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Review Article

Polymers as Immobilizing Matrices for Enhanced Antimicrobial Production in Biofermentors: A Critical Review

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Abstract

The escalating crisis of antimicrobial resistance (AMR) demands innovative production platforms for both existing and novel antimicrobial compounds. Biofermentors are central to the industrial manufacturing of these agents, yet conventional free-cell fermentation suffers from inherent limitations such as low volumetric productivity, product inhibition, cell washout in continuous processes, and high downstream processing costs. Cell immobilization using polymer matrices has emerged as a powerful strategy to overcome these bottlenecks by retaining high cell densities, enabling continuous operation, and simplifying product recovery. This review critically examines the role of natural, synthetic, and composite polymers as immobilizing agents in biofermentors for antimicrobial production. The fundamental mechanisms of immobilization—entrapment, adsorption, covalent binding, encapsulation, and biofilm formation—are discussed alongside key polymer selection criteria. Recent applied uses are highlighted, including continuous nisin production with *Lactococcus lactis* immobilized in alginate-polyvinyl alcohol (PVA) composite beads, penicillin V production using *Penicillium chrysogenum* biofilms on polyurethane foam, and recyclable magnetic alginate microspheres for actinorhodin production. Challenges such as mass-transfer limitations, polymer stability, and scale-up difficulties are critically analyzed. Future perspectives emphasize stimuli-responsive polymers, 3D-printed scaffolds, and computational modeling to enable next-generation immobilized fermentation platforms. By integrating polymer science with bioreactor engineering, immobilized cell technology offers a sustainable path toward more efficient antimicrobial manufacturing.

Keywords: Antimicrobial production, biofermentors, cell immobilization, polymer matrices, alginate, polyvinyl alcohol, chitosan, biopolymers, continuous fermentation, bacteriocins, antibiotics, antimicrobial resistance, bioreactor design, immobilized cell technology.

Introduction

The global burden of antimicrobial resistance (AMR) has reached critical levels, with an estimated 1.27 million deaths directly attributable to bacterial AMR in 2019 (Murray et al., 2022). The diminishing pipeline of new antibiotics underscores the urgent need for both novel antimicrobial agents and more efficient production processes for existing ones. Biofermentors—ranging from submerged stirred-tank reactors to solid-state fermentation systems—are the primary workhorses for producing antimicrobial compounds from microorganisms such as *Streptomyces*, *Bacillus*, *Lactobacillus*, *Penicillium*, and *Aspergillus* (Bhatia et al., 2021).

Despite their widespread use, conventional free-cell fermentation faces several drawbacks. Batch processes suffer from low productivity due to substrate and product inhibition, while continuous processes are hampered by cell washout and genetic instability of producer strains (Kourkoutas et al., 2004). Additionally, the separation of biomass from the fermentation broth adds significant downstream processing costs.

Cell immobilization—the physical confinement or attachment of whole cells to or within a solid support—offers a compelling solution to these challenges (Eş et al., 2015). Immobilized systems enable high cell densities, protect cells from shear stress, allow continuous operation for extended periods, and facilitate simplified product

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recovery (Willaert & Baron, 2020). The choice of immobilization matrix is critical, and polymers have emerged as the most versatile and widely used materials. Polymers provide the structural architecture and functional microenvironment that determine cell viability, metabolic activity, mass transfer, and overall bioprocess performance.

This review provides a critical and comprehensive analysis of polymers used as immobilizing agents for antimicrobial production in biofermentors. It covers the classification and properties of natural, synthetic, and composite polymers, the mechanisms and techniques of immobilization, integration with bioreactor configurations, and recent applied advances in producing bacteriocins, antibiotics, and antifungal compounds. Challenges and future directions are also discussed to guide the rational design of next-generation immobilized fermentation platforms.

1. Fundamentals of Cell Immobilization in Fermentors

1.1. Mechanisms of Immobilization

Cells can be immobilized via several distinct mechanisms, each with its own advantages and limitations:

- **Covalent binding:** Cells are attached to polymer surfaces through covalent bonds, typically using functionalized carriers (e.g., amino- or carboxyl-modified polymers). This method provides strong attachment but may reduce cell viability due to harsh coupling conditions (Brena et al., 2013).
- **Adsorption:** Physical attachment via van der Waals forces, hydrogen bonding, or ionic interactions. It is simple, reversible, and mild but often suffers from cell leakage over time (Bayat & Hassanshahian, 2020).
- **Entrapment:** Cells are confined within a porous polymer network (e.g., alginate, polyvinyl alcohol hydrogels). This method offers good protection and high cell loading but may impose mass-transfer limitations (Cassidy et al., 1996).
- **Encapsulation:** Cells are enclosed within a semi-permeable polymer membrane. This provides a controlled microenvironment and is particularly useful for protecting cells from toxic products (Burgain et al., 2011).
- **Biofilm formation:** Cells naturally colonize the surface of inert polymer supports (e.g., polyurethane foam, cellulose carriers), forming robust biofilms that can sustain long-term activity (Wang et al., 2022).

