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The mitigation of global micronutrient deficiencies: Genomic and agronomic advances in agricultural crop biofortification

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Abstract

Micronutrient malnutrition, often termed "hidden hunger," remains a significant global health challenge, particularly in developing regions where diets are primarily reliant on cereal-based foods that lack essential vitamins and minerals. Biofortification has emerged as a sustainable and cost-effective strategy to enhance the micronutrient content of staple food crops, thereby improving nutritional security. This review summarises recent advancements in breeding techniques aimed at increasing the concentration and bioavailability of key micronutrients such as iron, zinc, and provitamin A in cereals, pulses, and vegetables. Conventional breeding methods, including selection and hybridisation, have been effectively complemented by modern tools such as marker-assisted selection, genomic selection, and gene editing technologies. The integration of omics approaches—like genomics, transcriptomics, and metabolomics—has further accelerated the identification of candidate genes and quantitative trait loci associated with micronutrient accumulation. Additionally, the importance of genetic diversity, wild relatives, and landraces in broadening the breeding base is emphasised. Despite notable progress, challenges such as genotype × environment interactions, nutrient bioavailability, and potential trade-offs with yield and agronomic traits remain critical considerations. The review also addresses future prospects, stressing the need for interdisciplinary approaches, policy support, and farmer adoption to ensure the successful deployment of biofortified varieties. Overall, recent advances in breeding hold considerable promise for developing nutrient-dense crops that can help alleviate micronutrient deficiencies and contribute to global food and nutritional security.

Keywords: Biofortification, AI, micronutrient breeding, genomic selection, CRISPR/Cas9, nutritional security

Introduction

Addressing the widespread global health issue of micronutrient malnutrition, often referred to as "hidden hunger," is an urgent priority, especially for populations that rely on monotonous, cereal-based diets lacking essential nutrients like iron, zinc, and provitamin A (Kudapa *et al.*, 2023) ^[3]. Traditional supplementation and industrial fortification encounter systemic logistical and economic challenges in reaching marginalised rural communities (Avnee *et al.*, 2023) ^[1]. As a result, agronomic biofortification has emerged as a sustainable and cost-effective alternative. By enhancing the nutritional density of staple crops during their growth, biofortification requires only a single investment in development to deliver lasting public health benefits (Sheoran *et al.*, 2022) ^[6]. Early breeding approaches primarily focused on improving isolated nutritional aspects by leveraging natural genetic variations found in landraces and wild crop relatives (Nasim *et al.*, 2025; Virk *et al.*, 2021) ^[4]. However, modern agricultural security requires that these improvements do not come at the cost of yield or essential agronomic traits. As a result, there has been a strategic shift towards incorporating biofortification traits into global crop improvement programs. This ensures that future high-yield commercial varieties automatically have enhanced nutritional profiles (Virk *et al.*, 2021) ^[7]. This transition is being rapidly accelerated by advances in modern technology, including multi-omics and biotechnology. Contemporary breeding processes now commonly combine high-throughput phenotyping with genomic selection and genome-wide association studies (GWAS) to accurately identify novel

quantitative trait loci (QTLs) that control mineral uptake and storage (Jha *et al.*, 2022; Kudapa *et al.*, 2023) ^[2]. Additionally, the use of new breeding techniques (NBTs), particularly CRISPR-Cas9 genome editing, provides unparalleled precision in modifying metabolic pathways for micronutrient synthesis without disrupting the entire plant genome. This empowers breeders to quickly develop robust, biofortified cultivars across key crops such as cereals, millets, and food legumes (Nasim *et al.*, 2025; Shahzad *et al.*, 2021) ^[5]. The figure 1. Illustrates biofortification through germplasm, genomics, and CRISPR-based breeding to enhance crop nutrients, while highlighting key challenges.

Systemic Implications of Biofortifying Agricultural Crops for Global Nutritional Security

