Volume 4, Issue 6, 2026

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

RECOMBINANT PROTEIN EXPRESSION SYSTEMS: CURRENT PROGRESS, CHALLENGES, AND FUTURE DIRECTIONS

Muhammad Rizwan[1], Sabah Mansoor[2], Anjum Masood[3], Tariq Nadeem[4], Kinza Khan[5], Muhammad Awais[*6], Zohaib Saeed[7], Iram Murtaza[8], Muhammad Haseeb Qamar[9]

[1,*6,7,9]*Multan College of Veterinary Sciences, Multan University of Science and Technology, Multan Pakistan*
[2]*Department of Allied Sciences, University of Home Economics, Lahore, Pakistan*
[3]*Department of Theriogenology, University of Agriculture, Faisalabad, Pakistan*
[4]*Para Veterinary Institute Karor Lal Eason Layyah Sub Campus, University of Veterinary and Animal Sciences, Lahore*
[5]*Department of Microbiology, Faculty of Veterinary and Animal Sciences, The Islamia University of Bahawalpur, Pakistan*
[8]*Department of Biotechnology, Lahore College for Women University, Lahore, Pakistan*

[*6]awaisjutt646478@gmail.com

DOI:https://doi.org/10.5281/zenodo.20771691

Keywords
Recombinant DNA technology, Escherichia coli, yeast, insect, Recombinant protein expression

Article History
Received: 23 April 2026
Accepted: 05 June 2026
Published: 20 June 2026

Corresponding Author: *
Muhammad Awais

Abstract
The production of recombinant proteins in protein expression systems has become an essential tool in modern biotechnology for the mass production of proteins for pharmaceutical, industrial, agricultural and research purposes. Since the advent of recombinant DNA technology, major progress has been made in the evolution and optimization of various expression systems such as bacterial, yeast, insect, mammalian, plant-based and cell-free systems. The selection of an appropriate host is essential for the successful production of proteins, with each expression system having its own set of advantages, including but not limited to: protein yield, production cost, scalability and post-translational modifications. Escherichia coli is the most popular host and is the most widely used system for the production of simpler therapeutic proteins; while mammalian cell lines are used for the production of more complex therapeutic proteins that require more human-like post-translational modifications. With the recent development of genetic engineering, synthetic biology, metabolic pathway optimization and genome editing technologies, expression efficiency, product quality and process scalability have significantly improved. Nevertheless, there are several issues that still remain in the way of recombinant protein production such as protein misfolding and aggregation, degradation by proteases, low recombinant protein expression, and challenges of native post-translational modifications. Additionally, the growing trend towards biologics and personalized medicines requires the creation of more efficient, flexible and cost-effective manufacturing platforms. These will be expected to increase the yield of protein and product consistency, and cut manufacturing costs. Major recombinant protein expression systems are summarized in this review, with a focus on their current status, advantages, disadvantages and industrial applications. It also covers important problems encountered in protein expression, and explores trends that could impact the future of recombinant protein production technologies. Ongoing developments

Frontier in Medical & Health Research
ISSN: (e) 3007-1607 (p) 3007-1593

in this area will be vital to the global progress of biotechnology, health care and sustainable industrial development.

INTRODUCTION

One of the most outstanding advances of modern biotechnology and genetic engineering is the technology of recombinant protein expression (Liu, Xiao, Li, Zhao, & Huang, 2025). (Shakweer, Krivoruchko, Dessouki, & Khattab, 2023). Recombinant proteins have played a crucial role in many sectors since the development of the recombinant DNA technology in the seventies, such as medicine, agriculture, industrial biotechnology, environmental research, and research within academia (Sunday et al., 2025). Capable of mass production of proteins has transformed the way diseases are treated, vaccines have been developed and industrial enzymes and diagnostic reagents manufactured (Raina, Villingiri, Jehan, & Qadir, 2022). The commercialization of recombinant human insulin in 1982 was a major milestone in biotechnology and a proof of the potential of recombinant protein production (binti Hafizal, binti Shamsudin, & Mohamed). Prior to the advent of the recombinant DNA technology, proteins required for medical use were frequently obtained from animal tissue or human donors, thus with a risk of contamination, limited supply and high production costs (Shih et al., 2023). Recombinant protein expression systems offered a safer, more reliable and scalable method to generate biologically active proteins. Since then, many recombinant products have been developed and approved for clinical use such as growth hormones, clotting factors, monoclonal antibodies, cytokines and vaccines (Slathia et al., 2023). With the rise in biologics product demand, there has been a great deal of research aimed at optimizing biologics expression platforms (Bas, 2025). Selection of an appropriate expression system is a key factor that affects yield, functionality, quality, and cost of protein production. A number of different host systems are available to suit various protein production needs. They range from bacterial systems like Escherichia coli, yeast systems like Saccharomyces cerevisiae and Pichia pastoris, insect cell-based systems, mammalian cell cultures, plant expression systems and recently cell-free protein synthesis systems. Both platforms have their strengths and weaknesses in terms of growth, scalability, ability to perform post-translational modifications, and regulatory acceptance (Bas, 2025).

