

BIOPOLYMERS AS THERAPEUTIC ADJUVANTS

INNOVATIONS AND ADVANCEMENTS

Editors:

Sudhanshu Mishra

Smriti Ojha

Shashi Kant Singh

Rishabha Malviya

Saurabh Kumar Gupta

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Biopolymers as Therapeutic Adjuvants: Innovations and Advancement

Edited by

Sudhanshu Mishra

*Faculty of Pharmaceutical Sciences Mahayogi Gorakhnath
University
Gorakhpur 273007, Uttar Pradesh
India*

Smriti Ojha

*Department of Pharmaceutical Science & Technology
Madan Mohan Malaviya University of Technology
Gorakhpur, Uttar Pradesh
India*

Shashi Kant Singh

*Faculty of Pharmaceutical Sciences
Mahayogi Gorakhnath University
Gorakhpur 273007, Uttar Pradesh
India*

Rishabha Malviya

*Department of Pharmacy
Galgotias University
Greater Noida, Uttar Pradesh
India*

&

Saurabh Kumar Gupta

*Rameshwaram Institute of Technology & Management
Lucknow, Uttar Pradesh
India*

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FOREWORD

The field of biopolymers represents a remarkable confluence of biology, chemistry, and material science, offering innovative solutions to some of the most pressing challenges in medicine and therapeutics. From their humble beginnings as naturally occurring substances to their sophisticated modern-day applications, biopolymers have continuously evolved, providing the scientific community with tools for creating safer, more effective, and personalized healthcare solutions.

The book *Biopolymers as Therapeutic Adjuvants: Innovations and Advancement* arrives at a pivotal moment in this field, bridging the gap between foundational knowledge and the latest advancements. It captures the spirit of interdisciplinary collaboration that defines modern science, bringing together contributions from seasoned researchers and emerging scholars. Their collective effort paints a detailed picture of the transformative potential of biopolymers across diverse domains, including drug delivery, tissue engineering, cancer therapy, and beyond.

The book invites readers to not only absorb its wealth of knowledge but to actively participate in shaping the future of biopolymer applications. By fostering a community of inquiry and shared purpose, it becomes more than a resource; it is a catalyst for advancement in therapeutic science.

I commend Mr. Sudhanshu Mishra and his dedicated team of contributors for producing a publication that is both scientifically rigorous and forward-looking. This work serves as a beacon of inspiration, guiding researchers and practitioners toward the shared goal of improving human health through biopolymer innovation.

With best wishes.

Pranesh Kumar
Institute of Pharmacy
University of Lucknow
Lucknow, Uttar Pradesh
India

PREFACE

Biopolymers, derived from natural sources or synthesized to mimic biological molecules, have emerged as revolutionary tools in therapeutics and drug delivery systems. The unique combination of biocompatibility, biodegradability, and tunable properties positions biopolymers as pivotal components in advancing healthcare technologies. This book, ***Biopolymers as Therapeutic Adjuvants: Innovations and Advancement***, delves into the multidisciplinary realm of biopolymer science, encompassing its historical evolution, scientific fundamentals, and cutting-edge applications. The chapters are thoughtfully curated to provide a comprehensive understanding of the subject. The book begins with an exploration of the historical context and foundational principles of biopolymers, tracing their development from early discoveries to their contemporary therapeutic relevance. Subsequent chapters address the diverse biological sources, chemical characteristics, and extraction methods of biopolymers, providing readers with a solid scientific foundation.

A detailed discussion on synthetic methodologies and the physicochemical properties of biopolymers sets the stage for understanding their pharmacokinetics and pharmacodynamics. Moving beyond the basics, the text explores the role of biopolymers in modern therapeutics, including their use in chemotherapeutic regimens, synergistic drug combinations, and disease-targeting strategies through nano-based systems. Special emphasis is given to advancements in the field, such as the integration of artificial intelligence in biopolymer engineering and the development of stimuli-responsive and enzyme-activated drug delivery systems. Readers will also discover applications in tissue engineering, bone regeneration, and autoimmune disease immunotherapy, highlighting the transformative potential of biopolymers in addressing complex medical challenges.

Authored by a diverse group of experts and researchers, this book serves as a vital resource for professionals, academics, and students involved in pharmaceutical sciences, biomaterials research, and biomedical engineering. By merging theoretical insights with practical applications, it aspires to inspire further innovation and exploration in the burgeoning field of biopolymer therapeutics.

We hope this book enriches your understanding of biopolymers and motivates you to contribute to this fascinating and impactful area of research.

Sudhanshu Mishra

Faculty of Pharmaceutical Sciences Mahayogi Gorakhnath University
Gorakhpur 273007, Uttar Pradesh
India

Smriti Ojha

Department of Pharmaceutical Science & Technology
Madan Mohan Malaviya University of Technology
Gorakhpur, Uttar Pradesh
India

Shashi Kant Singh

Faculty of Pharmaceutical Sciences
Mahayogi Gorakhnath University
Gorakhpur 273007, Uttar Pradesh
India

iii

Rishabha Malviya
Department of Pharmacy
Galgotias University
Greater Noida, Uttar Pradesh
India

&

Saurabh Kumar Gupta
Rameshwaram Institute of Technology & Management
Lucknow, Uttar Pradesh
India

List of Contributors

Ajay Pandey	Department of Pharmaceutical Engineering and Technology, Indian Institute of Technology (Banaras Hindu University), Varanasi, India
Aamir Anwar	Department of Pharmacy, Integral University, Lucknow, Uttar Pradesh, India
Asad Ahmad	Department of Pharmacy, Integral University, Lucknow, Uttar Pradesh, India
Anindita De	Department of Pharmaceutics, College of Pharmacy, JSS University, Noida 201301, India
Anubhav Anand	Shri Ramswaroop College of Engineering and Management (Pharmacy), Lucknow, Uttar Pradesh, India
Aarti Tiwari	Institute of Pharmacy, Dr Rammanohar Lohia Avadh University, Ayodhya, Uttar Pradesh, India
Ajay Kumar Shukla	Institute of Pharmacy, Dr Rammanohar Lohia Avadh University, Ayodhya, Uttar Pradesh, India
Bharat Mishra	Institute of Pharmacy, DR. Shakuntala Misra National Rehabilitation University, Lucknow, 226017, India
Bhaveshwari Wagh	Institute of Pharmaceutical Sciences, Faculty of Pharmacy, Parul University, Vadodara, Gujarat, 391760, India
Bishambar Singh	PHTI Department, SMS Medical College and Hospital, Jaipur, Rajasthan, 302017, India
Deepak Kumar	Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur, Uttar Pradesh, 273007, India
Ganesh Lal	KJ College of Pharmacy, Babatpur, 221006, Varanasi, India
Gaurish Narayan Singh	Institute of Pharmacy, Deen Dayal Upadhyaya Gorakhpur University, Gorakhpur, 273009, Uttar Pradesh, India
Gowthamarajan Kuppusamy	Department of Pharmaceutics, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty 643001, Tamil Nadu, India
Juhi Tiwari	Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur, Uttar Pradesh, 273007, India
Kunal Agam Kanujia	Institute of Pharmacy, Dr Rammanohar Lohia Avadh University, Ayodhya, Uttar Pradesh, India
Manoj Kumar Mishra	Shambhunath Institute of Engineering and Technology, Prayagraj, Uttar Pradesh, India
Manya Modi	Department of Pharmacy, Banasthali Vidyapith, Rajasthan, 304022, India
Nancy Gupta	Department of Pharmacy, Banasthali Vidyapith, Rajasthan, 304022, India
Nandani Jayaswal	Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur, 273007, Uttar Pradesh, India
Piyush Anand	Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur, Uttar Pradesh, 273007, India

Pooja Pooja	Department of Pharmacy, Banasthali Vidyapith, Rajasthan, 304022, India
Pooja Jaiswal	Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur, 273007, Uttar Pradesh, India
Piyush Anand	Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur, Uttar Pradesh, 273007, India
Rufaida Wasim	Department of Pharmacy, Integral University, Lucknow, Uttar Pradesh, India
Rama Sankar Dubey	Department of Pharmacy, MMM University, Gorakhpur, Uttar Pradesh, India
Sharda Sambhakar	Department of Pharmacy, Banasthali Vidyapith, Rajasthan, 304022, India
Shreya Maddesiya	Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur, Uttar Pradesh, 273007, India
Taufik Mulla	Institute of Pharmaceutical Sciences, Faculty of Pharmacy, Parul University, Vadodara, Gujarat, 391760, India
Tarique Mahmood	Department of Pharmacy, Integral University, Lucknow, Uttar Pradesh, India
Srishti Verma	Department of Pharmacy, Banasthali Vidyapith, Rajasthan, 304022, India
Saba Parveen	Department of Pharmacy, Madan Mohan Malaviya University of Technology, Gorakhpur, Uttar Pradesh, India
Sonali Jayronia	Department of Pharmaceutics, College of Pharmacy, JSS University, Noida 201301, India
Young Joon Park	Department of Formulation and Drug Delivery, College of Pharmacy, Ajou University, 206 Worldcup-ro, Yeongtong-gu, Suwon-si 16499, Republic of Korea
Surbhi Gupta	Ashoka Institute of Technology and Management, Varanasi, Uttar Pradesh, India
Vimal Kumar Yadav	Institute of Pharmacy, Dr Rammanohar Lohia Avadh University, Ayodhya, Uttar Pradesh, India
Vishnu Prasad Yadav	Institute of Pharmacy, Dr Rammanohar Lohia Avadh University, Ayodhya, Uttar Pradesh, India

CHAPTER 1**Introduction and Historical Overview of Biopolymers as Therapeutics****Bhaveshwari Wagh^{1,*} and Taufik Mulla¹**¹ *Institute of Pharmaceutical Sciences, Faculty of Pharmacy, Parul University, Vadodara, Gujarat 391760, India*

Abstract: Biopolymers are naturally occurring polymers that are produced by living organisms. They include proteins, nucleic acids, polysaccharides, and other biomolecules. Due to their biocompatibility, biodegradability, and low toxicity, biopolymers have gained significant attention in medicine, particularly as therapeutic agents. As a class of materials, biopolymers offer unique advantages over synthetic polymers, including the ability to interact with biological systems more naturally. Their applications span drug delivery, tissue engineering, wound healing, and gene therapy, making them essential to modern biomedical research. The historical development of biopolymers as therapeutics spans from ancient uses in traditional medicine to modern biotechnology advancements. In the 19th century, the foundation was laid with the discovery of proteins and nucleic acids. In the early 20th century, therapeutic use of proteins such as insulin and polysaccharides like heparin emerged. The mid-20th century marked the rise of nucleic acids as therapeutic agents, while the late 20th century introduced biotechnology, enabling large-scale production of biopolymer-based drugs. In the 21st century, innovations in drug delivery, gene therapy, and regenerative medicine have further advanced the use of biopolymers in treating diseases.

Keywords: Biocompatibility, Biodegradability, Biopolymers, Drug delivery, Polysaccharides, Therapeutic agents, Tissue engineering.