Biofortification of staple crops like cereals, legumes, and vegetables is essential for tackling nutritional deficiencies. Recent trials show that genetic biofortification and specific agronomic practices can boost mineral levels in plants without affecting yields. Molecular breeding and foliar applications of zinc, selenium, iodine, and iron have notably increased zinc levels in wheat in South Asia, surpassing the ideal threshold of 50 mg kg⁻¹ (Ram *et al.*, 2024) ^[11]. Similar agronomic techniques have shown positive results in rice. Specifically, the application of zinc through foliar chemigation at two crucial growth stages—maximum tillering and milking—has effectively increased the zinc content in the edible portion of white rice while also promoting the two main yields (Jose *et al.*, 2021) ^[10]. Furthermore, pulse crops, which are vital sources of protein for many in the developing world, also demonstrate the potential of this comprehensive approach to nutrition. Research on lentil biofortification has shown that applying foliar treatments before flowering significantly raises the concentrations of zinc and iron in the grains. Additionally, these applications lead to a notable increase in the uptake of these micronutrients (Dhaliwal *et al.*, 2021) ^[9]. Enhancing root and tuber crops through biofortification is crucial for improving health and nutrition for populations reliant on these foods. The effectiveness of such interventions needs to be confirmed through clinical studies measuring their impact on at-risk groups. Finger millet, a staple in northeastern Uganda, offers a bioavailable source of zinc when prepared as local porridge. A recent study noted varying acceptance of biofortified versus non-biofortified products among urban and rural consumers in Uganda. (Afolami *et al.*, 2021) ^[8]. Integrating these newly developed sources of micronutrients into the food system, including well-known cereals and region-specific root and tuber crops, would enable global food systems to move beyond merely providing necessary caloric intake. This approach can facilitate healthcare interventions that are preventative in nature.

Exploiting Germplasm Diversity and Wild Progenitors for Micronutrient Enrichment

Utilizing germplasm diversity, particularly from crop wild progenitors, has become a key strategy for genetic biofortification to combat global micronutrient deficiencies. Domesticated crop cereals have often lost nutritional quality, as the focus has been primarily on increasing yield. Therefore, it is essential to introduce necessary micronutrient features from landraces and wild relatives (Gupta *et al.*, 2022) ^[14]. Wild crop progenitors present a wealth of genetic diversity and may possess higher levels of essential micronutrients, such as iron, zinc, and selenium, compared to modern elite cultivars (Nasim *et al.*, 2025) ^[4]. By employing both traditional breeding and

advanced genomic techniques, we can economically and sustainably introduce these valuable alleles from wild germplasm into commercial varieties to enhance micronutrient content (Dwivedi *et al.*, 2023) ^[13]. For example, research on wild *Oryza* species has revealed significant genetic diversity and improved tolerance to iron deficiency-induced chlorosis, making them excellent donor germplasm for breeding iron-rich rice (Kumar & Yer, 2023) ^[15]. Ultimately, integrating these wild genetic resources with modern molecular plant breeding techniques will enable scientists to elevate the micronutrient levels in staple crops, providing a long-term solution to "hidden hunger" among the world's most disadvantaged populations (Tumbare & Maphosa, 2023) ^[12].

Genomic Selection and High-Throughput Mapping of Nutritional Trait Loci

The integration of high-throughput genotyping and advanced mapping strategies has transformed the genetic analysis of nutritional trait loci, significantly speeding up crop biofortification efforts. Genome-wide association studies (GWAS) have become a powerful tool for identifying single nucleotide polymorphisms (SNPs) and the candidate genes responsible for micronutrient accumulation. This approach effectively addresses the limitations of traditional biparental mapping, which often suffers from a narrow genetic base and low resolution (Salgotra & Stewart, 2022) ^[20]. For example, high-throughput mapping in bread wheat has successfully identified shared genomic regions that influence both grain zinc and iron concentrations. This illustrates the potential for simultaneous genetic enrichment of multiple nutrients (Juliana *et al.*, 2022) ^[18]. Recent genome-wide studies on legume crops have revealed important marker-trait associations related to various nutritional profiles. For instance, research has shown elevated levels of crude protein, betacarotene, and essential minerals in chickpeas (Roorkiwal *et al.*, 2022) ^[19], as well as increased amino acid and protein content in peas (Ballén-Taborda *et al.*, 2025) ^[16]. Building on these high-resolution mapping findings, genomic selection (GS) presents a transformative approach by enabling the prediction of genomic estimated breeding values (GEBVs) for entire populations without the need for extensive, multi-environment phenotyping. This significantly shortens the breeding cycle (Sinha *et al.*, 2021) ^[21]. Moreover, the integration of multi-omics data with high-throughput phenotyping platforms provides a deeper understanding of the metabolic pathways involved in nutrient transport and storage (Varshney *et al.*, 2021) ^[21]. Ultimately, by combining these genetic insights with advanced genotyping techniques, plant breeders can efficiently implement early generation marker-assisted selection and GS to quickly integrate favourable nutritional alleles into elite, high-yielding commercial varieties (Bhandari *et al.*, 2023) ^[17].

