JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2025/48043

REVIEW ARTICLE

A Comprehensive Review on Sustainable Molecular Pharming of Plant-based Pharmaceuticals: Challenges and Future Prospects

Rajeev Kumar[1], Souraja Datta Majumder[1], Shruti Agarwal[1], Anshuman Shah[1,2], Shyam Kishor Thakur[3], Vishal Haribhai Patel[1], Nidhee Chaudhary[1] and Ravi Kant Singh[1*]

[1]Amity Institute of Biotechnology, Amity University, Sector 125, Noida – 201313, Uttar Pradesh, India; rksingh1@amity.edu

[2]Indian Council of Agricultural Research (ICAR) -National Institute for Plant Biotechnology, New Delhi – 110012, Delhi, India

[3]Department of Physics, Town Inter College, Hajipur, Vaishali – 844505, Bihar, India

Abstract

Medicinal plants have historically played a vital role in healthcare, with approximately 80% of the global population relying on traditional remedies. The emergence of molecular pharming, or biopharming, marks a significant advancement in biotechnology, enabling genetically modified plants to serve as biofactories to produce important therapeutic proteins. Molecular pharming is cost-effective and scalable compared to conventional systems, such as mammalian cell cultures. Plant genetic transformation techniques, including the use of *Agrobacterium tumefaciens* for gene insertion, have facilitated the expression of diverse proteins in a range of plant species. The integration of functional genomics has significantly advanced our understanding of the genetic and epigenetic mechanisms regulating secondary metabolite synthesis in plants. Techniques such as genome mining and high-throughput sequencing have facilitated the identification of biosynthetic gene clusters, leading to the discovery of novel therapeutic agents. Additionally, multiplex genome editing technologies, notably CRISPR-Cas9, have revolutionised the production of biologically active molecules, including therapeutic proteins, vaccines, antibodies, and industrial enzymes in plants. Nanoparticles also play a crucial role in molecular pharming, serving as versatile carriers for gene delivery and protein encapsulation, thereby improving transformation efficiency and product monitoring. This review explores the role of molecular pharming, or biopharming, as a cutting-edge biotechnological approach that utilises genetically modified plants to produce valuable proteins, therapeutic enzymes and other biologically active compounds.

Major Findings: The article explores the role of molecular pharming, or biopharming, as a cutting-edge biotechnological approach that utilises genetically modified plants to produce valuable proteins, therapeutic enzymes and other biologically active compounds. The article also addresses valuable insights into biopharming, therapeutic proteins, genetic transformation, *in vitro* production, and bioreactors.

Keywords: Biopharming, Bioreactor, Genetic Transformation, *In Vitro* Production, Therapeutic Proteins

1. Introduction

Throughout history, medicinal plants have been utilised for treating a wide range of diseases. According to a report from the World Health Organisation (WHO), approximately 80% of the global population depends on traditional remedies[1,2]. Many of these therapies involve the use of extracts and active compounds derived from medicinal plants[3]. Recently, there has been an increase in the consumption of medicinal plants worldwide, attributed to their demonstrated effectiveness in treating specific

*Author for correspondence

Article Received on: 03.01.2025 Revised on: 21.05.2025 Accepted on: 27.05.2025

ailments and their safety profiles[4,5]. Medicinal plants have played a vital role in healthcare since ancient times and remain important in drug development today[6,7]. Molecular pharming, also referred to as "biopharming", is a segment of biotechnology that employs genetically modified plants to act as biofactories for the production of valuable proteins and biologically active molecules. This approach enables the large-scale generation of therapeutic proteins, vaccines, antibodies, and industrial enzymes in a manner that is more cost-effective and scalable than traditional methods involving mammalian or microbial cell cultures. By utilising the inherent biochemical processes of plants, molecular pharming allows for the synthesis and accumulation of these proteins, which can subsequently be extracted and purified for pharmaceutical and industrial applications[8-10]. This process entails the insertion of genes that code for the desired proteins into the plant genome, followed by the cultivation of these genetically modified plants that express the target proteins. These proteins can then be harvested from the plant tissues and purified for various uses, including in medicine, agriculture, and industry. Initially, plants like tobacco (*Nicotiana tabacum*) were favoured as hosts due to their rapid growth, high biomass yield, and ease of genetic modification[11]. Over time, a broader range of plants, including maize, rice, potatoes, and even fruits like tomatoes and bananas, have been evaluated as potential biofactories, with selection based on factors such as the type of protein produced and the ease of purification. The concept of molecular pharming traces back to the 1980s, following early advancements in plant genetic engineering[12,13]. The first successful genetic transformation of plants occurred in 1983, using the bacterium *Agrobacterium tumefaciens* to insert foreign genes into tobacco plants. This pivotal moment laid the groundwork for using plants as biofactories for recombinant protein production[14]. Subsequent research expanded into expressing diverse proteins in plants, leading to the early development of plant-derived pharmaceuticals. Functional genomics plays a crucial role in understanding the complex relationships between genes and the biology of organisms, particularly in the context of medicinally important secondary metabolite research[15]. This field has emerged as a powerful tool for elucidating the genes involved in the biosynthesis and regulation of therapeutic proteins. The advent of high-throughput sequencing and functional genomics has revolutionised our understanding of secondary metabolite production by enabling the identification of entire Biosynthetic Gene Clusters (BGCs) in plants[16]. By integrating transcriptomics and metabolomics, researchers have analysed gene expression in *Artemisia annua*, gained insights into the complex production of artemisinin, a potent antimalarial compound[17]. Additionally, functional genomics has unveiled the intricate regulatory networks that control metabolite pathways in response to environmental signals, allowing researchers to activate previously silent gene clusters and discover new compounds. The synthesis of valuable secondary metabolites is intricately regulated by genetic and epigenetic factors. Functional genomics plays a pivotal role in elucidating the transcriptional networks, signalling pathways, and epigenetic modifications that govern the production of compounds[16]. For instance, key transcription factors such as MYB and WRKY have been identified as essential regulators of flavonoid and alkaloid biosynthesis in various plant species[18]. Epigenetic modifications, including DNA methylation and histone modifications, also significantly influence secondary metabolite biosynthesis. Research in fungal systems has shown that modifications to epigenetic markers can reactivate dormant biosynthetic pathways, leading to the discovery of previously unidentified secondary metabolites[19]. Cichewicz[20] highlights those functional genomics techniques, such as chromatin immunoprecipitation followed by sequencing (ChIP-seq), are effective for identifying specific epigenetic alterations associated with the regulation of secondary metabolite biosynthetic genes. Secondary metabolites remain a vital source of pharmaceutical compounds, and the methodologies of functional genomics are accelerating the identification of new bioactive molecules. Genome mining, a functional genomics approach that searches for BGCs in sequenced genomes, has proven effective in uncovering novel antibiotics and anticancer agents[16]. The integration of genomics, transcriptomics, and metabolomics facilitates a comprehensive understanding of secondary metabolite synthesis and regulation, paving

