and to ascertain the impact of Fe (II,III) oxide nanoparticles and K-humate (Kh) treatments. A randomised block design was employed, and the seedbed consisted of a mixture of 50% perlite and 50% peat, placed in transparent pots with a volume of 1.2 L. These pots, measuring 9 cm in width and 18 cm in height, were selected to provide sufficient space for root development and maintain adequate soil fertility. The experiment was conducted in a growth chamber with temperature settings maintained at 24-26°C during the day and 18±2°C at night, along with a 12-hour photoperiod. The photosynthetic process and plant growth were promoted by the use of red light at a wavelength of 630 nm. The sowing process commenced on 30 November 2023, with three seeds planted at a depth of 2 cm in each pot. Each pot was initially irrigated with 50 mL of water to optimise germination conditions, and subsequent irrigation was carried out at two-week intervals to support seedling emergence. The irrigation water is described below. The irrigation solution comprised 10 L of water, which was prepared with the following nutrients and applied equally in all condions The fertilizer solution comprised 4g of NPK (15:15:15), 2g of urea, and 20ml of liquid fertilizer (Multimicro® Fluid). The calculation of the NaCl concentration was as follows: The salt concentration in the irrigation water was calculated according to the following formula:

1 dS m^{-1} is equivalent to 10 mM NaCl, or 0.584 g L^{-1}. 130 mM NaCl is equivalent to 13 dS m^{-1}, or 7.592 g NaCl L^{-1}.

On 8 December 2023, the experiment commenced with two groups: a saline treatment group and a non-saline control group. The plants in the saline group were subjected to salt stress, whereas those in the control group were cultivated under non-saline conditions. The sixth set of leaves from the plants cultivated under non-saline conditions was harvested. All treatments were subject to periodic measurement and irrigation was provided every two days with 100 ml of water per pot.

2.1. Nanoparticle treatment

Iron oxide nanoparticles were procured from Sigma-Aldrich (product number 637106-25G, lot number MKBT3736V, particle size: 50-100 nm) and the concentration was adjusted to 0.3 mg/100 mL. The solution of K-humate was prepared at a concentration of 0.3 g/L. In this study, the plant nutrient elements were determined using the ICP-OES device in the laboratory of the Department of Soil Science and Plant Nutrition at Aydın Adnan Menderes University, Faculty of Agriculture.

3. Findings

Principal component analysis (PCA) is a powerful statistical approach to analyze and simplify complex and extensive datasets. In the case of cotton grown under conditions of optimal irrigation, the total variation was divided into seven principal components (PCs), as detailed in Table 1. It is noteworthy that the first three PCs exhibited eigenvalues greater than 1, indicating that they are significant in explaining the variation among traits (Figure 1A). The cumulative contribution of the first three PCs accounted for 90.845% of the total variability in traits, thereby reflecting their strong association with these traits in nonsaline conditions. In the analysis of nutrient accumulation under normal conditions, notable trait correlations and variability patterns were observed. Sodium, zinc, and copper exhibited a strong positive correlation with each other, while they showed a strong negative correlation with manganese, calcium, and phosphorus. Furthermore, a strong negative correlation was observed between potassium and iron. The length of the vectors originating from the biplot's centre depicted the correlations among traits. Among the nutrients, potassium, iron, sodium, zinc, and copper were associated with vectors of considerable length, indicating a high degree of variation among these traits. In contrast, calcium exhibited the lowest degree of variability, as indicated by its shortest vector length. This information is illustrated in Figure 1A, which provides a visual representation of the correlations and variability among traits under normal (nonsaline) conditions. In the case of cotton grown under saline conditions, the total variation was also divided into seven principal components (PCs), as detailed in Table 1. Once more, the first two PCs exhibited eigenvalues greater than 1, indicating their significance in explaining the variation among traits (Figure 1B). The PCA results derived from data obtained under saline conditions revealed that the cumulative contribution of the first three PCs accounted for 90.982% of the total variability in traits, reflecting their strong association with these traits in saline conditions. The analysis of nutrient accumulation under salinity revealed a strong positive correlation between iron, sodium, zinc, and copper, while they showed a strong negative correlation with calcium. Additionally, manganese and phosphorus exhibited strong positive correlations with each other. Among the nutrients, calcium, copper, and sodium were associated with long vectors, indicating higher variation among these traits. Nutrient analysis revealed strong positive correlations among iron, sodium, zinc, and copper, suggesting shared uptake mechanisms under stress. A notable negative correlation between these nutrients and calcium may indicate that elevated sodium levels inhibit calcium uptake, disrupting plant physiological balance (Sharma et al., 2016). Correlation analysis highlighted significant relationships among nutrients: iron, sodium, zinc, and copper showed strong positive correlations, suggesting shared uptake mechanisms. Conversely, calcium exhibited a strong negative correlation with these nutrients, possibly indicating disruptions in uptake due to salinity. Notably, manganese and phosphorus displayed a positive correlation, reflecting their synergistic roles in plant health (Munns and Tester, 2008). Additionally, the positive correlation between manganese and phosphorus reflects their cooperative role in stress adaptation (Graham et al., 2001).

