Technology and Policy for Plant Genetic Engineering: The Role of Nanomaterials

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Abstract

Food insecurity remains a common issue within the under-resourced communities of many nations. Genetic engineering of plants provides us a new method to improve agricultural yields, and thus help curtail food insecurity. Plant genetic engineering still faces limitations such as ongoing disputes with the ethicalities of such methods and several technical barriers. Nanomaterials are an emerging technology that can potentially surpass technical barriers, but we must still consider the development of regulations for them and their impact. In this Review, the potential of nanotechnology to enable the rapid growth of genetically modified plants is discussed, as well as potential policy/social implications for the use of nanotechnology in agriculture.

Introduction

Food insecurity still represents a major global challenge. Recent conflicts have exacerbated food insecurity, highlighting this problem. The Russia-Ukraine conflict, the Suez Canal crisis, Climate Change, and much more, have continued to showcase the critical importance of food security. The concept of food security has many definitions but is primarily based on the availability, accessibility, and stability of crop production.[1] Unfortunately, globally over 800 million people are chronically malnourished, a form of growth failure that causes both physical and cognitive delays in growth and development,[2] with Africa accounting for about one-third of this population.[3,4] Countries face immense challenges in achieving food security, which include nutrient-deficient crops, widespread use of chemicals, and the emergence of new pests and diseases. While agriculture is sensitive to environmental changes, agriculture simultaneously strains the environment; this is directly related to food security through globally falling crop yields.[3,5]

In light of the difficulties discussed above, agricultural systems require improvement to ensure food security. In recent decades, genetically modified (GM) crops have emerged as a potential solution. Genetic modification is a process that uses laboratory-based technologies to alter the DNA or genetic makeup of an organism (National Human Genome Institute 2024). For instance, scientists have created GM crops with higher vitamin A content and with increased resistance to abiotic stress such as ultraviolet-B radiation, along with the development of GM crops that reduce pesticide and insecticide use and are resistant to pathogens and the effects of droughts.[4] GM crops have been also created with shorter harvesting times and higher yields, improved nutrition composition, and decreased toxicology.[4] However, despite the potential GM crops have to improve agriculture, two primary challenges remain with GM crops. First, technically, GM crops remain difficult to produce, requiring significant research and development costing significant time and money. Second, the adoption of GM crops is limited globally, particularly in developing countries where societal resistance and policy issues prevent widespread adoption.[6] For example, East African countries like Kenya, Tanzania, and Uganda have largely been devoid of information about the use of GM crops.[4]

Table on food insecurity within developing regions[7]

Region	Prevalence of severe food insecurity (%)	Prevalence of moderate or severe food insecurity (%)	Prevalence of undernourished (%)
Central Africa	38.0	77.7	30.8
Southern Africa	10.9	24.9	9.6
East Africa	24.2	64.5	28.6
West Africa	18.8	61.4	16.0
Northern Africa	11.9	33.8	7.8
Central Asia	3.4	16.6	3.0
Southern Asia	19.1	41.1	13.9
Eastern Asia	1.0	6.3	<2.5
Western Asia	13.3	37.5	12.4
Latin America	7.3	26.0	5.4
Caribbean	28.6	58.8	17.2

Given the potential of GM crops, methods to more efficiently produce new GM crops and policies to encourage more widespread adoption of GM crops are necessary. One such avenue is Nanotechnology: an emerging genetic engineering method that remains underdeveloped. Nanotechnology is a novel method of genetic engineering that may be able to combat previous limitations and enable rapid, species-independent production of GM crops.[8] Additionally, nanotechnology may help bypass policy barriers to decrease the resources required to produce GM crops. Yet, it is important to acknowledge the novelty of the technology and the potential unintended negative externalities. Current nanotechnology research has been limited to small-scale experimentation, which does not account for large-scale farming.[5] Moreover, regulatory bodies face difficulties placing nanotechnology within existing policies. Amidst policy and technical limitations, nanotechnology has an uncertain role in the issue of food insecurity. This Review paper connects nanotechnology for use in the genetic modification of crops and agriculture policy to food security.

About the emerging gene editing method: Nanotechnology

Genetic modification of plants remains technically challenging. There are two primary steps in generating a GM crop, first reagents to generate an edit must be delivered to plant cells and second, edited plant cells must be regenerated into full plants capable of setting seeds.[8]

Delivering editing reagents to plant cells is challenging. Compared to animal cells, plant cells are not as permeable due to the cell wall.[8] Current techniques to deliver cargo to plant cells include biolistics and agrobacterium. Both of these delivery techniques lack plant species independence and are unable to deliver certain cargoes like proteins.[8] Nanotechnology may be poised to circumvent some of the limitations of the current delivery techniques. Second, even after the successful delivery of cargo and gene editing, plant tissues require regeneration. Regeneration is necessary for stable genetic transformation, which ensures that the edits can be passed down to progeny.[9] Regeneration requires long tissue culture periods that can take months, complicated culturing protocols, and time-intensive work to ensure complete regeneration.[8] Nanotechnology offers the potential to simplify regeneration or circumvent regeneration altogether through germline editing.