the way for the discovery and development of innovative drug candidates. This area of research holds tremendous potential for the identification of novel natural products with therapeutic applications. Multiplex genome editing enables the simultaneous modification of multiple genomic loci within an organism's genome, making it an essential tool across various biological fields, including medicine and functional genomics[17]. This approach leverages advanced technologies of genome-editing, such as CRISPR-Cas9 (clustered regularly interspaced short palindromic repeats), TALENs (Transcription Activator-Like Effector Nucleases) and ZFNs (Zinc Finger Nucleases) to target multiple genes concurrently, facilitating comprehensive investigations into gene function and the generation of complex proteins. Among these, CRISPR-Cas9 stands out as the most widely utilised technology, utilising a guide RNA (gRNA) that directs the Cas9 nuclease to specific DNA sequences, where it creates Double-Strand Breaks (DSBs). The cell's repair mechanisms then repair these breaks via Non-Homologous End Joining (NHEJ), which can disrupt genes, or homologous recombination (HR) for precise edits[21]. Multiplex genome editing with CRISPR-Cas9 typically involves delivering multiple gRNAs from a single vector or utilising synthesised gRNAs, allowing for targeted modifications at various loci simultaneously, as demonstrated by Cong *et al.*[22]. While TALENs and ZFNs are also applicable for multiplex editing, they are more complex to design and implement compared to the relatively straightforward RNA-DNA pairing used in CRISPR-Cas9, which has made CRISPR the preferred choice for most multiplex applications in molecular pharming and beyond[21]. On the other hand, Nanoparticles have shown great promise in molecular pharming due to their versatility and ability to be engineered with specific compositions, sizes, shapes, and surface chemistries for various biological applications[23]. Notably, liposomes serve as effective carriers for gene delivery, enhancing plant transformation methods since their introduction in 1965 as models of cellular membranes. Additionally, gold nanoparticles function as biolabels in *in vivo* and *ex vivo* imaging systems, enabling the monitoring of protein production and the detection of contaminants in plant-based expression systems. Polymeric nanoparticles facilitate the encapsulation of proteins, which aids in the protection and delivery of plant-synthesised pharmaceuticals. Furthermore, modifications such as the integration of targeting ligands, like antibodies, enhance the specificity of nanoparticle delivery to organs or organellar tissues, making them invaluable in molecular pharming[24,25]. Lastly, their enhanced permeability and retention properties allow for the effective supply of nutrients or growth factors to targeted areas within plant tissues, promoting overall plant health and productivity. Today, molecular pharming holds significant promise for transforming pharmaceutical production and industrial biotechnology, with ongoing research aimed at harnessing plants for a wide variety of therapeutic proteins. The molecular pharming market is expected to grow due to the increasing demand for modern medicines and pharmaceuticals, as well as the need for improved crop nutrition and protection. The global molecular pharming market is expected to expand at a Compound Annual Growth Rate (CAGR) of 14.8% from 2023 to 2030, with an anticipated market value of approximately $1,196 million by the end of this period[26]. The major factors driving the growth of the molecular pharming market include: increasing demand for proteins from the pharmaceutical industry, growing applications in the enzyme industry and increased funding and investment. Therefore, this review article discusses the technological developments in the production of therapeutic proteins, vaccines, antibodies, and industrial enzymes using various *in vitro* methods. Furthermore, the study offers a thorough synopsis of the technical, regulatory, economic, and societal challenges associated with molecular pharming.

2. A Key Survey on Molecular Pharming

In the bibliometric data study, we retrieved the 156 published articles between 2010 to 2024, which deal with biopharming and therapeutic proteins as per Scopus data. During bibliometric data analysis, we used the keywords "molecular pharming", and "genetic transformation" or "*in vitro* production of secondary metabolites" or "bioreactor" and gathered the data from the Scopus database (Figure 1).

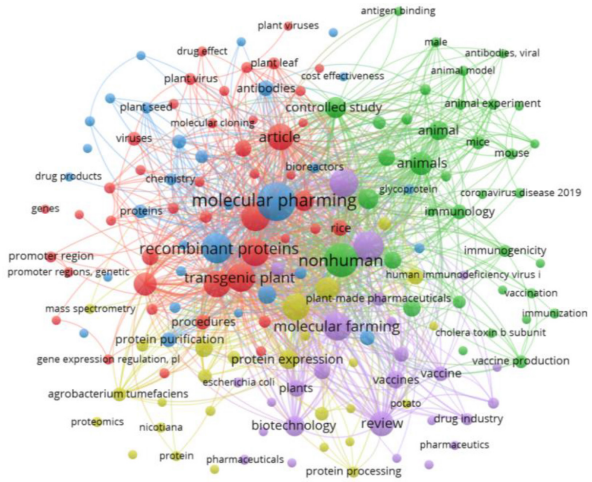


Figure 1. Network visualisation map displaying the key terms present in the title and abstract of the published article related to the molecular pharming and genetic transformation. Nodes of the same colour showed clusters of the interconnected phrases; however, the circle size indicates the number of publications larger size indicating a larger number of publications. The network has been created using the software VOS viewer processing software [v1.6.9].

3. Innovative Approaches to Enhance Molecular Pharming

Molecular pharming utilises an array of biotechnological techniques for genome modification in plants to produce recombinant proteins. These methods have advanced significantly, enhancing protein expression and addressing challenges such as yield optimisation and scalability (Figure 2). Authors have discussed the following important key techniques commonly employed in molecular pharming.

3.1 Biolistic Bombardment

This method, also known as particle bombardment, is often used when plant cells or tissues resist the uptake of foreign DNA. The gene gun technique is employed to introduce DNA into cells, utilising biologically inert particles like tungsten or gold coated with DNA or RNA constructs. A vacuum accelerates the DNA/gold-particle complex toward the target tissue, facilitating effective gene transfer in maize cells and soybean callus[27,28].

3.2 Electroporation

Significant advancements in nanotechnology have improved electroporation, a widely used non-viral method for cell transfection. Modern electroporation systems enhance cell viability and provide precise dose control, avoiding the safety concerns associated with viral vectors. These innovations are crucial for expanding biological applications in intracellular delivery[29,30].

3.3 PEG Techniques

This technique is primarily employed to introduce foreign genes or DNA into the protoplasts of plant cells, as cell walls pose a significant barrier to other transformation methods. In this process, the protoplasts take up foreign DNA through the reversible permeabilisation of the plasma membrane[31,32].

