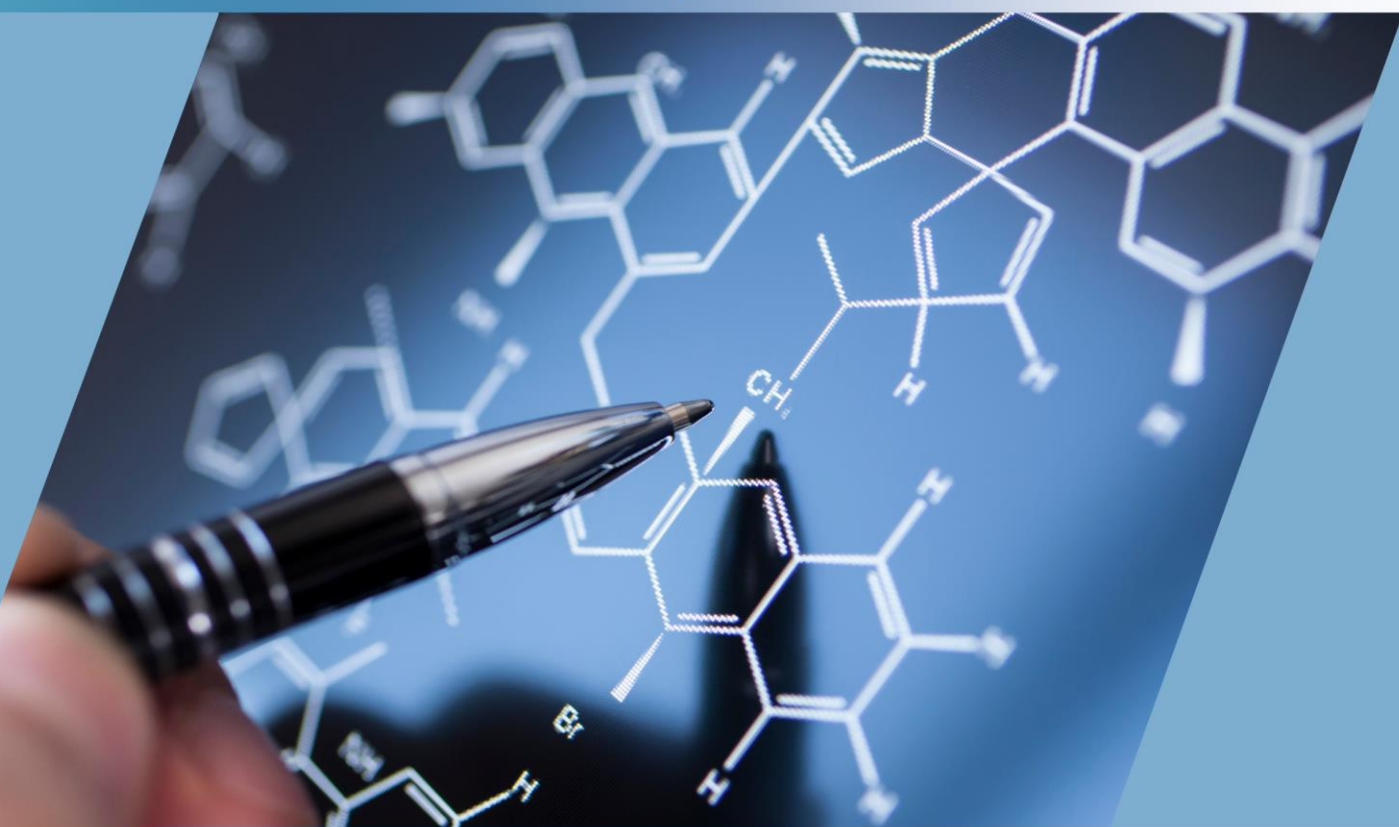




eISSN: 2789-858X

Scientific Journal for the Faculty of Science - Sirte University (SJFSSU)

Bi-annual, Peer- Reviewed, and Open Accessed e-Journal



VOLUME 4 ISSUE 1 APRIL 2024



10.37375/issn.2789-858X



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Effect of Exogenous Application of Nicotinic Acid on Genotypes of durum wheat (*Triticum aestivum* L.) under salt stress.

Sami M. salih* and Ahmed A. Abdulraziq

Biology Department, Education Faculty, Omar Al-Mukhtar University, Al-Bayda, Libya.