Table on characteristics, applications, advantages, and challenges of various nanomaterials [8,10,11]

Nanocarriers	Characteristics	Applications	Advantages	Challenges
Liposomes	Phospholipid vesicles consisting of lipid bilayers; biocompatible	Drug delivery; nucleic acid delivery	Efficient delivery to protoplasts	Tested only in protoplasts and not in intact plants
Carbon dots	Size <10 nm; high luminescence	Bio-imaging; drug delivery; treatment of neurological diseases	Small radius enable carrier internalization; non-nuclear genome targeting	Carriers >8 nm do not internalize and deliver cargo in plants
Gold nanoparticles	1 - 100 nm; low toxicity; great solubility in organic solvent	Electron microscopy; electronics; biomedicine	Carrier internalization	Tested in only one species
Iron-oxide nanoparticles	Biocompatible; tow toxicity; 1-100 nm	Contrast agents; drug delivery	Suitable for pollen transformation	Low efficiency; low reproducibility; species-dependent
Carbon nanotubes	Single-walled (1 nm diameter); multiwalled (5-20 nm outer and 2-6 nm inner diameter); tube-like hollow structure	Cancer therapy; medical treatment	High tensile strength enable carrier internalization; species-independent	Single-walled = limited to small cargoes Multi-walled = Larger carrier than single-walled carbon nanotubes

Nanotechnology has overcome some of the previously mentioned challenges in producing GM crops. In the last decade, numerous reports of different nanotechnologies used to deliver different cargoes to a variety of tissue types have emerged. In particular, carbon nanotubes, carbon dots, gold nano-clusters, gold nanoparticles, iron-oxide nanoparticles, silicon mesoporous nanoparticles, liposomes, and vesicles have all been used to deliver various cargoes to plant cells.[8] Carbon nanotubes specifically have been used to deliver plasmid DNA to plants in a species-independent manner including cotton, wheat, arugula, and Nicotiana benthamiana.[12] The ability to deliver plasmid DNA in a species-independent manner could be important in enabling genetic modification of a wider array of plant species including those which are not currently editable. Another experiment with gold nanoclusters (AuNCs) involved delivering small interfering RNA (siRNA) into plant cells to knock down target genes.[13] Originally, delivering siRNA was highly complicated when done with common methods like Agrobacterium-mediated delivery or viruses, since these methods limited the range of hosts and led to uncontrolled DNA integration into the plant genome.[8,13] The AuNCs were able to successfully deliver the siRNA through the cell wall without nuclease degradation, and the technology achieved high-efficiency gene knockdown rates when compared to conventional methods of delivery.[13] The tested achievements of nanotechnology for delivery showcase its potential in increasing the range and effectiveness of editing plants.

While nanotechnology is promising, controversy has emerged at times in the literature regarding the effectiveness of new techniques and the overall effectiveness of GM crops. Magnetofection of pollen with plasmid DNA via iron oxide nanoparticles was reported in 2017 and was an exciting advancement due to the potential to avoid regeneration while producing a GM crop.[14] However, a follow-up paper cast doubt on the species independence of this method, as researchers were unable to achieve magnetofection of monocots.[15] Furthermore, GM crops in general might be oversold as the only solution to food security.[16] While GM crops will play a role in food security, there are important research standards that should be considered while attempting to develop a new GM crop to avoid overhyping a new technology's potential. The role of nanotechnology is promising but still requires additional careful research.

The effect of Nanotechnology on food insecurity

GM crops can be used to increase crop yield without altering the nutritional composition of the crops. For instance, scientists engineered soybeans to accelerate the process of non-photochemical quenching (NPQ) relaxation to increase crop yields.[17] NPQ is a process that plants utilize to remove excess light energy, which would otherwise damage the plant in form, for example, of reactive oxygen species. However, the relaxation of NPQ in plants when excess light energy is no longer present is slow, leading to the loss of photochemical energy, which could otherwise be used for photosynthesis, and consequently decreases the yield of crops. Hence, soybean crops were engineered with faster NPQ relaxation rates, especially in fluctuating light conditions. A 33% increase in yield rates was observed in genetically modified soybean crops relative to wild-type crops without any change in seed protein or oil content.[17] The results of the experiment showcased the immense possibilities that GM crops create for food security around the world. Genetic modification can be applied to increase the nutritional value of crops as well. Golden rice is an example of this application. Golden rice was created to combat vitamin A deficiency (VAD) in South East Asian countries. VAD has caused millions of deaths in less-developed countries, greatly affecting children. Rice was genetically engineered to produce beta-carotene, a precursor that is synthesized into vitamin A when consumed.[18] While GM crops are promising, there are some challenges. First, adoption is not globally widespread, this is discussed further in section 3. Second, GM crops do not necessarily solve all food insecurity problems, hype is common for GM crops, and this is also discussed in section 3.