3.4 Agrobacterium-mediated Transformation

In this approach, the gene of interest is inserted into a plasmid vector and introduced into *Agrobacterium tumefaciens*. The bacterium then transfers the DNA into plant cells, where it integrates into the nuclear genome. As the transformed plants grow and reproduce, the new gene is inherited, allowing for the mass production of plants expressing the desired protein. Similarly, rice and *Arabidopsis* were used for transformation and DNA repair using T-DNA insertion[33,34].

3.5 Recombinant Virus Vectors

This technique employs modified plant viruses to introduce genes into plant cells. The virus's genome is altered to include the DNA encoding the desired protein, which is then introduced into host plants. As the virus replicates, it can rapidly produce high levels of the target protein[35]. However, this method requires immediate processing post-harvest due to the instability of green plant materials.

The field of plant improvement has evolved significantly with advancements in cytogenetics and chromosome engineering, facilitating the introduction of foreign genes into agricultural species, particularly wheat. Recent innovations in biotechnology for direct gene transfer have further enhanced plants for the production of valuable proteins.

4. Promoters and Expression Systems

The effectiveness of molecular pharming depends not only on the introduction of foreign genes into plants but

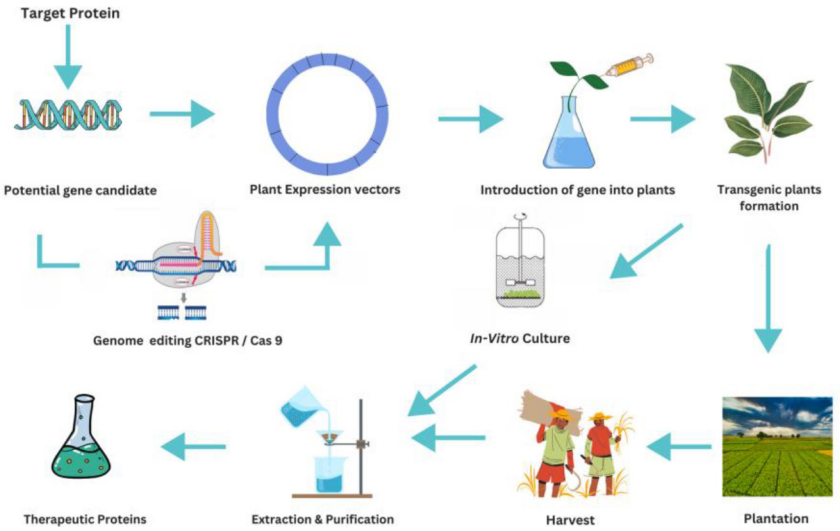


Figure 2. Schematic of the workflow from candidate gene selection to process development and scale-up. The process begins with the identification of the gene of interest, which may involve genome editing. The gene is then cloned into vectors and transformed into *Agrobacterium* for expression. This leads to the development of a transgenic cell line or plant. Subsequent steps include *in vivo* and *in vitro* cultivation, the establishment of downstream processing platforms, and the continuous operation of the process to produce the protein of interest.

also on their efficient expression. This necessitates the use of promoters and expression systems that regulate gene activity in plants. Promoters are specific DNA sequences that regulate the initiation of transcription, marking the initial phase of gene expression. Selecting the right promoter is essential to maximise protein production efficiency[36]. Common types of promoters listed below.

4.1 Constitutive Promoters

These promoters enable continuous expression of the transgene across all plant tissues throughout its life cycle. The Cauliflower Mosaic Virus (CaMV) 35S promoter is among the most frequently utilised constitutive promoters in plant genetic engineering.

4.2 Tissue-specific Promoters

These promoters restrict gene expression to specific tissues or organs, such as leaves, seeds, or roots. Tissue-specific promoters are beneficial when the target protein needs to be produced only in particular parts of the plant.

4.3 Inducible Promoters

These promoters allow for regulated expression of the transgene in response to external stimuli, such as light, temperature, or chemical inducers. Inducible promoters provide flexibility in determining when and where the protein is produced.

Expression Systems are equally important in optimising protein production. For instance, plant viral vectors can be employed to enhance gene expression, taking advantage of the rapid replication and spread of plant viruses within plant tissues, resulting in high protein levels in a short timeframe. Expression systems can be designed for transient expression-allowing short-term production without stable integration into the plant's genome, or for stable expression, which involves the long-term production of proteins through the integration of the gene into the genome of plants. Each system has its benefits, tailored to specific applications[37].

5. Plant Species Used in Molecular Pharming

Molecular pharming utilises various plant species as biofactories for the production of recombinant proteins, enzymes, vaccines, and other therapeutic compounds[12,13]. Each species offers distinct advantages based on its genetic traits, biomass yield, and cultivation ease. Below is a summary of significant plant species employed in this field.

5.1 Tobacco (*Nicotiana* spp.)

Tobacco is among the most extensively used plants in molecular pharming, notable for its high biomass, rapid

growth rate, and established transformation methods. Both *Nicotiana tabacum* and *Nicotiana benthamiana* are commonly used due to their capacity to produce a wide range of recombinant proteins and vaccines, including monoclonal antibodies and enzymes[38-42].

The flexibility of tobacco allows for transient expression systems, such as agroinfiltration, enabling the rapid and high-yield production of proteins without the need for creating stable transgenic lines. This characteristic is particularly advantageous for producing therapeutic proteins, including vaccines for diseases like Ebola and COVID-19. Additionally, tobacco's relatively low cultivation costs and the availability of established infrastructure for greenhouse and field growth make it an ideal choice for both research and commercial biopharmaceutical production.

5.2 Maize (*Zea mays*)

Maize provides significant advantages for large-scale protein production, primarily due to its high biomass yield and the abundance of seeds, which create stable environments for protein storage. As a cereal crop, maize has been utilised to produce industrial enzymes, therapeutic proteins, and even vaccines[13,45]. The stability of proteins within maize seeds allows for long-term storage, which is particularly beneficial in resource-limited settings.

Proteins produced in maize seeds can remain stable for extended periods, facilitating transport and storage without the necessity for cold chains. This protective environment also helps prevent protein degradation, ensuring that therapeutic proteins maintain their functionality. Maize has been used for producing a variety of proteins, including those for biofuels and antibodies, making it a versatile option for large-scale pharmaceutical production.

5.3 Rice (*Oryza sativa*)

Rice is leveraged in molecular pharming mainly to produce therapeutic proteins and vaccines, thanks to its ability to produce complex proteins with human-like post-translational modifications, including glycosylation. The use of rice in molecular pharming offers the potential for low-cost pharmaceutical production, especially in developing regions where rice is a staple food.

Rice can be cultivated in significant quantities using existing agricultural infrastructure, making it feasible to scale up production for global health needs. Research has explored rice for producing vaccines against diseases such as cholera and hepatitis, as well as therapeutic proteins for conditions like haemophilia. Its affordability, scalability, and capacity for high-quality protein production position rice as a promising platform in molecular pharming[14,41,46].