DOI: <https://doi.org/10.37375/sjfssu.v4i1.2680>

A B S T R A C T

ARTICLE INFO:

Received: 18 March 2024

Accepted: 12 April 2024

Published: 17 April 2024

Keywords: *Triticum aestivum* L, Salinity tolerance, Seawater Irrigation, Wheat genotypes, Nicotinic acid.

Two experiments were conducted (laboratory and pot). The laboratory experiment represented the tolerance of ten durum wheat genotypes (ACSAD) to levels (20, 30, 40%) of seawater. The pot experiment evaluated the efficiency of foliar spraying of nicotinic acid for three election genotypes of durum wheat (ACSAD 1671, 1711, and 1765), Under seawater levels (20, 30%). The results of the laboratory experiment showed that revealed significant ($p < 0.05$) differences in the genotypes' response to salinity, the genotypes' (1671, 1711 and 1765), were superior in recording the best average germination percentage and seedling length compared to the other genotypes. The results of the pot experiment showed, after 80 days of sowing, under seawater irrigation conditions, decreases in (Plant height, Leaf area /plant, Spike length, number of spikes/plant, number of grains/spike, chlorophyll a, chlorophyll b, carotenoids, and total pigments) of the three durum wheat genotypes (ACSAD), compared to control. In contrast, foliar application of Nicotinic acid led to a significant decrease in a negative effect resulting from salinity for all vegetative growth parameters and the contents of photosynthetic pigments, especially with low concentrations of seawater. The (1671) genotype performed better than the (1711 and 1765) genotypes in concern to high averages for all studied traits, under salinity and spraying with Nicotinic acid.

1 Introduction

Today agriculture faces challenges of high saltwater intrusion levels along coastal areas, which ruins the efficiency and quality of the cultivation of wheat crops, due to Sea level rise (Yanagi, 2024). This increases the salt concentration in the soil, causing Salt stress for wheat crops (Salih *et al.*, 2023). Through many negative reactions, represented by an osmotic stress, ionic imbalance, oxidative stress, membrane disorganization, reduction of cell division, and finally increased accumulation of reactive oxygen species (Ain *et al.*, 2024). To address the problem of changing climate conditions on crop growth, studies have dealt with the use of genotypes that can withstand abiotic stress (Cabusora, 2024). For example, the results of a study conducted on

40 genotypes of bread wheat at the germination stage under salinity conditions indicated, that only three genotypes were salt-tolerant (Ahmed *et al.*, 2024). Wheat genotypes adapt to climatic conditions changes, especially salinity, through reduced formation of oxygen species (ROS) by antioxidants (AOS), consisting of a complex of enzymes, which works to protect cells from salinity damage (Kononenko *et al.*, 2023). Furthermore, the role of osmolytes in quenching free radicals, regulating osmotic and ion homeostasis, and regulating phytohormones (Choudhary *et al.*, 2023). Nicotinic acid (NA) or vitamin B3 known as (niacin) of the water-soluble vitamins (Çatak and Yaman, 2019). Contributes to the biosynthesis of the enzymatic conjugates (NAD, NADP), Which has a role in giving cells plasticity to the response of plants to environmental conditions (Noctor *et*

al., 2011; Gasperi *et al.*, 2019), addition, as DNA repair or post-translational modification of proteins (Gakière *et al.*, 2018). The height of fresh weight and bulb dry weight of onion during salt stress was observed to be increased by foliar application of nicotinic acid and tryptophan (Hussein *et al.*, 2014). Also, (Farooq *et al.*, 2022), reported the potential of barley to tolerate water stress through foliar treatments with nicotinic acid. Consequently, this study aims to test the effect of irrigation with different seawater levels on the tolerance of ten durum wheat genotypes in a dish experiment and follow-up of salt-resistant genotypes in pot experiments through foliar application Nicotinic acid under seawater irrigation conditions.

2 Materials and Methods

2.1 Plant material and experimental setup:

The laboratory study was conducted in the Department of Biology/Faculty of Education at Omar AlMukhtar University. The experiment was conducted on ten genotypes of durum wheat, which included ACSAD (1595, 1651, 1671, 1695, 1697, 1711, 1729, 1735, 1747, and 1765). They were obtained from the Arab Center for the Studies of Arid Zones and Dry Lands ACSAD. They were soaked in 1% Sodium hypochlorite solution for 3 minutes for sterilization, and washed with distilled water.

