Biopharmaceutical Production in Plant-Based Systems: Current Status and Future Prospects

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Abstract: Biopharmaceutical production has witnessed significant advancements in recent years, with plant-based systems emerging as a promising platform. This review provides an overview of the current state of biopharmaceutical production in plant-based systems and explores the future prospects of this innovative technology. One of the key strengths of plant-based biopharmaceutical production is its ability to produce complex proteins, including monoclonal antibodies and enzymes, with glycosylation patterns similar to those found in humans. This is essential for ensuring the safety and efficacy of biopharmaceuticals. Furthermore, plant-based systems are free from the risk of contamination by human pathogens, a concern often associated with traditional mammalian cell culture-based production systems. The scalability of plant-based biopharmaceutical production is a significant advantage. Plants can be grown in large quantities in a relatively short period, making them suitable for the rapid production of biopharmaceuticals during pandemics or other health emergencies. Additionally, the production of biopharmaceuticals in plants reduces the reliance on expensive bioreactors and cell culture facilities, potentially leading to cost savings for both manufacturers and patients. Future prospects in plant-based biopharmaceutical production are promising. Researchers are continually exploring new plant species and optimizing expression systems to increase yields and production efficiency. The development of transient expression systems, such as viral vectors and agro infiltration, has enabled faster and more scalable protein production. Furthermore, advances in genome editing technologies, such as CRISPR/Cas9, hold the potential to further enhance the suitability of specific plant species for biopharmaceutical production.

Keywords: Biopharmaceuticals, Bioprocessing, Transgenics, Plant-made Recombinant protein, Expression system


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Introduction

Biopharmaceuticals, a class of therapeutic agents derived from living organisms or produced using biotechnological techniques, have emerged as a transformative force in modern medicine. Their profound impact on healthcare is evident in their ability to treat a wide array of diseases and
conditions, ranging from cancer and autoimmune disorders to rare genetic diseases (Lico et al., 2008). Biopharmaceuticals encompass a diverse group of products, including monoclonal antibodies, vaccines, gene therapies, and cell-based therapies, all of which are derived from biological sources such as living cells, proteins, and nucleic acids. Unlike traditional small-molecule drugs, biopharmaceuticals are intricately linked to the genetic and molecular makeup of their host organisms. This inherent complexity often translates into highly specific and targeted therapeutic interventions, reducing the risk of adverse effects and improving patient outcomes (Srivastav and Das, 2014).

In addition to their therapeutic prowess, biopharmaceuticals have also played a pivotal role in advancing personalized medicine, tailoring treatments to individual patients based on their genetic and molecular profiles (Srivastav Janahiraman, 2019). Furthermore, they have contributed significantly to the economic growth of the pharmaceutical industry and have become a cornerstone of pharmaceutical research and development.

**Plant-Based Systems: Revolutionizing Biopharmaceutical Production:**

The field of biopharmaceutical production is experiencing a transformative shift as researchers and industries increasingly turn their attention to plant-based systems as a powerful alternative platform. This paradigm shift is driven by the need for more sustainable, cost-effective, and scalable methods to produce therapeutic proteins, vaccines, and other biopharmaceuticals. Traditional mammalian cell culture systems (Fig. 1) have been the cornerstone of biopharmaceutical production for decades, but they come with significant challenges, including high production costs, limited scalability, and potential contamination risks (Srivastav and Das, 2015).

Plant-based systems, encompassing the use of plants such as tobacco, maize, and lettuce as bioreactors, have emerged as a promising solution to address these challenges. These systems offer several advantages, including lower production costs, rapid scalability, and reduced risk of human pathogens, making them an attractive choice for the pharmaceutical industry. Furthermore, plant-based platforms align with the growing demand for sustainable practices, as they are less resource-intensive and can be cultivated in large quantities with minimal environmental impact (Ma et al., 2003).

