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REVIEW ARTICLE

Unveiling the Potential of Cinnamon-Induced Hydrogels for Advanced Biomedical Applications: A Comprehensive Review

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ABSTRACT

Abstract: Cinnamon, a popular spice known for its aromatic properties and medicinal benefits, has recently gained attention in the field of biomedical research for its potential to develop advanced hydrogels. Hydrogels are three-dimensional polymeric networks that can absorb and retain significant amounts of water, making them highly suitable for various biomedical applications. This comprehensive analysis delves into the potential of cinnamon-induced hydrogels, exploring their synthesis, characterization, biocompatibility, and safety evaluation. Furthermore, the article explores the diverse range of advanced biomedical applications that cinnamon-based hydrogels can offer, including wound healing, tissue regeneration, drug delivery systems, and biomedical imaging. Additionally, the challenges and future perspectives of developing cinnamon-induced hydrogels for biomedical applications are discussed, shedding light on the optimization and commercialization potential of this innovative biomaterial.

Keywords Hydrogels, Cinnamon, Biomedical application, Synthesis, Characterization

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INTRODUCTION

Background and Overview

Cinnamon, that delightful spice we sprinkle on our oatmeal and add to our baked goods, is not just a flavour enhancer [1]. It turns out that cinnamon has some pretty amazing properties that make it a promising candidate for advanced biomedical applications[2]. In recent years, researchers have been exploring the use of cinnamon-induced hydrogels as a novel material for various biomedical purposes[3]. These hydrogels are gel-like structures that can absorb and retain large amounts of water, making them ideal for applications such as drug

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delivery and wound healing [4]. In this article, we will delve into the world of cinnamon-induced hydrogels and explore their potential in the field of biomedicine.

Significance of Cinnamon in Biomedical Applications

Cinnamon has long been recognized for its medicinal properties, and its use in traditional medicine can be traced back centuries [5]. It is rich in bioactive compounds, including cinnamaldehyde, responsible for its characteristic aroma and flavor[6]. These compounds have shown antibacterial, antifungal, antioxidant, and anti-inflammatory properties, among others [7]. In biomedical applications, cinnamon offers a natural and sustainable source for developing hydrogels that can mimic certain properties of human tissues [8]. This opens up a world of possibilities for the use of cinnamon-induced hydrogels in wound healing, tissue regeneration, drug delivery, and even biomedical imaging and diagnostics [3].

SYNTHESIS AND CHARACTERIZATION OF CINNAMON-BASED HYDROGELS

Preparation Methods of Cinnamon-Induced Hydrogels

There are several methods used to prepare these hydrogels, including covalent crosslinking, physical gelation, and enzymatic reactions [9]. These methods involve the combination of cinnamon extracts or cinnamon-derived compounds with other polymers or crosslinkers to form a gel-like structure [10]. Each method has its advantages and limitations, and researchers are constantly exploring new approaches to optimize the synthesis process for specific applications as explained below [10]:

COVALENT CROSSLINKING:

- **Definition:** Covalent crosslinking involves the formation of strong chemical bonds between different polymer chains or between polymers and other crosslinking agents.

- **Application:** In the context of cinnamon, covalent crosslinking could involve the use of cinnamon extracts or compounds derived from cinnamon, such as cinnamaldehyde or cinnamic acid, as components in the formation of covalent bonds within a polymer matrix.

PHYSICAL GELATION:

- **Definition:** Physical gelation relies on non-covalent interactions, such as hydrogen bonding or van der Waals forces, to form a gel-like structure.

• **Application:** Cinnamon extracts or compounds may participate in physical gelation by interacting with other polymers or crosslinkers through non-covalent forces. This method allows the formation of reversible gels, providing flexibility in applications like drug delivery or tissue engineering.

ENZYMATIC REACTIONS:

• **Definition:** Enzymatic reactions involve the use of enzymes to catalyze specific chemical reactions. In this context, enzymes can facilitate the crosslinking of polymers and compounds from cinnamon.

• **Application:** Cinnamon-derived compounds may undergo enzymatic reactions with other polymers or crosslinkers, resulting in the formation of a gel structure. This method offers specificity and control over the gelation process.

