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Smart biomaterial composites for controlled drug release: Mechanisms and applications

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A B S T R A C T

Smart biomaterial composites signify an important progress for biomedical engineering, particularly in the area of measuring drug release. These innovative materials are engineered to respond to specific stimuli from their environment, enabling precise and targeted delivery of therapeutic compounds. The integration of smart biomaterials into medication systems is key to enhancing treatment efficacy and safety, as they can diminish side effects and improve patient adherence by maintaining drug levels within the therapeutic window. The aim of this article is to explore the mechanisms and applications of smart biomaterial composites in controlled drug release, highlighting their potential to revolutionize therapeutic strategies in biomedical engineering.

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1. Introduction

Smart biomaterial composites combine natural and synthetic materials to create multifunctional systems that can interact dynamically with biological environments [1]. These composites can be tailored to continuing various properties, such as biocompatibility, biodegradability, and stimuli-responsiveness, which are essential for effective drug delivery applications [2]. The design of these materials often involves incorporating stimuli-sensitive moieties that activate drug release when exposed to internal or external signals, such as pH changes, temperature fluctuations, or electromagnetic fields [3]. There has been significant progress in the development of sophisticated systems capable of achieving controlled release profiles that enrich therapeutic consequences while diminishing the frequency of administration [4]. In addition, its' reputation in skillful drug release cannot be excessive [5]. The traditional methods of delivering drugs suffer from limitations including inconsistent publication rates and systemic side effects [6]. In contrast, smart biomaterials allow for programmable and on-demand drug release mechanisms customized to meet the needs of specific therapeutics [7]. This capability is particularly beneficial in treating chronic conditions where maintaining stable drug levels is critical for efficacy [8]. Understanding market trends is essential for anticipating future developments and investments in this field.

Using Google Scholar articles, Fig. 1 illustrates the advancements in smart biomaterial composites for controlled drug delivery. Additionally, we estimated enhancements until 2050. As these materials respond to specific stimuli like pH, temperature, or light, they can be used to enhance therapeutic efficacy and minimize side effects [9, 10]. In the last few decades, smart biomaterials have evolved from silicone rubber-based systems to polymers that can adapt to a variety of environmental changes [9, 11]. As an example, pH-sensitive materials can release drugs in acidic environments typical of tumors, improving cancer treatment outcomes by limiting systemic toxicity [9].

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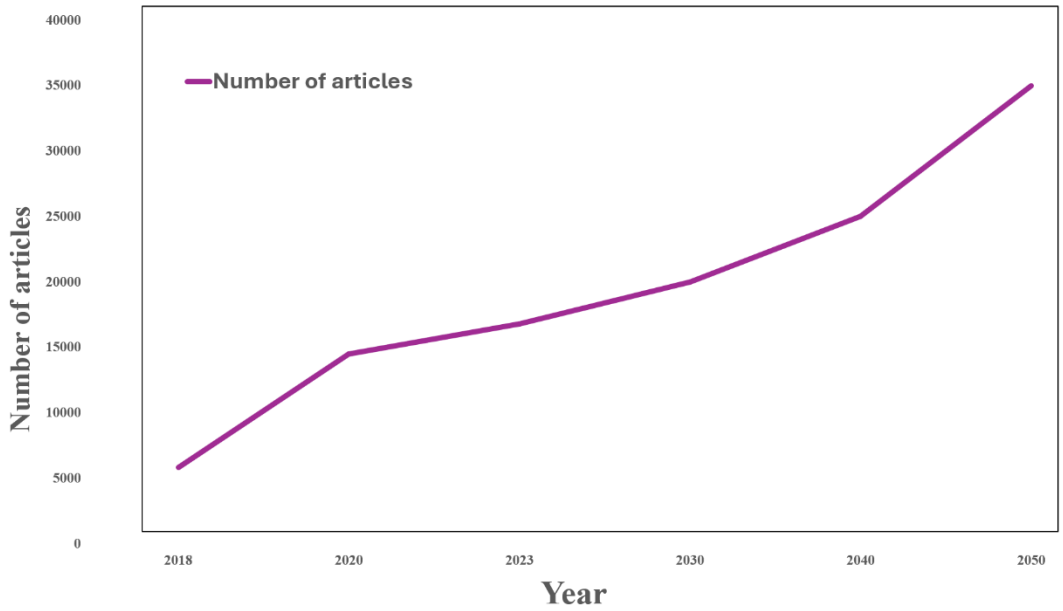


Fig. 1. Tracks the number of articles on biomaterial composites used for controlled drug release over recent years and forecasting up to 2050.

