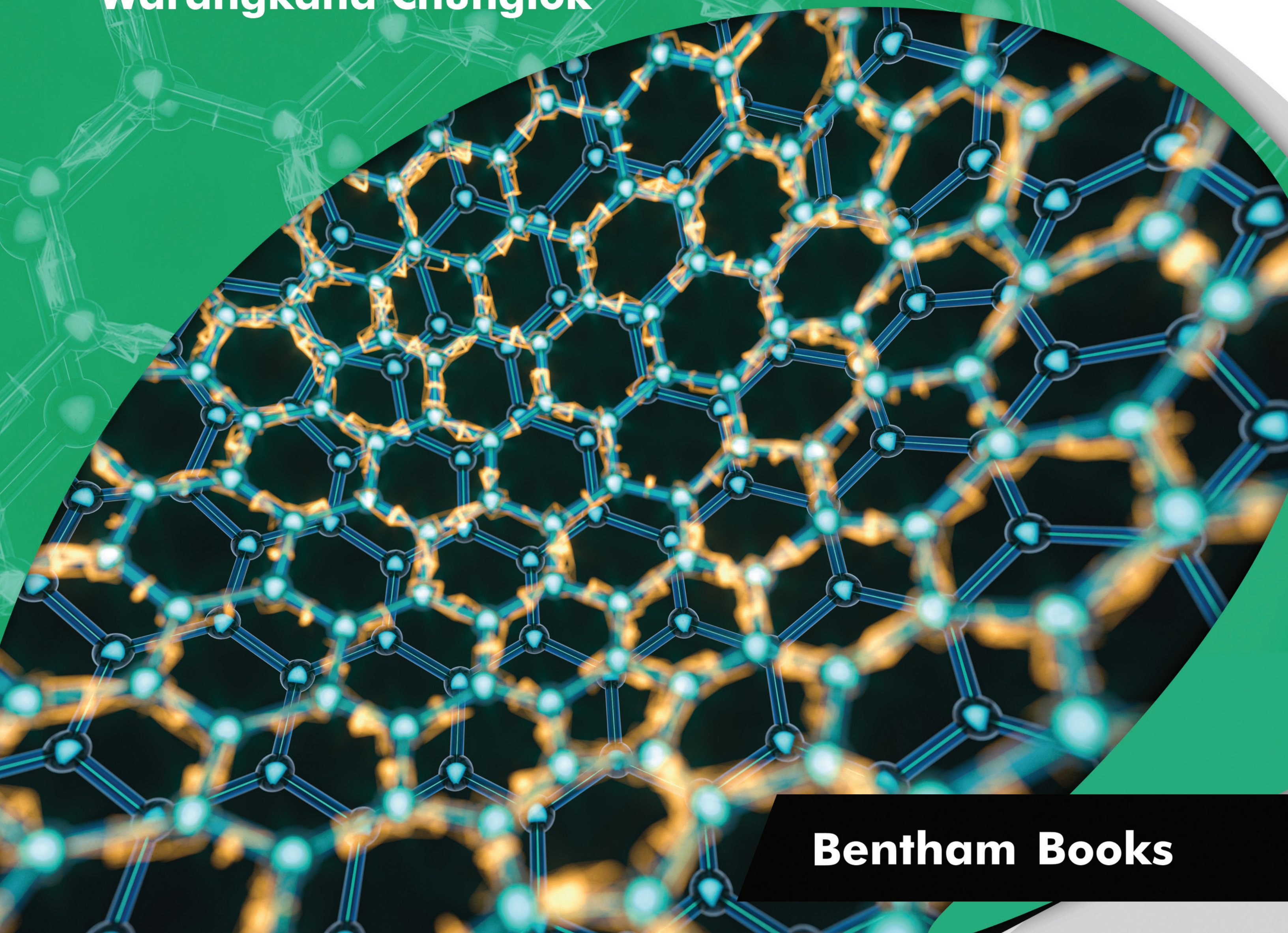
BIOPOLYMERS TOWARDS GREEN AND SUSTAINABLE DEVELOPMENT

Sudarshan Singh
Warangkana Chunglok



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Biopolymers Towards Green and Sustainable Development

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ISBN (Online): 978-981-5079-30-2

ISBN (Print): 978-981-5079-31-9

ISBN (Paperback): 978-981-5079-32-6

First published in 2022.

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FOREWORD

There has been growing concern about the negative impacts of environmental pollution from fossil fuels, waste from petroleum products, and non-biodegradable materials. A lot of research has been done into exploring another alternative to petroleum-based products which would be renewable as well as biodegradable and thus pose a lesser risk to the environment. Biopolymers are one such possible solution to the problem because they are typically biodegradable materials obtained from renewable sources. Moreover, biopolymers are produced by the cells of living organisms consisting of monomeric units that are covalently bonded to form large molecules. Some of the first modern biomaterials made from natural biopolymers include rubber, linoleum, celluloid, and cellophane. However, due to growing ecological concerns, the application of biopolymers enjoys renewed interest from the scientific community, the industrial sectors, and even other allied sectors.

Biopolymers towards green and sustainable development provide an up-to-date summary of polymeric materials characterized by biodegradability and sustainability. The book includes a thorough breakdown of the vast range of application areas, including pharmaceutical and medical, packaging, textile, biodegradable plastics, green synthesis of metallic nanoparticles, and many more, giving engineers critical materials information in an area that has traditionally been more limited than conventional inactive ingredients. This book aims to fulfill the current need of the researcher by providing an excellent bibliometric meta-analysis on bio-based polymers indicating potential collaboration between country, organization, institution, and authors. Moreover, a meta-analysis provided a view of recent ongoing trends in biopolymers.

I have, no doubt, that this book will be well-received by all those in the pharmaceutical and agro-industry, academia, and other research organizations who continually seek inactive functional biomaterials for improved drug formulation and development, especially scientists and students working with biopolymers.

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PREFACE

Biopolymers are polymers synthesized by living organisms. They can be polynucleotides, peptides, or polysaccharides. These consist of long chains made of repeated, covalently bonded units, such as nucleotides, amino acids, or monosaccharides. Cellulose is the most common organic compound, and about 33% of the plant matter is cellulose. Biopolymers can be sustainable and carbon neutral and are always renewable because they are made from plant materials that grow indefinitely. These plant materials come from agricultural non-food crops. Therefore, the use of biodegradable polymers creates a sustainable industry. In contrast, the feedstock for synthetic polymers derived from petrochemicals will eventually deplete and most of them are non-biodegradable. Non-biodegradability issues of synthetic inactive pharmaceutical ingredients strongly emphasized innovators towards the development of biopolymers. Recently natural biodegradable excipients gained significant attention due to their sustainability and engineered applications. Innovative technologies to transform these materials into value-added chemicals *via* novel graft-polymerization or co-processing techniques for the production of high-performance multifunctional and low-cost polymers with tunable structures are key parts of its sustainable development. Besides, the development of state-of-the-art advanced characterization techniques for these engineered materials is an essential component in uncovering their specific structure and facilitates the application of these materials in the new research area. This expansion is driven by a remarkable progress in the process of refining biomass feedstock to produce bio-based building blocks. The book has been written to provide a broad platform for innovators and researchers in the area of biopolymers' development with major biomedical and agro-industrial applications. Furthermore, to communicate the state-of-the-art work related to the transformation of natural materials into value-added pharmaceutical inactive ingredients, a brief on the modification and fabrication of new biopolymers, and their characterization including the application in the textile and plastic industry has been emphasized. Moreover, the book presents updated information and addresses various issues on emerging new sources of biopolymers with multifunctional efficacy, food, and drug administrative regulatory requirements, with their impact on the ecosystem and human health. Additionally, the book also provides updated information on a meta-analysis of bio-based pharmaceutical excipients.

There are numerous books about biopolymers covering the scientific research that is enabling the new generation of degradable plastics. The goal of this handbook is to bring together some of the core knowledge in the field to provide a practical and wide-ranging guide for engineers, product designers, and scientists involved in the commercial development of biopolymers and their use in the various biomedical, environmental, and agro applications. Additionally, information on the impact of non-biodegradable materials on human health and the environment has been taken into consideration. This book gives a brief account of inactive ingredients originating from plants and their characterization techniques with pharmacokinetics. The book also covers a summary of the bibliometric meta-analysis of bio-based polymers.

We acknowledge Walailak University for extending the library facility and providing access to Scopus. Moreover, Dr. Ozioma F Nwabor, Division of Infectious Diseases, Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand is acknowledged for the valuable suggestions and critical comments.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

KEY FEATURE

- Provides an up-date summary on recently discovered natural polymeric materials

- Recently discovered new sources of biopolymers have been presented in this book.

- Presents a thorough breakdown of the vast range of application areas including fabrication of conventional and novel drug delivery, polymeric scaffolds, composites, microneedles, and green synthesis of metallic nanoparticles.

- Bibliometric meta-analysis indicating potential collaboration between country, organization, institution, and authors with a view on recent ongoing trends with biopolymers.

- A summary of pharmacology and pharmacokinetics on the inactive pharmaceutical ingredient presented

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CHAPTER 1

Overview on Bio-based Polymers

Abstract: Synthetic polymers are an imperative manmade discovery that has long been under environmental scrutiny due to their several detriments such as slow or non-degradation, diminutive re-usage, and severe milieu effects. A rough estimate indicates that 8300 million metric tons of virgin plastic are produced using synthetic materials to date, of which only 9% have been recycled until 2015. The detrimental effects of a synthetic polymeric waste product on surroundings can be slowed down by replacing it with biopolymers. Biodegradable polymers are materials that degrade due to the action of either aerobic or anaerobic microorganisms and/or enzymes. Environmental protection agency and PlasticEurope indicated that biodegradable polymers have shown a promising impact on the environment with a decline in the waste and toxic gas produced by either burying or incinerating synthetic polymers and their products. Moreover, the replacement of plastic products with bio-polymeric material for general, pharmaceutical, and agricultural use has also shown a significant decline in waste plastic in landfills and oceans. Furthermore, the potential market share of biopolymers growing gradually and is projected to generate 10.6 billion US Dollars by 2026. However, the potential biodegradable polymers market capital share has yet not reached its peak, due to the non-availability of specific regulatory standards and approval process. Thus, a complete replacement of synthetic polymers with biodegradable polymeric materials can be a paradigm shift for nature and human beings. This chapter acmes on the history of biodegradable materials and their impact on nature with their regulatory requirements to gain market capital share.

Keywords: Biodegradable agro-materials, Biodegradable material, Biopolymer market, Biopolymers.

