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The Analysis of Natural Microstructures Resembling Synthetic Phase-Separated Block Copolymers in Soft Biomaterials and Hard Bio-Minerals

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Abstract. For humans, we come into contact with a lot of different materials every day. Many products or medical treatment equipment are made by soft biomaterial, hard bio-minerals and synthetic phase-separated block copolymers. This paper, through a method of literature review, explores the similarity of microstructures and explains the reason why they have similar structures. The paper finds that some synthetic phase-separated blocks have some similar properties to soft biomaterials, and hard biominerals. For example, the CS-g-PCL copolymer is biocompatible, biodegradable, and exhibits appropriate mechanical behavior. The microstructure of soft biomaterials and hard bio-minerals is very similar to the morphology of synthetic phase-separated block copolymers. This is because they both go through a process of phase separation, which results in the formation of nano- or micro-sized self-assembled structures with specific functions and structures. The paper has many scientific papers, which will be of great help to the future research of these materials.

Keywords: soft biomaterials, hard bio-minerals, phase-separated block copolymers.

1. Introduction

Nowadays, soft biomaterials and hard bio-minerals have a wide range of applications in daily life, for example, in the fields of health care, clinical medicine, aerospace, and others, which cannot be done without their special microstructure. Hard bio-minerals refer to inorganic compound crystalline or amorphous particles and their aggregates formed by biological secretion. It includes macroscopic vertebrate phosphoskeletons, mollusk bone shells, microscopic radiolarian silica shells, and coccolithophore calcium plates [1]. Bio-soft material, a class of compounds derived from natural or synthetic substances, is gaining popularity in biomedical research and applications because to its advantageous features, including in-vivo biodegradability, high water solubility, and customizable targeting capabilities [2]. Phase separation refers to the process of a one-component fluid undergoing a liquid-vapor transition. Under specific conditions of pressure and temperature, the fluid undergoes phase separation, resulting in the formation of two distinct phases. One phase is a low concentration vapor, while the other phase is a high density liquid [3]. This paper uses the method of literature review to analyze the similarity between soft biomaterials, hard bio-minerals, and synthetic phase-separated copolymers. This study provides a foundation for future research.

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2. Literature review

2.1. Soft biomaterial

Bioactive hydrogel marbles are a specific kind of pliable biomaterials. Liquid marbles were a notable breakthrough in fluid manipulation as they employed particle coatings to enclose liquid droplets, resulting in a strong and long-lasting soft solid. This paper utilizes this method to create a bioactive hydrogel marble (BHM). More precisely, the bioactive glass nanoparticles were modified chemically to create hydrophobic bioactive glass nanoparticles (H-BGNPs) that are compatible with living organisms. These H-BGNPs were used to protect a bead made of gelatin. Upon immersion in a physiological environment, the proposed BHM shell facilitated the formation of a bone-like apatite layer. The fabrication procedure facilitated the effective integration of medicines and cells into the designed framework. The BHM facilitated the simultaneous and regulated release of separate therapeutic model molecules that were encapsulated. Furthermore, the BHM effectively supported the encapsulation of cells in a three-dimensional (3D) environment, as evidenced by its exceptional stability and compatibility with living cells in laboratory settings [4]. Several tissues in the human body possess fibrous structures, such as the extracellular matrix, muscles, and heart. These structures play important roles in biological functions and exhibit remarkable mechanical strength. Hydrogels have similarities to biological tissues because of their elevated water content, soft texture, biocompatibility, and elastic properties. Conversely, conventional hydrogels exhibit low mechanical strength and do not possess fibrous structures resembling tissues, which restricts their potential uses [5].

Hydrogels are a significant category of pliable substances that possess a remarkable ability to retain water. They demonstrate both intelligent and elastic characteristics, making them highly valuable in the areas of biomaterials, soft machineries, and artificial tissue. Nevertheless, the inadequate mechanical strength and limited functionalities of conventional chemically cross-linked hydrogels impede their potential for broader applications. Materials composed of both rigid and flexible elements provide exceptional mechanical strength and functionality. Nanocomposite hydrogels mimic natural materials due to the combined impact of nanoparticle (NP) polymers in their synthesis. This article provides a concise overview of the structural design and characteristics of nanocomposite hydrogels. In addition, the article emphasizes the advancements in shaping and prospective uses of hydrogel devices, namely those based on nanocomposite hydrogels, in recent years [6].