In all these methods, the combination of cinnamon extracts or compounds with other polymers or crosslinkers is pivotal. The resulting gel-like structures can have diverse applications, ranging from drug delivery systems to tissue engineering scaffolds. These methods allow researchers to harness the unique properties of cinnamon in creating biomaterials with desirable characteristics, such as biocompatibility, controlled release, and sustainability. Additionally, the choice of the gelation method provides versatility in tailoring the properties of the final biomaterial to suit specific biomedical applications.

Some other studies have suggested some other methods to synthesis cinnamon-Induced hydrogels, including[9]:

• Free radical polymerization: This method involves the polymerization of cinnamon-derived monomers in the presence of a free radical initiator.

• Ionic crosslinking: This method involves the crosslinking of cinnamon-derived polymers with ionic crosslinkers, such as calcium ions or alginate.

• Schiff base formation: This method involves the crosslinking of cinnamon-derived polymers with aldehyde-containing crosslinkers, such as glutaraldehyde or benzaldehyde.

Characterization of cinnamon-based hydrogels

Once synthesized, cinnamon-based hydrogels can be characterized using a variety of techniques, including [11]:

2.2.1 Structural and Physicochemical Analysis of Cinnamon-Based Hydrogels

Once the hydrogels are synthesized, it is crucial to analyze their structure and physicochemical properties[11]. This involves techniques such as swelling studies are used to measure the water absorption capacity of hydrogels. In addition, morphological analysis is used to study the structure and morphology of hydrogels using techniques such as scanning electron microscopy (SEM) and transmission electron microscopy (TEM) [11].

Fourier-transform infrared spectroscopy (FTIR), and rheological analysis. These analyses provide valuable insights into the chemical composition, and mechanical properties of the hydrogels [12]. Understanding the structure and physicochemical characteristics of cinnamon-based hydrogels allows researchers to fine-tune their properties for specific biomedical applications[13].

Biocompatibility and Safety Evaluation of Cinnamon-Induced Hydrogels

Cytotoxicity and Cell Viability Studies It is crucial to assess the biocompatibility and safety of cinnamon-induced hydrogels before their utilization in biomedical applications[14]. Cell viability studies are conducted to assess the cytotoxicity of the hydrogels and their impact on cell growth and proliferation. An example of these methods are:

- MTT Assay measures cell viability through mitochondrial enzyme activity.
- LDH Release Assay indicates cell membrane damage.
- Live/Dead Staining visually distinguishes live and dead cells.

Researchers expose different cell types to hydrogels and monitor their viability over time[15]. These studies provide valuable information on the compatibility of cinnamon-based hydrogels with living cells, ensuring their safety and minimizing potential side effects[16].

Immunological Response and Inflammation Assessment Delving beyond cytotoxicity assessment, researchers are delving into the intricate realms of immunological responses and possible inflammation incited by the use of cinnamon-induced hydrogels. [3]. This involves studying the activation of immune cells and assessing the release of inflammatory mediators which involves the following techniques:

Activation of Immune Cells and Assessment of Inflammatory Mediators:

FLOW CYTOMETRY:

- **Activation:** Antibodies target cell surface markers.
- **Assessment:** Intracellular staining quantifies released cytokines.

ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA):

- **Activation:** Stimulated cells release cytokines.
- **Assessment:** ELISA kits quantify specific cytokines.

REAL-TIME POLYMERASE CHAIN REACTION (RT-PCR):

- **Activation:** Cells are stimulated, and RNA is extracted.
- **Assessment:** RT-PCR quantifies mRNA expression of inflammatory genes.

IMMUNOFLUORESCENCE MICROSCOPY:

- **Activation:** Cells are fixed and stained for activation markers.
- **Assessment:** Microscopy visualizes cellular changes and activation markers.

LUMINEX ASSAY:

- **Activation:** Stimulated cells release cytokines.
- **Assessment:** Luminex quantifies multiple cytokines simultaneously.

WESTERN BLOTTING:

- **Activation:** Cells are stimulated, and proteins are extracted.
- **Assessment:** Detects and quantifies protein expression, including inflammatory markers.

BIOPLEX ASSAY:

- **Activation:** Immune cells are activated, and supernatant is collected.
- **Assessment:** Measures multiple cytokines simultaneously.

ELECTROCHEMILUMINESCENCE (ECL ASSAY):

- **Activation:** Stimulated cells release cytokines.
- **Assessment:** Detects and quantifies cytokines with high sensitivity.

PHOSPHO-SPECIFIC FLOW CYTOMETRY:

- **Activation:** Measures phosphorylation events.
- **Assessment:** Phospho-specific antibodies target signalling molecules.