INTRODUCTION

Mankind was familiar with bio-based materials and their use since the beginning of civilizations. The synthetic polymer industry in its initial stage assured systematic preservation of the environment with progressive support to human beings. However, with the discovery of fossil fuels for the synthesis of petroleum-based polymers and their products, the development and innovation of natural polymers suffered major setbacks. Moreover, the innovation of single-use synthetic polymer-based plastic materials severely affected the ecosystem. In view of the potential disadvantages of synthetic polymers towards the environment, biodegradable polymer regained consideration among researchers,

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pharmaceutical manufacturers, and other allied industrial sectors. Biopolymers are polymeric materials synthesized by living organisms that can be polynucleotides, and polypeptides, or polysaccharides. Biopolymer mainly consists of long chains made of repeating covalently bonded units, such as nucleotides, amino acids, or monosaccharides. Furthermore, biodegradable polymers have received significant attention in the last few decades due to their various potential application including the development of novel dosage forms, fabrication of agro-biotechnological products, *etc*. The biodegradability of such polymers or polymeric materials results in the formation of by-products such as CO_2, N_2, H_2O, biomass, and inorganic salts upon breaking down either by aerobic or anaerobic microorganisms. However, this degradability does not include polylactides polymers that hydrolyze comparatively at a higher rate even at room temperature and neutral pH in the absence of hydrolytic enzyme. Moreover, biodegradation does not mean that all material can be processed into compost or humus. In addition, biodegradation significantly differs from the bio-erosion process. Bio-erosion is a process of conversion of initially water-insoluble material to a slow water-soluble material that may or may not involve any major chemical degradation. Polymers are versatile compounds and are classified based on several parameters such as the source of availability, type of polymerization, monomers in the repeating units of polymers, molecular forces, *etc*., as presented in Fig. (**1**). In this chapter, an overview is presented on the history of biopolymers and the impact of synthetic polymers on the ecosystem. Furthermore, a brief account of the regulation involved in the safety and efficacy of biopolymers and their market potential concerning the maintenance of the carbon cycle within the environment has been taken into consideration, with special attention to the use of the polymer-based product in the pharmaceutical and agroindustry.

HISTORY OF BIODEGRADABLE POLYMERS

The term excipient is derived from the Latin word, *excipiens*, which means either to receive, to gather, or to take out. The definition of excipients has changed from time to time with its functions. The International Pharmaceutical Excipients Council (IPEC) defines an excipient as any substance other than the active drug or prodrug that is included in the manufacturing process or is contained in the finished pharmaceutical and relevant products [1]. Several incidences including phenytoin toxicity in 1968 and lack of strict regulations raised serious concerns and steered IPEC to mandate the manufacture for providing material safety data directly or indirectly consumed. The synthetic polymer market is growing exponentially and has become an integral part of day-to-day human life due to the enormous use of polymer-based products. These polymers are out product of petroleum oil industries or chemically synthesized *via* polymerization of several monomers. The market available petroleum-derived synthetic polymers are designed to resist the biological attack and stabilized with antioxidants and heat stabilizers that protect them from environmental degradation. Furthermore, synthetic polymers' production was significantly accelerated by a global shift from reusable to single-use plastics and surpassed most manmade products. In consequence to that the share of plastics in municipal solid waste increased from less than 1% in 1960 to more than 10% by 2005 [2]. Although products made using synthetic polymers are a more economically feasible choice than biodegradable polymers, however, the scenario has changed as such synthetic polymers produce detrimental effects to the environment and health of several organisms on enduring use.

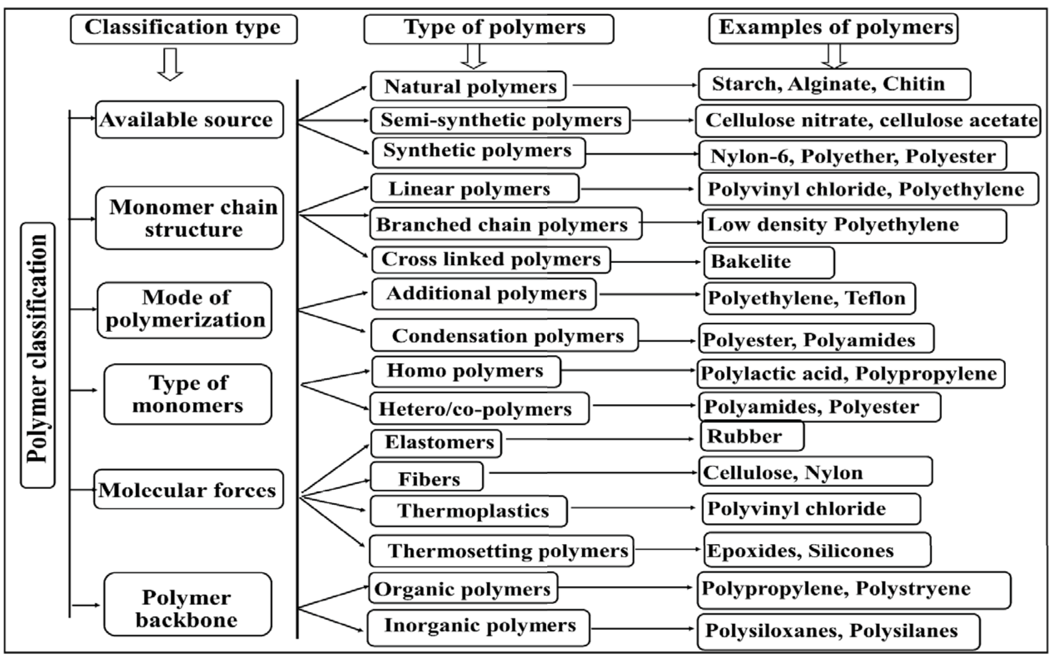

Fig. (1). Classification of polymers [4].

Decreasing the use of non-biodegradable polymers and reducing the solid waste generated from them have become a high priority due to the rising cost of petroleum oils with increasing concern about the preservation of ecological systems. In addition, the use of synthetic polymers generates substantial environmental pollution and damage to wildlife. Additionally, incineration of the synthetic polymer-made product presents serious environmental issues due to toxic emissions including dioxins, furans, mercury, and polychlorinated biphenyls [3]. Moreover, toughen legal requirements of several countries for the management of waste caused a concern to focus on the expansion of biodegradable functional polymers. For such different issues, it is necessary to

CHAPTER 2

Impact of Non-Biodegradable Polymers on the Environment and Human Health

Abstract: Synthetic polymers have been thriving in global industries over the past few decades due to their malleability, resilience, and economic value. But leaching of additives such as bisphenol-A, polybrominated diphenyl ether, and phthalates used in the manufacturing of polymeric products has raised serious concerns. However, the growing interest and investment in the development of biodegradable polymers could be a vital step toward reducing the impact of non-degradable polymers on the environment. Moreover, a combination of petroleum products with biopolymers can be a turning point for gradually replacing synthetic polymers to address or resolve these problems. In addition, a possible reduction in plastic polymer usage and manufacturing of products with materials that are less aggressive towards the environment can also reduce the impact of plastic on nature. Nature-derived biopolymers possess an enormous advantage over synthetic polymeric materials through cost-effectiveness, eco-, and user-friendly materials. Furthermore, the advanced applications of biopolymers in medical, tissue engineering, food industry, and fabrication of biotechnological products suggest that biopolymers are a boon for nature over synthetic polymers. This chapter discusses the advantage of biopolymers over synthetic polymers considering socioeconomic, human health, and environmental aspects. Additionally, the impact of petroleum-based polymeric materials on the environment compared to biodegradable polymers has been taken into consideration. The discussion is further extended to life cycle assessment, regulation, valorization, and utilization of polymer derived from waste with their potential use as inactive materials.

Keywords: Bio-based polymer, Environment, Life cycle assessment, Natural polymer, Valorization of waste.

INTRODUCTION

Living creatures produce a wide range of polymers as a significant part of their morphological, cellular, and dry matter. These biopolymers play a vital role in the life cycle of organisms to support their essential metabolic and cellular activities (Fig. **1**). Biopolymers are produced in the cytoplasm, organelles, cytoplasmic membrane, cell wall components, and the surface of cells even extracellularly by enzymatic processes. Today the life of human beings has become inconceivable without the use of polymeric products. Synthetic polymers are known to produce

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non-biodegradable products originating from the petroleum industry as monomers, which are subjected to specific chemical reactions including polymerization, poly-condensation, and poly-addition under a particular condition. Petrochemical plastics have many technical advantages that have significantly replaced other materials in many applications. These polymeric products can adopt different forms such as single-use plastics, bags, bottles, jars, thin films, multiple-use pipes, *etc*.

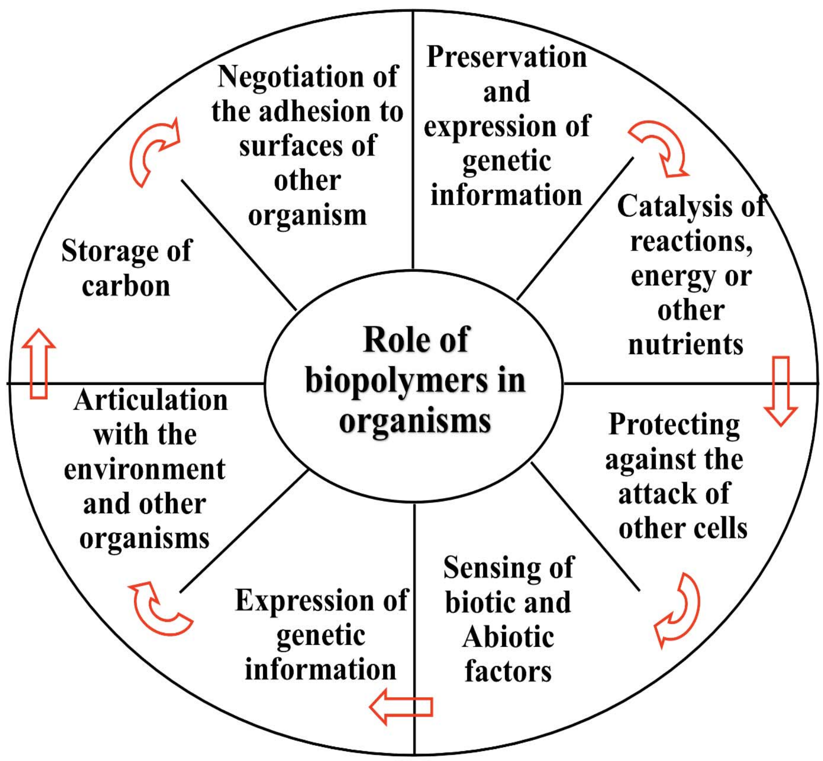

Fig (1). Biological role of biopolymers in a living organisms [1].

