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REVIEW

# Deciphering nutrient stress in plants: integrative insight from metabolomics and proteomics

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**Abstract**

To comprehend the responses and resilience of plants under unfavorable environmental conditions, it is crucial to study the metabolomics and proteomic insights into nutrient stress. Nutrient stress substantially challenges agriculture, impacting plant growth, development, and productivity due to a lack or imbalance of essential nutrients, which can happen due to poor soil quality, limited nutrient availability, or unfavorable climatic conditions. Although there has been significant progress in the study of plant nutrient stress using metabolomics and proteomics, several challenges and research gaps still need to be addressed, such as the standardized experimental protocols, data integration strategies, and bioinformatic tools are necessary for comparative analysis and interpretation of omics data. Hence, this review explores the theoretical frameworks of metabolomics and proteomics as powerful tools to decode plant responses to nutrient stress, addressing critical knowledge gaps in the field. This review highlights the advantages of integrative analyses, combining metabolomics, proteomics, and transcriptomics, to uncover the molecular networks governing nutrient stress resilience. Key findings underscore the potential of these techniques to enhance breeding strategies and genetic engineering efforts aimed at developing nutrient-efficient crops. Through metabolomics and proteomic analyses, novel molecular components and regulatory networks have been revealed as responsive to nutrient stress, and this breakthrough has the potential to bolster plant resilience and optimize nutrient utilization. Understanding the synergistic roles of metabolites and proteins in nutrient stress resilience has profound implications for crop improvement and agricultural sustainability. Future research should focus on refining integrative methodologies and exploring their applications across diverse plant species and environmental conditions, paving the way for innovative solutions to nutrient stress challenges.

**Keywords** Nutrient stress · Abiotic Stress · Metabolomics · Proteomics · Signal pathways · Agricultural sustainability

## Introduction

Plants face numerous environmental challenges regularly, including nutrient deficiencies that can significantly impact their growth, development, and overall efficiency (Tyagi et al. 2023; Jan et al. 2025; Bisht et al. 2024). Nutrient stress occurs when plants struggle to obtain sufficient nutrients from their environment due to soil deficiencies, nutrient imbalances, or competition with other organisms for limited resources (Qiu et al. 2023; Wang et al. 2025a). Nutrient stress is a significant hurdle for plant survival, development, crop quality, resistance to stresses and agricultural output, making it imperative to comprehend how plants react and adjust to these circumstances (Zenda et al. 2021; Vilakazi et al. 2025). Metabolomics is essential for identifying crucial metabolites in plant reactions to nutritional stress, as plants often alter

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their amino acid metabolism, accumulating nitrogen-rich substances like proline and polyamines, requiring detailed analysis of biological systems (Salam et al. 2023; Zhang et al. 2023). Metabolomics research has revealed changes in carbohydrate metabolism, lipid composition, and secondary metabolite production under nutrient stress (Xian et al. 2023; Rajkumari et al. 2023; Abdulraheem et al. 2024). Its involve various techniques, including sample preparation, metabolite extraction, separation (e.g., chromatography), detection (e.g., mass spectrometry), and data analysis. Advanced analytical platforms such as gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS) are frequently used for metabolite profiling (Brockbals et al. 2025; Rahayu et al. 2025).

Conversely, proteomics investigates the functions of proteins on a larger scale within cells or organisms which allows for thorough examination of a sample's protein composition, abundance, and post-translational modifications (Tyagi et al. 2023; Kruaweangmol et al. 2025). Proteomics aids in identifying the significant proteins that contribute to nutrient uptake, transport, storage, and utilization, as well as shedding light on signaling pathways and regulatory networks (Ribeiro et al. 2023). Protein extraction, separation (using methods like liquid chromatography or gel electrophoresis), protein identification (mass spectrometry), and data analysis are all part of proteomics (Brockbals et al. 2025). Shotgun proteomics and targeted proteomics are advanced mass spectrometry-based technologies that help discover and quantify various proteins within the same experiment. Specialized proteomic workflows allow for the analysis of post-translational modifications like phosphorylation, acetylation, and glycosylation, allowing researchers to understand how plants cope with nutrient stress at a molecular level (Naik et al. 2023). When plants are stressed, they collect osmoprotectants to preserve the photosystem II complex, enzymes, and protein structure, which helps with membrane integrity and ROS scavenging, which can significantly impact biomass and secondary metabolites (SMs) production (Xu et al. 2025). Recent research has indicated that certain mineral nutrients can either increase or repress growth, and biomass production can influence SM production, depending on the growth conditions and environmental factors, which may be influenced by the species' or genotype's status and physiological traits (Wellpott et al. 2023; Keya et al. 2025). Micronutrient availability can affect the production of bioactive compounds by activating enzymes in biosynthetic pathways, while macronutrients like nitrogen are crucial for biomass and SM biosynthesis (Lacrampe et al. 2023).

Plants can remarkably adapt to nutrient stress by making intricate changes to their metabolic and proteomic networks, ensuring the continuation of their vital functions (Prusty et al. 2022). However, to gain a deeper knowledge of these responses, pinpointing and measuring the metabolites involved in both primary (carbohydrates and amino acids) and secondary (phenolics and flavonoids) metabolism are crucial (Zenda et al. 2021). The proteomic analysis delves into the connection between nutrient stress and protein adaptations by closely examining protein interactions, expression levels (Shen et al. 2023; Yang et al. 2019). This method enables the identification of specific proteins that might rise or drop in response when subjected to nutrient stress, providing insight into the molecular mechanisms involved in the response (Tinte et al. 2021; Singh and Jwa 2013). Furthermore, proteomic investigations can reveal these proteins' functional roles and function in critical cellular processes like nutrient uptake, assimilation, signaling, and transporting.

An essential aspect of research in this field involves comprehending how plants can endure nutrient stress because plant species exhibit varying resistance to nutrient-limit conditions (Yang et al. 2021; Ampong 2022; Wang et al. 2025b). Through undertaking metabolomics and proteomic studies, scientists can pinpoint the crucial proteins and metabolites that bolster plant resilience in the face of nutrient stress (Shen et al. 2023). Applying metabolomics and proteomic methods has revolutionized our comprehension of how plants react to nutrient stress (Raza et al. 2021; Roychowdhury et al. 2023; Yang et al. 2019). These cutting-edge techniques offer a detailed outlook on plant molecular alterations when subjected to nutrient deficiencies, empowering scientists to decipher intricate networks that regulate plant functioning and aims to decode the molecular responses and resilience mechanisms that plants employ to cope with nutrient stress (Fig. 1). With this knowledge, we can improve crop yields and safeguard worldwide food supplies by understanding plant responses to nutrient stress (Wellpott et al. 2023; Liu et al. 2024b).

Figure 1 above outlines the processes of investigating the metabolomics and proteomics insights into nutrient stress, which involve the metabolic and protein profiles of plants in response to nutrient deficiencies or imbalances. The experimental design entails defining the research objectives, selection of the appropriate plant species and the establishment of environmental conditions for the proposed study. The collection of plant samples should be done at different time points during the stress treatment to capture dynamic changes in metabolite and protein levels, and there should be an adequate number of biological replicates to account for biological variation. In the metabolomics analysis, the extraction of samples (liquid-liquid and solid-phase extraction), metabolite profiling (GC-MS, LC-MS), and data analysis using specialized software tools to detect significant changes in metabolite abundance between control and stressed samples. The proteomic analysis includes protein extraction (trichloroacetic acid and phenol

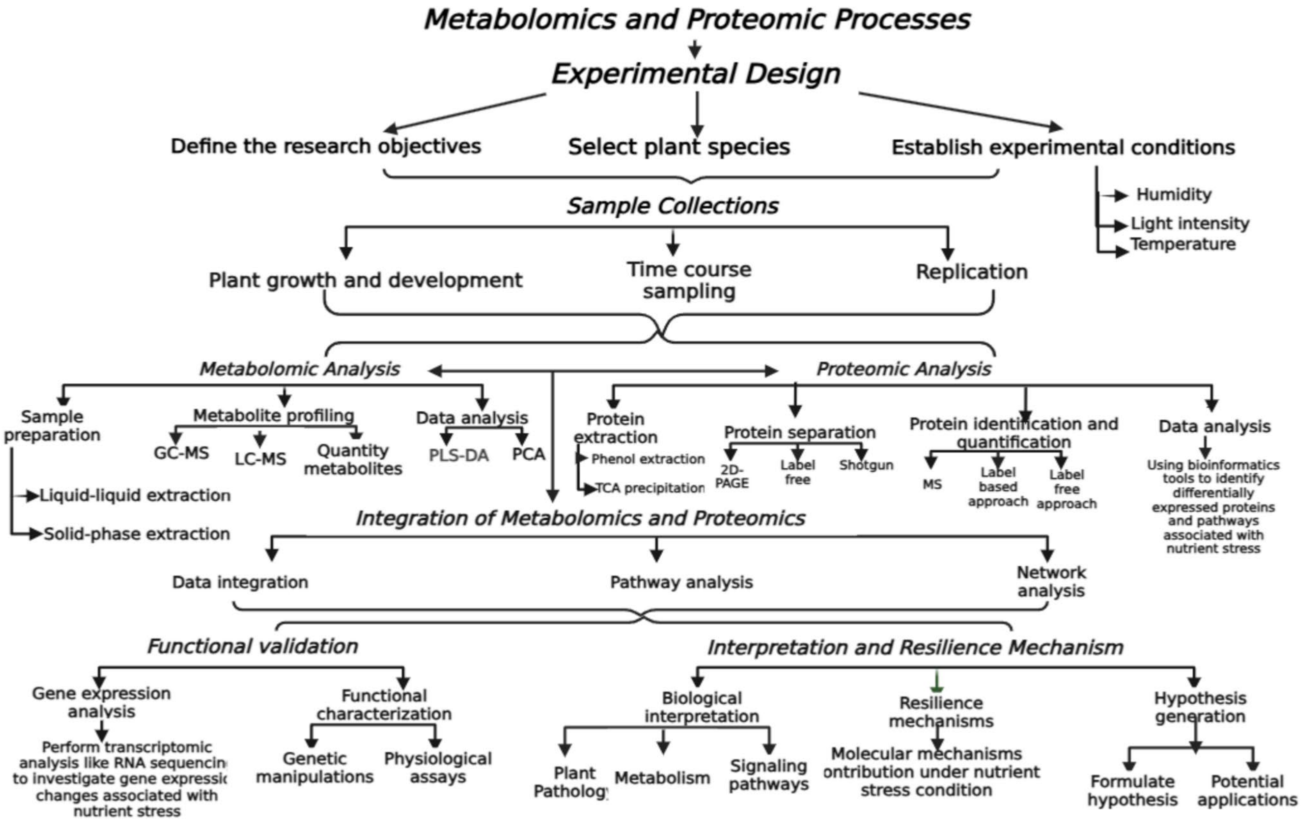

**Fig. 1** Schematic framework of metabolomics and proteomics stages, steps and analysis in response to nutrient stress

extraction) and protein separation, which employ techniques like (two-dimensional gel electrophoresis, shotgun and liquid chromatography-based methods. Mass spectrometry, label-free approach and label-based approach aid the identification and quantification of the protein where the data analysis was done using bioinformatics tools to identify differential protein expression and pathways associated with nutrient stress through the integration of metabolomics and proteomics, which include data integration, pathways and network analysis that elucidate the relationships between metabolites, proteins and regulatory elements involved in nutrient stress responses. The interpretation and resilience mechanism will give insights into the signal pathways, metabolism and plant physiology (biological interpretation). In contrast, the resilience mechanisms identify the molecular mechanisms contributing to plants under nutrient-stress conditions. The hypothesis generated will be further used for investigation and potential applications in crop improvement strategies.