Nanotechnology has practical applications in enabling food security by simplifying the process of producing GM crops. Nanotechnology has led to improvements in the delivery of a variety of cargoes such as genetic material, macromolecules like proteins, and hormones.[19,20] Various types of nanomaterials can deliver DNA as well as RNA to plant cells without mechanical assistance with application in producing GM crops.[19] Unfortunately, GM crop production is highly centralized currently due to the high cost of research and development as well as the regulatory burden. The process of bringing a GM crop to the market is costly and time-consuming. In 2019, the cost and time of bringing a GMO was 10.5 million dollars within 5 years if regulated as a conventional crop, and 24.5 million dollars within 14 years if regulated as GM.[21] This directly results in high seed costs for GM crops. Furthermore, seed companies do not risk investing in crops that might not adequately return on investments.[22] This accounts for the production of certain crops like GM soybean, wheat, maize, and other widely consumed crops.[23] Additionally, the high cost of producing a GM crop restricts production to big multinational agricultural companies and organizations in developed countries. Due to this, developing countries become increasingly reliant on developed countries for GM crops. Nanotechnology may help reduce the time and money invested in GM production, by for example reducing the duration of tissue culture.[8] The potential reduction in production costs can enable greater accessibility, which may lead to decentralization of GM crop production. Nanotechnology may broaden the applications of GM crop production from a set few crops. For instance, in Ethiopia, a crop named Teff, which feeds millions of people, is under stress due to climate conditions and mechanical stress which reduce yield.[24] However, since Teff is a non-traditional crop, biotechnological companies do not invest in the development of GM Teff. This showcases how there is limited research and development for the non-traditional crops that feed developing countries. However, through nanotechnology, the development of non-traditional GM crops can be possible, as the species-independent delivery achieved by nanotechnology can help in the production of other crop varieties that help developing countries combat food insecurity.[8,9] Nanotechnology can have a profound effect on our agricultural systems by improving GM crop production.

The policy landscape for Nanotechnology & GMO crops

Nanotechnology is a rapidly advancing avenue, developing at a pace at which policy and regulation are not able to keep up. Current definitions of nanotechnology are broad, creating complications for the implementation and advancement of research in nanotechnology. The definitions cannot assess the specific attributes of different nanomaterials which may or may not be dangerous.[25] To allow for steady and safe development, regulatory bodies have to invest in further definitions for nanotechnology and nanomaterials to create accurate safety assessments. Much of the regulatory effort thus far has resulted in nanotechnology and nanomaterials falling under the umbrella of previously developed policies designed for different materials such as micro-materials.[25] There remains uncertainty about the possible impacts of nanotechnology including potential environmental and toxicological impacts. Researchers in the field consistently argue nanotechnology requires regulation calling for precise standards involving material characterization, biological characterization, and experimental protocols.[26] Further highlighting the lack of policy, misunderstanding, and uncertainty has resulted in proposed bans on certain nanomaterials, rather than careful policy development. The creation of accurate definitions and regulations for nanotechnology can enable society to safely benefit from nanomaterials.

Table on the definitions of GMOs, Nanotechnology, and Nanomaterials in different organizations [27–32]

Organizations	Genetically Modified Organisms	Nanotechnology	Nanomaterials
United Nations (UN)	Living modified organism	Nanotechnology is the manipulation of matter at the nanoscale.	Materials with at least one internal or external dimension of less than 100 nm
European Food Safety Authority (EFSA)	A genetically modified organism (GMO) is an organism which contains genetic material that has been deliberately altered and which does not occur naturally through breeding or selection	Nanotechnology is a field of applied sciences and technologies involving the control of matter at the atomic and molecular scale, normally below 100 nanometres.	Materials that may exhibit different physical and chemical properties compared with the same substances at normal scale, such as increased chemical reactivity due to greater surface area.
International Organization for Standardization (ISO)	Organism in which the genetic material has been changed through modern biotechnology in a way that does not occur naturally by multiplication and/or natural recombination	Nanotechnology involves the understanding and control of matter at the nanoscale, typically below 100 nanometers in one or more dimensions	ISO defines nanomaterials as materials with any external dimension in the nanoscale (approximately 1 to 100 nanometers) or having internal structure or surface structure at the nanoscale.