Table 1. PCA obtained from Phosphorus (P) Potassium (K) Calcium (Ca) Magnesium (Mg) Sodium (Na) Iron (Fe) Zinc (Zn) Copper (Cu) Manganese (Mn) undernonsaline and saline irrigation condition

Number	**Nonsaline Condition**		**Saline Condition**	
	Eigenvalue	**Percent**	**Eigenvalue**	**Percent**
1	5.3161	59.067	5.3907	59.897
2	1.6071	17.857	2.1377	23.752
3	1.2529	13.921	0.6600	7.333
4	0.4352	4.836	0.4825	5.361
5	0.2429	2.699	0.2402	2.669
6	0.1057	1.174	0.0882	0.980
7	0.0402	0.446	0.0008	0.009

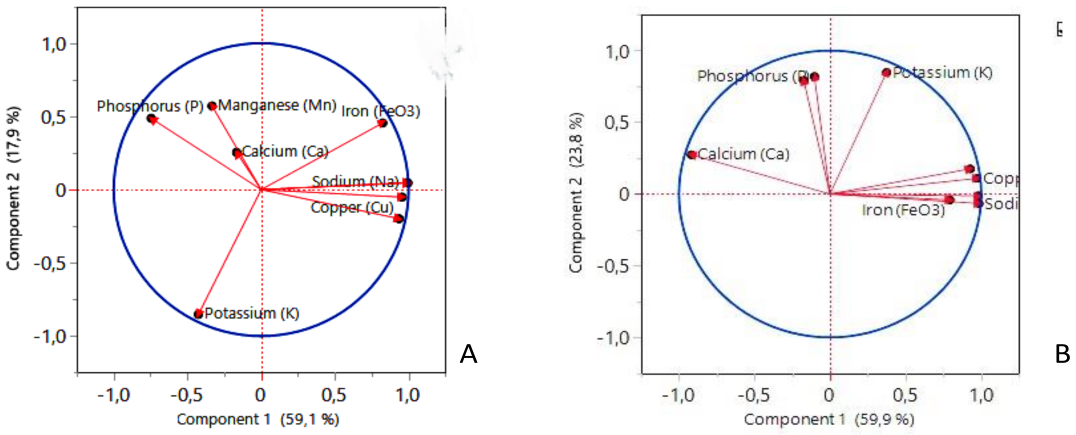

Figure 1. Summary of bar chart displaying eigenvalue and variation percentage contribution by all principal components (PCs), a biplot between PC1 and PC2 displaying the distribution of Nonsaline (A) and Saline (B) conditions