2.2 Preparation of seawater dilutions:

Five seawater dilution treatments were used in the experiment:

- 1- tap water (control).
- 2- 20% seawater + 80% tap water (20% seawater).
- 3- 30% seawater + 70% tap water (30% seawater).
- 4- 40% seawater + 60% tap water (40% seawater).

2.3 Seed germination:

The petri dishes were filled with 20 seeds and were lined with two Whatman No.1 filter papers and incubated at room temperature. Each treatment was repeated three times. The dishes were subjected to daily observation for 10 days and follow-up on germination in terms of addition of saline solution to the treated dishes. Distilled water was added to control as needed for each dish. The filter papers were changed once every two days to prevent salt accumulation due to evaporation, germination was calculated by recording the number of

germinated seeds in all treatments starting from the second day, which the first germination occurred, germination criterion is the appearance of radical outside seed cover. At the end of the experiment, the final results of the following qualities:

- Germination percentage (PG %) = the number of germinated seeds / total number of seeds cultured $\times 100$ (Salih *et al.*, 2023).
- Seedling lengths (cm): The seedling lengths were taken using a graduated ruler, and the averages were calculated by taking 5 seedlings from each plate.

2.4 Pots Experiment:

Three salt-tolerant genotypes of durum wheat were used, ACSAD (1671, 1711, and 1765), according to the results of the laboratory experiment. The pot experiment was carried out inside under greenhouse conditions, the soil samples were sterilized at (90°C for 48 h). Five kg of sterilized clay-sandy soil were put into pots, a ratio of 2:1 (weight to weight). Ten seeds of durum wheat were sown in each pot. Before the transactions take place, the quantity of seedlings is decreased to five per pot. After two weeks of planting, the saltwater irrigation began. and grown under greenhouse conditions of 54 pots, for 80 days of sowing. and with no chemical fertilizers. The experiment was set up in a completely random arrangement with six treatments and three repetitions as follows:

- T₁ without Salinity or spraying (control).
- T₂ 20% Seawater (Sw).
- T₃ 30% Seawater (Sw).
- T₄ Spraying of Nicotinic acid (NA) 75ppm without Salinity.
- T₅ Spraying NA75ppm+ 20% Sw. T₆ Spraying NA75ppm+ 30% Sw.

The application of nicotinic acid was carried out through foliar spraying thrice, the first, second and third sprays were done 30, 45 and 60 days after sowing, respectively. At the end of the experiment took final results of the following qualities:

Plant height and spike length (cm) were measured using a graduated ruler in three replicates, and the averages were calculated.

The number of spikes per plant and the number of grains per spike.

Leaf area / Plant (cm²) according to (Mokhtarpour *et al.*, 2010).

Photosynthetic pigments (chlorophyll a, b, and carotenoids) were determined spectrophotometrically according to (Metzner *et al.*, 1965).

Statistical Analysis:

The study experience was created using the complete random design (CRD). The statistical analysis was done using the Minitab 17 program and ANOVA variance analysis tables. The averages were compared using Tukey's test at P <0.05.

3 Results

3.1 Laboratory experiment:

Effect of different concentrations of seawater on germination percentage and seedling length in the laboratory :

The results presented in Tables (1 and 2), represented the effect of seawater irrigation levels (20, 30 and 40%) of ten ACSAD durum wheat genotypes, on the germination percentage and seedling length after 10 days of germination. Significant differences have been recorded in the germination percentage of tested genotypes. The lowest averages were for ACSAD genotypes (1697, 1729 and 1747), from 100% for the control to (53.25, 55.00 and 56.50 %), respectively. According to the findings, the germination percentage of all genotypes was not affected at a concentration of seawater of 20% but decreased at a concentration of 30%. while a concentration of 40% seawater suppressed all seed growth for all wheat genotypes except ACSAD (1671, 1711 and 1765) by (20, 20 and 36%) respectively. Moreover, the results showed a decrease in the average seedling length of ten wheat genotypes. The highest average seedling length was recorded (8.00, 8.52 and 8.30cm), for ACSAD (1671, 1711 and 1765) respectively. In contrast, there are no significant differences in seedling length between the rest of the wheat genotypes. In general, all tested concentrations of seawater significantly reduced seedling lengths.

Table (1) Effect of different concentrations of seawater on seed germination (%) of wheat genotypes.