Moreover, synthetic polymers are also widely used in the fabrication of pharmaceuticals and medical products to regulate the life cycle. In addition, synthetic polymers and their products demonstrate good thermal and electrical insulators that resist corrosion and other associated chemical reactions with ease of handling. Although synthetic polymers can produce economic products, but their non-biodegradability and increasing accumulation in the environment every year cause detrimental effects on the ecosystem. Additionally, when synthetic polymer-based plastic enters the natural environment as litter through poor waste management or incorrect disposal, this poses a threat to wildlife too. Moreover, the leaching of additives such as bisphenol A, polybrominated diphenyl ether, and phthalates used in the manufacturing of polymeric products has also raised serious concerns about human health. To address these complications, researchers developed several biodegradable polymers originating from nature or chemically synthesized materials that can partially or completely replace the non-biodegradable polymeric product. Biopolymers have emerged as potential alternatives, some of which are available commercially while others remain under research. A biopolymer made from annually renewable resources which biodegrade can appear to solve the major problems associated with non-biodegradable polymers and their materials. In this chapter, an overview is presented on the impact of non-biodegradable polymers on the environment and their life cycle assessments. Further, a summary of recent research and review published on the biodegradation of natural polymers is provided. Furthermore, the effect of non-biodegradable polymers on human health has been reviewed.

Sustainability and Life-Cycle Assessments of Polymers on Eco-System

Biopolymers are generally considered an eco-friendly alternative to petrochemical polymers due to the renewable feedstock used to produce them and their biodegradability. Natural polymers are biosynthesized by living organisms *via* various techniques in the biosphere. Generally, such materials are high molecular weight polymers that break down to lower macromolecular structures upon the action of micro or macro-organism and enzymes [2]. In addition, catalysts promoting the degradation in nature *via* catabolic reactions followed by enzymes are categorized in six different classes depending on the catabolism [3]. The biodegradable polymeric materials including proteins, peptides, nucleic acids, lipids, natural rubber, lignin, and polysaccharides are obtained from various sources originating either from plants or microorganisms, however, the degradation rate differs depending on the nature of the functional group and the degree of complexity. Biopolymers are organized and classified variously as briefed in Chapter 1. The categorization of natural polymers allows the usage of starting monomers of diverse sequence and conformations at molecular, nano, micro, and macroscale, forming biodegradable multifarious polymers [4 - 6]. Conversely, synthetic biodegradable polymers degrade *via* oxidation, hydrolysis, thermal degradation, or other modes. The major advantage of biopolymers over synthetic polymers includes the potential to create a sustainable industry as well as enhancement in various properties such as durability, flexibility, high gloss, clarity, and tensile strength. However, several questions and challenges are also associated with biopolymers, since biopolymers are somehow produced using renewable raw materials that do not imply they are sustainable. Moreover, the farming practices used to grow agro-based polymers often carry significant environmental burdens, and the production energy can be higher than for petrochemical polymers [7]. Therefore, it is necessary to understand the potential

CHAPTER 3

Potential Sources of Biodegradable Polymers

Abstract: Synthetic polymers are an important class of pharmaceutical excipients that contribute significantly to the fabrication of different dosage forms. However, due to biodegradability concerns, the highly publicized disposal problem of traditional oil-based thermoplastics with a detrimental effect on the environment, has promoted the search for alternative biodegradable polymers. Biodegradable polymers are an ecofriendly, economic, and safe alternative to synthetic polymers due to their biodegradable nature and the source of origin. Biopolymers and biomaterials are available in abundance with different pharmaceutical and medical applications including drug delivery, wound healing, tissue engineering, imaging agents, *etc*. Moreover, biopolymers possess certain specific properties such as biocompatibility, biodegradability, low antigenicity, functionality to support cell growth, and proliferation with appropriate mechanical strength. Biopolymers are obtained from sustainable natural resources and animal processing co-products and wastes. Polysaccharides such as cellulose and starch represent the major characteristics of the family of these natural biopolymers, while other biodegradable polymers such as bacterial cellulose and sericin are also used to develop biodegradable materials. Recent advancements and development in the field of natural polymers have opened up new possibilities for the rational engineering of natural gums and mucilage towards the expansion of functional excipients suitable for industrial and medical applications. This chapter highlights the potential sources of novel biodegradable polymers with recent expansion in the processing of different novel natural polymers to develop multifunctional excipients and valorization of waste biomass to produce biopolymers.

Keywords: Biodegradable polymers, Biopolymers, Carrageen, Lignin, Sericin, Source of polymers.

INTRODUCTION

Biodegradable functional polymers were introduced in the 1980s and since then, these have been applied in the design and development of various components including the pharmaceutical dosage form, packaging, agriculture, and in several other allied areas [1]. Biodegradable polymers have received attention in the last decades due to their potential application in the maintenance of physical health with low cost of production, environmental protection, and delivery of active drug moiety. Biodegradable polymers are broadly distinguished into two classes such as synthetic and natural excipients. Natural polymers are those that are present in

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or created by living organisms. Moreover, such polymers are available in abundant from renewable sources, while synthetics are developed from non-renewable petroleum resources. The future of biodegradable polymer depends not only on the cost of production but also on its effectiveness in delivering the active component in a controlled manner. The term natural polymers refers to macromolecules that occur naturally or are synthesized by a living organism [2], whereas synthetic polymers are fabricated macromolecules. The synthesis of natural polymers generally involves enzyme-catalyzed, chain-growth polymerization reactions of activated monomers that are typically formed within cells by complex metabolic processes. Moreover, the degradation of natural polymeric materials generally occurs through enzymatic actions or *via* chemical deterioration. The enzymatic degradations include the breakdown of polymers in lower molecular mass through abiotic reactions, while hydrolysis and oxidation are chemical degradation pathways as presented in Fig. (**1**). Furthermore, recent discoveries in the field of bacterial polymer biosynthesis have opened up other new avenues for the rational and medical applications of biodegradable polymers. Generally, petroleum-derived polymers resist degradation *via* oxidation or hydrolysis, however, the addition of additives including antioxidant or pro-oxidants can initiate the biodegradation process. Fortification of additives within such polymer chain initiates the biodegradation process in the presence of ultraviolet light *via* photo-oxidation, which propagates by a free radical chain reaction in which the first hydrogen peroxide is produced and later a hydrophilic low molecular mass is formed by pyrolysis [3].

The evolution process of biodegradable polymers is yet not complete, or commercially successful. However, biodegradable polymers gained significant attention among researchers considering the utilization of renewable resources to replace declining and increasingly expensive fossil resources as a source for monomers and polymers. The selection of a suitable composition substrate is an important factor for the optimization of biodegradable excipients production and characterization. Since the high cost of substrates is the major contributing factor in biopolymers development and production cost, thus the usage of waste and biomass could significantly reduce the total fabrication cost. In this chapter, a detailed overview is presented on recent advances in the sources of biodegradable functional polymers either from natural or from synthetic manufacturing, with an outline on various emerging processed techniques utilized for the improvement of pharmaceutical properties as *via*ble multifunctional commercial replacements for currently used polymers. These biodegradable polymers were selected based on the ease of availability, the extent of knowledge available to describe their formation, and their commercial relevance with applied potential.

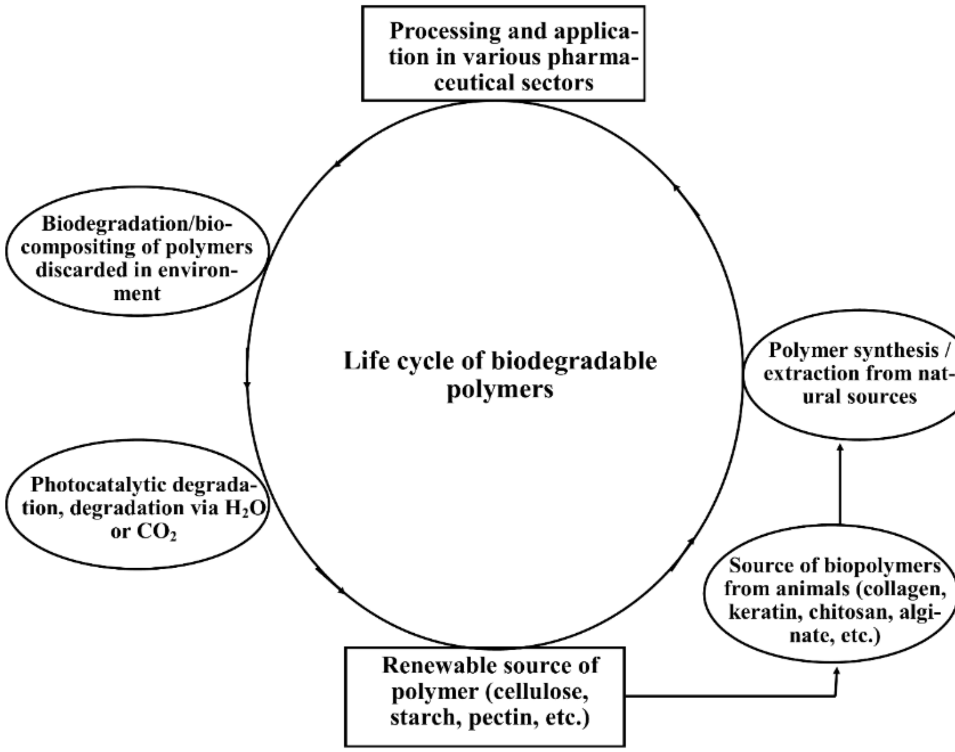

Fig. (1). The life cycle for biodegradable polymers obtained from natural resources.

Potential Polymers from Natural Resources

The source of excipients is often determined by nature and common practice with its potential applications. Depending on the source, traditionally excipients are distinguished as natural or synthetic. There are two main types of natural polymers (I) those that come from a living organism (carbohydrates and proteins) and (II) those that need to be polymerized and obtained from renewable resources (lactic acid and triglycerides). However, over the past few decades, a new class of multifunctional polymers resulted from the processing of natural and biodegradable synthetic polymers that have attracted significant pharmaceutical manufacturers and researchers. Some examples of such natural polymers are proteins and nucleic acid that occur in the human body, cellulose, natural rubber, silk, and wool. Several types of cellulose including starch and other carbohydrate-based natural polymers are made up of numerous glucose molecules linkage. Similarly, peptides, polypeptides, lignin, and proteins obtained from plants or animals have also been referred to as biodegradable natural polymers. Moreover, processed or grafted polymers are another class of naturally occurring excipients that are significantly used in the day-to-day life of human beings.

CHAPTER 4

Conformational, Morphological, and Physical Characterization of Bio-based Polymers

Abstract: Polysaccharides are the most pervasive form of pharmaceutical excipients, consisting of diverse functional properties that play a vital role in sustaining life. Moreover, polysaccharides are well-known for several benefits such as nutritional benefits, effects on immunity, and delectability with biocompatibility. Natural polysaccharides are an assembly of monosaccharides' long chain units bounded together with glycosidic linkage. In addition, polysaccharides are often quite heterogeneous, a slight alteration in the repeating unit produces distinct properties in biopolymers. Further engineered bio-based polymers produced to facilitate the regulated drug delivery system require information on structural conformation to meet the Food and Drug Administrative regulations. Furthermore, surface conformation and morphological imaging analysis are also of prime importance in the fabrication of drug delivery systems. Therefore, the amendment in the chemistry that brings about an alteration in the physicochemical property requires the use of various instrumental techniques for its characterization. In this chapter, a brief overview of compositional characterization techniques used for bio-based polymers is presented, focusing on analytical techniques that are generally applied. Moreover, the chapter promotes the application of suitable analytical techniques such as nuclear magnetic resonance spectroscopy, infrared spectroscopy, and varying chromatography in understanding the complex structure of polysaccharides. In addition, information on instruments used for surface morphological characterization of polymers is covered in this chapter.