INTRODUCTION TO BIOPOLYMERS IN THERAPEUTICS

Biopolymers are a remarkable class of naturally occurring polymers produced by living organisms, including plants, animals, and microbes. These polymers differ fundamentally from synthetic ones, as they are derived from renewable biological sources rather than petroleum-based resources [1]. Due to their inherent biodegradability and biocompatibility, biopolymers have garnered increasing attention in the medical field, where there is a constant need for materials that can

* **Corresponding author Bhaveshwari Wagh:** Institute of Pharmaceutical Sciences, Faculty of Pharmacy, Parul University, Vadodara, Gujarat 391760, India; E-mail: bhaveshwari.wagh35656@paruluniversity.ac.in

integrate seamlessly with human biology. This introduction will explore the unique qualities that set biopolymers apart, their essential role in therapeutic applications, and a high-level overview of the primary types of biopolymers in use today [2].

Definition of Biopolymers

Biopolymers are large, chain-like molecules composed of repeating subunits identified as monomers. Monomers, which are covalently bonded, make a long chain that can exhibit a diverse array of structures and functionalities. The variability in structure among different types of biopolymers contributes to their unique properties and functions, making each type suitable for specific applications [3]. For instance, the structural organization of protein-based biopolymers allows for complex three-dimensional forms, enabling them to perform precise biological functions. Nucleic acids, on the other hand, encode genetic information, while polysaccharides offer structural and energy storage solutions. This structural and functional diversity makes biopolymers indispensable in therapeutic applications [4].

Importance of Biopolymers in Therapeutics

The therapeutic potential of biopolymers can be attributed to several critical properties that make them well-suited for interaction with biological systems.

Biocompatibility

One of the most important features of biopolymers is their compatibility with biological tissues. Because biopolymers are typically well-tolerated by the body, they pose a lower risk of immune reactions, making them ideal to apply in drug delivery, tissue engineering, and wound care [5].

Biodegradability

Unlike synthetic polymers, which often persist in the body and environment, biopolymers can be broken down by natural enzymatic or hydrolytic processes. This eliminates concerns related to long-term accumulation and reduces potential complications. This property is advantageous in applications requiring a temporary scaffold or carrier, such as drug delivery systems or tissue engineering [6].

Customizability with Interactive Capabilities

Biopolymers can be modified or engineered to exhibit specific interactions with biological targets, increasing their efficacy and versatility in therapeutic

applications. For example, biopolymers can be designed for precise drug release, to target specific cells, or to facilitate tissue regeneration by promoting cell adhesion and growth [7].

Overview of Biopolymer Types

Biopolymers used in therapeutics can be classified into three main types: proteins, nucleic acids, and polysaccharides. Each class has unique properties and applications that make it suitable for specific therapeutic purposes [8].

Proteins

Proteins are perhaps the most versatile type of biopolymer, with roles that range from structural support to enzymatic catalysis. Composed of amino acids linked with peptide bonds, proteins adopt intricate three-dimensional shapes that determine their specific functions [9]. Within therapeutics, various types of protein-based biopolymers have specific applications.

Enzymes

As natural catalysts, enzymes accelerate biochemical reactions in the body. Therapeutic enzymes are used in enzyme-replacement therapy to treat metabolic disorders or as catalysts in drug synthesis, offering a biologically safe and efficient alternative to chemical catalysts [10].

Antibodies

Antibodies are crucial components of the immune system, identifying and neutralizing pathogens. Therapeutically, monoclonal antibodies are used in cancer immunotherapy and autoimmune disease treatments due to their ability to specifically target disease-causing cells or molecules [11].

Hormones

Hormones are regulatory proteins that modulate physiological processes. Synthetic hormone analogs, such as insulin for diabetes and growth hormone for growth disorders, are widely used in medicine [12].

Nucleic Acids

Examples include DNA and RNA, which store and transport genetic information, playing an essential role in cell functioning and gene expression. Advances in genetic engineering have expanded their potential in medicine.

CHAPTER 2

Biological Sources, Chemistry, and Extraction of Biopolymers

Sharda Sambhakar^{1,*}, Bishambar Singh², Srishti Verma¹, Nancy Gupta¹, Manya Modi¹ and Pooja¹

¹ Department of Pharmacy, Banasthali Vidyapith, Rajasthan 304022, India

² PHTI Department, SMS Medical College and Hospital, Jaipur, Rajasthan 302017, India

Abstract: To foster a green environment, considerable efforts have been made to replace synthetic polymers with biodegradable materials, such as biopolymers, particularly for the development of green drug delivery systems. Biopolymers are a prominent class of functional materials with high-value applications, generated either by biological systems or derived from biological sources. Natural sources of biopolymers include plants, animals, microorganisms, and agricultural wastes. Biopolymers exhibit excellent properties, including flexibility, tensile strength, stability, reusability, and many more. Biopolymers are composed of repetitive monomers bound covalently *via* polymerization reaction or enzyme-catalyzed assemblies of monomeric units that occur in the biosynthetic pathway within biological systems. Biopolymers can be classified based on their source, chemical composition, functional properties, degradability, type of charges, and other factors. The extraction of biopolymers involves a range of chemical and enzymatic processes that vary specifically for each biopolymer. Some of the extraction methods include the use of coagulating agents, hydrolysis, alkali and acid treatments, bleaching, deproteination, and demineralization, among others. Following extraction, purification, and often modification, biopolymers are prepared for potential applications. Due to their renewability, abundance, biodegradability, and unique properties, such as higher absorption capabilities and ease of functionalization, biopolymers have been explored for various industrial applications. This chapter examines the sources, chemistry, and extraction procedures for several important biopolymers, including polyhydroxyalkanoates, polylactic acid, chitosan, alginate, polyesteramide, starch, gelatin, polyglycolic acid, and pectin, as well as their biomedical applications.

Keywords: Biopolymers, Bio-based technology, Biodegradable polymers, Chemistry, Extraction.

* Corresponding author **Sharda Sambhakar:** Department of Pharmacy, Banasthali Vidyapith, Rajasthan 302017, India; E-mail: ssambhakar@yahoo.co.in

INTRODUCTION

The concept of biopolymers emerged when people became aware of the deleterious effects of synthetic polymers on the environment and human health. The increasing use of synthetic, non-biodegradable polymers in our daily lives has significantly increased the risks of cancers and other health hazards. These are costly and derived from petrochemical sources. Biopolymers are sustainable, biodegradable, and eco-friendly alternatives to synthetic polymers. The term “biopolymer” originates from the Greek prefix *bio* (life) and *polymer* (many parts), reflecting the biological origin and the large molecular structure of these materials, which are composed of repeating monomeric units covalently bonded, forming highly structured macromolecules [1]. Biopolymers are synthesized either through direct biosynthesis, a process involving living organisms, such as microorganisms or plants, which enables the production of polymers with specific structural and functional characteristics, or through chemical processes that utilize biological raw materials. The latter involves the chemical conversion of natural substrates, such as corn starch or cellulose, into polymeric forms. The chemical synthesis approach enables the tailored production of biopolymers with desired molecular properties, thereby facilitating the creation of specialized materials for various applications [2].

SOURCES OF BIOPOLYMERS

Biopolymers are sourced from various origins, including plants, animals, seaweed, mushrooms, and microorganisms like bacteria, fungi, and yeasts (Table 1).

Natural Sources

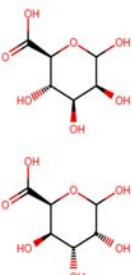
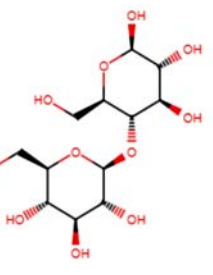
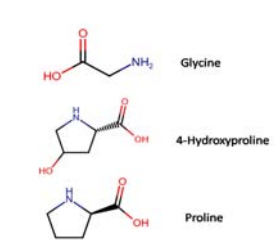
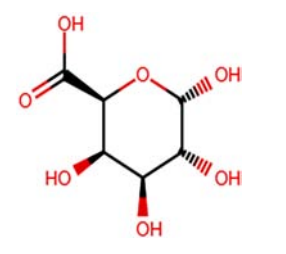
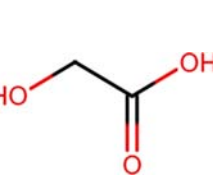
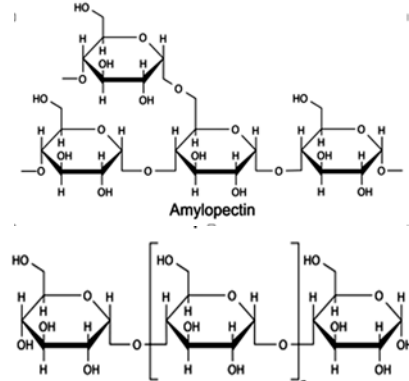
These biopolymers are formed organically from living organisms. Examples of polymers obtained from plants include cellulose, starch, and pectin, whereas collagen, chitin, gelatin, and hyaluronic acids are obtained from animals. Biotechnological techniques produce microorganism-based biopolymers (polyhydroxyalkanoates, polylactic acid), whereas polycaprolactone synthesis requires petrochemical sources (Table 1).

Synthetic Biopolymers

Synthetic biopolymers are produced or chemically modified by chemical reactions, either as biodegradable or non-biodegradable polymers. Synthetic polymers offer both stability and flexibility, making them suitable for a wide range of applications. Synthetic biopolymers are economically produced by enzymes and living cells in a controlled environment, utilizing biopolymer

synthesis, and they exhibit improved mechanical characteristics. They are widely used in tissue engineering. Commonly used biodegradable polymers in the pharmaceutical field include Polyglycolic acid (PGA), Polylactic Acid (PLA), Polycaprolactone (PCL), Polyhydroxybutyrate (PHB), Polypropylene Fumarate (PPF), and Polydioxanone (PDS), among others. The non-biodegradable polymers include Polyamide (PA), Polyvinyl Chloride (PVC), Polypropylene (PP), Polyethylene (PE), Polymethyl Methacrylate (PMMA), Polycarbonate (PC), and Polyurethane (PU), among others. They do not get degraded or metabolized inside the body and, therefore, accumulate and sometimes require surgical removal; hence, they are preferred for non-medical purposes [3, 4].

Table 1. Sources of biopolymers.

