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Hormonal modulation by omeprazole improves tomato growth under single and combined water and nitrogen deficits

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ABSTRACT

Omeprazole (OMP) has emerged as a promising protective compound against abiotic stress and a potential plant growth promoter, yet its role under combined stress and underlying mechanisms remains unclear. This study assessed the hormonal response of tomato plants to single and combined nitrogen (N) and water (W) deficits (50%N and/or 50%W) and the impact of OMP application to the root zone (0 and 1 μM) under these conditions. Combined deficit induced distinct hormonal shifts, including decreased shoots' abscisic acid (ABA) and indole-acetic acid (IAA), alongside increased salicylic acid (SA), jasmonic acid (JA) and jasmonic acid-isoleucine (JA-Ile). OMP consistently improved plant performance irrespective of the growth conditions, increasing total dry weight by 23% and enhancing nitrogen use efficiency and water use efficiency by 23% and 17%, respectively. Root growth stimulation in OMP-treated plants correlated with higher root IAA under control (+9%), N deficit (+27%), and W deficit (+20%) conditions, while combined deficit plants exhibited 35% lower root ABA without significant root biomass gain. OMP also improved photosynthetic rates and decreased shoots' lipid peroxidation, suggesting a protective effect. Hormonal modulation by OMP included lowering stress-related hormones - restoring JA and JA-Ile to control levels and reducing phaseic acid and SA under W deficit - while promoting IAA, a growth-related hormone. Collectively, these findings indicate that the combined deficit triggers a distinct hormonal profile from single deficits, and that OMP acts as both a stress alleviator and a growth promoter under N and W limitations by modulating hormonal, physiological and biochemical responses in a condition-specific manner.

1. Introduction

Water and nitrogen (N) availability are among the most critical factors limiting plant growth and productivity (Machado et al., 2022). N is a key component of essential biomolecules, while water acts as the universal solvent for biological reactions and nutrient transport (Araus et al., 2020; Machado et al., 2022). Consequently, water and N fertilization are often overused, exacerbating climate change impacts and environmental constraints such as eutrophication, greenhouse gas emissions, and groundwater contamination (Fernandes et al., 2022).

Although the effects of the single N and water deficits have been extensively studied (reviewed by Sun et al., 2020; Machado et al., 2022; Chen et al., 2024), their simultaneous occurrence in crops is not yet fully understood. Recent research on tomato plants has addressed the biological basis of combined water and N deficit, focusing on primary metabolism and antioxidant system (Machado et al. 2023a, 2023b, 2025). These studies concluded that plant responses to combined stresses are not additive to single-stress effects. N remobilization and plant osmoregulatory molecules were pivotal for plant acclimation, alongside the maintenance of redox homeostasis through enzymatic and non-enzymatic antioxidant processes. However, so far, the hormonal regulation underlying these mechanisms has not yet been studied. Phytohormones such as abscisic acid (ABA), indole acetic acid (IAA), jasmonates such as jasmonic acid (JA) and jasmonic acid-isoleucine (JA-Ile), and salicylic acid (SA) play key roles in stress responses, orchestrating stomatal regulation, growth adjustments, and defence signalling (Raza et al., 2022; Kazan, 2023), highlighting the need to investigate their profiles under combined stresses.

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Table 1

Morphological traits of tomato plants cv. Moneymaker grown under control (CTR), nitrogen deficit (N), water deficit (W) and combined deficit (N + W) conditions, with or without 1 μM Omeprazole (OMP). Values are means of 6 replicates (n = 6). P values indicate the F-probability for the interaction between deficit conditions and OMP application and for individual factors. Different letters denote significant differences according to Tukey's HSD test ($p < 0.05$). Abbreviations: DW = dry weight.

Growth Conditions	OMP application (μM)	Leaf DW (g)	Stem DW (g)	Root DW (g)	Plant Height (cm)	Root Length (cm)
CTR	0	2.39	0.740	0.310^{b}	28.1	23.6
	1	2.56	0.803	0.542^{a}	29.4	26.1
N	0	1.41	0.277	0.157^{c}	21.2	24.5
	1	1.60	0.433	0.332^{b}	24.5	27.4
W	0	1.70	0.275	0.203^{c}	22.7	23.4
	1	2.07	0.473	0.310^{b}	25.2	23.8
N + W	0	1.15	0.232	0.150^{c}	18.5	20.0
	1	1.34	0.308	0.243^{bc}	20.1	22.7
Deficit Mean	CTR	2.47^{a}	0.772^{a}	0.426	28.8^{a}	24.8^{a}
	N	1.50^{c}	0.355^{b}	0.244	22.8^{b}	26.0^{a}
	W	1.88^{b}	0.374^{b}	0.257	23.9^{b}	23.6^{ab}
	N + W	1.25^{d}	0.270^{c}	0.197	19.3^{c}	21.3^{b}
OMP Mean	0	1.66^{b}	0.381^{b}	0.205	22.6^{b}	22.9^{b}
	1	1.89^{a}	0.505^{a}	0.357	24.8^{a}	25.0^{a}
Fprob						
Deficit × OMP		*0.283*	*0.076*	***0.019***	*0.585*	*0.706*
Deficit		***<0.0001***	***<0.0001***	*< 0.0001*	***<0.0001***	***0.0028***
OMP		***<0.0001***	***<0.0001***	*< 0.0001*	***0.0003***	***0.0155***

Research on small bioactive molecules, that can contribute to the mitigation of climate change impacts while meeting the growing food demand, is of great interest to the scientific community. Hormone-like compounds are particularly promising due to their role in modulating stress responses (Wang et al., 2018). Omeprazole (OMP), a proton pump inhibitor belonging to the benzimidazole class and widely used in humans to treat gastric disorders (Carillo et al., 2019a), acts by targeting P-Type IIC H^{+}/K^{+} ATPases in gastric parietal cells. Although these ATPases have not been identified in plants (Cirillo et al., 2019), OMP has shown potential in mitigating abiotic stresses and promoting growth in several species such as tomato, basil, lettuce, and green beans (Van Oosten et al., 2017; Rouphael et al., 2018, Cirillo et al., 2019; Carillo et al., 2019a and b; Ramírez-Estrada et al., 2024). It has also improved N assimilation and uptake in corn (Van Oosten et al., 2019) and enhanced drought tolerance in peppermint by increasing leaf water potential, proline accumulation, and secondary metabolism (Elansary and Zin El-Abedin, 2019). While OMP's effects under individual water or N limitation have been reported (e.g., Elansary and Zin El-Abedin, 2019; Cirillo et al., 2019; Van Oosten et al., 2019), its impact under combined deficits remains unexplored. Furthermore, the mechanisms underlying its action - linked to the protection of photosystem II, hormonal modulation root growth, membrane lipid remodelling, and antioxidant responses - are not fully understood (Van Oosten et al., 2017; Rouphael et al., 2018). To date, no study has quantitatively assessed the effects of OMP on hormone concentrations under combined stress conditions.

This study aims to (i) quantify the impact of N and water deficits on the hormonal profile of tomato plants and (ii) elucidate OMP's role in the acclimation responses under single and combined N and water deficits. We hypothesize that a combined deficit of N and water induces a shift in the hormonal profile that cannot be inferred from the responses of each deficit alone, and that OMP will differentially modulate stress-responsive hormones, enhancing acclimation and improving resource use efficiency. To address these aims, we employed a multilevel approach to assess key morpho-physiological traits, oxidative stress markers, and endogenous phytohormonal concentrations.

2. Materials and methods

2.1. Plant growth conditions and experimental design

The experiment was conducted in a phytoclimatic growth chamber under controlled environmental conditions: day/night temperatures of 25 °C/23 °C, a 16h photoperiod with a photosynthetic photon flux density of 300 μmol s^{-1} m^{-2}, and 70% relative humidity. A completely randomized 4 × 2 factorial design was used, combining four deficit conditions with two levels of OMP application. This experimental design was implemented following previous studies on combined stresses (e.g., Vescio et al., 2022; Machado et al., 2023b; Machado et al., 2025).