Escherichia coli is one of the most common expression hosts due to its low cultivation cost, high protein expression yield, simple genetics and rapid growth rate (Pouresmaeil & Azizi-Dargahlou, 2023). But bacterial systems are frequently bound in their ability to produce eukaryotic proteins which have extensive post-translational modifications (Carabetta & Hardouin, 2022). Eukaryotic expression systems like yeast, insect and mammalian cells have become more important, as they can address these challenges. The advantage of using mammalian cells to produce therapeutic proteins is that they are capable of glycosylating proteins like human cells, and are known to fold proteins like human cells. Chinese Hamster Ovary (CHO) cells and Human Embryonic Kidney (HEK293) cells are regarded as the gold standard for therapeutic protein production because they can glycosylate proteins like human cells and they are known to fold them in a human-like manner. But the mammalian system is still too expensive and complex to grow cells, and alternative platforms continue to be explored (Lim, 2022). The efficiency of recombinant protein production has greatly benefited from recent advances in molecular biology, synthetic biology, metabolic engineering and genome editing technologies (J. Yadav, Marwah, & Kumar, 2025). The new techniques like codon optimization, promoter engineering, co-expression of chaperones, modification of metabolic pathways, and genome editing using CRISPR-Cas have been employed to increase the level of protein expression and improve the quality of the products in various host systems. Moreover, the optimization of the bioreactor design, fermentation process and downstream purification technologies have also

Frontier in Medical & Health Research
ISSN: (e) 3007-1607 (p) 3007-1593

helped achieve higher productivity and lower manufacturing costs. Although there has been significant progress, there are several aspects that still need to be overcome to produce recombinant proteins efficiently. Many expression systems still face challenges such as protein misfolding, aggregation, the formation of inclusion bodies, proteolytic degradation, and low expression levels. Further, introducing native post-translational modifications like glycosylation is still a significant challenge for non-mammalian hosts. The synthesis of membrane proteins, multi-subunit complexes and other structurally complex biomolecules are also technically challenging. Solving these challenges is key to enhancing product quality, boosting manufacturing productivity, and satisfying the global demand for the production of biopharmaceuticals (Shokoohi & Attar, 2024).
New opportunities have emerged in the past few years to address the limitations in the production of recombinant proteins with the advent of synthetic biology and artificial intelligence (AI). Synthetic biology methods provide opportunities to design customized genetic circuits and engineered host organisms that have increased production capacity (Hoces, Miguens Blanco, & Hernández-López, 2023). Likewise, AI and machine learning algorithms are being used ever more to design an optimized protein structure prediction, protein expression conditions, protein engineering, and bioprocess control (Nikolados & Oyarzún, 2023). The technologies can be instrumental in speeding up research and development as well as lowering production costs and increasing consistency of products (Suriyaamporn et al., 2024). Cell-free protein synthesis systems also have been receiving some attention for their novel approach as alternatives to cell-based platforms in recent years. The systems used are based on cell fragments from living organisms to be used for the in vitro synthesis of proteins, which have the advantage of being more flexible, faster, and are capable of synthesizing proteins that can be toxic to living cells. While there are scalability and cost challenges ahead, cell-free technologies are becoming more important as a factor in future protein manufacturing processes. The wide-ranging use of recombinant proteins, combined with the constant development of expression methods, makes it necessary to have a thorough knowledge of the available expression systems for researchers and industry(M. Yadav, Sarkar, & Kumar, 2024) . This review is intended to outline the major recombinant protein expression systems, review recent advances and innovations and discuss present problems and challenges, and outline future trends that could prove to be influential for the next generation of recombinant protein production. These advancements will further solidify the place of recombinant proteins in health care, agriculture, and industrial biotechnology, and drive scientific progress and economic expansion internationally (Jain).

Recombinant protein Expression

The recombinant protein expression is a biotechnological process in which a particular gene that codes for a desired protein is introduced into a host organism and the desired protein is expressed in large quantities (Srivastava). The technology is in recombinant DNA techniques, which enable scientists to isolate, manipulate and move genes from one organism to another (Kollabathula et al., 2025). Recombinant proteins have been invaluable in medical, agricultural, industrial biotechnology and research applications (Liu et al., 2025). The first step in the production of recombinant proteins is usually the identification and isolation of a target gene (Feng, Li, Fan, Zhu, & Chen, 2022). This recombinant vector is then introduced (transformed, transfected or infected) into a suitable host cell. Recombinant protein expression systems include: bacteria, yeast, insect cells, mammalian cells, plants and cell-free systems. Several factors including the level of modification required post-translationally, the protein complexity, the production volume and economic parameters are used in the selection of host (Z.-X. Zhang et al., 2022). The main reason they are used is that bacterial systems grow quickly, and Escherichia coli bacteria are easy to cultivate and produce high yields of protein (Z.-X. Zhang et al., 2022). However, they are not ideal for the production of complex proteins that need extensive post-translational modifications. In this case, eukaryotic hosts like yeast, insect cells, and mammalian cells are preferred because they can carry out protein folding and modification processes that are like those found in higher organisms (İncir & Kaplan, 2024).

Recombinant protein expression revolutionized the pharmaceutical industry by making it possible to produce therapeutic proteins like vaccines, monoclonal antibodies, interferons, erythropoietin, growth hormones and insulin (Slathia et al., 2023). In industrial applications, recombinant enzymes are applied in food industry, detergent industry, biofuel industry and environmental biotechnology. Furthermore, recombinant proteins are used in various areas of molecular biology research, diagnostics and drug discovery (Mohammed, Ibrahim, & Basher, 2025). Although there are many benefits of using recombinant proteins, there are also a number of challenges associated with the process of expressing them, such as low expression levels, aggregation, formation of inclusion bodies, degradation by proteases, and failure to properly post-translate the proteins. The development of genetic engineering techniques, synthetic biology, codon optimization and genome editing technologies have greatly enhanced protein production and quality (Khanal & Sharma, 2024). With the continuous advancement of research, the expression of recombinant protein has become an indispensable part of today's cutting-edge biotechnology, offering new solutions in healthcare, agriculture and industrial development, and meeting the increasing demand for biological products (Яковенко & Бородай, 2025).

