Nutritional quality of crops in a high CO\textsubscript{2} world: an agenda for research and technology development

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Abstract

Essential nutrients, including carbohydrates, proteins, fats, vitamins, and minerals, are required for human health and development. Inadequate intake can negatively affect development and result in a wide range of adverse health outcomes. Rice, maize, and wheat provide over 60\% of the world's food energy intake. Atmospheric carbon dioxide (CO\textsubscript{2}), water, nitrogen, and soil micronutrients are the basis of this plant material. Since 1850–1900, CO\textsubscript{2} concentrations have increased about 50\%, with most of that increase since 1950. Higher CO\textsubscript{2} concentrations increase photosynthesis, which then increases plant biomass, but also alters the nutritional quality of wheat, rice, and other C\textsubscript{3} plants. We review the possible impacts of rising CO\textsubscript{2} concentrations on human health, highlight uncertainties, and propose a research agenda to maintain the nutritional quality of C\textsubscript{3} plants. We also synthesize options for addressing this critical challenge to nutritional safety and security. A complete research agenda requires addressing data and knowledge gaps surrounding plant biology and policy responses. Data on key nutrients are lacking, leading to a limited mechanistic understanding of the response of the plant ionome to elevated CO\textsubscript{2} concentrations. Regular data are largely missing on nutritional status and food safety in low- and middle-income countries, limiting assessments of the magnitude of the risks. Research opportunities to fill gaps in data and understanding include herbaria studies, field-based natural and manipulative studies, leveraging natural plant variability, and innovations in seed quality. Improved models of cereal crop nutritional quality can project the magnitude and direction of possible future challenges; incorporating the effects of climate change into those models can further improve their robustness. Transdisciplinary research involving at least ecologists, plant physiologists, economists, and experts in human nutrition is essential for developing a systems-based understanding of the potential impacts of rising CO\textsubscript{2} concentrations for human nutrition and the attendant consequences for achieving the sustainable development goal on food security.

Acronyms

| Acronym | Definition |
|---------|------------|
| CO\textsubscript{2} | carbon dioxide |
| CWR | crop wild relatives |
| FACE | free air CO\textsubscript{2} enrichment (experiment) |
| LMIC | low- and middle-income countries |
| ONS | oral nutritional supplements |
| SSPs | small-scale producers |
1. Introduction

Plants are the foundation of human health and well-being. Of the 50 000 edible plants, just three grains—rice, maize, and wheat—provide over 60% of the world’s food energy intake (FAO undated). Terrestrial plant material is built from CO$_2$ in the atmosphere and water, nitrogen, and micronutrients drawn from soils. This means the biomass and nutritional quality of plants varies with the environment and with the quality of soils. As CO$_2$ increases rapidly in the atmosphere, there are anticipated changes in plant stoichiometry that will affect their nutritional status. These changes, in turn, risk compromising the nutritional integrity for all living things, including humans. Research is just beginning to understand the extent and nature of the effects of rising CO$_2$ on plants with its associated implications for human health and food security.

Increasing atmospheric CO$_2$ concentrations from emissions of greenhouse gases and deforestation also are driving global climate change. The Intergovernmental Panel on Climate Change (IPCC) recently reviewed the (primarily negative) impacts of climate variability and change on crop yields worldwide (Intergovernmental Panel on Climate Change 2019). While CO$_2$ concentrations and climate change may interact to alter the nutritional quality of crops, the focus here is on the possible separate impacts of CO$_2$.

Atmospheric CO$_2$ concentrations, a strong selective pressure that has been shaping the evolutionary history of plants on geological time scales (Beering 2012), have increased at an unprecedented rate of about 50% since 1850–1900, with most of that increase since 1950 (Intergovernmental Panel on Climate Change 2019). This increase caused mean surface air temperature over land in 2006–2015 to be higher by 1.5°C than in 1850–1900 (Osborn et al. 2021). Higher CO$_2$ concentrations increase photosynthesis, which then increases plant biomass (i.e. CO$_2$ is plant food) (Kimball 2016). Satellite observations over the last three decades have shown vegetation greening over most of the land surface (Zhu et al. 2016); causes included CO$_2$ fertilization, warmer temperatures, an extended growing season, nitrogen deposition, and land management (Intergovernmental Panel on Climate Change 2019). This greening should be good news for addressing the high burden of food insecurity. There are about 821 million people today who do not have secure access to sufficient amounts of food for normal growth and development, with over 20% of children (149 million) stunted and 7.3% wasted (FAO 2019). But achieving food security means addressing access to safe and nutritious foods, not just sufficient food. Already, 45% of mortality in children under five is attributable to insufficient calories and/or inadequate consumption of adequate nutrients (i.e. undernutrition) (Black et al. 2013).

Continued increases in CO$_2$ concentrations are expected to alter the nutritional quality of wheat, rice, barley, oats, potatoes, most trees, and other C3 plants (Loladze 2002, Taub et al. 2008, Myers et al. 2014, Zhu et al. 2018, Loladze et al. 2014a). C3 plants, approximately 95% of the plants on Earth, use one of three major photosynthetic pathways to take carbon from atmospheric carbon dioxide to incorporate it into carbohydrates.