Tomato seeds (cv. Moneymaker; ~220 seeds in total) were sown in trays filled with vermiculite (0.1 to 1.5 mm-grade), irrigated weekly with half-strength Hoagland solution and watered as needed. After approximately three weeks, at the third-leaf stage, uniform seedlings were selected and transplanted individually into pots (10.9 cm height, 14 cm diameter; ~1.7 L) containing 120 g of vermiculite. Plants were then assigned to eight treatments resulting from the combination of four deficit conditions [control (CTR; 100% N – 10.5 mmol/L; 100% field capacity – i.e FC], N deficit (N; 50% N – 5.3 mmol/L), water deficit (W; 50% FC) and combined deficit (N + W; 50% N – 5.3 mmol; 50% FC) and two OMP levels (0 or 1 μM), with 15 replicates per treatment.

OMP was supplied to the plants via the nutrient solution and the studied concentration was selected based on previous studies (Van Oosten et al., 2017, 2019; Cirillo et al., 2019). Prior to transplanting, the pots were watered to reach 100% FC (~400 mL) using nutrient solutions prepared according to Machado et al. (2023c): one with 10.5 mmol/L of N (for CTR and W treatments) and another with 5.3 mmol/L of N (for N and N + W treatments), each supplemented with 0 or 1 μM of OMP. To minimize soil water evaporation, pots were covered with black plastic sheets (with a slit from the edge to the centre to allow plant placement) secured with an elastic band (Fig. SM1). CTR and N-deficit pots were weighed daily and watered to maintain 100% of FC. W-deficit pots (W and N + W) did not receive further watering until they reached 50% FC (12 days after transplant), after which they were rewatered daily to maintain 50% of FC.

Plants were harvested 25 days after transplanting. Six replicates per treatment (n = 6) were used for morphological and physiological measurements. Roots were carefully washed, and plants were separated into roots, stem and leaves. The remaining nine plants per treatment were allocated for biochemical analyses, and these were divided into roots and shoots, immediately frozen in liquid N and stored at −80 °C. Tissues were subsequently ground in liquid N, and three biological replicates per treatment were prepared (n = 3; each consisting of a pooled sample of three plants).

2.2. Morphological traits

At harvest, plant height was measured from the stem base (at the substrate surface) to the apical meristem, and maximum root length from the root–shoot junction to the tip of the longest root. A LI-3100C area meter (LI-COR, Lincoln, Nebraska, USA) was used to measure total leaf area (LA) per plant. Dry weights of leaves (LDW), stems (SDW) and roots (RDW) were collected after drying the plant material at 105 °C for 48 h in a ventilator. Shoot-to-root ratio was calculated by dividing SDW by RDW (g/g DW).

2.3. *Chlorophyll relative content, photosynthesis and water use efficiency*

The physiological measurements described here were performed on six biological replicates, using the youngest fully expanded leaf. Chlorophyll relative content was measured non-destructively using a SPAD-502 meter (Konica Minolta, Tokyo, Japan) Photosynthesis was assessed with a portable infrared gas analyser (LI-COR 6400 IRGA, Lincoln, NE, USA) approximately 2 h after the start of the photoperiod and the overall readings took 2 h. The settings for the LI-COR were as follows: light intensity of 300 ± 1 μmol/m^2.s, CO_2 concentration of 400 ± 2 μmol/mol, leaf temperature of 25 ± 1 °C, and relative humidity of 67 ± 1%. The CO_2 assimilation rate (A, μmol CO_2/m^2.s) and the stomatal conductance (g_s, mol/m^2.s) were recorded. WUE was calculated as TDW divided by W consumption during the experiment (g/mL DW).

2.4. *Nitrogen use efficiency traits*

Nitrogen use efficiency (NUE) was calculated as TDW per unit of N applied (g TDW/mg N mL). NUE-related traits were calculated according to Abenavoli et al. (2016). Total N Accumulation (TNA) was calculated as the N concentration times the total plant dry weight (mg N); N Uptake Efficiency (NUpE) was calculated as TNA divided by root dry weight (mg N/g RDW); N Utilization Efficiency (NUtE) was calculated as the total plant dry weight divided by N concentration (g^2 TDW/mg N).

2.5. *Lipid peroxidation*

LP was estimated through the quantification of malondialdehyde (MDA) using 250 mg of frozen ground shoot or root tissues (n = 3; each biological replicate includes a pool of three plants) and following Machado et al. (2023a). Briefly, samples were homogenized in 0.1% (w/v) trichloroacetic acid, and (MDA) level was determined using the thiobarbituric acid reactive substances (TBARS) assay. Absorbance at 532 nm minus 600 nm was used with an extinction coefficient (ε) of 155 mM/cm. MDA concentration was expressed as nmol/g of fresh weight.

2.6. *Endogenous hormone analysis*

Hormones (ABA, PA, JA, JA-Ile, IAA, SA) were extracted and quantified following Durgbanshi et al. (2005) with modifications from Vives-Peris et al. (2023). Briefly, 50 mg of lyophilized shoots and 30 mg of lyophilized roots were extracted in 2 mL of ultrapure water, spiked with 25 μL of a solution containing internal standards, and then homogenized in a ball mill (MillMix20, Domel, Železniki, Slovenija). The following molecules were used as internal standards for structurally related hormones ([$^2H_6$]-ABA for ABA and PA; DHJA for JA and JA-Ile; [$^{13}C_6$]-SA for SA; and [$^2H_5$]-IAA for IAA). Following vigorous agitation with glass beads for 10 min at 17 rps, the samples were centrifuged at 12 000 g for 10 min at 4 °C. The resulting supernatants were collected, and their pH was adjusted to 3 using 30% acetic acid. Each extract was then subjected to two successive liquid–liquid extractions with 2 mL of diethyl ether. The organic phase was recovered and concentrated to dryness under vacuum using a centrifugal evaporator (Speed Vac, Jouan, Saint Herblain Cedex, France). The residues were subsequently reconstituted in 500 μL of a methanol:water solution (10:90, v/v) with mild sonication. Prior to analysis, samples were filtered through 0.22-μm polytetrafluoroethylene syringe filters and injected into an ultra-performance liquid chromatography system (Xevo TQ-S, Waters

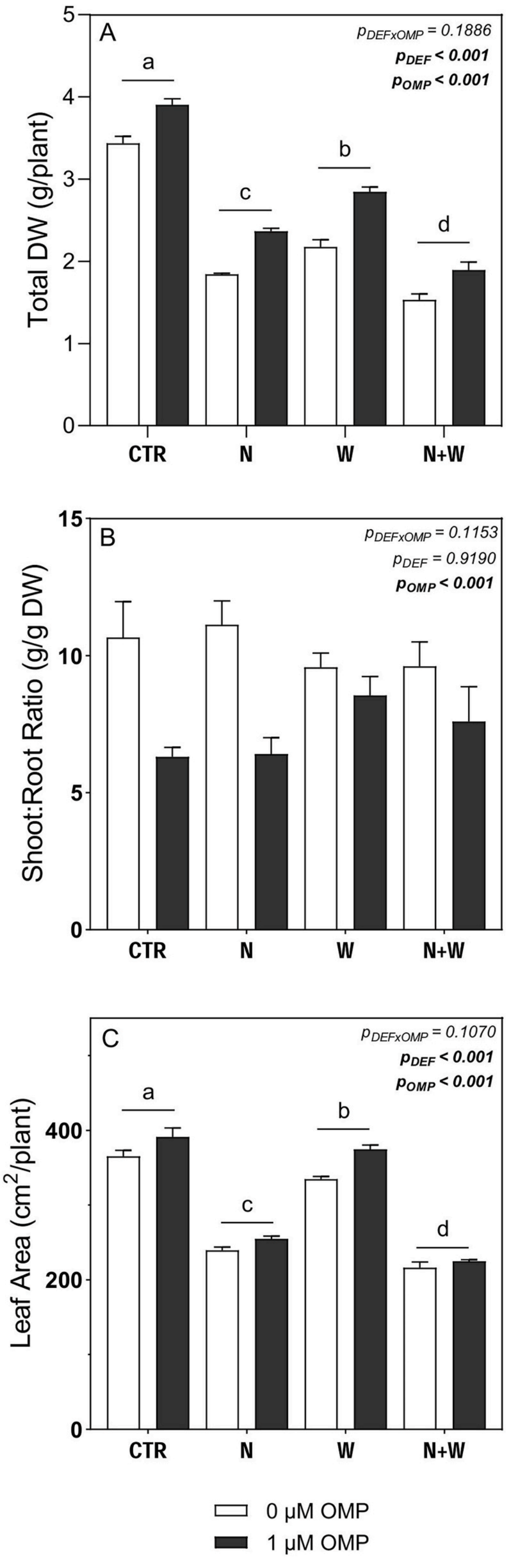

Fig. 1. Total dry weight (A), shoot:root ratio (B) and leaf area (C) of tomato plants grown under control (CTR), nitrogen deficit (N), water deficit (W) and combined deficit (N + W) with (black bars) or without (white bars) 1 μM of omeprazole (OMP). Values are means of six biological replicates ± standard error of the mean. P values indicate the F-probability for the interaction between deficit conditions and OMP ($P_{DEF \times OMP}$) and for their independent effects. Different letters denote significant differences according to Tukey's HSD test ($p < 0.05$).

