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Current development and future prospects of protein hydrogels

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Abstract. Protein hydrogels are a class of soft biomaterials that have attracted extensive attention due to their unique properties and potential applications in biomedicine in recent years. This paper explores the promise of protein hydrogels, discussing their advantages, limitations, and future prospects. The biocompatibility, high water content, and tunable mechanical properties of protein hydrogelsmake them appropriate for a variety of uses, including 3D bioprinting, drug delivery, wound healing, and biosensors. However, challenges such as stability and biodegradation, reproducibility and scalability, clinical translation, and a lack of understanding of their mechanisms of action must be addressed to fully realize their potential. The purpose of this paper is to understand the current development status and difficulties of protein hydrogels and to speculate on their future development.

Keywords: biocompatibility, 3D bioprinting, drug delivery, biodegradation.

1. Introduction

Because protein hydrogels have the potential to be used in such a wide variety of uses, such as drug delivery, tissue engineering, and biosensors, they have garnered a large amount of interest from researchers. The most recent developments in this area of research have centred on the creation of new protein-based materials that have enhanced degradation and mechanical properties, the improvement of the biocompatibility of protein hydrogels for use in in vivo applications, and the development of advanced manufacturing techniques for the mass production of protein hydrogels.

One recent breakthrough in protein hydrogel research is the development of self-healing hydrogels. These materials have the ability to repair themselves when damaged, which could be particularly useful for biomedical applications where mechanical strength and stability are critical. Researchers have developed self-healing protein hydrogels using various approaches, including introducing dynamic covalent bonds and using reversible protein-protein interactions. Another area of current research progress is the use of protein hydrogels in 3D printing. The ability to print complex structures using protein hydrogels could have significant implications for regenerative medicine and tissue engineering. Researchers have made progress in developing inkjet printing and extrusion-based printing techniques for protein hydrogels, as well as exploring the use of multiple protein components in 3D printing to create more functional structures.

Despite these advancements, several research gaps still exist in protein hydrogel research. The biocompatibility of protein hydrogels for in vivo applications requires additional study. While protein hydrogels have demonstrated promise in tissue engineering and drug delivery, additional research is

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necessary to completely comprehend their interactions with living tissues and to develop materials that can interact with the body without triggering an immune response.

This paper explores the promise of protein hydrogels, discussing their advantages, limitations, and future prospects, so as to to understand the current development status and difficulties of protein hydrogels and to speculate on their future development.

2. Current development of protein hydrogels

2.1. Protein hydrogels and its background

Hydrogels are biphasic substances composed of a porous, permeable solid and an interstitial fluid. For hydrogels, porous and permeable solids consist of a three-dimensional network of water-insoluble polymers and fluids that absorb large quantities of water or biological fluids [1]. These characteristics form the premise for numerous applications, particularly in the biological field. The majority of commercially available hydrogels are synthetic, but some are derived from natural substances.

Protein hydrogels are a type of soft biomaterial composed of protein networks absorbing a substantial amount of water. Protein hydrogels can be produced utilizing either natural or synthesized proteins as building blocks for three-dimensional networks, according to their underlying principle. Cross-linking these proteins produces hydrogel structures that are capable of absorbing large quantities of water, causing them to become extremely distended and hydrated [2]. Their unique properties make them suitable for various biomedical, tissue engineering and drug delivery applications.

2.2. Properties of protein hydrogels

Protein hydrogels are soft biomaterials that possess chemical, physical, and biological properties that are important for their formation, stability, and performance. The physical properties of protein hydrogels include their mechanical strength, swelling behavior, and porosity. The chemical properties include biodegradability, stability, and ability to be functionalized. The biological properties include biocompatibility, bioactivity, and cell adhesion.

2.2.1. Physical properties of protein hydrogels. Protein hydrogels' physical properties are determined by factors such as protein concentration and type, crosslinking density, and pH. Increasing the protein concentration and crosslinking density can increase the hydrogel's mechanical strength. This, however, can reduce the swelling behaviour and porosity of the hydrogel, which can impact cell adhesion and nutrient transport. The swelling behaviour of the hydrogel is also affected by the pH and ionic strength of the surrounding environment.

The mechanical, rheological, and swelling properties of protein hydrogels are essential for their stability and performance in various biomedical applications. Several factors can influence these properties, including the type and concentration of protein, the crosslinking density, the pH, the temperature, and the presence of ionic species.