Keywords: Bio-based polymer, Chromatography, Infrared spectroscopy, Nuclear magnetic resonance spectroscopy.

INTRODUCTION

Recent progress in biopolymers-based drug delivery technology has provided a prospect for the development of highly effective, efficient and compatible natural polymers that can regulate the release of therapeutics. Biopolymers are produced from biomaterials, where the term “bio” means biodegradable originating from a living organism. A wide variety of biomaterials resulting from biological sources such as plants and microorganisms are defined using the term bio-based polymers [1]. Whereas, excipients produced *via* the synthetic process from a biological source such as sugars, proteins, and amino acids are pronounced as modified or

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processed biopolymers [2]. The bio-based content of a biopolymer can be determined by calculating the number of carbon atoms that come from biomass as a raw material. Thus, biomaterials refer to materials in which carbon might emanate from non-fossil biological sources. Biopolymers are broadly classified as biodegradable and non-biodegradable polymers. Moreover, biopolymers are also classified according to occurrence and abundance as (i) polynucleotides, (ii) polypeptides/poly amino acids, and (iii) polysaccharides. Polynucleotides are long-chain polymers with 13 or more nucleotide monomers [3], while polypeptides are short polymers comprised of amino acids as monomeric units with amide bond linkage [4]. Polysaccharides are composed of sugar monomeric unit-linked *via* glycosidic linkage. Several polysaccharides have been identified and the most commonly used biopolymers are listed in Table **1**.

Table 1. Biopolymers classification [6].

Biodegradable				Non-Biodegradable
Bio-Based			Fossil-Based	Bio-Based
Plant	Microorganism	Animals		
Cellulose and derivatives	Polyhydroxy alkanoates	Chitin	Poly(alkylene dicarboxylates)	Polyethylene, polypropylene, polyvinyl chloride
Lignin	Polyhydroxy fatty acid	Chitosan	Polyglycolide	Poly(ethylene terephthalate)
Starch and derivatives	Bacterial cellulose	Hyaluronan	Poly(ε-caprolactone)	Polyurethane
Alginate	Hyaluronan	Casein	Poly(vinyl alcohol)	Polycarbonate
Lipids	Xanthan	Whey protein	Poly(ortho ester)	Poly(ether-ester)
Wheat, Corn	Curdlan	polyanhydrides	Polyanhydrides	Polyamides
Gums	Pullulan	Albumin	Polyphosphazenes	Polyester amides
Carrageenan	Silk	Keratin	-	Unsaturated polyester
Poly(lactic acid)	-	Leather	-	Epoxy

Exploring bio-based excipients, as the main component of pharmaceutical products can be a smart stratagem to mitigate cost associated issues in the development of novel drug delivery. The excellent polymeric properties of the bio-based polymers in several fields including pharmaceutical and industrial have gained a great deal of research interest. Polysaccharides are widely distributed in nature as they can be derived from plants, animals, and microorganisms. However, polysaccharides differ in their repetitive unit, and composition, which leads to a variation in physicochemical properties of biomaterials as well as fabricated pharmaceutical products. Thus, biopolymers are the promising candidate in the fabrication of a pharmaceutical product that could meet the dual requirement of sustainability and biodegradability.

Compositional characterization of bio-based polymers is considered the first step in understanding the chemistry behind the conformation of polysaccharides. Bio-based polymers are composed of monosaccharides or polysaccharides with *O*-glycosidic linkages [5]. Polysaccharides are often quite heterogeneous, hence a slight alteration in the repeating unit produces biopolymers with distinct properties. The amendment in the chemistry that brings alteration in the physicochemical property are characterized using various instrumental techniques including nuclear magnetic resonance spectroscopy, and infrared spectroscopy with various categories of chromatographic techniques. In addition, structural and chemical compositional studies of biopolymers provide information relevant for understanding compatible polymers with drug and dosage form design.

Chemistry Of Bio-Based Polymers

Advancement in the biological macromolecular structure of pharmaceutical polymers is more recent, however, less prevalent than the parallel progress in the protein, nucleic acid, and allied field [7]. Bio-based polysaccharides and gums are used in pharmaceuticals as well in textile industries due to their excellent material properties as a release retardant, suspending agent, gelling agent, wet granulator binder, fiber spinning, *etc*. The study of the molecular structure offers the most fundamental knowledge to the understanding of functional, conformational, and physiological properties of polysaccharides. However, the structural description of bio-based polymers is a perplexing task due to molecular complications. Geometric and chemical studies of biopolymers have gained significant consideration during the last decades with steady progress. The chemical characterization techniques including nuclear magnetic resonance (NMR), infrared spectroscopy (IR), chromatography, electron microscopy, x-ray diffractions, are employed for the conformational analysis of carbohydrate-derived polymers. Whereas physio-technical characterization includes moisture content, flowability, compressibility, particle size, size distribution, zeta potential, powder porosity, surface composition and morphology, contact angle and surface energy, and measurement of compressibility and compactibility.

Nuclear magnetic resonance spectroscopy is an effective tool for understanding the conformational structure, molecular dynamics, and interactional behavior of biopolymers either with therapeutics or with inactive pharmaceuticals. Combined with one-dimensional (1D) spectra, chemical shifts, and coupling coefficients in

CHAPTER 5

Thermo-Mechanical Properties of Bio-Based Polymers

Abstract: Bio-based polymers offer a broad range of applications in pharmaceutical engineering. However, their assortment gets constrained owing to variations in structural conformation, which affects the thermomechanical properties during complex formulation. The thermomechanical property of pharmaceutically inactive ingredients provides insight into the thermal expansion, glass transitions temperature, softening point, compositional, and phase changes of biomaterials with different geometries on the application of constant force as a function of temperature. In addition, thermomechanical properties provide fundamental information on network chemical structure, crosslink density, rubbery modulus, failure strain, and toughness. Moreover, the structural composition of polysaccharides also affects the composite's mechanical properties. Hence, analysis of thermomechanical properties provides valuable information that is applicable in different sectors including aviation, quasi-static loading, electroplating technology, micro-electric, construction, cosmetics, food packaging, and pharmaceutical products. This compilation highlights the basics of thermal and mechanical experiments on bio-based polymers with different fabrication for both technical and pharmaceutical formulations.

Keywords: Bio-based polymers, Differential scanning calorimetric, Differential thermal analysis, Thermogravimetric analysis, Thermomechanical.

INTRODUCTION

Natural resources, both renewable and non-renewable, significantly contribute to monetary benefits, *via* utilization in various manufacturing processes. The World Trade Organization, in 2010 recognized that natural resources are stocks of materials, that are both scarce and economically useful in production or consumption, either in their raw state or after a minimal expense of processing [1]. Geographic surface coverage has broadly classified natural resources into two types – *Point Resources* and *Diffused Resources*. The point resources include a narrow economic base such as oils and minerals, whereas diffused resources include agriculture and forest [2]. Moreover, diffused natural resources are a class of renewable natural sources that significantly contribute to the development of herbal therapeutics. Considering herbal therapeutics, active and inactive pharmac-

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eutical ingredients have gained importance due to their cytocompatibility and biodegradability.

Polysaccharides are pharmaceutical natural polymers with distinctive configurations and properties favorable in several biomedical applications. Polysaccharides are isolated from the plant, animal, microbial, and marine sources. Polysaccharides are carbohydrates that are comprised of monosaccharides attached with O-glycosidic linkages and are essential biomolecules required for the growth of living organisms [3]. Moreover, polysaccharides can be homogenous, containing only one kind of sugars, whereas heterogeneous polysaccharides contain 8-10 types of sugar moiety [4]. Among them, plant polysaccharides have gained enormous attention as bio-based polymers with a wide range of applications in pharmaceuticals, prosthetics, imaging analysis, and food industries [1] as presented in Fig. (**1** and **2**). Recent reports indicated that more than 300 different kinds of bio-based polymers have been identified for drug delivery applications [5]. Moreover, several biomaterials have been chemically modified to regulate the release of active ingredients as well as to support the requirement of formulations.

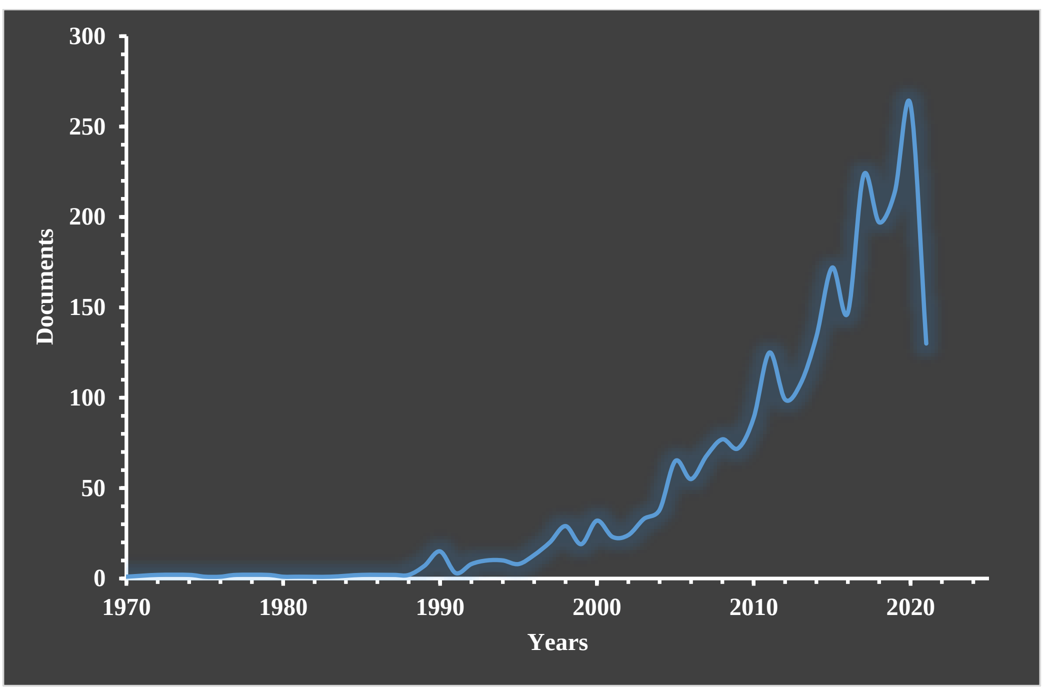

Fig. (1). Publication of documents from 1970 to 2020, data retrieved from Scopus database on 07th of June 2021 using keywords “biodegradable*” “polysaccharides*”.