Expected changes in the nutritional quality of C3 crops are of deep concern because of their dietary importance, particularly in LMICs where larger proportions of the population are undernourished. Rice is the most consumed cereal crop in the world led by the regions of Asia, sub-Saharan Africa, and South America; it is the primary staple for more than half of the world’s population (FAO 2013, USDA 2021). Wheat is the primary staple for another 2.5 billion people, providing about 20% of the protein consumed worldwide (Phys.Org. 2020). An estimated 2 billion people are already micronutrient deficient (e.g. iron, zinc, and other micronutrients) (FAO 2018). Production of rice and wheat is increasing to address demand (FAO 2013). But an increasing reliance on these crops, which are vulnerable to declining nutritional quality, can aggravate deficiencies that adversely affect cognitive development, metabolism, obesity, diabetes, and other health outcomes, thereby potentially affecting health and welfare across the life course (Tulchinsky 2010).

Experiments exposing wheat, rice, and other C3 plants to concentrations of CO$_2$ expected later this century show declines of about 10% in protein, 5%–10% in iron and zinc (and potentially other micronutrients), and up to an average of 30% in individual B vitamins (Taub et al. 2008, Myers et al. 2014, Zhu et al. 2018, Loladze et al. 2019). There is limited evidence suggesting that declines in nutrition may have already occurred in response to recent CO$_2$ increases (figure 1). As protein concentrations decline, the stoichiometric ratios of carbon to nitrogen (C:N) and to other minerals increase (Loladze 2002). In addition, elevated CO$_2$ decreases transpiration and alters plant carbon allocation patterns, allocating more carbon below ground in an elevated CO$_2$ environment as additional root biomass and/or carbon released into the surrounding soil (Norby and Zak 2011, McGrath and Lobell 2013, Thompson et al. 2017). These changes alter root access to soil elements, affect the soil microbial community that processes soil compounds, and can both compete with and facilitate access to nutrients and contaminants in the soil.

There are additional poorly understood potential indirect effects. Through effects on plant nitrogen content, higher concentrations of CO$_2$ could affect the livestock that contribute ≥15% of the global human protein supply. For example, Craine et al. (2017) examined dietary quality over 22 years for US cattle and found that cattle have been
Percent Change in Protein Concentration
300-400 ppm CO2

Figure 1. Changes in protein concentrations of unhulled rice seeds of eight genetically diverse rice cultivars in response to an increase in CO2 concentrations from 300 ppm (mid-20th century) to 400 ppm (today). Plants were grown to maturity in controlled environment chambers at their respective CO2 concentrations with sufficient nutrient supply. IR-72 is a semi-dwarf indica cultivar; NERICA is a cultivar derived from interspecific hybridization between Asian (Oryza sativa) and African (Oryza glaberrima) rice; Cypress is a long-grain cultivar bred in California, USA; Nipponbare is a short-grain temperate japonica cultivar bred in Japan; Italica Carolina was chosen because of its known high protein content. Cypress is representative of lines grown in the United States, and 075–158 is a mutant of Cypress, but with higher protein content. Protein was determined by nitrogen content. Additional details regarding the methods are available in Wang et al (2016) and Ziska et al (2010). (Note that some of these cultivars are old and not widely planted anymore.)

Increasingly protein-stressed, likely reducing cattle weight gain from reductions in nitrogen availability in grasslands. Changing carbon:nitrogen ratios also are affecting other compounds within plants. For example, concentrations of artemesinin (part of a widely used combination therapy for Plasmodium falciparum malaria) increased between 1905 and 2009 in parallel with CO2 concentrations (Zhu et al 2015). Impacts on other cultural and medicinal uses of plants, and on various phytonutrients, are generally unexplored. For example, while plants and humans share the need for xanthophylls to defend against light-induced oxidative stresses, the concentration of xanthophylls and other carotenoids might decline under elevated CO2 conditions (Loladze et al 2019).

Climate change projections indicate biomass production and yields could be affected by changes in the length of the growing seasonal and transpiration (Ahmed et al 2017), with likely interactions with nutrient density and quality. Interactions between temperature and CO2 (positive and negative) are likely, although whether they facilitate or negate nutritional quality is uncertain (Augustine et al 2018, Kohler et al 2019). Projections of future nutrient adequacy combine country-specific biophysical (climate) scenarios with socioeconomic futures under different income and population growth assumptions. These models project adequate average macronutrient availability in all but the lowest-income countries (e.g. Nelson et al 2018). But even without factoring in the effect of CO2 on nutritional quality, micronutrient challenges are projected to be more widespread and continue in low-income countries. ‘Nutrients of public health concern in lower income countries today, such as iron, zinc and vitamin A, are likely to remain problematic in 2050 under all modelled scenarios’ (Nelson et al 2018, p 775).