Major Recombinant Protein Expression Systems

In response to the growing demand for proteins for research, medical, agricultural and industrial applications, a range of recombinant protein expression systems has been created (Liu et al., 2025). The choice of expression system is influenced by the protein complexity, yield, cost of expression, production scale and the requirement for post-translational modifications (Z.-M. Li, Fan, Wang, & Wang, 2022).

Escherichia coli is the preferred host for bacterial expression system because it can be easily manipulated and it grows quickly and cheaply (Hayat, Farahani, Golichenari, & Sahebkar, 2018). While they can yield a large amount of recombinant protein in a short time, they may not be able to carry out the complex post-translational modifications of many eukaryotic proteins.

Yeast expression systems such as Saccharomyces cerevisiae and Pichia pastoris have the best features of both prokaryotic and eukaryotic hosts (Garvey, 2022). They can execute some post-translational modifications without compromising on their relatively high growth rate and production yield. The enzymes, vaccines and therapeutic proteins are produced by yeast systems.

Standard expression systems for insects can be used to produce complex proteins with proper folding and post-translational modification (PTM). They are often used in vaccine manufacturing and structural biology research (Koff, Rappuoli, & Plotkin, 2023).

The preferred cells for therapeutic protein and monoclonal antibody production are mammalian cells, especially Chinese Hamster Ovary (CHO) and Human Embryonic Kidney (HEK293) cells (L. Zhang et al., 2024). They offer human like PTMs and create highly biologically active proteins; however they are more expensive and require longer cultivation (V. Kumar et al., 2024).

The plant-based expression system has become a cost-effective and environmental friendly option for recombinant protein production (Jadhav & Khare, 2024). Also, the cell-free protein synthesis systems are able to rapidly produce proteins without using living cells, which are useful for special applications and high throughput screening (Gu et al., 2023).

These expression systems offer a variety of options for the production of recombinant proteins, allowing researchers and industries to choose the appropriate system for their needs and goals (Liu et al., 2025).

Frontier in Medical & Health Research
ISSN: (e) 3007-1607 (p) 3007-1593

Current Progress in Recombinant Protein Expression Technologies

The recombinant protein expression technology has made tremendous progress over the last decades, and is now an important backbone of biomedical research, pharmaceutical development and modern biotechnology (Sobti & Sobti, 2023). Genetic engineering has been used to produce proteins on a large scale, which has led to the production of therapeutic proteins, vaccines, industrial enzymes, and research reagents (V. Kumar et al., 2024). With the recent innovation, efficiency in expressing proteins, protein quality, and scalability of the production yield has been significantly improved (Liu et al., 2025).

Advanced expression hosts are one area of progress. Although modern systems like P. fluorescence and Bacillus thuringiensis are increasingly available, the traditional systems (E. coli) are still widely used due to their fast growth, low cost and ease of genetic manipulation. In more recent engineered bacterial strains, however, efforts have been made to improve protein folding, to achieve a decrease in the formation of inclusion bodies, and to produce complex proteins. Likewise, the expression systems based on yeast were optimized, especially those based on Saccharomyces cerevisiae and Pichia pastoris, to yield proteins at higher levels and to provide more accurate post-translational modifications (Liu et al., 2025).

Mammalian cell expression systems, notably Chinese Hamster Ovary (CHO) cells, still maintain their position as the leading method for making therapeutic proteins and monoclonal antibodies. The cell-line engineering and development of genome editing tools, like CRISPR-Cas9, and the refinement of culture media have improved yield and lowered production expenses. The improvements have led to efficient manufacturing of very complex biopharmaceuticals (Liu et al., 2025).

Another major breakthrough is the CFPS systems. These systems have no requirement for living cells, and can be used to produce proteins rapidly in a controlled environment. CFPS is especially valuable for generation of toxic proteins, screening of protein variants and for vaccine development (Liu et al., 2025).

Table 1: Recombinant Proteins Expression

Expression System	Future Directions	Major Challenges	Key Advantages	Current Progress	Refernces
Yeast (Saccharomyces cerevisiae, Pichia pastoris	The introduction of glycosylated pathways, engineering of strains using CRISPR, optimization of high density fermentation	Hyperglycosylation, inconsistent glycan patterns	The advantages of PTM in eukaryotes are: eukaryotic PTMs, scalable fermentation, low cost.	Enhanced glycoengineering and secretion systems; ubiquitous in the case of industrial enzymes and vaccines	(Crnoglavac Popović, Stanišić, & Prodanović, 2024)
Mammalian Cells (CHO, HEK293)	These are all considered innovations that facilitate the scaling up of single-use bioreactor production in the	Expensive, slow growing, hard to culture.	Immediate human-like PTMs, correct folding and quality biologics.	Advanced bioprocessing/bioreactor scaling; advanced bioreactor technology; scaling up therapeutic	(Guna, Nguyen, Stevens, & Voorhees, 2026)