Recent studies have highlighted that the exogenous application of melatonin enhances plant resilience under nutrient stress. For instance, melatonin application has been shown to improve peanut field productivity and quality while reducing nitrogen usage, offering a sustainable solution to optimize nutrient management (Li et al. 2024b). Also, research has indicated that mineral nutrients can either increase or repress growth, and biomass production can influence sensing mechanism production, depending on the growth conditions and environmental factors involved (Dalal et al. 2023). Hence, the adoption of the integration of metabolomics and proteomics allows for examining how various stresses signaling pathways interact where plants experience multiple stressors simultaneously (Kausar and Komatsu 2023). These methods can detect overlapping or distinct molecular signatures, which aids in the understanding of the interdependence of stress responses (Shen et al. 2023). Omics sciences, such as metabolomics, genomics, proteomics, and transcriptomics, can offer unparalleled opportunities to establish a comprehensive and predictive understanding of how plants react to particular circumstances (Fernie et al. 2020; Wang 2019). Transcriptomics has improved millet's salinity and drought tolerance, while proteomics and metabolomics have identified critical proteins and metabolic pathways linked to stress resilience and nutrient synthesis (Mazumder et al. 2024). When metabolite levels and protein expression patterns are combined, we learn about the metabolic pathways and regulatory mechanisms that govern nutrient stress responses (Vo et al. 2021; Prusty et al. 2022). This integrative approach identifies key metabolic nodes and regulatory hubs critical for plants to adapt to nutrient limitations (McKetney et al.

2022). Furthermore, these changes are reflected in the plant metabolome, making metabolomics and proteomics a powerful tool for studying the impact of stress (Castro-Moretti et al. 2020; Tinte et al. 2021). Thus, this review addresses the resilience of plants to nutrient stress, examines how plant species or genotypes exhibit enhanced tolerance to nutrient limitations or imbalances and provides an overview of the current research on metabolomics and proteomic insights into nutrient stress in plants.

## Metabolomics insights into nutrient stress

Metabolomics is a rapidly advancing field that analyzes metabolite molecules in biological systems, offering valuable insights into metabolic changes triggered by various stimuli, including nutrient stress (Haddadi et al. 2023). Nutrient stress occurs when an organism experiences insufficient or imbalanced intake of essential nutrients required for normal growth and development. This stress disrupts metabolism by affecting nutrient uptake, utilization, and storage, leading to metabolic imbalances (Marchev et al. 2021; Pandey et al. 2024). Metabolomics research has provided a deeper understanding of the complex metabolic adaptations that organisms undergo under nutrient-stress conditions, shedding light on underlying mechanisms and potential strategies for alleviating these effects (Xian et al. 2023). By analyzing metabolic changes under nutrient limitations, metabolomics reveals how organisms prioritize and allocate resources during periods of scarcity (Oh et al. 2023). Key findings include alterations in amino acid metabolism and an increase in secondary metabolite production as a defense mechanism against stressors (Pinto et al. 2023; Shahid et al. 2023; Lacrampe et al. 2023). These insights highlight metabolomics as a powerful tool for addressing the challenges posed by nutrient stress.

Plant metabolism categorized into primary and secondary metabolites, which play crucial roles as regulators, antioxidants, and defense mechanisms against pathogens (Patel and Parida 2023). This metabolites often accumulate in response to external stressors, resulting in the production of unique natural products (Ballhorn 2011). However, extreme environmental stress can disrupt metabolic pathways affecting the synthesis of secondary metabolite production which are derived from primary metabolites such as amino acids, carbohydrates, and lipids through specialized biosynthetic pathways (Chandran et al. 2020). These metabolites enable plants to adapt to their environment challenges, underscoring their important in plant survival and stress responses (Pott et al. 2019). Over time, plants have evolved genetically encoded pathways to synthesize secondary metabolites essential for their development and resilience (Fig. 2).

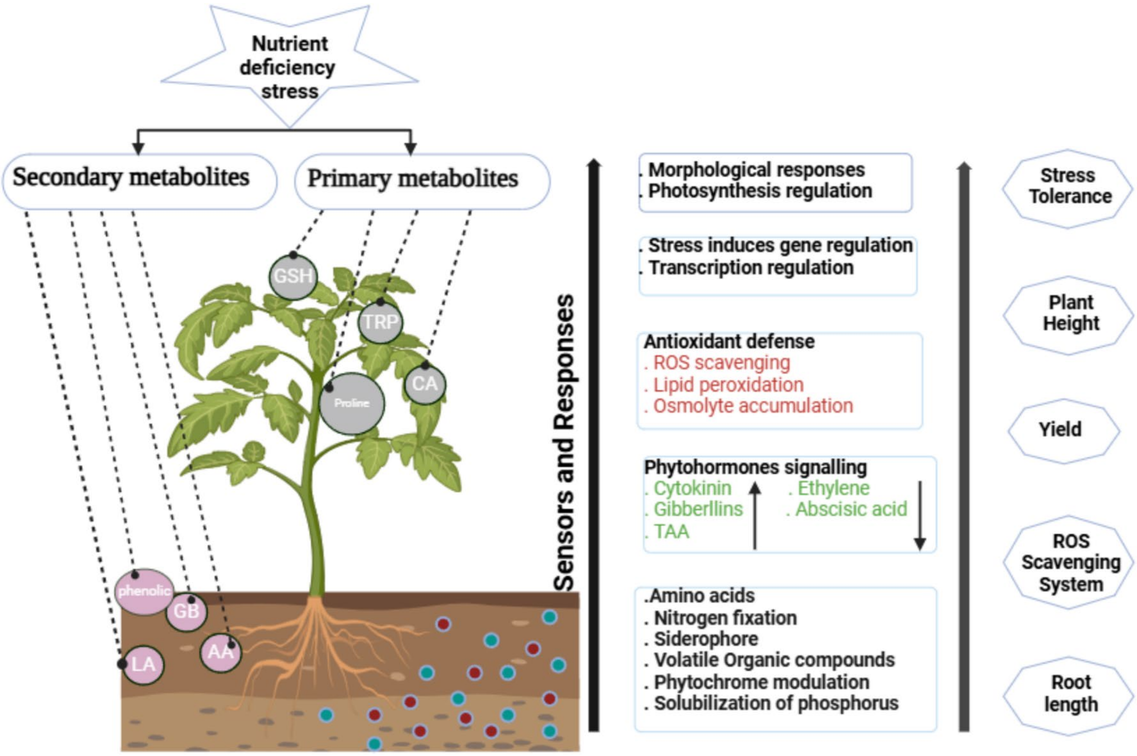

**Fig. 2** Overview of metabolites responses to various nutrient stresses in plant

The Fig. 2 highlights how nutrient deficiency stress affects primary metabolites (e.g., proline, citric acid) and secondary metabolites (e.g., glutathione, glycine betaine) that play roles in osmotic adjustment, ROS scavenging, and stress signaling. Stress induces transcriptional and physiological changes, including antioxidant defenses and photosynthesis regulation. Phytohormones (cytokinins, gibberellins, abscisic acid, and ethylene) regulate growth, nutrient uptake, and stress tolerance. Root exudates, such as siderophores and organic acids, aid in nutrient mobilization and these processes collectively enhance stress tolerance, plant height, yield, and ROS regulation. When plants experience a shortage of phosphorus, their lipid metabolism can undergo significant changes. Phospholipids are necessary components of cell membranes and may be altered to maintain the membrane's integrity and function under a low-phosphorus environment (Asakura et al. 2021). Plants can enhance phosphorus absorption by increasing the production of organic acids and phosphatases, aiding in nutrient mobilization from soil. Metabolomics studies have also provided insights into how microorganisms respond to nutrient stress (Lacrampe et al. 2023). Under nutrient limitation, bacteria undergo metabolomics adjustments, such as increased glycolysis and reduced energy-consuming processes, such as nucleotide biosynthesis (Shahid et al. 2023; Rani et al. 2025). Additionally, bacteria may produce siderophores to scavenge essential nutrients like iron from the environment (Pintus et al. 2023).

Metabolomics offers several advantages in studying nutrient stress. It enables the identification of metabolic modifications, detects both known and unknown metabolites, and facilitates the discovery of novel biomarkers or metabolic signatures associated with nutrient limitations (Asakura et al. 2021). These insights can be applied to enhance crop productivity, optimize microbial bioprocesses, and address nutritional deficiencies in both human and animal health. Furthermore, integrating metabolomics with other omics approaches, such as genomics and proteomics, can provide a more comprehensive understanding of nutrient stress responses.

## Metabolomics techniques for studying plant responses to nutrient stress

By identifying specific metabolic pathways and networks involved in nutrient stress response, metabolomics allows for a better understanding of these complex biological processes (Foito and Stewart 2018). Nuclear magnetic resonance (NMR), gas chromatography-mass spectrometry (GC-MS), mass spectrometry (Benjamin et al.), and liquid chromatography-mass spectrometry (LC-MS) are examples of metabolomics techniques that have revolutionized the study of plant responses to nutrient stress (Salam et al. 2023; Lang et al. 2023). These techniques provide high-resolution information on the metabolic changes in plants under stress conditions, enabling researchers to identify specific metabolic pathways and networks involved in nutrient stress response (Table 1). The specific research question and experimental system under consideration determine the approach chosen. In this section, we will discuss the various metabolomics techniques used to study plant responses to nutrient stress and their respective advantages and limitations.

Plants adapt to environmental stresses during development by undergoing transcriptional and post-transcriptional changes to maintain homeostasis (Dalal et al. 2023). These changes help the plants to reconfigure regulatory networks to adapt to stressors such as nutrient limitation, extreme temperature, flood, severe radiation, metal ion stress, oxidative stress and drought (Ampong 2022; Wan et al. 2024). Activation of stress-responsive genes triggers the production of specialized metabolites (Hu et al. 2023; Wang et al. 2025b). Stressed plants produce more secondary metabolites due to impeded growth and carbon fixation, directing the carbon they fix towards these compounds (Lacrampe et al. 2023). For instance, a study on *Daucus carota callus* showed that anthocyanin's dry weight% increased from 5.4 to 7.2% under phosphate stress (Juarez et al. 2017). Furthermore, nutrient stress has been shown to impact phenolic levels in plant tissues (Juarez et al. 2017). The absence of nitrogen and phosphate can result in the accumulation of phenylpropanoids and lignification (Wellen and Thompson 2010a). Under nutrient stress, the level of anthocyanidins in *Lycopersicon esculentum* increases three-fold, while quercetin-3-O-glucoside doubles simultaneously (Mannino et al. 2022). When the urea concentration is increased in the nutrient solution, it increases the putrescine content in the cell suspensions of *Phaseolus vulgaris* (Zeid 2009). At the same time, anthocyanin production is regulated by osmotic stress from sucrose and other agents in a *Vitis vinifera* culture (Benjamin et al. 2019). Fast analyses of plant metabolic responses to environmental changes are crucial for identifying phenotypic responses to nutrient stresses, selecting stress-tolerant plants, and understanding plant plasticity (Hong et al. 2016).