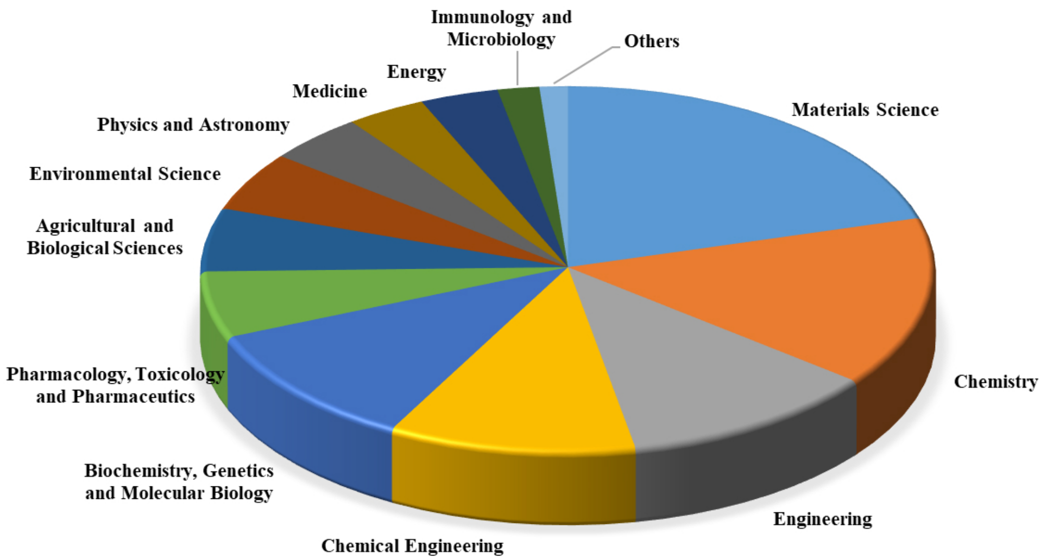

Fig. (2). Publication of documents on various subjects from 1970 to 2020, data retrieved from Scopus database on 07th of June 2021 using keywords "biodegradable*" "polysaccharides*"(for interpretation of the results to color in this Fig. legend, the reader referred to either web version of this chapter or color print).

The pharmaceutical formulation consists of both active and inactive constituents where the individual may experience phase transitions during formulation and storage in the varied range of temperature and pressure. The molecular changes exerted during the phase transitions promote variation in the thermomechanical properties. Therefore, the phase transitions analysis of pharmaceutical formulation is of major importance in maintaining the integrity of the product during shelf life. The phase transitional thermal analysis technologies include thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), and differential thermal analysis (DTA).

Thermal Analysis

Thermal analysis of pharmaceutical excipients includes a series of temperature dependency measurements aimed to understand the physicochemical property of the substance. Several techniques can be employed for the measurement of thermo-analytical properties as listed in Table **1**, however only the most popular techniques used for characterization of excipients have been elaborated in this chapter.

CHAPTER 6

Pharmaceutical and Biomedical Applications of Bio-Based Excipients

Abstract: The success of an active pharmaceutical depends on how efficiently and precisely the polymeric dosage form can deliver it for effective treatment. Polymers are recognized as inactive pharmaceutical excipients and the backbone of the drug delivery system that plays an essential role in the design of dosage forms. Biodegradable polymer-based drug delivery system has gained significant attention among researchers and manufacturers in the last few decades, compared to synthetic non-biodegradable and their analog polymers. Synthetic biodegradable biopolymers demonstrate excellent efficacy in the design and development of drug delivery that enables the incorporation of active pharmaceuticals into the body. Despite the wide effectiveness of currently available polymers in the design of drug delivery systems, the quest for biocompatible, biodegradable, and easily accessible novel polymers with multifarious applications is still protractile. Due to safety and regulatory approval requirements in the development of novel inactive pharmaceuticals, the introduction of new excipients is much limited. However, the development of bio-based polymers with modification as required could be a valuable way to address the problem associated with synthetic polymers. In this chapter, an overview has been presented on the various applications of bio-based polymers ranging from oral conventional drug delivery to reduction and capping of metallic materials. Moreover, details are presented on the technology-based use of biopolymers in the fabrication of modified oral drug delivery, microneedles, packaging film, and biogenic synthesis of metallic nanoparticles.

Keywords: Bio-based polymers, Biogenic metallic nanoparticles, Electro-spinning, Modified drug delivery, Tissue engineering.

INTRODUCTION

Today polymer industry has grown significantly due to its wide applicability in various sectors. The manufacturing and output of polymers per unit volume have left behind several other industrial materials such as aluminum, copper, steel, and other major metallic materials [1]. Polymers are a large structural linkage of the monomeric unit and frequently form a chain-like arrangement. The application of polymers has widened day by day, compared to other classes of materials developed by humans. The first man-made polymers have been studied since 1832 [2]. The contemporary applications of polymers extend from a

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pharmaceutical dosage form to packaging materials, composites, textile, coating, foams, adhesives, electronic devices, optical devices, industrial fibers, and the development of advanced ceramics (Fig. **1**).

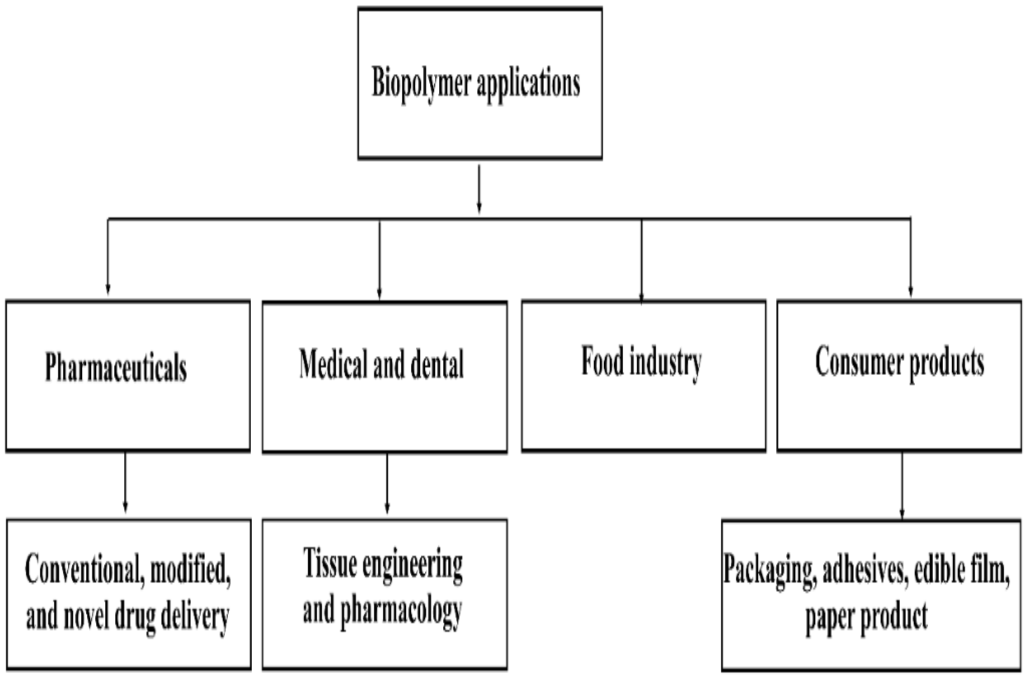

Fig. (1). Application of bio-based polymers in various fields.

Approximately 140 million tons of synthetic polymers are produced around the globe annually for various applications by the manufacturer [1]. Most synthetic polymers and integrated polymer products are stable and require an unlimited time for degradation. Moreover, due to stability and resistance to degradation of synthetic polymer products, they accumulate in the environment at a rate of 8% by weight and 20% by volume in landfills, which causes a serious impact on the ecosystem [3]. Although the acceptance of synthetic polymers and intended products is higher than biopolymers, still bio-based polymers are gaining significant attention among researchers and manufacturers for extending application in various sectors. Bio-based polymers are natural polymers produced or synthesized from animals, plants, bacteria, and fungi. In addition, biopolymers could also be developed by a chemical reaction among biological materials such as sugars, amino acids, oils, or natural fats [4]. Analogous to synthetic biopolymers excipients, bio-based polymers consist of monomeric units covalently bonded to form a larger structure. Perhaps, several limitations are associated with bio-based polymers but research has indicated potential applications in various drug delivery systems and allied areas. In this chapter, a brief account is presented on several applications of polymers in conventional, modified, and novel drug delivery, fabrication of nanofibers and scaffolds using electrospinning techniques, development of microneedles, and in the bio-reduction of metallic nanoparticles.

Polymers in Conventional Drug Delivery System

Several routes for the administration of drugs are available such as oral, mucosal, parenteral, transdermal, pulmonary, *etc*. Among these delivery routes for a therapeutic agent, oral route is widely accepted. Oral formulations have been broadly classified based on the local or systemic efficacy as a conventional and modified or novel drug delivery system. Recent advancements in drug delivery and polymer chemistry shifted the fabrication technology from conventional to modified drug delivery systems with an enhancement in bioavailability and therapeutic efficacy. However, conventional drug delivery is still the most promising drug administration route, due to several advantages including the ease of self-administration, non-invasiveness, patient preference, and low cost-o--production [5]. The conventional drug delivery system has been the most accepted delivery system among pharmaceutical manufacturers and patients. However, drugs with poor solubility, stability, and permeability exhibit low bioavailability and pharmacological efficacy when administered orally [6]. Fabrication and development of oral drug delivery system require the addition of inactive materials such as additives, binder, diluents, lubricants, glidants, *etc*. to produce a suitable dosage form with the effective release of active pharmaceuticals. These inactive materials are denoted as excipients derived from either synthetic or natural sources. Although synthetic polymers have been effectively used in the development of oral conventional and novel drug delivery systems, however biodegradability is still of concern. Whereas, natural polymers are gaining interest among scientists and manufacturers due to their excellent biodegradability within nature.