Frontier in Medical & Health Research
ISSN: (e) 3007-1607 (p) 3007-1593

	biopharmaceutical industry.All of these are regarded as innovations that help scale single-use bioreactor production in the biopharmaceutical industry.			proteins (antibodies, hormones), etc.	
Plant-based Systems (Nicotiana benthamiana, transgenic plants)	The development of molecular farming, chloroplast engineering, and quick transient expression systems.Development of molecular farming, chloroplast engineering, and rapid transient expression systems.	Dealing with processing difficulties downstream, variable expression levels, regulatory issues	Low cost, scalable, low risk of human pathogen contamination ,	Increasingly being used in vaccines and biopharmaceuticals; some approved biologics successfully produced	(Sliwczynski, 2022)
Cell-free Expression Systems	Cost reduction strategies, continuous cell-free systems, industrial-scale adaptation	High cost, limited scalability, short reaction time	Fast production, no living cells required, easy control of conditions	Growing use in vaccines and biopharmaceuticals; successful production of some approved biologics	(Zawada et al., 2022)
Bacterial (E. coli)	Engineering strains for better folding, synthetic biology tools, improved secretion systems, co-expression of chaperones	Lack of post-translational modifications (PTMs), protein misfolding, inclusion body formation	Fast growth, low cost, high yield, easy genetic manipulation	Most widely used; high-yield expression of simple proteins; advanced vector systems and codon optimization widely adopted	(Guna et al., 2026; Mohite et al., 2026)

The applications of synthetic biology and metabolic engineering have drastically changed the production of recombinant proteins. Researchers are now able to create optimized synthetic promoters, codon-optimized genes and genetic circuits to achieve the highest expression levels. In addition, AI- and machine-learning-based tools are becoming more and more prevalent in predicting protein structures, optimizing expression conditions, and working towards more efficient production (Tepap, Anissi, & Bounou, 2023).

Frontier in Medical & Health Research
ISSN: (e) 3007-1607 (p) 3007-1593

Despite these developments, there are still challenges including protein mis-folding, aggregation, production costs and regulatory requirements. Despite these developments, new advances in recombinant protein expression technologies such as genetic engineering, bioprocess optimization, and computational biology still hold promise for improved efficiency and cost-effective production of valuable proteins for medical, industrial, and research purposes (Kathirvel & Gayathri Ganesan, 2024).

Applications of Recombinant Proteins

Recombinant proteins are one of the most important products of modern biotechnology, with a wide variety of applications in medicine, agriculture, industry and scientific research (Liu et al., 2025). Recombinant proteins are heavily used in the medical field to treat a number of diseases. The first and most successful recombinant insulin is recombinant human insulin, which is used to treat diabetes mellitus. Other therapeutic recombinant proteins are human growth hormone for growth disorders, erythropoietin to treat anemia, interferons for viral infections and some cancers, and blood-clotting factors for hemophilia (Johnson, 2023). The recombinant monoclonal antibodies have revolutionized the field of cancer treatment, autoimmune disorder treatment, and inflammatory diseases with their highly targeted treatment approach. Recombinant proteins are also crucial factors used in the production of modern vaccines. Recombinant vaccines, like the ones created against hepatitis B and the human papillomavirus (HPV), are safer, as they are made up of just a few of the antigenic proteins instead of the entire organism. Recombinant proteins are also extensively used in diagnostic applications such as enzyme-linked immunosorbent assays (ELISA), immunoblotting, and rapid diagnostic tests, where their high specificity and sensitivity aid in the accurate detection and monitoring of diseases (P. Li, Zheng, Zhang, Yin, & Ren, 2025).

In addition to medicine, recombinant proteins have an important role in industrial biotechnology, agriculture and research. Recombinant enzymes like amylases, proteases, lipases, cellulases etc. are widely used in food processing, detergent industry, textile industry, paper industry and biofuel industries (Regmi & Yoo, 2025). These enzymes are used in manufacturing for improved production efficiency, lower manufacturing costs and environmentally friendly industrial processes (Patel, Dong, Chen, Pandey, & Singhania, 2023). In agriculture, the use of recombinant proteins has led to the production of transgenic crops that are resistant to pests, pathogens, and environmental factors (Collinge & Sarrocco, 2022). In agriculture, recombinant proteins have been used to produce genetically modified crops that are resistant to pests, diseases, and environmental stressors (S. Kumar et al., 2024). An important one is the expression of Bacillus thuringiensis (Bt) proteins in crops for effective protection against insect pests and reduction in the use of chemical pesticides (Ali, Abdellah, & Eletmany, 2023). Recombinant proteins also find applications in veterinary medicine, such as vaccines, diagnostics and therapeutics, in order to enhance animal health and productivity (Ali et al., 2023). They are essential for scientific research to elucidate protein structure and function, cellular signaling pathways, gene regulation, and disease mechanisms (Nadhan, Isidoro, Song, & Dhanasekaran, 2022). Recombinant proteins are utilized during the discovery of drugs, in structural biology and in the development of novel therapeutic approaches (Mohammed et al., 2025). The ability to produce high quantities of highly pure proteins has greatly aided in the research of the biological field and spurred innovation in several fields (Nath, 2026). Recombinant proteins remain vital in biotechnology, driving progress in global science, medicine, biotechnology, and food production, and will continue to play an important role in human health in the future (Jain).