The results of a Principal Component Analysis (PCA) on the nutrient elements phosphorus (P), potassium (K), calcium (Ca), magnesium (Mg), sodium (Na), iron (Fe_2O_3), zinc (Zn), copper (Cu) and manganese (Mn)) in both stem and root of plants. For the stem, the first principal component (PC1) has an eigenvalue of 3.74 and explains 41.54% of the total variance, indicating that this component captures a significant part of the nutrient variation. The second component (PC2) explains a further 25.14% with an eigenvalue of 2.26, while the third (PC3) and fourth (PC4) components explain 13.81% and 13.63% respectively. Together, these four components account for 94.13% of the total variance in the stem nutrient data, suggesting that a small number of components can effectively summarise the nutrient profile. In the root, PC1 is even more dominant with an eigenvalue of 4.90, explaining 54.54% of the total variance. This indicates that a large part of the nutrient variation in the root is captured by the first component. PC2 and PC3 contribute 21.32% and 10.81% of the variance respectively. The first three components together explain 86.67% of the variance, and the fourth component (PC4) adds an additional 8.32%, bringing the total variance explained to 94.98%. Overall, the analysis shows that the nutrient composition of both stem and root is effectively captured by the first few principal components, with the root showing a stronger contribution from PC1 compared to the stem. This suggests that fewer factors are needed to describe nutrient variability in the root than in the stem (Table 2). In the biplot analysis for the plant stem (Figure 2A) and the plant root (Figure 2B), different nutrient patterns are observed. For the stem, Component 1 (explaining 41.5% of the variance) and Component 2 (25.1%) capture a significant part of the variation in nutrient composition. Potassium (K), sodium (Na) and phosphorus (P) show strong positive associations with Component 1, indicating their major influence on stem nutrient variation. Copper (Cu) and zinc (Zn) are also significant contributors, while magnesium (Mg), calcium (Ca), manganese (Mn) and iron (Fe) have weaker or even negative associations with Component 1, especially for manganese and iron. In contrast, nutrient variation in the plant root (Figure 2B) is dominated by Component 1, which explains 54.5% of the variance, while Component 2 accounts for 21.3%. Iron (Fe) and magnesium (Mg) are the most influential elements, with strong positive contributions to component 1. Calcium (Ca) also contributes, but to a lesser extent. Nutrients such as zinc (Zn), copper (Cu), phosphorus (P) and sodium (Na) are clustered together and show moderate contributions to both components. Comparing the two, the stem nutrient variation is mainly driven by potassium, sodium and phosphorus, whereas the root variation is more influenced by iron and magnesium. This difference reflects the different physiological roles of stem and root, each with unique nutrient requirements and accumulation patterns. Salinity stress is a significant abiotic factor that adversely affects plant growth and development by disrupting osmotic and ionic balances within plant cells. This disruption leads to nutrient imbalances and metabolic dysfunctions, ultimately impacting plant health and productivity. Understanding how salinity affects nutrient accumulation in both roots and stems is crucial for developing strategies to enhance plant resilience in saline environments.

Table 2. PCA obtained from Phosphorus (P) Potassium (K) Calcium (Ca) Magnesium (Mg) Sodium (Na) Iron (Fe) Zinc (Zn) Copper (Cu) Manganese (Mn) for plant stem and plant root

Number	**Plant Stem**		**Plant Root**	
	Eigenvalue	**Percent**	**Eigenvalue**	**Percent**
1	3,7389	41,544	4,9090	54,544
2	2,2630	25,144	1,9187	21,319
3	1,2428	13,809	0,9724	10,805
4	1,2270	13,633	0,7484	8,315
5	0,3703	4,115	0,3512	3,902
6	0,1044	1,160	0,0961	1,068
7	0,0535	0,594	0,0043	0,047

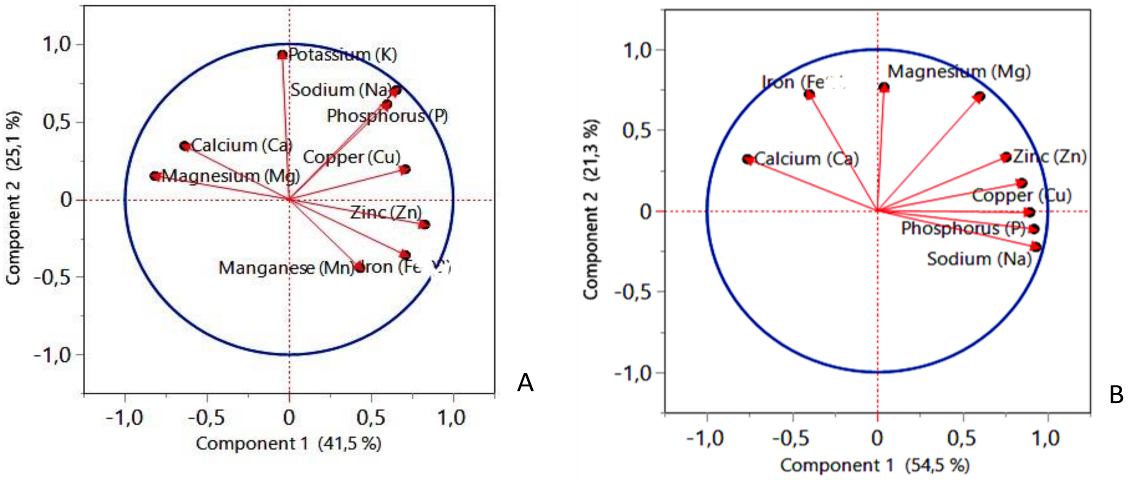

Figure 2. Summary of bar chart displaying eigenvalue and variation percentage contribution by all principal components (PCs), a biplot between PC1 and PC2 displaying the distribution of plant-stem (A) and plant root (B)