## Metabolite profiling of plants under nutrient stress

Metabolite profiling identifies plant characteristics, including ecotypes, species fingerprinting, and metabolite responses to stimuli and chemicals. This method also aids in understanding plant symbiotic relationships and developmental processes, as well as comparing the metabolite content of transgenic and wild-type plants (Alseekh and Fernie 2018; Lou et al. 2024). Metabolomics profiling involves multiple steps, including sample preparation, metabolite extraction, separation, detection, and

**Table 1** Advantages and disadvantages of some common analytical techniques used in metabolomics

| Techniques | Properties | Mechanism | Functions | Advantages | Disadvantages | References |
|---|---|---|---|---|---|---|
| Mass Spectrometry (Benjamin et al.) | Mass range: < −50 kDa<br>Sensitivity: Low ($10^{-6}$ M) | It involves the ionization of metabolites, followed by mass analysis using a mass spectrometer | can detect and quantify a wide range of metabolites in plant tissues | High sensitivity and specificity<br>Can detect a wide range of metabolites and quantify metabolite levels | Expensive, Requires specialized equipment and expertise, Sample preparation can be time-consuming and challenging | (Obata and Fernie 2012b) |
| Liquid Chromatography-Mass Spectrometry (LC-MS) | Mass range: <1500 Da;<br>Accuracy: 50–100 ppm<br>Sensitivity: High ($10^{-15}$ M) | Combines the separation power of liquid chromatography (LC) with the mass analysis capabilities of MS | Detecting and quantifying a wide range of metabolites in plant tissues, including amino acids, sugars, and neurotransmitters. | Highly sensitive, Quantifying, separation and detecting wide range of metabolites | Expensive, time consuming, technical know-how, specialized equipment, tedious | (Salam et al. 2023) |
| Nuclear Magnetic Resonance (NMR) Spectroscopy | Mass range: < −50 kDa<br>Sensitivity: Low ($10^{-6}$ M) | non-destructive technique that uses magnetic fields and radio waves to detect and quantify metabolites in plant tissues | High-resolution information on the chemical shift and coupling constants of metabolites | High resolution, non-destructive, sensitivity and detecting wide range of metabolites | Limited to soluble metabolites, time-consuming, specialized equipment and expertise | (Katam et al. 2022) |
| Gas Chromatography-Mass Spectrometry (GC-MS) | Mass range: <350 Da<br>Accuracy: <50 ppm<br>Sensitivity: High ($10^{-12}$ M) | combines the separation power of gas chromatography (Li et al.) with the mass analysis capabilities of MS | Detecting and quantifying lipids, carbohydrates, and other polar metabolites in plant tissues. | Available database, High sensitivity, specificity, quantification, detection, and separation | Time-consuming, expensive, destructive, specialized equipment and expertise | (Hong et al. 2016) |

data analysis. To identify and quantify metabolites, analysts commonly use different analytical platforms such as gas chromatography-mass spectrometry (GC-MS), liquid chromatography-mass spectrometry (LC-MS), and nuclear magnetic resonance (NMR) spectroscopy (Fig. 3). NMR, GC-MS, LC-MS, capillary electrophoresis-mass spectrometry (CE-MS), and FT-IR spectroscopy are among these techniques (Wishart et al. 2022; Vignoli et al. 2019). Metabolite profiling is often combined with other omics tools to study regulatory networks in stress conditions (Foito and Stewart 2018). For example, GC-MS and LC-MS profiling have been successfully used to investigate metabolic regulation under sulfur deficiency in *Arabidopsis*, providing insights into nutrient stress adaptation mechanisms (Nikiforova et al. 2005). The study utilized transcriptomics to establish gene-metabolite correlation networks in response to sulfur deficiency in *Arabidopsis*. Also, Hernández et al. (2007) studied bean plant responses using transcriptomics and metabolomics under different conditions. GS-TOF-MS analysis showed changes in metabolites, including amino acids, polyols, and sugars, in P-stressed *Arabidopsis* roots where the bean plants produce more metabolites in response to phosphorus stress. The *Arabidopsis* seedlings experienced a reduction in carbohydrates and organic acids due to a lack of carbon, whereas the majority of amino acids showed an increase, suggesting the occurrence of proteolysis (Shumilina et al. 2023). Sucrose reintroduction reversed most of these changes. Using extended dark treatment, (Usadel et al. 2008) induced C starvation in *Arabidopsis* rosettes and found that the metabolite changes were comparable to liquid culture seedlings.

The GC-MS platform is a sophisticated analytical tool utilized for plant metabolite profiling. It has a long-standing history as one of the earliest high-throughput metabolite profiling techniques and is still widely used today (Wishart et al. 2022). Typically, GC-MS analysis is conducted using either electron impact (EI) quadrupole or time-of-flight mass spectrometry (Vignoli et al. 2019; Foito and Stewart 2018). Multiple chemical groups can be analyzed using GC-MS, resulting in the identification of hundreds of individual compounds (Wishart et al. 2022). The convenience of commercially and publicly available EI spectral libraries makes GC-MS a valuable tool for metabolomics (Vignoli et al. 2019). Table 2 summarizes key metabolic markers identified in plants under specific nutrient stress conditions, highlighting their roles, pathways, and recent findings.

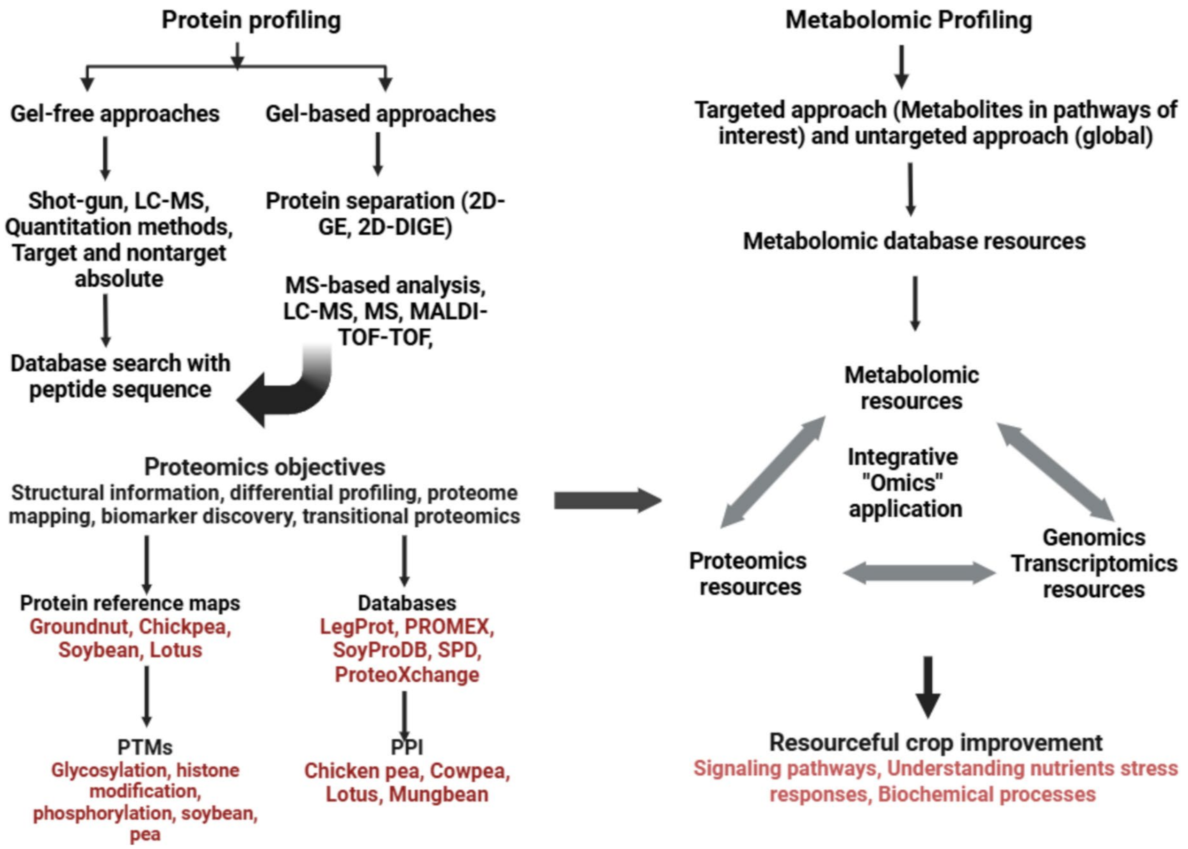

**Fig. 3** Metabolomics and proteomic advancement for integrative approaches in response to nutrient stress

**Table 2** Metabolic markers responsive to nutrient stress in plants

| Nutrient Stress | Metabolic Markers | Type (Primary/Secondary) | Function in Stress Response | Metabolic Pathways | References |
|---|---|---|---|---|---|
| Nitrogen (N) Deficiency | Proline | Primary | Osmoprotection, ROS scavenging, nitrogen storage | Amino acid metabolism | (Salam et al. 2023; Zhang et al. 2023) |
| | γ-Aminobutyric acid (GABA) | Primary | Regulates carbon/nitrogen balance, stress signaling | GABA shunt pathway | (Haddadi et al. 2023; Oh et al. 2023) |
| | Phenylpropanoids (Lignin, Flavonoids) | Secondary | Reinforces cell walls, stress adaptation | Phenylpropanoid pathway | (Juarez et al. 2017) |
| Phosphorus (P) Deficiency | Organic acids (Malate, Citrate) | Primary | Enhances P solubilization and root exudation | Tricarboxylic Acid (TCA) cycle | (Asakura et al. 2021) |
| | Phospholipid-derived jasmonates | Secondary | Modulates root growth and signaling | Lipid metabolism | (Qiu et al. 2023) |
| | Anthocyanins | Secondary | Antioxidant activity, stress signaling | Flavonoid biosynthesis | (Pintus et al. 2023) |
| Potassium (K) Deficiency | Polyamines (Putrescine, Spermidine) | Primary | Maintains ion homeostasis, regulates membrane potential | Polyamine metabolism | (Dalal et al. 2023) |
| | Sugars (Sucrose, Raffinose) | Primary | Osmoregulation, energy storage | Carbohydrate metabolism | (Lacrampe et al. 2023) |
| Iron (Fe) Deficiency | Nicotianamine | Primary | Enhances Fe transport and bioavailability | Phytosiderophore pathway | (Ghorbanzadeh et al. 2023) |
| | Flavins (Riboflavin) | Secondary | Enhances Fe uptake and stress tolerance | Riboflavin biosynthesis | (Wishart et al. 2022) |
| Zinc (Zn) Deficiency | Phytochelatins | Secondary | Detoxifies excess metals, enhances Zn mobility | Glutathione metabolism | (Castro-Moretti et al. 2020) |
| | Terpenoids | Secondary | Enhances stress tolerance, antioxidant function | Terpenoid biosynthesis | (Pinto et al. 2023) |
| Sulfur (S) Deficiency | Glutathione | Primary | Antioxidant defense, sulfur storage | Sulfur assimilation | (Yan et al. 2022a) |
| | Methionine-derived volatiles | Secondary | Signaling molecules, stress adaptation | Methionine metabolism | (Wang and Lei 2018) |
| Magnesium (Mg) Deficiency | Chlorophyll precursors | Primary | Photosynthetic function, energy transfer | Chlorophyll biosynthesis | (Shen et al. 2023) |
| | Lignins | Secondary | Structural integrity, stress resistance | Phenylpropanoid metabolism | (Dalal et al. 2023) |

