

# Plant Molecular Farming: Production Platforms, Applications and Challenges

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Plant molecular farming, or plant biopharming, is an innovative biotechnology approach that uses plants to produce valuable compounds, such as pharmaceuticals, industrial enzymes, and other essential proteins. This method harnesses the natural biological systems of plants to manufacture complex molecules that are otherwise challenging to produce.

## Production Platforms for Plant Molecular Farming

Plant molecular farming leverages various production platforms with unique advantages and applications. These platforms include a range of plant species and plant-based systems that have been genetically engineered to produce desired proteins, enzymes, and other valuable compounds.

## Commonly Used Plants

### Tobacco (*Nicotiana tabacum*)

- Advantages: Fast growth, high biomass yield, and well-established genetic modification techniques.
- Applications: Production of vaccines, antibodies, and therapeutic proteins.
- Example: ZMapp, an antibody treatment for Ebola.

### Maize (*Zea mays*)

- Advantages: Large-scale agricultural production and significant biomass.
- Applications: Production of industrial enzymes and pharmaceuticals.
- Example: Production of recombinant proteins for industrial use.

### Rice (*Oryza sativa*)

- Advantages: Well-characterized genome, ease of genetic manipulation, and existing infrastructure for large-scale cultivation.
- Applications: Production of vitamins and pharmaceutical proteins.
- Example: Golden Rice, engineered to produce beta-carotene (a precursor of vitamin A).

### Soybeans (*Glycine max*)

- Advantages: High protein content and well-established agricultural practices.
- Applications: Production of therapeutic proteins and nutraceuticals.
- Example: Production of proteins used in dietary supplements.

## Other Prominent Plant Systems

### Alfalfa (*Medicago sativa*)

- Advantages: High biomass production and the ability to fix nitrogen, reducing the need for fertilizers.
- Applications: Production of enzymes and therapeutic proteins.
- Example: Production of alfalfa-derived biopharmaceuticals.

### Peas (*Pisum sativum*)

- Advantages: Nitrogen-fixing capabilities and suitability for producing recombinant proteins.
- Applications: Production of antibodies and other therapeutic proteins.

### Barley (*Hordeum vulgare*)

- Advantages: Ability to produce high levels of recombinant proteins in seeds.
- Applications: Production of pharmaceutical proteins and enzymes.

## Specialized Plant Systems

### Mosses (e.g., *Physcomitrella patens*)

- Advantages: Simple growth requirements, genetic stability, and ability to produce complex proteins.
- Applications: Production of pharmaceutical proteins and research reagents.
- Example: Production of human blood-clotting factors.

#### Microalgae (e.g., *Chlamydomonas reinhardtii*)

- Advantages: Rapid growth, ease of cultivation in bioreactors, and ability to produce a wide range of compounds.
- Applications: Production of biofuels, pharmaceuticals, and nutraceuticals.
- Example: Production of omega-3 fatty acids and bioactive peptides.

#### 4. Innovative Plant-Based Systems

##### Transient Expression Systems

- Description: Utilize plant viruses or Agrobacterium-mediated transient expression to produce proteins quickly in plants like tobacco.
- Advantages: Rapid production, scalability, and high yields.
- Applications: Production of emergency vaccines and therapeutic proteins.
- Example: Rapid production of COVID-19 vaccine candidates in tobacco plants.

##### Stable Transgenic Plants

- Description: Plants are genetically modified to stably express the desired protein throughout their life cycle.
- Advantages: Long-term production and integration into existing agricultural systems.
- Applications: Continuous production of pharmaceuticals and industrial enzymes.
- Example: Genetically modified rice producing human serum albumin.

The choice of production platform in plant molecular farming depends on the target product's specific requirements, including the protein's complexity, the required yield, and the intended application. Tobacco and maize are famous for their high biomass and ease of genetic manipulation, while systems like mosses and microalgae offer specialized advantages for specific applications. Transient expression systems are precious for rapid protein production, making them suitable for responding to urgent needs such as vaccine production during pandemics.

#### Applications of Plant Molecular Farming

**1. Pharmaceuticals:** Plants are used to produce a variety of pharmaceutical products, including:

- a) Vaccines: Plants can produce antigens used in vaccines against diseases such as influenza, hepatitis B, and COVID-19.
- b) Antibodies: Plantibodies, or plant-produced antibodies, can be used for therapeutic and diagnostic purposes. An example is ZMapp, a cocktail of monoclonal antibodies for Ebola treatment.
- c) Therapeutic Proteins: These include enzymes, hormones, and other proteins used to treat diseases. Taliglucerase alfa, produced in carrot cells, is used for treating Gaucher's disease.
- d) Blood Substitutes: Hemoglobin and other blood substitutes can be produced in plants for use in medical emergencies and surgeries.

**2. Industrial Enzymes:** Enzymes produced in plants can be used in various industrial processes:

- a) Biofuels: Enzymes that break down biomass into fermentable sugars can enhance biofuel production.
- b) Food Processing: Enzymes such as amylases, proteases, and lipases are used to process food and beverages.
- c) Textile Industry: Enzymes are used in the processing of fibers and fabrics, including in the treatment of raw materials and the finishing of textiles.

**3. Nutraceuticals and Functional Foods:** Plants can be engineered to enhance their nutritional profile or produce health-promoting compounds:

- a) Vitamins and Minerals: Fortified crops with higher levels of vitamins (e.g., Golden Rice enriched with beta-carotene) and essential minerals.
- b) Antioxidants and Polyphenols: Plants can be enhanced to produce higher levels of antioxidants, which are beneficial for health.
- c) Amino Acids and Fatty Acids: Engineering plants to have higher concentrations of essential amino acids and omega-3 fatty acids.