Bio-based natural polymers have been extensively used as a tablet binder and explored in the design of various oral drug delivery systems including fast disintegrating, orodispersible, bio and mucoadhesive tablets, *etc*. In addition, bio-based polymers have been tested successfully in the fabrication of several novel drug delivery systems such as microsphere, nanoparticles, microbeads, transdermal films, wound dressing scaffolds, thermo-responsive gel, continuous or pulsatile release systems, *etc*. Moreover, advancements in pharmaceutical technology with a modification in polymer chemistry have significantly changed the formulation aspects of conventional drug delivery systems. Several conventional oral solid dosage forms incorporated with synthetic polymers have

CHAPTER 7

Potential Application of Biopolymers as Biodegradable Plastic

Abstract: Today, on average, we produce yearly about 300 million tons of plastic waste, equivalent to the entire human population weight around the globe. The single-use plastics and plastic products are produced using high molecular weight polymers in combination with additives that could not be completely reprocessed. So far, only 9% of overall plastic waste produced has been recycled and around 12% has been incinerated while the remaining 79% has been accumulated as debris in terrestrial and aquatic environments. Biodegradability and recycling of plastics depend on various physicochemical properties including molecular weight, hydrogen bonding, Van der Waals forces, and electrostatic forces. Moreover, biodegradability depends on macromolecular chain distresses that not only affect polymer aggregates but also affect the structural and functional properties of plastic products. However, due to unlimited production and utility with distressing effects on the environment, it is deemed necessary to replace such non-biodegradable polymers used in the fabrication of plastics with biodegradable polymers. The use of biodegradable polymers in the fabrication of plastic products is a creative way to resolve the plastic disposal problem. In this chapter, a brief overview has been presented on the fabrication of biodegradable plastic using biopolymers to reduce its detrimental effects on the environment.

Keywords: Bio-based polymer, Bioplastic, Plastic, Plastic-packaging, Thermoplastic.

INTRODUCTION

Today nearly everyone globally every day comes in contact with plastic or products packed with plastics, which are inexpensive, gauzy, and durable materials. The term plastic was derived from *Plasticus* a Latin term and *Plastikos* a Greek word that was common in practice during the 17^{th} century for molded materials [1]. Plastics are a pivotal material in modern life and are popularly used in water supply, food packing, and in various medical devices including surgical equipment including drips, aseptic medical packaging, and blister packs for pills [2]. Although plastic has various benefits, however, its bioburden became obvious day by day due to its short first-use cycle. Currently, plastic packaging represents 26% of the total produced volume of plastic with a direct economic boost that significantly contributes to productivity resources [3]. The first use of synthetic

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plastic was recorded in 1907 as Bakelite in Belgium [4]. While the commercial production of plastic materials started during the 1950s with remarkable global annual percentage production of 393 million metric tons including textile fabrics [5]. The mismanaged accumulation of plastic waste in the environment has raised a global concern. Statistical data indicates about 60 to 99 million metric tons of mismanaged plastic waste were produced globally in 2016 (Fig. **1**), and the Figs could triple to 155-265 metric tons per year by 2060 [6]. A previous report indicated that 32% of plastic packaging escapes from collection systems and 91% of the mismanaged plastic causes significant economic loss with detrimental effects on the ecosystem by clogging drainage and disposal to the ocean via rivers [7] (Fig. **2**). Moreover, approximately 4% of the fossil fuel extracted is consumed as raw material in the production of plastic [8]. The rise in the demand for plastic in packaging and construction materials indicates higher consumption of alternative energy during production, with an additional 4% increase in the emission of greenhouse gases [3]. In addition, the expected demand by 2050 for fossil fuel and other natural resources of energy as well as associated carbon emission by plastic producing industries may account for 20% of petroleum's consumable with 15% of carbon emission [7].

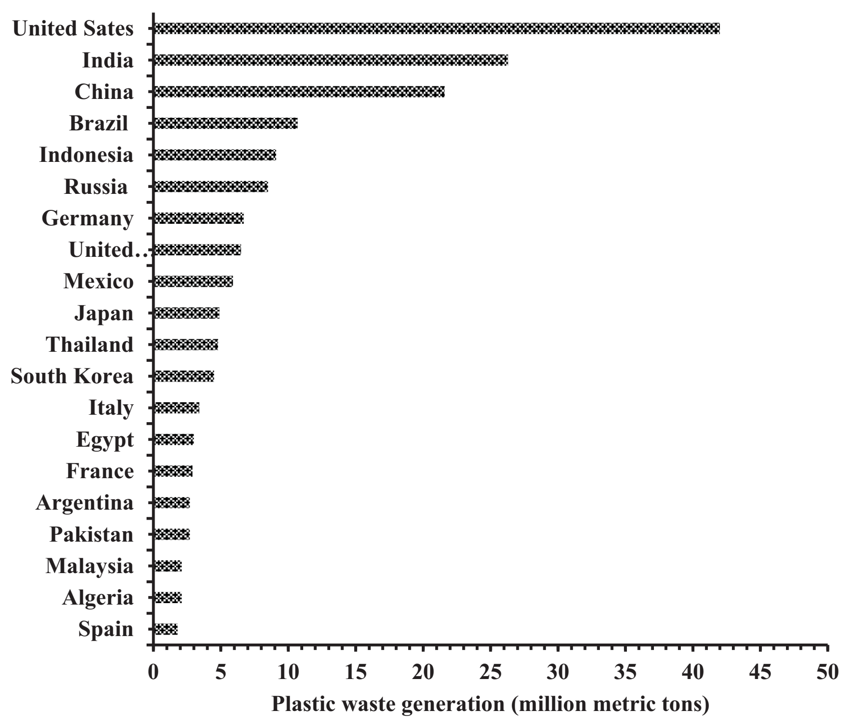

Fig. (1). The highest number of plastic waste was generated by the selected country in 2016 (in million metric tons).

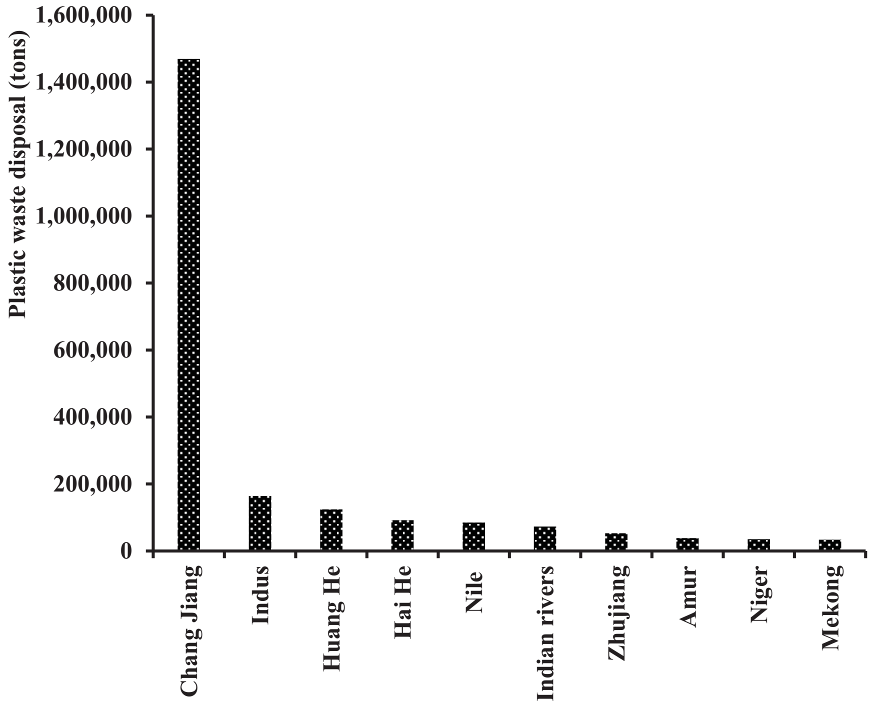

Fig. (2). Plastic waste disposal (tons) in top 10 rivers across the globe [9].

Presently 95% of plastic packaging materials costing 80-120 billion dollars annually are lost due to a short life cycle [3]. More than 4 decades after the launch of the universal plastic recycling process, only 14% of plastic packaging is collected with a 5% material loss during sorting and reprocessing causes a huge economic loss [10]. Moreover, the recycled plastics that do get recycled in general are used for a lower-value application that further cannot be reused. The recycling of plastic depends on the types of polymer used, package design, and product type. The plastic that is constituted of a single polymer is easier and more cost-effective to recycle, compared with complex plastic products. Different terminologies used for the plastic and plastic products during the recycling and recovery process are indicated in Table **1**.

Table 1. Different terminologies are used for plastic and plastic products during the recycling and recovery process.

ASTM D5033 Approach	ISO 15270 Correspondent	Analogous Expressions
Primary recycling	Mechanical recycling	Recycling with closed-loop
Secondary recycling	Mechanical recycling	Downgrading

CHAPTER 8

Potential Application of Biopolymers in the Textile Industry

Abstract: Textile configurations are derived from two major sources such as ancient handicraft and modern scientific inventions. Textile fabrication using polymeric fiber is one of the fastest-growing sectors since the 19th century and is currently the second-largest manufacturing industry after information technology. Although polymers are predominantly used in the development of dosage forms, however recent devolvement in natural polymer chemistry reflects its association with the production of plastics, fibers, elastomers, *etc*. Innovation using natural polymer fibers-based textile could serve as an alternative capable of replacing synthetic polymer-based fibers. Polymers, especially fibers contribute significantly to the manufacturing of textiles. Moreover, copolymerization of fabrics fibers with excipients demonstrated potential for the development of materials useful in various biomedical applications. Furthermore, to understand the fundamental characteristics of polymeric fibers including structural composition, morphological features such as crystallinity, and orientation, a comprehensive skill is necessary. This chapter discusses the basic materials used in the fabrication of textile products, with emphasizes on bio-based polymers as an alternative to synthetic polymers in the production of fabrics.

Keywords: Bio-based polymer, Chitosan, Fabrics, Fibers, Textile.

INTRODUCTION

The invention of rayon in 1903 prompted a revolution that led to the development of synthetic fiber in 1935 [1]. The use of fiber or yarns in the manufacturing of fabrics is one of the unique creations of human history. Today fiber industry has evolved into a complex field with rising interest among researchers. The word textile is derived from the Latin word "*textilis*" and a French word "*texere*", denoting "*to weave*" refed to woven fabric [2]. Textile materials are fabricated by the interweaving of either yarns or fibers (Fig. **1**). Textile Exchange's new preferred fiber and materials market report reveals that the global fiber production has doubled in the last 20 years, reaching an all-time high of 111 million metric tons and could potentially progress to 146 million metric tons by 2030 [3]. The annual global fabric market and production in percentage are presented in Figs. (**2** and **3**). The fibers are manufactured through the process of interlacing such as twisting, knitting, spinning, *etc*. Twisting or weaving includes basic weaves, twill,

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and stain while knitting includes weft and wrap process. Recent reports indicate that knitting is rapidly gaining interest among textile manufacturers [4].

