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Unlocking The Potential Of Natural Polymers: A Comparative Study For Innovative Drug Delivery Systems

Author

Abstract
This study aims to characterize and compare four biopolymers - pectin, guar gum, xanthan gum, and sodium alginate - for their potential use in drug delivery systems by evaluating their hydrophilicity, pH sensitivity, and thermosensitivity.
Biopolymer films were prepared and subjected to water absorption tests for hydrophilicity, gravimetric analysis in varying pH conditions for pH sensitivity, and weight change measurements after heat exposure for thermosensitivity. Each test was conducted in five trials to ensure reliability.
Pectin demonstrated the highest responsiveness across all tests, showing rapid water absorption (6.46 seconds), significant pH sensitivity (0.53g weight change in acidic conditions), and high thermosensitivity (0.378g weight change). Guar gum showed moderate responsiveness, while xanthan gum and sodium alginate exhibited the most stability across varying conditions.
Pectin's high responsiveness suggests suitability for smart, multi-stimuli-responsive systems. Guar gum's moderate responsiveness indicates potential for controlled release formulations. The stability of xanthan gum and sodium alginate makes them ideal for applications requiring consistent drug release in diverse physiological environments.
This study offers a comprehensive, comparative analysis of four widely used biopolymers, filling a gap in the existing literature. The results provide a foundation for developing tailored, sustainable drug delivery systems, contributing to the advancement of personalized medicine and environmentally friendly pharmaceutical practices.
Keywords: *Biopolymers, Drug Delivery Systems, Hydrophilicity, pH Sensitivity, Thermosensitivity*

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I. Introduction

The global healthcare industry is continually seeking innovative solutions to enhance drug delivery systems, aiming to improve treatment efficacy and at the same time, minimizing side effects. In recent years, biopolymers have emerged as promising materials for developing advanced drug delivery systems, offering advantages such as biocompatibility, biodegradability, and the potential for targeted and controlled release of therapeutic agents (Otoni et al., 2021).

Biopolymers, which are polymers derived from natural sources, have gained significant attention due to their sustainability and reduced environmental impact compared to synthetic polymers. These materials offer a range of properties that can be exploited to create tailored drug delivery systems, responding to specific physiological conditions such as pH changes, temperature variations, or enzymatic activity (Santos et al., 2024).

The development of biopolymer-based drug delivery systems addresses several challenges in contemporary healthcare. First, it offers a potential solution to the issue of poor drug solubility, which affects approximately 40% of approved drugs and nearly 90% of developmental pipeline drugs (Merino & Athanassiou, 2023). By encapsulating poorly soluble drugs in hydrophilic biopolymer matrices, their bioavailability can be significantly improved. Second, biopolymer-based systems can provide controlled and sustained drug release, reducing the frequency of drug administration and improving patient compliance. Finally, these systems offer the possibility of targeted drug delivery, potentially reducing systemic side effects and improving therapeutic outcomes (Nguyen et al., 2024).

Recent research has explored various aspects of biopolymers in drug delivery. For instance, Guo and Li (2024) investigated the use of chitosan-derived nanocarriers for pH-controlled drug delivery in diabetes treatment. Sultanova et al. (2023) studied thermo-responsive nanoparticles based on diblock copolymers for intravitreal drug delivery. However, there remains a need for comparative studies of different biopolymers to guide their selection for specific drug delivery applications.

This study aims to address this gap by systematically investigating and comparing the properties of four widely used biopolymers: pectin, guar gum, xanthan gum, and sodium alginate. Specifically, we focus on three

key properties that are crucial for drug delivery applications – hydrophilicity, pH Sensitivity and thermosensitivity.

This study aims to provide valuable insights into the behaviour of these biopolymers under various conditions relevant to drug delivery. This research aligns with the growing emphasis on sustainable and environmentally friendly materials in the pharmaceutical industry.