Genotypes	Seawater Concentration %				Genotypes average
	Control	20	30	40	
A1595	100	100	36	0	59.00 bc
A1651	100	100	50	0	62.50 bc
A1671	100	100	100	20	80.00 a
A1695	100	100	40	0	60.00 bc
A1697	100	100	13	0	53.25 c
A1711	100	100	80	20	75.00 ab
A1729	100	100	20	0	55.00 c
A1735	100	100	40	0	60.00 bc
A1747	100	100	26	0	56.50 c
A1765	100	100	100	36	84.00 a

Table (2) Effect of different concentrations of seawater on seedling length of wheat genotypes.

Genotypes	Seawater Concentration %				Genotypes average
	Control	20	30	40	
A1595	10.8	6.4	3.6	0	5.20 b
A1651	11.2	8.5	3.2	0	5.72 b
A1671	14.5	10.0	7.0	0.5	8.00 a
A1695	12.0	8.0	3.2	0	5.80 b
A1697	11.0	7.5	2.5	0	5.25 b
A1711	14.0	11.0	8.3	0.8	8.52 a
A1729	9.7	7.0	2.0	0	4.67 b
A1735	10.9	9.5	4.1	0	6.12 b
A1747	10.0	7.0	2.0	0	4.75 b
A1765	13.8	11.5	7.0	9.0	8.30 a

3.2 Pots Experiment:

Effect of different concentrations of seawater on some morphological and photosynthetic pigment parameters of the three-durum wheat genotypes (ACSAD).

Current work is shown in tables (3 and 4) an effect of seawater irrigation levels (0, 20, and 30%) on some morphological and photosynthetic pigment parameters of wheat genotypes after 80 days of sowing. The results showed that irrigation with seawater 20% caused a significantly decrease (p<0.05) in (plant height, leaf area /plant, spike length, No of spikes/plant, No. of grains/spike, chlorophyll a, chlorophyll b, carotenoids, and total pigments), for all genotypes from (100%) of the control to (84.03, 87.16, 88.33, 75.47, 81.27, 81.31, 86.14, 71.69 and 82.02%), for ACSAD 1671, and (76.39, 76.23, 74.13, 71.73, 63.90, 80.86, 83.87, 62.50 and 82.41%), for ACSAD 1711, and (79.89, 79.20, 81.66, 71.42, 75.95, 83.94, 84.37, 65.38 and 82.43%) for ACSAD 1765, respectively. In addition, genotypes grown under a seawater concentration of 30% exhibited significantly lower performance in all previously studied parameters compared to control (100%), to (63.02, 59.24,

61.66, 56.60, 65.77, 51.26, 77.71, 49.05 and 61.23%), for ACSAD 1671, (42.61, 47.33, 51.72, 56.52, 44.96, 51.26, 77.71, 49.05 and 61.23%), for ACSAD 1711, and (54.98, 55.24, 48.33, 53.57, 61.73, 50.52, 75.62, 48.07 and 57.09%) for ACSAD 1765, respectively. The ACSAD 1671 genotype exhibited the highest averages for all studied parameters under Salt stress conditions, whereas the ACSAD 1711 genotype exhibited the lowest averages.

Effect of foliar application of Nicotinic acid on some morphological and physiological characteristics of three wheat genotypes (ACSAD), under seawater irrigation levels.

The data presented in Tables (3 and 4) show the effect of foliar application of nicotinic acid on some morphological and photosynthetic pigment parameters for three genotypes of wheat (ACSAD), under seawater irrigation levels after 80 days of sowing. The results showed a significant increase in plant height for the three genotypes (ACSAD 1671, 1711 and 1765) by (17.31,

22.45, and 15.81%), leaf area /plant, (11.51, 10.94 and 11.09%), spike length, (5.00, 12.07 and 8.34%), the number of spikes/plant, (30.19, 15.22 and 5.36%), the number of grains/spike, (16.06, 16.57 and 14.21%), Chlorophyll a,(27.52, 13.21 and 21.58%), Chlorophyll b, (12.65, 13.54 and 5.63%), carotenoids, (13.21, 12.50 and 17.31%), and Total pigments, (22.04, 10.96 and 16.89%), respectively of treatment (T5), compared to (T2). As indicated by the treatment (T6) indicated a clear increase in plant height for the three genotypes (ACSAD 1671, 1711 and 1765) by (10.25, 18.81, and 12.20%), leaf area /plant, (8.49, 8.68 and 6.54%), spike length, (13.34, 8.62 and 18.33%), the number of spikes/plant, (18.87, 15.21 and 17.85%), the number of grains/spike, (13.37, 34.32 and 12.58%), Chlorophyll a,(25.76, 3.24 and 22.90%), Chlorophyll b, (10.24, 9.67 and 6.88%), carotenoids, (11.32, 10.42 and 7.69%), and total pigments, (17.30, 3.84 and 17.23), respectively compared to (T3).