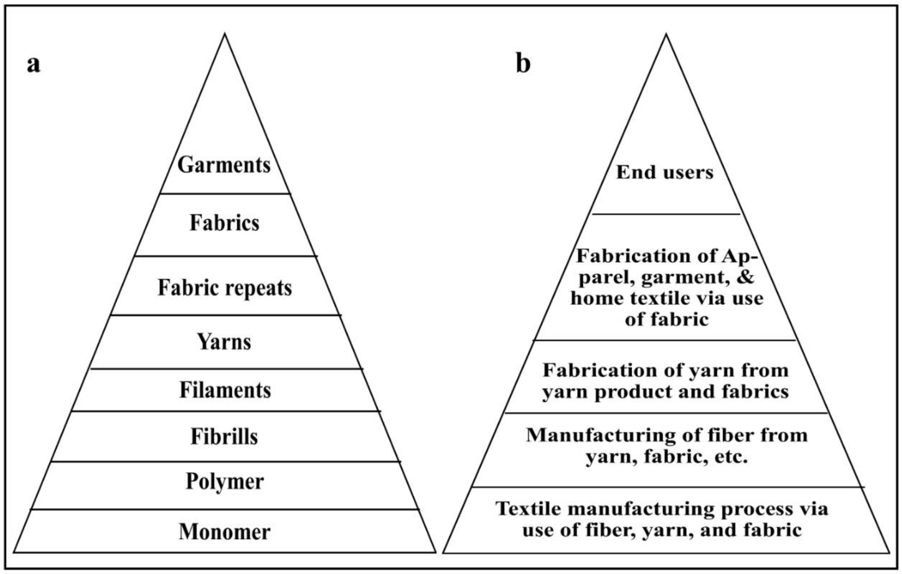

Fig. (1). The hierarchy of textiles (a), textile manufacturing process from fiber to fabrics (b).

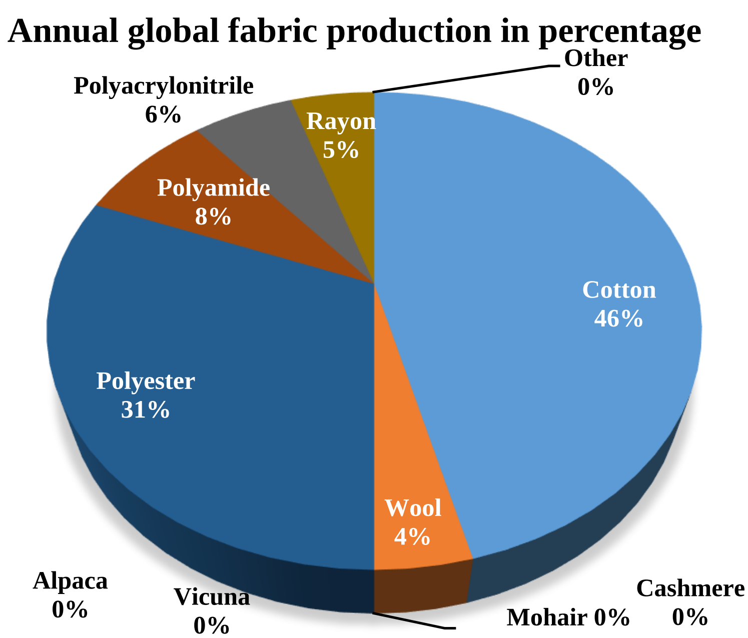

Fig. (2). The global market of fiber in pounds (for interpretation of the results to color in this Fig. legend, the reader is referred to either web version of this chapter or color print).

Textile fibers are symbolized as essential components of modern society that provide a physical structure for human comfort with sustainability. Textile fabrics are used in clothing, bedding, home furnishings, liquid filtrations, insulation materials in buildings, cleaning wipes, dental brush, wound bandages, sutures, *etc*. Currently, textile fabrics' manufacturer principally relies on synthetic petroleum-based fibers, which adversely impact the environment through global warming and pollution [5]. The rise in demand, as well as diminution in petroleum oil reserves with fluctuation in the international market value, indicates a transition from petroleum-based resources to bio-based polymers. Bio-based polymers are gaining interest in textile industries and are considered as a green alternative to synthetic petroleum fibers. Moreover, the challenges are not only associated with the pricing, but also with the derisory properties of the synthetic polymers for the textile industry.

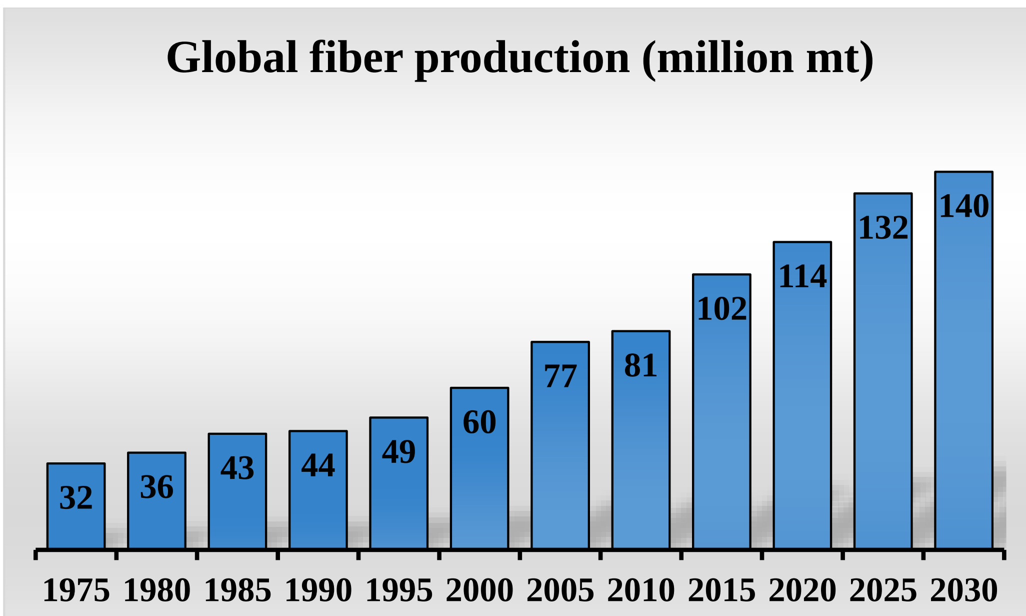

Fig. (3). Global fiber production in million metric ton projection until 2030.

Biopolymers in the Textile Industry

The earliest evidence of weaving, closely related to basketry, dates from the Neolithic culture of about 5000 BC [6]. Silk, cotton, and wool are among the natural fibers used in the manufacturing of fabrics for thousands of years, around 3000 BC in India [7]. However, due to their inherent deficiencies, applications are limited to raw form. Bernigaud de Chardonnet in 1884 invented and patented synthetic fiber also known as artificial silk, which was the first manmade fiber [8].

CHAPTER 9

Pharmacokinetics and Toxicology of Pharmaceutical Excipients

Abstract: Progress, innovation, and development of new chemical entities fetched new defies in the drug delivery arena, and also put forward several issues including bioavailability with intestinal metabolism or efflux mechanism. However, some excipients such as surfactants have demonstrated improvement in drug bioavailability. Thus, these excipients can no longer be considered inert and require attention from a pharmaceutical regulatory perception. Biopolymers and their derivatives are gaining attention in pharmaceutical manufacturing due to their biodegradability and compatibility. However, based on the Food and Drug and Administration (FDA) guidelines, the manufacturers are required to evaluate their pharmacokinetic and toxicological properties. Several methods including Rule-of-Five and Biopharmaceutical Classification System (BCS) are used for early pharmacokinetic prediction of active and inactive pharmaceutical ingredients. Although polymers differ from therapeutic agents, similar methods can be smeared for the understanding of the absorption, distribution, metabolism, and excretion profile of bio-based pharmaceutical excipients. This chapter explores pharmacokinetic and pharmacodynamics information of biopolymers used in the design, and development of several pharmaceutical formulations.

Keywords: Biopharmaceutical classification system, Biopolymer, Lipinski rule, Pharmacokinetics.

INTRODUCTION

Nature is augmented with an extensive assortment of phytoconstituent such as biomedicine and polysaccharides that are directly or indirectly beneficial for the persistence of consistent health. Pharmaceutical excipients are traditionally known as inert components used in the formulation of pharmaceutical products that contain active constituents essential to assuring quality and safety with the effectiveness of the product [1]. Pharmaceutically inactive ingredients are the backbone of the formulation, whereas these excipients are incorporated in finished dosage forms to maintain the physicochemical stability of active pharmaceuticals during *in vitro* and *in vivo* analysis. Considering this, an excipient in pharmaceutical formulation could convert the most effective drug substance into

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an ineffectual one by modifying and conjugating the formulated product. While on the other hand, some drug molecules/products with poor pharmacokinetics can be improved by the use of excipients. Pharmaceutical excipients such as preservatives, colorants, fillers, sweeteners, binders, flavoring agents, film coating agents, encapsulating materials, lubricating agents, and their derivatives originating from plants, minerals, and animals source, are gaining importance in the development of pharmaceutical products [2]. Pharmaceutically inactive ingredients are used to expedite the pharmacodynamics and pharmacokinetics of active moiety added in the formulations. In addition, excipients also impact the physiochemical properties of medicine including consistency, solubility, and release kinetics which are a basic prerequisite for the attainment of therapeutic efficacy after administration. Natural excipients hold several advantages including biodegradability, cytocompatibility, inertness, and low cost of production over synthetic polymers. This has gained interest among pharmaceutical manufacturers for the development of various formulations as well as food products [3]. Several alternative polymers are available with pharmaceutical manufacturers that have been continuously used for the formulation of various dosage forms including solid, liquid, semisolid, *etc*. However, some of these synthetic excipients indicated side effects during *in vivo* analysis [4]. Source and the active constituent of bio-based polymers are presented in Table **1**.

Table 1. Source and active constituents of biopolymer-based polysaccharides.

Source	Composition	Properties	Reference
Buchanania lanzan Spreng	Arabinose, rhamnose, fructose, mannose, fixed oil used as permeation enhancer	Mw: 7012; ζ: 1.56 mV	[5 - 7]
Manilkara zapota (Linn.)	Rhamnose, xylose, arabinose, mannose, fructose	Mw: 2903837; ζ: 18.05 mV	[8]
Diospyros melonoxylon Roxb	Arabinose, fructose, mannose, rhamnose, xylose, and glucose	Mw: 8760; ζ: 5.90mV	[9]
Aloe vera leaves	Arabinan, arabinorhamnogalactan, galactan, galactogalacturan, glucogalactomannan, *etc*.	Mw: 30-40kDa	[10, 11]
Moringa oleifera	Glucose, rhamnose, galacturonic acid, arabinose, xylose, rhamnose	Mw: 190kDa;	[12]
Caesalpinia spinose	Galactomannans, mannose, galactose	Mw: 10^6 - 2.33 x 10^6 g/mol	[13, 14]
Prosopis juliflora	Sucrose, galactomannans, mannose, glucose, glactose	Mv x 10^6: 1.14; Viscosity: 1178 ml/g	[15 - 17]
Pithecellobium Dulce	Carbohydrate 65.79 -72.76 (%), arabinose, galactose, glucose, rhamnose	ζ: -8.6mV	[18, 19]
Annona squamosal	Carbohydrate 12.45 - 14.26 (%)	-	[20, 21]

(Table 1) cont.....