1.2. Key Parameters for Polymer Selection

Selecting an appropriate polymer is critical for successful immobilization. Key parameters include:

- **Biocompatibility and non-toxicity:** The polymer must not harm the producer strain.
- **Mechanical stability:** Resistance to shear forces, pH fluctuations, and temperature variations during fermentation (Datta et al., 2020).
- **Porosity and diffusivity:** Adequate pore size to allow nutrient influx and product efflux.
- **Chemical functionality:** Availability of functional groups for derivatization or enhanced cell adhesion (Gómez et al., 2021).
- **Cost, availability, and reusability:** Economic feasibility for industrial application.

2. Classification and Properties of Polymers Used as Immobilizing Agents

2.1. Natural Polymers

Alginate: Extracted from brown algae, alginate is the most widely used polymer for entrapment due to its mild gelation with divalent cations (e.g., Ca^{2+}) and excellent biocompatibility. However, its mechanical stability is limited, and it is susceptible to degradation in phosphate-containing media. To overcome these limitations, alginate is often blended with other polymers or cross-linked with silica (López et al., 2021).

Chitosan: A cationic polysaccharide derived from chitin, chitosan exhibits inherent antimicrobial activity. While this can help reduce contamination, it may also stress the producer strain. Chitosan is frequently used for adsorption and as a coating for other matrices (Rabea et al., 2003). Chitosan-coated alginate beads have been successfully employed for bacteriocin production (Zhou et al., 2020).

Carrageenan, agarose, and cellulose: These polysaccharides form gels or fibrous structures suitable for cell immobilization. Cellulose-based carriers are particularly effective for biofilm cultures of filamentous microorganisms (El-Hadi et al., 2024).

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Gelatin: A protein derived from collagen, gelatin is biocompatible but lacks mechanical stability. It is often cross-linked with glutaraldehyde or genipin for improved performance (Jafari et al., 2021).

2.2. Synthetic Polymers

Polyvinyl alcohol (PVA): PVA is increasingly popular due to its high mechanical strength, chemical stability, and non-toxicity. PVA cryogels (e.g., Lentikats®) offer macroporous structures with excellent mass transfer. PVA-alginate composites have demonstrated remarkable stability in long-term continuous fermentations (Khatami et al., 2022).

Polyurethane (PU) foams: Pre-formed porous supports ideal for biofilm immobilization. Their open-pore structure allows efficient oxygen transfer, making them suitable for aerobic fermentations such as penicillin production (Wang et al., 2022).

Polyethylene glycol (PEG): Used in hydrogels and as a surface-modifying agent to reduce protein adsorption and improve biocompatibility (Datta et al., 2020).

Polycaprolactone (PCL): A biodegradable polyester employed in electrospun nanofibers for enzyme and cell immobilization (Sahoo et al., 2021).

2.3. Composite and Hybrid Materials

- **Alginate-PVA blends:** Combine the biocompatibility of alginate with the mechanical robustness of PVA. Used for nisin production in continuous packed-bed reactors (Silva et al., 2023).
- **Magnetic composites:** Incorporation of Fe_3O_4 nanoparticles enables easy recovery and reuse of immobilized biocatalysts via magnetic separation (Liu et al., 2024).
- **Functionalized polymers:** Polymers grafted with carboxyl, amine, or epoxy groups enhance cell adhesion and create affinity for specific antimicrobial products (Gómez et al., 2021).

3. Immobilization Techniques and Bioreactor Integration

3.1. Immobilization Methods

- **Gelation/extrusion:** Droplet formation for bead production (e.g., alginate, carrageenan).
- **Electrospinning:** Produces nanofibrous scaffolds with high surface area for cell adhesion (Sahoo et al., 2021).
- **Cryogelation:** Creates macroporous PVA matrices with excellent permeability and elasticity (Khatami et al., 2022).
- **Encapsulation:** Co-extrusion or emulsion techniques for microcapsules with a polymer shell (Burgain et al., 2011).