Challenges in Recombinant Protein Expression

Recombinant protein expression is one of the basic techniques in biotechnology which is commonly employed for the production of therapeutic, industrial or research proteins (Jayakrishnan et al., 2024). Although many developments have been made, there are still some

Frontier in Medical & Health Research
ISSN: (e) 3007-1607 (p) 3007-1593

obstacles to be overcome before efficient production of high quality recombinant proteins can be achieved. High levels of target protein expression is one major challenge (Tepap et al., 2023). Factors such as the strength of the promoter, bias of codon usage, mRNA stability, and host physiology can influence the expression of foreign genes in host systems such as bacteria, yeast, insect cells and mammalian cells (S. Zhang et al., 2025). In bacterial systems, particularly Escherichia coli, proteins are frequently synthesized as protein aggregates which are not biologically active, and have to undergo complex refolding procedures. An additional challenge is the correct folding and post-translational modifications of proteins (Bradley, 2022). Glycosylation, phosphorylation, disulfide bond formation, and other modifications are required for many eukaryotic proteins to function and/or be structurally correct. But bacteria are incapable of these modifications without complex expression systems that would generate inactive or unstable proteins (Lee, Hammarén, Savitski, & Baek, 2023).

Beyond these are problems of protein degradation, product toxicity and problems associated with the downstream processing (Shanu, Choudhary, Kumari, Anu, & Devi, 2024). Host proteases can degrade recombinants during expression, thus lowering yield and quality of the product (Z.-X. Zhang et al., 2022). There are some proteins that are toxic to the host cell, which will affect growth and reduce production efficiency (Z.-X. Zhang et al., 2022). However, challenges in large-scale manufacturing arise, such as consistency of expression, optimization of fermentation conditions and reduction of production costs (Du et al., 2022). Recombinant protein purification is often complicated and costly, especially when high levels of purity are necessary for pharmaceutical use (Eskandari, Leow, Rahman, & Oslan, 2024). In addition, it is essential to keep the level of such contaminants as host-cell proteins, endotoxins, or impurities at a level that is acceptable for regulatory requirements (Janghorban, Kazemi, Tormon, Ngaju, & Pandey, 2023). Suitable expression systems that combine high productivity, protein processing and cost-effectiveness are still an important research focus in biotechnology (Ahmad et al., 2026). These challenges are being addressed and efficiency of recombinant protein manufacturing is increasing with the use of genetic engineering, synthetic biology and bioprocess optimization (Tepap et al., 2023). However, obtaining reproducible yields of useful and quality recombinant proteins still remains as a major challenge in academic and industrial applications (Liu et al., 2025).

Future Directions and Emerging Technologies

Recombinant protein expression is a fast evolving field, fueled by the developments in molecular biology, genetic engineering, synthetic biology and bioprocess technology (Jayakrishnan et al., 2024). Future developments will focus on increased protein yield, protein quality, scalability and cost-effectiveness, and resolve current protein production limitations (Nath, 2026). Synthetic biology has been one of the most promising areas for designing and optimizing host cells to express their protein of interest (Listov, Goverde, Correia, & Fleishman, 2024). Cellular pathways can be altered, genes that are unwanted can be deleted, and hosts can be engineered to be better for protein folding, secretion and post-translational modification using genome editing methods like the CRISPR-Cas9 system. In addition, synthetic promoters, optimized codon usage, and artificial regulatory circuits are also being developed and optimized for precise control of gene expression and maximum recombinant protein production (Tepap et al., 2023).

A newer field of interest is cell-free protein synthesis systems, which are composed of purified cellular components used to synthesize proteins. These systems provide quick production, lower level of potential contamination, and are more flexible in expressing complex or toxic proteins (İncir & Kaplan, 2024). In addition, improvements in mammalian, insect and plant-based expression platforms are also increasing the possibilities for producing therapeutic proteins with human-like post-translational modifications. Furthermore, the use of artificial intelligence (AI) and machine learning has been expanded in order to anticipate protein structures, optimize

Frontier in Medical & Health Research
ISSN: (e) 3007-1607 (p) 3007-1593

expression conditions and enhance the design of bioprocesses (Phillip, 2026). The adoption of automation, high throughput screening, and digital biomanufacturing technologies are likely to speed up the process of protein development and lower production costs. New technologies like continuous bioprocessing, single use bioreactors and innovative purification technologies are improving manufacturing processes and product quality (Samaras, Micheletti, & Ding, 2022). In addition, new uses of recombinant proteins are under investigation for personalized medicine, tissue engineering, regenerative medicine, gene therapy and vaccine development (Akhtar & Gupta, 2024). However, the increasing need for biologics, biosimilars, and next generation therapeutics remains to be a major force in propelling innovation in protein expression technologies (Bas, 2025). The production of recombinant proteins is likely to be more efficient, sustainable, and widespread with the development of scientific knowledge and technological advancements (Popkova, De Bernardi, Tyurina, & Sergi, 2022). The future developments will be very important for solving the problems of the health care in the world and also for increasing the productivity of agricultural production, industrial biotechnology and opportunities for biomedical research (Dwivedi, 2025). In summary, emerging technologies will change the recombinant protein expression into a more sophisticated, precise and powerful platform for both science and commercial applications (Liu et al., 2025).