 β-D-Mannuronic acid α-L-Guluronic acid Alginate(β-D-mannuronic acid and α-L-guluronic acid) Source: Brown algae and some bacteria	 Cellulose(Cellubiose) Source: Plants and agricultural residues	 Glycine 4-Hydroxyproline Proline Gelatin(Collagen: composed of glycine, proline and hydroxyproline) Source: Pig skin, bovine bones, tendons and ligaments
 Pectin(α-D-galacturonic acid) Source: Citrus fruits and their byproducts	 Glycolic acid monomer (PGA) Source: Glycolic acid present in fruits and vegetables	 Amylopectin Amylose Starch(Amylose and amylopectin) Source: Potato, maize, rice

CHAPTER 3

Various Synthetic Pathways and Properties of Biopolymers

Piyush Anand¹, Deepak Kumar¹, Juhi Tiwari¹ and Shashi Kant Singh^{1,*}

¹ Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur, Uttar Pradesh 273007, India

Abstract: Biopolymers are naturally occurring macromolecules, such as proteins, nucleic acids, and polysaccharides, which are produced by living organisms. Over time, interest developed in both their natural synthesis and various synthetic pathways due to their importance in a variety of applications. Enzymatic reactions within organisms synthesize biopolymers through intricate biochemical processes known as natural biosynthesis. Nowadays, microbes may be engineered to produce unique biopolymers with specialized functions, indicating developments in synthetic biology. Moreover, synthetic variations that retain desirable capabilities can be carried out by using chemical synthesis techniques to mimic the architectures of genuine biopolymers. The combination of biopolymers with clay can enhance mechanical properties, leading to the development of new materials known as biopolymer–clay nanocomposites. These nanocomposites may represent a significant innovation in the development of biopolymers with enhanced features. The functionality of biopolymers depends on their features, which include good mechanical properties, biocompatibility, and biodegradability. These features facilitate their use in areas ranging from environmental sustainability to medicine. For example, polylactic acid (PLA) is a well-known artificial biopolymer that is being used in biomedical equipment and packaging because of its strength and biodegradability. As research advances, biopolymers are becoming increasingly attractive as alternatives to traditional petroleum-based materials, addressing environmental challenges and enabling innovative solutions across diverse industries.

Keywords: Biopolymers, Bioavailability, Bio-synthesis, Biocompatibility, Biodegradability, Enzymatic reactions.

INTRODUCTION

Natural materials often contain organic compounds known as biopolymers. The term “biopolymer” is derived from the Greek word “*bio*”, meaning life, and “*polymer*”, referring to many units. Biopolymers are long, repeating

* Corresponding author Shashi Kant Singh: Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur, Uttar Pradesh 273007, India; E-mail: shashikantsingh59@gmail.com

macromolecules composed of several components. As biopolymers are both biocompatible and biodegradable, they can be used in a wide range of applications. These applications include their uses in food and pharmaceutical industries, such as “wound healing” and “tissue scaffolding”, edible films, emulsions, drug transport materials, and implants. The most common macro-level compounds include biopolymers, such as proteins, carbohydrates, lipids, and nucleic acids, as well as larger non-polymeric molecules like macrocycles and lipids. Genetic manipulation of microorganisms facilitates the biotechnological production of various biopolymers with distinct properties, making them suitable for highly valuable medicinal applications, such as medicine delivery and tissue engineering [1].

Biopolymers are synthetic materials with superior qualities, including flexibility, tensile strength, stability, and reusability. They originate from biological sources and occur naturally, particularly during the growth cycle of various living organisms. The combination of two or more biopolymers yields the creation of “biocomposites”, which have numerous innovative applications. Several processes have been discovered that enable the efficient synthesis of biopolymers from various life forms, including microorganisms, plants, and animals. The structure and functionality of biopolymers vary depending on their source. The environmental benefits and biodegradability of biopolymers make them a preferable alternative to chemically manufactured polymers. A key component of the pharmaceutical industry is biopolymers. Biopolymers have the potential to be utilized in both regenerative medicine and drug delivery, offering optimal therapeutic performance and minimal immunogenicity in treated patients [2].

The Role of Biopolymers in Nature and Industry

Directly derived from biomass sources, such as animal proteins and polysaccharides, biopolymers are most commonly used in the production of food packaging materials. The use of biopolymers from renewable resources can help solve the worldwide plastic pollution problem. Researchers and scientists have been working on creating packaging materials derived from biopolymers for a long time. However, due to their chemical makeup and structure, animal proteins and natural polysaccharides have certain unfavorable characteristics [3].

Biopolymers play a definite role in nature and industry. Natural biopolymers are macromolecules derived from microbes, plants, or animals. To expand the spectrum of applications for different polymers, they can be developed through particular chemical alterations or used directly. Since proteins are inexpensive and uncommon, materials derived from them have been used in a wide range of industries, including the food, cosmetic, textile, and biomedical sectors.

Biopolymers are biologically degradable and biocompatible. Typically, biomaterials are composed of natural proteins, such as collagen, keratin, silk, and gelatin. The primary protein in connective tissue is gelatin, a biopolymer created when collagen is heated to a low temperature. It possesses several remarkable qualities, including the ability to enhance cell attachment and growth, biodegradability, low antigenicity, and excellent biocompatibility. It is used in various industries, including the food industry as an emulsifier and gelling agent, the pharmaceutical industry for capsules and ointments, and the cosmetics industry as a cosmetic ingredient. Fig. (1) illustrates how the biopolymer-clay nanocomposites are made and processed using the melt insertion method [4].

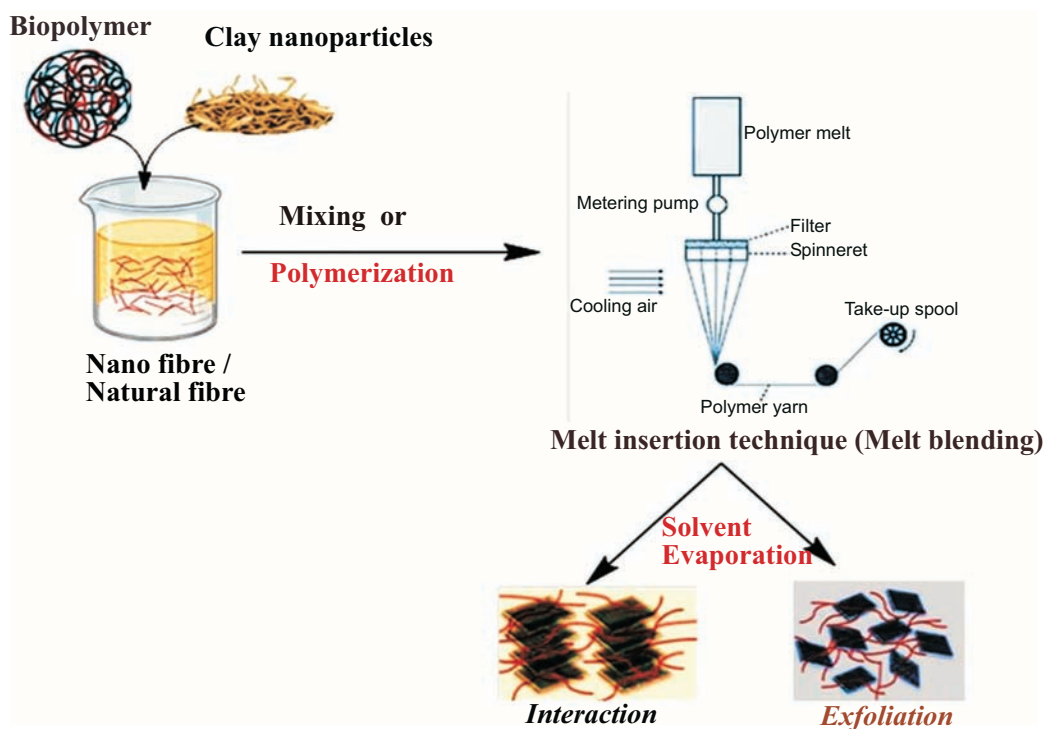


Fig. (1). Illustration of how the biopolymer-clay nanocomposites are made and processed using the melt insertion method.

In the pharmaceutical and medical sectors, alginate is one of the most commonly utilized biopolymers. This is due to its unique encapsulating properties and its role in wound healing. Since its initial isolation in the 1980s, it has evolved into a multifaceted compound with a broad range of applications. Starch has been utilized in the medical and pharmaceutical sectors as a plasma volume expander, controlled-release polymer, pharmaceutical excipient, and superdisintegrant (for

Biopolymer Mechanism: Pharmacokinetics and Pharmacodynamics

Ajay Pandey^{1,*} and Bharat Mishra²

¹ Department of Pharmaceutical Engineering and Technology, Indian Institute of Technology (Banaras Hindu University), Varanasi, India

² Institute of Pharmacy DR. Shakuntala Misra National Rehabilitation University, Mohan Road, Lucknow 226017, India

Abstract: Biopolymers have become apparent as a potential therapeutic material, which shows an important role in treating different diseases like cancer, neurological disorders, cardiovascular disorders, infectious diseases, diabetes, and drug delivery. Due to its biocompatible and biodegradable properties, it is widely used for therapeutic purposes. This chapter provides detailed information regarding the pharmacokinetic and pharmacodynamic properties of biopolymers. It involves a comprehensive analysis of how these materials are involved in drug absorption, distribution, metabolism, excretion, and their interaction with physiological systems. The pharmacokinetic properties of biopolymers depend on various factors such as molecular weight, degradation behavior, and structure of biopolymers, which are important for therapeutic efficacy. On the other hand, pharmacodynamic properties provide detailed information regarding mechanisms like cellular uptake and internalization, modulation in immunological responses, and physical and chemical interactions by which these materials show therapeutic responses by targeting specific cells or tissues, extending beyond the target consequences, and receptor-associated interactions. Recent advancements in the field of biopolymers involve their utilization for specific therapeutic effects, enhancing patient compliance and outcomes, with various mechanisms of action involved for showing therapeutic responses by biopolymers mentioned in this chapter. By gathering information regarding biopolymers' pharmacokinetic and pharmacodynamic properties, this chapter aims to provide detailed information on various mechanisms involving the effectiveness and efficacy of biopolymer-based therapeutics in clinical utilization.

Keywords: Applications, Biopolymers, Mechanism of action, Pharmacodynamics, Pharmacokinetics.

* Corresponding author Ajay Pandey: Department of Pharmaceutical Engineering and Technology, Indian Institute of Technology (Banaras Hindu University), Varanasi, India; E-mail: pandeyajay.1633@gmail.com

Sudhanshu Mishra, Smriti Ojha, Shashi Kant Singh, Rishabha Malviya & Saurabh Kumar Gupta (Eds.)
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INTRODUCTION

Biopolymers are macromolecular compounds that are obtained from resources found in nature and can be synthesized chemically with the help of biological elements or can be fully biosynthesized by living things [1]. The structural composition of these compounds is carbon, nitrogen, and oxygen, which makes biopolymers susceptible to degradation. The broken parts of biopolymers, like organic macromolecules, water, and some other natural products, do not cause any harm to nature. Biopolymers combine bio and polymers, respectively, meaning life and nature [2].

Biopolymers are utilized for their emerging properties like biocompatibility, no immunogenic reactions, lack of toxicity, extended systemic circulation, and biodegradability. Apart from these properties, these are non-carcinogenic and non-thrombogenic, which makes them eco-friendly and excellent materials for the delivery of larger as well as smaller drugs [3, 4]. A comparison of different biopolymers for drug delivery is mentioned in Table 1. Biopolymers consist of recurring sequences with various recurring functional moieties (such as carboxyl, hydroxyl, and amino) and a large range of chemical constituents, which makes biopolymers vulnerable to cross-linking [5]. Applications of biopolymers are mentioned in Fig. (1).

Table 1. Characteristics and applications of biopolymers [4, 6, 7].