## Metabolite signaling pathways and their role in nutrient stress responses

Metabolomics is an effective method for investigating metabolites changes, which can reveal organismal phenotypes, cellular signaling, attributes, and metabolic processes (Katam et al. 2022; Lacrampe et al. 2023). By capturing the dynamic system of the metabolome, this analytical approach can offer valuable insights into the workings of living organisms. For instance, a year-long analysis of *Fucus vesiculosus* bioactivity profiles revealed that metabolites varied depending on the sampling time (Heavisides et al. 2018). The metabolite profiles of citrus rootstocks have been found to offer insight Margalinto the tolerance of their scions to pathogens, as noted in a study (Killiny et al. 2018). Further metabolomics research on *Triticum aestivum* (Lavergne et al. 2018; Zhang et al. 2023), *Solanum lycopersicum* (Lacrampe et al. 2023) and *Capsicum* (Calumpang et al. 2020) has demonstrated differences in metabolite composition and levels across cultivars and tissues. Recent research has shown that plants exposed to challenging growth conditions can shift their carbon resources from producing biomass to creating defensive plant secondary compounds, but only if they detect the stress signal accurately (Narayani and Srivastava 2017). Research shows plants use salicylic and jasmonic acids, calcium, abscisic acid, polyamines, and nitric oxide to produce secondary compounds (Rejeb et al. 2014). Recently, stress physiology related to plant secondary compounds received acknowledgement and evidence from various literature sources that emphasize the significance of metabolites in fortifying plant cell structures under stress-induced growth conditions, both in vivo and in vitro (Szabó et al. 2017).

## AMP-activated protein kinase (AMPK) pathway

The AMPK pathway is a highly conserved kinase that senses cellular energy. It gets activated when the ratio of AMP-to-ATP in the cell increases, indicating low energy levels. The activation leads to the phosphorylation of various downstream targets involved in energy metabolism, such as enzymes responsible for glucose uptake, fatty acid oxidation, and mitochondrial biogenesis. By activating these processes, AMPK helps restore energy balance during nutrient stress. However, the binding of AMP to the γ subunit results in a notable alteration in the molecular makeup of the AMPK heterotrimer complex, leading to AMPK kinase activation (Wang and Lei 2018). Subsequently, the α subunit communicates this signal of energy depletion to protein targets further downstream through phosphorylation, which involves the suppression of lipid and cholesterol synthesis by phosphorylating sterol regulatory element-binding protein 1c and acetyl-CoA carboxylase 1 (Hardie et al. 2012).

## Target of the rapamycin (TOR) pathway

TOR is a protein kinase that regulates growth and metabolism by integrating signals, including nutrients, growth factors, and energy status (Wellen and Thompson 2010b). When nutrients are abundant, it promotes protein synthesis and cell proliferation. Conversely, when nutrients are scarce, TOR activity is hindered, causing a shift towards catabolic processes such as autophagy. This enables cells to recycle their components and generate energy from internal stores, enhancing their ability to cope with nutrient scarcity (Li et al. 2017). This pathway regulates cellular processes such as protein synthesis, autophagy, and nutrient uptake, allowing cells to adapt to varying nutrient stress conditions (Kim et al. 2021). There has been progress in understanding how the TOR regulatory module impacts plant defense against stress (Kim et al. 2021), the molecular mechanisms that facilitate communication between energy and nutrient availability, growth, and defense still need to be discovered (Dalal et al. 2023).

According to (Li et al. 2017), under the same growth conditions, glucose and light are required to restore the inhibited activity of TOR in the shoot meristem of plants. Previous research has found that osmotic stress, cold stress, and sulfate depletion reduce TOR phosphorylation or activity in *Arabidopsis* (Wang et al. 2017). Surprisingly, the effect of sulfate deficiency on TOR was discovered to be indirect, as it entered the TOR pathway via the downregulation of glucose metabolism, where the glucose supplementation improved *Arabidopsis* sulfur deficiency phenotypes (Ghorbanzadeh et al. 2023). Hence, the protein kinase complex may be involved in TOR regulation.

## Sirtuins

The families of NAD$^+$-dependent protein deacetylases, that are crucial in regulating cellular processes like metabolism, stress response, and ageing. These processes, along with AMPK and TOR pathways, are closely monitored by the Sirtuins, which sense the cell's metabolic state by gauging the cellular NAD+/NADH ratio. When the cell experiences nutrient stress, Sirtuins are activated due to high NAD + levels, which promotes catabolic processes like autophagy and fatty acid oxidation while inhibiting anabolic processes. This regulation of Sirtuins is crucial in helping cells adapt to nutrient stress by conserving energy and maintaining cellular homeostasis. Metabolite signaling pathways, such as AMPK, TOR, and sirtuins, play crucial roles in responding to nutrient stress by regulating cellular metabolism, energy balance, and stress adaptation (Wellen and Thompson 2010b). These pathways enable cells to detect and respond to variations in nutrient availability, ensuring their survival and maintaining cellular homeostasis.

## Metabolomics as a tool for identifying potential biomarkers for nutrient stress tolerance

The ability to tolerate nutrient stress is essential in agriculture as it can significantly affect crop yields and quality (Fernie et al. 2020; Marchev et al. 2021). To identify potential biomarkers for nutrient stress tolerance, studying the complete metabolites in a biological system, known as metabolomics, has proven to be a powerful tool (Brennan et al. 2021). In this response, we will explore how metabolomics can aid in identifying such biomarkers and provide examples of previous studies that have utilized this approach. Biomarkers serve as measurable indicators showing biological processes or responses (Tebani and Bekri 2019). In the case of nutrient stress tolerance, biomarkers can be utilized to distinguish plants capable of surviving under challenging conditions, such as drought or nutrient deficiency. Biomarkers come in different types, including molecular, physiological, and biochemical, and can be measured through several techniques, such as gene expression, protein, and metabolite analysis (Brennan et al. 2021).

Metabolomics is a valuable tool for researchers seeking to identify biomarkers associated with nutrient stress tolerance (Gibbons et al. 2015). By comparing metabolic profiles between plants capable of enduring nutrient stress and those not, reliable biomarkers that display differential expression can be pinpointed with precision (Tebani and Bekri 2019). Metabolomics offers a significant benefit in identifying biomarkers for nutrient stress tolerance, as it allows researchers to measure stress's effects on various metabolic pathways instead of just focusing on a single gene or protein (O'Gorman and Brennan 2017; Gibbons et al. 2015). This comprehensive approach leads to a better understanding of the metabolic changes that occur as a response to stress, and it aids in identifying reliable and robust biomarkers. Various studies have employed Metabolomics to discover possible crop nutrient stress tolerance biomarkers (Marchev et al. 2021; Tebani and Bekri 2019; Brennan et al. 2021; Qiu et al. 2023; Ghorbanzadeh et al. 2023). For instance, a study (Rahman et al. 2017) utilized metabolomics to determine metabolic biomarkers for drought tolerance in *Triticum aestivum*. The study's findings revealed that drought-resistant *Triticum aestivum* plants recorded increased antioxidant levels and decreased sugar levels and amino acids compared to drought-sensitive plants. Additionally, the study identified several metabolites expressed differentially and associated with drought tolerance. One of these metabolites is quebrachitol, which plays a role in synthesizing cell walls and membranes.

A recent study (Raza 2022) utilized metabolomics to uncover markers indicating nutrient stress tolerance in *Arabidopsis thaliana*. The findings shows that plants that exhibited tolerance to nutrient stress had increased stages of amino acids and decreased stage of sugars compared to non-tolerant plants. The study also identified several metabolites differentially expressed and linked to nutrient stress tolerance, including the essential compound 'glutamate,' which aids protein synthesis and other metabolic processes. Also, (Ghorbanzadeh et al. 2023) utilized metabolomics to identify biomarkers indicating tolerance to nutrient stress in rice. The study found that rice plants with increased levels of antioxidants and decreased levels of sugars and amino acids were more tolerant to nutrient stress. Additionally, the research identified various metabolites expressed differently in tolerant plants, such as sorbitol - a compound crucial for synthesizing cell walls and membranes.

Metabolomics plays a crucial role in detecting biomarkers for crop nutrient stress tolerance and help researchers can pinpoint metabolites that serve as reliable biomarkers by analyzing the metabolic profiles of both tolerant and non-tolerant plants (Haddadi et al. 2023; Zhang et al. 2023). This approach enhances our comprehension of metabolic changes caused by stress and ensures the identification of dependable biomarkers.

## Proteomic insights into nutrient stress

### Proteomic techniques for studying plant responses to nutrient stress

Proteomic insights into nutrient stress involve studying protein expression and function changes in response to limited availability or imbalances of essential nutrients (Cai et al. 2021; Gao et al. 2020; Ribeiro et al. 2023; Bawa et al. 2022). Nutrient stress can affect plants, animals, and microorganisms, and comprehending how proteins respond to such stress can offer a valuable update about molecular mechanisms that regulate nutrient homeostasis and adaptation (Thangaraj et al. 2020). Two-dimensional gel electrophoresis (2-DE), which separates proteins based on their isoelectric point (pI) and molecular weight, is a widely used method in proteomic research on nutrient stress (Xu et al. 2019; Stryiński et al. 2020). By scrutinizing protein profiles across varying nutrient-stressed and control conditions, researchers can pinpoint differentially expressed proteins linked to the response to nutrient stress (Christie-Oleza et al. 2012; Ribeiro et al. 2023). These particular proteins can then be subjected to further analysis, employing mass spectrometry-based techniques for protein identification. In proteomic research, Mass spectrometry technology is crucial for identifying and characterizing proteins based on their mass-to-charge ratio (m/z). Prominent MS-based techniques such as matrix-assisted laser desorption/ionization (MALD) (Yan et al. 2006) and LC-MS/MS are employed for detecting post-translational modifications and measuring protein abundance levels (Gao et al. 2020).