Conclusion

Recombinant protein expression is one of the most powerful and transformative technologies of modern biotechnology. It has allowed the production of large quantities of human life-saving, industrial, agricultural and scientific research proteins. This technology has enabled the development of life-saving therapeutic drugs, including insulin, erythropoietin, and monoclonal antibodies, to the production of safer recombinant vaccines, making it possible to dramatically advance disease treatment and prevention strategies around the world. Recombinant proteins have improved the precision, sensitivity and reliability of diagnostic tests for diseases, leading to improved clinical decisions and public health efficacy in diagnostics.Besides medicine, the recombinant protein technology has had a tremendous impact on industrial biotechnology, as it enabled developing highly efficient enzymes for use in food processing, detergent formulation, textile manufacturing and production of biofuels. Its use in agriculture has aided the development of more resistant and productive genetically improved crops, decreasing the need for chemical pesticides. In research, recombinant proteins remain invaluable tools for elucidating disease mechanisms, protein functions, and biological processes, and have proved to be invaluable in speeding up discoveries in molecular biology and drug development.Although tremendous progress has been made, limitations to the potential capabilities of recombinant protein technologies remain, including low expression yields, misfolded protein production, lack of post-translational modifications, protein degradation and the high costs of production. But ongoing developments in genetic engineering, synthetic biology, host optimization and bioprocess engineering are gradually correcting these shortcomings. In summary, recombinant protein expression is a pivotal technique in modern life sciences, connecting basic scientific research with its applications. It has continued to grow in several fields and is providing novel solutions to the challenges facing the world in the areas of health, food security and industrial sustainability. As technology advances, the use of recombinant protein technology is likely to continue to grow its versatility and applicability and will continue to impact the welfare and economies of the world.

References

Ahmad, T., Esposito, F., Rauf, M. A., Inam-ur-Raheem, M., Cirillo, T., & Aadil, R. M. (2026). A Review on Recent Processing and Bioprocessing Developments in Alternative Proteins: Sources, Modification Methods, Economic Feasibility, and Future Challenges. *Food and Bioprocess Technology, 19*(2), 54.

ISSN: (e) 3007-1607 (p) 3007-1593

Akhtar, Z. B., & Gupta, A. D. (2024). Advancements within molecular engineering for regenerative medicine and biomedical applications an investigation analysis towards a computing retrospective. *Journal of Electronics, Electromedical Engineering, and Medical Informatics, 6*(1), 54-72.

Ali, M. A., Abdellah, I. M., & Eletmany, M. R. (2023). Towards sustainable management of insect pests: Protecting food security through ecological intensification. *International Journal of Chemical and Biochemical Sciences, 24*(4), 386-394.

Bas, T. G. (2025). Formulation of Recombinant Therapeutic Proteins: Technological Innovation, Regulations, and Evolution Towards Buffer-Free Formulations. *Pharmaceutics, 17*(9), 1183.

binti Hafizal, R. A., binti Shamsudin, S. H., & Mohamed, E. PRODUCTION OF INSULIN USING RECOMBINANT DNA TECHNOLOGY.

Bradley, D. (2022). The evolution of post-translational modifications. *Current Opinion in Genetics & Development, 76*, 101956.

Carabetta, V. J., & Hardouin, J. (2022). Bacterial post-translational modifications. *Frontiers in Microbiology, 13*, 874602.

Collinge, D. B., & Sarrocco, S. (2022). Transgenic approaches for plant disease control: Status and prospects 2021. *Plant Pathology, 71*(1), 207-225.

Crnoglavac Popović, M., Stanišić, M., & Prodanović, R. (2024). State of the art technologies for high yield heterologous expression and production of oxidoreductase enzymes: Glucose oxidase, cellobiose dehydrogenase, horseradish peroxidase, and laccases in yeasts P. pastoris and S. cerevisiae. *Fermentation, 10*(2), 93.

Du, Y.-H., Wang, M.-Y., Yang, L.-H., Tong, L.-L., Guo, D.-S., & Ji, X.-J. (2022). Optimization and scale-up of fermentation processes driven by models. *Bioengineering, 9*(9), 473.

Dwivedi, D. (2025). Recent Trends in Biotechnology Engineering: Innovations and Applications across Sectors. AG *Volumes*, 82-90.

Eskandari, A., Leow, T. C., Rahman, M. B. A., & Oslan, S. N. (2024). Utilization and prospect of purification technologies in natural proteins, peptides and recombinant proteins. *Journal of Proteins and Proteomics, 15*(2), 233-257.

Feng, Z., Li, X., Fan, B., Zhu, C., & Chen, Z. (2022). Maximizing the production of recombinant proteins in plants: from transcription to protein stability. *International Journal of Molecular Sciences, 23*(21), 13516.

Garvey, M. (2022). Non-mammalian eukaryotic expression systems yeast and fungi in the production of biologics. *Journal of Fungi, 8*(11), 1179.

Gu, Y., Fan, F., Liu, Y., Chai, Y., Yuan, Y., & Chen, X. (2023). Cell-free protein synthesis system for bioanalysis: Advances in methods and applications. *TrAC Trends in Analytical Chemistry, 161*, 117015.

Guna, A., Nguyen, V. N., Stevens, T. A., & Voorhees, R. M. (2026). Membrane Protein Insertion in Mammalian Cells. *Annual Review of Biochemistry, 95*.

Hayat, S. M. G., Farahani, N., Golichenari, B., & Sahebkar, A. (2018). Recombinant protein expression in Escherichia coli (E. coli): what we need to know. *Current pharmaceutical design, 24*(6), 718-725.

Hoces, D., Miguens Blanco, J., & Hernández-López, R. A. (2023). A synthetic biology approach to engineering circuits in immune cells. *Immunological Reviews, 320*(1), 120-137.

