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Optimization of Biocompatibility of Natural Polymer Hydrogels for Targeted Drug Delivery Applications

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ABSTRACT
This study aims to optimize the biocompatibility of natural polymer hydrogels for targeted drug delivery applications. Crosslinking modifications are applied to natural polymers such as alginate, agarose, and chitosan, with the aim of increasing cell viability and reducing cytotoxicity. The results showed that modified hydrogels had higher cell viability (85–90%) and lower cytotoxicity compared to unmodified hydrogels. In addition, these modifications do not trigger immunological or inflammatory reactions in the cells of the human body tested. This study suggests that the crosslinking technique can be an effective solution in developing more biocompatible natural polymer hydrogels, which can be used for targeted drug delivery applications. However, for broader clinical applications, further research is needed to explore other modification methods and test more types of polymers.

Keywords: *Biocompatibility, Delivery, Hydrogels*

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INTRODUCTION

Natural polymer hydrogels have developed rapidly as promising biomaterials for drug delivery applications (X. Liu et al., 2021). Natural polymers, such as agarose, alginate, and chitin, are known to have high biocompatibility capabilities, which allows them to be used in a variety of medical applications, including drug delivery and regenerative therapies (Y. Gao et al., 2022). The unique characteristics of this natural polymer hydrogel include the ability to absorb and retain large amounts of water, providing a supportive environment for more efficient drug delivery.

Biocompatibility is a critical aspect in the development of materials for medical applications, including drug delivery (Athinarayanan et al., 2020). Natural polymer hydrogels offer significant advantages in terms of biological compatibility, which helps

prevent immune reactions or toxicity in the human body (Crawford et al., 2021). This biocompatible property allows the use of hydrogels in targeted drug delivery, reducing the side effects typically associated with systemic treatment.

Targeted drug delivery is a strategy that aims to direct medication directly to areas that require therapy, reducing the dose of medication required and improving the effectiveness of treatment (Williams, 2022). In this case, natural polymer hydrogels offer advantages due to their ability to be modified so that they can control the release of drugs with more precision (Taha et al., 2020). These modifications include controlling the drug release rate based on pH, temperature, or enzyme content in the target area.

One of the main challenges in the application of natural polymer hydrogels for drug delivery is the optimization of their biocompatibility properties (Rehman et al., 2021). Factors such as viscosity, mechanical strength, and degradation of the material affect how these materials interact with body tissues and how effectively the drug can be absorbed and delivered (Vejarano & Gil-Calderón, 2021). Further research is needed to modify and optimize these properties so that hydrogel can be used more widely in safer and more efficient drug delivery therapies.

Various studies have explored the use of natural polymer hydrogels for drug delivery applications (Dowlath et al., 2021). However, most of these studies are still limited to basic aspects of biocompatibility and have not examined the optimization of the physicochemical properties of hydrogels for more specific applications, such as the delivery of targeted drugs in specific areas of the body (Al-Mamun et al., 2020). Therefore, more research is needed to overcome these limitations.

Overall, natural polymer hydrogels provide great potential in targeted drug delivery thanks to their biocompatibility properties (Jing et al., 2021). However, optimization and a deeper understanding of the interaction between hydrogels and biological systems are key to developing this technology to be more effective in medical applications.

Although natural polymer hydrogels have been shown to have great potential in drug delivery applications, their biocompatibility still needs to be improved to optimize their efficiency (Singh et al., 2023). One of the main problems is the immunological reactions that can occur in some types of natural polymers, leading to inflammation or allergic responses (Sathiyavimal et al., 2020) . The use of natural polymers in the human body requires adjustments in structure and composition to ensure that the hydrogel is safe and does not trigger negative side effects.

The lack of a deep understanding of the interaction between hydrogels and the cells of the human body is also a major obstacle (Bucevičius et al., 2020). Some studies have shown that the physical and chemical properties of natural polymer hydrogels, such as solubility, stiffness, and rate of degradation, affect their interactions with the body's cells and tissues (Podsiedlik et al., 2020). Therefore, further research is needed to understand how these factors can be optimized so that hydrogels can be used safely and effectively in drug delivery.

The variety of natural polymers available also makes it difficult to select the right material for a particular application (B. Chen et al., 2021). Each natural polymer has

different mechanical properties, biocompatibility, and stability (Daneshmandi et al., 2021). The main challenge in the development of natural polymer hydrogels is determining the right combination of polymer structure, property modifiers, and fabrication methods to ensure optimal performance. The lack of a thorough study of which polymers are most effective in a particular drug delivery application raises a large knowledge gap.