Plants change protein expression due to nutrient stress, including alterations in nutrient transporters, ion channels, and proteins that play a role in photosynthesis, respiration, and carbon metabolism (Thangaraj et al. 2020). The resulting impact is on energy production and allocation. In microorganisms, proteomic analyses have shed light on the adaptive strategies employed by these organisms under nutrient-stress conditions (Cai et al. 2021). For example, bacteria may upregulate proteins involved in scavenging alternative nutrient sources or enhancing stress tolerance mechanisms (Xu et al. 2019; Gao et al. 2020; Stryiński et al. 2020). Understanding these proteomic responses can aid in developing strategies for improving microbial bioproduction processes or combating pathogenic bacteria (Li et al. 2024a). Investigating how organisms' proteins react to restricted access or imbalanced levels of vital nutrients offers invaluable knowledge regarding their response to nutrient stress (Christie-Oleza et al. 2012).

There are various techniques for studying plant responses to nutrient stress, and one of the most commonly used is *shotgun proteomics*. This method involves breaking down proteins into peptides, separating them using LC, and then analyzing them using MS. Unlike 2-DE, shotgun proteomics does not require protein separation based on pI and molecular weight (Bawa et al. 2022). Instead, it relies on modern mass spectrometers' impressive sensitivity and resolution to detect and quantify thousands of proteins in just one experiment (Liu et al. 2019). In plant research, gel-free proteomic methods have become famous for investigating nutrient stress responses, which involve analyzing peptides directly without needing prior separation on gels (Ahmad et al. 2016). Such techniques include label-free quantification, selected reaction monitoring (SRM), and multiple reactions monitoring (MRM). Label-free quantification involves comparing peptide ion intensities between control and stressed samples to determine variations in protein abundance. In contrast, SRM and MRM are targeted proteomic approaches that utilize specific peptide ion transitions to measure selected proteins of interest (Ghosh and Xu 2014).

The application of proteomic techniques has aided in the understanding of the molecular mechanisms that drive plant responses to nutrient stress (Ahmad et al. 2016; He et al. 2025). These techniques have enabled researchers to identify crucial proteins responsible for nutrient uptake, transport, assimilation, and signaling pathways (Liu et al. 2019). Scientists can develop strategies to improve plant nutrient utilization efficiency and crop productivity under nutrient-limited conditions by gaining insights into these processes at the protein level (Prusty et al. 2022). Researchers can reveal the fundamental molecular mechanisms in nutrient stress response by scrutinizing different aspects of protein function, such as expression, modifications, and interactions. Such findings carry significant weight in diverse fields, ranging from agriculture and biotechnology to human health.

## Protein profiling of plants under nutrient stress

Examining the protein profiles of plants experiencing nutrient stress can aid in comprehending alterations in protein expression resulting from inadequate nutrients because when essential elements are lacking, nutrient stress can hinder the growth and development of plants (Wang 2019; Ahmad et al. 2016). By analyzing protein profiles, we can gain valuable insights into the molecular processes that plants employ to adapt and flourish in demanding surroundings. Protein profiling refers to identifying and quantifying proteins in a biological sample. This can be accomplished through various methods, including gel-based techniques, LC-MS/MS, or high-throughput sequencing-based approaches (Schulze et al. 2021; Lang et al. 2023).

When experiencing nutrient stress, plants undergo changes in their physiology and biochemistry, which can be observed through variations in protein expression and through analyzing protein profiles of stressed and non-stressed plants; we can identify differentially expressed proteins and potentially shed light on nutrient uptake pathways (Pandey et al. 2024). Protein profiling in nutrient stress aims to recognize nutrient-responsive proteins that undergo significant expression level changes in response to nutrient availability (Liu et al. 2019). These identified proteins aid researchers in comprehending nutrient homeostasis and devising techniques to enhance plant nutrient acquisition efficacy and tolerance towards nutrient stress (Rodziewicz et al. 2014). Protein profiling studies have investigated the impact of nutrient stress on a range of plant species (Schulze et al. 2021). Crops like rice, wheat, maize, soybean, and model plants such as *Arabidopsis thaliana* have been extensively researched, and these studies have identified nutrient-responsive proteins involved in various biological processes (Schulze et al. 2021; Zhang et al. 2023; Rajkumari et al. 2023). It should be noted that proteomics detects protein abundance, interactions, and regulations, providing insights into changes under nutrient stress (Li et al. 2019).

### Nitrogen (N) stress

*This* is a widely studied form of nutrient stress that affects plants and is essential for many physiological processes in plants, including protein synthesis. In the face of nitrogen deficiency, plants undergo significant changes in their protein profiles to optimize the use of available nitrogen and conserve energy (Barkla 2016). Scientists have identified several N-responsive proteins critical for N uptake, assimilation, and remobilization. These proteins include nitrate transporters, reductases, glutamine synthetases, and various enzymes involved in amino acid metabolism. Using a proteomics methodology, (Ma et al. 2011) investigated proteins responding to N-deficiency stress in two rice cultivars with varying N use efficiency. The gel analysis revealed 31 protein spots shared by both cultivars, four of which were induced by stress in both varieties. Nitrogen deficiency significantly affects amino acid metabolism, leading to the downregulation of glutamine synthetase (GS) and nitrate reductase (NR), enzymes crucial for nitrogen assimilation. In response, plants activate aminotransferases (AspAT, AlaAT) to redistribute nitrogen-containing compounds, ensuring metabolic homeostasis under limited nitrogen availability. Stress-responsive proteins, such as dehydrins (DHNs), are also upregulated to protect cellular structures from nitrogen deficiency-induced oxidative stress, thereby improving plant resilience (Bisht et al. 2024; Wang et al. 2025a).

### Phosphorus (P) stress

This is a crucial nutrient stress that impacts the growth and development of plants. P is required for nucleic acids, ATP (adenosine triphosphate), and phospholipids. When plants face a scarcity of P, they exhibit adaptive responses to enhance P acquisition and utilization efficiency. Studies on protein profiling have identified proteins that are responsive to P, and they are involved in various processes such as phosphate transport, P remobilization from older tissues to younger ones, and the activation of alternative metabolic pathways to compensate for P limitation. P deficiency disrupts ATP synthesis and impairs membrane integrity, necessitating the activation of purple acid phosphatases (PAPs) to mobilize organic phosphorus from the soil. Simultaneously, phosphate transporters (PHT1, PHT2) facilitate phosphate uptake and remobilization to sustain metabolic activities. The structural stability of cellular membranes under phosphorus stress is maintained by lipid transfer proteins (LTPs), which play a role in membrane lipid remodeling. Additionally, MYB transcription factors regulate root growth and phosphate acquisition strategies, enhancing plant adaptability to phosphorus-limited conditions (Ghorbanzadeh et al. 2023; Naik et al. 2023).

### Potassium (K) stress

This affects various physiological processes in plants, such as osmoregulation, enzyme activation, and stomatal regulation (Li et al. 2019). In K-deficient conditions, plants adjust their protein expression to maintain K homeostasis and minimize the adverse effects of K limitation (Zhao et al. 2016). Proteomic studies have identified proteins responsive to K and involved in K uptake from soil, transport of K within plant tissues, and regulation of K-dependent enzymes (Li et al. 2019). Recently, substantial advancements were made regarding knowledge of K nutrition molecular mechanisms, as studies on Arabidopsis and rice demonstrated that Calcineurin B-like (CBL)-interacting protein kinases (CIPK) complexes effectively regulate the activities of Arabidopsis K transport 1 (AtAKT1), OsAKT1, and HAK5 (K + transporter 5), which are required for high-affinity K + transport in plants. These complexes are essential for plant adaptation to K + deficiency (Zhao et al. 2016). K-starved plants also show higher levels of peroxidases (POX) to mitigate oxidative damage and heat shock proteins (HSPs) to stabilize protein structures under potassium stress (Dalal et al. 2023; Zhao et al. 2023; Niu et al. 2025).

In addition to macronutrients such as N, P, and K, plants also require micronutrients in small quantities to support proper growth and development. Micronutrient deficiencies can result in various physiological disorders and reduced crop productivity (Zhao et al. 2016).

### Iron stress

Plants can suffer from stunted growth and damage to cellular components due to the accumulation of reactive oxygen species (ROS) caused by iron stress. To cope with the problem of iron deficiency, plants have developed different mechanisms, such as the upregulation of iron uptake, transport and storage proteins. Protein profiling studies have provided insights into how plants respond to micronutrient stress (Yang et al. 2014). Iron deficiency severely impacts chlorophyll biosynthesis and electron transport, necessitating the induction of ferritin (FER1, FER2) for intracellular iron storage and release. To enhance iron uptake, iron-regulated transporter 1 (IRT1) is upregulated, facilitating Fe transport from the soil to root cells. Additionally, superoxide dismutases (SODs) play a crucial role in mitigating oxidative stress induced by Fe deficiency. The synthesis of nicotianamine (NAS1, NAS2) further supports Fe mobility and bioavailability, ensuring efficient iron distribution within plant tissues (Michaletti et al. 2018; Shen et al. 2023; Zenda et al. 2021).

### Zinc stress

This can also hinder plant growth and development, leading to the accumulation of ROS. However, plants have mechanisms to deal with zinc deficiency, including the upregulation of zinc transport and storage proteins. Proteins that respond to zinc have been identified in plants grown under zinc-deficient conditions (Liu et al. 2019).

### Carbon and Calcium stress

Carbon can significantly impact plants' growth and development, resulting in the accumulation of reactive oxygen species (ROS). To cope with carbon deficiency, plants have developed mechanisms such as the upregulation of photosynthetic enzymes and the downregulation of non-photosynthetic processes. Calcium stress affects plant growth, development and accumulates ROS. Plants have evolved mechanisms such as the upregulation of calcium transport and storage proteins to cope with calcium deficiency.

Examining plants' protein profiles under nutrient stress is critical to agriculture and crop advancement because by comprehending the molecular mechanisms behind nutrient stress responses, experts can create successful tactics to enhance nutrient usage, improve crop output, and cultivate nutrient-efficient plant varieties through genetic engineering or breeding techniques and identifying proteins responsive to nutrient shortages empowers researchers to comprehend the adaptive mechanisms of plants under such stress and devise effective strategies to enhance crop productivity in demanding environmental circumstances(Schulze et al. 2021).

## Protein signaling pathways and their role in nutrient stress responses

Protein signaling pathways play an important role in controlling cellular responses to nutrient stress which, occurs when there is a deficiency between the availability of nutrients and the nutrient requirements of the cell (Hotamisligil and Davis 2016). In response to nutrient stress, specific protein signaling pathways are activated to coordinate the allocation of limited nutrients and maintain cellular homeostasis (Kim et al. 2021).

