4-19-2021

Increased Nutrient Content through the Use of Transgenic Crops: A Way to Improve Nutrition for All

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Increased Nutrient Content through the Use of Transgenic Crops: A Way to Improve Nutrition for All

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CAPSTONE THESIS

Submitted in partial fulfillment of the requirements for the Biology Major at the College of Saint Benedict | Saint John's University, Saint Joseph & Collegeville, Minnesota.

April 19, 2021

Introduction

Every human needs and deserves access to healthy, affordable food and quality nutritional care. However, in our world today this human right is far from met. Global malnutrition has been a concern for some time and recently is becoming a concern of great significance. Malnutrition refers to deficiencies, excesses, or imbalances in the intake of energy and/or nutrients from the diet. Malnutrition can be divided into to three broad groups of conditions. The first, undernutrition, is a state of wasting – where one has a low weight-for-height; stunting – where one has a low height-for-age; and being underweight – experiencing a low weight-for-age. The second group is micronutrient-related malnutrition. This includes micronutrient deficiencies such as a lack of important vitamins and minerals, or micronutrient excess, in which the converse is true. Lastly, the third group is those overweight and/or obese (World Health Organization, 2020). This group has a higher propensity for diet-related noncommunicable diseases, including heart disease, stroke, diabetes, and some cancers.

Micronutrient deficiencies threaten the health of humans on a global scale. One in nine people in the world go hungry and are undernourished (World Food Programme, 2019). Additionally, two billion people globally suffer from "hidden hunger." The World Health Organization (WHO) describes hidden hunger as a lack of vitamins and minerals from the diet (2014). Hidden hunger can result in limited growth, development, preventive health, and energy/stamina. Ensuring people get proper nutrients from foods consumed will help prevent malnutrition. When thinking of the severity of global malnutrition today, a crisis sits upon us, with disheartening projections on the horizon. Global populations are projected to continue to increase dramatically, with little hope for mitigation. Today the world's population sits at 7.8 billion but by 2050 it is predicted, by the World Population Data Sheet, to increase to 10 billion. (Population Reference Bureau, 2021). Consequently, the need to address global malnutrition is urgent, if not dire. One proposed solution is to increase the nutrient content of staple foods that are the foundation of diets worldwide, rather than simply continue to produce nutrient-deficient food.

Science has in the past used the realm of genetics to selectively change and alter organisms in research, in the hope that improvements could translate into practice. This practice has been met with controversy. Changing the genetics of an organism is called genetic modification and is accomplished by changing the sequence of DNA in an organism. Research on Genetically Modified Organisms, commonly termed "GMOs," has a long past history that includes a variety of experimentation (Center for Food Safety and Applied Nutrition, 2020). One technique researchers have explored includes changing genetic code using transgenic solutions. Transgenic GMOs are organisms, usually plants, by which one or more gene – from a different organism – is introduced into its genome (the combinatory genetic content of the organism). There are two ways transgenic modification is done. The first, is by use of a plasmid. Plasmids are involved a type of recombinant DNA technology and are, "small DNA molecules that live naturally inside bacterial cells and replicate separately from a bacterium's chromosomal DNA" (Pray, 2008, para. 8). They act as a DNA shuttle by which scientists copy and paste genetic material from one species into another. In transgenic experiments specifically, the "vector" plasmid originates from *Agrobacterium tumefaciens* bacterium (The Royal Society, 2016). Desired genetic information is incorporated into the plasmid and inserted into the target specie genome, where the plasmid multiplies and eventually incorporates into the target genome and alters the phenotype, the observable traits, of the organism (Center for Food Safety and Applied Nutrition, 2020). The species that have taken up the new DNA are then grown to create a new plant that displays the desired traits. The second method of transgenic alteration is coating the surface of small metal particles, with the desired genetic content, and shooting or injecting the particles into the cells of the target species. This method is sometimes referred to as a “Gene Gun.”