PCA analysis revealed significant differences related to nutrients (phosphorus, potassium, calcium, magnesium, sodium, iron (Fe_2O_3), zinc, copper and manganese) between the control, Fe_2O_3, Fe (II, III) oxide + K-humate and K-humate treatments. In the control group, the first principal component (PC1) explained a large proportion of the total variance, 61.052%, with an eigenvalue of 5.4946. In the Fe (II,III) oxide treatment, PC1 provided 55.058% of the variance with an eigenvalue of 4.9552. In the Fe (II,III) oxide + K-humate treatment, this value increased to 5.4087, contributing 60.096%. The most impressive result was obtained in the K-humate treatment; PC1 explained 66.093% of the variance with an eigenvalue of 5.9484, highlighting the decisive influence of this treatment on the nutrients. These results clearly demonstrate that nutrients play a critical role in the response of cotton plants to different treatment groups and the profound impact of these treatments on plant development. Principal Component Analysis (PCA) biplots comparing nutrient distribution in four treatment conditions: Control (A), Fe (II,III) oxide (B), Fe (II,III) oxide + K-humate (C) and K-humate (D). In the control (A), copper, zinc and iron showed a strong and positive correlation with each other, while the same strong and positive correlation was found between manganese, phosphorus and potassium. Calcium (Ca) contributes largely to the first principal component (PC1), while copper (Cu), zinc (Zn) and magnesium (Mg) show strong correlations with both PC1 and PC2. Sodium (Na), manganese (Mn), phosphorus (P), and potassium (K) have weaker effects on the total variance. In the Fe (II,III) oxide treatment (B), the relationships between the nutrients change. Potassium (K) and sodium (Na) show an increasing correlation with PC2, while the contribution of calcium decreases compared to the control. Copper and magnesium continue to group, but their orientation shifts towards PC2. In the combined Fe (II,III) oxide + K-humate treatment (C), manganese (Mn) and calcium are closely aligned with PC1, while phosphorus, zinc, copper and sodium are associated with PC2, revealing a more distinct pattern indicating changes in nutrient interactions under dual treatment. In the K-humate treatment alone (D), calcium continues to dominate PC1, while manganese and phosphorus align strongly with PC2 and potassium, sodium, copper, zinc and iron (Fe) cluster together, showing similar behaviour. Calcium contributes consistently to PC1 in all conditions, but its influence is slightly reduced in the Fe (II,III) oxide treatment. Potassium and sodium show considerable variability between the control and Fe (II,III) oxide treatments, while the combination of Fe (II,III) oxide and K-humate significantly alters the nutrient correlations, particularly affecting manganese and phosphorus. K-humate application alone leads to different interactions between phosphorus, manganese and potassium, highlighting how different treatments affect nutrient dynamics in unique ways.

Table 3. PCA obtained from Phosphorus (P) Potassium (K) Calcium (Ca) Magnesium (Mg) Sodium (Na) Iron (Fe) Zinc (Zn) Copper (Cu) Manganese (Mn) for Control, Fe_2O_3, Fe (II,III) oxide +K-humate and K-humate

Number	Control		Fe (II,III) oxide		Fe (II,III) oxide +Kh		K-humate	
	Eigenvalue	Percent	Eigenvalue	Percent	Eigenvalue	Percent	Eigenvalue	Percent
1	5,4946	61,052	4,9552	55,058	5,4087	60,096	5,9484	66,093
2	3,0070	33,411	3,3167	36,852	2,8619	31,799	2,7431	30,479
3	0,4983	5,537	0,7281	8,090	0,7294	8,105	0,3085	3,428