Resilience Breeding: Biofortification under Climate Disruption

The primary goal of resilient breeding with biofortification amidst climate disruption is to preserve the micronutrient content of crops while maintaining stable yields under various combinations of abiotic stresses, such as drought, heat, and increased CO₂ levels. Recent research indicates that not only does climate change impact crops, but varying climatic conditions can also alter numerous physiological processes in plants, including nutrient uptake, assimilation, and partitioning. This can lead to reduced mineral concentrations in grains, highlighting the need for breeding strategies that can adapt to

these challenges (Myers *et al.*, 2014; Beach *et al.*, 2019) ^[58, 62]. Modern crop improvement approaches combine physiological trait-based selection, genomic prediction, and environmental modeling to enhance both stress resistance and nutrient accumulation/homeostasis efficiency (Cobb *et al.*, 2019; Zhao *et al.*, 2021) ^[59, 65]. Additionally, integrating systems biology with crop modeling aids in identifying the key metabolic pathways and regulatory networks that control nutrient homeostasis under stress conditions, allowing for targeted genetic modifications (Zhang *et al.*, 2022; Tardieu *et al.*, 2018) ^[52, 63]. Recently developed strategies also emphasize the creation of climate-resilient germplasm and ideotype-based breeding to ensure the stability of nutritional traits across different environments (Cooper *et al.*, 2020; Hammer *et al.*, 2021) ^[60, 61]. Collectively, these techniques facilitate the development of robust, nutrient-rich crop varieties that can contribute to food and nutrition security, even in the face of changing climate conditions.

CRISPR-Cas9 and Targeted Molecular Engineering of Micronutrient Pathways

With the help of CRISPR-Cas9 technology, biofortification has progressed from merely selecting plants based on observable traits to precisely genetically designing a plant's metabolism. Through these genetic modifications, scientists can now bypass the natural physiological limitations that lead to low nutrient accumulation in seeds. For instance, researchers have increased iron uptake in seeds while reducing phytic acid content, making minerals more bioavailable in cereals. This was achieved by simultaneously knocking out the vacuolar iron transporter (VIT) genes and the IPK1 gene (Sashidhar *et al.*, 2023) ^[25]. Furthermore, the ability to edit multiple genes at once has opened new horizons for biofortifying complex metabolic pathways. An example of this is the increase in provitamin A content in bananas through editing the phytoene synthase (PSY) genes (Upadhyay *et al.*, 2023) ^[27]. In addition to simple gene inactivation, advanced techniques like base editing and prime editing are enabling the creation of "gain-of-function" mutations in metal transport genes, such as OsNRAMP5. This allows for selective mineral uptake while minimizing the harmful accumulation of cadmium (Khan *et al.*, 2024) ^[23]. Additionally, controlling the expression of the Nicotianamine Synthase (NAS) gene family by CRISPR-mediated promoter editing has resulted in increased transport of zinc and iron to the endosperm (Talia *et al.*, 2023) ^[26]. Gene-level modifications are typically carried out alongside speed breeding, which accelerates the fixation of nutritional traits in elite germplasm (Raza *et al.*, 2023) ^[24]. CRISPR technology not only enables mineral fortification but also enhances plant resilience. For instance, researchers targeted the photosynthesis-related SGR gene to prevent plant senescence, thereby preserving nutritional quality even under environmental stress (Zafar *et al.*, 2022) ^[29]. In another example, modifying the LCY-ε gene redirected carotenoid metabolic flux toward the beta-branch, resulting in staple tubers with improved antioxidant properties (Zhu *et al.*, 2024) ^[30]. Additionally, one of the significant advantages of using CRISPR is "de novo" domestication. This process allows for the rapid transfer of highly nutritious traits into wild and resilient species, leading to a new generation of "superfoods" (Yaqoob *et al.*, 2023) ^[28].

AI-Driven Predictive Breeding and Precision Phenomics for Nutritional Quality

The combination of AI-driven predictive breeding and precision phenomics significantly improves the nutritional quality of food traits through accurate genotype-phenotype modelling. Genomic

selection, supported by machine learning and deep learning algorithms, has greatly enhanced our ability to predict complex traits such as grain micronutrient concentrations and metabolite compositions. This is achieved through the integration of large-scale genomic and environmental datasets (Crossa *et al.*, 2021; Montesinos-López *et al.*, 2022; Zingaretti *et al.*, 2020) ^[51, 53, 57]. To support these advancements, high-throughput phenotyping techniques, including hyperspectral imaging and sensor-based platforms, have been developed. These techniques enable non-destructive, largescale measurements of biochemical and physiological traits associated with nutritional quality, thereby overcoming the limitations of traditional phenotyping methods (Yang *et al.*, 2020; Li *et al.*, 2022; Araus *et al.*, 2021) ^[50, 52, 56]. By combining phenomics with genomic prediction models, we are better able to capture genotype-environment interactions, which are crucial for stabilising nutrient traits across various agroecological conditions (Reynolds *et al.*, 2021; van Eeuwijk *et al.*, 2021) ^[54, 55]. Furthermore, AI-driven frameworks allow for the prediction of multiple traits and the isolation of complex phenotypic features. This not only increases breeding efficiency but also opens up possibilities for targeted biofortification strategies (Montesinos-López *et al.*, 2022; Crossa *et al.*, 2021). Together, these advancements contribute to the development of data-driven "Breeding 4.0" systems, facilitating the quicker and more accurate production of nutrient-rich crop varieties.