**4. Cosmetics:** Active ingredients for cosmetic products can be produced in plants, including:

- a) Collagen and Elastin: Used in anti-aging creams and lotions.
- b) Antioxidants: Such as resveratrol and flavonoids, used in skin care products to prevent oxidative damage.

**5. Biodegradable Plastics and Polymers:** Plants can be engineered to produce biodegradable plastics, reducing reliance on petroleum-based plastics:

- a) Polyhydroxyalkanoates (PHAs): Produced by plants as a renewable source of biodegradable plastics.

**6. Agricultural and Veterinary Products:** Molecular farming can also produce products for animal health and agriculture:

- a) Vaccines for Livestock: Plants can be used to produce vaccines to prevent diseases in animals, improving animal health and food security.
- b) Feed Additives: Enzymes and nutrients produced in plants can be added to animal feed to enhance nutrition and growth.

**7. Research and Development Tools:** Plants can be used to produce research reagents and diagnostic tools:

- a) Molecular Probes and Markers: Used in various biological research applications.
- b) Diagnostic Kits: Components for diagnostic tests can be produced in plants, making these tests more accessible and affordable.

**8. Environmental Applications:** Phytoremediation and bioremediation strategies can benefit from molecular farming:

- a) Pollutant-Degrading Enzymes: Plants can be engineered to produce enzymes that break down environmental pollutants.
- b) Heavy Metal Accumulation: Plants designed to accumulate heavy metals can be used to clean contaminated soils.

Plant molecular farming presents a versatile and sustainable approach to producing a wide array

of high-value products, leveraging the natural capabilities of plants to address needs in medicine, industry, nutrition, and environmental management.

### Challenges in Plant molecular farming

Despite its promising potential, faces several challenges that need to be addressed to fully realize its benefits. These challenges span technical, regulatory, economic, and public perception aspects.

#### 1. Technical Challenges

##### Gene Expression Levels

- Issue: Achieving high and consistent levels of recombinant protein expression in plants can be difficult.
- Solution: Optimize genetic constructs, promoters, and codon usage to enhance expression levels. Use tissue-specific promoters or inducible systems to control protein production.

##### Protein Stability and Accumulation

- Issue: Recombinant proteins may degrade or not accumulate efficiently in plant tissues.
- Solution: Target proteins to specific cellular compartments (e.g., chloroplasts, vacuoles) to enhance stability. Use fusion proteins or peptide tags to improve accumulation.

##### Post-Translational Modifications

- Issue: Plants may not perform human-like post-translational modifications, affecting protein functionality.
- Solution: Engineer plants to perform human-like glycosylation. Use glycoengineering techniques to modify plant glycosylation pathways.

##### Protein Purification

- Issue: Efficiently extracting and purifying recombinant proteins from plant tissues can be complex and costly.
- Solution: Develop robust and scalable purification methods. Utilize affinity tags and streamlined purification protocols to reduce costs.

## 2. Regulatory Challenges

### Approval Processes

- Issue: Regulatory pathways for genetically modified organisms (GMOs) and biopharmaceuticals are stringent and vary by region.
- Solution: Engage with regulatory agencies early in the development process. Ensure compliance with all regulatory guidelines and conduct thorough safety and efficacy testing.

### Environmental Concerns

- Issue: Potential risks of transgene escape and cross-contamination with non-GMO crops.
- Solution: Implement containment strategies, such as using non-food or non-feed crops, physical barriers, and genetic containment methods (e.g., male sterility).

## 3. Economic Challenges

### Cost of Production

- Issue: Initial costs of developing genetically engineered plants and setting up production systems can be high.
- Solution: Scale up production to achieve economies of scale. Develop cost-effective cultivation and processing methods.

### Market Competition

- Issue: Competition with established production systems, such as microbial fermentation and mammalian cell cultures.
- Solution: Focus on niche markets where plant molecular farming offers clear advantages, such as complex protein production or low-cost scalability.

## 4. Public Perception Challenges

### GMO Concerns

- Issue: Public skepticism and opposition to GMOs can impact the acceptance of plant-produced products.
- Solution: Communicate transparently about the safety, benefits, and regulatory compliance of plant molecular farming. Highlight success stories and address misconceptions.

## Ethical Issues

- Issue: Ethical concerns related to the use of genetic engineering in plants.
- Solution: Ensure ethical practices in genetic modification and address ethical concerns through public engagement and dialogue.

## 5. Infrastructure and Expertise

### Technical Expertise

- Issue: Requires specialized knowledge in plant biotechnology, genetic engineering, and protein purification.
- Solution: Invest in training and education programs to build expertise. Collaborate with academic and research institutions to advance knowledge and innovation.

### Infrastructure Needs

- Issue: Setting up controlled environments, like greenhouses and bioreactors requires significant investment.
- Solution: Seek partnerships and funding opportunities to develop necessary infrastructure. Utilize existing agricultural systems when possible.

## 6. Consistency and Yield Variability

### Yield Fluctuations

- Issue: Protein yield variation due to environmental conditions, plant health, and genetic factors.
- Solution: Develop robust cultivation practices and genetically stable plant lines. Use controlled environment agriculture (CEA) to minimize variability.

Addressing these challenges involves a multifaceted approach, including advances in genetic engineering, improved regulatory frameworks, effective public communication, and strategic economic planning. By overcoming these obstacles, plant molecular farming can become a mainstream method for producing a wide array of valuable bioproducts, contributing to advancements in medicine, industry, and sustainability.

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