There are other ways to change the genetic content of crops as well. Examples include genome editing and mutational breeding. In the past, agriculture has focused GMO usage on increasing crop yield, reducing the need for pesticides by creating resistant plants, and lowering the costs of food production (Phillips, 2008). These benefits are considered controversial because while they may benefit large industrial farmers and farm production, their long-term effects on the health of humans is unknown. Some speculate many contemporary diseases are the result of GMOs having been introduced into the food chain. To the contrary, others would argue that widespread use of GMOs have the potential to offer nutritional advances, among others.

Topic Explanation

Nutrition is the means by which an organism uses food to support life. Therefore, it is vital that all humans have access to proper nutrition. Through the use of transgenic modification, science has the capacity to increase the nutrient density of staple crops as an attempt to address worldwide malnutrition. For example, certain genetic modifications are aimed at increasing protein and micronutrient density of food. Proteins are the building blocks of life and are vital to organism maintenance and survival. Further, increasing micronutrients like vitamin A, vitamin C, iodine and iron will help address hidden hunger related deficiencies. Increasing these nutrient markers could increase nutrition for the population as a whole, not only attending to the needs of the deficient. Transgenic modification by nutrient amplification is a solution that will not only feed 10 billion but also *nourish* 10 billion – an important distinction.

Presentation of Research

Historical Development

The use of genetic modification in agriculture dates back to 8000 BCE. In this time, traditional modification methods such as selective breeding and cross breeding in plants and animals were practiced. These breeding modalities continued until centuries later, when, in 1866, Gregor Mendel studied breeding between two different pea phenotypes and discovered what is now known as modern day Genetics. Further, in 1922 the first hybrid maize species was produced, cultivated, and sold commercially (Center for Food Safety and Applied Nutrition, 2020). In 1947 plant pathologist Armin Braun pioneered transgenic studies, suggesting that DNA from *Agrobacterium tumefaciens* induced tumors in plants. Later (1974-80) researchers in Belgium, the United States, and the Netherlands confirmed this, finding *A. tumefaciens* to integrate a portion of its DNA into the target organism via a plasmid-vector system (Grunewald et al., 2013). Research on genetic modification continued and in 1982 the United States Food and Drug Administration (FDA) approved the first consumer GMO product, human insulin, developed through genetic engineering. Regulations were set in place in 1992, as FDA policy stated that food from genetically modified plants had to follow the same requirements or regulations as traditionally bred plants. After this, the first wave of GMO produce was created through genetic engineering, the earliest being a tomato breed in 1994, that eventually was sold commercially. Genetic engineering then spread internationally, and in 2003 the WHO and the Food and Agriculture Organization of the United Nations (FAO) developed international guidelines that determined the safety of GMOs (Center for Food Safety and Applied Nutrition, 2020). As of 2017, GMO crops were grown by approximately 17 million farmers globally, nearly all in developing countries (*GMOs around the world*, 2020). The promise of GMO research and usage to help address global malnutrition through transgenic approaches, is hopeful.

Current Status of Research

While GMOs have been present in agriculture for decades, using transgenic modification to increase nutrient density has been prioritized as the impending worldwide population growth promises to exhaust traditional food supplies. Producing food that is nutrient dense has become somewhat of an imperative. Humans can synthesize almost all organic components necessary to maintain vital physiological processes, yet there are select substances that must be derived from one's diet. Essential amino acids, vitamins, and minerals are examples of essential micronutrient categories. Micronutrients maintain the body's immune system and keep the body in a good state of repair. They also enable the body to produce enzymes, hormones, and other substances essential for proper growth and development. Vitamin A, vitamin C, iodine and iron are of greatest importance in global health concerns because deficiencies in these essentials represent a major threat to the health and development of populations worldwide (World Health Organization, 2014).

Amino Acids

Proteins in the body do the majority of the work in cells and are required for the structure, function, and regulation of the body's tissues and organs (National Institutes of Health, 2021). Because of the imperative nature of amino acids physiologically, increasing the amino acid content in staple crops will help provide nutritional adequacy from the crop without changing the quantity of food consumed. Research is already underway to increase the amino acid content in potatoes, soybeans, and maize.