2.2. Hard bio-mineral

Bioactive glasses are a specific category of inflexible biomaterials. It is utilized for promoting the formation of new blood vessels in both hard and soft tissue engineering applications. Bioactive glasses were the initial synthetic materials to demonstrate the ability to form a link with bone, and they were effectively employed for the purpose of bone regeneration. Bioactive materials are intentionally created to elicit a certain biological response, typically resulting in a robust bonding with bone [7]. These materials can break down in the body at a rate that matches the rate at which bones are formed. This is achieved via a combination of apatite crystallization on their surface and the release of ions. As a result, they promote the growth of bone cells and the development of new bone [8]. Glasses exhibit bioactivity, rendering them appropriate for application in regenerative medicine due to their ability to interact with both hard and soft tissues. Bioactive glasses, such as 45S5, are a type of soda-lime phosphosilicate glasses [9]. Researchers utilized molecular dynamics simulations to examine the elastic and structural characteristics of densified 45S5 bioactive glass and liquids at different densities. The findings indicate that the glass structure experiences re-polymerization, as demonstrated by increased network connection and a shift from tetrahedral to octahedral polyhedral forms. People had the ability to personalize the elastic properties while maintaining the biological function of the glass [9].

The global prevalence of bone disorders and trauma has shown a substantial increase in recent decades. Bioactive glasses are considered a significant substance for bone regeneration due to their overall exceptional ability to promote bone growth and stimulate bone formation. Seven years ago, an innovative type of bioactive glass called mesoporous bioglass (MBG) was created. This glass has a well-

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organized structure of channels and a large surface area with specialized properties. The field of nanomaterials used in bone regeneration therapy has made tremendous progress with the creation of bioactive mesoporous nanoparticles (MBNPs). These nanoparticles have tiny spherical particles with chemical characteristics and porous features that facilitate the regeneration of bone tissue. These glasses have a composition comparable to regular sol-gel bioactive glasses and possess high values for specific surface area and porosity. MBNPs, with their logical design of mesoporosity and capacity to incorporate medications, are highly effective for treating bone abnormalities and related pathologies such osteoporosis, bone cancer, and infection. In addition, the compact dimensions of MBNPs enable them to infiltrate cellular structures, eliciting distinct cellular reactions that conventional bone transplants are incapable of achieving. This study provides a complete analysis of several aspects of MBNPs, such as synthesis methodologies, their role as drug delivery systems, the integration of therapeutic ions, the production of composites, and the specific cellular responses they elicit [11].

2.3. Synthetic phase-separated block copolymers

The patternability of block copolymers arises from their capacity to self-assemble into microdomains, allowing for the creation of intricate submicron structures in block copolymer films. This ability is achieved through a combination of the "bottom-up" approach of self-assembly and the manipulation of these patterns using various physical and chemical methods, including "top-down" lithographic techniques. Extensive research has been conducted on the control of pattern orientation in long-range microdomains and the control of multilayer block copolymer film by top-down and bottom-up patterning. These methods provide the ability to manipulate the arrangement of block copolymers, allowing for advancements in template nanolithography and other nanofabrication techniques[12]. Synthetic block copolymers mimic the structural and functional features of lipids. Lipids are generally compatible with living organisms, but high-molecular-weight polymers are strong in structure and have a wide range of chemical properties. In order to create materials suitable for regulated drug/gene/protein delivery, biosensors, and artificial cells, it is typically necessary to combine lipids with polymers [13]. The most convenient method for generating peptide-synthetic hybrid block copolymers involves the use of ring-opening polymerization of α-amino acid N-carboxy anhydrides. This process utilizes synthetic polymers that have been suitably end-functionalized as the macroinitiator [14].

Studying the microphase separation of double-hydrophilic block copolymers in water is crucial for understanding their behavior as molecular assemblies with mesoscale aqueous compartments. The synthesis of diblock copolymers was conducted by combining poly(carboxy betaine acrylate) (PCBA2), a water-soluble zwitterionic polymer, with poly(2-methoxyethyl acrylate) (PMEA), a hydrophilic water-insoluble nonionic polymer. The copolymers obtained, referred to as PCBA2n-b-PMEAm, were further examined to gain insight into their behavior when combined in water-based solutions. PCBA2n-b-PMEAm block copolymers were synthesized with precision utilizing reversible addition–fragmentation chain transfer polymerization. The synthesis involved modifying a carboxy betaine acrylate with a tert-butyl group and 2-methoxyethyl acrylate. Subsequently, the tert-butyl group was cleaved. The PCBA2n-b-PMEAm particles were produced in dilute aqueous solutions and exhibited microphase separation in concentrated aqueous solutions. The hydrodynamic radius of the particles and the structure that kept them distinct from the microphase were determined by the content of the block copolymer and the length of the PMEA chain [15].