İncir, İ., & Kaplan, Ö. (2024). Escherichia coli as a versatile cell factory: Advances and challenges in recombinant protein production. *Protein Expression and Purification, 219*, 106463.

ISSN: (e) 3007-1607 (p) 3007-1593

Jadhav, R. R., & Khare, D. (2024). Green biotherapeutics: overcoming challenges in plant-based expression platforms. *Plant Biotechnology Reports, 18*(4), 465-486.

Jain, N. INTRODUCTION TO BIOTECHNOLOGY: BIOLOGY FOR INNOVATION AND ADVANCEMENT. *BIOPROCESS ENGINEERING*, 1.

Janghorban, M., Kazemi, S., Tormon, R., Ngaju, P., & Pandey, R. (2023). Methods and analysis of biological contaminants in the biomanufacturing industry. *Chemosensors, 11*(5), 298.

Jayakrishnan, A., Wan Rosli, W. R., Tahir, A. R. M., Razak, F. S. A., Kee, P. E., Ng, H. S., . . . Tan, C. S. (2024). Evolving paradigms of recombinant protein production in pharmaceutical industry: a rigorous review. *Sci, 6*(1), 9.

Johnson, E. D. (2023). Hematology and immunology review. *Pediatric CCRN® Certification Review: Comprehensive Review, PLUS 300 Questions Based on the Latest Exam Blueprint*, 141.

Kathirvel, I., & Gayathri Ganesan, N. (2024). Computational strategies to enhance cell-free protein synthesis efficiency. *BioMedInformatics, 4*(3), 2022-2042.

Khanal, B., & Sharma, A. (2024). Codon Usage in Biotechnology: A Review of Strategies and Applications across Multiple Domains. *Authorea Preprints*.

Koff, W. C., Rappuoli, R., & Plotkin, S. A. (2023). Historical advances in structural and molecular biology and how they impacted vaccine development. *Journal of Molecular Biology, 435*(13), 168113.

Kollabathula, P., Katru, S., Tumarada, P., Ravuri, S., Zainab, A., & Velagala, S. K. (2025). Harnessing Recombinant DNA Technology for Modern Innovations: A Review. *International Journal of Dental Materials, 7*, 27-31.

Kumar, S., Singh, D., Mohan, S., Shakya, A., Diwakar, S. K., & Yadav, V. K. (2024). Genetically Modified Crops: Resistant To Pest And Environmental Stress: A Review. *Journal of Advanced Zoology, 45*(2).

Kumar, V., Barwal, A., Sharma, N., Mir, D. S., Kumar, P., & Kumar, V. (2024). Therapeutic proteins: developments, progress, challenges, and future perspectives. *3 Biotech, 14*(4), 112.

Lee, J. M., Hammarén, H. M., Savitski, M. M., & Baek, S. H. (2023). Control of protein stability by post-translational modifications. *Nature communications, 14*(1), 201.

Li, P., Zheng, J., Zhang, G., Yin, R., & Ren, L. (2025). Recent Progress on Rapid Diagnostic Methods for Viral Diseases. *Animals and Zoonoses*.

Li, Z.-M., Fan, Z.-L., Wang, X.-Y., & Wang, T.-Y. (2022). Factors affecting the expression of recombinant protein and improvement strategies in Chinese hamster ovary cells. *Frontiers in Bioengineering and Biotechnology, 10*, 880155.

Lim, W. A. (2022). The emerging era of cell engineering: Harnessing the modularity of cells to program complex biological function. *Science, 378*(6622), 848-852.

Listov, D., Goverde, C. A., Correia, B. E., & Fleishman, S. J. (2024). Opportunities and challenges in design and optimization of protein function. *Nature Reviews Molecular Cell Biology, 25*(8), 639-653.

Liu, M., Xiao, R., Li, X., Zhao, Y., & Huang, J. (2025). A comprehensive review of recombinant technology in the food industry: Exploring expression systems, application, and future challenges. *Comprehensive Reviews in Food Science and Food Safety, 24*(2), e70078.

Mohammed, A., Ibrahim, N. A., & Basher, N. S. (2025). Protein Engineering and Drug Discovery: Importance, Methodologies, Challenges, and Prospects. *Biomolecules, 15*(11), 1628.

Mohite, A., Shrivastava, D., Pawar, J. R., Bharti, N., Parveen, F., & Vikram, V. (2026). Recombinant Protein Production in Escherichia coli: Optimization Strategies. *Vascular and Endovascular Review, 9*(1), 15-30.

Nadhan, R., Isidoro, C., Song, Y. S., & Dhanasekaran, D. N. (2022). Signaling by LncRNAs: structure, cellular homeostasis, and disease pathology. *Cells, 11*(16), 2517.

Nath, S. (2026). Integration of microbial proteins into traditional food systems: innovations, challenges, and future perspectives. *Food Reviews International, 42*(3), 1532-1557.

Nikolados, E.-M., & Oyarzún, D. A. (2023). Deep learning for optimization of protein expression. *Current opinion in biotechnology, 81*, 102941.

Patel, A. K., Dong, C.-D., Chen, C.-W., Pandey, A., & Singhania, R. R. (2023). Production, purification, and application of microbial enzymes. In *Biotechnology of microbial enzymes* (pp. 25-57): Elsevier.

Phillip, A. (2026). The Role of Artificial Intelligence in Modern Biotechnology: A Comprehensive Review. *Journal of Applied Biotechnology Reports, 13*(1), 1899-1921.