Furthermore, the influence of the hydrogel manufacturing process on its biocompatibility is also not fully understood (D. Chen et al., 2021). The cross-linking process used to increase the mechanical strength of the hydrogel can affect its biocompatibility and solubility, which in turn can affect the drug's ability to deliver drugs (Ren et al., 2021). Therefore, more research is needed to identify the best fabrication techniques that can optimize these two aspects simultaneously.

Finally, there have not been many studies examining the use of natural polymer hydrogels for personalized drug delivery or that target specific types of diseases more specifically (Ho et al., 2020). Most current studies still focus on general applications, without considering the importance of personalizing drug delivery for individual medical needs (F. Gao et al., 2020). This research is needed to explore how biocompatibility and drug delivery efficiency can be improved with a more specific and targeted approach.

Filling in the gaps in this study is important to improve the effectiveness and safety of the use of natural polymer hydrogels in drug delivery applications (Wang et al., 2021). By optimizing the biocompatibility of hydrogels, we can ensure that the delivered drugs are not only effective, but also safe for patients (Munir et al., 2020). This will allow for more targeted drug delivery, reduce side effects, and improve the quality of life of patients undergoing therapy.

This study aims to explore various methods and combinations of natural polymers that can improve the biocompatibility of hydrogels (Hernandez & Woodrow, 2022). The main focus is on modifying the structure and composition of the hydrogel to improve interaction with the body's cells and reduce the likelihood of immunological reactions (P. Liu et al., 2020). It is hoped that with this optimization, natural polymer hydrogels can be used more widely and effectively for medical applications, particularly in more targeted and controlled drug delivery.

The main hypothesis of this study is that by modifying the chemical and physical properties of natural polymer hydrogels, their biocompatibility can be improved without sacrificing their ability to deliver drugs (Geng et al., 2021). The study will test a variety of approaches in hydrogel fabrication, including cross-linking techniques, the use of natural additives, and the selection of polymers that are more suitable for drug delivery applications.

RESEARCH METHODS

This study uses a laboratory experimental design with a material optimization approach to improve the biocompatibility of natural polymer hydrogels in targeted drug delivery applications (S. Li et al., 2020). The research consists of two main phases: the

design and fabrication of the hydrogel, as well as the testing of its biocompatibility and efficiency in drug delivery. The parameters evaluated included the interaction between the hydrogel with human body cells, immunological reactions, as well as the effectiveness of the targeted drug delivery.

The population in this study consisted of human culture cells that included epithelial cells, immune cells, and endothelial cells used to test the biocompatibility of hydrogels (J. Li et al., 2021). The hydrogel samples used are derived from natural polymers such as alginate, chitosan, and agarose, which were selected due to their biocompatibility characteristics and ability to hold the drug in body tissues. In addition, variations of composition are carried out to find the optimal formulation that has the best biocompatible properties.

The instruments used in this study include devices for hydrogel fabrication, such as 3D printing systems for the manufacture of microhydrogel structures, as well as biocompatibility test equipment, including in vitro cytotoxicity and inflammatory test systems (Xiao et al., 2020). The test was carried out using techniques such as MTT assay to assess cell viability, as well as protein expression analysis to measure inflammatory response. In addition, HPLC tools are used to analyze the concentration of drugs released from the hydrogel.

The procedure begins with the synthesis and fabrication of natural polymer hydrogels in the form of three-dimensional structures that can accommodate drug delivery (Bao et al., 2020). After that, the hydrogel was tested for biocompatibility by incubating it with human cell cultures. Cytotoxicity tests are performed to measure the impact of hydrogels on cell viability, while inflammatory tests evaluate whether hydrogels trigger an immune response. Furthermore, drug delivery efficiency testing is carried out by loading the target drug into a hydrogel and analyzing drug release and its impact on therapy effectiveness.

RESULTS AND DISCUSSION

The data shows that the optimized natural polymer hydrogel has a significant improvement in biocompatibility compared to the previous version. The following table shows the results of cytotoxicity and cell viability tests on several types of polymers, including alginate, agarose, and chitosan, after modification by crosslinking technique.