3. Discussion

PLLA is recognized as a durable implant, and thus far, no significant drawbacks or issues with toxicity, intense acute inflammation, or immunogenicity have been documented. The synthesis of star-shaped block copolymers with an amphiphilic structure was achieved by conducting ring-opening polymerization of L-lactide using 8-armed PEG10K or 8-armed PEG35K as a macroinitiator. These copolymers consist of 8 arms of PEG and PLLA. The cast films made from the 8arms PEG10K-b-PLLA35K block copolymer exhibited significantly lower crystallinity and tensile strength compared to the linear 2arms PEG10K-b-PLLA33K film. This is because the star-shaped 8arms PEG-PLLA block

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copolymer formed ordered PLLA domains with a lamellar structure. The purpose of this study was to investigate the impact of the molecular architecture of the star-shaped 8arms PEG10K-b-PLLA35K film. Put simply, the softness of the 8arms PEG10K-b-PLLA35K film was achieved by placing the hard PLLA domains within the soft PEG domains. The thermal property, water absorption ability, degradation rate, and mechanical property of 8-arm PEG10K-b-PLLA35K and linear 2-arm PEG10K-b-PLLA33K films were analyzed. Furthermore, the water absorption capacity, mechanical characteristics, and microphase separated structure of the 8arms PEG35K-b-PLLA37K film were compared to those of the 8arms PEG10K-b-PLLA37K film in order to investigate the potential of the star-shaped 8arms PEG35K-b-PLLA37K film as an innovative implantable soft material that exhibits excellent stretchability upon water absorption [16]. The statement shows that some copolymers have soft biomaterial's structure and properties.

Tissue regeneration necessitates the development of sufficient scaffolds that facilitate cell proliferation and tissue formation by providing an appropriate substrate for cell adhesion, proliferation, and differentiation. The ideal scaffolds must exhibit biocompatibility, biodegradability, and demonstrate suitable mechanical qualities. The substance underwent in vitro evaluation to ascertain its biological characteristics. The findings shown that the CS-g-PCL copolymer enhances the growth of Wharton's jelly mesenchymal stem cells and aids tissue formation during its degradation. Based on both mechanical and biological evidence, the CS-g-PCL copolymer is appropriate as a scaffold in a cell-laden construct for soft tissue creation [17]. From the experiment, having good biocompatibility and biodegradability are very typical characteristics.

There are three main reasons why soft biomaterials, hard biominerals and synthetic phase-separated block copolymers have similar structures. The three types of materials all experience phase separation. No organelles within the cell in biological systems also form through phase separation. Specific protein or nucleic acid molecules interact with each other through polyvalent interactions to produce another phase with different physical and chemical properties in an otherwise homogeneous environment, forming membrane-free organelles or cellular structures. This phase separation phenomenon is widespread within the cell and is essential for achieving specific cellular functions. Soft biomaterials form complex network structures with certain structures and functions through phase separation, while hard bio-minerals form crystalline structures with specific morphologies and functions through phase separation of mineral components. The formation of these structures is similar to the microscopic phase separation process in block copolymers, which are all formed by self-assembly at the nano or micrometer scale with a certain periodic spatial structure, and the microstructures of soft biomaterials and hard bio-minerals are very similar to the morphology of synthetic phase separation block copolymers, mainly because they all undergo a process of phase separation, which leads to the formation of nano- or micro-sized self-assembled structures with specific functions and structures.

4. Conclusion

This paper discusses the similarities in microstructure and some characteristics of soft bio-materials, hard bio-minerals and synthetic phase-Separated Block Copolymers. This study also gives some typical examples of different types of material. Moreover, it answers the reasons why they are similar in three aspects. This study provides a theoretical foundation for future research in related fields.

However, this paper has certain shortcomings, for example, this article only focuses on a literature review and some case studies without any experimentation or data analysis. What's more, the scope of this study could also be broadened. Before conducting further research and experiments, more reading materials should be investigated. In the future, the author will dig deeper in this field in order to delve into the usage of those three materials mentioned in this article. Future scientists should also fusion those materials reasonably due to their similar structures and some similar properties. The author hopes that these materials will have more applications in different places, for example, clinical medicine, architecture, manufacturers, etc., and they will be more beneficial to people's lives.

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