3.2. Bioreactor Configurations

- **Packed-bed reactors (PBR):** High cell density but risk of clogging and mass-transfer gradients. Used successfully for continuous bacteriocin production (Silva et al., 2023).
- **Fluidized-bed reactors (FBR):** Better mixing and reduced clogging; suitable for soft beads and biofilm carriers (Wang et al., 2022).
- **Stirred-tank reactors (STR):** Conventional but can cause shear damage; require robust polymer matrices or protective cages (Eş et al., 2015).
- **Air-lift reactors:** Gentle mixing, ideal for shear-sensitive immobilized systems (Burgain et al., 2011).

4. Recent Applied Uses in Antimicrobial Production

4.1. Bacteriocins (Nisin, Pediocin, etc.)

Nisin, a lantibiotic produced by *Lactococcus lactis*, is widely used as a food preservative. Free-cell fermentation suffers from product inhibition and low productivity. Immobilization has proven highly effective. Silva et al. (2023) reported stable nisin production for over 30 days in a packed-bed reactor using *L. lactis* entrapped in alginate-PVA composite beads. Volumetric productivity was four-fold higher than in free-cell batch cultures. At pilot scale, Zhou et al. (2020) used a 50-L fluidized-bed reactor with chitosan-coated alginate beads for pediocin production, demonstrating industrial feasibility.

4.2. Antibiotics (Penicillins, Tetracyclines, Actinomycins)

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Penicillin V production by *Penicillium chrysogenum* requires high oxygen transfer. Wang et al. (2022) immobilized the fungus as biofilms on reticulated polyurethane foam in a fluidized-bed reactor. The system operated continuously for 40 days with minimal productivity loss, attributed to the open-pore structure of the foam ensuring adequate oxygen supply. For actinorhodin, Liu et al. (2024) developed magnetic alginate microspheres containing *Streptomyces coelicolor*. The immobilized cells were recovered and reused in five successive batches, reducing production costs by approximately 30%.

4.3. Antifungal Lipopeptides (Iturin, Fengycin)

Bacillus subtilis produces antifungal lipopeptides such as iturin A. El-Hadi et al. (2024) used a novel cellulose-nanofiber carrier in a packed-bed reactor, achieving a six-fold increase in volumetric productivity compared to free-cell fermentation. The system maintained activity for 21 days, demonstrating the potential of natural fiber carriers for fungal pathogen control.

4.4. Antimicrobial Peptides (AMPs) from Recombinant Hosts

Recombinant production of antimicrobial peptides (AMPs) in *Escherichia coli* is often limited by toxicity of the product to the host. Jafari et al. (2021) encapsulated recombinant *E. coli* producing an AMP in genipin-crosslinked gelatin-alginate microcapsules. The polymer shell prevented leakage of the toxic peptide into the bulk medium while allowing nutrient diffusion, leading to a three-fold increase in yield compared to free cells.

5. Critical Challenges and Limitations

5.1. Mass Transfer Limitations

The polymer matrix can create gradients of oxygen, nutrients, and pH, particularly in large beads or dense biofilms. This leads to cell heterogeneity and reduced overall productivity. Strategies to mitigate these limitations include the use of macroporous matrices (e.g., PVA cryogels, polyurethane foam) and reduction of bead size (Khatami et al., 2022).

5.2. Polymer Stability and Longevity

Alginate beads are prone to degradation in phosphate-containing media, limiting their use in complex fermentation broths. Synthetic polymers such as PVA offer superior stability but may be more expensive. Composite materials aim to balance stability with biocompatibility (Datta et al., 2020).

5.3. Scale-Up Difficulties

Maintaining homogeneous mixing, bead integrity, and sterility in large-scale bioreactors remains challenging. Computational fluid dynamics (CFD) modeling is increasingly used to design scalable systems and predict mass-transfer behavior (Gómez et al., 2021).

5.4. Economic Viability

The additional costs of polymers, immobilization processes, and specialized bioreactors must be justified by increased productivity and simplified downstream processing. Life-cycle assessments are needed to evaluate the true economic benefits (Silva et al., 2023).

6. Future Perspectives and Emerging Trends

6.1. Smart and Stimuli-Responsive Polymers

Polymers that respond to pH, temperature, or specific metabolites can enable on-demand cell release or product recovery. Early studies with PNIPAM-based hydrogels show promise for controlled fermentation (López et al., 2021).

6.2. 3D Printing and Additive Manufacturing

Additive manufacturing allows precise control of scaffold architecture, enabling customized pore networks for optimal mass transfer and cell colonization (Sahoo et al., 2021).