MULTIPARAMETER FLOW CYTOMETRY:

- **Activation:** Uses multiple surface markers and intracellular stains.
- **Assessment:** Provides detailed information on immune cell subsets and activation status.

These techniques offer insights into immune cell behavior, activation, and the release of inflammatory mediators, aiding in understanding immune responses and developing therapeutic strategies.

[17]. By understanding the immune response triggered by the hydrogels, researchers can ensure that they do not induce unwanted immune reactions and are compatible with the body's natural defence mechanisms. [18].The mechanism that triggers the immune response using hydrogels typically involves the interaction between the hydrogel material and the immune system. Hydrogels can be designed to release specific molecules, such as antigens or immunomodulatory agents, which then interact with immune cells. This interaction may lead to the activation of immune cells, the release of inflammatory signals, and the initiation of an immune response. Additionally, the physical properties of hydrogels, such as their structure and biocompatibility, can influence how immune cells respond to the material. The overall goal is often to design hydrogels that can modulate the immune response for applications like drug delivery, vaccines, or tissue engineering.

ADVANCED BIOMEDICAL APPLICATIONS OF CINNAMON-BASED HYDROGELS

Wound Healing and Tissue Regeneration

One of the most exciting applications of cinnamon-induced hydrogels is in the field of wound healing and tissue regeneration[3]. The unique properties of these hydrogels, such as their ability to absorb and retain moisture, promote cell migration, and provide a favourable environment for tissue growth, make them excellent candidates for accelerating the healing process[19]. Researchers are exploring the use of cinnamon-based hydrogels for chronic wound management, tissue engineering, and regenerative medicine, bringing us one step closer to more effective treatments for challenging wounds and tissue defects[13,15,16].

Drug Delivery Systems

Cinnamon-induced hydrogels also show great potential as drug delivery systems. The porous structure of these hydrogels allows for the encapsulation and controlled release of therapeutic molecules, such as drugs or growth factors[20]. By incorporating these molecules into the hydrogels, researchers can achieve targeted and sustained delivery, enhancing the efficacy and reducing the side effects of various medications [21]. This opens up new possibilities for personalized medicine and improved treatment strategies for a wide range of diseases [21].

Biomedical Imaging and Diagnostics

In addition to wound healing and drug delivery, cinnamon-based hydrogels can be utilized in biomedical imaging and diagnostics[22]. By incorporating imaging agents or contrast agents into the hydrogel matrix, researchers can develop innovative materials for imaging modalities such as magnetic resonance imaging (MRI) or computed tomography (CT)[23] . These hydrogels can also serve as diagnostic platforms, allowing for the detection and monitoring of specific biomarkers or analytes in patient samples[23] . The versatility of cinnamon-induced hydrogels makes them a valuable tool in advancing medical imaging and diagnostics [23] .In conclusion, cinnamon-induced hydrogels hold tremendous potential for a wide range of advanced biomedical applications. From wound healing and tissue regeneration to drug delivery systems and biomedical imaging, these hydrogels offer a natural and versatile platform for innovative solutions in healthcare. As researchers continue to unravel the mysteries of cinnamon and explore its capabilities, it is possible to look forward to exciting developments that may revolutionize the field of biomedicine[23] .

CINNAMON-INDUCED HYDROGELS FOR WOUND HEALING AND TISSUE REGENERATION

Cinnamon has long been known for its aromatic and flavorful properties in the culinary world, but recent research has unveiled its hidden potential in the field of biomedical applications [24]. Specifically, cinnamon-induced hydrogels have shown promising results in wound healing and tissue regeneration.

Mechanisms of Action in Wound Healing

When applied to wounds, cinnamon-induced hydrogels work their magic by facilitating the natural healing process[24]. The active compounds in cinnamon, such as cinnamaldehyde and eugenol, have antimicrobial properties that can help prevent infections in the wound site[25]. Additionally, cinnamon-induced hydrogels have been found to stimulate the production of collagen and promote angiogenesis, which is crucial for wound closure and tissue regeneration[25].