Mechanical properties refer to the ability of protein hydrogels to withstand external forces or deformation without breaking. The stiffness or elasticity of hydrogels can be measured using mechanical testing methods such as compression, tensile, and shear tests. The mechanical properties of protein hydrogels are influenced by the concentration and type of protein, the crosslinking density, and the temperature. Increasing the protein concentration and crosslinking density can increase the mechanical strength and stiffness of hydrogels. The temperature also plays a major role in the mechanical properties of protein hydrogels, as changes in temperature can affect the protein conformation and crosslinking density, thereby affecting the mechanical strength of the hydrogel [3].

Rheological properties refer to the flow behavior of protein hydrogels under external forces, and it is important for the processing and handling of hydrogels. Rheological properties of hydrogels are measured using techniques such as shear rheology, oscillatory rheology, and creep tests. The rheological properties of protein hydrogels are influenced by factors such as protein concentration, crosslinking density, pH, and temperature. Increasing the protein concentration and crosslinking density can increase the viscosity and elasticity of the hydrogel, while changes in pH and temperature can affect the hydrogel's gelation time and viscoelastic properties [4].

Protein hydrogels' swelling properties refer to their capacity to incorporate water and expand. As it affects the diffusion of molecules and cells, the swelling behaviour of hydrogels is crucial for their efficacy in tissue engineering and drug delivery applications. The swelling properties of protein hydrogels are affected by variables such as protein type and concentration, pH, the presence of ionic species, and crosslinking density [5]. Increasing the protein concentration and crosslinking density can reduce the swelling ratio of hydrogels, whereas changes in pH and ionic strength can affect the swelling behaviour of hydrogels.

*2.2.2. Chemical properties of protein hydrogels.*The chemical properties of protein hydrogels are affected by variables such as the crosslinking agent, protein source, and presence of functional groups. Crosslinking agents like glutaraldehyde and genipin can enhance the hydrogel's stability and mechanical properties, but they can also cause cytotoxicity and inflammation. The choice of protein source can also affect the biodegradability and biocompatibility of the hydrogel [3]. Additionally, functionalization of the hydrogel with specific biomolecules or ligands can enhance the biological activity and specificity of the hydrogel for applications [6].

2.2.3. Biological properties of protein hydrogels. The biological properties of protein hydrogels are determined by their biocompatibility, bioactivity, and cell adhesion. Protein hydrogels are from natural sources such as fibrin, collagen, and gelatin are biocompatible and can support cell adhesion and proliferation. The bioactivity of the hydrogel can be enhanced through functionalization with growth factors or other bioactive molecules [7]. However, factors such as protein denaturation, mechanical instability, and immune response can limit the performance and biocompatibility.

3. Advantages of protein hydrogels and their current applications

3.1. Advantages of protein hydrogels

Compared to other synthetic polymers, protein hydrogels have several advantages. The biodegradability and biocompatibility of protein hydrogels make them ideal for use in medical applications [3]. Additionally, protein hydrogels can be easily functionalized to respond to specific stimuli such as ionic strength, temperature, and pH.

3.2. Applications of protein hydrogels

Protein hydrogels are used in a wide range of fields, including medical, food, and cosmetics. These applications are principally made possible by their special qualities, which include biocompatibility, biodegradability, and stimuli-responsiveness, among others.

Protein hydrogels are frequently used in medical fields such as drug delivery, tissue engineering, and wound healing. Due to its excellent biocompatibility and biodegradability compared with other materials. For example, it can be loaded and released through artificial control, so it is often used to deliver targeted drugs. Second, because they can mimic the extracellular matrix, they also be applicable as scaffolds in tissue engineering applications and provide an environment conducive to cell differentiation and growth. In addition, they are used in wound healing as they absorb exudate and promote healing [6]. Protein hydrogels are utilized as gelling agents, emulsifiers, and stabilizers in the food industry. The unique properties of protein hydrogels such as water-binding capacity and ability to form gels make them suitable for use in various food products such as meat products, desserts, and beverages. Protein hydrogels can also be used as fat replacers in low-fat food products [8].

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4. Prospect of protein hydrogels and existing problems

4.1. Prospect

The rapidly expanding discipline of regenerative medicine focuses on repairing or replacing damaged tissues or organs. As a result of their capacity to imitate the extracellular matrix and provide an optimal environment for cell proliferation and differentiation, protein hydrogels have the potential to be used as scaffolds in tissue engineering applications. To optimize the degradation and mechanical propertiesrates of protein hydrogels for specific tissue engineering applications, additional research is required.

