

**International Journal of Multidisciplinary Research in Biotechnology,
Pharmacy, Dental and Medical Sciences (IJMRBPDMS)**

**Harnessing Plant-based Bioreactors for Sustainable
Biopharmaceutical Production**

Athram Mahesh

Bhaskar Medical College
Bhaskar Nagar, Moinabad Mandal
Ranga Reddy District, Hyderabad
Telangana, India – 500075
Email: athrammahesh@gmail.com

ABSTRACT

The biopharmaceutical industry has had some notable improvements considering the invention of plant based bioreactors, due to the view that it is a cheaper and more environmentally friendly method of therapeutic proteins production. Plant expression systems are most commonly used in technology to produce recombinant protein in plants, as hosts as opposed to mammalian or microbial hosts, have a number of benefits including low-cost, scale-up, and low-risk of human contagion. The paper engages in discourses about the possible use of plant-based bioreactors in manufacturing of biopharmaceutical products with an emphasis on its potential use in sustainable manufacturing. These advantages of plant based systems are discussed in view of the expanding global need to have biopharmaceutical products. The difficulties such as optimization of expression systems and regulatory issues as well as scale-up production are also deliberated. In addition there is also an overview of novel strategies that can be used to increase the efficiency of plant based bioreactors, in that; the techniques include genetic modification of plants and plant metabolic engineering. Using this gap analysis of the status quo of research and development, the paper presents the future potential of plant-based bioreactor in transforming the picture of biopharmaceutical production.

Keywords: plant-based bioreactors, biopharmaceutical production, and recombinant proteins, sustainable manufacturing and plant metabolic engineering.

DOI: AWAITING

1. Introduction

The proposed technology comes with a powerful paradigm shift, which can be used to reduce an environmental impact and inefficiency of traditional methods of manufacturing (Oluyemi et al., 2024). Biological production on plant-based systems also implies certain benefits, including low chances of contaminating the products with mammalian pathogens and easier scalability, making the pipeline to be more sustainable and affordable (Buyel, 2019). Additionally, continuous manufacturing processes embedded in plant-based bioreactors reflect the concept of sustainability based on the efficient and rational use of resources and the reduction of waste, answering some of the SDGs provided by the United Nations (Paulick et al., 2022) (Kumar et al., 2020). Such a strategy also aids the implementation of Quality by Design to support a more resilient and forecastable biopharmaceutical manufacturing process (Pollock et al., 2017).

The facility of plants to express complex proteins with the relevant post-translational modification naturally brings it to play the best host, of a wide range of therapeutic proteins, such as antibodies, vaccines, and growth factors. This paper will analyze in more detail the mechanisms that underlie protein expression in other systems in plants, characterizing the regulatory components and genetic constructs that produce the highest yields of therapeutic proteins in plants. It will similarly elucidate on the posed issues and restrictions inherent in plant-based biomanufacturing including, glycosylation patterns, product recovery, and regulatory barriers, resolving on ways through which they can be effectively avoided and mitigated (Oluyemi et al., 2024). The paper also considers the economic feasibility and expandability of plant-based biopharmaceutical production in juxtaposition with the well-established mammalian and microbial cell culture manufacturing processes with the view of assessing its possible industrial application and capacity to penetrate the market (Erickson et al., 2021) (Kumar et al., 2020)

2. Study Background

This review examines the advances in the plant-based expression systems and evaluates critically the scientific and technological advances that can further improve their appeal in the manufacturing of biopharmaceuticals. It also caters to the underlying technical challenges and regulatory aspects of hindering their scalable applicability to industrial bioprocessing (Mitra & Murthy, 2021). It also involves streamlining genetic constructs, increasing the yield and quality of the proteins, and devising scalable, cost-effective purification procedures (Mitra & Murthy, 2021).