Enhanced Tissue Regeneration with Cinnamon-Based Hydrogels

Beyond wound healing, cinnamon-induced hydrogels have shown great potential in tissue regeneration[25]. These hydrogels provide a supportive environment for cells to grow and differentiate, thus aiding in the regeneration of damaged tissues [26]. Furthermore, cinnamon-induced hydrogels have been found to enhance the recruitment of stem cells to the site of injury, boosting the regenerative potential of the body [26–28]

CINNAMON-INDUCED HYDROGELS FOR BIOMEDICAL IMAGING AND DIAGNOSTICS

The applications of cinnamon-induced hydrogels extend beyond wound healing and drug delivery. These hydrogels have also shown promise in the field of biomedical imaging and diagnostics[29].

Contrast Agents and Imaging Applications

By incorporating contrast agents into cinnamon-induced hydrogels, they can be used as imaging agents for various diagnostic techniques[30]. The hydrogel matrix provides stability and prolonged retention of the contrast agents, improving imaging quality and allowing for better visualization of specific tissues or organs[30].

Biosensors and Diagnostic Tools

Cinnamon-induced hydrogels can be utilized as a platform for biosensors and diagnostic tools[31]. These hydrogels can be engineered to respond to specific biological markers or signals, enabling the detection of diseases or abnormalities[31]. Additionally, the biocompatibility of cinnamon-induced hydrogels makes them suitable for use in various diagnostic applications, such as point-of-care testing[31].

CHALLENGES AND FUTURE PERSPECTIVES IN THE DEVELOPMENT OF CINNAMON-INDUCED HYDROGELS

While the potential of cinnamon-induced hydrogels is exciting, there are still challenges and considerations to be addressed for their successful development and widespread use.

Optimization of Cinnamon-Based Hydrogel Formulations

Further research is needed to optimize the formulation of cinnamon-induced hydrogels, including factors such as the concentration of cinnamon extract and the choice of crosslinking agents [30]. Fine-tuning these parameters can enhance the performance and stability of the hydrogels, ensuring their effectiveness in various biomedical applications[31].

Regulatory Considerations and Commercialization Potential

As with any biomedical product, regulatory considerations are essential for the development and commercialization of cinnamon-induced hydrogels. Safety and efficacy evaluations, along with adherence to regulatory guidelines, must be rigorously addressed to ensure the acceptance and marketability of these innovative hydrogels[32].

CONCLUSIONS AND PROSPECTS

Conclusions

Cinnamon-induced hydrogels have emerged as promising candidates for advanced biomedical applications. From wound healing and tissue regeneration to drug delivery systems and biomedical imaging, these hydrogels offer exciting possibilities for improving healthcare outcomes. While there are challenges ahead, with further research and development, cinnamon-induced hydrogels hold tremendous potential to revolutionize the field of biomedicine. In conclusion, the study of cinnamon-induced hydrogels has unveiled their immense potential for advanced biomedical applications. The unique properties of these hydrogels, combined with the beneficial properties of cinnamon, have opened up new avenues in wound healing, tissue regeneration, drug delivery, and biomedical imaging. However, further research is needed to optimize their formulation and address regulatory considerations for their widespread use. With continued exploration and advancements, cinnamon-induced hydrogels could revolutionize the field of biomedicine, offering innovative solutions for improved patient outcomes and enhanced healthcare practices.

Future prospects of cinnamon-induced hydrogels in the biomedical field

The future prospects of cinnamon-induced hydrogels are promising. Further optimization of their formulation, understanding their mechanism of action, and addressing regulatory considerations can lead to their widespread use in various biomedical applications. These hydrogels have the potential to revolutionize healthcare practices, offering innovative solutions for wound healing, drug delivery, and diagnostic imaging.

DECLARATIONS

1. **Authors contribution**

Contributor Role	Degree of Contribution		
	Lead	Equal	Supporting
Conceptualization	KZ	RW	EY
Data curation	KZ	RW	EY
Formal analysis	KZ	EY	RW
Funding acquisition	EY	AEA	RW
Investigation	KZ	EY	AEA
Methodology	RW	KZ	EY
Project administration	EY	KZ	RW
Resources	KZ	RW	EY
Software	KZ	AEA	RW
Supervision	EY	KZ	AEA
Validation	EY	KZ	RW
Visualization	KZ	EY	RW
Writing-original draft	KZ	RW	EY
Writing-review & editing	EY	KZ	AEA

2. Conflict of interest

- There is no conflict of interest in this manuscript.

3. Ethical approvals

3. Ethical approvals (The research study has obtained ethical approvals from both Al-Nahrain University and University of Baghdad.).

4. Funding resources

- Al-Nahrain University and University of Baghdad

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