We review the breadth of possible impacts of rising CO2 concentrations on human nutrition, highlight uncertainties, and propose a research agenda to monitor changing plant nutritional content and associated health impacts and to develop potential strategies for addressing nutritional health impacts. We also synthesize options for addressing this critical challenge to achieving the sustainable development goal on food security.
2. Overview of the range of factors that affect plant nutrient levels

Concentrations of nutrients and toxins in grains reflect (a) availability of elements to the plant root, which is related to soil concentration, chemical form, and transport rate from bulk soil to the root; (b) plant uptake of the element, which is related to plant demand for element (toxins are often chemical analogues of nutrients); (c) translocation of element into grain, which is related to internal transport of the element from roots to grain; and (d) the total accumulation of carbohydrates in amyloplasts and other cellular parts, including vacuoles. Elevated CO$_2$ increases carbohydrate synthesis and increases leaf-level water-use efficiency almost universally; however, canopy level water use and carbon assimilation fluxes are still unclear (Donohue et al 2017).

Elevated CO$_2$ and temperature can alter all four of these aspects for many elements, both nutrients and toxins. Higher photosynthetic rates often correspond with a greater release of carbon from plant roots into soil, which can fuel microbial reactions that dissolve minerals and/or alter soil pH. These chemical changes can modify the partitioning of elements between soil particles and soil water. Increased photosynthetic efficiency decreases plant nutrient demand relative to carbon gain that can lead to less root uptake and carbon dilution of elements. Higher water use efficiency reduces transpiration while higher temperature increases transpiration (at a given relative humidity), and transpiration controls mass-flow delivery of elements in soil water to the root surface and influences internal plant transport. Reaction kinetics increase with temperature, and thus, rates of reactions that mobilize and sequester elements from soil will increase with temperature (Farhat et al 2021). Plant physiology is also sensitive to temperature, which can alter uptake and translocation patterns.

Most experiments on grain quality measured changes in grain nutrient concentrations in response to a single variable—atmospheric CO$_2$. The experiments that included increases in both temperature and CO$_2$ showed a more complex relation with some indicating that elevated temperature can worsen grain quality (Ziska et al 1997), while others showing that it can ameliorate the negative effects of elevated CO$_2$ on grain nutritional quality (Köhler et al 2019, Wang et al 2019, 2020).

The financial incentives in grain production often do not align with higher grain nutritional quality; producers are incentivized financially to produce higher yields. While a few physical and chemical aspects of grain quality (e.g. moisture, milling quality, vitreousness, protein content) do affect grain price, many aspects of grain quality that are central to the ‘hidden hunger’ problem, such the concentration of bioavailable zinc, are usually ignored in the grain price determination. Consequently, producers have little or no incentive to increase grain micronutrient density.

In addition to decreased macro- and micronutrients (e.g. nitrogen, protein, zinc, copper), there is also some evidence that rice grown under elevated CO$_2$ has increased concentrations of contaminants, such as cadmium, arsenic, and methylmercury (Lieffering et al 2004, Taub et al 2008, Guo et al 2011). It is also notable that recent studies have shown that rice grown in elevated temperature have increased concentrations of contaminants such as arsenic (Muehe et al 2019, Farhat et al 2021). Further decreases in the quality of rice would exacerbate and extend the health threat posed by micronutrient deficiency and toxin exposure if such trends are confirmed by additional experiments.

3. Implications for human health

There is ample evidence of the benefits of reducing nutrient deficiencies, including enjoying improvements in health and cognition, and societal returns via higher educational attainments, work productivity, and lower healthcare costs (Bailey et al 2015). These benefits are pronounced for pregnant women and young children, where micronutrient deficiencies are associated with infant mortality and reduced disease resistance (Moore et al 2006, Moore 2016). Globally, half of anemia is attributable to iron deficiency, and zinc and protein insufficiency are associated with stunting in children (García-Casal et al 2016). Some of the most common deficiencies—folate, iron, and zinc—are the same vitamins and minerals as those most compromised by rising CO$_2$ (Bailey et al 2015).

Carbohydrate intensive grains are often lacking in protein or essential micronutrients, resulting in undernutrition (too few micro and macro nutrients)—or overnutrition (too many calories and carbohydrates), or what is commonly referred to as the double burden of malnutrition, especially among poorer countries (Zhu et al 2018, Nugent et al 2020). More recent work also considers obesity for understanding the value of nutrient density per calorie consumed (Nugent et al 2020). While malnutrition was commonly thought of as chronic nutrient deficiencies, there is mounting evidence that even seasonal hunger—regular short-term pre-harvest food insecurity—can have long-term health and cognitive human development consequences (Moore et al 1997, Anderson et al 2018). Further understanding is needed of the benefits of raising the quantity of available calories versus raising or maintaining the nutritional density of each calorie, and the importance of consumption smoothing. As these ‘hidden hunger’ effects have become recognized, there is a greater research emphasis on providing nutrient-rich crops. Nutritional fortification and supplementation programs are an essential part of combating hidden hunger. However, such approaches are often reliant on
external funding that may be inconsistent over time (Dwyer et al. 2018).