Table (3) The effect of Nicotinic acid on the morphological characteristics of election genotypes of ACSAD wheat under different levels of salinity.

Genotypes	Con	Plant height		Leaf area /plant		Spike length		No. of spikes/plant		No. of grains/spike	
		(cm)	%	(cm ²)	%	(cm)	%	number	%	number	%
A1671	T ₁	59.5 cd	100	53.0 b	100	6.0 abc	100	5.30 abc	100	62.33 bc	100
	T ₂	50.0 h	84.03	46.2 e	87.16	5.3 abcde	88.33	4.00 bcde	75.47	50.66 f	81.27
	T ₃	37.5 l	63.02	31.4 h	59.24	3.7 defg	61.66	3.00 de	56.60	41.00 h	65.77
	T ₄	68.2 a	115.20	61.5 a	116.03	6.4 a	106.66	6.60 a	124.52	67.00 a	107.49
	T ₅	60.3 c	101.34	52.3 bcd	98.67	5.6 abcd	93.33	5.60 ab	105.66	60.67 cd	97.33
	T ₆	43.6 j	73.27	35.9 g	67.73	4.5 abcdefg	75.00	4.00 bcde	75.47	49.33 g	79.14
Genotype average		53.18		46.71		5.25		4.75		55.16	
A1711	T ₁	52.1 g	100	50.7 cd	100	5.8 abc	100	4.60 abcde	100	56.33 e	100
	T ₂	39.8 k	76.39	38.5 f	76.23	4.3 bcdefg	74.13	3.30 bcde	71.73	36.00 ij	63.90
	T ₃	22.2 n	42.61	24.0 j	47.33	3.0 fg	51.72	2.60 e	56.52	25.33 k	44.96
	T ₄	57.3 ef	109.98	52.9 bc	104.33	6.0 abc	103.44	5.00 abcd	108.69	59.00 d	104.73
	T ₅	51.5 gh	98.84	44.2 e	87.17	5.0 abcdef	86.20	4.00 bcde	86.95	45.33 g	80.47
	T ₆	32.0 m	61.42	28.4 i	56.01	3.5 efg	60.34	3.30 cde	71.73	34.66 j	79.28
Genotype average		42.48		39.78		4.60		3.80		42.77	
A1765	T ₁	58.2 de	100	50.5 cd	100	6.0 abc	100	5.60 ab	100	61.00 bcd	100
	T ₂	46.5 i	79.89	40.0 f	79.20	4.9 abcdefg	81.66	4.00 bcde	71.42	46.33 g	75.95
	T ₃	32.0 m	54.98	27.9 i	55.24	2.9 g	48.33	3.00 de	53.57	37.66 i	61.73
	T ₄	64.3 b	110.17	54.5 b	107.92	6.1 ab	101.66	6.00 ab	107.14	63.33 b	103.81
	T ₅	55.7 f	95.70	45.6 e	90.29	5.4 abcde	90.00	4.30 bcde	76.78	55.00 e	90.16
	T ₆	39.1 kl	67.18	31.2 h	61.78	4.0 cdefg	66.66	4.00 bcde	71.42	45.33 g	74.31
Genotype average		49.30		41.61		4.88		4.58		51.44	

Table (4) The effect of Nicotinic acid on photosynthetic Pigment of election genotypes of ACSAD wheat under different levels of salinity.