Biopolymer	Advantages	Disadvantages	Suitable Drug Types	Delivery Routes A
PLGA (Poly(lactic-co-glycolic acid))	Biodegradable, biocompatible, controlled drug release, FDA-approved	Acidic degradation byproducts, burst release possible	Small molecules, peptides, and proteins	Injectable, implantable, oral
PLA (Polylactic Acid)	Biocompatible, slow degradation, good mechanical strength	Hydrophobic, low protein adsorption, acidic degradation	Hydrophobic drugs, proteins, and peptides	Injectable, implantable, transdermal
Polysaccharides	Natural, biocompatible, mucoadhesive, controlled drug release	Variable properties, stability concerns, batch-to-batch variations	Small molecules, peptides, proteins, and vaccines	Oral, injectable, transdermal
Collagen	Biodegradable, promotes cell adhesion, widely used in tissue engineering	Expensive, potential immunogenicity	Proteins, peptides, growth factors	Injectable, implantable, transdermal

(Table 1) cont.....

Biopolymer	Advantages	Disadvantages	Suitable Drug Types	Delivery Routes A
Gelatin	Biocompatible, thermosensitive gelation, widely used in drug delivery	Enzymatic degradation, poor mechanical strength	Hydrophilic drugs, proteins, and vaccines	Injectable, transdermal
Starch	Biodegradable, easily modifiable, widely available	Swelling issues, limited mechanical strength	Small molecules, peptides	Oral, transdermal, injectable
Hyaluronic Acid	Biodegradable, enhances drug permeability, high water retention	Rapid degradation, expensive	Hydrophilic drugs, peptides, and proteins	Ocular, injectable, transdermal
Polynucleotides	Biocompatible, essential in gene therapy, highly specific	Stability issues, enzymatic degradation	Gene-based drugs, oligonucleotides	Injectable, transdermal
DNA	Highly specific, enables gene therapy, stable when encapsulated	Prone to enzymatic degradation, immune activation risk	Gene-based drugs, plasmids	Injectable, oral
RNA	High specificity, potential for mRNA vaccines, and gene silencing	Unstable, rapid enzymatic degradation	mRNA vaccines, siRNA, gene therapy	Injectable, nasal
Proteins and Peptides	High specificity, biocompatible, diverse functionality	Short half-life, requires stabilization	Therapeutic peptides, enzymes, and hormones	Injectable, oral, transdermal
Zinc-containing Proteins	Important for enzyme activation, immune modulation	Potential toxicity at high doses, stability concerns	Enzyme-based drugs, protein therapies	Injectable, oral
Bovine Serum Albumin (BSA)	High drug binding capacity, stabilizes drugs, biocompatible	Potential immunogenicity, batch variability	Small molecules, proteins, and peptides	Injectable, oral, transdermal
Chitosan	Biodegradable, mucoadhesive, enhances drug permeation	Limited solubility at physiological pH, possible immunogenicity	Peptides, proteins, and hydrophilic drugs	Oral, nasal, transdermal, ocular

Chemically, biopolymers comprise different functional groups such as amino, hydroxyl, and carboxyl. They become reactive and vulnerable to cross-linking as a result. Thus, large molecular weight molecules with repetitive sequences are known as biopolymers, and they may have a high potential for chemical reactions with different substances [5].

Biopolymer-based Chemotherapeutics: Combination Therapies and Synergistic Effects

Rufaida Wasim¹, Tarique Mahmood^{1,*}, Saba Parveen², Aamir Anwar¹ and Asad Ahmad¹

¹ Department of Pharmacy, Integral University, Dasauli, Kursi Road, Lucknow, Uttar Pradesh, India

² Department of Pharmacy, Madan Mohan Malaviya University of Technology, Gorakhpur, Uttar Pradesh, India

Abstract: Applications of nanotechnology have increased the importance of research and nanocarriers, which have revolutionized medication delivery in recent years to treat a range of diseases, including cancer. Due to its multidrug resistance to several chemotherapeutic treatments, cancer, one of the most dangerous diseases in the world, has drawn the attention of experts. Scientists have created a different way to deliver chemotherapeutic drugs to the desired location while reducing side effects and enhancing delivery efficacy on healthy cells by incorporating them into nanocarriers such as synthetic polymers, nanotubes, micelles, dendrimers, magnetic nanoparticles, Quantum Dots (QDs), lipid nanoparticles, nano-biopolymeric substances, *etc.* Nanotechnology applications have made research and nanocarriers—which have recently transformed drug delivery to treat a variety of illnesses, including cancer—even more crucial. One of the most deadly illnesses in the world, cancer, has caught the attention of scientists because of its multidrug resistance to several chemotherapeutic therapies. By integrating chemotherapeutic drugs into nanocarriers like synthetic polymers, nanotubes, micelles, dendrimers, magnetic nanoparticles, Quantum Dots (QDs), lipid nanoparticles, nano-biopolymeric substances, *etc.*, researchers have developed an alternative method of delivering these medications to the intended site while minimizing side effects and improving delivery efficacy on healthy cells. Preclinical and clinical research on cancer treatment has yielded promising results. Biopolymers stand out as viable options for anticancer nano drug delivery systems due to their exceptional biocompatibility. Moreover, the presence of ligands in some biopolymers that are naturally present on the surface of human cells enables active targeting.

Keywords: Biopolymers, Chemotherapeutics, Drugs, Nanocarrier, Nanotechnology.

* Corresponding author Tarique Mahmood: Department of Pharmacy, Integral University, Dasauli, Kursi Road, Lucknow, Uttar Pradesh, India; E-mail: tmahmood@iul.ac.in

Sudhanshu Mishra, Smriti Ojha, Shashi Kant Singh, Rishabha Malviya & Saurabh Kumar Gupta (Eds.)
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INTRODUCTION

The dramatic rise in cancer as the world's top cause of death highlights the pressing need for scientific research and healthcare initiatives. Ten million people died from cancer in 2020 alone, according to estimates, and the World Health Organization estimates that number might triple by 2040 [1 - 3]. A wide range of adverse effects are linked to modern cancer treatments, including hormone therapy, immunotherapy, radiation, chemotherapy, and surgery [4 - 6]. Chemotherapy's infamous side effects, which include myelotoxicity and cardiotoxicity, are caused by non-specific delivery and the exacerbation of unintentional cellular damage [7 - 11]. This makes it abundantly evident how urgently anticancer medications are needed. In light of this, nanomedicine has become more than just a substitute; it is a revolutionary tool in pharmaceutical research, particularly in the field of drug delivery [12 - 14].

Cancer therapy is being revolutionized by nanomaterials, which provide new and improved therapeutic alternatives. Their special qualities—such as their compact size, high surface area-to-volume ratio, and capacity to be surface-engineered for precise targeting—make them perfect for use in cancer therapy applications. By restricting drug exposure to healthy cells, they are used to deliver pharmaceuticals directly to tumor cells, significantly reducing the adverse consequences linked to conventional chemotherapy. Furthermore, thermal treatment makes use of nanomaterials, which are designed to absorb particular light wavelengths to heat up and kill cancer cells with the least amount of harm to the surrounding tissues. They are also essential in diagnostic applications, where they improve imaging techniques to increase the sensitivity and specificity of cancer detection procedures. The use of nanomaterials in cancer therapy has enormous potential to enhance therapeutic results, lessen adverse effects, and open the door to more individualized and effective cancer care [15].

Because of their inherent biomimetic qualities, design flexibility, and biocompatibility, biopolymers (which have particle sizes ranging from 10 to 1000 nm) have emerged as the focal point of this research revolution [16, 17]. Because of their increased specificity and bioavailability, recent research has highlighted the potential of naturally derived nanomedicines, ranging from complex composite nanocarriers to lipid nanocarriers for targeted drug delivery [18 - 21]. However, due to their possible cytotoxicities, their synthetic equivalents raise doubts [22 - 24].

Research to enable precision-targeted medication delivery has traditionally focused on the combination of polymer conjugates and nanomedicine [25 - 29].

Innovative developments like polylactic acid conjugates, which are intended for better medication penetration, highlight this story [30 - 41].

PRODUCTION AND CHARACTERIZATION OF BIOPOLYMERIC NANOPARTICLES (NCS) UTILIZED IN DRUG DELIVERY SYSTEMS (DDS)

Anticancer medication-loaded NCs provide several benefits over free medication. They guarantee target-specific tumor cell death by preventing medicines from degrading too quickly and interacting with nonspecific substances [42 - 44]. One of the most crucial characteristics of NCs is their biocompatibility, which increases their effectiveness and prolongs the drug's shelf life in use [45].

Natural materials with nontoxic, biocompatible, and biodegradable qualities are called biopolymers. For the creation of NC formulations, only polymers have been studied thus far [46 - 49]. Both natural and synthetic polymers can be used for encapsulation; natural polymers, such as chitosan, silk, alginate, albumin, starch, carbohydrates, proteins, and lipid materials, can be used without the medication having to be chemically altered [50]. Over the past few decades, several biopolymeric NP formulations and methodologies have produced effective nanotransporting capabilities with outstanding anticancer effects [51 - 53].

LIPID-BASED BIOPOLYMER

In the past few decades, organic polymers have been used [54]. Proteins, liposomes, and solid lipid nanoparticles are examples of organic polymers that have been considered appropriate nanocarriers for Drug Delivery Systems (DDSs) [55, 56]. The widespread use of lipid polymers may be attributed to their effective ability to encapsulate both hydrophilic and hydrophobic medications [57 - 60]. Water-insoluble medications have recently been administered *via* lipid nanoparticles (LPNs) [61]. Stearic acid-modified polyglycerol adipate (PGAS) is a lipid substance that has been demonstrated by Weiss *et al.* to be a potential drug delivery vehicle that does not require a surfactant [62]. Only N-(2-hydroxypropyl) methacrylamide (HPMA) copolymer coating, either covalently or non-covalently, was carried out [62]. Despite having comparable particle sizes, these nanoparticles can show lower or negative zeta-potentials [62]. The fluorescent dyes DiR and DYOMICS, which were covalently bonded to an HPMA copolymer, were used to double-label the NPs in a non-covalent fashion [63]. Using optical imaging based on various spectra, the biodistribution was examined noninvasively. The pharmacokinetics and biodistribution of cancer-bearing and healthy mice were altered by coating (Fig. 1).