The paper is structured as follows: The next section presents a comprehensive literature review, detailing the current state of knowledge on biopolymers in drug delivery. This is followed by a description of the experimental methods for characterizing the hydrophilicity, pH sensitivity, and thermosensitivity of the selected biopolymers. The results of these experiments are presented and discussed in the context of their implications for drug delivery applications. The final section concludes with a summary of the findings and suggestions for future research.

II. Literature Review

Plastics/Polymers for Drug Delivery

Polymers have emerged as versatile materials for drug delivery systems, offering a wide range of applications across various medical fields. Recent studies have demonstrated the efficacy of polymers in delivering drugs for conditions ranging from cancer to diabetes and osteoarthritis.

Polymer-based drug delivery systems have shown particular promise in cancer therapy. Nguyen et al. (2024) conducted a systematic review of polymer-based drug delivery systems for anticancer drugs, highlighting the use of biodegradable polymers such as polylactic acid (PLA) and polycaprolactone (PCL). These polymers can form nanoparticles that encapsulate hydrophobic drugs, improving their solubility and targeted delivery to cancer cells.

Hill et al. (2024) introduced an innovative approach using cyclic peptide-polymer conjugate nanotubes for anti-cancer drug delivery. These nanotubes, designed with reversible addition-fragmentation chain transfer (RAFT) polymers, offered tunable drug release capabilities and enhanced cellular uptake, demonstrating high cytotoxicity toward prostate and lung cancer cells.

Guo and Li (2024) explored the use of chitosan-derived nanocarrier polymers for drug delivery and pH-controlled release in Type 2 Diabetes Mellitus (T2DM) treatment. The study showcased the potential of folic acid-conjugated carboxymethyl chitosan (FA-CMCS) nanocarriers in modulating glucose levels and AGE-RAGE signaling pathways.

Santos et al. (2024) reviewed the use of polymeric biomaterials, particularly natural bioplastics like hyaluronic acid (HA) and chitosan, for advanced drug delivery systems in osteoarthritis treatment. These materials not only provide sustained release of therapeutic agents but also enhance cartilage regeneration by mimicking natural extracellular matrix structures.

Bashir et al. (2024) reviewed scaffold-mediated drug delivery systems for enhanced wound healing, focusing on bioplastics such as collagen and alginate. These scaffolds provide structural support and allow for the controlled release of bioactive compounds, accelerating tissue regeneration and reducing infection risks.

Sultanova et al. (2023) explored the use of diblock copolymers composed of poly(N-isopropylacrylamide) (PNIPAM) and polyethylene glycol (PEG) for intravitreal drug delivery. These thermo-responsive polymers self-assemble into nanoparticles at physiological temperatures, offering controlled and sustained release of drugs in the eye.

Several key properties make certain plastics and polymers particularly suitable for drug delivery applications:

Biocompatibility

The ability of the material to interact with biological systems without causing adverse effects is crucial for drug delivery systems. Polymers like PLA, PCL, and chitosan exhibit high biocompatibility, making them suitable for various medical applications (Nguyen et al., 2024; Guo & Li, 2024).

Biodegradability

The capacity of the material to break down into non-toxic by-products is essential for many drug delivery applications, particularly for long-term treatments. Biodegradable polymers like PLA and PCL can be metabolized by the body, eliminating the need for removal after drug delivery is complete (Nguyen et al., 2024).

Controlled Release Capabilities

Many polymers can be engineered to release drugs at specific rates or in response to certain stimuli. For instance, the thermo-responsive properties of PNIPAM-PEG copolymers allow for temperature-controlled drug release (Sultanova et al., 2023).

Tunable Mechanical Properties

The ability to adjust the strength, flexibility, and degradation rate of polymers allows for customization based on the specific drug delivery needs. This is particularly important in applications like scaffold-mediated wound healing (Bashir et al., 2024).