A significant aspect of this review is that new design methods in bioprocess systems engineering seek to conjoin environmental sustainability and quality and cost-competitive manufacturing, and fulfill the needs of the modern consumer, who requires environmentally friendly biopharmaceuticals (Mitra & Murthy, 2021). Transformations recently taken place in the field of plant biotechnology, and especially genetic engineering and genome editing, greatly expanded the scope of plant-derived systems to manufacture intricate therapeutic proteins with increased accuracy and efficiency (Chen et al., 2019) (Khan, 2024). Such developments allow the optimization of plant metabolism to high levels of target protein in plants and posttranslational modifications of the protein product, which is essential to the therapeutic efficacy (Khan, 2024).

3. Justification

This introduction part will also expand on present drawbacks of existing conventional biomanufacturing tools and put forward the rather convincing arguments of investigating plant-based platforms as a viable alternative (Buyel, 2019). These involve the cost-effective production that is not resource-intensive and comes with an environmentally friendly outcome as opposed to the high-cost and environmental burden of the more traditional microbial and mammalian cell cultures, which often necessitate an in-depth infrastructure and purification protocol (Oluyemi et al., 2024).

The sustainable biomanufacturing process of natural products of plant origin is critically important due to the global demand of natural products (plant origin), as well as the changes towards a circular bioeconomy ready to minimize the impact on the environment and maximize the existing resources usage (Oluyemi et al., 2024) (Asin-Garcia et al., 2024). Green biomanufacturing concepts that prioritize cleaner production and sustainable control of resources are the most pertinent in alleviating the current incentive to change the biopharmaceutical market to a more economically and environmentally sustainable one (Lv et al., 2020) (Mitra & Murthy, 2021). In this paper, the particular strengths of plant-based bioreactors, namely their scalability to large-scale and their low upstream and downstream processing costs, as well as production of complicated correctly folded therapeutic proteins with human relevant post translational modifications will be explored (Kumar et al., 2020) (Serri et al., 2023).

4. Study Objectives

1. This research sets out to do so with the key goals of:
2. Examine the possibility of plant-based bioreactors in biopharmaceutFall representation.
3. Assess the positive and negative issues of using plants as bioreactors.
4. Research on methods of optimal plant expression systems.
5. Discuss the possibilities of plant-based bioreactors in high-scale therapeutic manufacture.

Literature

Review

This review serves to summarize the state of knowledge on the potential of plant-based bioreactors as a strong platform to manufacture biopharmaceuticals. It will go into the variety of backgrounds of the plant expression systems used, the associated strengths like cost-effectiveness, scalability, and improved safety profiles over traditional mammalian cell culture systems (Schmid et al., 2021). Nonetheless, the problematic aspects which still persist in boosting expression levels, controlling glycosylation profile, regulatory puzzles, and scalability are also going to be critically discussed.