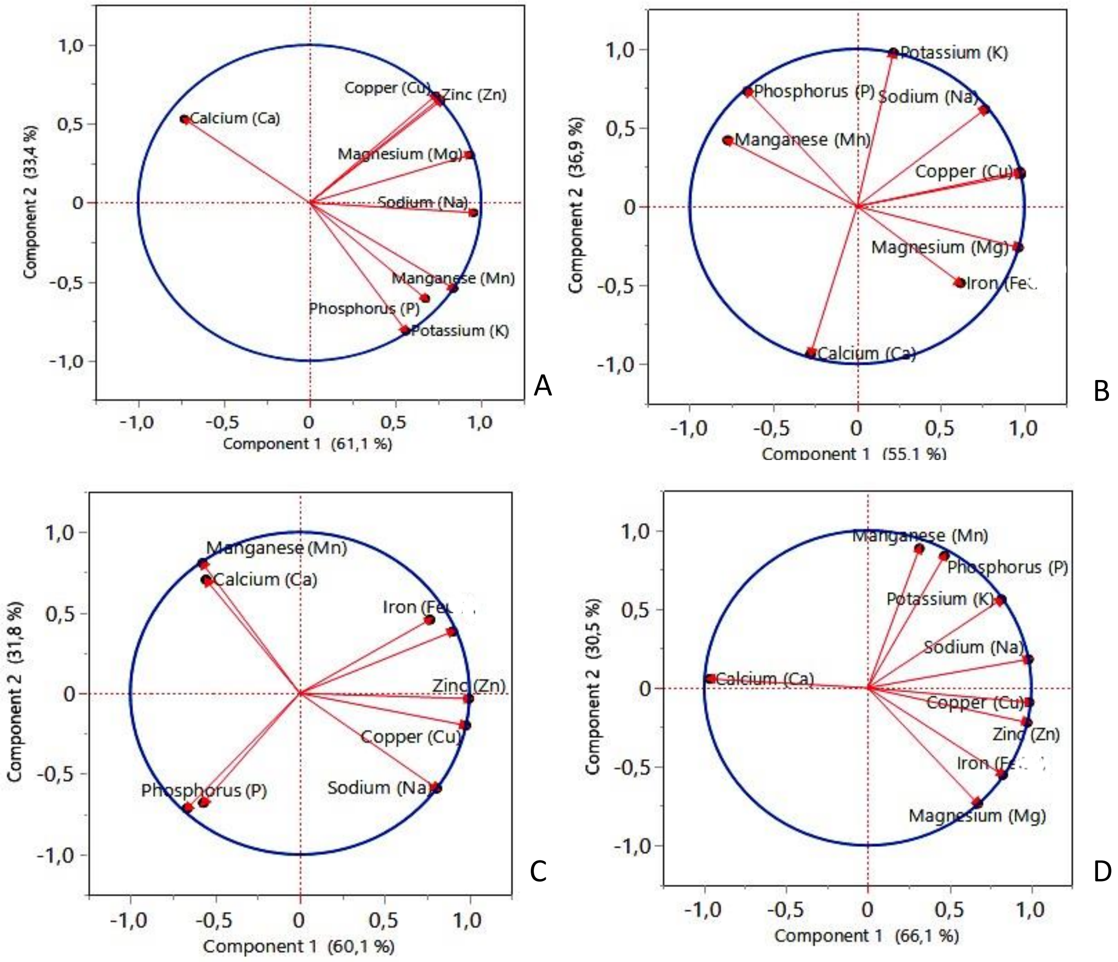

Figure 3. Summary of bar chart displaying eigenvalue and variation percentage contribution by all principal components (PCs), a biplot between PC1 and PC2 displaying the distribution of Control (A) Fe (II,III) oxide (B), Fe (II,III) oxide +K-humate (C) and K-humate (B) factors