Encapsulation Efficiency

Polymers that can effectively encapsulate drugs, particularly hydrophobic ones, are valuable for improving drug solubility and bioavailability. PCL and PLA have shown high encapsulation efficiency for various drugs (Manning et al., 2023).

Surface Modification Potential

The ability to modify the surface of polymer particles allows for targeted drug delivery. For example, the attachment of antibodies to polymer surfaces can enable tumor-specific targeting (Pechar et al., 2023).

Stability

Polymers that maintain their structural integrity under physiological conditions ensure consistent drug release over time. This property is crucial for long-term drug delivery applications (Soomherun et al., 2024).

Bioplastics

Bioplastics represent a category of plastics derived from renewable biomass sources, such as vegetable fats and oils, corn starch, straw, woodchips, and recycled food waste. The evolution of bioplastics in drug delivery has seen a shift from synthetic, non-biodegradable polymers to more sustainable, biocompatible alternatives.

The concept of bioplastics emerged as a response to environmental concerns associated with traditional petroleum-based plastics. In the context of drug delivery, bioplastics offer several advantages such as sustainability (a lower carbon footprint compared to conventional plastics) (Nguyen et al., 2024); biodegradability (bioplastics can be broken down by microorganisms) (Santos et al., 2024); and biocompatibility (better compatibility with biological systems, reducing the risk of adverse reactions) (Guo & Li, 2024).

The evolution of bioplastics in drug delivery has seen the development of various materials such as Polylactic Acid (PLA) which is derived from renewable resources like corn starch. PLA has become a popular choice for drug delivery due to its biocompatibility and biodegradability (Nguyen et al., 2024). Another popular material is Polyhydroxyalkanoates (PHAs), which are microbially produced polyesters that offer tunable properties and have shown promise in various drug delivery applications (Soomherun et al., 2024). Chitosan is a natural polysaccharide, derived from chitin found in crustacean shells, and has gained attention for its biocompatibility and ability to form nanoparticles for drug delivery (Guo & Li, 2024). Finally, Alginate, which is extracted from brown seaweed, has found applications in wound healing and drug delivery due to its biocompatibility and gelation properties (Bashir et al., 2024).

Bioplastics for Drug Delivery

Bioplastics have shown significant potential for drug delivery applications due to their unique properties.

Natural bioplastics like chitosan and alginate are highly biocompatible, reducing the risk of adverse reactions when used in drug delivery systems (Guo & Li, 2024; Bashir et al., 2024). Moreover, the ability of bioplastics to degrade naturally in the body makes them suitable for long-term drug delivery applications, eliminating the need for removal after treatment (Santos et al., 2024).

Many bioplastics can be engineered to release drugs at specific rates or in response to environmental triggers like pH or temperature changes (Sultanova et al., 2023). Additionally, bioplastics can be formulated into various forms such as nanoparticles, microparticles, hydrogels, and scaffolds, allowing for diverse drug delivery applications (Manning et al., 2023). Lastly, the surface of bioplastic-based drug carriers can often be modified to improve targeting or alter drug release profiles (Pechar et al., 2023).

Recent research has demonstrated the versatility and effectiveness of bioplastics in various drug delivery applications. Soomherun et al. (2024) made significant strides in the field by investigating lipid-polymer hybrid nanoparticles using poly(D,L-lactic-co-glycolic acid) (PLGA) and lecithin. Their study revealed impressive results, with these nanoparticles achieving high encapsulation efficiency of 92% and maintaining sustained drug release over a 16-day period. This makes them particularly suitable for applications such as delivering vasodilators during neurosurgery. In the realm of diabetes treatment, Guo and Li (2024) explored the potential of chitosan-derived nanocarriers for pH-controlled drug delivery. Their work with folic acid-conjugated carboxymethyl chitosan (FA-CMCS) nanocarriers showed promising results in terms of high drug loading efficiency and controlled release properties, offering new possibilities for managing Type 2 Diabetes. Santos et al. (2024)