The objective of this review paper is to comprehensively examine the current state of biopharmaceutical production within plant-based systems and to outline the future prospects in this burgeoning field. We aim to provide a detailed analysis of the recent advancements and breakthroughs in plant-based biopharmaceutical production, emphasizing the potential benefits, challenges, and regulatory considerations. Our review will encompass a wide range of topics, including the utilization of various plant platforms, such as tobacco, maize, and Arabidopsis, for the expression of therapeutic proteins, vaccines, and monoclonal antibodies. We will delve into the latest technologies and strategies employed in optimizing plant-based production systems, such as gene editing and molecular farming. Furthermore, this review will explore the ecological and economic advantages associated with plant-based production, such as scalability, cost-effectiveness, and reduced environmental impact. We will also discuss the regulatory landscape and ethical considerations surrounding plant-derived biopharmaceuticals. Ultimately, this review aims to provide valuable insights for researchers, industry professionals, and policymakers, facilitating informed decision-making and fostering the continued growth of this promising field.

**HISTORY OF BIOPHARMACEUTICAL PRODUCTION:**

The history of biopharmaceutical production is a captivating journey that has evolved significantly over the years. Beginning in the mid-20th century, the development of biopharmaceuticals marked a pivotal shift in medicine (Fig. 2). Initially,
biopharmaceuticals were produced using conventional techniques like fermentation, where microorganisms were employed to produce therapeutic proteins, such as insulin and vaccines. However, these methods were laborious and limited in scalability (Walsh, 2018).

The turning point came in the 1970s with the advent of recombinant DNA technology, allowing for the creation of genetically engineered organisms capable of producing complex biopharmaceuticals. This breakthrough led to the production of groundbreaking drugs like recombinant insulin and the first genetically engineered vaccine (Leader et al., 2008).

As biopharmaceuticals gained prominence, manufacturing processes underwent continuous refinement. Advances in cell culture techniques, downstream processing, and analytical technologies improved product yields, quality, and safety. The introduction of monoclonal antibodies in the 1980s marked another milestone, paving the way for personalized medicine and targeted therapies (Geisse and Hemke, 2005).

The 21st century has witnessed further innovation in biopharmaceutical production, including single-use bioreactors, continuous manufacturing, and the emergence of gene and cell therapies. These advancements have transformed the industry, making biopharmaceuticals more accessible and effective.

Thus, the history of biopharmaceutical production reflects a remarkable journey from rudimentary fermentation methods to sophisticated biotechnological processes. This evolution has been driven by pioneering research, technological breakthroughs, and a commitment to improving healthcare. The future holds promise for even more innovative approaches in the production of biopharmaceuticals.

**Evolution of Plant-Based Systems in Biopharmaceutical Production:**

Historically, the concept of plant-based biopharmaceutical production gained momentum with the development of plant molecular farming in the early 1990s (Fig. 3). Initially focused on the production of vaccines and antibodies, this approach has expanded to encompass a wide

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**Fig. 1: Cultivating Biopharmaceuticals: Mammalian Cells vs. Revolutionary Plant-Based Systems Unveiled.**

**Fig. 2: Evolution of biopharmaceutical production techniques.**
range of therapeutic proteins, enzymes, and other biopharmaceuticals. The evolution has been fueled by the development of robust expression systems, including transient and stable transformation techniques, such as agro infiltration and viral vectors (Das and Srivastav, 2021).

One of the pivotal advancements in this field is the emergence of plant cell suspension cultures, which offer controlled and scalable production of biopharmaceuticals in bioreactors, reducing the reliance on field-grown plants. Moreover, the engineering of plants to produce complex glycoproteins with human-like glycosylation patterns has addressed an important limitation of earlier systems, enhancing the functionality and safety of plant-derived biopharmaceuticals (Ma, 2015).

The adoption of molecular tools for precise gene editing, such as CRISPR-Cas9, has further accelerated the development of high-expression plant lines, reducing production timelines and costs. Additionally, increased emphasis on containment strategies and good manufacturing practices has improved the regulatory acceptance of plant-based systems (Das and Janahiraman, 2019).

Notably, recent breakthroughs in transient expression platforms like MagnICON® and HyperTrans™ have demonstrated the potential for rapid and flexible production of biopharmaceuticals at commercial scale. These systems have been successfully used to produce monoclonal antibodies, vaccines, and therapeutic proteins, offering a competitive edge in responding to emerging health crises (Holtz, 2015).

Thus, the evolution of plant-based systems in biopharmaceutical production has transformed them into a viable and versatile platform for the production of a wide range of biopharmaceuticals. With ongoing advancements in molecular biology, gene editing, and process optimization, plant-based systems are poised to play an increasingly important role in addressing global health challenges while ensuring sustainability and cost-efficiency (Mercx, 2020).