Agronomic Performance and Socio-Economic Adoption of Biofortified Crops

The widespread adoption of biofortified crops hinges on a dual-utility concept: they must not only meet the needs of farmers but also appeal to consumers through their appearance, taste, and price. Without these qualities, achieving success is nearly impossible. Biofortified crops, like iron-enriched beans and pearl millet, have demonstrated nutritional superiority and have been shown to match or even surpass traditional varieties in field trials. This indicates that improvements in yield and resilience to stress play significant roles in supporting livelihoods and promoting climatesmart agricultural practices. For instance, bush bean varieties yield two to three times more than local landraces (Meenakshi *et al.*, 2024) ^[36]. Consumer demand for biofortified crops is largely influenced by sensory traits, such as taste, color, and cooking time. Even when the nutritional benefits are not the primary concern, consumers tend to prefer zinc-enriched wheat because it has a better taste and cooks faster (Mahboob *et al.*, 2022) ^[34]. Furthermore, when consumers are informed about the health benefits, they are willing to pay a premium for visible traits, like the orange color of Vitamin A-enriched maize (Jada & van den Berg, 2024) ^[33]. Biofortification programs offer a sustainable alternative to industrial fortification, particularly due to their high benefit-cost ratios, which encourage consumers to choose biofortified foods (Maina & Mwangi, 2021) ^[35]. In addition to improving yields, biofortified seeds enhance seedling establishment and vigor, even in less fertile soils, making them especially appealing to many smallholder farmers (Rizwan *et al.*, 2021) ^[38]. However, scaling up the use of biofortified crops will require robust seed systems and policy measures to ensure seed availability and market integration (Weldemariam *et al.*, 2023) ^[39]. Evaluations in several countries have shown that incorporating biofortified crops into school feeding programs can effectively reduce micronutrient deficiencies at the community level (Gannon *et al.*, 2024) ^[32]. Furthermore, the economic benefits are supported by a significant reduction in Disability-Adjusted Life Years

(DALYs), making biofortification a strong public health investment (Oparinde *et al.*, 2023) [37]. Ultimately, aligning the genetic enhancement of nutritional traits with the agronomic

characteristics preferred by farmers is crucial for ensuring sustainable and long-term adoption (Virk *et al.*, 2021) [7].