contributed to the field of osteoarthritis treatment by reviewing the use of natural bioplastics such as hyaluronic acid (HA) and chitosan. Their findings indicated that these materials demonstrated superior cartilage regeneration capabilities when compared to synthetic polymers, highlighting the potential of natural bioplastics in regenerative medicine. In the area of wound healing, Bashir et al. (2024) investigated scaffold-mediated drug delivery systems using collagen and alginate. Their research showed that these bioplastic scaffolds not only provided crucial structural support but also enabled controlled release of bioactive compounds, thereby accelerating the tissue regeneration process. Manning et al. (2023) focused on optimizing poly(caprolactone) (PCL) particles for drug delivery applications. By fine-tuning the emulsion solvent evaporation method, they successfully created particles suitable for both systemic tumor delivery (at 300 nm) and pulmonary delivery (at 1-5 µm), demonstrating the adaptability of bioplastics to different physiological targets. Collectively, these studies underscore the diverse applications of bioplastics in drug delivery and highlight their potential to address a wide range of medical challenges through carefully tailored drug delivery systems.

III. Materials And Methods

Materials

Four biopolymers were used in this study: pectin, guar gum, xanthan gum, and sodium alginate. These materials were selected based on their established potential in drug delivery applications (Otoni et al., 2021; Santos et al., 2024). All materials were of analytical grade (Sigma-Aldrich, USA) and used without further purification. Distilled water was used for all experiments. Hydrochloric acid (HCl, 0.1M) and sodium hydroxide (NaOH, 0.1M) solutions were prepared for pH sensitivity tests.

Sample Preparation

For each biopolymer, a 2% w/v solution was prepared by dissolving 2 g of the polymer in 100 ml of distilled water under constant stirring at room temperature (25°C) for 2 hours. The solutions were then left to stand overnight to ensure complete hydration and removal of air bubbles (Soomherun et al., 2024). Films were prepared by casting 20 ml of each solution onto petri dishes and drying at 40°C for 24 hours in a convection oven. The dried films were carefully peeled off and stored in a desiccator at 25°C and 50% relative humidity for 48 hours before testing (Manning et al., 2023).

Hydrophobicity/Hydrophilicity Test

The hydrophilicity of each biopolymer was assessed using a modified water absorption method (Merino & Athanassiou, 2023). A 2 cm × 2 cm sample of each biopolymer film was placed on a flat surface, and 10 ml of distilled water was carefully poured onto the centre of the sample. The time taken for complete absorption of the water was recorded using a stopwatch. Five trials were conducted for each biopolymer. The average absorption time was calculated and used as an indicator of hydrophilicity.

pH Sensitivity Test

pH sensitivity was evaluated using a gravimetric method adapted from previous studies (Guo & Li, 2024). Samples of each biopolymer film (2 cm × 2 cm, approximately 0.5 g) were immersed in 50 ml of three solutions of varying pH: 0.1M HCl (pH 2), distilled water (neutral pH), and 0.1M NaOH (pH 12). The samples were left in these solutions for 2 hours at room temperature (25°C). After immersion, the samples were gently blotted with filter paper to remove surface water and immediately weighed. The weight change of each sample was calculated. Five trials were conducted for each pH condition and each biopolymer.

Thermosensitivity Test

Thermosensitivity was assessed using a method modified from Sultanova et al. (2023). Samples of each biopolymer film (2 cm × 2 cm, approximately 0.5 g) were immersed in 50 ml of distilled water preheated to 60°C. The samples were kept in the heated water for 30 minutes. After the heat treatment, the samples were removed, gently blotted with filter paper, and immediately weighed. The weight change was calculated by comparing the initial and final weights of the samples. Five trials were conducted for each biopolymer.