Modeling estimates project negative effects of rising CO₂ levels on human nutrition by mid-to late-century. Smith and Myers (2018) assumed no changes in diets and accounted for nutrient declines in crops to project that an additional 175 million people could be zinc deficient and an additional 122 million people could become protein deficient. Weyant et al. (2018) projected that CO₂-induced reductions in the zinc and iron levels in crops alone could induce 125.8 million disability-adjusted life years (DALYs) globally, with South-East Asian and sub-Saharan African countries most affected. Zhu et al. (2018) estimated 600 million people at risk past mid-century in the highest rice-consuming countries in Asia with the lowest overall gross domestic product per capita.

Beach et al. (2019) projected a 2.4% to 4.3% penalty on expected gains in global availability of protein, iron, and zinc by mid-century because of technology change, market responses, and the fertilization effects of CO₂ on yield. These penalties are expected to slow progress in achieving reductions in global nutrient deficiencies, disproportionately affecting countries with high levels of nutritional deficiencies. The nutrient effects of CO₂ more than negate any benefits of CO₂ fertilization for protein, iron, and zinc availability.

Millions of people are exposed to unsafe levels of arsenic, lead, cadmium, and methylmercury through C3 crops that take these elements from soil (Gibb et al. 2019). Chronic exposure to these contaminants can lead to intellectual disability, multiple diseases, cancers, and death (Oberoi et al. 2019). Malnourishment further compromises chronically exposed individuals (Gibb et al. 2019).

4. Options for improving the nutritional quality of cereal crops

In addition to the core climate and physiological research necessary for understanding the magnitude and pattern of risks from rising CO₂ concentrations on animal and human health, the socioeconomics require consideration because nutritional quality can be affected not only by a changing environment, but also by the responses addressing those changes. Decision-makers will want to first understand the feasible and effective options to adapt to the declining nutritional quality of crops and then prioritize according to the estimated benefits and costs across options, including continuing with the status quo.

Options for responding to a changing nutritional composition of crops include adaptations at the consumer (depending on resources) or producer (mostly farmer) level. Consumers can adapt via changes in their food choices or dietary supplements, or nutritional losses can be minimized through fortification or biofortification via conventional plant breeding, genetic modification, or better agronomic practices.

Choosing among feasible options requires understanding their relative costs and trade-offs, at a minimum, by country and farming system. Evaluating options for increasing or maintaining the density of zinc, iron, and folate per carbohydrate in C3 crops requires evidence on the ‘effectiveness’ of reducing nutritional deficiencies and the cost. Cost considerations include the economic consequences arising from the state of scientific knowledge of technical, policy, and behavior changes needed, risk perceptions (including a country’s position on approving the domestic cultivation of genetically modified organisms (GMOs)), the distribution of costs by stakeholder and subpopulation, and measurement costs, including data and methods to estimate perceived risks and value short and long-term nutritional outcomes that do not trade in markets.

The following sections examine research gaps on the evidence of ‘effectiveness’ and ‘costing’ under the options of dietary diversity, nutritional supplements, and the three biofortification approaches: conventional breeding, bio-engineering, and agronomic. Where relevant, we distinguish between SSPs and urban consumers in LMICs.

4.1. Evidence on relative costs by option

There is a relatively small literature that values the health outcomes from improved nutrition via the costs of inputs and value of outputs including fewer years of life lost or DALYs or more quality-adjusted life years (Levin et al. 2019). Although promising work toward a more integrated approach for nutritional goals and a standard set of metrics and economic evaluation is emerging, most evaluations focus on cost-effectiveness rather than benefit-cost analysis (Levin et al. 2019). The benefits, however, vary by micronutrient, the degree and speed at which nutritional gains are realized, the distribution of those gains by region and subpopulation, sustainability, effects on secondary markets, and spillover benefits (Pingali 2012). Promoting dietary diversity, for example, through educational campaigns or subsidies, may have long-lasting generational returns, but require often slow behavior change and funding, and does not lead to the same scientific knowledge of research and discovery—in theory a public good—as does biofortification. Fully articulating, if not precisely valuing, these differential benefits could be useful inputs into evidence-based decision making.

4.2. Dietary diversity and nutritional supplements

Although reliant on cereal staples, LMIC household baseline diets also draw on other planted, wild, and purchased foods (Powell et al. 2015, Ickowitz et al. 2019). In theory, changing the mix of food produced and consumed to respond to lower concentrations of, for example, iron and zinc in staple crops, should
be effective. As a feasible option for SSPs, however, it depends on whether baseline diets and soils are nutrient adequate, and how much access and substitutability via planted—or perhaps more importantly purchased—diversity exists (Ickowitz et al 2019). Two recent reviews (Jones 2017, Shibhatu and Qaim 2018) find on net a positive association between production diversity and dietary diversity, but with Jones (2017, p 774) concluding that ‘…a potentially large and unrealistic increase in crop species richness may be required to have a nutritionally meaningful impact on the diversity of household diets.’