**ADVANTAGES OF PLANT-BASED BIOPHARMACEUTICAL PRODUCTION:**

Plant-based biopharmaceutical production offers several distinct advantages that make it an attractive alternative to traditional production systems. The key benefits of using plants for biopharmaceutical production include scalability, cost-effectiveness, and safety (Fig. 4).

**Scalability:** Plant-based systems are highly scalable, allowing for the production of a wide range of biopharmaceuticals, from small-scale research projects to large-scale commercial production. Plants such as tobacco, rice, and maize can be cultivated in the field or in greenhouses, providing flexibility in production volume and
Fig. 4: Advantages of plant-based biopharmaceutical production.

enabling rapid scale-up when needed. This scalability ensures a reliable and efficient supply of biopharmaceuticals, particularly important during pandemics or sudden spikes in demand (Gleba et al., 2004).

**Cost-Effectiveness:** Plant-based production is cost-effective due to several factors. First, plants can be grown in low-cost, controlled environments, reducing the need for expensive bioreactors and fermentation facilities. Second, plant-based systems eliminate the risk of pathogen contamination, reducing the need for costly sterilization processes. Additionally, plants can be engineered to produce high yields of biopharmaceuticals, further reducing production costs. Overall, plant-based production offers a cost-efficient alternative to traditional mammalian cell culture systems (Buyel and Fischer, 2012).

**Safety:** Plant-based biopharmaceutical production is inherently safer than some other systems. Plants do not harbor human pathogens or produce endotoxins, minimizing the risk of contamination and the need for extensive purification steps. Furthermore, plant-produced biopharmaceuticals are devoid of animal-derived components, reducing the potential for allergic reactions and transmission of zoonotic diseases. This safety profile aligns with regulatory agencies’ stringent requirements for the production of biopharmaceuticals.

These advantages make plant-based systems an attractive and viable choice for producing a wide range of biopharmaceuticals, from vaccines to therapeutic proteins. As biotechnology continues to advance, plant-based platforms are likely to play an increasingly pivotal role in meeting global healthcare needs.

**SUCCESSFUL PRODUCTION OF BIOPHARMACEUTICALS IN PLANTS:**

Plants have emerged as a promising platform for the production of biopharmaceuticals due to their cost-effectiveness, scalability, and ability to perform complex post-translational modifications. Several successful examples highlight the potential of plant-based expression systems in this field.

**ZMapp:** ZMapp, a therapeutic antibody cocktail against Ebola virus, gained prominence during the 2014-2016 outbreak. The biopharmaceutical was produced in tobacco plants, demonstrating rapid response capabilities in emergency situations (Qiu, 2014).

**Elelyso (Taliglucerase alfa):** This enzyme replacement therapy for Gaucher’s disease was the first plant-derived biopharmaceutical approved by the FDA. It is expressed in carrot cells and provides an alternative source to costly mammalian cell culture production (Shaaltiel, 2007).

**Avidin:** Avidin, used in various research applications, is produced in transgenic maize. This plant-based source offers advantages such as cost reduction and increased stability compared to traditional sources (Kirienko, 2016).

**Artemisinin:** An antimalarial drug precursor, artemisinin, is synthesized in yeast with the help of genes from sweet wormwood (*Artemisia annua*). This innovative approach tackles supply chain issues in malaria-endemic regions (Paddon, 2013).
**Duckweed-based Biopharmaceuticals:** Duckweed, an aquatic plant, has been explored for the production of various biopharmaceuticals due to its rapid growth and ease of cultivation (Lam, 2014).

These examples underscore the versatility and potential of plant-based systems in biopharmaceutical production. As plant biotechnology continues to advance, it promises to offer cost-effective and sustainable solutions for the manufacturing of life-saving drugs.

**RECENT DEVELOPMENTS:**

**CRISPR-Cas9 Technology:** The utilization of CRISPR-Cas9 has revolutionized plant biotechnology by enabling precise genome editing. Researchers are now able to engineer plants for improved production of pharmaceutical proteins, optimizing yields and quality.

**Transplastomic Plants:** Plastids, particularly chloroplasts, have been increasingly explored as ideal compartments for protein expression due to their high protein synthesis capacity. Recent studies have shown remarkable advancements in engineering plastid genomes for biopharmaceutical production.