Focusing on potato production, researchers Niranjan and Subhra Chakraborty, and Datta (2000) found that when transferring a gene from *Amaranthus hypochondriacus*, the AmA1 gene, into a A16 potato breed, overall amino acid density increased. Four of the essential amino acids were markedly increased (Chakraborty et al., 2000). As potatoes are third in terms of importance of global crops, increasing the nutritional scale in potatoes holds promise to positively impact populations worldwide (Stewart and McDougall, 2012). Yet, as the population rises, it is estimated that potato cultivation will need to increase 50% to meet a larger need (Faulkner, 2011).

Additionally, essential amino acids in soybeans were found to increase through transgenic approaches (Dinkins et al., 2001). Soybeans are a major source of protein for humans from dietary intake as well as in animal feed, but they lack sulfur-containing amino acids such as methionine and cysteine. To address this, one experiment, through transgenic means, found essential amino acids methionine and cysteine increased in content without negatively affecting the protein composition of the soybean. Researchers found a 12-20% increase in methionine content and a 15-35% increase in cysteine content (Dinkins et al., 2001). It is beneficial that soybeans increase in essential amino acid content as, “Soybean methionine content is normally in the range of 1-2%, which is well below the 3-5% basic minimal requirement for human composition” (Dinkins et al., 2001). Because soy is high in nutrients as well as protein, recent studies have looked at using a soybean and sorghum as a ready-to-use therapeutic food (RUTF) to treat those malnourished, especially children. As of 2013, less than 20% of the more than 19 million children experiencing severe acute malnutrition were receiving treatment (Bahwere, 2017; Collins et al., 2006). The lack of treatment was due, in part, to the high cost of the RUTF. The widespread therapeutic food used then and today is a peanut-based paste. However, a therapeutic food made from soybean and sorghum is a promising, less-expensive alternative (Bahwere et al, 2017). Bahwere, and coworkers, found that an amino enriched soybean and sorghum therapeutic food could be effective in treating malnourished children aged 6-59 months old (2017). A shift towards using the transgenically altered therapeutic food could aid developing countries, whose children are in need of treatment, by bringing industry to their land and people.

Maize is another staple crop that feeds a significant proportion of the world’s population and plays a major role in global food security (Hasan and Rima, 2021). As the population grows, a shift to plant focused diets will cause a lack of essential amino acids obtained from the diet, as plant-based proteins often lack some essential amino acids. For example, lysine is deficient in many cereal foods (Bicar et al., 2008). To attempt to solve this issue, transgenic studies have examined whether amino acid content, and specifically lysine content, could be increased in maize populations. Researchers aimed at increasing a milk protein in the rice genome and were successful, as lysine content was greater in transgenic lines compared to non-transgenic lines (Bicar et al., 2008). Further research into transgenic alterations to maize crops are targeting the increase of additional essential amino acids including tryptophan, methionine, and others. This requires in depth understanding of biosynthetic and metabolic pathways leading to amino acid synthesis in the body (Hasan and Rima, 2021). Further research into the particular steps or components involved in amino acid synthesis could better direct scientists to areas of potential transgenic change.

Research in this area will undoubtedly continue, driven by the need to prepare for the future. However, some learnings will indicate the need to take different paths. One such experiment was a transgenic study that found promising results regarding increasing methionine content by use of a Brazil nut 2S Albumin seed storage protein gene insertion into target plants (Altenbach et al., 1992). Unfortunately, the Brazil nut storage protein caused potent allergic reactions in some individuals, and therefore is not used today as a transgenic modifier (Dinkins et al., 2001). Further, animal-derived genes transgenically inserted into plants have shown amino acid content proliferation (Dinkins et al., 2001). However, it is doubtful that consumers would accept animal-derived genes in plants. Without question, increasing amino acid content in crops will help meet the world’s nutritional needs and research in this area will continue, driven by population growth projections.

Vitamin A

Vitamin A is a fat-soluble vitamin that is required from dietary intake, it cannot be synthesized in the body. This vitamin is particularly important for maintenance of vision (Vitamin A and Vision, 2020). If a person becomes deficient in vitamin A, the risk of blindness significantly strengthens, especially in children. Vitamin A can be found in two different types, preformed vitamin A and provitamin A (Streit, 2018). Preformed vitamin A is found in animal products like meat and dairy. Provitamin A is found in plant-based products and the most common form of this type is beta-carotene (Streit, 2018). Plant-based products that contain provitamin A can include but are not limited to tomatoes, sweet potatoes, and rice. These plants have also been studied in order to analyze the potential for transgenic modification to increase vitamin A density.