Polyculture may have other tradeoffs; for example, the increase in labor energy required to manage a more complex cropping system has been speculated to explain lower BMIs among Nepalese women in more agro-diverse households (Malapit et al 2015 in Jones 2017), but it can provide other advantages such as more resilience to environmental stressors and greater biomass output efficiency. At a minimum, supporting dietary diversity would likely require information and incentives to change behaviors, as a new crop’s adoption is limited by agro-ecological zone, the dominant farming systems, and functioning markets—making this option potentially less viable, although arguably more important, for subsistence producers and rural consumers in LMICs, relative to urban consumers near markets or home gardens.

Nutritional supplements provide another option. Supplements come in a variety of forms, most taken orally, and may be synthetic or naturally sourced. They have the advantage of likely requiring less substantive behavior change and the ability to more precisely target particular deficiencies and subpopulations. In a systematic review of ONSs, many clinically relevant outcomes associated with ONS relative to the control were reported: ‘improved quality of life, reduced infections, reduced minor post-operative complications, reduced falls, and functional limitations’ (Elia et al 2016). Another systematic review concluded that the majority of studies found food products to produce higher anthropometric gains than supplements (Lelijveld et al 2020). However, compliance and cost are issues in all countries, particularly in poorer populations.

Much of the concern around dietary diversity and nutritional supplements centers on measuring access—cost and availability—particularly for populations relying on C3 staple crops in LMICs. For food product options, there are advancements in methods, including a new cost of diet diversity index, to standardize and measure the lowest-cost way to reach international standards of diet quality, taken as a measure of nutritional effectiveness (Masters et al 2018). Initial results in Ghana find that the cost of diet diversity has been rising ‘10% per year faster than national inflation’ (Masters et al 2018). Lower costs were found in Tanzania, but more adjustment in the mix of food groups was required.

The use of ONS depends on cost, but it is also influenced by consumer and policy-maker perceptions of effectiveness and risk. Regulation of nutritional supplements is uneven; the US Food and Drug Administration, for example, considers supplements a food product rather than a medicine. Companies must have evidence that their products are safe and truthfully labeled, but they do not need to provide this evidence or receive approval before marketing, whereas the EU Food Supplements Directive of 2002 requires a demonstration of safety. Of the cost-effectiveness analyses involving quality adjusted life years or functional limitations across supplements used in care settings, results were associated with modest (<10%) but positive cost savings (Elia et al 2016).

4.3. Fortification and biofortification options

The nutritional composition of food can be altered pre- or post-harvest and through breeding and/or crop management practices. Pre-harvest options include biofortification through breeding (conventional trait selection and genetic engineering) and agronomic techniques, and post-harvest includes manual fortification, and improved storage, preservation, and processing.

Food has been manually fortified post-harvest with selected nutrients during crop processing for decades. Recent systematic reviews found that fortifying rice with iron alone or in combination with other micronutrients had little discernible effect on the risk of anemia, although it may have other benefits, including in combination with vitamin A or folic acid (Peña-Rosas et al 2019). Similarly, evidence is limited of the effectiveness of flour fortification for reducing the prevalence of anemia, although evidence of other iron related effects, in particular the prevalence of low ferritin in women, was more consistent (Pachón et al 2015). Although improvements in post-harvest storage, preservation, and processing do not fortify the plant per se, they are a potential means of reducing nutrient loss and toxins (in particular, aflatoxins) (Kumar and Kalita 2017).

Biofortification involves increasing nutrient levels in crops during plant growth. Biofortification reflects three over-arching strategies (Saltzman et al 2017, Garg et al 2018). The first is agronomic methods that can be applied to increase nutrient content in situ without a breeding program by applying nutrient-rich fertilizers to foliage or soil to increase the micronutrient concentration in edible crop parts. Improved farming practices, like fallowing and intercropping, can also increase soil nutrient levels (Nestel et al 2006, Garcia-Casal et al 2016). The second strategy is conventional crop breeding, i.e. identification and selection of desired traits, long practiced...
by farmers. Currently, the thousands of crop varieties available in global seed banks provides biofortified germplasm that can target minerals or produce higher concentrations of vitamins to generate nutrient rich breeding lines (Nestel et al 2006, Garcia-Casal et al 2016, Bouis and Saltzman 2017). Recent research finds indications of evolutionary adaptation to CO2 increases in weedy and CWRs that may be useful for increasing crop growth, but Ziska (2021, p 6) notes ‘any efforts to adapt CWRs and cultivars to recent CO2 increases must include concurrent selection efforts or the co-development of suitable management practices that will maintain the desired quality and nutritional characteristics necessary for human health.’ Whether or not landraces managed on-farm and evolved in-situ will exhibit the same CO2 sensitive traits is unknown. Finally, the nutritional composition of crops can be altered via genetic engineering, for example, through gene-editing (such as the CRISPR method) or transgenic modification (inserting foreign DNA into the host organism’s genome), when the desired nutrient does not exist at necessary levels (Stokstad 2019). Traits that cannot be targeted by conventional breeding or gene-editing because they are not present in the target crop can instead be introduced through transgenic manipulation to create GMOs. One example of a biofortified GMO is golden rice that was modified to produce beta-carotene (provitamin A) using a chimeric trait developed from daffodils and bacteria (Ye et al 2000, Paine et al 2005).