Definitions regarding genetically modified organisms have come much farther on the other hand. The United Nations Cartagena Protocol on Biosafety defines a GMO or GM crop as a living modified organism. Per this definition, a modified organism contains a novel combination of genetic material, achieved through the use of modern biotechnology.[33] The definition of GMOs in the Cartagena Protocol on Biosafety was proposed to act as a baseline for the creation of policies in countries. Once a GMO is determined to exist, the GMO undergoes heavy monitoring and in-the-field testing to meet safety requirements. However, with the formation of new techniques of genetic modification like nanotechnology, definitions for GMOs become vague leading to a lack of oversight in some cases and too much oversight in other cases.[34] There are two primary frameworks for regulating GMOs: process-based regulation and product-based regulation.[33] Process-based regulation is triggered based on the use of certain biotechnology methods in creating the end GMO product. In contrast, product-based regulation considers only the nature of the final GMO product, not how the product was created. Many researchers believe that a product-based review process is more effective in determining the safety and assessment of GMOs. However, most countries use a process-based regulation instead. There is a widespread fear of the possible effects GMOs can have. The lack of accessibility to GMOs, as well as knowledge about them, creates a huge barrier between the people and the acceptance of the technology.[6]

Nanomaterials and nanotechnology lack a global consensus definition. Different organizations and jurisdictions use different types of metrics and identification systems for nanomaterials.[25] For instance, the European Union uses particle size distribution based on particle numbers to identify nanoforms. However, the US EPA identifies nanoparticles using the weight fraction of nanoscale particles. Some countries use both metrics when regulating nanomaterials further emphasizing the lack of global consensus. This further divides the definitions and policies for nanotechnology across the globe, posing a barrier for nanotechnology to serve as a solution for food insecurity. Furthermore, policy should consider the application of nanotechnology not just the nature of the nanotechnology (ie size). For example, thus far nanotechnology is primarily used in a lab setting and not in field settings where environmental release of nanomaterials could occur.[5] There are several risks for nanotechnology in application to agriculture, yet how the nanomaterial is used ultimately dictates the risk. The current policy does not yet fully consider usage.

Conclusion & Perspective

Here we reviewed the potential of nanotechnology for reducing food insecurity by reducing the time and cost to produce GM crops. Conventional delivery practices fall behind, as they are species-dependent and have low rates of regeneration within plant species, making the process of creating GM crops difficult. On the other hand, nanotechnology has applications in editing plants by delivering cargo in a species-independent manner and potentially enabling germline editing to circumvent tissue culture/regeneration. Thus, due to the comparatively lower investment of time and money, nanotechnology can expand the range of species that can be edited, including niche crops that are not typically targeted by large seed companies. The production of non-traditional GM crops could allow countries to be more self-sufficient and enable diet cultures that suit the environment of various regions. However, the full potential of GM crops as well as the application of nanotechnology to GM crops has yet to be fully achieved due to the lack of fully developed policy frameworks in the case of nanotechnology and the heterogeneous regulatory landscape in the case of GM crops. The lack of global consensus in the definition of GM crops, nanotechnology, and nanomaterials complicates research, the production of GM crops, and the transportation of GM crops to other developing countries.

To fully enable the exploitation of nanotechnology in the production of GM crops, additional work is needed in a few key areas. First, field-based testing and environmental studies of nanotechnology are lacking. Rather than developing policies for the safe development of nanotechnology, some countries are considering outright bans that harm research and development advances. New policy needs to be developed to properly regulate nanotechnology. Second, controversy in the scientific community on the application of nanotechnology and GM crops needs clarifying. Specifically, instances of unrepeatable experiments demonstrating editing of germline tissues with magnetic nanoparticles as well as overhype about the impact of GM crops. Third, amongst the public, increased awareness and knowledge of nanotechnology and GM crops, along with the positive and negative aspects, is necessary. The spread of information on GM crops and nanotechnology can ensure the safe and widespread usage of GM crops within developing countries.

Many countries have already made an initiative attempting to ban certain nanomaterials, even if proper research is still required to know the effects of the materials. Regulatory bodies need to structure their policy-making bodies so that they can implement informed policies that will still allow for research to progress safely. The scientific community has to put more effort into ensuring the accuracy of the results of nanotechnology-based studies. This will reduce misinformation and avoid the exaggeration of results. The governments of developing countries have to start investing in more informational programs on GM crops to enable the incorporation of GM crops to ensure food security. Since, even if nanotechnology becomes a highly developed and valid technique for GM crop production, the effect of nanotechnology on food security will be negligible if populations lack the understanding or trust to use GM crops safely and efficiently.

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