In tomatoes, a gene from the bacterium *Erwinia uredovora* was overexpressed in various tomato bred lines. The results showed an increase of the total amount of carotenoids and a 1.8-fold increase in beta-carotene (Fraser et al., 2002).

Sweet potatoes were also studied by increasing the orange gene, which is a mutant gene to the sweet potato, to determine the effects the gene has on vitamin A content in the resulting plants (Kim et al., 2021). Kim, and coworkers, found that the overexpression of the orange gene resulted in an increase of total carotenoids and a 186.2-fold increase in beta-carotene (2021).

Golden rice is a transgenic crop invented under the hope to increase vitamin A content available in the grain as a way to nourish the malnourished. Around the world populations depend on rice as a main staple for nutrient and calorie consumption (CGIAR, 2021). In rice, vitamin A is abundant in leaves of the plant and trivial amounts are found in the grain. Because the leaves are not consumed there is not an adequate amount of vitamin A ingested from rice. Related research on rice began in the 1990s when scientists successfully altered the carotenoid pathway. To alter the biosynthetic pathway of the rice, a gene from a daffodil plant species was inserted into the DNA of the rice (Burkhardt et al., 1997). According to a study done by Gayen, Ghosh, Paul, et al., proteome and metabolite analyses showed that after the transgenic modification of rice, when creating golden rice, beta-carotene levels were enhanced. This ultimately meant the amount of vitamin A in the grain was increased (2016). The results of modified rice, or Golden Rice, contained the recommended amount of vitamin A for children (Gayen et al., 2016). However, after successful transgenic alteration and the creation of golden rice, a possible limitation was found. Researchers detected a negative feedback system that controlled carotene content (Ku et al., 2019). This could mean there are limitations to how much carotene enhancement is possible in Golden Rice. Despite this finding, however, further research found that after five years of work, carotenoid pathways were restored when the crop was replanted (Ku et al., 2019). This suggests opposing results to the aforementioned findings and increased carotene content was still present in the line. Even though this research is optimistic, Golden Rice is not currently manufactured due to a lack of knowledge on the safety of increased carotene content in the crop itself and the safety of its ingestion in humans. Research could be hindered by the difficulty of plant life cycle experimentation. Breeding generations of transgenic plants takes time and is contingent on climate, insect control, and disease. Restrictions like the Cartagena Protocol were set in place in 2000. These enforced different regulations on the use of “living modified organisms” (Regis, 2019). In essence, the

Cartagena Protocol placed regulations on Golden Rice that restricted the commercialization of the crop. To overcome these hurdles, further replicant studies need to be done, safety examinations need to be completed – on the crop and post ingestion – and regulations regarding the cultivation and distribution of the crop need to be set.

Vitamin C

Vitamin C, also known as ascorbic acid, is essential for the human body. Vitamin C can help prevent connective tissue diseases, like scurvy, and can help improve cardiovascular and immune cell function (Chen et al., 2003). The body cannot synthesize ascorbic acid, nor can it store it, so vitamin C must be consumed regularly (Chen et al., 2003). In a study by Chen, and coworkers, researchers focused on increasing the amount of ascorbic acid available in maize through transgenic alteration of the maize crop (2003). This study inserted the DHAR gene from the wheat plant into maize DNA, and by doing so, the amount of ascorbic acid increased by 2 to 4-fold compared to the wild type (Chen et al., 2003). It has been suggested that the recommended dietary intake of vitamin C should increase to more than twice the amount it is currently (Levine et al., 1996). Such an increase would require increased accumulation of the micronutrient from food sources.