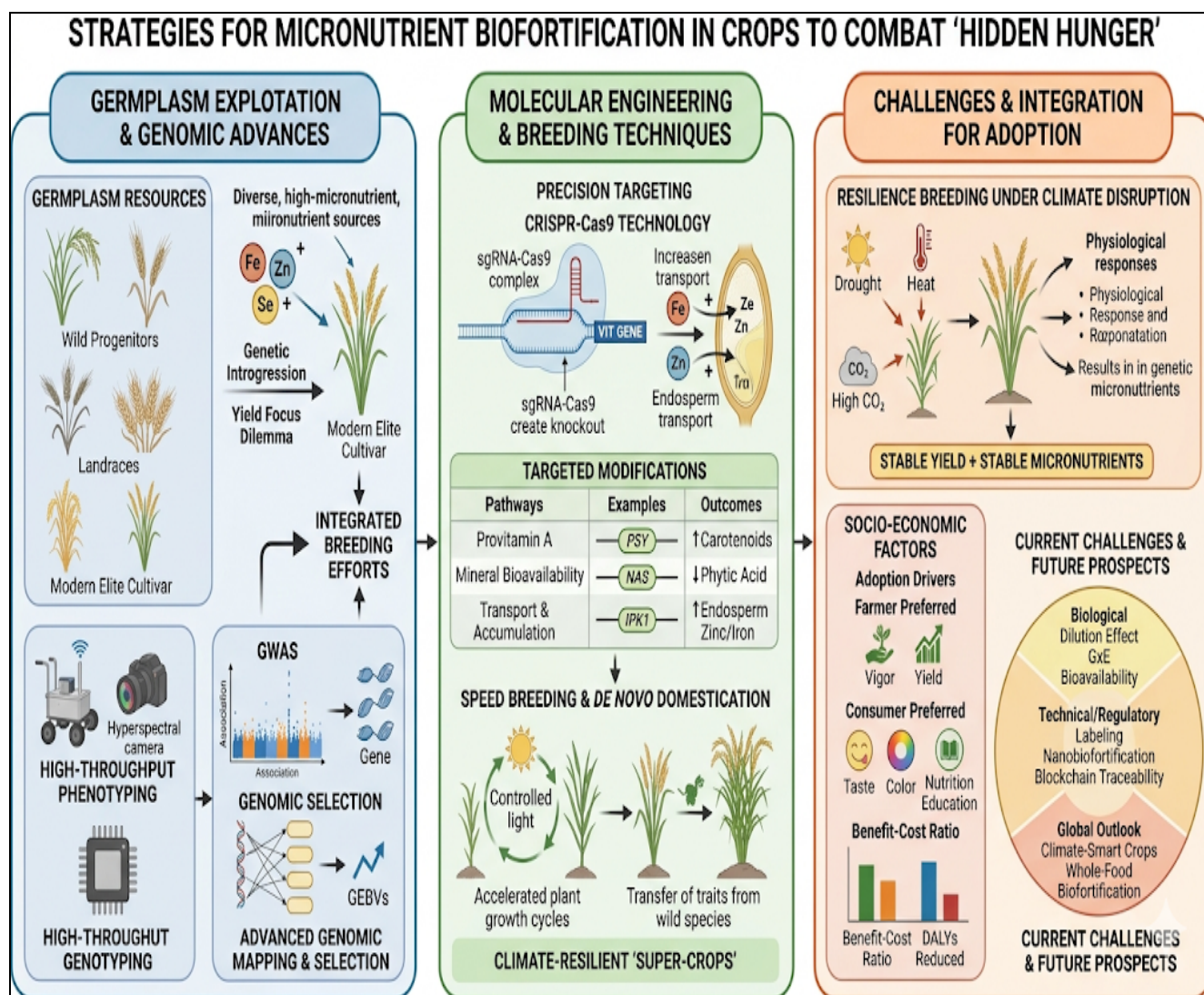


Fig 1: The figure illustrates biofortification through germplasm, genomics, and CRISPR based breeding to enhance crop nutrients, while highlighting key challenges.

Challenges and future prospects of biofortification in agricultural crops

The journey from experimental success to the global implementation of biofortified crops faces numerous challenges that must be addressed. One of the most significant challenges is genotype-by-environment (G×E) interaction, which can cause micronutrient levels in genetically identical crops to vary significantly depending on the soil and climate in which they are grown (Saini *et al.*, 2022) [45]. Another biological challenge is that plants typically exhibit the highest grain mineral density at the lowest yield, a phenomenon known as the "dilution effect." As a result, many new high-yielding crop varieties fail to maintain their nutrient concentrations (Velu *et al.*, 2023) [48]. Additionally, mineral bioavailability is often limited by the presence of polyphenols and phytates in certain staple crops, which can restrict consumers' nutritional intake (Maqbool *et al.*, 2021) [42]. Additionally, there are regulatory hurdles to overcome, as there are currently no internationally harmonised standards for labelling and certifying "biofortified" products. This lack of standardisation complicates international trade and makes it challenging to obtain market premiums (Birol *et al.*,

2021) [40]. Looking ahead, it is expected that the integration of high-throughput phenomics techniques with satellite imagery will simplify the process of assessing food nutrients at the regional level (Prasad *et al.*, 2024) [44]. One of the emerging directions in this area involves the development of "climate-smart" biofortified crops that can maintain their nutrient levels even when exposed to increased atmospheric CO₂, which typically lowers the mineral content in cereals (Soares *et al.*, 2021) [46]. Additionally, nanobiofortification, which involves using nano-carriers to deliver micronutrients, is considered a promising short-term technological solution that can complement genetic approaches (Zulfiqar *et al.*, 2022) [49]. Conversely, the concept of circular biofortification aims to improve soil fertility by recycling nutrient-rich organic waste, presenting a sustainable alternative for agricultural systems (Garg *et al.*, 2022) [41]. Meanwhile, the use of digital tools and blockchain-based traceability is becoming more prevalent as a method to validate the nutritional claims of biofortified grains to consumers, thereby fostering trust (Pal *et al.*, 2023) [43]. Ultimately, the future focus of biofortification is likely to prioritize whole foods that are nutrient-dense, providing a

simultaneous supply of various vitamins and minerals to address complex malnutrition issues (Strobbe & Van Der Straeten, 2022) [47].

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