Genotypes	Con	Chlorophyll a		Chlorophyll b		Carotenoids		Total pigments	
		mg/ g	%	mg/ g	%	mg/ g	%	mg/ g	%
A1671	T ₁	3.96 abcd	100	1.66 ab	100	0.53 abc	100	6.15 de	100
	T ₂	3.22 abcd	81.31	1.43 abc	86.14	0.38 abcde	71.69	5.03 gh	82.02
	T ₃	2.03 cd	51.26	1.29 bc	77.71	0.26 de	49.05	3.58 j	61.23
	T ₄	5.04 a	127.27	1.87 a	112.65	0.62 a	116.98	7.53 a	122.43
	T ₅	4.31 ab	108.83	1.64 ab	98.79	0.45 abcd	84.90	6.40 cd	104.06
	T ₆	3.05 abcd	77.02	1.46 abc	87.95	0.32 cde	60.37	4.83 hi	78.53
Genotype average		3.60		1.55		0.42		5.58	
A1711	T ₁	3.71 abcd	100	1.55 abc	100	0.48 abcd	100	5.74 ef	100
	T ₂	3.00 abcd	80.86	1.30 bc	83.87	0.30 cde	62.50	4.60 hi	82.41
	T ₃	2.06 cd	55.52	1.05 c	67.74	0.20 e	41.66	3.31	59.29
	T ₄	4.53 ab	122.10	1.60 ab	103.22	0.53 abc	110.41	6.66 bc	116.02
	T ₅	3.49 abcd	94.07	1.51 abc	97.41	0.36 bcde	75.00	5.36 fg	93.37
	T ₆	2.18 cd	58.76	1.20 bc	77.41	0.25 de	52.08	3.63 j	63.13
Genotype average		3.16		1.36		0.35		4.88	
A1765	T ₁	3.80 abcd	100	1.60 ab	100	0.52 abc	100	5.92 e	100
	T ₂	3.19 abcd	83.94	1.35 abc	84.37	0.34 bcde	65.38	4.88 h	82.43
	T ₃	1.92 d	50.52	1.21 bc	75.62	0.25 de	48.07	3.38 j	57.09
	T ₄	4.74 ab	124.73	1.71 ab	106.87	0.58 ab	111.53	7.03 b	118.75
	T ₅	4.01 abc	105.52	1.44 abc	90.00	0.43 abcd	82.69	5.88 e	99.32
	T ₆	2.79 bcd	73.42	1.32 bc	82.5	0.29 cde	55.76	4.40 i	74.32
Genotype average		3.40		1.43		0.40		5.24	

4 Discussion

Wheat plays a crucial role in ensuring global food and nutritional security production. However, soil salinity poses a significant environmental, that hampers productivity and quality (El Sabagh *et al.*, 2021). Nevertheless, the detrimental impacts of salinity can be alleviated by identifying genotypes that are tolerant to salinity (Salih *et al.*, 2023). Therefore, this study was conducted with two experiments (laboratory - pots), To find out the impact of irrigation with seawater at the concentrations (20, 30 and 40%) on the tolerance of ten ACSAD durum wheat genotypes at the early seedling stage (laboratory experiment). According to the results of this experiment, the effect of foliar application of Nicotinic acid was evaluated for three salt-tolerant genotypes (ACSAD 1671, 1711 and 1765), under seawater salinity conditions at the concentrations 20 and 30% (pot experiment). Results indicated this study, laboratory experiment revealed significant differences when ($P < 0.05$) in reducing average germination percentage, and seedling length in wheat genotypes compared to control. Differences in germination rates were documented between wheat genotypes based on their tolerance to salinity (Ramadan *et al.*, 2023; Khanishova *et al.*, 2024). Hmissi *et al.* (2023) outlined that the primary factor hindering germination in low-

salinity conditions is the osmotic effect, while the toxic impact of sodium ions is observed in high-salinity environments. The negative effect of salinity attributed to Increased Na⁺ disorganizing ionic balance in cells, disturbs cell division, genetic circuits and protein synthesis machinery of plants, It also higher cellular membrane damage, and alters the nutrient level (Sarkar and Sadhukhan, 2023). Likewise, (Sghayar *et al.* 2023) stated that Na⁺ accumulation in wheat seedling tissues significantly impaired carbohydrate and protein mobilization by inhibiting amylase and protease enzymes. The ACSAD (1765, 1671 and 1711) genotypes scored the highest average germination percentage (84.00, 80.00 and 75.00%), respectively. On the other hand, she exhibited significantly greater seedling length than other genotypes. Observed by (Mahboob *et al.*, 2023) Differences between genotypes in salt tolerance are a polygenic trait controlled by multiple genes. Wheat's salt tolerance mechanisms include osmoregulation and scavenging reactive oxygen species. These mechanisms are supported by accumulated compounds such as sugars, polyhydric alcohols, amino acids, and quaternary ammonium compounds (Slama *et al.*, 2015). Moreover, plants possess both enzymic and non-enzymatic mechanisms for scavenging ROS, through the antioxidant defense system (Singh, 2022). It was observed that increased salinity from 30 to 40% Sw