The nutritional effectiveness of biofortification depends on the method, crop, micronutrient, and country context. Led by the efforts of HarvestPlus, the evidence is growing that biofortification of staple crops via conventional breeding, such as zinc rice and zinc wheat, appear to be nutritionally effective, particularly when the crops represent regular dietary intake (Rosado et al 2009, Khush et al 2012, Signorell et al 2015, Brnic et al 2016, Garcia-Casal et al 2016, Bouis and Saltzman 2017, Saltzman et al 2017). But there is a need to further assess independently whether biofortified crops can, in fact, make measurable improvement on human nutrition.

Evidence is also emerging that biofortification is cost-effective (Meenakshi et al 2010). In Uganda, orange sweet potato was demonstrated to cost US$15–20 per DALY. Other studies similarly found biofortification to be a good return on investment, including Hodginott et al (2012) finding as much as US$17 of benefits for every dollar invested, and the Copenhagen Consensus ranking biofortification investments among the highest value-for-money (Bouis and Saltzman 2017). Although the Copenhagen Consensus ranking included interventions that reduce micronutrient deficiencies more generally, more recent opinion suggests biofortification is more cost-effective than supplementation or fortification. (Meenakshi et al 2010, Birol et al 2014, Fan et al 2019).

Biofortification of staple food crops may offer an economically sustainable means to provide ongoing crop cultivars of high quality to low-income consumers (Saltzman et al 2017). But the efficacy and adoption of biofortification will, in turn, depend on pragmatic considerations. An additional challenge for biofortification is the tendency of rising CO2 concentrations to diminish the concentrations of multiple nutrients concomitantly (Loladze 2014a, 2014b) in contrast to biofortification that targets only one or a few selected nutrients. Any attempt to improve fertilization to enhance micronutrient availability must be economically viable; it cannot decrease yields and must be incentivized within the food chain. Acceptance regarding the production and consumption of transgenic biofortified crops must be considered. Garg et al (2018) conclude that although a greater emphasis is being laid on transgenic research, conventional breeding has a much higher success rate and acceptability, perhaps due to the higher uncertainties or perceived risk around environmental and health effects of GMOs that temper demand and lead to more burdensome regulatory processes and restrictions on GMOs, for example, within the EU.

Overall, there is an obvious need to better understand the impact of climate and CO2 on the world’s most important crops, and the efficacy and cost-effectiveness of alternative strategies for improving nutritional quality considering slow behavior change, limited resources, and the political economy of food systems, as the following example indicates.

4.4. Example of the policy opportunities and challenges: India

The Green Revolution transformed Indian agriculture and nearly tripled cereal production over the last 50 years, (ICRISAT 2015) through promoting high-yielding varieties of rice and wheat via policy changes that made their cultivation more profitable (Pingali 2012). Consequently, rice and wheat now contribute three-quarters of India’s total cereal production and consumption of these cereals increased dramatically at the expense of C4 cereals such as millet and sorghum (DeFries et al 2018). Increased access to these cereals was facilitated by their inclusion in the nation’s public distribution system (PDS) that provides subsidized grains to nearly two-thirds of the country’s population.

This homogenization of crop production and related reduced diversity in diets contributed to lower per capita supplies of key nutrients such as iron and vitamin A in diets (e.g. DeFries et al 2018, Rao et al 2018). The ability of millet to grow in poorer soils (DeFries et al 2018, Rao et al 2018, Davis et al 2019) led the Indian government to introduce it into the PDS in 2018 to incentivize its production and consumption. The Indian government also increased the minimum support price for these cereals, which is a
5. Research agenda

A complete research agenda requires addressing data and knowledge gaps surrounding both plant biology and policy response. The global nature of rising CO\textsubscript{2} levels suggests a strong role for publicly funded and distributed research.

6. Data and knowledge gaps

Data on key nutrients are lacking. Every chemical element essential for plants is also essential for humans. But the reverse is untrue: several elements that humans need, including sodium (Na), iodine (I), fluorine (F), lithium (Li), selenium (Se) and chromium (Cr), are non-essential to most plants (Loladze 2002). While plant tissues can contain useless or harmful elements, no minimum concentrations exist, e.g. wheat grains can contain Li in concentrations nutritionally relevant for humans but also may be Li free, depending on the amount of Li in the soil. This means that plant-based foods may be insufficient for meeting human needs for sodium, iodine, fluorine, lithium, selenium, or chromium (Loladze et al 2014a).

To address this elemental gap between human and plant requirements, humans devised supplementation schemes. The most ancient and familiar one is table salt that addresses the sodium gap between plant and human needs. Since 1920s, iodine has been added to table salt in Switzerland and the United States, followed by around 120 countries later in the twentieth century, largely eliminating iodine deficiency in those countries. The fluorine gap has been addressed in many municipalities by fluorinated water and also by the introduction in 1950s of fluoride-containing toothpastes that are now readily available in most countries. Lithium is essential for mental health, and lithium prescriptions revolutionized psychiatry in the second half of the twentieth century; lithium remains a commonly used medicine for treating bipolar disorder. There are no established supplementation programs for selenium (important for thyroid and immune system functions) or chromium (may improve insulin sensitivity and metabolism); selenium (and possibly chromium) deficiencies might be widespread.