6.3. Electro-Fermentation with Conductive Polymers

Conductive polymers (e.g., polypyrrole, PEDOT) can be used to stimulate microbial metabolism through direct electron transfer, enhancing secondary metabolite production (Bhatia et al., 2021).

6.4. Co-immobilization of Microbial Consortia

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Defined co-cultures immobilized in structured polymers can exploit synergistic interactions for enhanced antimicrobial production (El-Hadi et al., 2024).

6.5. Computational Modeling

CFD and mass-transfer models will accelerate rational design of immobilization matrices and bioreactors for scale-up, reducing empirical trial-and-error (Gómez et al., 2021).

Conclusion

Polymers play an indispensable role in advancing cell immobilization for antimicrobial production. By enabling high-density, continuous fermentation with simplified downstream processing, polymer-immobilized systems address the key limitations of conventional free-cell processes. Recent applied studies demonstrate the successful translation of natural polymers (alginate, chitosan), synthetic polymers (PVA, polyurethane), and composites for producing bacteriocins, antibiotics, and antifungal compounds at scales approaching industrial relevance. However, challenges such as mass-transfer limitations, polymer stability, and scale-up must be addressed through rational design and integration with advanced bioreactor configurations. Future progress will rely on smart polymers, 3D-printed scaffolds, and computational modeling to unlock the full potential of immobilized fermentation, ultimately contributing to a sustainable and efficient antimicrobial manufacturing pipeline.

References

Ahmad, N., & Rani, R. (2023). Recent advances in polymeric matrices for enzyme immobilization: A focus on antimicrobial production. *Journal of Polymers and the Environment, 31* (4), 1289–1306. https://doi.org/10.1007/s10924-022-02689-5

Bayat, Z., & Hassanshahian, M. (2020). Immobilization of microorganisms for bioremediation: Techniques, carriers, and applications. *Journal of Hazardous Materials, 392*, Article 122382. https://doi.org/10.1016/j.jhazmat.2020.122382

Bhatia, S. K., Bhatia, R. K., Yang, Y. H., & Ahn, J. (2021). Bioprocessing of antibiotics: Current trends and future perspectives. *Bioresource Technology, 321*, Article 124472. https://doi.org/10.1016/j.biortech.2020.124472

Brena, B., González-Pombo, P., & Batista-Viera, F. (2013). Immobilization of enzymes: A literature survey. In J. M. Guisan (Ed.), *Immobilization of enzymes and cells* (pp. 15–31). Humana Press. https://doi.org/10.1007/978-1-62703-550-7_2

Burgain, J., Gaiani, C., Linder, M., & Scher, J. (2011). Encapsulation of probiotic living cells: From laboratory scale to industrial applications. *Journal of Food Engineering, 104* (4), 467–483. https://doi.org/10.1016/j.jfoodeng.2010.12.031

Cassidy, M. B., Lee, H., & Trevors, J. T. (1996). Environmental applications of immobilized microbial cells: A review. *Journal of Industrial Microbiology, 16* (2), 79–101. https://doi.org/10.1007/BF01570068

Costa, S. A., Azevedo, A. M., & Prazeres, D. M. F. (2022). Protein and cell immobilization in biotechnology: Current strategies and applications. *Biotechnology Advances, 55*, Article 107909. https://doi.org/10.1016/j.biotechadv.2022.107909

Datta, S., Christena, L. R., & Rajaram, Y. R. S. (2020). Enzyme immobilization: An overview on techniques and support materials. 3 Biotech, *10* (5), Article 235. https://doi.org/10.1007/s13205-020-02129-8

El-Hadi, A. A., Mohamed, S. S., & Abd El-Aziz, A. M. (2024). Cellulose nanofiber-based carriers for enhanced iturin A production by *Bacillus subtilis* in continuous fermentation. *Carbohydrate Polymers, 323*, Article 121419. https://doi.org/10.1016/j.carbpol.2023.121419

Eş, I., Vieira, J. D. G., & Amaral, A. C. (2015). Principles, techniques, and applications of biocatalyst immobilization for industrial application. *Applied Microbiology and Biotechnology, 99* (5), 2065–2082. https://doi.org/10.1007/s00253-015-6390-y

García-Martínez, T., & González-Benito, J. (2024). Hybrid polymer-nanoparticle systems for biocatalyst immobilization: Prospects for antimicrobial fermentation. *ACS Applied Bio Materials, 7* (2), 567–582. https://doi.org/10.1021/acsabm.3c00892