**Virus-Like Particle (VLP) Production:** Plant-based systems have been harnessed for the production of VLPs, a promising approach for vaccine development. The hepatitis B surface antigen produced in plants is a notable example.

**RESEARCH FINDINGS:**

**COVID-19 Vaccine Production:** The COVID-19 pandemic underscored the agility of plant-based systems for vaccine production. Companies like Medicago, Kentucky BioProcessing, and iBio demonstrated the rapid production of COVID-19 vaccines in plants.

**Monoclonal Antibodies:** Plant-produced monoclonal antibodies against various diseases, including cancer and Ebola, have shown great promise in preclinical and clinical trials, highlighting the versatility of plant systems.

**KEY PLAYERS:**

**Medicago:** A leading biopharmaceutical company known for its plant-based platform, they developed a COVID-19 vaccine candidate that received emergency use authorization.

**iBio:** Renowned for their FastPharming technology, iBio specializes in plant-based biomanufacturing and has worked on vaccines and therapeutic proteins.

**Kentucky BioProcessing (KBP):** A subsidiary of British American Tobacco, KBP gained recognition for its work in producing a COVID-19 vaccine using tobacco plants.

**CHALLENGES AND LIMITATIONS:**

Plant-based biopharmaceutical production holds great promise for cost-effective and scalable production of therapeutic proteins, vaccines, and antibodies. However, it faces several challenges and limitations that must be addressed for widespread adoption.

**Regulatory Hurdles:** One of the primary challenges in plant-based biopharmaceutical production is regulatory approval. The regulatory landscape varies across countries, and obtaining approvals for plant-derived biopharmaceuticals can be time-consuming and costly. Stringent safety and quality standards must be met to ensure patient safety and product efficacy.

**Yield Variability:** Plant-based production systems can exhibit significant yield variability due to factors like environmental conditions, plant genetics, and growth stages. Achieving consistent product yields can be challenging, making it essential to optimize production processes, select suitable plant hosts, and implement robust quality control measures.

**Potential Contamination Risks:** Another concern is the risk of contamination, which can arise from unintended cross-pollination with wild plants or the introduction of pathogens into the production facility. Strict containment strategies and monitoring protocols are necessary to mitigate
contamination risks and maintain product integrity.

Additionally, downstream processing and purification of plant-produced biopharmaceuticals can be complex and may require tailored purification methods to remove plant-specific impurities and contaminants.

While plant-based biopharmaceutical production offers numerous advantages, it faces notable challenges and limitations related to regulatory approvals, yield variability, and contamination risks. Collaborative efforts among researchers, industry, and regulatory bodies are crucial to address these issues and unlock the full potential of this innovative technology.

**Regulatory Frameworks and Safety Considerations in Plant-Based Biopharmaceutical Production:**

Plant-based biopharmaceutical production has gained significant attention due to its potential advantages in terms of scalability, cost-effectiveness, and reduced environmental impact. However, ensuring the safety and efficacy of plant-based biopharmaceuticals requires stringent regulatory oversight and adherence to safety considerations (Ma, 2005).

Regulatory frameworks play a pivotal role in governing plant-based biopharmaceutical production. Agencies like the U.S. FDA and the European Medicines Agency (EMA) have established guidelines to ensure product quality, safety, and efficacy. These guidelines encompass various aspects, such as Good Manufacturing Practices (GMP), Good Laboratory Practices (GLP), and the necessity for comprehensive regulatory submissions.

Safety considerations are paramount in plant-based biopharmaceutical production. These considerations encompass containment measures to prevent cross-contamination, risk assessment to mitigate potential hazards, and rigorous testing to ensure the absence of allergens or contaminants in the final product. Additionally, the development of transgenic plants must follow strict regulations to address environmental concerns (Srivastav and Suriyakala, 2023).

Several successful plant-based biopharmaceuticals, including vaccines and therapeutic proteins, have been produced and approved by regulatory agencies, underscoring the feasibility of this technology. Nevertheless, continuous monitoring and adaptation of regulatory frameworks are essential to keep pace with advancements in plant-based biopharmaceutical production.

**The Importance of Quality Control and Traceability:**

Plant-based biopharmaceutical production has gained prominence due to its potential for cost-effective and scalable production of therapeutic proteins. Rigorous quality control measures are essential at every stage of production, from plant selection and genetic engineering to downstream processing and formulation. These measures ensure consistent product quality, thereby meeting regulatory requirements and assuring patient safety (Fischer, 2015).