5.4 Utility of Commercial Crops in Molecular Pharming

Other crops, including potatoes, tomatoes, alfalfa, and lettuce, are being investigated for their ability to produce recombinant proteins and vaccines. Potatoes and tomatoes, being edible, have been explored for oral vaccine delivery systems, making them especially valuable in regions with limited healthcare access. These crops provide versatility in the production of both therapeutic and industrial proteins[38,43,47-50,53,54].

The variety of plant species used in molecular pharming highlights the adaptability of plants as production platforms for a wide range of biotechnological applications (Table 1). Each crop offers specific advantages tailored to the desired products and production scales.

6. Application of Molecular Pharming

Molecular pharming, also referred to as plant-based biomanufacturing, has transformed the production of high-value biomolecules by utilising plants as biofactories. This novel approach has found extensive applications in various fields, including therapeutic proteins, plant-derived vaccines, enzymes, and antibodies, offering sustainable and cost-effective solutions for biomanufacturing. Since plants have long been used as sources of medicinal compounds, molecular pharming offers an innovative approach to producing molecular medicines, including plasma proteins, enzymes, growth factors, vaccines, and recombinant antibodies, with well-defined molecular applications in medicine.

Applications of Recombinant proteins expressed in plants: Proteins produced in plants for molecular pharming can be categorised into four main types: (1) therapeutic proteins and pharmaceutical intermediates,

Table 1. List of plants used for molecular pharming as an expression system, for important protein and their medical application

Expression system	Recombinant protein	Medical applications	References
Nicotiana tabacum	Glucocerebrosidase	Glycolipid metabolism	37-40
Nicotiana tabacum	Erythropoietin	Hormone activity, protein kinase activator activity, protein binding	41
Nicotiana tabacum	Protein C	Anticoagulant	42
Nicotiana tabacum	Immunoglobin A and M	First, IGM expressed in plants	39,40,42
Nicotiana tabacum	Polyhydroxybuterate	Plastic production, diabetes	37-39
Nicotiana tabacum	Insulin	Hormone activity	40,42
Nicotiana tabacum	Interleukin 2	Therapeutic uses	37-39
Nicotiana tabacum	M12 (antibody)	Therapeutic uses	40
Nicotiana tabacum	Antibody	Non-Hodgkin's lymphoma	40
Nicotiana tabacum	Antibody	Dental caries	40
Zea mays	Beta glucuronidase	Cancer prodrug therapies	13
Zea mays	Expansin	Biofuel production	45
Zea mays	Vaccine	Diarrhea	13,45
Zea mays	Therapeutic enzyme	Cystic fibrosis, pancreatitis	13,45
Zea mays	Dietary	Gastrointestinal infection	13,45
Oryza sativa	Lysozyme	Antimicrobial enzyme	46
Oryza sativa	Alpha 1 antitrypsin	Protein	41
Oryza sativa	Lactoferrin	Globular glycoprotein	14
Glycine max	Aspergillus phytase	Food formulations	56
Glycine max	Immunoglobin G	Therapeutic agent	57
Daucus carota	Glucocerebrosidase	Gaucher disease treatment	51,52
Spinacia oleracea	Rabies Glycoprotein	Vaccine	58
Artemisia sps.	Artemisinin	Malaria treatment	59
Daucus carota	Elelyso (enzyme)	Gaucher's disease treatment	38,50
Solanum tuberosum	Rotavirus Enterotoxin	Oral feeding protection	38,47-50
Solanum tuberosum	Human serum albumin	Animals vaccine	38,48,49
Solanum lycopersicum	Lactoferrin	Antimicrobial activity	38,50
Solanum lycopersicum	Rabies virus glycoprotein	Antimicrobial activity	47,48
Solanum lycopersicum	Vaccine	Hepatitis B	38,50
Solanum lycopersicum	Vaccine	Norwalk virus infection	47,48
Brassica napus	Hirudin	Thrombin inhibitor	53,54
Carthamus tinctorius	Hormone	Diabetes	50

(2) industrial proteins, such as enzymes, (3) monoclonal antibodies (Mabs) and (4) antigens intended for edible vaccines[57].

6.1 Therapeutic Proteins and Pharmaceutical Intermediates

This category includes proteins directly applied as pharmaceuticals, along with those utilised in pharmaceutical manufacturing. The range of these proteins is extensive and continuously expanding, featuring therapeutic examples like thrombin and collagen, as well as intermediates such as trypsin and aprotinin. One of the primary applications of molecular pharming is the production of therapeutic proteins and enzymes. Enzymes have become essential in the pharmaceutical industry due to their high

efficiency and selectivity in catalysing biochemical reactions within living systems. Over the past century, various therapeutic enzymes - such as L-asparaginase, streptokinase, collagenase, ribonuclease, uricase, and glucosidase have gained significant applications in this field. Given their profound impact on human health, enzyme-based drugs are increasingly the focus of research[57,58]. These therapeutic enzymes are largely produced industrially through diverse fermentation methods within suitable expression systems. Genetically engineered plants can express proteins vital for treating various conditions. For instance, crops like rice and tobacco have been modified to produce insulin for diabetes management and erythropoietin for treating anaemia. The ability of plants to perform post-translational modifications, such as glycosylation, is essential for the functionality of these proteins[18,28,42,47]. Although glycosylation patterns in plants may differ slightly from those in humans, advancements in genetic engineering are enabling the customisation of plants to produce proteins with human-like glycosylation, ultimately reducing production costs compared to traditional mammalian cell cultures. Additionally, the scalable nature of plant-based production allows for rapid responses to global healthcare needs, making it a vital player in pharmaceutical manufacturing. Another significant application lies in the development of plant-made vaccines, which could revolutionise global immunisation strategies. Unlike traditional vaccine production methods that rely on egg-based or microbial systems, transgenic plants can be used to produce antigens that trigger immune responses against various infections. Crops such as tobacco, maize, and potatoes have been engineered to produce antigens for vaccines targeting diseases like influenza, hepatitis B, and cholera. A compelling advantage of plant-made vaccines is the potential for oral delivery[27,35,42]. Research has explored producing edible vaccines in crops like tomatoes and potatoes, where the plant tissues can serve as the vaccine delivery system, eliminating the need for needles and cold chain logistics. This approach enhances accessibility and cost-effectiveness, particularly in developing regions. Moreover, the rapid production cycles of plants enable timely vaccine development during outbreaks, as evidenced during the COVID-19 pandemic when plants were utilised to produce spike proteins for vaccine formulations[60]. Advances in recombinant DNA technology, protein engineering, enzyme immobilisation, and nanotechnology have created a robust foundation for developing enzymatic drugs with applications across a wide spectrum of diseases. Therapeutic enzymes can be broadly categorised into those used in fibrinolysis, cancer treatment, enzyme replacement therapies, and the treatment of various rare and common diseases[59]. Techniques such as rational design, PEGylation, and glycoengineering have improved these enzymes' half-life, stability, and solubility, optimising them for therapeutic use. Progress in producing stable enzymes with enhanced biocatalytic activity is opening new possibilities in medicine, supporting both therapeutic and diagnostic applications[59]. Therefore, in the context of therapeutic enzymes, molecular pharming has the potential to revolutionise the production and availability of enzyme-based therapies, especially in cases where the production of therapeutic enzymes is traditionally costly or complex.