## The mTOR pathway

When nutrients are abundant, mTOR activity increases, leading to cell growth and proliferation. Conversely, under nutrient scarcity, mTOR activity decreases, causing cells to enter a dormancy state or undergo programmed cell death (apoptosis) to conserve resources. The mTOR pathway integrates signals from nutrient sensors, such as the amino acid sensor GCN2, to maintain cellular metabolism and growth (Liao et al. 2022). In response to nutrient conditions, autophagy is regulated by Yeast TORC through the phosphorylation of autophagy-related (ATG13). *Arabidopsis* TORC may also play a role in modulating autophagy, as evidenced by identifying several TOR phosphorylation sites on ATG13 through large-scale phosphoproteomics (Van Leene et al. 2019). Energy and nutrient sensors collaborate with other signaling pathways to regulate autophagy, which is for maintaining plant development equilibrium and stress responses (Liao et al. 2022).

## The AMP-activated protein kinase (AMPK) pathway

The AMPK pathway is crucial in maintaining cellular energy balance and responding to nutrient stress. In nutrient scarcity, the AMPK pathway springs into action, conserving energy by inhibiting anabolic pathways and activating catabolic pathways (Hotamisligil and Davis 2016). Moreover, AMPK takes charge of the genes responsible for glucose and lipid metabolism, and it can even promote autophagy, recycling damaged or dysfunctional cellular components.

## The unfolded protein response pathway

When cells experience nutrient stress due to misfolded proteins in the endoplasmic reticulum (ER), they activate the UPR pathway (Hotamisligil and Davis 2016). This pathway prompts the activation of transcription factors like XBP1 (X-box binding protein 1), ATF6 (activating transcription factor 6), and CHOP (C/EBP homologous protein), which manage the expression of genes involved in protein folding, degradation, and the ER's stress response. Moreover, the JNK (c-Jun N-terminal kinase) and IRE1 (inositol-requiring enzyme 1) signaling pathways are also stimulated by the UPR pathway, regulating the body's stress responses and protein folding (Guo et al. 2024).

Protein signaling pathways are integral to regulating cellular responses to nutrient stress. These pathways, which include mTOR, AMPK, and UPR, are tasked with managing the distribution of scarce nutrients to maintain cellular homeostasis while governing metabolism, growth, and stress responses (Hotamisligil and Davis 2016). A more profound comprehension of these pathways and their role in nutrient stress responses may aid in creating practical therapeutic approaches for treating ailments associated with nutrient stress, such as cancer, diabetes, and neurodegenerative disorders (Kadowaki and Nishitoh 2013).

## Protein-protein interactions in nutrient stress responses

Nutrient deficiencies trigger complex molecular responses in plants, which are largely mediated by protein-protein interactions (PPIs) that regulate nutrient uptake, transport, and metabolic adaptation. These interactions form intricate protein networks, known as the interactome, that enable plants to adjust to changing environmental conditions, and provide valuable insights into how plants optimize resource allocation under nutrient-deficient conditions. Table 3 summarizes key protein-protein interactions associated with different nutrient deficiencies, highlighting their functional roles in plant stress responses.

### Nitrogen deficiency and protein interactions

Nitrogen starvation affects protein networks involved in nitrogen assimilation and metabolic regulation. The glutamine synthetase (GS)-glutamate synthase (GOGAT) complex plays a central role in nitrogen remobilization, ensuring efficient nitrogen use. Additionally, the nitrate reductase (NR)-nitric oxide (NO) synthase interaction regulates nitrogen signaling and root architecture under nitrogen-deficient conditions. The TOR (Target of Rapamycin) kinase complex (TOR-RAPTOR-LST8) is also activated during nitrogen starvation, controlling metabolic adaptation by balancing energy production and amino acid biosynthesis (Zhang et al. 2023).

**Table 3** Protein-protein interactions regulating plant responses to nutrient deficiences

| Nutrient Deficiencies | Protein-Protein Interactions | Functions | References |
|---|---|---|---|
| **Nitrogen (N) Deficiency** | GS-GOGAT Complex | Regulates nitrogen assimilation and remobilization | (Wang et al. 2025a) |
| | NR-NO Synthase Complex | Controls root architecture and nitrogen uptake | (Li et al. 2024b) |
| | TOR-RAPTOR-LST8 Complex | Adjusts metabolism under nitrogen starvation | (Pinto et al. 2023; Rahman et al. 2017) |
| **Phosphorus (P) Deficiency** | SPX-PHT Transporter Complex | Enhances phosphate uptake and homeostasis | (Yang et al. 2021) |
| | PHR1-SPX Complex | Regulates phosphorus-responsive gene expression | (Ghorbanzadeh et al. 2023) |
| | LTP-Phospholipase Complex | Maintains membrane stability under P stress | (Naik et al. 2023) |
| **Potassium (K) Deficiency** | HAK5-CIPK23 Complex | Regulates potassium transport and uptake | (Wang 2019; Xian et al. 2023) |
| | HKT1-SOS1 Complex | Maintains Na+/K + balance | (Zhao et al. 2016) |
| | HSP90-Ion Transporter Complex | Stabilizes proteins under K-deficient conditions | (Dalal et al. 2023) |
| **Iron (Fe) Deficiency** | IRT1-bHLH Complex | Regulates iron uptake from soil | (Shen et al. 2023) |
| | Ferritin-SOD Complex | Mitigates oxidative stress from Fe deficiency | (Zenda et al. 2021) |
| | NAS1-YSL Transport Complex | Facilitates long-distance Fe transport | (Michaletti et al. 2018) |

### Phosphorus deficiency and regulatory protein complexes

Phosphorus deficiency disrupts energy metabolism, prompting plants to activate protein interactions that optimize phosphate acquisition. The SPX domain proteins interact with phosphate transporters (PHT1, PHT2) to enhance phosphate uptake and maintain homeostasis. Additionally, PHR1 (Phosphate Starvation Response 1) forms a complex with SPX proteins, which acts as a transcriptional regulator to control phosphate-responsive gene expression. To preserve membrane integrity under phosphorus limitation, lipid transfer proteins (LTPs) interact with phospholipases, enabling adaptive lipid remodeling (Yang et al. 2021).

### Potassium deficiency and ion transport networks

Potassium deficiency leads to disrupted ion homeostasis and metabolic imbalances, activating essential protein interactions to restore K + balance. The high-affinity K + transporter (HAK5) interacts with CBL-Interacting Protein Kinase 23 (CIPK23) to regulate potassium uptake and transport. Additionally, the HKT1-SOS1 interaction plays a crucial role in maintaining Na+/K + homeostasis, preventing excessive potassium loss under stress conditions. Moreover, heat shock proteins (HSP90) interact with ion transporters, stabilizing key proteins under potassium-limited stress (Wang et al. 2025a; Zhao et al. 2016).

### Iron deficiency and redox-responsive protein complexes

Iron starvation impairs chlorophyll synthesis and disrupts cellular redox balance, necessitating specialized protein interactions to enhance Fe uptake and distribution. The iron-regulated transporter 1 (IRT1) interacts with bHLH transcription factors (FIT1, bHLH38, bHLH39) to regulate iron acquisition from the soil. The ferritin (FER1) complex interacts with superoxide dismutase (SODs) to mitigate oxidative stress induced by Fe deficiency. Additionally, nicotianamine synthase (NAS1) interacts with YSL transporters, facilitating long-distance iron transport from roots to shoots (Shen et al. 2023; Zenda et al. 2021).

### The role of the nutrient stress interactome in systems biology

Recent advances in proteomics and bioinformatics have led to the large-scale mapping of nutrient deficiency interactomes, revealing key protein complexes that regulate plant stress responses. Co-expression networks, phosphorylation cascades, and ubiquitin-mediated proteolysis play critical roles in fine-tuning nutrient stress adaptation. Integrating interactomics with metabolomics and proteomics provides a holistic view of nutrient stress responses, enabling the identification of molecular targets for crop improvement (Dalal et al. 2023; Michaletti et al. 2018).

### Proteomics as a tool for identifying potential biomarkers for nutrient stress tolerance

The proteomics field involves identifying and characterizing proteins, which offers valuable insights into their functions and interactions, which holds great potential for detecting biomarkers associated with nutrient stress tolerance in various organisms (Amiri-Dashatan et al. 2018; Qiu et al. 2023). Proteomics offers an all-encompassing perspective of protein expression patterns in reaction to nutrient stress, facilitating the recognition of distinct biomarkers. In response to nutrient stress, proteomics can identify post-translational modifications (PTMs) in addition to proteins (Barkla 2016). Protein tyrosine phosphate (PTMs) regulates protein function, affecting stability, localization, and interactions with other molecules, providing insight into nutrient stress tolerance (Ballhorn 2011).

Proteomics is a valuable tool for researchers studying protein interactions and complexes during nutrient stress responses (Qiu et al. 2023). By identifying proteins that interact or form complexes under such conditions, researchers can gain insights into the complex signaling networks and pathways that enable organisms to tolerate nutrient stress (Halder et al. 2022). To identify biomarkers for nutrient stress tolerance through proteomics, researchers gather and analyze samples from both stressed and non-stressed organisms (Vignoli et al. 2019; Qiu et al. 2023). Through various extraction techniques, proteins are isolated and subsequently separated by size, charge, or hydrophobicity utilizing either gel electrophoresis or liquid chromatography (Roos and McArdle 2008; Liu et al. 2024a). Enzymes such as trypsin are utilized to separate and digest proteins into peptides. Subsequently, mass spectrometry is employed to determine the peptides' mass-to-charge ratio and abundance, thus yielding essential insights into their identity and relative abundance across varied samples (Barkla 2016; Liu et al. 2024b).

Bioinformatics tools and databases are utilized to analyze mass spectrometry data and identify proteins present in the samples (Roos and McArdle 2008). Differentially expressed proteins are identified through statistical analysis when comparing expression levels between stressed and non-stressed samples under nutrient-stress conditions. To establish the correlation between potential biomarkers and nutrient stress tolerance, it is recommended to employ Western blotting or ELISA techniques to measure protein expression levels in a larger sample (Roos and McArdle 2008). Functional studies can also be conducted to delve deeper into the role of these biomarkers in nutrient stress responses. Proteomics has identified potential biomarkers that aid nutrient stress tolerance across multiple organisms with specific proteins related to nutrient uptake, transport, and storage in plants that are upregulated during nutrient-stress conditions (Halder et al. 2022). These proteins could serve as valuable biomarkers for enhancing crop breeding to improve nutrient stress tolerance.

Understanding nutrient stress tolerance is crucial in identifying biomarkers, and proteomics is vital in this endeavour (Liu et al. 2019). Proteomics can provide a comprehensive overview of this tolerance and its molecular mechanisms through an analysis of protein expression patterns, detection of PTMs, and investigation of protein-protein interactions. Such insights can inform the development of strategies for food security, animal health, and human nutrition.