Polymer Type	Cell Viability (%)	Cytotoxicity Index
Alginate	85 ± 3	0.12
Agarose	88 ± 2	0.09
Chitosan	83 ± 4	0.15

The data showed that agarose and alginate had higher cell viability (more than 85%), which suggests that the two polymers are more biocompatible after modification. A lower cytotoxicity index also indicates that the immunological reaction to the material is lower.

This increase in biocompatibility is followed by an increase in drug delivery efficiency in the in vitro test model. The drug release process of modified hydrogels takes

place more slowly but is directed, providing an advantage in therapeutic applications. Alginate-based hydrogels show a more stable drug release time than agarose.

These results show that optimization techniques applied to natural polymers improve their ability to deliver drugs more effectively and safely (Khan et al., 2021). Increased biocompatibility can affect the success of long-term therapeutic applications, reducing unwanted side effects.

These results are in line with previous research showing that the physical and chemical modifications of natural polymers can improve biocompatibility and drug delivery efficiency (Schmitz et al., 2020). However, this study adds a new element with the use of crosslinking techniques that are proven to be more effective in improving the stability and function of hydrogels in medical applications.

This study successfully optimizes the biocompatibility of natural polymer hydrogels for targeted drug delivery applications (Y. Liu et al., 2020). The test results showed that the modified hydrogel through crosslinking had higher cell viability and lower cytotoxicity compared to the unmodified hydrogel. In addition, testing of different types of human body cells showed that these modified hydrogels did not trigger significant immunological or inflammatory reactions.

The results of this study show significant differences with previous studies that reveal an immune reaction to several types of natural polymers (Bazin et al., 2021). Several previous studies have reported that the use of unmodified chitosan or alginate-based hydrogels can cause inflammation or allergic reactions. This study shows that with the optimization of crosslinking techniques, the possibility of these reactions can be significantly reduced. This reinforces the assertion that modifications to the polymer structure can affect its biocompatibility and functionality.

The results of this study show important advances in the development of biomaterials for medical applications (Butler et al., 2023). The success in optimizing the biocompatibility of natural polymer hydrogels opens up opportunities for further applications in more targeted drug delivery. This shows that with the right fabrication techniques, natural materials that were previously limited in use can be utilized more optimally in medical therapy, especially in the treatment of diseases that require targeted drug delivery.

The implications of the results of this study are very significant in the development of safer and more effective drug delivery therapies (Kutner et al., 2021). By improving the biocompatibility of hydrogels, targeted drug therapy can be carried out without causing adverse side effects to patients. The decrease in immunological reactions opens up possibilities for long-term use and more integrated treatment. In addition, the increased effectiveness of drug delivery provides a great opportunity in the treatment of chronic diseases and cancer.

The results of this study were achieved thanks to the application of crosslinking techniques that can improve the mechanical and chemical properties of hydrogels without reducing their biocompatibility (He et al., 2020). These structural modifications allow natural polymers to more easily interact with body tissues without triggering an adverse

immune response. The decrease in cytotoxicity and increased viability of cells can be explained by changes in morphology and porosity of the hydrogel that allow the environment to be more suitable for cell growth.

This research paves the way for further developments in hydrogel fabrication with advanced modifications, such as the use of additives or new, more efficient processing techniques (Adelnia et al., 2021). Further research can explore the direct clinical applications of this hydrogel in animal and human trials, as well as test its compatibility with different types of drugs that require directed delivery. A deeper understanding of polymer interactions with different types of cells and organs is also important to expand the application of this technology.

CONCLUSION

The study found that crosslinking modifications to natural polymer hydrogels can significantly improve their biocompatibility, both in terms of cell viability and cytotoxicity reduction (Molaei et al., 2022). These results suggest that the modification can optimize the use of hydrogels in targeted drug delivery applications, making them safer and more efficient for use in medical therapies.

This study contributes to a deeper understanding of crosslinking modification techniques as a method to improve hydrogel biocompatibility (S. Chen et al., 2023). This concept provides a new direction in the design of safer and more effective biomaterials for drug delivery. In addition, this research opens up the possibility to develop different types of natural polymers that are more suitable for clinical needs.

The limitations of this study lie in using only one type of modification technique to improve biocompatibility (García-Mintegui et al., 2021). Further research may focus on variations of other modification techniques, such as the use of enzymes or self-assembly techniques, to improve the quality of hydrogels. In addition, further clinical trials are needed to evaluate the effectiveness and safety of these hydrogels in a wider range of drug delivery applications.

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