Source	Composition	Properties	Reference
Shorea wiesneri	α-resin, β-resin, dammarol acid	Average Mw: 180	[22]
Mimosa Pudica	D-xylose and D-glucuronic acid, tubulin, gallic acid, calcium oxalate crystals, Cglycosylflavones	Viscosity of 0.5% solution is 50,000 cps	[23]
Opuntia ficus indica	Arabinose, galactose, xylose, galacturonic acid, rhammnose	Mw: 15.3 – 15.7 x 10^6 g/mol	[24, 25]
Hibiscus rosasinensis	Rhamnose, galactose, xylose, arabinose, galacturonic acid	Viscosity: 12.234 poise	[26]
Azadirachta indica	Arabinose, galactose, xylose, rhammnose	Mw: 6.4 – 12.0 x 10^5; intrinsic viscosity: 2400-3600 cPs	[27]
Cassia tora Linn.	Galactomannans	Mw: 198 kDa	[28, 29]
Zizizphus jujube	Rhamnose, arabinose, glactose, glucose, xylose	-	[30, 31]
Cassia angustifolia	Rhamnose, arabinose, glactose, glucose, xylose, mannose	-	[32, 33]
Caesalpinia pulchirrima	Galactomannan	-	[34, 35]

Pharmacokinetic and Toxicology of Excipients

Pharmacokinetic and pharmacodynamics are relevant to understanding the absorption, distribution, metabolism, elimination (ADME), and therapeutic efficacy of administered medicine and/or inactive ingredient following oral, topical, intravenous, intramuscular administration. Moreover, recently a new terminology “Liberation” has been included considering studying the release kinetic process controlled by the used excipients. Toxicological screening and ADME profiling are conducted during the discovery and development of new drug entities to estimate the safety and efficacy of new drug molecules. Excipients are known as pharmacologically inactive substances and in parenthesis, their regulatory requirements to those of new drug substances require several evaluations during the development process that cost between 10 to 50 million dollars [36]. Therefore, there is a need to investigate the pharmacokinetic and pharmacodynamic profile of biopolymers as alternatives to synthetic excipients.

Basics of Pharmacokinetic and Pharmacodynamics

Pharmacokinetic and pharmacodynamics are the basis for understanding and estimating the action of active and inactive moiety administered in the body. The term pharmacokinetic is derived from the Greek word “pharmakon” and “kinetikos” meaning “drug” and “putting in motion”, respectively [37]. Pharmacokinetic is also defined as a quantitative assessment of absorption,

CHAPTER 10

Bibliometric Analysis of Bio-Based Pharmaceutical Excipients

Abstract: Recently bibliometric analysis has gained significant importance in quantitative assessment for analyzing scientific outputs, the linkage between universities, authors, funding organizations, and development enactment, with several other applications. Therefore, the scientific community needs an advanced tool to analyze a wide range of scientific data with precision and accuracy. This chapter aims to provide up-to-date bibliometric analysis on bio-based pharmaceutical excipients including network and overlay visualization for publication from 2000 to 2021, retrieved from the Scopus database. The documents considered were original research and conference proceedings numbering 2923. The bibliometric analysis revealed that research interests in bio-based are expanding throughout the globe, as a potential source of biomaterial for allied pharmaceutical sciences.

Keywords: Bibliometric analysis, Bio-based polymer, Bio-based polysaccharides, Natural polysaccharides, Plant mucilage.

INTRODUCTION

A comprehensive understanding of the physicochemical properties of inactive pharmaceuticals is necessary to develop quality pharmaceutical products and promote the required therapeutic efficacy. In both conventional and modified pharmaceuticals, active pharmaceuticals have been reported to be incompatible in various instances with several synthetic excipients including bulk pharmaceuticals [1, 2]. Synthetic excipients have been extensively modified to minimize issues related to incompatibility, however, due to several drawbacks including biodegradability, compatibility, and physicochemical properties of active pharmaceuticals, poor bioavailability is observed. Thus, the development of natural pharmaceutical excipients with multifunctional properties is an urgent need.

Polymers are pharmaceuticals that serve as a backbone for the development of several drug delivery categories including targeted delivery, tissue engineering, modified drug delivery, probiotics, *etc*. Both synthetic and semisynthetic excipients play important roles in the formulation and development of numerous

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dosages forms labelled as finished pharmaceuticals. The increase in dependence towards synthetic and semisynthetic polymers is partly due to the datum of unconstrained and cost-effective possibilities available for amendment in the basic skeleton to develop products with exact requisites. Subsequently, many of the widely used pharmaceutical excipients are obtained by amendments in some natural derivatives to improve their functionality. However, despite several benefits with synthetic and semisynthetic excipients, pharmaceutical manufacturers need to address various challenges before their expansion and utility can be accepted effectively. Biological macromolecules have gained significant importance due to their biodegradability with ease of availability and multi-functionality. Bio-based polysaccharides can be obtained from plants or other living things, and agriculture resources. Natural polysaccharides are macromolecules composed of repeating monomeric units interlinked by covalent bonding. The word "polymer" derived from the Greek term *polus,* which means much or many whereas *meros*, means part. The word was first devised by Jons Jacob Berzelius with a distinct definition from the IUPAC nomenclature definition [3].

Bio-based pharmaceutical excipients are one of the fastest-growing products within the pharmaceutical market due to their sustainability including biodegradability, biocompatibility, low production cost, with abundance in availability, compared to synthetic and semisynthetic polymers. Moreover, biological macromolecules originating from natural resources are renewable and proper harvesting with cultivation can provide a constant supply. The current chapter focuses on the bibliometric analysis of bio-based excipients with pharmaceutical applications (Table **1**). Several reviews and monographs with scientific data are available on natural excipients, however a comprehensive bibliometric analysis of natural originating pharmaceutical inactive ingredients is lacking. The content presented in this chapter provides the reader a brief on scientific data available from the last two decades with a considerable preference on the keywords, major funding associated with bio-based polymer research, the linkage between potential authors, and leading countries with maximum citations on bio-based polymer research.

Table 1. Bio-based excipients with pharmaceutical applications.

Polysaccharides	Application	Reference
Photo-cross linkable alginic acid and hyaluronic acid	*In situ* photo-polymerization	[4]
Alginate from brown algae	Pharmaceutical microsphere	[5, 6]
Guar gum	Deflocculants	[7]
Graft vinyl monomers with chitosan	Pharmaceutical excipients	[8]

(Table 1) cont.....

Polysaccharides	**Application**	**Reference**
Fenugreek mucilage	Flocculating agent	[9]
Plantago psyllium mucilage	Pharmaceutical excipients	[10, 11]
Chitosan and alginic acid	Gel beads	[12]
Hyaluronan	Biomedical application	[13]
Lacquer polysaccharide	Anti-tumor efficacy	[14]
Misgurnus anguillicudatus polysaccharide	Immunomodulation	[15]
Cassava starch polysaccharide	Packaging	[16]
Apple pectin	Sorption properties	[17, 18]
Tamarindus indica pods seeds mucilage	Food grade flocculant	[19 - 24]
Coccinia indica fruits mucilage	Removal of dyes	[25]
Conyza canadensis polysaccharides	Anti-aggregatory and anti-oxidant	[26]
Psyllium husk	Colon specific drug delivery	[27 - 29]
Pullulan	Nanoparticles	[30]
Hibiscus esculentus and *Trigonella foenum graceum*	Pharmaceutical flocculants	[31]
Gellan gum	Injectable vehicle and bead	[32, 33]
Cassia auriculata seed mucilage	Tablet binder	[34]
Zizyphus jujuba lamk. Seed mucilage	Tablet binder	[35]
Cassia tora of seed mucilage	Tablet binder	[36]
Cassia sophera Linn seed mucilage	Tablet binder	[37]
Prosopis juliflora seed mucilage	Tablet binder	[38]
Cassia aungostifolia seed mucilage	Tablet binder	[39]
Caesalpinia pulchirrima and *Leucaena leucocephala* seed mucilage	Mucoadhesion	[40]
Cassia fistula seed mucilage	Tablet binder	[41]
Diospyros melonoxylon Roxb, *Buchanania lanzan* Spreng, and *Manilkara zapota* (Linn.) *P. Royen* syn seed mucilage	Mucoadhesion	[42 - 51]
Aloe vera (L.) Burm. f leaves mucilage	Mucoadhesion	[52, 53]
Pithecellobium dulce seed mucilage	Mucoadhesion	[54]
Annona squamosa (L.) Burm. fruit mucilage	Mucoadhesion	[55]
Konjac-graft-poly (acrylamide)-co-sodium xanthate	Flocculant	[56]
Schizophyllan polysaccharides from fungi Schizophyllum	Collagen	[57]
Lycium barbarum L polysaccharides	Antioxidant	[58]
Bora rice starch	Pharmaceutical excipients	[59, 60]
Xanthan gum, guar gum, and chitosan	Colon drug delivery	[61]
Okra gum	Sustained-release tablets	[62]

SUBJECT INDEX

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Sudarshan Singh

Dr. Sudarshan Singh is presently working as a University Reinventing Postdoctoral research scholar at Chiang Mai University, Thailand. He has authored several technical books and book chapters and more than hundreds of research papers in reputed peer-reviewed journals. He has registered three patents to his credit. He is an editorial board member of Science Domain International and guest editor of biomaterials theme in Frontiers in Bioengineering and Biotechnology Journal. He is a reviewer of various international journals. He has ten years of teaching experience in undergraduate and postgraduate courses of pharmacy with more than five years of research experience. He has guided several undergraduate and postgraduate students in their project works. Moreover, during his postdoctoral research at Prince of Songkhla University and Walailak University, Thailand, he co-supervised the doctoral students. He is a life member of professional bodies such as the Society of Pharmacovigilance India and a registered pharmacist at the State Pharmacy Council of Chhattisgarh, India.

Warangkana Chunglok

Dr. Warangkana Chunglok is presently working as Associate Professor at the School of Allied Health Sciences, Walailak University, Thailand. She received Royal Golden Jubilee Scholarship from Thailand Research Fund, Thailand, and Deutscher Academischer Austausch Dienst (DAAD), Germany for pursuing her Ph.D. Furthermore, she has received several awards from Walailak University, Thailand. She has more than sixteen years of teaching and research experience. She is one of the expert scientists in molecular biology of cancer, natural product- based drug discovery for cancers and inflammatory-related diseases, and therapeutic agents from medicinal plants for muscle wasting following stroke. Her research works are conducted both in national collaboration with other universities in Thailand and international collaboration with European Union research institutes. Her background experience includes experiments in molecular biology, in vitro and in vivo study, natural products drug discovery, evaluation of natural compounds and their synthetic analogues from medicinal plants as potential drug leads for the treatment of various types of cancers, inflammatory diseases, and stroke.