Furthermore, traceability systems, including molecular markers and labeling, play a vital role in monitoring and tracking the origin and handling of plant materials. This not only aids in compliance with Good Manufacturing Practices but also facilitates the identification and recall of products in case of adverse events (Srivastav and Suriyakala, 2022). Several case studies underscore the significance of quality control and traceability, emphasizing their role in preventing contamination, ensuring batch-to-batch consistency, and building trust in plant-based biopharmaceuticals. These practices are pivotal in advancing this promising field and promoting its integration into mainstream pharmaceutical production.

**FUTURE PROSPECTS:**

One of the most promising applications is the production of vaccines. Plant-based systems have demonstrated their ability to rapidly respond to emerging infectious diseases, offering a flexible and efficient solution. For instance, the recent development of plant-based COVID-19 vaccines
has showcased their speed and versatility (Rybicki, 2020).

Furthermore, plant-based systems can be tailored for personalized medicine, allowing for the production of patient-specific biopharmaceuticals, which is particularly relevant in the context of cancer immunotherapy and rare diseases.

Despite these promising prospects, challenges remain, including regulatory approval, public acceptance, and scalability issues for certain complex proteins. However, ongoing research and technological advancements are steadily addressing these concerns.

Thus, plant-based systems hold tremendous potential for the future of biopharmaceutical production. Their scalability, cost-effectiveness, and adaptability make them a compelling choice for the rapid and sustainable production of biologics, vaccines, and personalized medicines. As research in this field continues to advance, we can anticipate a transformation in the way we produce and access critical pharmaceuticals, ultimately benefiting both healthcare providers and patients (Capell and Twyman, 2018).

The Future of Biopharmaceutical Production: Plant-Based Systems:

The future of biopharmaceutical production from plant-based systems is poised for remarkable growth. Firstly, advancements in genetic engineering and synthetic biology will enable the development of designer plants with enhanced expression capabilities and glycosylation patterns, yielding high-quality biopharmaceuticals. Secondly, the recognition of the safety and scalability of plant systems by regulatory agencies will accelerate their adoption.

Moreover, the environmental sustainability of plant-based systems aligns with the global trend towards green biomanufacturing. Reduced energy consumption, decreased resource usage, and minimal waste generation make plant-based platforms appealing for the biopharmaceutical industry.

The evolution of biopharmaceutical production from plant-based systems is anticipated to continue its upward trajectory. Collaborations between academia, industry, and regulatory bodies will play a pivotal role in shaping this future, making plant-based systems a vital component of the biopharmaceutical landscape (Buyel, 2019).

Emerging Technologies and Strategies for Enhancing Plant-Based Production:

In recent years, the global demand for plant-based products has surged, driven by concerns over environmental sustainability and health benefits. To meet this growing demand, researchers and agricultural experts have been exploring innovative technologies and strategies to improve plant-based production.

**Precision Agriculture:** Precision agriculture utilizes data-driven approaches, such as satellite imagery and IoT sensors, to optimize crop management. This allows for precise monitoring of plant health, resource allocation, and pest control, ultimately increasing crop yields and resource efficiency.

**Genome Editing:** CRISPR-Cas9 and other genome editing techniques enable targeted modifications in plant genomes to enhance traits like disease resistance, drought tolerance, and nutritional content. These technologies accelerate breeding programs and reduce the time required to develop improved crop varieties.

**Vertical Farming:** Vertical farming involves growing plants in stacked layers, often indoors or in urban environments. Controlled environments, LED lighting, and hydroponic systems ensure year-round production with minimal water usage and reduced pesticide needs.

**Biological Pest Control:** Beneficial insects and microorganisms are harnessed to control pests, reducing the reliance on chemical pesticides. This sustainable approach safeguards plant health while preserving ecosystems.

**Advanced Crop Monitoring:** Remote sensing technologies, including drones and satellite
imagery, provide real-time data on crop conditions. This data helps farmers make informed decisions regarding irrigation, fertilization, and disease management.

**Plant-Based Meat Alternatives:** Innovation in plant-based meat substitutes, such as lab-grown meat and plant-based proteins, offers sustainable alternatives to traditional livestock farming, reducing greenhouse gas emissions and land use.