Biosensors are devices that can detect biological molecules and are widely used in medical diagnostics and environmental monitoring. Protein hydrogels can be used as sensing elements in biosensors due to their ability to selectively bind to specific molecules. Further research is needed to optimize the sensitivity and selectivity of protein hydrogel-based biosensors for different applications.

3D printing is an emerging technology that allows the fabrication of complex structures with high precision. Protein hydrogels have the potential to be used as bioinks in 3D printing for tissue engineering applications. To optimize the printing parameters and enhance the mechanical properties of protein hydrogel-based constructs, additional research is required.

4.2. Limitations of protein hydrogels

Challenges that need to be overcome to advance the field of protein hydrogels include improving their mechanical strength, stability, and biocompatibility. Protein hydrogels typically have lower mechanical strength compared to synthetic polymers, which limits their use in certain applications [3]. Improving the stability of protein hydrogels under different environmental conditions is also critical to expanding their applications. In addition, protein hydrogels may induce an immune response in vivo, which limits their biocompatibility. Further research is needed to address these challenges and optimize the properties of protein hydrogels for specific applications.

5. Conclusion

Protein hydrogels have shown great potential for a wide range of applications, including drug delivery, tissue engineering, biosensors, and 3D printing. As a result, the future prospects for protein hydrogels are very promising, with many new opportunities for innovation and research. One area of potential for further research is the development of new protein-based materials that can exhibit improved mechanical and degradation properties. In particular, researchers are working to enhance their mechanical strength and stability so that they can be used in load-bearing such as bone and cartilage repair.

One approach is to engineer the structure of the proteins themselves, either through genetic modification or chemical modification, to enhance their mechanical properties. Another area of emphasis for future study is the development of protein hydrogels that can be utilized in in vivo applications. In vivo applications require materials that are biocompatible and can safely interact with living tissues without causing an immune response. Researchers are exploring different methods for enhancing the biocompatibility of protein hydrogels, such as modifying the surface of the hydrogel to reduce protein adsorption and cell adhesion.

Finally, there is a need for further research into the manufacturing processes for protein hydrogels, particularly in the context of 3D printing. Current techniques for fabricating protein hydrogels are often time-consuming and require specialized equipment, making them difficult to scale up for mass production. Researchers are investigating new methods for fabricating protein hydrogels using 3D printing techniques, such as inkjet printing and extrusion-based printing, which could enable the production of more complex and functional structures. These efforts will help to unlock new applications for protein hydrogels and further contribute to the advancement of biomedical engineering and regenerative medicine.

References

[1] Wichterle, O., Lím, D. (1960). "Hydrophilic Gels for Biological Use". Nature. 185 (4706): 117–

118.
[2] Yang, Y.J., Holmberg, A.L., Olsen, B.D. (2017) Artificially engineered protein polymers. Annu. Rev. Chem. Biomol. Eng., 8, pp. 549-575.
[3] Jiang, L.B., Su, D.H., Ding, S.L., Zhang, Q.C., Li, Z.F., Chen, et al. (2019) Salt-Assisted Toughening of Protein Hydrogel with Controlled Degradation for Bone Regeneration. Adv. Funct. Mater, 29, p. 1901314.
[4] Wang, J.J., Wang, Y., Yang, J., Chen, L., et al. (2019) Mechanically Strong and Highly Tough Prolamin Protein Hydrogels Designed from Double-Cross-Linked Assembled Networks. ACS Appl. Polym. Mater., 1 (6), pp. 1272-1279.
[5] Li, H., Zhao, L., Chen, X.D., Mercade-Prieto, R. (2016) Swelling of whey and egg white protein hydrogels with stranded and particulate microstructures. Int. J. Biol. Macromol., 83, pp. 152-159.
[6] Bae, K.H., Kurisawa, M. (2016) Emerging hydrogel designs for controlled protein delivery. Biomater. Sci., 4 (8), pp. 1184-1192.
[7] Gao, X., Fang, J., Xue, B., Fu, L., Li, H. (2016) Engineering Protein Hydrogels Using SpyCatcher-SpyTag Chemistry. Biomacromolecules, 17 (9), pp. 2812-2819.
[8] de Kruif, C.G., Anema, S.G., Zhu, C.J., Havea, P., Coker, C. (2015) Water holding capacity and swelling of casein hydrogels. Food. Hydrocoll., 44, pp. 372-379.