6.2 Industrial Proteins

This category includes hydrolases, which consist of both glycosidases and proteases. Molecular pharming is also gaining traction in the production of enzymes and industrial proteins, showcasing its versatility beyond pharmaceuticals. This group majorly includes hydrolases, encompassing both glycosidases and proteases. Plants can be engineered to produce enzymes essential for various industrial processes, such as biofuel production, food processing, and textile manufacturing. For instance, maize has been employed to produce cellulase, an enzyme critical for converting cellulose into sugars for biofuel applications. The plant-based production of industrial proteins is not only cost-effective but also environmentally sustainable compared to traditional microbial or chemical synthesis methods. Large-scale plant cultivation allows for mass enzyme production with reduced costs, lower energy consumption, and fewer greenhouse gas emissions. Additionally, plants provide a natural system for producing proteins that can be easily harvested, stored, and processed[18,21,25,34,43,48].

6.3 Monoclonal Antibodies (Mabs)

It encompasses various antibody types (e.g., IgA, IgG, IgM, secretory IgA) and antibody fragments (such

as Fv). These can be produced in plants in either glycosylated or non-glycosylated forms. Transgenic plants have been utilised to produce antibodies targeting conditions such as dental caries, rheumatoid arthritis, cholera, *E. coli* infections, malaria, several cancers, Norwalk virus, HIV, rhinovirus, influenza, hepatitis B, and herpes simplex virus. Molecular pharming is also significant for producing antibodies and biosimilars. Monoclonal antibodies (mAbs) are crucial for treating various diseases, including cancer and autoimmune disorders[16,27]. Traditionally, these antibodies are produced in mammalian cell cultures, a costly and time-consuming process. In contrast, plants offer a more economical and scalable platform for antibody production. For example, *Nicotiana benthamiana* has been utilised to produce functional antibodies with therapeutic potential, such as those targeting cancer cells or neutralising viruses[28,35]. The production of biosimilars—nearly identical copies of biologic drugs—can also be efficiently achieved in plants, addressing the growing demand for affordable alternatives as many biologics approach the end of their patent periods.

6.4 Antigens Intended for Edible Vaccines

Edible vaccines are made by inserting genes for microbial antigens into plants, which then produce the antigens in their edible parts. The antigens trigger an immune response when the plant is eaten, e.g. Hepatitis B surface antigen (HBsAg) used in edible vaccines for hepatitis B. Potatoes are often used for this vaccine; HBsAg is more expressed in the roots of the plant. Bananas are being developed to produce antigens that can be used as an edible vaccine against diarrhea caused by E. coli. Edible vaccines can protect against a range of diseases, including measles, cholera, foot-and-mouth disease, and hepatitis B, C, and E *etc*.

7. Future Aspects and Research

Molecular Pharming is an area that can serve as an unprecedented opportunity to manufacture affordable modern medicines and make them available at the global level. Its greatest potential lies in the prevention of infectious diseases, particularly in underdeveloped countries where access to medicines and vaccines has been limited. Molecular pharming presents significant opportunities for sustainable biomanufacturing and biopharmaceutical production. However, to fully realise its potential, several substantial challenges must be addressed. These challenges can be classified into technical, regulatory, economic, and societal dimensions, each requiring targeted efforts for effective implementation and acceptance of molecular pharming technologies.

7.1 Technical Challenges

Technical obstacles are among the most pressing issues facing molecular pharming. A primary concern is optimising plant expression systems to produce complex proteins with proper folding and post-translational modifications. While plants have shown the ability to generate therapeutic proteins, ensuring that these proteins are correctly modified to maintain their biological activity is essential. Variability in glycosylation patterns between plants and mammals can influence the efficacy and safety of the produced proteins, particularly in therapeutic contexts. Functional genomics has revolutionised our understanding of secondary metabolite production in plants, revealing intricate regulatory networks that control biosynthesis proteins. Techniques such as chromatin immunoprecipitation followed by sequencing (ChIP-seq) have also enabled the identification of epigenetic factors influencing secondary metabolite pathways. Moreover, multiplex genome editing technologies, notably CRISPR-Cas9, have streamlined the modification of multiple genomic loci, enhancing the capabilities of molecular pharming. Nanoparticles also play a crucial role in this field, improving gene delivery and enabling the monitoring of protein production in plant systems. Ongoing research is needed to advance genetic engineering techniques, such as CRISPR/Cas9, to enhance precision in modifications and to develop more robust plant expression systems that can consistently yield high-quality proteins. This is because modifying Cas9 was used to remove immunogenic epitopes that regulate immune reactions, and shorten its expression period[22,23]. In addition to optimisation, the scalability of *in vitro* production of proteins remains a significant technical hurdle. Automation of the *in vitro* cultivation of plants in a bioreactor has been advanced as a possible way of reducing costs. The large-scale production of essential medicinal compounds

through molecular pharming using bioreactors presents a complex challenge that requires careful consideration of various scaling factors. However, many plant species exhibit sensitivity to liquid media, often resulting in hyperhydricity in tissues cultured in or on such media. Transitioning from laboratory-scale processes to industrial-scale production necessitates a thorough understanding of the necessary conditions and criteria for successful scale-up. Key aspects to focus on include ensuring geometrical, kinematic, and dynamic similarities between the scales. To achieve this, it is crucial to maintain consistent Reynolds, Froude, and Weber numbers throughout the process, as these dimensionless numbers help characterise the flow and mixing behaviour of the culture. Additionally, maintaining a constant power per unit volume of the culture is vital to ensure optimal growth conditions for the organisms involved. These scale-up principles provide valuable insights into the rheological (flow-related), inertial, and viscous behaviours of the culture during industrial-scale production. By addressing these factors, we can optimise the bioreactor environment, enhancing the efficiency and yield of medicinal compounds while ensuring the stability and viability of the biological systems employed in molecular pharming[16,17,22-25].

7.2 Regulatory Challenges

Regulatory hurdles are also critical for the future of molecular pharming. The regulatory landscape for Genetically Modified Organisms (GMOs) varies widely across different countries, creating complexities that can hinder international collaboration and trade. In many regions, stringent regulations and lengthy approval processes slow the development and deployment of plant-based products, affecting timely responses to global health needs. Policymakers should establish clear, science-based guidelines that distinguish between traditional GMOs and the innovative methodologies employed in molecular pharming, thereby facilitating quicker approvals without compromising safety[8,52,55].