Nano-based Biopolymer for Disease Targeting

Gaurish Narayan Singh¹, Nandani Jayaswal^{2,*}, Pooja Jaiswal² and Ganesh Lal³

¹ Institute of Pharmacy, Deen Dayal Upadhyaya Gorakhpur University, 273009, Gorakhpur, Uttar Pradesh, India

² Faculty of pharmaceutical sciences, Mahayogi Gorakhnath University Gorakhpur, 273007, Gorakhpur, Uttar Pradesh, India

³ KJ College of Pharmacy, Babatpur, 221006, Varanasi, Uttar Pradesh, India

Abstract: Nano-based biopolymers are emerging as a powerful tool in targeted disease therapy, offering a promising combination of the precision of nanotechnology and the biocompatibility of natural polymers. In administering therapeutic chemicals specifically to certain disease areas, these nanoscale (1–100 nm) materials are intended to maximize therapeutic effectiveness while decreasing systemic adverse reactions. The integration of biopolymers, which are biodegradable and non-toxic, with nanoparticles allows for the creation of advanced drug delivery systems capable of responding to specific biological signals. This book chapter covers almost all current evolutions in nanomaterial-based medicament delivery techniques, with a focus on biopolymers such as polysaccharides (chitosan, alginate, cellulose, and starch) and proteins (albumin, collagen, gelatin, and silk fibroin). In cancer therapy, nano-based biopolymers can deliver chemotherapeutic agents precisely to tumour cells, minimizing damage to good tissues and overcoming the possible adverse effects linked with traditional radiation therapy. Additionally, these materials can be used for diagnostic purposes, enhancing imaging methods such as CT or MRI scans to better locate or characterize tumors. Regarding gene therapy, biopolymer-based nanoparticles can transfer genetic material, such as RNA or DNA, directly to specific cells, offering potential treatments for genetic disorders by correcting or silencing defective genes. Infectious diseases also benefit from this technology, with nano-based biopolymers delivering antimicrobial agents directly targeted to the site of infection, thereby increasing the drug's local concentration and efficacy. Furthermore, because these materials may carry anti-inflammatory medications straight to inflammatory tissues, they are being investigated for the treatment of inflammatory illnesses like rheumatic arthritis, which would lessen systemic protection against the negative effects. The possibilities of nano-based biopolymers in personalized medicine are examined in this chapter, along with issues including stability, scalability, and regulatory compliance.

* Corresponding author Nandani Jayaswal: Faculty of pharmaceutical sciences, Mahayogi Gorakhnath University Gorakhpur, 273007, India; E-mail: nandani.jaiswal123@gmail.com

Keywords: Biopolymers, Cancer therapy, Drug delivery systems, Gene therapy, Infectious diseases, Nano-based, Nanotechnology, Personalized medicine, Targeted disease therapy, Therapeutic agents.

INTRODUCTION

Drug administration often applies naturally occurring biodegradable polymers due to their accessibility, biodegradability, biocompatibility, and less toxic effects. In addition to polysaccharides, including chitosan, dextran, hyaluronic acid, agarose, carrageenan, cyclodextrin and alginate, it contains protein-based polymers such as gelatin, collagen, albumin, and soy. Because of their wide molecular weight ranges and batch variability, natural polymers present significant hurdles as drug carriers. Chitosan is the most often utilized natural polymer for drug administration because of its good cell and tissue integration, minimal cytotoxicity, capacity to change its surface, and lack of immunogenicity. It can also combine well with a range of different polymers. Although some biodegradable polymers have shown efficacy in various pre-clinical investigations, almost none of the actively targeted nanocarriers have progressed past clinical trials, and few passively targeted nanocarriers have been authorized for clinical usage. It is crucial to investigate novel candidates from this polymer family in order to achieve targeted and long-lasting medication release [1]. Protein and polysaccharide-based biopolymers are being researched because of their low levels of antibacterial activity, biodegradability, immunogenicity, and biocompatibility. Drugs, bioactive substances, and scaffolds for tissue engineering can all be transported by these nanoparticles. The DDS program utilizes nanotechnology to solve challenges facing the biomedical industry, such as low absorption, limited solubility, and adverse reaction. Nanoparticles' high surface area to volume ratio suggests that they might be useful in medicine. However, the mononuclear phagocyte system quickly clears non-modified nanoparticles. Synthetic approaches can manipulate nanoparticle characteristics and particle sizes, making them commonly used in the therapeutic sector. Covalent bonds between synthetic or biopolymers can modify nanoparticle surfaces [2]. Natural biopolymers are being explored for their biocompatibility, low toxicity, and immunogenicity, making them a valuable alternative to synthetic materials in nanomedicine. Their structural and chemical alterations are guaranteed by their biodegradability [3]. New developments in biopolymer technology are opening up the possibility for novel medication delivery methods that can enhance treatment results and patient compliance. These systems consider biopolymers' attributes like extraction technique, sustainable production, chemistry, surface characteristics, and biocompatibility [4]. The process of transporting an agent from the external environment to a designated target within the body is known as delivery. The possibility for specific cellular and molecular illness treatment is

presented by developments in diagnostic agents, medications, and biological tools such as gene operators and nanotechnology. In order to transport to the target and shield them from deterioration, nanoparticles are usually integrated into vehicles. Current design paradigms focus on physical aspects, as nanoparticles interact with biological systems and can accumulate in non-target areas, affecting formulation effectiveness [5]. The first biopolymer nanoparticles were created using albumin [6]. Albumin and gelatin are the first naturally occurring proteins used to create nanoparticles, offering biodegradability, low immunogenicity, toxicity, stability, simplicity, and large-scale production. These nanoparticles offer surface modification and covalent drug attachment options [7]. Therapeutic chemicals may be delivered to the target tissue in a high-dose, targeted, and safe manner helpful to nanotechnology. It is possible to design biodegradable polymers into multilayered complex nanoparticles, which improves the therapeutic index and allows for drug targeting. Physical and chemical targeting strategies are used, with physical targeting influencing tissue accumulation and cell uptake. Chemical targeting uses molecular recognition units sensitive to external stimuli or pathological conditions. Advanced nanoparticles employ conjugation chemistry for tissue-specific chemical targeting and stimuli-responsive nanoparticles for chemical targeting [8]. This book chapter discusses the optimization of nanoparticle shape, size, and surface characteristics to improve physical targeting and chemical targeting. It also discusses the use of natural biopolymers to create biocompatible, low-immunogenic nanoparticles that offer improved drug encapsulation, controlled release, decreased toxicity, and biocompatibility. Understanding interactions between nanoparticles and biological barriers can improve medication delivery design and patient compliance.

FUNDAMENTALS OF NANOTECHNOLOGY AND BIOPOLYMERS

The twentieth century has been altered by advances in nanotechnology and its use in the fields of drugs and medicine. The field of nanotechnology studies incredibly microscopic structures. The Greek word “*nano*,” which means “small,” refers to minuscule size. Nanotechnology is a technique used to manufacture materials and devices with special properties by structuring small atoms, particles, or combinations. In nanotechnology, work is done either top-down, from immense structures to smaller ones, as in the case of optical photonics applications in semiconductor technology in this sector, or bottom-up, from individual atoms and molecules to nanostructures, which is more akin to chemistry and biology. Unique properties of materials include electrical conductivity, chemical reactivity, magnetism, visual effects, and nanotechnology, which focuses on materials with physical strength and sizes between 0.1 and 100 nm. Advances in nanotechnology and nanofabrication have significantly impacted drug delivery, enabling designs of nanoscale secondary structures and delivery systems made entirely of

CHAPTER 7**AI-powered Biopolymers Engineering:
Advancements in Drug Delivery and Efficacy****Anindita De^{1,*}, Sonali Jayronia¹, Gowthamarajan Kuppusamy² and Young Joon Park³**¹ Department of Pharmaceutics, College of Pharmacy, JSS University, Noida 201301, India² Department of Pharmaceutics, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty 643001, Tamil Nadu, India³ Department of Formulation and Drug Delivery, College of Pharmacy, Ajou University, 206 Worldcup-ro, Yeongtong-gu, Suwon-si 16499, Republic of Korea

Abstract: The application of AI within biopolymer engineering is a monumental step in the advancement of drug delivery systems. With the aid of AI, it is possible for researchers to design and develop biopolymer materials to the highest degree, which means that drug effects, targeting accuracy, and treatment modulation for each patient can be improved to a large extent, which brings out the concept of personalized medicine. This chapter presents the state-of-the-art knowledge concerning the topic of biopolymer engineering utilizing AI, with a focus on Nanomedicine and Drug Delivery, respectively, in the context of the most fundamental and interesting areas—drug delivery and therapy and Machine Learning for Polymer Design. The developing frontiers of AI and biopolymer technology have the potential to alter drug discovery, delivery and administration processes with the patient in mind, leading to better compliance and control of the remedy for the patient.

Keywords: Advanced drug delivery systems, AI-driven biopolymer engineering, Machine learning, Personalized medicine, Precision drug targeting.

INTRODUCTION

In recent years, the focus has shifted towards the use of biopolymers as carriers of drugs. These substances are naturally occurring polymers obtained from renewable biological sources such as plants, animals, and microorganisms. The biocompatibility and biodegradability of these materials make them a good choice for building structures for drug delivery systems, providing safety and efficacy with respect to the environment [1]. In addition, the biopolymers also provide a

* **Corresponding author Anindita De:** Department of Pharmaceutics, College of Pharmacy, JSS University, Noida, India; E-mail: aninditanirupa@gmail.com

unique approach for controlled and sustained delivery of drugs, which makes them very useful for a number of therapeutics. Drug delivery is an example of biopolymers that include chitosan, alginate and gelatin and polylactic acid, PLA: each of which can be used based on its unique characteristics to increase drug action [2].

Nevertheless, the classic techniques for engineering these biodegradable materials for the purpose of drug delivery have posed considerable challenges. One of the main drawbacks is the ability to foresee and fine-tune the behavior of biopolymers within the subsets of biological systems. For instance, polymer degradation rate, interactions between the drug and the polymer, as well as the immune response of the body, are parameters that are hard to predict using normal methods. More often than not, these challenges lead to a semblance of an arduous process which is prone to wastage of resources and time and in certain instances, does not work at all [3].

The use of Artificial Intelligence (AI) in combination with machine learning (ML) in the synthesis of biopolymers is changing the perspective of designing these materials and optimizing them for drug delivery systems. Generally, the process of developing biopolymers has been overly reliant on experimentation, which is slow, expensive, and lengthy due to biological complexities. On the contrary, AI and ML make the whole process more accurate and efficient. With AI, it becomes possible to design new structures of biopolymers, knowing how they will behave biologically based on extensive polymer properties, biological interactions, and clinical data. For example, it is possible to employ complex learning algorithms to hyperparameterize the collected data to perform inference tasks. Specifically, key attributes such as polymers' degradation rates, drug release kinetics, and overall biocompatibility can be predicted accurately [4]. This predictive capability encourages scientists to engineer biopolymers for specific purposes and minimize the extent of trial analytics required. By way of illustration, one can use Generative Adversarial Networks (GANs), which have generative capabilities in creating new types of polymers with specific desired characteristics in mechanical strength and chemical properties. A study was conducted where they used a GAN to fabricate a new biopolymer with better stability and drug encapsulation efficiency for the delivery of tedious-to-formulate hydrophobic drugs [5].

Such an approach, driven by AI, not only streamlines the development process but also makes it possible to fabricate biopolymers with newer functionalities that the conventional methods could not realize. The use of AI in the engineering of biopolymers is a significant step in dealing with the deficiency mentioned earlier. In this respect, AI, especially those programs that employ ML and deep learning techniques, create an avenue for designing and developing biopolymers with

better properties and functions for specific needs. For example, such AI mechanisms can comprehend and process large volumes of information about the existing polymers, their architecture, and even predict their behavior within biological systems. With this ability, they can design advanced drug delivery systems in the form of biopolymers that can target specific sites, reduce side effects and enhance the quality of life of the individuals [6]. A significant example of using AI in the field of biopolymer engineering is the development of custom drug delivery systems. AI can facilitate the design of such bio-polymeric drug delivery systems considering individual genetic information, disease state and it can help optimize a specific biopolymeric delivery system by controlling the release profile of the drug from the biopolymer in order to administer the drug at the right time and appropriate dosage for the maximum therapeutic efficacy [7].