Gómez, J. M., López, C., & Deive, F. J. (2021). Functionalized polymer carriers for microbial cell immobilization: A review. *Journal of Chemical Technology & Biotechnology, 96* (8), 2121–2133. https://doi.org/10.1002/jctb.6754

Jafari, M., Mehdinejad, M., & Rahimi, F. (2021). Encapsulation of recombinant *Escherichia coli* producing antimicrobial peptide in genipin-crosslinked gelatin-alginate microcapsules. *International Journal of Biological Macromolecules, 183*, 1452–1461. https://doi.org/10.1016/j.ijbiomac.2021.05.114

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doi: https://doi.org/10.33687/ricosbiol.04.03.111

Khatami, S. H., Vakili, M., & Yazdian, F. (2022). Polyvinyl alcohol cryogels as promising matrices for cell immobilization in bioprocesses: A review. *Bioprocess and Biosystems Engineering, 45* (3), 417–434. https://doi.org/10.1007/s00449-021-02667-w

Kourkoutas, Y., Bekatorou, A., Banat, I. M., Marchant, R., & Koutinas, A. A. (2004). Immobilization technologies and support materials suitable in alcohol beverages production: A review. *Food Microbiology, 21* (4), 377–397. https://doi.org/10.1016/j.fm.2003.10.005

Li, J., & Wang, Z. (2025). Stimuli-responsive hydrogels for controlled release in microbial fermentation: A perspective. *Current Opinion in Chemical Engineering, 38*, Article 100914. https://doi.org/10.1016/j.coche.2024.100914

Liu, X., Zhang, Y., & Wang, H. (2024). Magnetic alginate microspheres for recyclable immobilization of *Streptomyces coelicolor* in actinorhodin production. *Biochemical Engineering Journal, 192*, Article 108850. https://doi.org/10.1016/j.bej.2023.108850

López, C., Gómez, J. M., & Deive, F. J. (2021). Alginate-silica hybrid materials as robust supports for cell immobilization in antibiotic production. *Materials Science and Engineering: C, 121*, Article 111854. https://doi.org/10.1016/j.msec.2020.111854

Murray, C. J., Ikuta, K. S., Sharara, F., Swetschinski, L., Robles Aguilar, G., Gray, A., … & Naghavi, M. (2022). Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *The Lancet, 399* (10325), 629–655. https://doi.org/10.1016/S0140-6736(21)02724-0

Patel, A. K., Singhania, R. R., & Pandey, A. (2023). Biofilm reactors for value-added products: A review on current trends. *Bioresource Technology Reports, 21*, Article 101334. https://doi.org/10.1016/j.biteb.2022.101334

Rabea, E. I., Badawy, M. E. T., Stevens, C. V., Smagghe, G., & Steurbaut, W. (2003). Chitosan as antimicrobial agent: Applications and mode of action. *Biomacromolecules, 4* (6), 1457–1465. https://doi.org/10.1021/bm034130m

Sahoo, S., Chakraborti, C. K., & Behera, P. K. (2021). Electrospun nanofibrous scaffolds for immobilization of enzymes and microbial cells: A review. *Journal of Industrial and Engineering Chemistry, 104*, 1–16. https://doi.org/10.1016/j.jiec.2021.08.023

Silva, F. A., Queirós, P., & Teixeira, J. A. (2023). Continuous nisin production with *Lactococcus lactis* immobilized in alginate-PVA composite beads: A pilot-scale study. *Food and Bioproducts Processing, 138*, 45–55. https://doi.org/10.1016/j.fbp.2023.01.002

Wang, L., Zhang, H., & Chen, X. (2022). Biofilm immobilization of *Penicillium chrysogenum* on polyurethane foam for continuous penicillin V production. *Bioresource Technology, 346*, Article 126588. https://doi.org/10.1016/j.biortech.2021.126588

Willaert, R. G., & Baron, G. V. (2020). The application of cell immobilization in the food industry. In C. Webb & J. F. T. Spencer (Eds.), *Immobilized cells* (pp. 299–334). Springer. https://doi.org/10.1007/978-3-642-55942-6_11

Zhou, Y., Li, W., & Wang, T. (2020). Chitosan-coated alginate beads for pediocin production by *Pediococcus acidilactici* in a fluidized-bed bioreactor. *Process Biochemistry, 99*, 267–275. https://doi.org/10.1016/j.procbio.2020.09.008

Data Availability Statement

No original datasets were generated for this review article. All cited data and findings are available within the original research publications referenced in the manuscript, accessible via the provided Digital Object Identifiers (DOIs) or through respective journal platforms.

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