Moreover, potential environmental impacts of transgenic plants and concerns about gene transfer to wild relatives necessitate comprehensive risk assessments. Ensuring the biosafety of transgenic plants and addressing public concerns regarding GMOs are crucial for gaining acceptance and support for molecular pharming technologies. Regulatory agencies must engage with the scientific community and the public to effectively communicate the safety and benefits of these innovative approaches[55].

7.3 Economic Challenges

Economic barriers are significant and impact the feasibility of molecular pharming. While there is considerable potential for cost savings, initial investments in research, development, and infrastructure can be substantial. Companies and research institutions must navigate the costs associated with developing transgenic plants, optimising production systems, and securing regulatory approvals[52,55]. Additionally, there is a pressing need for investment in cultivation, harvesting, and processing infrastructure to ensure efficient scaling of production. Market acceptance of plant-derived products is vital for economic success. Despite the advantages of molecular pharming, consumers may hesitate to embrace products from genetically modified plants due to safety concerns and limited understanding. Education and awareness campaigns are essential to inform the public about the safety, efficacy, and benefits of these products, fostering broader market acceptance.

7.4 Societal Challenges

On a societal level, public perception and acceptance of molecular pharming technologies present significant challenges. Concerns regarding the safety of GMOs, ethical considerations, and potential impacts on traditional pharming practices can influence consumer attitudes. Building trust and transparency through engagement with stakeholders—including farmers, consumers, and regulatory bodies—is critical to addressing these concerns. Involving the public in discussions about the benefits and safety of molecular pharming can help alleviate fears and misconceptions, paving the way for greater acceptance.

Furthermore, integrating molecular pharming into existing agricultural systems requires consideration of the socio-economic context. Issues such as access to technology, intellectual property rights, and potential impacts on smallholder farmers must be addressed to ensure equitable distribution of molecular pharming benefits[8,44,52,55]. Strategies

that support smallholder farmers in adopting these technologies can promote inclusive growth and ensure that the advantages of molecular pharming extend to all stakeholders.

7.5 Global Collaboration

Ultimately, promoting global collaboration and the exchange of knowledge among researchers, policymakers, and industry stakeholders is crucial for effectively tackling these challenges. The rapid evolution of molecular pharming necessitates cooperation to share best practices, research findings, and technological advancements. International partnerships can help harmonise regulatory frameworks and standards, promoting a more integrated approach to molecular pharming globally. By working collaboratively, stakeholders can leverage their expertise and resources to overcome obstacles and maximise the potential of molecular pharming for global health and sustainable development[52,53,55].

8. Conclusion

Molecular pharming represents a transformative approach for biomanufacturing high-value biomolecules using key plant species (tobacco, maize, rice, potato and cereal crops) that serve as bioreactors and leveraging their unique characteristics to enhance the yield and stability of therapeutic compounds. Besides, molecular pharming expedites the production of recombinant proteins and enzymes with successful results to cure devastating diseases, including hepatitis and coronavirus. It employs a diverse array of advanced biotechnological techniques for the genetic modification of plants, enabling the efficient production of recombinant proteins. The potential of molecular pharming is vast, but challenges remain, including technical optimisation, regulatory hurdles, economic feasibility, and societal acceptance. Addressing these challenges through global collaboration and knowledge sharing among researchers, policymakers, and industry stakeholders will be essential for realising the full potential of molecular pharming. Its applications span therapeutic proteins, plant-derived vaccines, enzymes, and monoclonal antibodies, offering sustainable and cost-effective solutions in healthcare. Ultimately, this approach could significantly enhance the availability of affordable medicines and vaccines, contributing to improved global health outcomes.

9. Author Contribution

RK: Conceived the idea, designed investigation and wrote the manuscript. SDM and SA: Contributed to writing the manuscript, AS, VHP, SKT, NC and RKS: Data curation, analysed results and contributed in providing constructive feedback. All authors have read and agreed to the published version of the manuscript.

10. References

1. Theodoridis S, Drakou EG, Hickler T, Thines M, Nogués-Bravo D. Evaluating natural medicinal resources and their exposure to global change. Lancet Planet Health. 2023; 7(2):e155-e163. https://doi.org/10.1016/S2542-5196(22)00317-5 PMid:36754471
2. Rahman MH, Roy B, Chowdhury GM, Hasan A, Saimun MS. Medicinal plant sources and traditional healthcare practices of forest-dependent communities in and around Chunati Wildlife Sanctuary in southeastern Bangladesh. Environ Sustain. 2022; 5(2):207-241. https://doi.org/10.1007/s42398-022-00230-z PMid:37521586 PMCid:PMC9170557
3. Craig WJ. Health-promoting properties of common herbs. Am J Clin Nutr. 1999; 70(3):491S-499S. https://doi.org/10.1093/ajcn/70.3.491s PMid:10479221
4. Prasathkumar M, Anisha S, Dhrisya C, Becky R, Sadhasivam S. Therapeutic and pharmacological efficacy of selective Indian medicinal plants: A review. Phytomedicine Plus. 2021; 1(2):100029. https://doi.org/10.1016/j.phyplu.2021.100029
5. Atanasov AG, Waltenberger B, Pferschy-Wenzig EM, Linder T, Wawrosch C, Uhrin P, *et al.* Discovery and resupply of pharmacologically active plant-derived natural products: A review. Biotechnol Adv. 2015; 33(8):1582-1614. https://doi.org/10.1016/j.biotechadv.2015.08.001 PMid:26281720 PMCid:PMC4748402
6. Sinha D, Odoh UE, Ganguly S, Muhammad M, Chatterjee M, Chikeokwu I, *et al.* Phytochemistry, history, and progress in drug discovery. Phytochemistry, computational tools and databases in drug discovery. Elsevier; 2023. p. 1-26. https://doi.org/10.1016/B978-0-323-90593-0.00001-0
7. Chaachouay N, Zidane L. Plant-derived natural products: a source for drug discovery and development. Drugs Drug Candidates. 2024; 3(1):184-207. https://doi.org/10.3390/ddc3010011
8. Schillberg S, Finnern R. Plant molecular farming for the production of valuable proteins: Critical evaluation of achievements and future challenges. J Plant Physiol. 2021;