This section of the book investigates the way AI is changing the landscape of biopolymer engineering, particularly in drug delivery systems. AI techniques allow researchers to design and fabricate biopolymer materials with great accuracy and speed, which seems likely to benefit the pharmaceutical R&D processes greatly. Such an AI revolution in this field is driven by the technology's ability to process large datasets, forecast outcomes, and restructure biopolymers to enhance effectiveness in pharmaceutical applications. In this chapter, we tried to provide different examples and case studies that highlight the role of AI in the development of biopolymers, among other advanced materials. These unique materials made *via* AI techniques and processes offer enhanced targeting and efficacy of drug delivery systems, but create a better environment for more effective treatments, making modern medicine more personalized.

AI IN BIOPOLYMER DESIGN AND SYNTHESIS FOR DRUG DELIVERY

AI has contributed to the development of biopolymer creation and design methodologies by allowing scientists to explore chemical space in a matter of hours. Forming biopolymers was very labour-intensive in the olden days; a lot of time was also wasted trying to experiment on the best possible material for drug delivery, which mostly depended on trial and error. However, the coming of AI, particularly the ML algorithms, has made it possible for scientists to assess and estimate the properties of numerous hypothetical polymer structures in a very short time (Fig. 1). This aspect minimizes the time taken to search for suitable biopolymers that are required for a certain application in drug delivery, for instance, when controlled release, targeted delivery, and biocompatibility of the biopolymer are of concern. For instance, random polymer interactions can be modelled, and the efficiency of drug encapsulation, and it is how long it takes to degrade and how long it takes to release them, can also be modelled in this way

CHAPTER 8

Biopolymers in Stimuli-triggered and Enzyme-activated Drug Delivery Systems

Surbhi Gupta¹ and Anubhav Anand^{2,*}

¹ Ashoka Institute of Technology and Management, Varanasi, Uttar Pradesh, India

² Shri Ramswaroop College of Engineering and Management (Pharmacy), Lucknow, Uttar Pradesh, India

Abstract: Biopolymers have emerged as a crucial component in advanced drug delivery systems due to their low toxicity, biodegradability, and inherent biocompatibility. Their ability to respond to specific stimuli or enzymes offers enhanced control over the release of therapeutic agents, making them highly valuable in precision medicine. Stimuli-triggered systems utilize external or internal signals such as pH, magnetic fields, temperature, redox potential, and light to precisely control drug release at targeted sites. For example, pH-sensitive biopolymers can release drugs in the acidic environment of tumors, while temperature-responsive systems adapt to local heat variations in tissues. This method ensures efficient drug delivery while minimizing side effects by targeting specific diseased areas. Enzyme-activated systems, on the other hand, rely on the presence of specific enzymes in the body to trigger the degradation of biopolymers and release the encapsulated drugs. These systems are beneficial in diseases such as cancer or infections, where overexpressed enzymes can be exploited for localized drug delivery. Biopolymers such as chitosan, dextran, alginate, and hyaluronic acid have been widely used in these enzyme-responsive systems, showing promising results in selective drug release. The precision and adaptability of biopolymer-based systems provide numerous benefits, including reduced systemic toxicity, controlled drug release, and enhanced therapeutic efficacy. However, challenges such as ensuring the stability of biopolymers in physiological conditions and scaling up production remain key obstacles. Ongoing research into novel biopolymers and more specific response mechanisms continues to push the boundaries of personalized medicine. Overall, biopolymer-based delivery systems signify a cutting-edge approach to achieving precise and controlled therapeutic interventions.

Keywords: Anti-bacterial, Anti-inflammatory, Biopolymer, Cancer, Enzyme-responsive systems, pH-responsive, Stimuli-responsive systems, Targeted drug delivery system.

* Corresponding author Anubhav Anand: Shri Ramswaroop College of Engineering and Management (Pharmacy), Lucknow, Uttar Pradesh, India; E-mail: anubhavanand2000@gmail.com

INTRODUCTION

Drug delivery is an interdisciplinary field combining expertise from chemistry, pharmaceutical sciences, medicine, and engineering. It relies on drug formulation, dosage, and delivery methods. Drug delivery systems (DDS) address the limitations of traditional approaches by improving solubility, extending drug activity, reducing side effects, and maintaining bioactivity. These systems also enhance bioavailability, increase drug absorption, maintain concentration through controlled release, and reduce side effects by targeting specific cells. Advances in material chemistry have driven the development of biodegradable carriers and biocompatible carriers with increased responsiveness. The creation of molecularly engineered biomaterials aims to address the challenges of delivering hydrophobic drugs and large biomolecules, such as proteins and nucleic acids. Smart materials that react to biological signals offer promising solutions for more efficient therapeutic delivery [1].

Biopolymers are a diverse and versatile class of compounds derived from natural sources or synthesized from biological materials. Like other polymers, they consist of repeating monomer units linked together. Due to their distinct characteristics, including biodegradability, availability, and the ability to modify their physicochemical properties, biopolymers are increasingly utilized in novel formulations. As the shift toward sustainable living gains momentum, biopolymers offer a promising platform for eco-friendly solutions. They have garnered significant attention for designing DDS, which delivers therapeutic agents precisely to diseased sites with minimal side effects. An ideal DDS could be one that controls drug release and protects drugs from degradation during transport. Both natural and synthetic polymers are considered suitable materials for developing DDS due to their biocompatibility and biodegradability [2].

Responsive polymers are materials that adapt their chemical or physical properties to respond to external stimuli.

Responsive polymers can alter characteristics like:

- a. **Chain dimensions/size:** The polymer chains might expand or contract.
- b. **Secondary Structure:** Modifications to the polymer chains' coiling or folding.
- c. **Solubility:** The polymer's ability to dissolve in solvents may vary.
- d. **Intermolecular Association:** Changes in the degree to which polymer molecules associate with each other.

These changes are typically driven by external factors such as:

- **Secondary Forces:** Like electrostatic interactions, hydrophobic effects, or hydrogen bonding.
- **Simple Chemical Reactions:** Acid-base reactions involving functional groups attached to the polymer.
- **Osmotic Pressure Differentials:** Changes in osmotic conditions caused by the external environment [3].

To reduce adverse effects, these biomaterials are designed to release therapeutic agents in response to biological, physical, or chemical triggers [4]. Enzymes, which are specific to certain organs and sites within the body, play a crucial role in this process. In enzyme-activated systems, drug release is triggered by enzymatic reactions. Prodrugs, liposomes, nanoparticles, and microparticles are some of the several types of enzymatic drug delivery systems. The key components in these systems include the drug, carrier, moiety, coating polymer, and ligand [5]. Stimuli-responsive polymers are particularly appealing due to their reactivity to both endogenous triggers, namely pH changes, redox conditions, and biomolecule recognition, as well as external stimuli like temperature and light [6]. These triggers can be categorized into intrinsic (internal) and extrinsic (external) stimuli. Intrinsic stimuli are linked to the pathological characteristics of diseased tissues, such as altered pH, redox environments, temperature, and the overexpression of specific biomolecules. External stimuli, conversely, are applied externally, namely heat, light, ultrasound, or magnetic fields [7].

Biopolymers are polymers derived from natural sources, either through chemical processes or synthesized entirely by living organisms. They consist of chain-like molecules made up of repeating chemical units obtained from renewable resources that are environmentally degradable. Biopolymers have been widely researched for pharmaceutical and biomedical applications owing to their diverse compositions, adaptable physical properties, and broad spectrum of potential products. They are generally categorized into two types based on their origin: natural biopolymers which include polysaccharides (such as alginate, chitin/chitosan, starch, and hyaluronic acid derivatives) and proteins (like silk, collagen, fibrin, gelatin, and soy) and synthetic polymers examples include poly(vinyl alcohol), poly(lactic acid), poly(glycolic acid), poly(caprolactone), poly(urethane), poly(propylene fumarate), and poly(hydroxybutyrate) [8].

Biopolymers offer several advantages due to their natural origin and inherent properties:

- a. **Biocompatibility:** Biopolymers are typically more compatible with biological systems compared to synthetic polymers. This makes them well-suited for

Biopolymer-based Nanofibers in Tissue Engineering

Aarti Tiwari¹, Ajay Kumar Shukla^{1,*}, Vimal Kumar Yadav¹, Kunal Agam Kanujia¹, Vishnu Prasad Yadav¹, Rama Sankar Dubey² and Manoj Kumar Mishra³

¹ Institute of Pharmacy, Dr Rammanohar Lohia Avadh University, Ayodhya, Uttar Pradesh, India

² Department of Pharmacy, MMM University Gorakhpur Uttar Pradesh, India

³ Shambhunath Institute of Engineering and Technology, Prayagraj, Uttar Pradesh, India

Abstract: Natural materials such as wood, shells, fungi, bacteria, and plants can be used to make biopolymer nanofibers (BPNFs), which are natural polymeric materials. Nanofibers (NFs) are the class of nanostructured materials that are widely used in tissue engineering (TE) and regenerative medicine (RM). These biomaterials aim to promote bone tissue regeneration at the defect location, whereupon they will eventually degrade naturally and be replaced by freshly produced bone tissue. Nanocomposite biomaterials are a relatively new class of materials that combine readily resorbable, bioactive fillers that are nanoscale in size with biopolymeric and biodegradable matrix architectures. The biocompatibility, tissue regeneration, and incorporation of nanomaterials have been assessed with alginate, fucoidan, chitosan (CS), collagen (Col), cellulose, and silk fibroin (SF). Examples of synthetic polymer-based nanocomposites in this chapter include polyethylene glycol (PEG), polycaprolactone (PCL), poly (lactic-co-glycolic) acid (PLGA), poly (lactic acid) (PLA), and polyurethane (PU) based nanocomposites. In bone tissue regeneration research, a wide range of nanofillers are used, such as graphene oxide (GO), nano titanium dioxide (nTiO₂), nano silica (nSi), nano zirconia (nZr), nano-hydroxyapatite (nHA), and nano silver nanoparticles (AgNPs). Biopolymer-based nanofibers have unique properties that replicate the extracellular matrix (ECM) of natural tissues, making them a promising tool for tissue engineering. These nanofibers, which can be made from synthetic or natural biopolymers, have customizable mechanical properties, biocompatibility, and biodegradability, making them ideal scaffolding materials for tissue regeneration. Cell attachment, proliferation, and differentiation are essential for the successful use of nanofibers in tissue engineering applications because of their high surface area-to-volume ratio. Further improving the functionality of biopolymer-based nanofibers and encouraging targeted tissue regeneration and healing is the addition of growth factors, medications, and bioactive compounds. The latest developments in biopolymer-based nanofibers for tissue engineering emphasize their properties, techniques of production,

* Corresponding author Ajay Kumar Shukla: Institute of Pharmacy, Dr Rammanohar Lohia Avadh University, Ayodhya, Uttar Pradesh, India; E-mail: ashukla1007@gmail.com

Sudhanshu Mishra, Smriti Ojha, Shashi Kant Singh, Rishabha Malviya & Saurabh Kumar Gupta (Eds.)