## Integration of metabolomics and proteomic insights

### Complementarity of metabolomics and proteomic approaches in response to nutrient stress

Metabolomics and proteomics are distinctive techniques that reveal valuable information about how organisms react to nutrient stress (Shu et al. 2022). Metabolomics captures a momentary glimpse of an organism's metabolic condition by tracking changes in metabolite levels, indicating which metabolic pathways are influenced by nutrient stress and which metabolites function as signaling agents (Akpunarlieva et al. 2017). Conversely, proteomics identifies and measures the proteins within an organism, disclosing which proteins increase or decrease when under nutrient stress (Kausar and Komatsu 2023). These two approaches together provide a complete and thorough understanding of an organism's response to nutrient stress (Ramalingam et al. 2015). Proteomics provides information about how much protein is expressed and post-translational modifications, which aids in the identification of essential proteins involved in nutrient uptake, transport, assimilation, and stress response (McKetney et al. 2022). It provides an in-depth awareness concerning the molecular mechanisms that govern nutrient stress response (Akpunarlieva et al. 2017).

Pattern recognition in non-targeted metabolomics often involves principal and independent component analysis. To enhance the effectiveness of these techniques, external factors such as protein concentration and enzyme activities can be considered, leading to the creation of metabolite correlation networks. (Weckwerth et al. 2004) demonstrated the utility of independent components analysis in separating the principal components of genotype in Arabidopsis plants throughout a diurnal rhythm. In a similar study, an integrative approach was used to analyze *Arabidopsis thaliana's* starch and raffinose metabolisms response to different temperatures, involving independent components analysis (Wang et al. 2017). The technique of transcript profiling is widely recognized as a cornerstone of systems biology, with numerous publicly available databases capable of automatically annotating candidate information (Rahim et al. 2023). While the fields of proteomics and metabolomics pose significant technical obstacles, there are now specialized databases containing highly annotated data.

When metabolomics and proteomic data are combined, researchers can pinpoint vital regulatory nodes that connect metabolic pathways to protein expression and function (Gioria et al. 2016). This innovative approach enables the identification of new biomarkers or targets that can enhance nutrient utilization efficiency or alleviate the effects of nutrient stress on living organisms (Ramalingam et al. 2015). To gain a comprehensive understanding of how organisms respond to nutrient stress, advanced tools like metabolomics and proteomics are required (Shu et al. 2022; McKetney et al. 2022). Metabolomics allows us to observe changes in metabolite levels and metabolic pathways, while proteomics provides information on protein expression and function (Yan et al. 2022a). By combining these two approaches, we can better comprehend the molecular mechanisms influencing the response to nutrient stress.

## Integration of metabolomics, proteomics and epigenomics a comprehensive understanding of plant responses to nutrient stress

Metabolomics and proteomics are powerful omics technologies that provide valuable insights into metabolic and protein-level changes in plants under various environmental conditions, including nutrient stress (Oh et al. 2023; Yan et al. 2022b). Integrating metabolomic and proteomic data allows researchers to unravel how plants adapt to nutrient deficiencies or excesses by simultaneously analyzing metabolic shifts and protein regulation (Oh et al. 2023). This approach enables the identification of key metabolic pathways, stress-responsive proteins, and regulatory mechanisms that contribute to nutrient stress tolerance. The combined analysis of metabolomics and proteomics facilitates the discovery of distinctive biomarkers that indicate early nutrient stress. These biomarkers can be used for early nutrient deficiency detection or as targets for genetic improvements to enhance nutrient use efficiency in crops (Roychowdhury et al. 2023Obata and Fernie 2012a). Since plant responses to nutrient stress involve complex molecular events—including changes in gene expression, protein synthesis, and metabolic fluxes—integrating omics data allows researchers to construct regulatory networks that decipher the molecular mechanisms governing plant adaptation (Budzinski et al. 2019; Srivastava et al. 2013).

Beyond metabolomics and proteomics, epigenetic modifications play a crucial role in regulating gene expression under nutrient-deficient conditions. DNA methylation, histone modifications, and chromatin remodeling influence transcriptomic changes that, in turn, impact proteomic and metabolomic responses (Abdulraheem et al. 2024). For example, nutrient deficiencies alter DNA methylation patterns, affecting genes involved in nutrient assimilation pathways. Epigenomics has revealed DNA methylation and chromatin changes under abiotic stress, and next-generation sequencing enables advanced genome analysis for stress-responsive genes and biotechnological interventions (Mazumder et al. 2024). Additionally, histone acetylation is reduced under glucose and energy starvation, leading to chromatin compaction and repression of metabolic genes, which directly affects protein synthesis and metabolic pathway regulation (Yao et al. 2024).

At the proteomic level, epigenetic modifications influence post-translational regulation of stress-responsive proteins. The AMP-activated protein kinase (AMPK), a central energy sensor, modulates epigenetic states by phosphorylating histone-modifying enzymes, linking nutrient sensing with proteomic and metabolic adjustments. On the metabolomic level, epigenetic regulation impacts primary and secondary metabolite accumulation, influencing plant stress tolerance mechanisms (Ramekar and Dutt 2025). The integration of metabolomics, proteomics, and epigenomics provides a holistic understanding of plant responses to nutrient stress by linking transcriptional control with protein function and metabolic adaptation. This systems-level approach enables the identification of novel metabolic pathways and regulatory proteins that contribute to nutrient stress resilience. These insights can be leveraged to develop nutrient-efficient crops through targeted breeding, genetic engineering, and epigenetic modifications, ensuring improved nutrient use efficiency and stress tolerance in agricultural systems (Roychowdhury et al. 2023). Thus, integrating metabolomics, proteomics, and epigenomics presents a promising strategy for enhancing crop resilience, optimizing nutrient management, and advancing sustainable agricultural practices (Budzinski et al. 2019; Srivastava et al. 2013).

## Cross-talk between signaling pathways under combined nutrient stress

Plants frequently experience multiple nutrient deficiencies simultaneously, triggering complex interactions between metabolic, proteomic, and transcriptomic pathways to optimize nutrient acquisition and stress adaptation. Unlike individual nutrient deficiencies, combined stresses result in distinct metabolic reprogramming, where plants adjust carbon allocation, secondary metabolite synthesis, and hormone signaling to cope with multiple limitations. For example, nitrogen (N) and phosphorus (P) co-limitation enhances organic acid accumulation (malate, citrate) to facilitate both N and P mobilization, while potassium (K) and magnesium (Mg) deficiency leads to sugar accumulation and flavonoid production to balance osmotic stress and ATP deficiency (Kumar et al. 2024; Budzinski et al. 2019). Additionally, iron (Fe) and sulfur (S) co-deficiency triggers the upregulation of sulfate and iron transporters, demonstrating interdependent regulation of these nutrients (Vignoli et al. 2019; Vilakazi et al. 2025). At the proteomic level, combined nutrient stress influences protein interactions, transporter activity, and post-translational modifications. HSP90 chaperones stabilize ion transporters under K and Mg deficiency, while SPX-PHT transporter complexes regulate phosphate homeostasis in response to N-P co-limitation (Ghorbanzadeh et al. 2023). Proteomic studies also reveal hierarchical regulation, where plants prioritize nitrogen uptake over phosphorus transport when both are deficient, indicating a nutrient-dependent response trade-off (Gupta et al. 2023; An et al. 2023). Transcriptomic analyses show that combined nutrient deficiencies lead to cross-regulation of stress-responsive genes, with shared induction of WRKY and NAC transcription factors across multiple stress conditions. In N-P co-deficiency, phosphate starvation-induced genes are suppressed when nitrogen levels are critically low, highlighting the dominance of nitrogen signaling (Yao et al. 2024). Ethylene and jasmonic acid pathways are activated in K-Mg deficiency, enhancing lipid remodeling and ion homeostasis (Ramekar and Dutt 2025).

## Translating multi-omics findings into practical applications for nutrient stress mitigation

Advancements in integrative metabolomics, proteomics, and transcriptomics have provided valuable insights into plant responses to nutrient stress. These applications include breeding nutrient-efficient crops, biotechnological innovations, and precision nutrient management strategies, all aimed at improving plant resilience under nutrient-limited conditions and sustainable farming practices.

### Breeding nutrient-efficient crops

Multi-omics research has identified key genes, proteins, and metabolic pathways that enhance nutrient uptake and utilization, enabling targeted crop improvement. Genomic selection (GS) and marker-assisted breeding have successfully used NRT1 (nitrate transporter), PHT1 (phosphate transporter), and HAK5 (potassium transporter) as markers for improving nitrogen (N), phosphorus (P), and potassium (K) use efficiency (Kumar et al. 2024). Additionally, CRISPR-Cas9 gene editing has modified genes like NRT2.1 (for nitrogen uptake) and PHO1 (for phosphate transport), improving nutrient acquisition in rice and wheat (Li et al. 2023; Roychowdhury et al. 2025). Engineering root system architecture by selecting key transcription factors (MYB, ARF, WRKY) has also enhanced soil nutrient foraging, making crops more adaptable to nutrient-limited conditions (An et al. 2023). Marker-assisted breeding and genotyping technologies are enhancing millet breeding for climate change mitigation and agronomic sustainability (Mazumder et al. 2024). Multi-omics data have highlighted the role of transcription factors like MYB, ARF, and WRKY in regulating root elongation and branching, which can be selected for in breeding programs to enhance soil nutrient foraging (Gupta et al. 2023).

### Biotechnological solutions for enhancing nutrient uptake

Biotechnology has facilitated the development of microbial inoculants, transgenic crops, and synthetic biology solutions to enhance nutrient acquisition. Plant growth-promoting microbes (PGPMs), including rhizobacteria (Azospirillum, Pseudomonas) and mycorrhizal fungi (Glomus species), improve nutrient uptake by secreting organic acids, siderophores, and phosphate-solubilizing enzymes (Singh et al. 2022; Khan et al. 2024). Transgenic approaches, such as overexpressing NRT1.1B in rice and PHO2 in soybean, have improved nitrogen and phosphorus uptake efficiency (Zhu et al. 2022). Advances in synthetic biology have further optimized nutrient homeostasis, for example, by integrating nitrate and phosphate signaling pathways via SPX-PHR regulatory interactions, which fine-tune nutrient sensing and transport.

### Precision agriculture, sustainable nutrient management, and real-world application of integrative omics

Omics-based approaches have revolutionized precision nutrient management by optimizing fertilizer application, improving soil health, and enhancing crop resilience. Nanotechnology-based slow-release fertilizers provide controlled nutrient availability, reducing nutrient losses and environmental impacts (Beig et al. 2022; Rani et al. 2025). Additionally, AI-driven nutrient diagnosis systems use leaf metabolomic signatures and protein expression profiles for real-time nutrient monitoring, enabling site-specific fertilization and resource-efficient nutrient management (Roychowdhury et al. 2025). Metagenomic and proteomic studies have also facilitated the development of biofertilizers enriched with beneficial microbes, enhancing soil nutrient cycling and plant nutrient uptake efficiency (Jagadesh et al. 2024). Integrative omics applications in different plant species have demonstrated success in improving nutrient use efficiency and stress resilience. For example, multi-omics studies have identified key genes, proteins, and metabolites associated with nutrient stress responses, leading to the development of nutrient-efficient rice varieties that maintain high productivity under low-fertility conditions (Zhao et al. 2023). Also, a study in cotton provided detailed insights into the integrative omics-based approaches employed to elucidate the molecular mechanisms underlying nutrient stress resilience (Prakash et al. 2023). In barley (*Hordeum vulgare*), multi-omics analysis identified metabolic pathways associated with drought resilience, guiding breeding efforts to develop stress-tolerant varieties (González-Rodríguez et al. 2025). Another study demonstrated that exogenous melatonin application increased peanut productivity and quality while reducing nitrogen inputs, highlighting its potential as an eco-friendly intervention in sustainable agriculture (Li et al. 2024b). Omics-driven studies have also enhanced understanding of beneficial plant-microbe interactions, identifying microbial traits that improve nutrient uptake, enhance plant growth, and increase stress resistance. This research has contributed to biofertilization strategies and sustainable soil management practices (Jagadesh et al. 2024; Gupta et al. 2023). However, challenges remain in translating omics-driven discoveries into large-scale agricultural solutions, such as standardized data pipelines, validation under field conditions, and the adoption of CRISPR-based gene editing and transgenic approaches.