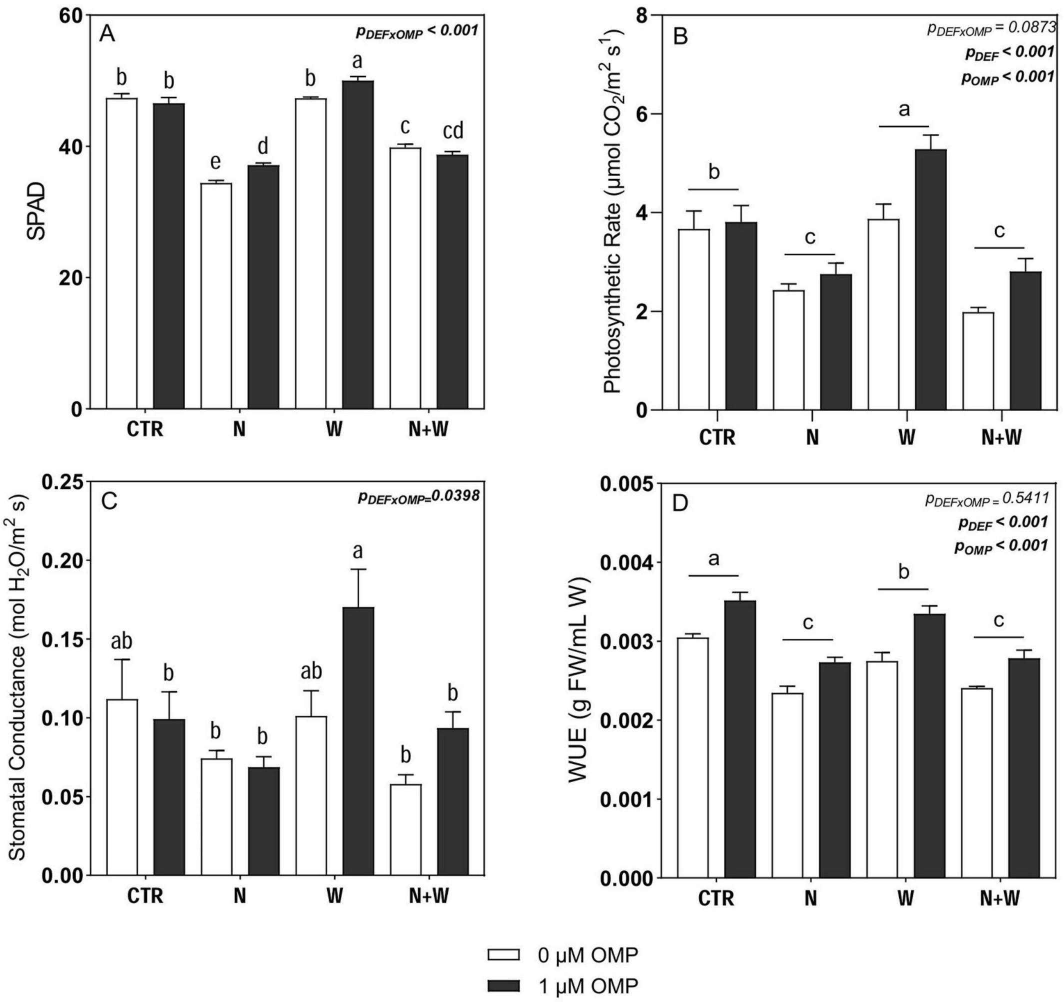

Fig. 2. Chlorophyll relative content (SPAD; A), photosynthetic rate (B), stomatal conductance (C) and water use efficiency (WUE; D) of tomato plants grown under control (CTR), nitrogen deficit (N), water deficit (W) and combined deficit (N + W) with (black bars) or without (white bars) 1 μM of omeprazole (OMP). Values are means of three biological replicates ± standard error of the mean. P values indicate the F-probability for the interaction between deficit conditions and OMP ($P_{DEF \times OMP}$) and for their independent effects. Different letters denote significant differences according to Tukey's HSD test ($p < 0.05$).

Corp., Milford, MA, USA, or Waters Alliance 2695, Waters Corp.). Phytohormone separation was conducted on a C18 reversed-phase column (Luna Omega, 50 × 2.1 mm 1.8-μm particle size, Phenomenex, Torrance, CA) using an acetonitrile:water (both supplemented with 0.1% acetic acid) gradient at a flow rate of 300 μL min^{-1}. Hormones were quantified using a UPLC-MS system consisting of a UPLC system connected to a triple quadrupole mass spectrometer by an orthogonal Z-spray interface (Xevo TQ-S, Waters Corp., Milford, MA, USA). The spectrometer was operated in negative electrospray ionization mode, and plant hormones were detected using a multi-residue mass spectrometric approach based on compound-specific transitions. Metabolites were monitored at m/z: SA 137 > 93, [$^{13}C_6$]-SA 143 > 99, IAA 176 > 130, $^{2}H_5$]-IAA 181 > 134, JA 209 > 59, [$^{2}H_6$]-ABA 269 > 159, ABA 263 > 153, JA-Ile 322 > 130, PA 279 > 139. MassLynx v4.2 software was used to process the data, and the relative quantification was obtained by comparing the areas of the different samples.

2.7. Statistical analysis

Differences among treatments were analysed by two-way ANOVA with deficit condition (CTR, N, W, and N + W deficits), OMP application (0 or 1 μM), and their interaction as fixed factors. Tukey's test ($p \leq 0.05$) was used for mean separation. Analysis was performed using GraphPad prism 9 software.

3. Results

3.1. Morphological traits

Two-way ANOVA revealed significant independent effects of the deficit conditions and the OMP application for most of the analysed traits (Table SM1, Table 1 and Fig. 1A–C).

In general, combined N + W deficit caused the greatest reductions in growth compared to CTR: TDW (−53%), LDW (−50%), SDW (−65%), plant height (−33%), maximum root length (−14%), and LA (−42%). Individual deficits led to less severe effects but still significant, reducing TDW by 43% under N deficit and 32% under W deficit. OMP consistently promoted plant growth across treatments, even under CTR conditions, significantly increasing TDW by an average of 23% (Table 1). Additional OMP-induced benefits were observed for LA (+8%), LDW (+14%), SDW (+33%), plant height (+10%), and maximum root length (+9%). A significant interaction between deficit condition and OMP application was only found for RDW, where OMP enhanced RDW under all single deficits (53% to 111%) but had no effect under combined stress (Table 1). Shoot-to-root ratio decreased by 30% in OMP-treated plants, indicating greater biomass allocation to roots, independently of the growth conditions.