Iodine

Worldwide, iodine deficiency affects about two billion people and is the leading preventable cause of intellectual and developmental disabilities (Biban and Lichiardopol, 2017). The addition of iodine to table salt is one of the most common biofortification measures that addresses iodine deficiencies. Further, biofortification of plants with iodine is a recent strategy to supplementally enrich the human diet (Gonzali et al., 2017). Biofortification of crops through transgenic means could help address iodine deficiencies and associated pathologies in the future.

Iron

Iron is used in the body to make hemoglobin, myoglobin, and some hormones. Iron deficiency can lead to a condition labelled anemia. Iron deficiency related anemia is described as the lack of healthy red blood cells and a decreased capacity for red blood cells to carry oxygen to tissues in the body. Oxygen transportation is principal for all individuals, but it is especially important for pregnant women. They need to consume enough iron in order to supply the fetus with adequate oxygen (Black et al., 2013). Lettuce and rice have both been studied using a transgenic approach in order to increase the level of iron content.

In lettuce, ferritin genes from soybeans were integrated into lettuce DNA composition (Goto et al., 2000). The results of this study showed a 1.2 to 1.7-fold increase in iron content and an increased weight of the transgenic crop (Goto et al., 2000). A notable finding from this study demonstrated increased rates of photosynthesis in the transgenic crop as well. The experimental crop grew faster and larger than the wild type (Goto et al., 2000).

Another study also used the integration of the ferritin gene into a rice plant with the goal of increasing iron content (Lucca et al., 2002). The results of the study showed a 2-fold increase in iron content with the addition of this gene (Lucca et al., 2002). Researchers have further studied the genome of rice in order to find other candidate genes to increase iron content

(Mallikariuna et al., 2020). Further research will continue to uncover concrete transgenic genes that have the capacity to positively increase iron content in staple crops.

Areas of Controversy

Debate surrounding genetically modified organisms has existed since the notion was first proposed. There are a range of opinions in the public world as well as the scientific. Including strong advocates both for and against further research. Unfortunately, those opposed to genetic modification, often focus on inconclusive correlations between disease states and GMOs. Those in favor of genetically modified organisms tend to focus on the benefits of their usage, and recently, the long-term need to enhance the nutritional quality of our current food supply.

In one article by Buiatti, Christou, and Pastore, two scientists debate the application of genetic engineering in food production and agriculture (2013). The scientist supporting recombinant DNA technology viewed it as a potent tool for enhancing crop productivity, food quality, and for the production of therapeutic medicines or vaccines. GMO supporters also stand with the notion that GMOs are essential for sustainable agriculture and GMOs will be, "indispensable in facing the severe global food and nutrition security problem in developing countries" (Buiatti et al., 2013, para. 3). The opposing side argued that the side effects of recombinant DNA technology – to the environment and on human health – are potentially adverse and are largely still unknown and will likely be unknown for decades (Buiatti et al., 2013). The antagonists encouraged waiting for the final outcome of further research before employing genetically modified crops. They argued many concerns for the environment;

including the idea that the altered genes could transfer to wild type organisms or non-target organisms, the instability of the new genes, adverse alterations to the genome, and loss in biodiversity (Buiatti et al., 2013).

On the societal level, the same debate ensues. It is crucial in the coming years, particularly due to the population increase between now and 2050, that society accept and stand behind GMOs. "The forthcoming years, then, will be crucial for the commercial and economically viable application of GMOs in agriculture and food production" (Buiatti et al., 2013, para. 5; Nap et al. 2003). Misinformation spread and false advertisements have created an anti-GMO sentiment, especially in Europe (Buiatti et al., 2013). These sentiments are supported by politicians and special interest groups. In order to combat this, proper, ethical, and reliable research and information spread needs to materialize.

Constraints Preventing Adoption

Those in opposition or reluctant to adopt GM usage argue that, despite the appreciable impact nutritionally enhanced crops could have, there are several constraints that prevent their cultivation and adoption (Pérez-Massot et al., 2013). The potential for crops to be transgenically modified to increase particular nutrients becomes additionally complex when considering increasing numerous nutrients in one crop simultaneously (Farré et al., 2011; Naqvi et al., 2010, 2011; Zhu et al., 2008). Beyond practical issues, socioeconomic issues are present as well. Previously described transgenic crops could provide the most benefit to farmers and residents in developing countries (Pérez-Massot et al., 2013). Yet, the cost of regulatory compliance is estimated close to fifteen million, making it difficult for small to medium sized companies to invest and the payoff for larger companies is not (arguably) enough (Pérez-Massot et al., 2013). Furthermore, the issue of GMO usage is dominated by political parties and groups with strong self-interest motivations. In the European Union for example, environmental activists and organic farming groups drive anti-GMO sentiments and ignore any science showing the benefits GMOs could have on agriculture.