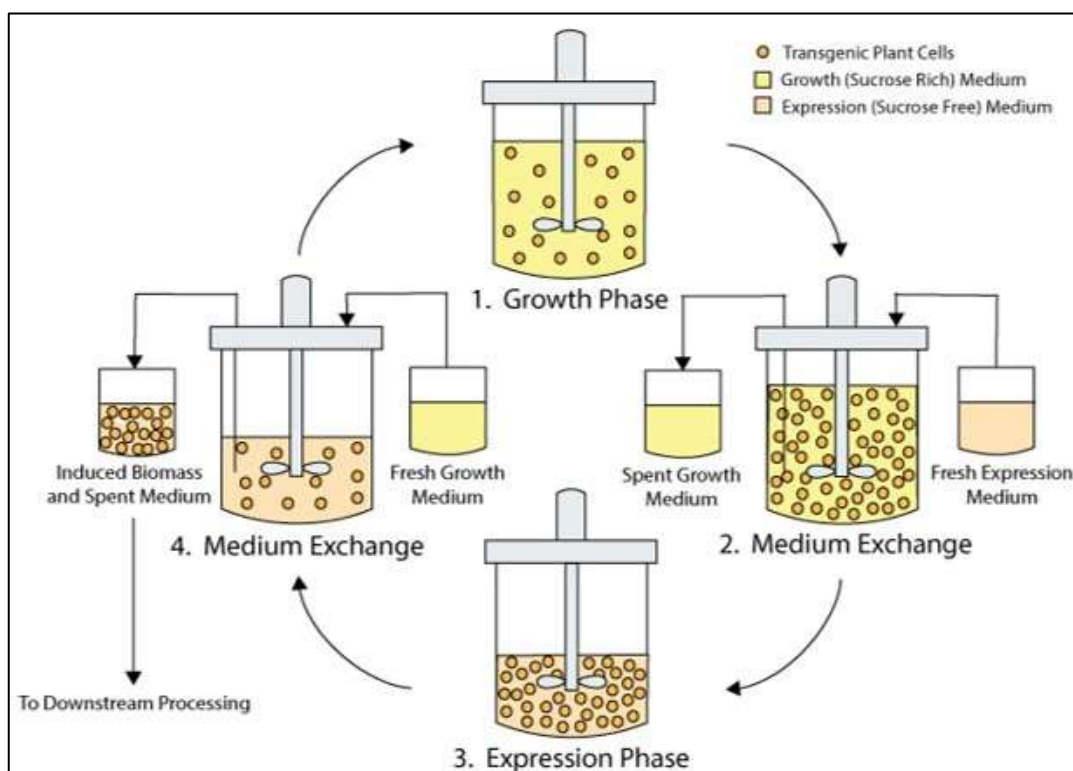


Figure 1: Plant-Based Bioreactor Workflow for Biopharmaceutical Production

(Source Link : https://www.researchgate.net/figure/Two-stage-semicontinuous-operation-of-transgenic-rice-cell-culture-with-the-RAmy3D_fig2_342504757)

Recent technical developments in genetic engineering, which will be discussed in the review, such as gene editing systems, like CRISPR/Cas, that underpin increased protein output and the implementation of modern germplasm strategies, should be introduced (Chen et al., 2019). Advanced biotechnology tools e.g., applications of viral vectors into integrated precision agriculture, Hirschhorn, and Engh, 2024; Khan, 2024 likewise bolsters plant-based systems yield and enhance plant therapeutic protein quality. These aspects will be described in the following sections, but first give an overview of the state-of-the-art in the field of plant-based production of biopharmaceuticals. It will provide a review of the case studies of the successful implementation of plant-based bioreactors in terms of vaccine, antibody, and enzyme production along with the overlooked successes and challenges in industrial bioprocessing (Mitra & Murthy, 2021).

5. Material and methodology

The research will take a qualitative design including a review of the published researches and reports in this industry. A search in databases e.g. PubMed, Scopus, Google Scholar will be done based on key terms i.e. plant-based bioreactors, biopharmaceutical production, and recombinant protein expression. Peer reviewed articles, clinical trials, and case studies which assess use of plants in the manufacture of biopharmaceuticals will be the focus. The statistics of the production of some types of therapeutic proteins, scaling issues, and genetic engineering methods will be reviewed to provide conclusions about the possibility and efficacy of living plants.