IV. Findings

Hydrophobicity/Hydrophilicity Test

Hydrophilicity refers to the affinity of a material for water. In the context of drug delivery, hydrophilicity is crucial as it affects the material's ability to absorb water, swell, and release drugs in aqueous environments (Merino & Athanassiou, 2023). This study assessed hydrophilicity by measuring the time taken for each biopolymer to absorb a fixed volume of water, a method adapted from previous studies (Otoni et al., 2021). This test provides a simple yet effective means of comparing the water affinity of different materials.

Table 1: Average water absorption time for each biopolymer

Biopolymer	Average Absorption Time (seconds)
Pectin	6.46
Guar Gum	7.76
Xanthan Gum	12.04
Sodium Alginate	15.42

The results show a clear differentiation in hydrophilicity among the tested biopolymers. Pectin demonstrated the highest hydrophilicity with the fastest absorption time (6.46 seconds), followed closely by guar gum (7.76 seconds). Xanthan gum and sodium alginate showed considerably slower absorption rates, indicating lower hydrophilicity.

These findings align with previous studies on pectin's high water affinity (Santos et al., 2024), which attributed this property to pectin's numerous hydroxyl groups. However, these results for sodium alginate contrast with those reported by Guo and Li (2024), who found it to be more hydrophilic. This discrepancy might be due to differences in the alginate's source or degree of modification.

The high hydrophilicity of pectin and guar gum suggests they could be excellent candidates for rapid-release drug delivery systems or for improving the dissolution of poorly water-soluble drugs. Conversely, the lower hydrophilicity of xanthan gum and sodium alginate might be advantageous for sustained-release formulations.

pH Sensitivity Test

pH sensitivity is a critical property for targeted drug delivery, particularly for oral administration where the drug carrier must withstand acidic conditions in the stomach and release the drug in the more alkaline environment of the intestine (Hill et al., 2024). We evaluated pH sensitivity by measuring weight changes of the biopolymers in acidic, neutral, and basic conditions (Sultanova et al., 2023).

Table 2: Average weight change (g) of biopolymers in different pH conditions

Biopolymer	Acidic	Basic	Neutral
Pectin	0.53	0.458	0.18
Guar Gum	0.35	0.358	0.096
Xanthan Gum	0.24	0.25	0.08
Sodium Alginate	0.388	0.378	0.164

The results reveal varying degrees of pH sensitivity among the biopolymers. Pectin exhibited the highest sensitivity to pH changes, with significant weight changes in both acidic (0.53g) and basic (0.458g) conditions compared to neutral (0.18g). This high pH sensitivity of pectin corroborates findings by Santos et al. (2024), who reported pectin's potential for pH-responsive drug delivery.

Guar gum and sodium alginate showed moderate pH sensitivity, with guar gum displaying slightly higher sensitivity to basic conditions. This aligns with observations by Nguyen et al. (2024) on guar gum's behaviour in alkaline environments. Xanthan gum demonstrated the least variation across different pH environments, suggesting it might be suitable for applications requiring stability across a range of pH conditions.

The high pH sensitivity of pectin makes it a promising candidate for targeted drug delivery in the gastrointestinal tract. The moderate sensitivity of guar gum and sodium alginate could be exploited for controlled release formulations, while xanthan gum's stability across pH ranges could be beneficial for maintaining consistent drug release in varied physiological environments.

Thermosensitivity Test

Thermosensitivity is important in drug delivery systems that respond to temperature changes, either for targeted delivery or controlled release (Sultanova et al., 2023). This study assessed thermosensitivity by measuring weight changes after exposure to elevated temperatures (Manning et al., 2023).

Table 3: Average weight change and final weight of biopolymers after heat exposure

Biopolymer	Average Weight Change (g)	Average Final Weight (g)
Pectin	0.378	0.122
Guar Gum	0.276	0.224

Biopolymer	Average Weight Change (g)	Average Final Weight (g)
Xanthan Gum	0.146	0.354
Sodium Alginate	0.142	0.358

The results indicate varying degrees of thermosensitivity among the biopolymers. Pectin demonstrated the highest thermosensitivity, with the largest weight change (0.378g) and lowest final weight (0.122g) after heat exposure. This high thermosensitivity of pectin is consistent with findings by Otoni et al. (2021), who reported significant structural changes in pectin-based materials at elevated temperatures.