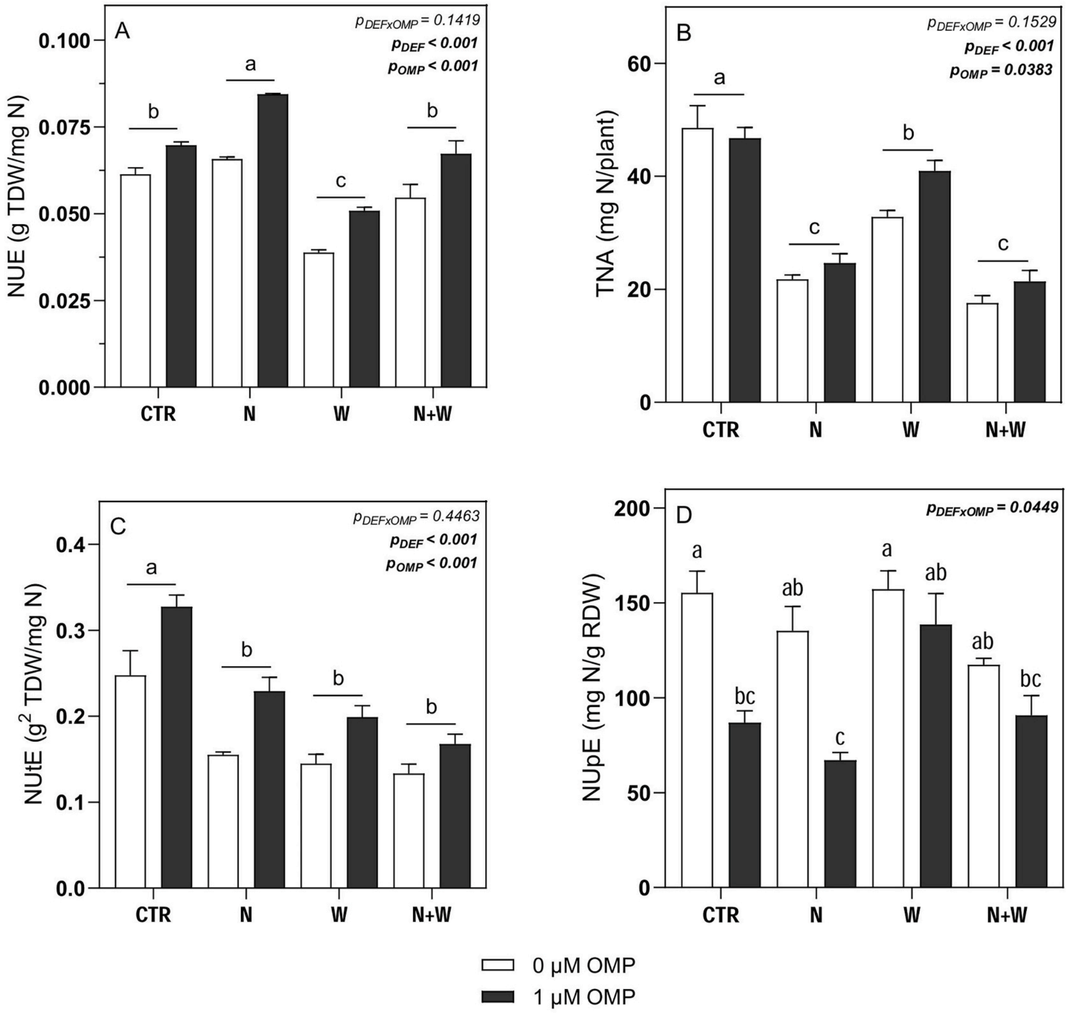

Fig. 3. Nitrogen use efficiency (NUE; A), Total nitrogen accumulation (TNA; B), Nitrogen utilization efficiency (NUtE; C) and Nitrogen uptake efficiency (NUpE; D) of tomato plants grown under control (CTR), nitrogen deficit (N), water deficit (W) and combined deficit (N + W) with (black bars) or without (white bars) 1 μM of omeprazole (OMP). Values are means of three biological replicates ± standard error of the mean. P values indicate the F-probability for the interaction between deficit conditions and OMP ($P_{DEF \times OMP}$) and for their independent effects. Different letters denote significant differences according to Tukey's HSD test ($p < 0.05$).

3.2. *Chlorophyll relative content, photosynthesis and water use efficiency*

Chlorophyll relative content (SPAD level) and stomatal conductance exhibited a significant interaction between deficit treatment and OMP application (Table SM1; Fig. 2A and C). SPAD decreased by 27% under single N deficit and 16% under combined deficit compared with CTR plants, while water deficit alone had no impact on this trait. OMP supplementation increased SPAD levels only under single deficit conditions (with increases of 8% under N deficit and 6% under W deficit). In contrast, photosynthetic rate (Fig. 2B) and water-use efficiency (WUE; Fig. 2D) were influenced independently by deficit treatments and OMP application, with no significant interaction between these factors. Photosynthetic rate declined by 31–36% under single or combined N deficits but increased under W deficit relative to CTR conditions (by ~22% on average). Similarly, WUE decreased under all deficit conditions, with the strongest reduction observed under N deficit (23% lower than CTR). OMP enhanced photosynthesis and WUE across treatments, with average improvements of 23% and 17%, respectively.

3.3. *Nitrogen use efficiency traits*

Two-way ANOVA results for NUE (Fig. 3A), TNA (Fig. 3B), and NUtE (Fig. 3C) showed an independent main effect of both studied factors (Table SM2). Deficit treatments strongly influenced N-related traits. Plants subjected to single N deficit exhibited a 15% increase in NUE, whereas those under single W deficit experienced a 32% reduction compared to CTR. TNA and NUtE declined significantly across all deficit conditions, with the combined deficit resulting in the largest decreases (59% for TNA and 48% for NUtE). OMP supplementation exerted a consistent positive effect on NUE, TNA, and NUtE across all deficit conditions, increasing these traits by 23%, 11%, and 35%, respectively. NUpE (Fig. 3D) decreased significantly upon OMP application under CTR and N-deficient conditions, by 44% and 50%, respectively, resulting in a significant interaction between the deficit condition and OMP application.

3.4. *Lipid peroxidation*

Two-way ANOVA revealed a significant interaction between deficit treatment and OMP application for LP in the shoots, assessed as MDA level (Table SM2; Fig. 4A). Plants exposed to N deficit (single or combined) had a significantly higher MDA concentration at shoot level, (by 24% and 34%, respectively), while, OMP application was able to bring it to the values found in plants under CTR conditions. In roots, MDA concentration was not significantly impacted by the deficit conditions, whereas OMP lead to an overall increase of 9% in this parameter

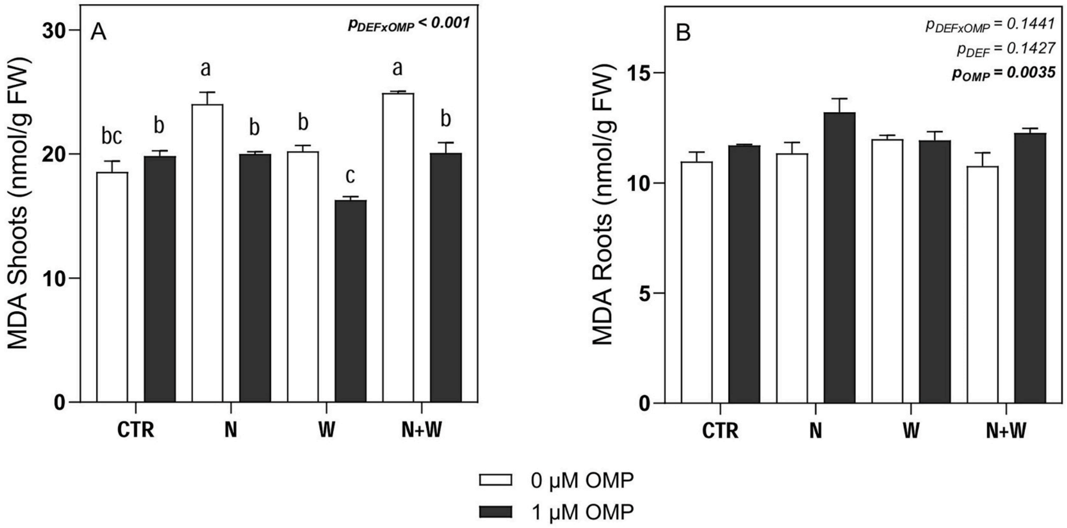

Fig. 4. Malondialdehyde (MDA) concentration in shoots (A) and roots (B) of tomato plants grown under control (CTR), nitrogen deficit (N), water deficit (W) and combined deficit (N + W) with (black bars) or without (white bars) 1 μM of omeprazole (OMP). Values are means of three biological replicates ± standard error of the mean. P values indicate the F-probability for the interaction between deficit conditions and OMP ($P_{DEF \times OMP}$) and for their independent effects. Different letters denote significant differences according to Tukey's HSD test ($p < 0.05$).