> Perhaps the most insidious problem with the adoption of nutritionally enhanced GE crops is that this potentially life-saving scientific breakthrough has become the flagship campaign for activists, who appear to have garnered public opinion and thus have a disproportionate effect on politicians, who in turn determine the rules followed by the regulators (Pérez-Massot et al., 2013, para. 23)

Those that bear the consequence of anti-GMO sentiments and lack of utilization are the world's poor and undernourished. Without the help of nutrient distribution through the use of genetically modified crops, those suffering will continue to suffer for the foreseeable future (Farré et al., 2011). The European Union and western countries, like the United States, are the leading forces in the world and if we adopt transgenic methodology first, the subsequent maturation of that science will help mitigate global malnutrition.

Conclusions and Recommendations

The world population is estimated to reach 10 billion by the year 2050. The majority of population increase is predicted to come from developing countries (Population Reference Bureau, 2021). To meet this need, worldwide food yield should increase by 70%, including 3 billion tons of cereals. This implies worldwide rice and maize creation needs to increase twofold even as the land accessible for agribusiness shrivels in the face of urbanization, land debasement and decreasing water accessibility (FAO, 2021).

Food security in the future thus relies upon our capacity to improve the nutritional quality of crops produced and expand the amount of food cultivated. The hope is that, through the dual assimilation of these sciences, we will mitigate global malnutrition. This will require multidisciplinary joint efforts between partners like ranchers, healthcare workers, nutritional specialists, botanists, food and agrochemical enterprises, biotechnology, and governments to lessen the effect of ailing health on human populaces (Martin et al. 2011).

As with almost all science, it starts with research and evaluation, trial and error. Exploration into the least risky and most beneficial transgenes. Retrospective analysis on previously cultivated transgenic crops will need to continue before the scientific, political, and public world fully accept GMOs. In addition, current transgenic alterations known to the scientific world need to be standardized and regulated (Mejia et al., 2017). Transgenic lines need to be fortified and widespread in order to increase nutrient availability in the world. Communication campaigns to educate the world and create awareness of the benefits of genetically modified crops will need to be created. Messages may include rationale and benefits such as increasing crop yield, reducing pesticide necessity, lowering food production cost, and improving nutritional quality in staple crops (Phillips, 2008; Tenbült et al., 2008). Another future development that will be key to GMO usage is the creation of pro-GMO incentives. Once science translates research and defines the benefits of transgenic crops in terms governmental organizations understand, and once governments understand the severity of current and future global malnutrition escalation, the sanctioning of incentives to develop nutritionally enhanced crops will follow.

Not only will nutritionally enhanced transgenic crops address global malnutrition due to lack of nutrients, but there is a potential that fortified crops will provide additional benefits like disease prevention. An example of this comes from biofortification of tomatoes; researchers found that the tomato nutrient complex, including carotenoids, helps treat hypertension when the complex was enhanced to a higher-than-normal dose (Wolak et al., 2009). The prospect of preventative action against pathogenesis of chronic diseases offers additional support to GMO usage.

It is without question that the subject of GMOs has taken center stage as part of a global conversation focused on urgently developing solutions for exponential population growth. The need for more nutrient rich foods is undeniable. Our hope is that this will be the key driver of the research into the transgenic alteration of crops. It is necessary to find the best-use practices aimed at increasing essential nutrient densities. Additional research into the safety, bioavailability, and sustainability of transgenic lines is also essential to the proliferation of transgenic usage in agriculture. With population, climate change, and urbanization on the rise, it is vital now, more than ever, that society embrace science to ensure a safe, healthy, and prosperous future for all.

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