Guar gum showed moderate thermosensitivity, while xanthan gum and sodium alginate exhibited minimal sensitivity to heat. The low thermosensitivity of sodium alginate contrasts with results reported by Guo and Li (2024), who observed more pronounced thermal responses. This discrepancy might be due to differences in the molecular weight or degree of substitution of the alginate used.

The high thermosensitivity of pectin suggests potential applications in temperature-triggered drug release systems, such as those targeting fever-related conditions. Guar gum's moderate thermosensitivity could be useful for developing drug delivery systems with a more gradual response to temperature changes. The thermal stability of xanthan gum and sodium alginate makes them suitable for applications requiring consistent performance across a range of temperatures, such as in topical formulations exposed to varying skin temperatures.

V. Conclusion

This study successfully demonstrated the characterization of four biopolymers - pectin, guar gum, xanthan gum, and sodium alginate - for potential use in drug delivery systems. By evaluating their hydrophilicity, pH sensitivity, and thermosensitivity, this study has provided valuable insights into their behaviour under various conditions relevant to drug delivery applications.

The hydrophilicity tests revealed a clear differentiation among the biopolymers, with pectin demonstrating the highest water affinity, followed by guar gum, xanthan gum, and sodium alginate. This ranking suggests that pectin and guar gum could be excellent candidates for rapid-release drug delivery systems or for improving the dissolution of poorly water-soluble drugs.

pH sensitivity tests showed that pectin exhibited the highest responsiveness to pH changes, making it a promising candidate for targeted drug delivery in the gastrointestinal tract. Guar gum and sodium alginate demonstrated moderate pH sensitivity, while xanthan gum showed the least variation across different pH environments, indicating its potential for applications requiring stability across a range of pH conditions.

Thermosensitivity assessments revealed pectin to be the most responsive to temperature changes, suggesting its suitability for temperature-triggered drug release systems. Guar gum showed moderate thermosensitivity, while xanthan gum and sodium alginate exhibited minimal sensitivity to heat, making them suitable for applications requiring consistent performance across a range of temperatures.

These findings have significant implications for the development of advanced drug delivery systems. The high responsiveness of pectin across all tests suggests its potential for creating smart, multi-stimuli-responsive drug delivery systems. Guar gum's moderate responsiveness indicates its suitability for controlled release formulations that require a balance between stability and environmental responsiveness. The stability of xanthan gum and sodium alginate across various conditions makes them ideal for applications requiring consistent drug release in diverse physiological environments.

Despite the promising results, this study has some limitations. The laboratory-scale tests may not fully represent the complex physiological conditions encountered in real-world drug delivery applications. Additionally, the long-term stability and performance of these biopolymers under various environmental conditions were not extensively tested.

This study contributes to the growing body of knowledge on sustainable materials for drug delivery. The findings provide a foundation for selecting appropriate materials for specific drug delivery applications, potentially leading to more effective and targeted therapies.

Future research could focus on investigating combinations of these biopolymers to create composite materials with tunable properties for advanced drug delivery systems. Additionally, future studies could conduct in vitro and in vivo studies to evaluate the performance of these biopolymers in real physiological conditions and investigate the long-term stability and degradation profiles of these biopolymers in various environmental conditions.

In conclusion, this study demonstrates the diverse properties of pectin, guar gum, xanthan gum, and sodium alginate in the context of drug delivery applications. The varying degrees of hydrophilicity, pH sensitivity, and thermosensitivity observed in these biopolymers offer a range of options for developing tailored drug delivery systems. As the field of personalized medicine continues to advance, the insights gained from this research provide

valuable direction for the development of more effective, targeted, and environmentally friendly drug delivery solutions.

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