(Fig. 4B).

3.5. *Hormonal analysis*

This study comprehensively analysed root and shoot phytohormone levels, revealing a significant interaction between deficit treatments and OMP application for all quantified phytohormones, except for PA in roots (Table SM2; Figs. 5–7).

ABA concentration decreased in shoots under N deficit by 41% and under combined deficit 25% compared to CTR (Fig. 5A). OMP increased ABA in shoots under N deficit (+28%) and reduced ABA in roots under combined deficit (−35%) (Fig. 5A and B). PA increased in shoots under single W deficit (+14%) and decreased under N deficit (−27%), while OMP reduced PA levels by 22% in the shoots under W deficit (Fig. 5C and D).

IAA declined in shoots under N deficit (−27%) and combined deficit (−19%), and in roots under all deficit conditions by about 24% (Fig. 6A and B). OMP significantly increased root IAA in CTR (+12%), N deficit (+27%), and W deficit (+20%), but not under combined deficit conditions (Fig. 6B). Plants grown under combined deficit increased SA concentration in the shoots and roots (up to 55% higher compared to CTR plants) (Fig. 6C and D). Water deficit also led to a significant increase in SA, but only in shoots (Fig. 6C). OMP application resulted in a significant reduction of the SA concentration in shoots of plants subjected to W deficit (−33%) (Fig. 6D).

In general, the biosynthesis of jasmonates (JA and its conjugate JA-Ile) was strongly enhanced under deficit conditions (Fig. 7). For instance, shoot JA increased up to 13-fold under W deficit (single or combined), whereas root JA increased 6- to 7-fold across all deficit treatments (Fig. 7A and B). Similarly, JA-Ile was significantly enhanced under all deficit conditions at shoot and root level. Interestingly, OMP supplementation was highly effective in bringing jasmonates levels to those found in the CTR plants, particularly in the shoots, where JA decreased by 93% under single N and W deficits and by 96% under combined deficit (Fig. 7A). Meanwhile, in roots, JA decreased by 69% under N deficit and 70% under combined deficit (Fig. 7B). JA-Ile in shoots decreased by 93% under N deficit, 94% under W deficit, and 97% under combined deficit upon OMP application (Fig. 7C). In roots, JA-Ile decreased under all deficits with OMP application by 85% in N deficit, 79% in W deficit, and 84% in combined deficit (Fig. 7D).

4. Discussion

Omeprazole promoted plant growth and conferred tolerance against different abiotic stresses (Fig. 8). Nonetheless, its effects under combined stress have never been tested, and its precise mode of action in plants remains poorly understood. Our findings highlight that OMP is a promising elicitor-like compound capable of modulating plant physiological, biochemical and hormonal responses under both single and combined water and N deficits, with the potential to enhance crop performance and resource-use efficiency. Furthermore, this study demonstrates that OMP regulates tomato responses in a condition-specific manner (Fig. 8).

4.1. *OMP influences biomass accumulation and partitioning*

N deficit in combination with W deficit, imposed the most severe reductions in biomass production, corroborating previous findings (Machado et al., 2023b). OMP supply at very low concentration (1 μM) significantly improved overall plant growth, irrespective of the growth conditions, i.e., from the CTR non-stressed plants to plants exposed to combined deficit (Fig. 1A). Previous reports have also demonstrated this dual OMP effect, as a growth-promoting molecule and plant elicitor, namely in tomato under control and salinity stress (Van Oosten et al., 2017) and in peppermint under non-stressed conditions and water stress (Elansary and Zin El-Abedin, 2019). Moreover, Ramírez-Estrada et al. (2024), who evaluated the effect of foliar-applied OMP (1, 10 and 100 μM) on green bean under non-stress conditions, reported enhanced biomass accumulation regardless of the OMP concentration.

Concerning biomass partitioning, OMP enhanced RDW under all growth conditions (including in CTR plants), with the deficit plants reaching the root biomass levels comparable to those of CTR plants without OMP, suggesting that OMP promotes root development as a tolerance mechanism. This conclusion is aligned with a significantly lower shoot-to-root ratio in OMP treated plants (Fig. 1B), a trend previously reported in tomato treated with OMP under salinity (Van Oosten et al., 2017). Increased root growth compared to the shoots by OMP may reflect its hormonal crosstalk with other phytohormones, as indicated by elevated IAA levels in the roots of OMP treated plants which had significant increases of RDW, and decreased root ABA levels of combined deficit plants supplemented with OMP, which can improve nutrient and water uptake under stresses such as salinity, drought, and N deficiency

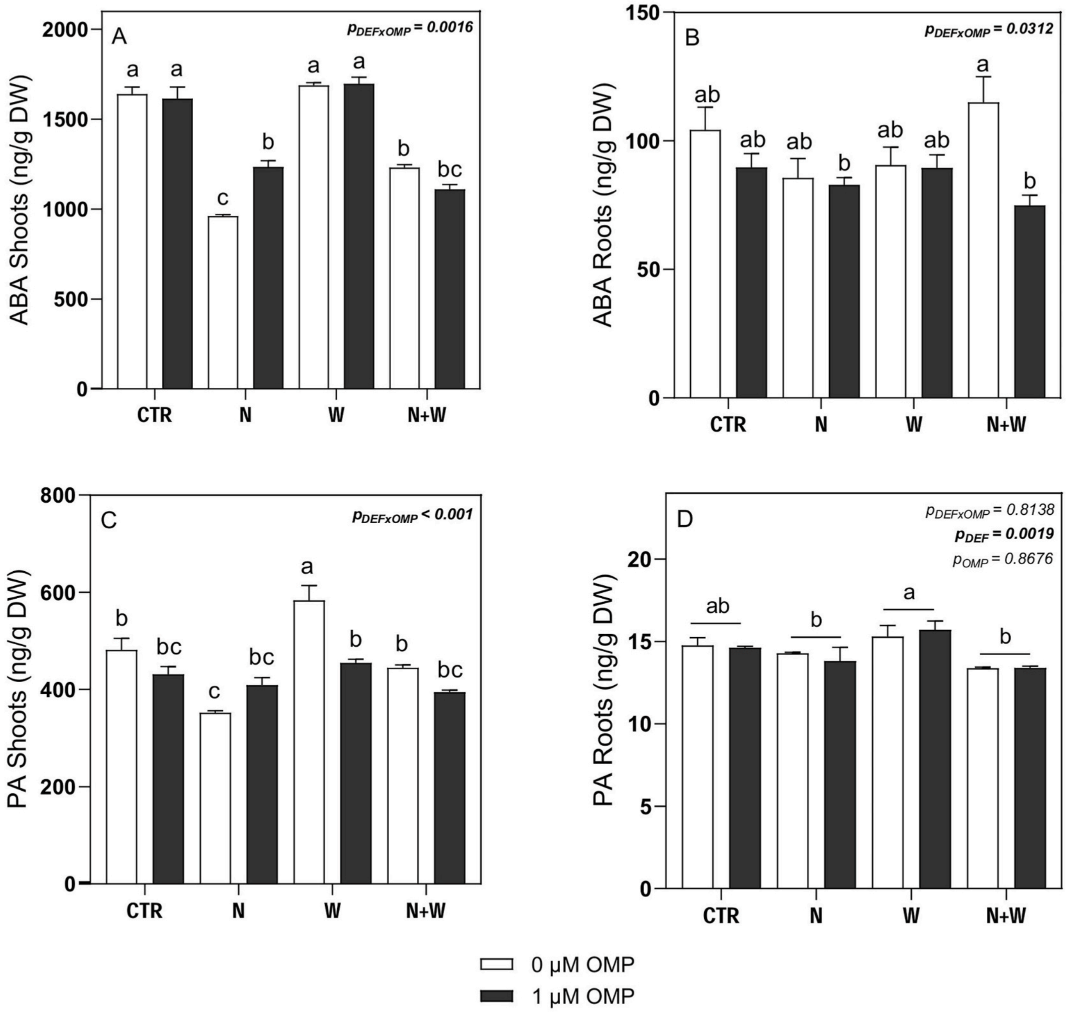

Fig. 5. Abscisic acid (ABA) concentration in shoots (A) and roots (B), and phaseic acid (PA) concentration in shoots (C) and roots (D) of tomato plants grown under control (CTR), nitrogen deficit (N), water deficit (W) and combined deficit (N + W) with (black bars) or without (white bars) 1 μM of omeprazole (OMP). Values are means of three biological replicates ± standard error of the mean. P values indicate the F-probability for the interaction between deficit conditions and OMP ($P_{DEF \times OMP}$) and for their independent effects. Different letters denote significant differences according to Tukey's HSD test ($p < 0.05$).