**Artificial intelligence and Machine Learning:** Artificial intelligence and machine learning algorithms analyze vast datasets to optimize crop management. These technologies predict disease outbreaks, suggest optimal planting times, and optimize resource allocation.

**Circular Agriculture:** The concept of circular agriculture emphasizes recycling and reusing waste materials in farming. This approach minimizes waste, reduces resource consumption, and enhances soil health.

The adoption of emerging technologies and innovative strategies is pivotal for enhancing plant-based production to meet the increasing global demand sustainably. These advancements promise improved crop yields, reduced environmental impacts, and healthier plant-based products. Continuous research and collaboration between scientists, farmers, and policymakers will be crucial to realizing the full potential of these innovations (Srivastav et al., 2021).

**Advancements in Plant-Based Production: A Paradigm Shift for the Pharmaceutical Industry:**

Firstly, advancements in genetic engineering, such as CRISPR-Cas9, have enabled precise modification of plants to produce complex pharmaceutical compounds. This allows for the sustainable and scalable production of high-value drugs, reducing the reliance on traditional chemical synthesis methods. Moreover, plant-based systems offer a versatile platform for the expression of a wide range of biologics, including vaccines, monoclonal antibodies, and therapeutic proteins (Pogue et al., 2020).

Secondly, the cost-effectiveness of plant-based production is a game-changer. Traditional biomanufacturing systems are expensive and resource-intensive, leading to high drug prices. Plant-based production significantly reduces production costs, making life-saving medications more affordable and accessible to a global population (Rosales and Angulo, 2015).

Furthermore, plants offer a rapid production cycle compared to mammalian cell cultures, enabling quicker responses to emerging health threats like pandemics. This agility can save lives and reduce economic burdens associated with healthcare crises. The environmental impact is another crucial aspect. Plant-based production is more sustainable and environmentally friendly than traditional methods, reducing the carbon footprint of drug manufacturing (Rybicki, 2014).

**COMPARATIVE ANALYSIS OF PLANT-BASED SYSTEMS VS. TRADITIONAL PRODUCTION METHODS IN BIOMANUFACTURING:**

Biomanufacturing is a crucial field for producing biopharmaceuticals and bio-based products. This review aims to compare plant-based systems with traditional production methods (mammalian cell culture and microbial fermentation) in terms of cost, scalability, and safety.

**Cost:** Plant-based systems offer cost advantages due to lower upfront infrastructure expenses, reduced facility maintenance, and lower raw material costs. Traditional methods often require costly bioreactors, growth media, and complex purification steps, making them more expensive.

**Scalability:** Plant-based systems demonstrate scalability advantages. They can be cultivated in open fields or greenhouses, allowing for large-scale production with minimal facility adjustments. In contrast, traditional methods may face challenges in scaling up due to the need for larger bioreactors and increased complexity.

**Safety:** Plant-based systems are considered inherently safer for biopharmaceutical production as they reduce the risk of contamination by mammalian or microbial pathogens. This
enhances product safety, reducing the need for extensive downstream processing and ensuring a purer end product. Traditional methods may pose higher risks of contamination and require stringent quality control measures.

Plant-based systems offer a cost-effective and scalable alternative to traditional production methods in biomanufacturing. They provide inherent safety advantages by minimizing contamination risks. However, the choice between these systems should consider specific product requirements, production volumes, and regulatory constraints. Further research and development in plant-based systems hold the potential to revolutionize biomanufacturing processes (Buyel et al., 2017).

**Conclusion**

Plant-based systems, such as transgenic plants and plant cell cultures, have proven to be efficient hosts for the production of various biopharmaceuticals, including monoclonal antibodies, vaccines, and therapeutic proteins. They offer cost-effective and scalable production, with the ability to rapidly respond to emerging global health crises.

Additionally, plant-based systems boast superior safety profiles, reducing concerns about contamination and viral vectors often associated with mammalian cell cultures. They also offer glycosylation patterns similar to humans, ensuring product efficacy and safety.

In conclusion, plant-based systems have evolved as a promising avenue for biopharmaceutical production, offering scalability, safety, and versatility. Their potential in producing critical biopharmaceuticals, such as vaccines and antibodies, signifies a significant stride towards a sustainable and accessible healthcare future. Continued research and development in this field will undoubtedly shape the future of biopharmaceutical manufacturing (Mor and Daniell, 2011).

**References**