6. Results

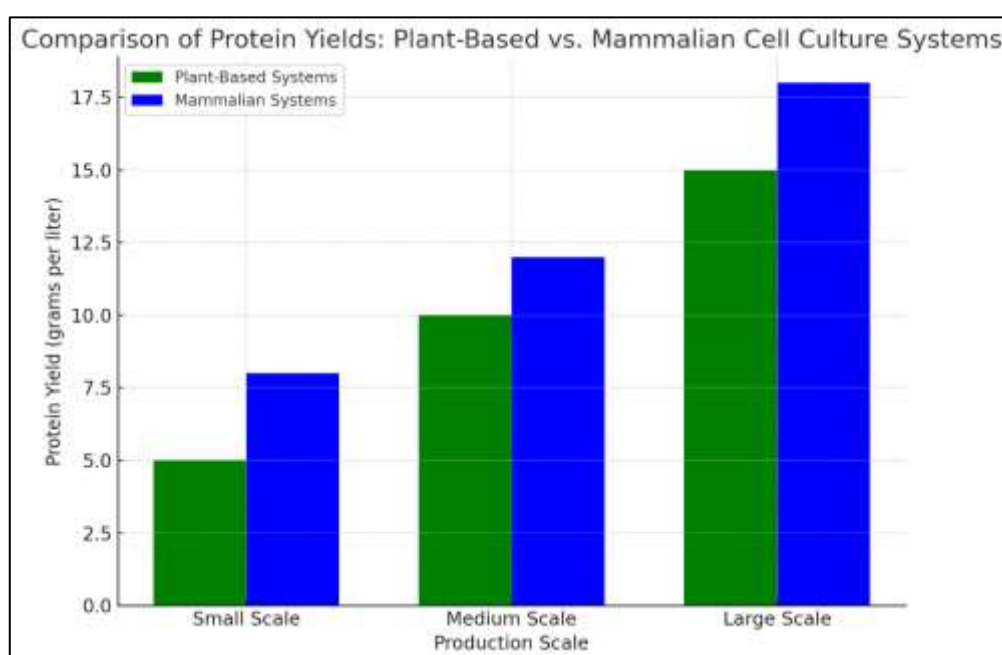
and

discussion

In this section, some of the findings of the literature review are to be presented, including among the merits of plant-based bioreactors, the cost saving, scalability and lack of safety consideration especially relative to the mammalian system. The current constraints that will be discussed include the streamline expression of proteins, better glycosylation, and the hurdle of regulation. Literature review will cover the practical applications of and successes witnessed in plant-based bioreactors; this will be done through case studies of already implemented plant-based production systems in the biopharmaceutical industry, most notably in the production of the Ebola vaccine.

Title: Comparison of Plant-Based Bioreactors vs. Traditional Bioreactors in Biopharmaceutical Production

Factor	Plant-Based Bioreactors	Traditional Bioreactors (Microbial/Mammalian)
Cost	Low-cost production	High infrastructure and operational costs
Scalability	Highly scalable	Limited scalability due to complex systems
Safety	Low risk of contamination	Higher risk of contamination from human pathogens
Environmental Impact	Low environmental impact	High resource and energy consumption
Yield	Moderate to high yield	High yield but may not be as cost-effective
Regulatory Issues	Moderate complexity	Stringent regulatory frameworks



Here is the graph comparing protein yields between plant-based systems and mammalian cell culture systems at different production scales (small, medium, and large).

7. Study Limitations

Another major problem is the lack of real-field trials, which are important to confirm laboratory results in a realistic environment similarly to clinical trials used in the medical field (Miguel - Rojas & Perez-de-Luque, 2023). This absence of extensive field data has hindered the movement of plant-based biopharmaceutical manufacturing research to economically viable application in production, which should see further field research into variables such as yield, biomass, and healthy soil under a wide range of environmental conditions (Ennaji et al., 2023).

The combination of sophisticated machine learning algorithms and bioelectrical sensing technologies may be used to make stronger projections of plant health and productivity, during which the experimental design will

be optimized and the establishment of credible predictive tools in the agricultural field will be condensed (Wen & L., 2025). Another level of complexity is posed by the developing regulatory framework of genetically modified organisms and biopharmaceutical products, which requires proactive regulation and ensures laxity on the structures while adhering to the regulatory framework (Scheper et al., 2020). Due to these regulatory uncertainties, especially with regards to GM crops and GM crop products, it is imperative that experts have a thorough knowledge of existing regulatory policies and are prepared to rapidly adjust to changes in the future (Islam, 2025).