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and uses in the regeneration of various tissues, such as skin, bone, cartilage, and neural tissues. The necessity for multidisciplinary research to enhance nanofiber-based scaffolds for therapeutic applications is highlighted by the exploration of the possible obstacles and future prospects in this quickly developing sector. This chapter discusses a few biomaterials that have the potential to regenerate bone tissue in the form of polymeric nanocomposites.

Keywords: Biodegradability, Biopolymer-based nanofibers, Natural or synthetic biopolymers, Offer biocompatibility, Tissue engineering.

INTRODUCTION

The naturally occurring substances found in natural sources are known as biopolymers. The Greek terms bio and polymer, which stand for nature and living things, are the roots of the term biopolymer. Biopolymers are large macromolecules composed of many repeating units. A macromolecule, according to the IUPAC definition, is a single molecule. Because the biopolymers are biocompatible and biodegradable, they can be used in a variety of applications, including the food industry for edible films and emulsions, as well as in the pharmaceutical industry for wound healing, tissue scaffolds, dressing materials, drug transport materials, and medical implants such as organs [1].

The most common macromolecules are biopolymers (Fig. 1), which include proteins, carbohydrates, lipids, nucleic acids, and huge non-polymeric molecules like macrocycles and lipids. Synthetic macromolecules include plastics, synthetic fibers, and experimental materials like carbon nanotubes [2]. Their molecular backbones may include repeating units of amino acids, saccharides, or nucleic acids as well as a range of chemical side chains that support the molecules' functions. Using conventional chemical techniques, biopolymers such as polylactic acid (PLA) and polyhydroxyalkanoates (PHAs) are identified in microbes or genetically engineered organisms. These consist of proteins from milk or collagen and carbohydrates from cellulose. The genetic manipulation of microorganisms enables the biotechnological manufacture of biopolymers with specific properties appropriate for high-value medicinal applications, such as tissue engineering and drug delivery. The classification of biopolymers based on their origin is displayed in Table 1

Some synthetic polymers based on chemicals are harmful to microbiological organisms, plants, animals, and people. To make them suitable for use in biomedical applications, biopolymers have been proposed as a substitute. Although biopolymers have useful biomedical uses, they can be harmful in some situations and are unstable in biological fluids. Recent developments in nanotechnology have increased its practical relevance across a range of fields,

particularly in the development of biopolymers to create nanoparticles for a wide range of biomedical uses. To improve their biological qualities and be used for specific biomedical applications, biopolymers are specifically created as nanofibers [3].

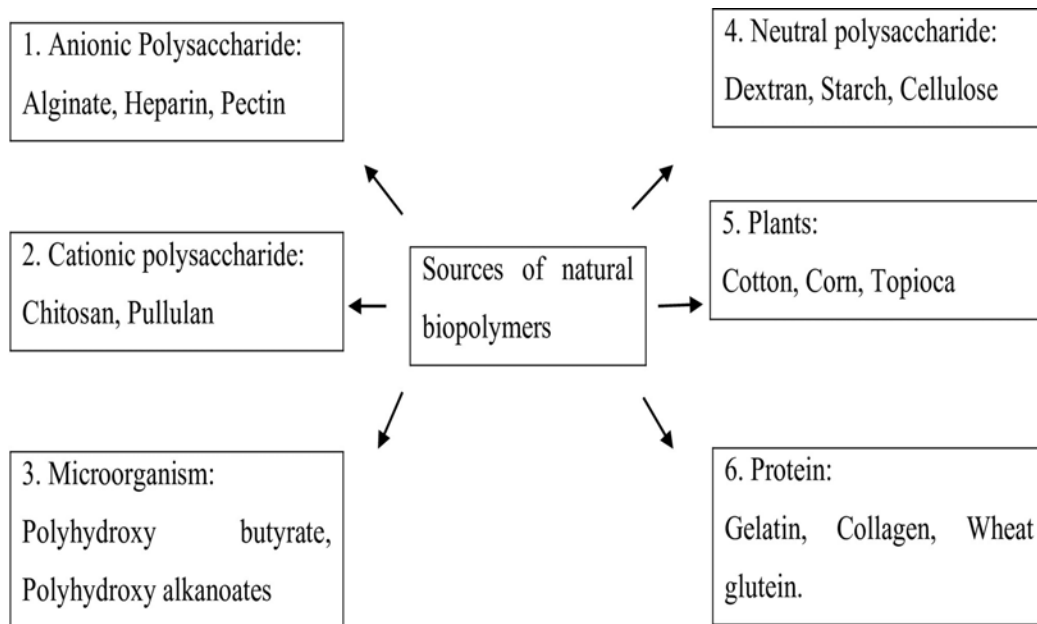


Fig. (1). Sources of natural biopolymers.

Table 1. A list of types of biopolymers, advantages and disadvantages.

Type	Advantages	Disadvantages	References
Natural biopolymers	Biodegradable, biocompatible, non-toxic, bioadhesive, biofunctional, and biologically renewable	Structurally more complicated, low melting point, high surface tension, and less stable.	[2]
Synthetic biopolymers	Improved mechanical and chemical stability, increased repeatability, and biocompatibility	Costly, toxic, and non-biodegradable synthesis process.	[2]

A nanofibrous structure is designed for a variety of medicinal applications using synthetic and/or natural polymers (biopolymers). The biopolymers are more biocompatible and have fewer toxicities and immunogenic effects on the body than synthetic polymers. Biopolymer-based electrospun nanofibrous materials have found extensive applications in drug delivery, tissue engineering, regenerative medicine, and wound dressing. To create composite nanofibers with

CHAPTER 10

Role of Biopolymer in Bone Regeneration & Replacement

Shashi Kant Singh^{1,*} and Shreya Maddesiya¹

¹ Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur , Uttar Pradesh 273007, India

Abstract: Bone regeneration and replacement are always challenging conditions, and with treatments, the chances of falling are often the least than expectations. This chapter emphasizes the function of biopolymers in bone replacement and regeneration, highlighting biopolymers that can be converted into scaffolds, hydrogels, and composites that mimic the extracellular matrix, facilitating the growth and repair of new bone. Their ability to promote cell adhesion, proliferation (rapid increase in the number or amount of cells), and differentiation makes them an alternative to traditional synthetic materials. Also, the biopolymer-based materials can be arranged in such a manner as to release bioactive molecules, enhancing osteogenesis, a genetic or heritable disease in which bones fracture or break easily, often without any major reason or minor injury. Angiogenesis is the process by which the body creates new capillaries from existing blood vessels. This chapter describes biopolymers in-depth and their role in the current biopolymer-based strategies for bone regeneration and replacement, including their mechanical properties, degradation rates, and osteoconductive potentials. It also focuses on the potential of biopolymers of composites and hybrid materials to enhance the regeneration the bones, combining the benefits of natural and synthetic materials. This chapter examines the potential of biopolymers for developing innovative solutions for bone replacement and regeneration, such as 3D-printed biopolymer-based implants and bioactive coatings. By harnessing the potential of biopolymers, the researchers can develop revolutionary treatments for bone regeneration and replacements, which lead to improvement in patient outcomes and enhances quality of life.

Keywords: Biocomposites, Biopolymer scaffolds, Bone cells, Bone healing, Bone replacement, *In vitro* testing, Novel biopolymer, Properties of biopolymer, Recent advancement, Stem cell therapy.

* Corresponding author Shashikant Singh: Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur , Uttar Pradesh 273007, India; E-mail: Shashikantsingh59@gmail.com

INTRODUCTION TO BONE BIOLOGY AND STRUCTURE

Composition of Bone (Organic and Inorganic Component)

Bone is a complex organ with both organic and inorganic components that support its structure and functionality. Collagen, more especially type I collagen, which gives the organic matrix its flexibility and tensile strength, makes up the majority of the material. Because it enables energy dissipation and fracture resistance, this collagen framework is essential to the properties of bone mechanics [1]. The structure of hierarchy in the collagen fibers allows mineral crystals to be integrated into the collagen matrix, increasing bone toughness [2, 3]. Collagen cross-links stabilize the collagen network, which affects the overall strength and toughness of the skeletal tissue, which further adds to the mechanical integrity of bone [4, 5]. Hydroxyapatite, a primary inorganic constituent of bone, is primarily composed of crystalline calcium phosphate with the chemical formula $\text{Ca}_5[\text{PO}_4]_3[\text{OH}]$. The compressive strength and stiffness of bone are attributed to this mineral phase [6]. At the nanoscale, the mineralization process entails the highly ordered deposition of HA crystals inside the collagenous framework. The degree of mineralization can influence the size and crystallinity of mineral crystals, and this can vary based on factors such as age and mechanical loading [7, 8]. Moreover, the mineral phase stores significant ions like calcium and phosphate, which are required for several physiological processes [9]. The interaction between the organic and inorganic components primarily examines the mechanistic features of bone. The collagen matrix shields the mineral crystals from mechanical stressors and serves as a framework for mineral deposition. Because of its composite nature, bone can tolerate a variety of stresses without losing its structural integrity or usefulness.

Role of Bone Cells

The following three primary cell types regulate the ongoing remodeling of bone:

Osteoblasts

The process of making new bone is carried out by specialized cells known as osteoblasts. They are derived from mesenchymal stem cells and play a crucial role in generating and secreting collagen type I and other vital components of the bone matrix, including osteocalcin and osteopontin. The mineralization of the bone matrix is dependent on osteoblasts, which facilitate the crystallization of hydroxyapatite, ultimately imparting strength and stiffness to the bone. Additionally, by secreting signaling molecules like Osteoprotegerin and RANKL, which influence the differentiation and function of osteoclasts, osteoblasts help control osteoclast activity. Osteoblasts and hematopoietic stem cells have a spatial

relationship in the bone marrow that suggests a functional interdependence, with osteoblasts providing a niche that promotes the maintenance of hematopoietic stem cells [10, 11].

Osteoclasts

Macrophage lineage multinucleated cells and osteoclasts are principally responsible for bone resorption. Osteoclasts cling to the bone's surface and release an acidic microenvironment that encourages mineralized materials to break down bone and cause the deterioration of the organic matrix [12, 13]. The necessary components of the macrophage colony-stimulating factor (M-CSF) and RANKL are highly regulated processes of osteoclast precursor differentiation through mature osteoclasts [14, 15]. To remove deteriorated or outdated bone tissue, this resorption process is necessary for appropriate bone remodeling. Additionally, osteoclasts show dynamic behavior that can change their functional capability through fission and fusion processes [16, 17]. Osteoporosis and other metabolic bone diseases can result from excessive osteoclastogenesis, hence, controlling osteoclast activity is essential [18].