(Van Oosten et al., 2017; Elansary and Zin El-Abedin, 2019; Van Oosten et al., 2019).

Reductions in LA under N and W deficits align with adaptive strategies to minimize water loss (Salehi-Lisar and Bakhshayeshan-Agdam, 2016; Zhou et al., 2017). OMP counteracted these reductions, likely through improved osmotic regulation in the cytosol and vacuole, as suggested for lettuce under salt stress (Carillo et al., 2019a), thereby sustaining photosynthetic capacity. Collectively, these findings confirm OMP's role in promoting biomass accumulation and modifying partitioning patterns to favour root development while maintaining leaf area, as previously observed under salt, drought, and N stress in tomato, peppermint, and corn plants, respectively (Rouphael et al., 2018; Elansary and Zin El-Abedin, 2019).

4.2. Chlorophyll relative content and photosynthetic regulation by OMP

N deficit (alone or combined) reduced chlorophyll content and photosynthetic rate (Fig. 2A and B), likely due to the remobilization of N from photosynthetic components (Mu and Chen, 2021). However, OMP was able to significantly increase SPAD values in plants grown under single N deficit and increase the photosynthetic rate under all deficit conditions. This effect may be related to the ability of OMP to preserve the photosynthetic apparatus under deficit conditions. Previous studies have shown that OMP can enhance antioxidant capacity and stimulate the accumulation of protective metabolites such as carotenoids and phenolic compounds, which contribute to maintaining chloroplast integrity and photosynthetic efficiency (Van Oosten et al., 2017; Rouphael et al., 2018).

In agreement with previous findings in tomato (Machado et al. 2023b, 2025), SPAD values decreased under N-deficient conditions but remained unaffected under W-deficit conditions. This likely reflects the relatively mild severity of the imposed W deficit (50% FC for 15 days with daily adjustments), which allowed plants to acclimate and maintain water status. Machado et al. (2025) also reported that a moderate water deficit in tomato (comparable to the one applied in this study) did not induce stomatal closure, thereby sustaining photosynthesis and suggesting the involvement of more subtle acclimation mechanisms. In this study, hormonal adjustments might have contributed to the observed responses. Despite this acclimation, OMP application improved SPAD and photosynthetic rate in plants under W deficit. Altogether, these results suggest that OMP plays a protective role in the photosynthetic apparatus. Similar findings have been reported in tomato plants under salt stress, where OMP improved photosynthesis and upregulated genes involved in photosystem II repair (Van Oosten et al., 2017). Likewise, Elansary and Zin El-Abedin (2019) reported improved chlorophyll content and photosynthetic capacity in W-stressed

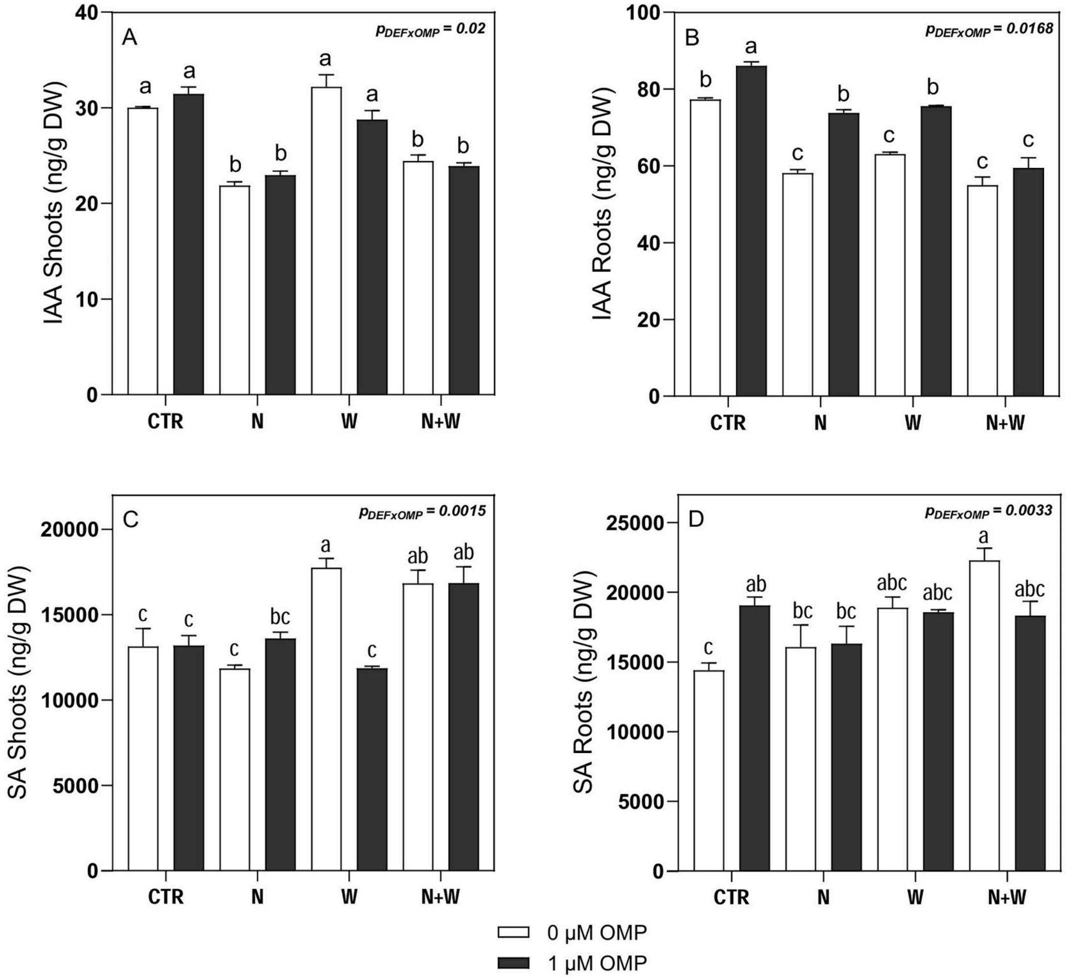

Fig. 6. Indole-acetic acid (IAA) concentration on shoots (A) and roots (B), and salicylic acid (SA)concentration in shoots (C) and roots (D) of tomato plants grown under control (CTR), nitrogen deficit (N), water deficit (W) and combined deficit (N + W) with (black bars) or without (white bars) 1 µM of omeprazole (OMP). Values are means of three biological replicates ± standard error of the mean. P values indicate the F-probability for the interaction between deficit conditions and OMP ($P_{DEF\times OMP}$) and for their independent effects. Different letters denote significant differences according to Tukey's HSD test ($p < 0.05$).

peppermint following OMP application.