258:153359. https://doi.org/10.1016/j.jplph.2020.153359 PMid:33460995
9. Sethi L, Kumari K, Dey N. Engineering of plants for efficient production of therapeutics. Mol Biotechnol. 2021; 63(12):1125-1137. https://doi.org/10.1007/s12033-021-00381-0 PMid:34398446 PMCid:PMC8365136
10. Velankar R, Nerkar G, Nagpurkar M. Genetically modified crops: A pivotal endeavor in biotechnology. Genetically modified organisms, Intech Open; 2024. https://doi.org/10.5772/intechopen.1005578
11. Saxena J, Rawat S. Edible vaccines. Advances in Biotechnology; 2014. p. 207-226. https://doi.org/10.1007/978-81-322-1554-7_12 PMCid:PMC7120417
12. Gerszberg A, Hnatuszko-Konka K. Compendium on food crop plants as a platform for pharmaceutical protein production. Int J Mol Sci. 2022; 23(6):3236. https://doi.org/10.3390/ijms23063236 PMid:35328657 PMCid:PMC8951019
13. Shanmugaraj B, Bulaon CJ, Phoolcharoen W. Plant molecular farming: A viable platform for recombinant biopharmaceutical production. Plants. 2020; 9(7):842. https://doi.org/10.3390/plants9070842 PMid:32635427 PMCid:PMC7411908
14. Eidenberger L, Kogelmann B, Steinkellner H. Plant-based biopharmaceutical engineering. Nat Rev Bioeng. 2023; 1(6):426-439. https://doi.org/10.1038/s44222-023-00044-6 PMid:37317690 PMCid:PMC10030082
15. Rai A, Yamazaki M, Saito K. A new era in plant functional genomics. Curr Opin Syst Biol. 2019; 15:58-67. https://doi.org/10.1016/j.coisb.2019.03.005
16. Alami MM, Ouyang Z, Zhang Y, Shu S, Yang G, Mei Z, *et al*. The current developments in medicinal plant genomics enabled the diversification of secondary metabolites' biosynthesis. Int J Mol Sci. 2022; 23(24):15932. https://doi.org/10.3390/ijms232415932 PMid:36555572 PMCid:PMC9781956
17. Wani KI, Choudhary S, Zehra A, Naeem M, Weathers P, Aftab T. Enhancing artemisinin content in and delivery from *Artemisia annua*: A review of alternative, classical, and transgenic approaches. Planta. 2021; 254:1-5. https://doi.org/10.1007/s00425-021-03676-3 PMid:34263417 PMCid:PMC8279915
18. Tong Y, Xue J, Li Q, Zhang L. A generalist regulator: MYB transcription factors regulate active ingredient biosynthesis in medicinal plants. J Exp Bot. 2024; erae225. https://doi.org/10.1093/jxb/erae225 PMid:38767602
19. Verma A, Tiwari H, Singh S, Gupta P, Rai N, Singh SK, *et al*. Epigenetic manipulation for secondary metabolite activation in endophytic fungi: Current progress and future directions. Mycology. 2023; 14(4):275-291. https://doi.org/10.1080/21501203.2023.2241486 PMid:38187885 PMCid:PMC10769123
20. Cichewicz RH. Epigenome manipulation as a pathway to new natural product scaffolds and their congeners. Nat Prod Rep. 2010; 27(1):11-22. https://doi.org/10.1039/B920860G PMid:20024091 PMCid:PMC2958777
21. Pacesa M, Pelea O, Jinek M. Past, present, and future of CRISPR genome editing technologies. Cell. 2024; 187(5):1076-1100. https://doi.org/10.1016/j.cell.2024.01.042 PMid:38428389
22. Cong L, Ran FA, Cox D, Lin S, Barretto R, Habib N, *et al*. Multiplex genome engineering using CRISPR/Cas systems. Science. 2013; 339(6121):819-823. https://doi.org/10.1126/science.1231143 PMid:23287718 PMCid:PMC3795411
23. Baig N, Kammakakam I, Falath W. Nanomaterials: A review of synthesis methods, properties, recent progress, and challenges. Mater Adv. 2021; 2(6):1821-1871. https://doi.org/10.1039/D0MA00807A
24. Eidenberger L, Kogelmann B, Steinkellner H. Plant-based biopharmaceutical engineering. Nat Rev Bioeng. 2023; 1(6):426-439. https://doi.org/10.1038/s44222-023-00044-6 PMid:37317690 PMCid:PMC10030082
25. Shanmugaraj B, Bulaon CJI, Phoolcharoen W. Plant molecular farming: A viable platform for recombinant biopharmaceutical production. Plants. 2020; 9(7):842. https://doi.org/10.3390/plants9070842 PMid:32635427 PMCid:PMC7411908
26. Molecular Farming: Global Markets Report; 2024.
27. Klein TM, Fromm M, Weissinger A, Tomes D, Schaaf S, Sletten M, *et al*. Transfer of foreign genes into intact maize cells with high-velocity microprojectiles. Proc Natl Acad Sci. 1988; 85(12):4305-4309. https://doi.org/10.1073/pnas.85.12.4305 PMid:16593942 PMCid:PMC280417
28. Christou P, McCabe DE, Swain WF. Stable transformation of soybean callus by DNA-coated gold particles. Plant Physiol. 1988; 87(3):671-674. https://doi.org/10.1104/pp.87.3.671 PMid:16666205 PMCid:PMC1054818
29. Cunningham FJ, Goh NS, Demirer GS, Matos JL, Landry MP. Nanoparticle-mediated delivery towards advancing plant genetic engineering. Trends Biotechnol. 2018; 36(9):882-897. https://doi.org/10.1016/j.tibtech.2018.03.009 PMid:29703583 PMCid:PMC10461776
30. Wu K, Xu C, Li T, Ma H, Gong J, Li X, *et al*. Application of nanotechnology in plant genetic engineering. Int J Mol Sci. 2023; 24(19):14836. https://doi.org/10.3390/ijms241914836 PMid:37834283 PMCid:PMC10573821
31. Kofer W, Eibl C, Steinmüller K, Koop HU. PEG-mediated plastid transformation in higher plants. *In Vitro* Cell Dev Biol - Plant. 1998; 34:303-309. https://doi.org/10.1007/BF02822739
32. Sharma S, Pawar S, Sagwal V, Mishra CN. Genetic transformation methods in plants - A review. Int J Agric Sci. 2023; 8.
33. Gelvin SB. Integration of *Agrobacterium* T-DNA into the plant genome. *Annu Rev Genet*. 2017; 51(1):195-217.