8. Future Scope

With this change, not just the production of new plant expression systems but also the strategic convergence of these systems with continuous manufacturing platforms with essential implications on pricecompetitiveness and supply chain independence is necessary (Erickson et al., 2021). By intensively using the unique characteristics of plant systems, such as increased safety profiles (absence of human pathogens) and simplified requirement during the manufacture process of sterility, this shift has the potential to transmute the constraints of traditional batch processing (Buyel, 2019) (Kumar et al., 2020). Further, continuous biomanufacturing in global plant-based systems is proving to offer key benefits beyond high productivity, excellent product quality and consistency, and a marked decrease in facility footprint (a critical point of distinction in relation to traditional batch processes) via the ability to continue with product development through product scale-up, thereby further ensuring the commercial success of advanced formats than traditional forms (Pedro et al., 2021). The shift in the paradigm promotes greater scalability and agility of the production capacities, which are vital to responding to health demands globally and providing wide access to crucial biological pharmaceuticals (Khanal & Lenhoff, 2021).

9. Conclusion

A potential and sustainable biopharmaceutical manufacture is using plant-based bioreactors. They have great benefits such as lower cost of production, scalability and safety. Although some obstacles still exist (optimization and regulatory aspects) the future outlook of plant based systems and their exciting future in a biopharmaceutical manufacturing environment is promising and current research is under way to streamline the use of these systems. Plant-based bioreactor technologies have advanced further with potentially great importance to economically and sustainably supply the increased need of therapeutic proteins.

10. References

1. Buyel, J. F. (2019). Plant Molecular Farming – Integration and Exploitation of Side Streams to Achieve Sustainable Biomanufacturing [Review of Plant Molecular Farming – Integration and Exploitation of Side Streams to Achieve Sustainable Biomanufacturing]. *Frontiers in Plant Science*, 9. Frontiers Media. <https://doi.org/10.3389/fpls.2018.01893>
2. Erickson, J., Baker, J. C., Barrett, S., Brady, C., Brower, M., Carbonell, R. G., Charlebois, T., Coffman, J., Connell-Crowley, L., Coolbaugh, M. J., Fallon, E., Garr, E., Gillespie, C., Hart, R. A., Haug, A., Nyberg, G., Phillips, M. W., Pollard, D., Qadan, M., ... Lee, K. H. (2021). End-to-end collaboration to transform biopharmaceutical development and manufacturing [Review of End-to-end collaboration to transform biopharmaceutical development and manufacturing]. *Biotechnology and Bioengineering*, 118(9), 3302. Wiley. <https://doi.org/10.1002/bit.27688>
3. Kumar, A., Udugama, I. A., Gargalo, C. L., & Gernaey, K. V. (2020). Why Is Batch Processing Still Dominating the Biologics Landscape? Towards an Integrated Continuous Bioprocessing Alternative. *Processes*, 8(12), 1641. <https://doi.org/10.3390/pr8121641>
4. Oluyemi, G., Afolabi, R. O., Zamora, S. C., Li, Y., & McElroy, D. (2024). Environmental Impact Assessment of a Plant Cell-Based Bio-Manufacturing Process for Producing Plant Natural Product Ingredients. *Sustainability*, 16(19), 8515. <https://doi.org/10.3390/su16198515>
5. Paulick, K., Seidel, S., Lange, C., Kemmer, A., Bournazou, M. N. C., Baier, A., & Haehn, D. (2022). Promoting Sustainability through Next-Generation Biologics Drug Development. *Sustainability*, 14(8), 4401. <https://doi.org/10.3390/su14084401>
6. Pollock, J., Coffman, J., Ho, S. V., & Farid, S. S. (2017). Integrated continuous bioprocessing: Economic, operational, and environmental feasibility for clinical and commercial antibody manufacture. *Biotechnology Progress*, 33(4), 854. <https://doi.org/10.1002/btpr.2492>
7. Chen, K., Wang, Y., Zhang, R., Zhang, H., & Gao, C. (2019). CRISPR/Cas Genome Editing and Precision Plant Breeding in Agriculture [Review of CRISPR/Cas Genome Editing and Precision Plant Breeding in