4.3. OMP improves WUE and NUE

WUE and NUE are key indicators of crop resource utilization (Hatfield and Dold, 2019). In this study, single and combined deficits did not significantly impact the intrinsic WUE (i.e., photosynthetic rate/stomatal conductance – A/gs; data not shown), indicating an efficient stomatal regulation (carbon gain vs. stomatal opening). However, when WUE was calculated at the plant level during the growth period (i.e., dry matter produced per unit of water consumed; g/mL), WUE declined under all deficits, particularly combined stress, but improved with OMP application, suggesting enhanced water conservation while maintaining growth (Fig. 2D). NUE and N uptake efficiency (NUpE) also increased with OMP application (Fig. 3A and C), being consistent with reports of enhanced nitrate reductase activity and amino acid accumulation in low N conditions (Van Oosten et al., 2019). Interestingly, NUpE decreased under CTR and N-deficient conditions, possibly reflecting altered root growth and nutrient uptake dynamics. These findings indicate that OMP primarily enhances N utilization rather than uptake, supporting growth under limited N availability.

4.4. OMP alleviates lipid peroxidation

LP, a marker of oxidative stress (Awasthi et al., 2018), increased in shoots under N-deficits but was significantly reduced by OMP, indicating mitigation of oxidative damage (Fig. 4). Previous studies linked OMP to enhanced antioxidant enzyme activity, including catalase and ascorbate peroxidase, promoting ROS detoxification (Van Oosten et al., 2017; Cirillo et al., 2019; Elansary and Zin El-Abedin, 2019). The observed LP reduction aligns with improved chlorophyll content and photosynthesis in OMP treated plants, suggesting maintenance of cellular integrity under stress. In roots, OMP caused a slight LP increase, which may relate to auxin-mediated root development, as ROS and lipid-peroxidation by-products can enhance auxin signalling and lateral root formation (Biswas et al., 2019). This interpretation is consistent with elevated root IAA and RDW observed in this study.

4.5. Combined deficit and OMP regulate tomato hormonal responses

Hormonal signalling is central to plant acclimation under resource limitations, coordinating growth, water relations, and stress responses. In this study, OMP application modified the hormonal balance in tomato plants, particularly affecting jasmonates, salicylic acid and auxin levels, which were associated with improved plant performance under N and W deficits. *4.5.1. ABA and PA dynamics.*

ABA, a key regulator of stomatal closure and water conservation, typically accumulates under drought and nutrient deficiency, limiting CO_2 uptake and photosynthesis (Lawson and Blatt, 2014; Verma et al., 2016). N deficiency is often associated with enhanced ABA

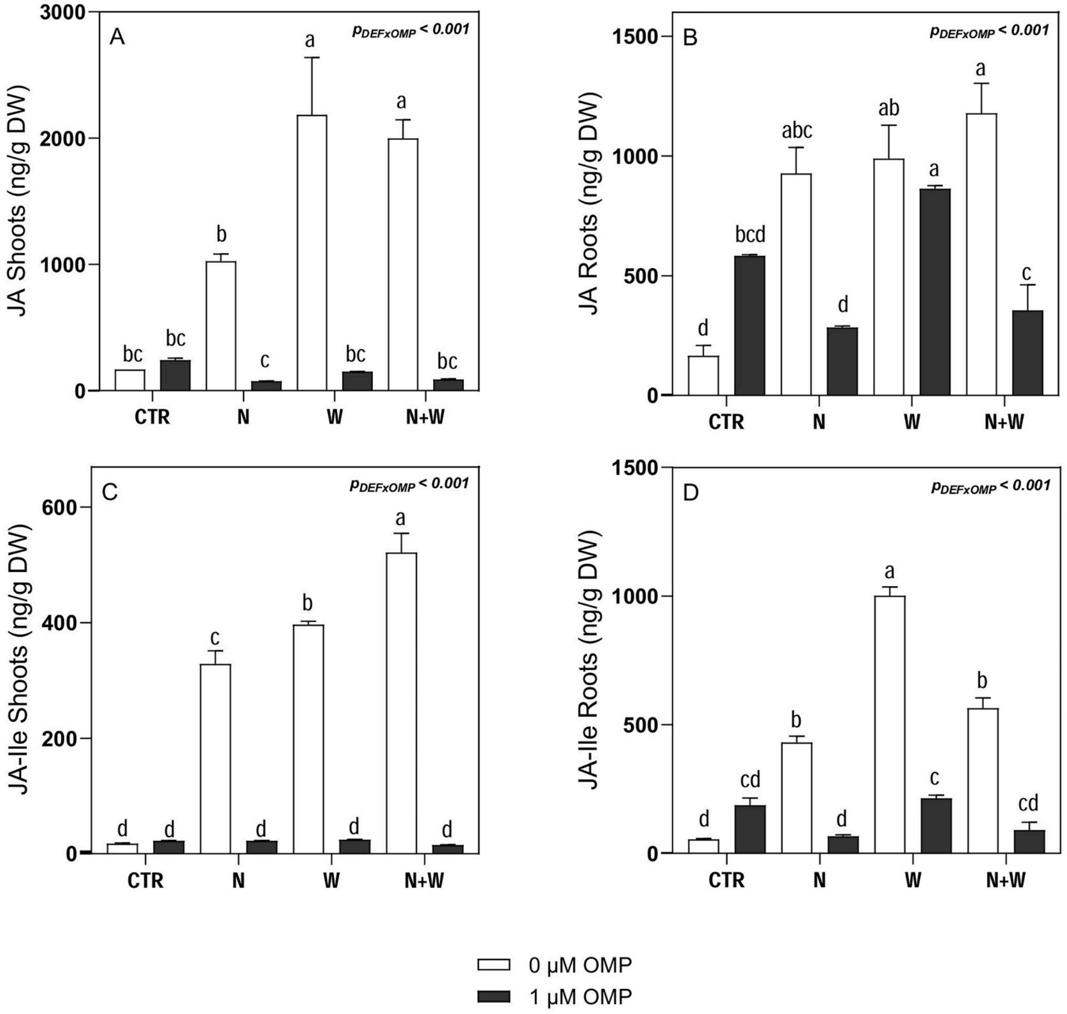

Fig. 7. Jasmonic acid (JA) concentration in shoots (A) and roots (B), and jasmonic acid-Isoleucine (JA-Ile) concentration in shoots (C) and roots (D) of tomato plants grown under control (CTR), nitrogen deficit (N), water deficit (W) and combined deficit (N + W) with (black bars) or without (white bars) 1 μM of omeprazole (OMP). Values are means of three biological replicates ± standard error of the mean. P values indicate the F-probability for the interaction between deficit conditions and OMP ($P_{DEF \times OMP}$) and for their independent effects. Different letters denote significant differences according to Tukey's HSD test ($p < 0.05$).

concentration in the plant tissues, triggering senescence and stress-adaptive pathways (Asad et al., 2025). Here, ABA levels in shoots and roots were unaffected by W deficit (Fig. 5A), consistent with the mild deficit imposed and the absence of major physiological changes, as previously reported for this type of deficit (Zhao et al., 2020). Nonetheless, under N deficit (single and combined), ABA levels have decreased, diverging from studies on short-term severe stress where ABA accumulation was observed (Hsieh et al., 2018; Asad et al., 2025). This can be due to differences in stress duration and intensity since ABA is highly dependent on both (Khan, 2025). In general, OMP application did not alter ABA levels, except for a significant increase at shoot level in plants grown under N deficit and a marked reduction at root level under combined N + W stress. PA, an ABA catabolite involved in stomatal regulation (Bulley et al., 2021), increased in shoots under W deficit, declined under N deficit, and remained near-control under combined stress, suggesting a buffering effect of simultaneous deficits. Interestingly, as ABA levels in shoots remained similar to CTR under W deficit while PA concentration increased, this may reflect enhanced ABA turnover, suggesting that ABA catabolism contributes to maintaining hormonal homeostasis in shoots under mild water deficit conditions. OMP reduced PA content in shoots under W-deficit (single and combined), consistent metabolomic evidence from Rouphael et al. (2018), potentially supporting higher photosynthetic capacity. Previous reports (Van Oosten et al., 2017; Rouphael et al., 2018) suggested OMP increases ABA in shoots and decreases it in roots under salinity — potentially enhancing root growth — our results only partially reflected this pattern under combined deficit, likely due to stress-type differences and the use of direct hormone quantification rather than gene-expression proxies.