When designing and carrying out experiments on crops or wild plants, ecologists and plant physiologists rarely seek input from specialists in human nutrition, which means that selection for quality is not often a consideration. Such disciplinary silos resulted in a sharp divide between the amount of data available for elements essential to plants and those only essential to humans. Collectively thousands of observations have been generated on the effect of elevated CO\textsubscript{2} on nitrogen, phosphorus, and other elements essential to plants, but no single observation has been published on Li response to CO\textsubscript{2}, and only 1–4 observations exist for sodium, iodine, fluorine, lithium, selenium, or chromium.

Our mechanistic understanding of the response of the plant ionome (the mineral and trace-element composition of a plant) to elevated CO\textsubscript{2} suggests that the concentrations of the majority of minerals and trace elements should decrease in C3 plants, including those that are essential for human but not plant nutrition. Despite the importance of Li, Se, Cr, I and F to human nutrition, we currently lack empirical evidence of their response to rising atmospheric CO\textsubscript{2} levels. Filling this critical data gap will be instrumental for quantifying mitigation responses to the declining nutrient density in crops.

Mechanistic understanding of the grain-quality response is required to (a) project when, where, and for which crops grain quality could change in major C3 growing regions under higher CO\textsubscript{2} concentrations; (b) evaluate the health consequences of diminished grain quality and identify the populations most at risk; and (c) develop solutions that will help maintain plant nutritional quality in the future. Further, systems-based understanding is needed of the interactions of CO\textsubscript{2} with climate and other environmental changes. Solutions will be dramatically different if climate-plant-soil interactions dominate the grain quality response versus if climate-plant physiology interactions dominate. The first situation would likely involve solutions focused on soil management while the latter situation would likely involve solutions focused on plant breeding. Knowledge of the health consequences, the most at-risk populations, and the mechanisms responsible for reduced grain quality can motivate developing and implementing solutions targeted to the areas with the greatest need.

Finally, regular data on nutritional status and food safety in particular is largely missing, particularly for LMICs. Greater investments are needed to establish baselines that can be monitored over time to increase understanding of the extent to which populations are being affected by any changes in nutrient density.

7. Research opportunities

Herbariums as Natural Indicators of Nutritional Quality. Since 1950, atmospheric CO\textsubscript{2} has increased by ~30% from 312 to 408 ppm, raising the question of whether recent increases in CO\textsubscript{2} are evident in plant samples collected and stored in herbaria. Analysis of such samples may not provide direct estimates
of protein (i.e., protein will degrade over time); however, elemental analysis of N as a protein proxy and estimates of mineral density would help quantify CO₂ induced changes in micronutrition that may have already occurred. Such analyses would be simple, and ostensibly, cost-effective, albeit with caveats:

- The regional levels of non-CO₂ industrial pollution changed dramatically since 1950 (e.g., drastic declines in high-income countries and concomitant increases in South, Southeast and East Asia). Air, water, and land pollution alter the plant ionome to the point that plants can be used as biomonitors of air pollution (Wolterbeek 2002). Hence, selecting herbarium samples from regions that have not experienced drastic changes in pollution levels is important for isolating the causative effect of CO₂.

- Temporal analyses of plants, some of which relied on herbarium samples, found declines in mineral concentrations (Penuelas and Matamala 1993, Duquesnay et al 2000, Davis et al 2004, Ekholm et al 2007, Fan et al 2008, Jonard et al 2009). Isolating the effect of CO₂ is challenging here due to other potential contributing factors (e.g., changes in agricultural practices, ambient temperatures, and precipitation patterns).

These analyses may prove effective in tracking CO₂ induced changes in protein. For example, hundreds of samples obtained from the Smithsonian Institution's Museum of Natural History were used to estimate pollen protein (using N as a proxy) for the C3 plant Canada goldenrod (Solidago canadensis), goldenrod pollen being a major protein source for domestic bees prior to overwintering (Ziska et al 2016). These data indicated a proximate 30% decline in nitrogen during the 20th century (and concomitant increase in C:N ratio) that corresponded with recent CO₂ increases (Ziska et al 2016); however, it is unclear whether these results are ubiquitous for other plant species.

7.2. Leveraging natural variability

Given that intraspecific variability in nutritional components exists among crop cultivars in response to climate and CO₂, quantifying the consistency of the variation to these parameters is essential. For example, if a given cultivar regularly demonstrates no decline in protein with additional CO₂ or reductions in Zn with high temperatures, then the physiological or phenological basis for the response may provide selection clues for maintaining nutritional integrity in the context of climate change. Such clues would help elucidate the influence of environmental factors on crop and plant quality and would be essential in any long-term breeding efforts.