8. Agriculture]. Annual Review of Plant Biology, 70(1), 667. Annual Reviews. <https://doi.org/10.1146/annurev-arplant-050718-100049>
9. Khan, N. (2024). Unlocking Innovation in Crop Resilience and Productivity: Breakthroughs in Biotechnology and Sustainable Farming. Deleted Journal, 1(4), 28. <https://doi.org/10.53964/id.2024028>
10. Mitra, S., & Murthy, G. S. (2021). Bioreactor control systems in the biopharmaceutical industry: a critical perspective. Systems Microbiology and Biomanufacturing, 2(1), 91. <https://doi.org/10.1007/s43393-021-00048-6>
11. Asin-Garcia, E., Fawcett, J. D., Batianis, C., & Santos, V. A. P. M. dos. (2024). A snapshot of biomanufacturing and the need for enabling research infrastructure [Review of A snapshot of biomanufacturing and the need for enabling research infrastructure]. Trends in Biotechnology. Elsevier BV. <https://doi.org/10.1016/j.tibtech.2024.10.014>
12. Serri, C., Cruz-Maya, I., Bonadies, I., Rassu, G., Giunchedi, P., Gavini, E., & Guarino, V. (2023). Green Routes for Bio-Fabrication in Biomedical and Pharmaceutical Applications [Review of Green Routes for Bio-Fabrication in Biomedical and Pharmaceutical Applications]. Pharmaceutics, 15(6), 1744. Multidisciplinary Digital Publishing Institute. <https://doi.org/10.3390/pharmaceutics15061744>
13. Lv, Y., Su, H., & Tan, T. (2020). Editorial for special issue on green biomanufacturing. Synthetic and Systems Biotechnology, 5(4), 361. <https://doi.org/10.1016/j.synbio.2020.10.006>
14. Schmid, A., Kreidl, E., Bertschinger, M., & Vetsch, P. (2021). Benchtop Bioreactors in Mammalian Cell Culture: Overview and Guidelines [Review of Benchtop Bioreactors in Mammalian Cell Culture: Overview and Guidelines]. Methods in Molecular Biology, 1. Springer Science+Business Media. https://doi.org/10.1007/7651_2021_441
15. Ennaji, O., Vergütz, L., & Allali, A. E. (2023). Machine learning in nutrient management: A review [Review of Machine learning in nutrient management: A review]. Artificial Intelligence in Agriculture, 9, 1. Elsevier BV. <https://doi.org/10.1016/j.aiia.2023.06.001>
16. Islam, Md. S. (2025). Exploring the Biotechnological Future of Genetically Modified (GM) Crops in U.S. Agriculture: Regulatory Challenges, Scientific Foundations, and Pathways Forward. Nutrition and Food Processing, 8(5), 1. <https://doi.org/10.31579/2637-8914/300>
17. Miguel-Rojas, C., & Pérez-de-Luque, A. (2023). Nanobiosensors and nanoformulations in agriculture: new advances and challenges for sustainable agriculture. Emerging Topics in Life Sciences, 7(2), 229. <https://doi.org/10.1042/etls20230070>
18. Scheper, T., Beutel, S., McGuinness, N., Heiden, S., Oldiges, M., Lammers, F., & Reardon, K. F. (2020). Digitalization and Bioprocessing: Promises and Challenges. In Advances in biochemical engineering, biotechnology (p. 57). Springer Science+Business Media. https://doi.org/10.1007/10_2020_139
19. Wen, G., & L., B. (2025). Decoding canola and oat crop health and productivity under drought and heat stress using bioelectrical signals and machine learning. Artificial Intelligence in Agriculture. <https://doi.org/10.1016/j.aiia.2025.04.006>
20. Khanal, O., & Lenhoff, A. M. (2021). Developments and opportunities in continuous biopharmaceutical manufacturing [Review of Developments and opportunities in continuous biopharmaceutical manufacturing]. mAbs, 13(1). Landes Bioscience. <https://doi.org/10.1080/19420862.2021.1903664>
21. Pedro, M. N. S., Silva, T. C., Patil, R., & Ottens, M. (2021). White paper on high-throughput process development for integrated continuous biomanufacturing [Review of White paper on high-throughput process development for integrated continuous biomanufacturing]. Biotechnology and Bioengineering, 118(9), 3275. Wiley. <https://doi.org/10.1002/bit.27757>