4.5.1. *IAA and root development*

IAA, a central growth regulator, decline under all deficits, indicating broad down-regulation of auxin-mediated signalling during both water and N limitations. OMP significantly increased root IAA under CTR, N and W deficits aligning with enhanced root biomass. This suggests a strategy favouring lateral root proliferation for improved water and nutrient uptake (Roychoudhry and Kepinski, 2022). Similarly, the OMP-induced root growth under salinity stress has been linked to auxin-mediated signalling (Van Oosten et al., 2017). Under combined deficit an increase of IAA was not found which shows a novel response by this deficit profile and could possibly be explained by the higher need of survival-oriented hormonal and metabolic reprogramming, which can exceed the capacity of OMP to sustain auxin biosynthesis.

4.5.2. *SA and stress perception*

SA, a phenolic acid primarily associated with biotic defence, also

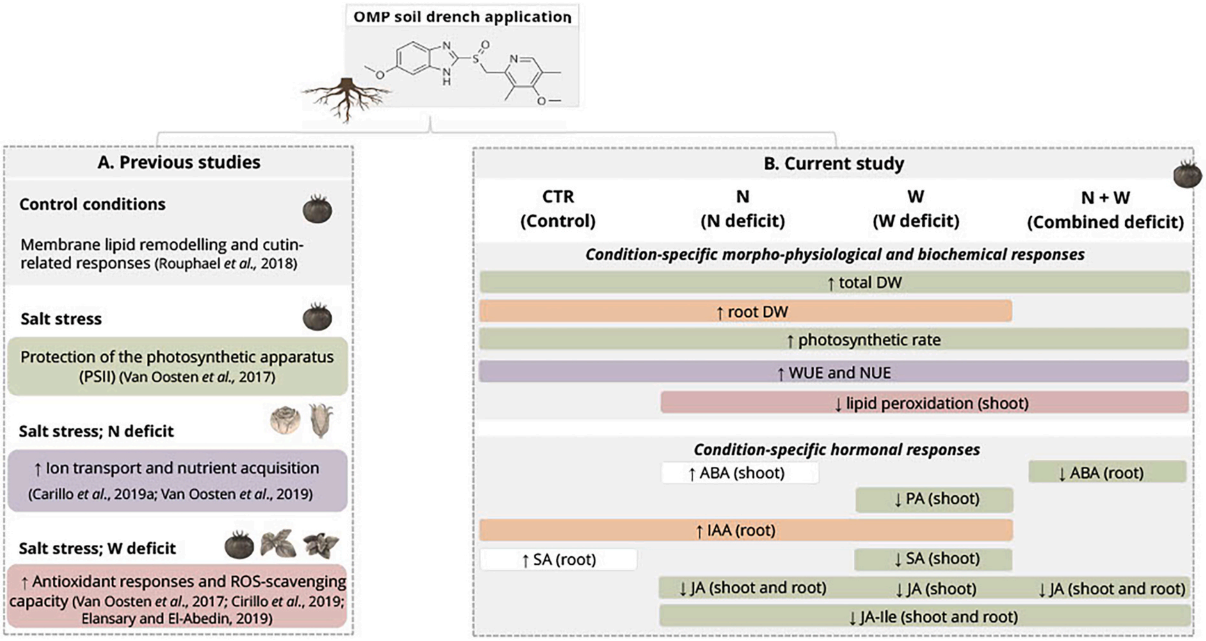

Fig. 8. Schematic representation of omeprazole (OMP) effects integrating information available from previous studies in different crops (A) with the condition-specific morpho-physiological, biochemical and hormonal responses observed in this study under single and combined N and W deficits in tomato (B). Processes and parameters with the same background colour represent functionally related responses (except for white boxes).

mediates abiotic stress responses (Khan et al., 2015; Koo et al., 2020). SA levels rose under water deficit in shoots and under combined deficit in both organs, indicating heightened stress perception when deficits co-occur. OMP application lowered shoot SA levels in water-stressed plants (Fig. 6C), and together with reduced shoot PA under the same conditions (Fig. 5C), suggests decreased stress sensitivity. Elevated SA in roots of CTR plants treated with OMP may explain growth stimulation even under non-stress conditions, given SA's role in nutrient uptake and growth regulation (Koo et al., 2020).

4.5.3. *JAs and photosynthetic resilience*

JA and its active conjugate JA-Ile, key stress signalling molecules (Ali and Baek, 2020; Ghorbel et al., 2021), were strongly induced by all deficits but reduced by OMP. Jasmonates can accumulate rapidly in response to abiotic stress and act as early signals in drought responses (Ali and Baek, 2020). They have been reported to interact with ABA signalling pathways, further supporting their role as early regulators of plant stress responses under drought conditions (Ghorbel et al., 2021; De Ollas et al., 2015), promoting stomatal closure and chlorophyll degradation (Creelman and Mullet, 1997; Ali and Baek, 2020; Wang et al., 2020; Ghorbel et al., 2021; Li et al., 2021). Interestingly, jasmonates accumulation may actually precede and contribute to ABA biosynthesis during dehydration. This relationship was demonstrated in *Arabidopsis*, where JA and JA-Ile production in roots was shown to be required for the subsequent increase in ABA levels, highlighting the cross-talk between these hormonal pathways during drought signalling (De Ollas et al., 2015, 2018). In this context, the reduction of JA and JA-Ile observed in OMP-treated plants suggests that OMP may attenuate early stress signalling, thereby limiting downstream stress responses. This reduction likely contributed to higher chlorophyll content and photosynthetic activity observed under single deficits and may also indicate resource allocation toward cutin biosynthesis, as jasmonate and cutin pathways share precursors (Li et al., 2019), consistent with metabolomic evidence of increased cutin in OMP-treated tomato (Rouphael et al., 2018). Enhanced cutin and possible cuticle formation could further improve drought tolerance by reducing water loss (Salehi-Lisar and Bakhshayeshan-Agdam, 2016).

4.6. *OMP mode of action is condition-specific*

OMP appears to act as a signalling modulator rather than a simple osmo-protectant, reducing the endogenous levels of several stress-related hormones while promoting the synthesis of the growth-related hormone IAA. Fig. 8 integrates previously reported OMP-induced processes with the morpho-physiological, biochemical, and hormonal responses observed in this study. Together, these findings highlight that OMP functions as a context-dependent hormonal modulator, fine-tuning the balance between growth and stress responses. However, the magnitude and nature of these effects depended on the growth conditions and the plant organ. For instance, IAA increased only in roots and exclusively under control and single-deficit conditions, with no impact observed under combined deficits. In contrast, OMP markedly decreased JA and JA-Ile levels irrespective of the deficit conditions, reflecting a preserved modulation of these two hormones under N and W deficits. Future studies should focus on elucidating OMP's molecular pathways, validating its effectiveness across diverse crops and environments, and assessing safety aspects, including residue accumulation in edible tissues and environmental impacts.

5. Conclusion

Combined N and W deficits induced a distinct hormonal signature characterized by reduced ABA in the shoots, lower shoot and root IAA, and elevated SA and JA levels, revealing a complex adaptive mechanism not predictable from single-deficit responses. OMP application mitigated many adverse morpho-physiological effects, improving biomass accumulation, root dry matter allocation, photosynthetic performance and resource use efficiency (NUE and WUE). Moreover, OMP reduced oxidative damage and modulated the endogenous levels of several stress-related hormones under both single and combined N and W deficits, in an organ- and deficit-specific manner. These findings position OMP as a promising elicitor-like compound, capable of decreasing stress perception while activating growth-supporting pathways, with potential to improve crop performance and resource use efficiency in sustainable agriculture even under combined deficit scenarios.

Author contribution statement

SMPC, MWV and JM were responsible for the conception and design of the experimental work. APGF implemented the full experiment and carried out the lipid peroxidation analysis. APGF and JM did the plant sampling and the morpho-physiological analysis. APGF, VVP and AGC were responsible for hormonal quantification. APGF wrote the manuscript, all authors provided critical revision of the manuscript and approved the final version of the manuscript. SMPC, as APGF grant supervisor and responsible for funding acquisition, assumes responsibility for the integrity of the present work, from inception to finished article.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Ana Patricia Fernandes reports financial support was provided by Foundation for Science and Technology. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.plaphy.2026.111342.

Data availability

Data will be made available on request.

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