Osteocytes

Osteoblasts that become embedded in the mineralized matrix differentiate into osteocytes, the most prevalent cell type in bone tissue. These are essential for mechanotransduction because they detect mechanical loads and communicate with other bone cells to start remodeling processes. Through a network of dendritic processes that extend through canaliculi in the bone matrix, osteoblasts and osteoclasts can communicate with one another. Coordination of bone production and resorption depends on this communication, which guarantees that bone remodeling adapts to mechanical and metabolic demands. Additionally, osteoblasts and osteoclasts are influenced by the signaling molecules that these cells create. Fig. (1) shows the bone cells responsible for bone regeneration. As a result, osteoclasts and osteoblasts work together to preserve bone homeostasis.

BONE REMODELING AND REGENERATION PROCESSES

Bone remodeling and regeneration are complex biological processes that involve the coordinated function of several cell types, primarily osteoblasts, osteoclasts, and osteocytes [19].

Bone Remodeling Process

When stimulated, osteoclasts, which directly resorb bone, break down the mineralized matrix of bone and resorb aging or damaged bone tissue in this phase,

Mechanisms of Immunotherapeutic Biopolymers in Autoimmune Disease

Deepak Kumar¹, Piyush Anand¹ and Shashi Kant Singh^{1,*}

¹ Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University Gorakhpur, Uttar Pradesh 273007, India

Abstract: Autoimmune disorders result from dysregulated immune responses directed against the body's tissues; immunotherapeutic biopolymers are becoming increasingly important as transformational agents in this regard. These biopolymers, which comprise organic materials like peptides and polysaccharides, function in different ways to help the immune system's restoration to equilibrium. A noteworthy method pertains to the control of immune cell function, wherein biopolymers augment the functionalities of regulatory T cells while inhibiting the generation of pro-inflammatory cytokines. Furthermore, certain biopolymers, such as hyaluronic acid and chitosan, have anti-inflammatory qualities that are vital in lowering tissue damage and inflammation linked to autoimmune diseases. By influencing the gut microbiota, which has been linked to the etiology of several autoimmune disorders, these biopolymers can also balance the immune system. The adaptability of immunotherapeutic biopolymers is further demonstrated by their capacity to target particular pathways, such as the NF- κ B signaling cascade and cytokine production. Recent developments in nanotechnology have made it possible to create delivery systems based on biopolymers that improve the bioavailability and effectiveness of medicinal drugs. Not only does this novel method increase therapeutic specificity, but it also reduces systemic adverse effects that are frequently linked to traditional medications. Personalized and efficient therapy techniques might transform the management of autoimmune diseases as research advances and immunotherapeutic biopolymers are incorporated into clinical practice.

Keywords: Antigen presentation, Autoimmune diseases, Gut microbiota, Immunological regulation, Immunotherapeutic biopolymers, Inflammation, Regulatory T cells.

INTRODUCTION

Autoimmune diseases can be triggered by genetics, bacterial or viral infections, or other factors, including the body's immune cells activating abnormally and

* Corresponding author Shashi Kant Singh: Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University Gorakhpur, Uttar Pradesh 273007, India; E-mail: Shashikantsingh59@gmail.com

destroying host tissues or organs. An estimated 24 million Americans suffer from more than 100 autoimmune disorders, with 80% of those affected being women, according to data made available online by the American Autoimmune Disorders Association. In addition, five to ten percent of Americans suffer from one or more autoimmune disorders. Patients frequently have abnormal T lymphocyte activation and autoantibodies that impact specific organs. Type I diabetes (pancreas) includes pernicious anemia (stomach), Hashimoto's thyroiditis (thyroid gland), and Addison's disease (adrenal glands). Additional organs and tissues may be impacted by rheumatoid arthritis, dermatomyositis, Systemic Lupus Erythematosus (SLE), and other conditions of a similar kind. Autoimmune diseases frequently recur with long delays. During clinical diagnosis, the majority of patients frequently exhibit tissue damage and persistent problems. Currently, anti-inflammatory, nonspecific, broad-spectrum, or immunosuppressive medications (such as tacrolimus, corticosteroids, or cyclosporine) are used to treat autoimmune diseases. These therapies mostly lessen the body's inflammatory cell proliferation and immune response, which can lessen clinical symptoms but not the disease's underlying cause or its consequences. Furthermore, using cytotoxic and immunosuppressive medications often over an extended period will weaken the body's defense against infection and cancer [1]. The objective has been to restore immunological equilibrium, and in the last several years, research has concentrated on creating treatments that may precisely reduce immunity without compromising healthy immune function. Because of their vital roles in preserving and enhancing immunological tolerance, immunoregulatory tolerogenic dendritic cells (Tol DCs), as opposed to earlier immunosuppressive therapies, have garnered a lot of attention in the treatment of autoimmune diseases. Currently, the *in vitro* harvesting of autologous tolerogenic DC is costly and has a risk of transfusion-associated failure. Another outcome of the *in vitro* culture of tolerogenic DCs is non-specific immunosuppression. However, disease-specific autoantigens must be loaded into these DCs for them to produce autoimmune cells that are specific to the targets [2].

Key Features and Types

Immunotherapeutic biopolymers are a cutting-edge approach to treating autoimmune diseases because of their unique capacity to successfully alter immune responses. These biopolymers are designed to interact with the immune system in a way that reduces aberrant immune activity, which is characteristic of autoimmune diseases and increases tolerance [3]. Biocompatibility is one of the most important characteristics of immunotherapeutic biopolymers. This feature guarantees that the substances utilized do not cause negative responses when ingested. Biopolymer synthesis and characterization are also important factors for establishing their biocompatibility, efficacy, and stability in drugs. Different

techniques of synthesis, such as chemical polymerization, enzymatic polymerization, and microbial fermentation, are utilized based on the biopolymer type. For instance, chitosan is generally derived through the deacetylation of chitin, whereas hyaluronic acid is biosynthesized through bacterial fermentation by utilizing *Streptococcus* species. Characterization of biopolymers is needed to determine their purity, molecular weight, and structural integrity, which further determines their functionality in immunotherapeutic applications. Gel Permeation Chromatography (GPC) is typically used for the determination of molecular weight distribution, while Fourier-Transform Infrared Spectroscopy (FTIR) and Nuclear Magnetic Resonance (NMR) spectroscopy confirm structural composition. These biopolymers' surface topography and nano-scale interactions are also elucidated by Atomic Force Microscopy (AFM) and Scanning Electron Microscopy (SEM). High-Performance Liquid Chromatography (HPLC) identifies purity, where contaminants are kept as low as possible, and batches can be reliably identical. Biodegradability as well as potential for drug-loading are important physical properties that guide biopolymer performance. Thermogravimetric Analysis (TGA) and Differential Scanning Calorimetry (DSC) are most frequently applied in assessing thermal stability, which dictates storage and formulation stability. All these sophisticated characterization methods together enhance our knowledge of biopolymer-based drug delivery systems and how they can potentially be used for the treatment of autoimmune diseases. Maintaining patient safety and improving the treatment's overall efficacy depends heavily on biocompatibility [4]. The regulated release aspect is also crucial. It is possible to construct immunotherapeutic biopolymers such that their therapeutic chemicals are released in a controlled way. This regulated release is crucial for maintaining therapeutic levels of the medicine over an extended period, which can contribute to improved patient outcomes by guaranteeing constant exposure to the treatment [5].

These biopolymers also possess the important quality of versatility. They may be engineered to carry nucleic acids, proteins, and peptides, among other medicinal substances. This flexibility enables customized treatment plans that may be modified under the requirements of each unique patient and the particular autoimmune disorder.

Types of Biopolymers Used in Immunotherapy

At present, several immunotherapeutic biopolymers are being investigated for their potential to treat autoimmune diseases. One of the most promising types of biopolymers is *nanoparticles*. To improve treatment precision, they can target certain immune cells and encapsulate therapeutic molecules. Nanoparticles can

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Sudhanshu Mishra

Prof. Sudhanshu Mishra completed M. Pharm in pharmaceuticals from the School of Pharmaceutical Science, Rajiv Gandhi Proudyogiki Vishwavidyalaya, Bhopal, and is pursuing a Ph.D. from Dr. APJ Abdul Kalam Technical University, Lucknow, Uttar Pradesh. He is currently working as an assistant professor at the Faculty of Pharmaceutical Sciences, Mahayogi Gorakhnath University, Gorakhpur. His areas of interest include novel formulations, nano-herbal formulation, transdermal drug delivery, localized drug delivery, etc. He has authored over 50 research/review articles for national/international journals. He is a reviewer and editorial board member of national and international journals. He holds international ranking positions in medical & health sciences and pharmacy & pharmaceutical sciences as per the AD Scientific Index 2025.



Smriti Ojha

Prof. Smriti Ojha earned a doctorate in pharmaceutical sciences from Dr. A. P. J. Abdul Kalam Technical University, Lucknow. Her doctoral research focused on the development of solid lipid nanoparticles for better management of multiple sclerosis. She has teaching and research experience of around 18 years and is currently working as an associate professor in the Department of Pharmaceutical Science and Technology, Madan Mohan Malaviya University of Technology, Gorakhpur, Uttar Pradesh. She is actively engaged in the research area of oral and controlled drug delivery and nanotechnology. She has published more than 50 peer-reviewed research papers in prestigious national and international journals.



Shashi Kant Singh

Prof. Shashi Kant Singh is currently working as a professor and head of the Faculty of Pharmaceutical Sciences at Mahayogi Gorakhnath University, Gorakhpur. His research interests encompass a wide range of fields, including pharmacognosy and phytochemistry, with a strong interdisciplinary focus that integrates organic, medicinal, and analytical chemistry. Throughout his illustrious career, he has made significant contributions to the scientific community, evidenced by his five international publications and ten national publications. Additionally, he holds two granted patents and has authored two books, highlighting his commitment to advancing knowledge in the pharmaceutical sciences.



Rishabha Malviya

Prof. Rishabha Malviya did a Ph.D. in pharmacy in the area of novel formulation development techniques. He has 12 years of research experience and has been working as a professor in the Department of Pharmacy, School of Medical and Allied Sciences, Galgotias University, for the past 8 years. His area of interest includes formulation optimization, nanoformulation, targeted drug delivery, localized drug delivery, and characterization of natural polymers as pharmaceutical excipients. He has authored more than 150 research/review papers for national/international journals of repute. He has 51 patents (12 granted, 38 published, 1 filed) and publications in reputed national and international journals. He received an outstanding reviewer award from Elsevier. He has authored/edited 21 books and 15 book chapters. He is a reviewer/editor/editorial board member of more than 50 national and international journals of repute.



Saurabh Kumar Gupta

Prof. Saurabh Kumar Gupta is an associate professor of pharmaceutical chemistry at Rameshwaram Institute of Technology and Management, Lucknow, with over ten years of teaching and two years of industry experience. He began his career as a quality assurance officer at Macleods Pharmaceuticals and Ciron Drugs, gaining expertise in analytical validation and regulatory compliance. He holds an M. Pharm in pharmaceutical chemistry and is pursuing his Ph.D. from AKTU. His research interests include nanotechnology-based drug delivery, neurodegenerative diseases, diabetes, and cancer therapeutics, with several publications and book chapters to his credit.