Popkova, E. G., De Bernardi, P., Tyurina, Y. G., & Sergi, B. S. (2022). A theory of digital technology advancement to address the grand challenges of sustainable development. *Technology in Society, 68*, 101831.

Pouresmaeil, M., & Azizi-Dargahlou, S. (2023). Factors involved in heterologous expression of proteins in E. coli host. *Archives of microbiology, 205*(5), 212.

Raina, A., Villingiri, V., Jehan, S., & Qadir, S. A. (2022). Diagnostic and therapeutic biotechnology. In *Fundamentals and advances in medical biotechnology* (pp. 285-324): Springer.

Regmi, S., & Yoo, J. C. (2025). Recent trends in industrial resource manufacturing processes using biocatalysts. *Nepal Journal of Biotechnology, 13*(1), 90-102.

Samaras, J. J., Micheletti, M., & Ding, W. (2022). Transformation of biopharmaceutical manufacturing through single-use technologies: current state, remaining challenges, and future development. *Annual Review of Chemical and Biomolecular Engineering, 13*(1), 73-97.

Shakweer, W. M. E., Krivoruchko, A. Y., Dessouki, S. M., & Khattab, A. A. (2023). A review of transgenic animal techniques and their applications. *Journal of Genetic Engineering and Biotechnology, 21*(1), 55.

Shanu, K., Choudhary, S., Kumari, S., Anu, K., & Devi, S. (2024). Downstream processing for bio-product recovery and purification. In *Recent advances in bioprocess engineering and bioreactor design* (pp. 139-169): Springer.

Shih, S., Askinas, C., Caughey, S., Vernice, N., Berri, N., Dong, X., & Spector, J. A. (2023). Sourcing and development of tissue for transplantation in reconstructive surgery: A narrative review. *Journal of Plastic, Reconstructive & Aesthetic Surgery, 83*, 266-275.

Shokoohi, M., & Attar, T. (2024). Biomanufacturing for a sustainable future: unleashing the potential of biotechnology in pharmaceutical raw material production. *International Journal of New Findings in Health and Educational Sciences (IJHES), 2*(2), 142-153.

Slathia, P. S., Sagrika, Sharma, E., Khan, I. A., Thakur, R. S., & Sharma, P. (2023). Recombinant production of therapeutic proteins. In *Protein-based Therapeutics* (pp. 101-129): Springer.

Sliwczynski, L. (2022). A novel in planta strategy to identify inhibitors of malarial HSP101 proteins.

Sobti, R. C., & Sobti, A. (2023). *Biomedical research, medicine, and disease*: CRC Press.

Srivastava, M. P. GENETIC CODE AND PROTEIN SYNTHESIS: A COMPREHENSIVE OVERVIEW. *ELEMENTS OF*, 52.

Sunday, R. M., Iwuozor, C. R., Ujah-Samuel, I. R., Ibrahim, Z. R., Yussuff, N., Asala, T. M., & Ifedilichukwu, N. H. (2025). A Review on the Impact of Biotechnology on Agriculture, Medicine, Industries and the Environment. *NABDA JOURNAL OF BIOTECHNOLOGY RESEARCH, 4*(1), 6-14.

Frontier in Medical & Health Research
ISSN: (e) 3007-1607 (p) 3007-1593

Suriyaamporn, P., Pamornpathomkul, B., Patrojanasophon, P., Ngawhirunpat, T., Rojanarata, T., & Opanasopit, P. (2024). The artificial intelligence-powered new era in pharmaceutical research and development: A review. *Aaps Pharmscitech, 25*(6), 188.

Tepap, C. Z., Anissi, J., & Bounou, S. (2023). Recent strategies to achieve high production yield of recombinant protein: A review. *Journal of Cellular Biotechnology, 9*(1), 25-37.

Yadav, J., Marwah, H., & Kumar, C. (2025). Synthetic biology and metabolic engineering paving the way for sustainable next-gen biofuels: a comprehensive review. *Energy Advances, 4*(10), 1209-1228.

Yadav, M., Sarkar, S., & Kumar, A. (2024). Diversifying expression platforms for biopharmaceuticals and industrial enzymes. In *Industrial Microbiology and Biotechnology: A New Horizon of the Microbial World* (pp. 573-603): Springer.

Zawada, J. F., Burgenson, D., Yin, G., Hallam, T. J., Swartz, J. R., & Kiss, R. D. (2022). Cell-free technologies for biopharmaceutical research and production. *Current opinion in biotechnology, 76*, 102719.

Zhang, L., Gao, J., Zhang, X., Wang, X., Wang, T., & Zhang, J. (2024). Current strategies for the development of high-yield HEK293 cell lines. *Biochemical Engineering Journal, 205*, 109279.

Zhang, S., Wang, Z., Luo, Q., Zhou, L., Du, X., & Ren, Y. (2025). Effects of microbes on insect host physiology and behavior mediated by the host immune system. *Insects, 16*(1), 82.

Zhang, Z.-X., Nong, F.-T., Wang, Y.-Z., Yan, C.-X., Gu, Y., Song, P., & Sun, X.-M. (2022). Strategies for efficient production of recombinant proteins in Escherichia coli: alleviating the host burden and enhancing protein activity. *Microbial cell factories, 21*(1), 191.

Яковенко, Д., & Бородай, В. (2025). Global market of biological products: trends, challenges, and future outlook. *Агроекологічний журнал*(4), 19-28.