4. Discussion

Salinity stress is a major environmental challenge that disrupts crop growth and productivity by affecting nutrient uptake and metabolic functions. The accumulation of nutrients in plant roots and stems under saline conditions is influenced by various physiological mechanisms, which differ across plant species. Recent studies have shed light on how salinity impacts nutrient accumulation, revealing the complex dynamics involved. Salinity stress causes osmotic and ionic imbalances in plant tissues, severely impairing nutrient absorption. For example, Cova et al. (2016) found that high salinity reduced both root growth and nutrient accumulation in *Ricinus communis*, suggesting that although roots can adjust osmotically, excessive salinity still leads to significant nutrient loss. Similarly, AbdElgawad et al. (2016) observed that salt stress led to Na^+ accumulation in maize roots, disrupting the critical K^+/Na^+ balance required for cellular function, resulting in physiological stress and reduced productivity. Taha et al. (2020) further demonstrated that salinity reduces the levels of essential nutrients like nitrogen (N), phosphorus (P), potassium (K), manganese (Mn), iron (Fe), and boron (B), all vital for plant metabolism and defense against oxidative stress. Salinity poses significant challenges to plant growth, often leading to nutrient deficiencies and imbalances (Neue et al. 1998; Santos et al. 2002). Numerous studies have shown that salinity can reduce nutrient uptake and accumulation or disrupt nutrient distribution within the plant (Fernández-García et al. 2004). The ability to maintain higher nutrient ratios, such as K^+ and Ca^{2+} to Na^+, particularly in young, rapidly growing tissues, is an important mechanism that contributes to improved salt tolerance in plants (Wei et al. 2003). Nutrient profiles in roots and stems differ under salinity stress. Al-Zahrani et al. (2021) showed that applying zinc improved growth and nutrient uptake in Vigna radiata, highlighting that targeted nutrient applications can mitigate the harmful effects of salinity. However, roots often accumulate harmful ions like Na^+ and Cl^-, leading to toxicity and nutrient imbalances. Umar et al. (2011) emphasized the role of potassium in maintaining ionic balance, particularly in combating Na^+ toxicity in plants like Brassica campestris under salt stress. Similarly, Seleiman et al. (2020) found that antioxidants helped restore ionic balance in salt-stressed cucumber plants, stressing the importance of managing oxidative stress for improved nutrient uptake. Research also indicates that salinity significantly alters nutrient composition in plant tissues. For example, Arslan (2020) reported that salinity reduces water uptake, limiting essential nutrients and impairing plant metabolism. Tarakçıoğlu (2023) demonstrated that applying organic amendments improved nutrient uptake in lettuce under saline conditions, suggesting that organic matter can counteract the negative effects of salinity by enhancing nutrient availability. Bayram and Üzal (2020) confirmed that salinity causes Na^+ and Cl^- accumulation in roots, which can lead to toxicity and imbalances in nutrient distribution within plant tissues. In summary, salinity stress affects nutrient uptake by altering the osmotic potential of soil, making it difficult for plants to absorb water and essential nutrients. The accumulation of Na^+ and Cl^- ions inhibits the uptake of key nutrients like potassium (K) and calcium (Ca), which are essential for vital physiological functions. Understanding these mechanisms is crucial for developing effective crop management strategies. Approaches such as applying micronutrients, using mycorrhizal fungi, and incorporating organic amendments can enhance nutrient uptake and improve plant resilience to salinity. By optimizing these practices, future research can help crops perform better in saline environments.

5. Conclusion

This study demonstrates the significant effect of Fe (II,III) oxide NPs, K-humate and their combination on nutrient accumulation in cotton plants under saline and non-saline conditions. The use of Principal Component Analysis (PCA) revealed distinct patterns of nutrient uptake between stem and root, showing that each treatment affected nutrient dynamics differently. The results indicate that the application of K-humate had the most profound effect on nutrient uptake, particularly in enhancing the accumulation of essential elements such as calcium, phosphorus and potassium. Fe (II,III) oxide NPs alone contributed to improved antioxidant activity and nutrient regulation, especially sodium and potassium, which are critical for managing osmotic stress under salinity. The combined Fe (II,III) oxide + K-humate treatment showed synergistic effects with enhanced nutrient interactions, reflecting an optimised balance between nutrient uptake and stress tolerance mechanisms. Under saline conditions, nutrients such as sodium, calcium and copper showed high variability, indicating their critical role in plant differentiation and adaptation to salinity stress. The results shows the potential of using K-humate and Fe (II,III) oxide NPs, individually or in combination, as a strategy to mitigate the negative effects of salinity stress by improving nutrient balance and plant resilience. Overall, this research provides valuable insights into the physiological responses of cotton to salinity stress and highlights the importance of nanomaterials such as Fe (II,III) oxide NPs and K-humate to enhance cotton growth under challenging environmental conditions. Further research could focus on optimising application rates and investigating long-term effects on crop productivity. These findings can contribute to sustainable agricultural practices and help in the development of salt-tolerant cotton varieties.

Declaration of Author Contributions

The authors declare that they have contributed equally to the article. All authors declare that they have seen/read and approved the final version of the article ready for publication.

Declaration of Conflicts of Interest

All authors declare that there is no conflict of interest related to this article.

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