https://doi.org/10.1146/annurev-genet-120215-035320 PMid:28853920
34. Su W, Xu M, Radani Y, Yang L. Technological development and application of plant genetic transformation. Int J Mol Sci. 2023; 24(13):10646. https://doi.org/10.3390/ijms241310646 PMid:37445824 PMCid:PMC10341552
35. Lico C, Chen Q, Santi L. Viral vectors for production of recombinant proteins in plants. J Cell Physiol. 2008; 216(2):366-377. https://doi.org/10.1002/jcp.21423 PMid:18330886 PMCid:PMC7166642
36. Grunennvaldt RL, Degenhardt-Goldbach J, Gerhardt IR, Quoirin M. Promoters used in genetic transformation of plants. Int J Biol Sci. 2025; 10:1-9.
37. Villao-Uzho L, Chávez-Navarrete T, Pacheco-Coello R, Sánchez-Timm E, Santos-Ordóñez E. Plant promoters: their identification, characterization, and role in gene regulation. Genes. 2023; 14(6):1226. https://doi.org/10.3390/genes14061226 PMid:37372407 PMCid:PMC10298551
38. Shanmugaraj B, Bulaon CJI, Phoolcharoen W. Plant molecular farming: A viable platform for recombinant biopharmaceutical production. Plants. 2020; 9(7):842. https://doi.org/10.3390/plants9070842 PMid:32635427 PMCid:PMC7411908
39. Burnett MJ, Burnett AC. Therapeutic recombinant protein production in plants: Challenges opportunities. Plants People Planet. 2020; 2(2):121-132. https://doi.org/10.1002/ppp3.10073
40. Klocko AL. Genetic containment for molecular farming. Plants. 2022; 11(18):2436. https://doi.org/10.3390/plants11182436 PMid:36145835 PMCid:PMC9501302
41. Kumari K. Plant Molecular farming: An emerging opportunity for biopharmaceuticals. J Adv Sci Res. 2024; 15(06):1-8. https://doi.org/10.55218/JASR.2024150601
42. Liu H, Timko MP. Improving protein quantity and quality - The next level of plant molecular farming. Int J Mol Sci. 2022; 23(3):1326. https://doi.org/10.3390/ijms23031326 PMid:35163249 PMCid:PMC8836236
43. Abiri R, Valdiani A, Maziah M, Shaharuddin NA, Sahebi M, Yusof ZN, *et al*. A critical review of the concept of transgenic plants: Insights into pharmaceutical biotechnology and molecular farming. Curr Issues Mol Biol. 2016; 18(1):21-42.
44. Hood EE, Witcher DR, Maddock S, Meyer T, Baszczynski C, Bailey M, *et al*. Commercial production of avidin from transgenic maize: Characterization of transformant, production, processing, extraction and purification. Mol Breed. 1997; 3:291-306. https://doi.org/10.1023/A:1009676322162
45. Zhong GY, Peterson D, Delaney DE, Bailey M, Witcher DR, Register JC III, *et al*. Commercial production of aprotinin in transgenic maize seeds. Mol Breed. 1999; 5:345-356. https://doi.org/10.1023/A:1009677809492
46. Geilfus CM, Ober D, Eichacker LA, Mühling KH, Zörb C. Down-regulation of ZmEXPB6 [Zea mays β-expansin 6] protein is correlated with salt-mediated growth reduction in the leaves of Z. mays L. J Biol Chem. 2015; 290(18):11235-11245. https://doi.org/10.1074/jbc.M114.619718 PMid:25750129 PMCid:PMC4416831
47. Gharelo RS, Oliaei ED, Bandehagh A, Khodadadi E, Noparvar PM. Production of therapeutic proteins through plant tissue and cell culture. J BioSci Biotechnol. 2016; 5(1).
48. Ghag SB, Adki VS, Ganapathi TR, Bapat VA. Plant platforms for efficient heterologous protein production. Biotechnol Bioprocess Eng. 2021; 26(4):546-567. https://doi.org/10.1007/s12257-020-0374-1 PMid:34393545 PMCid:PMC8346785
49. Abd-Aziz N, Tan BC, Rejab NA, Othman RY, Khalid N. A new plant expression system for producing pharmaceutical proteins. Mol Biotechnol. 2020; 62:240-251. https://doi.org/10.1007/s12033-020-00242-2 PMid:32108286
50. Sathishkumar R, Kumar SR, Hema J, Baskar V, editors. Advances in plant transgenics: Methods and applications. Berlin/Heidelberg, Germany: Springer; 2019. https://doi.org/10.1007/978-981-13-9624-3
51. Ritala A, Häkkinen ST, Schillberg S. Molecular pharming in plants and plant cell cultures: A great future ahead? Pharm Bioprocess. 2014; 2(3):223-236. https://doi.org/10.4155/pbp.14.21
52. Rosales-Mendoza S, Tello-Olea MA. Carrot cells: A pioneering platform for biopharmaceuticals production. Mol Biotechnol. 2015; 57:219-232. https://doi.org/10.1007/s12033-014-9837-y PMid:25572939
53. Chung YH, Church D, Koellhoffer EC, Osota E, Shukla S, Rybicki EP, *et al*. Integrating plant molecular farming and materials research for next-generation vaccines. Nat Rev Mater. 2022; 7(5):372-388. https://doi.org/10.1038/s41578-021-00399-5 PMid:34900343 PMCid:PMC8647509
54. Boothe JG, Saponja JA, Parmenter DL. Molecular farming in plants: oilseeds as vehicles for the production of pharmaceutical proteins. Drug Dev Res. 1997; 42(3-4):172-181. https://doi.org/10.1002/(SICI)1098-2299(199711/12)42:3/4<172::AID-DDR9>3.0.CO;2-N
55. Chandrakanth RK, Gubbewad S, Oli AK. Molecular Pharming. Applications of synthetic biology in health, energy, and environment. IGI Global; 2023. p. 152-161. https://doi.org/10.4018/978-1-6684-6577-6.ch007
56. Mor TS. Molecular pharming's foot in the FDA's door: Protalix's trailblazing story. Biotechnol Lett. 2015; 37:2147-2150. https://doi.org/10.1007/s10529-015-1908-z PMid:26149580 PMCid:PMC4583803
57. Horn ME, Woodard SL, Howard JA. Plant molecular farming: Systems and products. Plant Cell Rep. 2004; 22(10):711-720. https://doi.org/10.1007/s00299-004-0767-1 PMid:14997337 PMCid:PMC7079917

58. Hajibehzad SS, Mohseni A, Dolati M, Shafaroudi SM, Hefferon K, Makhzoum A. Plant molecular pharming methods, tools, challenges ahead for production of recombinant proteins, and potential solutions. Applications in Plant Biotechnology. CRC Press; 2022. p. 165-203. https://doi.org/10.1201/9781003008866-9
59. Tandon S, Sharma A, Singh S, Sharma S, Sarma SJ. Therapeutic enzymes: Discoveries, production and applications. J Drug Deliv Sci Technol. 2021; 63:102455. https://doi.org/10.1016/j.jddst.2021.102455
60. Kumar M, Kumari N, Thakur N, Bhatia SK, Saratale GD, Ghodake G, *et al*. A comprehensive overview on the production of vaccines in plant-based expression systems and the scope of plant biotechnology to combat against SARS-CoV-2 virus pandemics. Plants. 2021; 10(6):1213. https://doi.org/10.3390/plants10061213 PMid:34203729 PMCid:PMC8232254