It is expected that as research advances in this field, the potential applications will expand into other areas such as regenerative medicine and personalized healthcare. Customizable smart biomaterials provide precise control over drug-release kinetics, maximizing bioavailability and reducing side effects [12]. A number of stimuli-responsive mechanisms will be integrated with advanced technologies like nanotechnology and 3D printing in the future[13]. The integration of these therapies will likely result in more effective therapies tailored to the needs of individual patients. Moreover, these materials may be engineered to target particular tissues or cells, further improving treatment precision and minimizing off-target effects [10]. This article aims to explore the mechanisms behind smart biomaterial composites used for controlled drug release, discuss their types, examine their characterization techniques, provide insights into future perspectives on these technologies, and highlight applications in cancer therapy and chronic disease management.

2. Types of Smart Biomaterial Composites

Smart biomaterial composites can be categorized based on their responsiveness to different stimuli [13]. PH-Sensitive composites materials release drugs in response to changes in pH levels, making them particularly useful for targeting body parts where pH varies, for instance tumors or inflamed tissues. The mechanism often involves the use of polymers that swell or degrade at certain pH thresholds, facilitating the publication of encapsulated drugs [14]. Also, Temperature-Sensitive Composites respond to temperature fluctuations, which can be utilized for precise drug release in various therapeutic applications [15]. Thermoresponsive materials can undergo phase transitions at specific temperatures, allowing for the release of drugs when they reach the target site or when subjected to external heat sources [16]. Moreover, Light-responsive biomaterials apply light as a trigger for drug release [17]. These materials can change their properties upon exposure to specific wavelengths of light, enabling precise control over when and where drugs are unconstrained [18]. According to Fig. 2, the four levels of smartness for biomaterials are inert, active, responsive, and autonomous. The classification distinguishes biomaterials according to their degree of interaction with the (bio)environment and, specifically, with biological/cellular processes [19].

3. Mechanisms of Controlled Release

Measured release mechanisms are fundamental to pharmaceutical delivery systems, allowing for the sustained administration of medicines [20]. The primary mechanisms include diffusion, degradation, and swelling, each playing a crucial role in determining how drugs are unconfined from their carriers [21]. Also, Fig. 3 clearly and concisely convey the key information about the mechanisms of drug release.

3.1 Diffusion

Diffusion is one of the most widely studied tools in controlled drug release systems. It involves the movement of drug molecules from an area of higher concentration within the delivery system to an area of lower concentration in the surrounding environment [22]. This manner can occur through various types of systems like Monolithic Systems which the drug is uniformly dispersed within a polymer matrix [23]. The release rate is meticulous by the diffusion of drug molecules through the polymer network, which can be designed to achieve specific release profiles [24]. Further, Reservoir Systems which consist of a core containing the drug surrounded by a rate-controlling polymeric membrane [25]. The drug is out by diffusion through this membrane, which can be engineered to provide zero-order kinetics, maintaining a constant publication rate over time [26]. Overall, Diffusion-controlled release is advantageous for delivering drugs at a steady rate, which helps maintain therapeutic levels in the bloodstream or target tissues [27].

3.2 Degradation

Degradation-controlled release mechanisms rely on the breakdown of the polymeric carrier itself to relief the encapsulated drug. This can occur through [28]. Water molecules penetrate the