significantly affected the initial growth traits. After the laboratory experiment, the germination data results of the laboratory experiment categorize ACSAD durum wheat genotypes into tolerant genotypes (1671, 1711 and 1765), moderate (1595, 1651, 1695 and 1735), and sensitive (1697, 1729 and 1747). Results of the pot experiment showed significant ($P < 0.05$) decreases in vegetative growth parameters and the contents of photosynthetic pigments, of the three-durum wheat genotypes (ACSAD), under seawater irrigation conditions, after 80 days of sowing. The harmful effect of saline stress was clear, especially in a concentration (30% Sw), which recorded the largest rates of decline in general. Similar findings were reported for wheat under seawater irrigation conditions by (Nassar *et al.*, 2020; Bashasha *et al.*, 2021; Elfanah *et al.*, 2023). In another study, Stojšin *et al.* (2023) reported that a decrease in plant height, spike length, and number of grains per spike was significant under the effect of salinity, for 27 wheat genotypes. The higher level of salts causes cell damage, reactive oxygen species (ROS) generation increased rate of lipid peroxidation, inhibiting apical growth, and inhibiting protein synthesis, (Alharbi *et al.*, 2022). The detrimental effects of salt stress on photosynthetic pigments were reported in studies on wheat (Salih and Abdulrazziq, 2023). The reduction in photosynthetic pigment parameters under salinity could be due to osmotic stress limits CO_2 fixation in the leaves by stomatal closure, downregulation of the Calvin cycle, as well as increased proteolytic enzymes chlorophyllase responsible for the degradation of chlorophyll, and decreased activity of ribulose biphosphate (Kwon *et al.*, 2019; Sharma *et al.*, 2020). The results of the data analysis showed that foliar application of Nicotinic acid alleviated the adverse effects of salinity levels in all morphological and the contents of photosynthetic pigments Parameters of wheat, compared to the untreated plant. Our results are consistent with many studies that showed Vitamin treatment successfully increases the productivity of crops (Khudair *et al.*, 2019; Al-Jboory *et al.*, 2022). The results are similar to (Farooq *et al.*, 2022), who suggested the foliar application of Nicotinic acid increases plant height, leaf area, and the number of leaves. also increases stomatal conductance, improves cell wall integration and enzymatic activities, and increases photosynthetic and transpiration rates. These results agree with those published by (Yaseen *et al.*, 2017) on the effects of vitamins on plant species organogenesis in vitro. The (1671) genotype performed better than the (1711 and

1765) genotypes in concern to high averages for all studied traits, under salinity and spraying with Nicotinic acid. foliar application of Nicotinic acid reduced salt stress and increased wheat growth through an increase in the levels of IAA, GA3, and cytokinins, and a decrease in ABA content (El-Bassiouny, 2005). Reduces the damage caused by cell membrane lipid peroxidation and improves plants' antioxidant capacity, contributing to cell osmotic regulation, and ROS detoxification according to (Chi *et al.*, 2021). In addition, Nicotinic acid is required by plants for synthesizing the amino acids and also helps in carbohydrate metabolism (Tomar *et al.*, 2018). Nicotinic acid counteract the formation of DNA strand breaks caused by oxidative stress, and prevent cell leakage and glutathione depletion caused by oxidative stress (Berglund *et al.*, 2017).

5 Conclusion

The laboratory experiment showed that the genotypes (1671, 1711 and 1765), were superior in recording the best average germination percentage and seedling length compared to the other genotypes, Under different seawater levels. Also, the pot experiment showed, under seawater irrigation conditions, decreases in all vegetative growth parameters and the contents of photosynthetic pigments, of the three durum wheat genotypes (ACSAD1671, 1711 and 1765), foliar application of Nicotinic acid led to a significant decrease in a negative effect resulting from salinity. The (1671) genotype performed better than the (1711 and 1765) genotypes in concern to high averages for all studied traits, under salinity and spraying with Nicotinic acid.

Conflict of interest: The authors declare that there are no conflicts of interest

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