## Advantages of integrated proteomic, and metabolomics analysis

- **Improved understanding of disease mechanisms**: By examining changes in gene expression, protein abundance, and metabolite levels simultaneously, researchers can identify dysregulated pathways and key molecular players driving disease progression. This knowledge can aid in the development of targeted therapies and the discovery of novel drug targets, ultimately leading to improved treatment strategies.
- **Elucidation of complex biological networks**: Integrating multiple omics datasets enables the construction of comprehensive biological networks, unravelling the intricate interplay between genes, proteins, and metabolites. Using network-based approaches, researchers can identify key regulatory elements, signaling pathways, and functional modules involved in specific cellular processes.
- **Enhanced data interpretation**: Integration of transcriptomic, proteomic, and metabolomics data provides a more complete picture of cellular processes. By considering the dynamic interactions between genes, proteins, and metabolites, researchers can decipher complex biological pathways and gain insights into functional relationships between molecules.
- **Facilitating personalized medicine**: Transcriptomic, proteomic, and metabolomics data integration holds significant promise in advancing personalized medicine. This can be utilized to tailor medical interventions to individual patients, optimizing therapeutic outcomes and minimizing adverse effects.
- **Identification of novel biomarkers**: Integration of transcriptomic, proteomic, and metabolomics data from both healthy and diseased individuals, researchers can identify specific molecular signatures associated with various physiological and pathological conditions. These biomarkers can be utilized for early disease detection, prognosis, and monitoring treatment responses.

Despite significant advancements in metabolomics, proteomics, genomics, and transcriptomics, several challenges and limitations hinder their full potential in understanding plant responses to nutrient stress. These challenges include technical constraints, data integration issues, reproducibility concerns, and the complexity of multi-omics interpretation, which must be addressed to enhance the reliability and applicability of omics-based studies in agricultural research. Table 4 summarizes the key limitations and potential solutions for each omics approach.

## Future directions for research using integrative metabolomics and proteomic approaches

Based on this extensive review, the following future research directions in integrating metabolomics and proteomics approaches are listed:

- *Comprehensive understanding of plant metabolic and protein networks*: Integrating metabolomics and proteomics has yielded significant knowledge about plant metabolic and protein networks (Yan et al. 2022b). Nevertheless, there is a need for further research that aims to comprehensively grasp these networks and devise novel analytical methods and computational tools to interpret extensive datasets.
- **Species-Specific Nutrient Stress Responses**: Comparative studies across diverse crop species will provide insights into shared and unique pathways, facilitating targeted breeding programs. For instance, a recent study in cotton elucidated the molecular basis of nutrient stress resilience, offering valuable insights for other economically important crops (Prakash et al. 2023).
- *Identification of novel stress-responsive genes and proteins*: Additional research is necessary to uncover novel stress-responsive genes and proteins in plants and gain insight into their roles (Tao et al. 2023). Cutting-edge genomic and proteomic methods, such as RNA sequencing, chromatin immunoprecipitation sequencing, and mass spectrometry, will be essential in this pursuit (Naik et al. 2023).
- *Field-Based Validation*: Future studies must bridge the gap between controlled experimental conditions and

**Table 4** Challenges and solutions in Metabolomics, Proteomics, Genomics, and Transcriptomics for Nutrient Stress Research

| Omics Approach | Challenges | Impact on Nutrient Stress Research | Potential Solutions | References |
|---|---|---|---|---|
| Metabolomics | Metabolite Diversity & Detection Limitations | Many low-abundance metabolites remain undetected due to instrument sensitivity constraints. | Develop high-resolution MS-based detection techniques and expand metabolite databases. | (Mazumder et al. 2024) |
| | Analytical Variability | Differences in LC-MS, GC-MS, and NMR platforms cause inconsistencies across studies. | Establish standardized workflows and cross-platform validation methods. | (Brockbals et al. 2025) |
| | Metabolite Identification Bottleneck | Many detected metabolites are uncharacterized, limiting pathway reconstruction. | Use AI-based metabolite annotation and increase functional metabolomics studies. | (Chen et al. 2022) |
| Proteomics | Low-Abundance Proteins Detection | Signaling proteins (e.g., transcription factors, kinases) exist in low concentrations, making them hard to detect. | Improve protein enrichment techniques and adopt single-cell proteomics. | (Nalla et al. 2025) |
| | Dynamic Range & Sensitivity Issues | Lack of amplification steps makes protein quantification difficult compared to RNA-seq. | Use deep fractionation methods and enhance high-sensitivity MS platforms. | (Liang et al. 2025) |
| | Post-Translational Modifications (PTMs) Complexity | PTMs (e.g., phosphorylation, glycosylation) are crucial for stress responses but difficult to analyze. | Develop advanced PTM-specific enrichment and detection techniques. | (Yao et al. 2024) |
| Genomics | High Cost & Computational Burden | Whole-genome sequencing and variant analysis require large datasets and advanced computing power. | Optimize cost-effective sequencing technologies and AI-driven data processing. | (Gupta et al. 2023; Xian et al. 2023) |
| | Linking Genotypic Variations to Phenotypes | Many genomic variations have small effect sizes, complicating trait selection. | Integrate functional genomics with gene-editing approaches like CRISPR. | (Li et al. 2023) |
| Transcriptomics | Transient vs. Stable Gene Expression | Rapid transcriptomic shifts may not correlate with long-term metabolic changes. | Use time-course RNA-seq and integrate transcriptomics with proteomics and metabolomics. | (Xu et al. 2019, 2025) |
| | Large Data Complexity & Interpretation Challenges | Multi-condition transcriptome studies generate massive datasets requiring complex bioinformatics. | Develop AI-based data interpretation frameworks. | (Singh et al. 2022) |
| Multi-Omics Integration | Heterogeneous Data Formats | Metabolomics, proteomics, transcriptomics, and genomics generate incompatible datasets. | Create cross-platform data standardization and universal omics pipelines. | (An et al. 2023) |
| | Lack of Universal Integration Pipelines | No standard framework exists for integrating multi-omics findings. | Implement machine learning algorithms for cross-omics correlations. | (Kumar et al. 2024) |
| | Reproducibility Across Species | Many omics studies focus on model plants, limiting cross-species application. | Conduct comparative multi-species omics studies to expand findings. | (Yao et al. 2024) |

field environments to ensure the translational application of laboratory findings in sustainable agriculture.

- *Advanced Biotechnological Interventions*: The application of CRISPR-based gene editing and synthetic biology offers promising avenues for developing nutrient-efficient crops. Regulatory frameworks and public acceptance should be aligned to accelerate their adoption.
- *Elucidation of the regulatory mechanisms of plant nutrient stress responses*: The responses of plant nutrients to stress are controlled by intricate networks of transcription factors, hormones, and signaling molecules (Shumilina et al. 2023). To advance our understanding of this process, further research should concentrate on identifying crucial transcription factors and hormone signaling pathways. This can be achieved by utilizing cutting-edge genomic and proteomic techniques such as ChIP-seq, RNA-seq, and mass spectrometry.
- *Artificial Intelligence and Predictive Modeling*: AI-driven models can revolutionize nutrient stress research by predicting stress responses, identifying optimal nutrient management strategies, and enabling real-time monitoring in precision agriculture.
- *Exogenous Application of Stress Mitigators*: Exploring eco-friendly solutions such as melatonin application and engineered biofertilizers enriched with beneficial microbes could enhance resilience under nutrient-limited conditions (Li et al. 2024b).
- *Developing novel biomarkers for plant nutrient stress*: Using biomarkers requires monitoring and determining effective stress-alleviating methods (Roychowdhury et al. 2023). To advance this research, developing new biomarkers utilizing cutting-edge techniques such as mass spectrometry and NMR spectroscopy is crucial.
- *Integration of metabolomics and proteomics with other omics technologies*: Plant nutrient stress responses are the result of intricate molecular interactions, which include transcriptomics, epigenomics, and metabolomics (Shen et al. 2023). To thoroughly understand these responses, future research should combine metabolomics and proteomics with other omics technologies like transcriptomics and epigenomics. Advanced computational tools and methods, such as machine learning and network analysis, will be required to achieve this integration.
- *Development of novel stress-alleviating strategies*: Plant nutrient stress significantly impacts crop productivity and food security (Tao et al. 2023). Therefore, future research should develop innovative stress-alleviating strategies using genetic engineering, biotechnology, and synthetic chemistry, integrating metabolomics and proteomics with other disciplines like agriculture and environmental science.

In conclusion, integrative metabolomics and proteomic approaches have provided significant insights into plant responses to nutrient stress. To advance plant science, it is essential to prioritize research focused on comprehending metabolic and protein networks, identifying genes and proteins that respond to stress, clarifying the mechanisms behind nutrient stress responses, creating new biomarkers, integrating omics technologies, and devising strategies to alleviate stress.

## Conclusion

In conclusion, the fields of metabolomics and proteomics have provided valuable insights into how plants respond to nutrient stress. These studies revealed the complex and dynamic metabolic and protein networks that enable plants to adapt and survive in challenging environments. It has become clear that plants use advanced mechanisms to sense and respond to nutrient availability, which regulates critical metabolic pathways, modulates hormone signaling, and alters protein expression and function. Integrating metabolomics and proteomics has uncovered crucial molecular mechanisms that underlie plant nutrient stress responses. These findings have pinpointed targets for enhancing crop resilience and identifying critical pathways and enzymes where genetic and biotechnological solutions have emerged to improve nutrient utilization and boost productivity. Furthermore, it should be noted that integrating metabolomics and proteomics methods has provided a complete understanding of how plant nutrient stress responses work. These findings have identified potential targets for improving crop resilience to environmental stressors, which could have significant implications for human health and food security. Despite advances in the field, significant challenges and limitations include the intricate complexity of plant metabolism, making it difficult to pinpoint the specific metabolic and proteomic changes that arise in response to varying nutrient conditions. Additionally, there is a need to conduct further research to comprehend better how nutrient stress interacts with other environmental factors, including temperature, drought, and salinity, which can profoundly influence plant growth and development.

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## Declarations

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