A fundamental challenge in identifying shifts in the quality of plants is the inherently high variability of the plant ionome (e.g., the concentration of an element can vary several-fold within the same plant species or cultivar). This variability, when combined with small sample sizes (three to six replicates) routinely used in ecological and agricultural studies due to monetary and logistical constraints, results in a low statistical power that obscures genuine cultivar-driven differences in the crop mineral density. Increasing sample sizes in FACE experiments is particularly difficult because such experiments are much costlier and logistically more challenging than enclosure experiments. Yet statistical power analyses of CO₂ effects on the plant ionome show that elevated CO₂ distinctly downshifts the plant ionome (i.e., decrease the concentrations of most elements except for carbon, hydrogen, and oxygen) in both FACE and enclosure experiments once a high statistical power is achieved (Loladze 2014a, 2014b). Hence, constraining future CO₂ experiments on plants solely to FACE experiments, which are costlier and more difficult to run than enclosure experiments, also would constrain the amount of new data produced. Furthermore, there is concern that FACE experiments may underestimate the CO₂ responses (Allen et al 2020). For the above reasons, we strongly recommend prioritizing new and rich data generation, including high-throughput methods, over experimental setups.
7.3. Innovations for seed quality

Methods are available to visualize and screen thousands of field-grown crop lines to accelerate selection for desired characteristics, e.g. disease resistance (Shakoor et al. 2017). Results from these methods can supplement other genetic information, including from SNP, GWAS, CRISPER, etc, to genetically select among a wide array of phenotypes. Such a strategy is essential for developing improved varieties, but in turn, is dependent on high resolution, high throughput field-based technologies that can screen cultivars across multiple environments.

At present, high throughput screening is a promising tool, with gene-level insight into the yield potential of rice (Yang et al. 2014) and the potential to reveal key genes associated with bread-making (Rasheed et al. 2019). However, the use of such technologies to illicit information on intra-specific crop quality, in conjunction with climate change or elevated CO$_2$, among multiple crop lines is uncertain. Use of these methods could provide fundamental insight into selection efforts to ensure nutritional integrity in the future.

7.4. Improved crop models for nutritional qualities

Crop simulation models play a critical role in projecting the risks of climate change for crop production (e.g. Bassu et al. 2014). Many existing crop models are responsive to the changes in atmospheric CO$_2$ through photosynthesis to account for the effects of elevated CO$_2$ on crop yield (e.g. Durand et al. 2018). However, crop models capable of projecting crop nutritional qualities remain rare with a few exceptions for grain protein content (Asseng et al. 2019). Statistical models have been applied to relate elevated CO$_2$ with micronutrient deficiencies such as zinc (Myers et al. 2015) and their impacts on human nutrition, but these approaches remain largely empirical. More mechanistic, process-based models are critically needed for projecting complete crop nutrient dynamics and nutritional qualities, and for assessing their integrated impacts on human nutrition. Improved crop models need to include crop nutritional responses to key environmental factors (e.g. temperature extremes, drought, soil qualities) beyond the direct effect of CO$_2$ for quantifying the health metrics related to crop products and produce in a changing climate.

Most of these research opportunities are directed at better understanding and projecting the effects of changing CO$_2$ on the nutritional composition of plants and associated effects on human nutrition. Although there is more research on how consumers respond to nutritional information, the burgeoning double burden of malnutrition suggests there remain large gaps in how and what information is translated to consumers, the monetary and convenience (time) trade-offs consumers are willing and able to make for better nutrition, and the risk attitudes toward transgenic options (Nugent et al. 2020).

8. Conclusion

Rising CO$_2$ concentrations will challenge nutritional security worldwide. However, the extent to which nutrient density is reduced in staple crops and other terrestrial and aquatic food sources remains understudied, as is how these added pressures could influence decisions on new crop adoption and agromic support programs. Other factors, such as limited markets, lack of access to substitute foods, and limited processing capacity could prevent dietary diversity and fortification from being effective solutions in low- and middle-income countries, and the widespread use of nutritional supplements will continue to be constrained by individual income. Among the biofortification options, conventional crop breeding appears to be the most cost-effective. There is less evidence on the relative cost-effectiveness of agromic options (which face behavioral and information-dissemination obstacles) or of bioengineered options under trade and regulatory barriers that limit current adoption. The effectiveness in particular of CRISPR gene-editing method has yet to be studied in crop applications aimed at nutritional fortification. The cost-effectiveness of any all these options must be evaluated under increasing atmospheric CO$_2$ concentrations, climate change, and the impacts of climate change on other important non-cereal crops.

Climate change is a social justice issue; those responsible for most of the CO$_2$ emissions are not the ones who will suffer the greatest negative consequences (Levy and Patz 2015). Reduced grain quality is an example of these disproportionate impacts; everyone could be affected, but those with access to diverse diets will suffer less (Wu et al. 2020). Policies and personal actions taken to reduce CO$_2$ emissions will help address this problem.

Multidisciplinary research and implementation are needed to ensure that a growing global population, particularly those in low- and middle-income countries, will have sufficient access to plentiful, safe, and nutritious food. Understanding the magnitude and pattern of the problem, and effectiveness of potential solutions, is critical for ensuring the health and well-being of future populations.

Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).
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