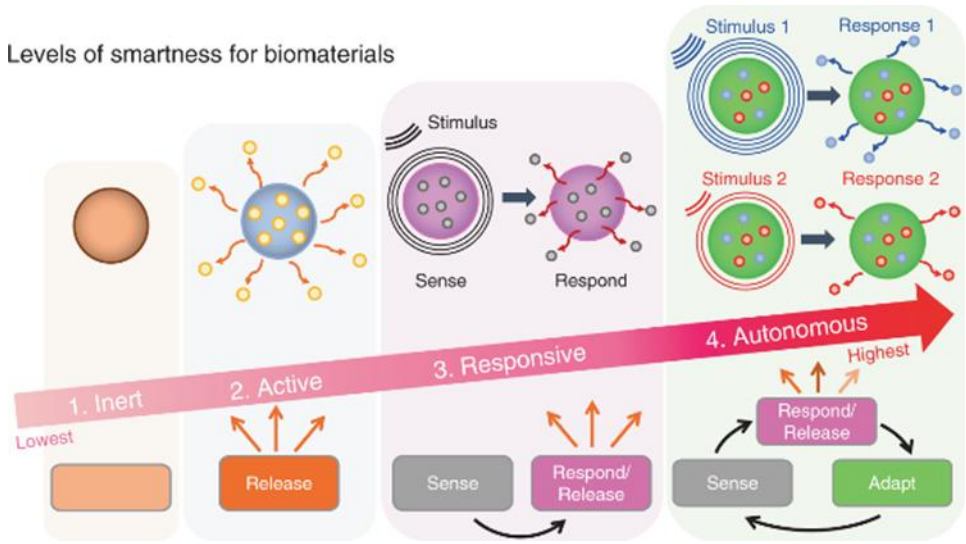


Fig. 2. There are four increasing levels of smartness for biomaterials: inert, active, responsive, and autonomous. There is no toxic reaction in or to the body when inert biomaterials are used. Inert biomaterials offer "merely" biocompatibility. Biomaterials that release therapeutics in a one-way, uncontrolled manner are active biomaterials. It is possible to release therapeutics from responsive biomaterials by sensing signals in the environment or biological processes. To continue providing additional, advanced, and/or alternative therapeutics, autonomous biomaterials sense a signal, release a specific payload, and adapt their properties to changing conditions [19].

polymer matrix, which lead to chemical reactions that break down the polymer chains and facilitate drug release [27]. This method is commonly used with biodegradable polymers that disintegrate into non-toxic byproducts that can be easily eliminated from the body [29]. Besides, Some systems are designed to respond to specific enzymes present in target tissues [30]. The cleavage of drug-polymer linkages by these enzymes allows for controlled release at desired sites, enhancing targeting and decreasing systemic side effects [31]. So, degradation apparatuses provide a natural way to achieve sustained drug release without requiring surgical removal of the delivery system after treatment [32].

3.3 Swelling

Swelling-controlled release methods involve changes in the physical dimensions of the polymeric carrier in response to environmental conditions, such as hydration or temperature changes. When exposed to aqueous environments Hydrophilic Polymers absorb water and swell, leading to an increase in pore size and facilitating drug diffusion out of the matrix [33]. This swelling can be finely tuned to control the rate at which drugs are unconfined [27]. While Temperature-Sensitive Polymers exhibit phase transitions at specific temperatures (e.g., lower critical solution temperature), causing them to swell or shrink dramatically. Such behavior can be exploited for on-demand drug release triggered by body temperature or external heat sources [34]. Swelling mechanisms allow for dynamic control over drug release rates, making them suitable for applications where precise timing is critical [27].

4. Characterization of Smart Biomaterial Composites

Characterization of smart biomaterial composites is critical for understanding their performance and functionality in applications such as drug delivery, tissue engineering, and regenerative medicine. This characterization encompasses a variety of techniques that assess physical, chemical, mechanical, and biological properties [35]. Among these, the evaluation of release kinetics and modeling is particularly important as it provides insights into how effectively these materials can deliver therapeutic agents over time [36].

4.1 Release Kinetics

Release kinetics refers to the study of the rate at which a drug is unconstrained from its carrier system. This understanding of kinetics is essential to designing drug delivery systems that maintain therapeutic levels of medication in the body [21]. The release kinetics of smart biomaterial composites can be influenced by several factors. The composition and structure of the biomaterial significantly affect drug release rates [37]. For instance, hydrophilic polymers may facilitate faster drug diffusion compared to hydrophobic materials [38]. Additionally, the solubility and molecular weight of the drug also play a crucial role. Highly soluble drugs tend to be discharged more quickly than those with lower solubility [39]. Furthermore, factors such as pH, temperature, and ionic strength can alter the statement profile. For example, pH-sensitive materials may emancipate their payload more rapidly in acidic environments, such as those found in tumors [40]. Also, several mathematical models are used to describe the release kinetics of drugs from biomaterial composites. Zero-Order Kinetics model describes a constant release rate over time, independent of the concentration of the drug remaining in the system [26]. It is often ideal for sustained-release formulations. Meanwhile, First-Order Kinetics model, the publication rate is proportional to the concentration of the drug remaining in the system. This behavior is common in systems where diffusion plays a significant role [41]. Besides that, Higuchi Model is specifically used for matrix systems where drug release occurs primarily through diffusion. It provides a way to relate the amount of drug released to time based on Fick's laws of diffusion [42]. Likewise, Peppas model accounts for both diffusion and swelling mechanisms and is often applied to polymeric systems that conserving complex proclamation behaviors [43].

4.2 Modeling Techniques

Modeling techniques are essential for predicting drug release profiles and optimizing biomaterial designs. These models can be developed using various approaches. First of all, Empirical Models

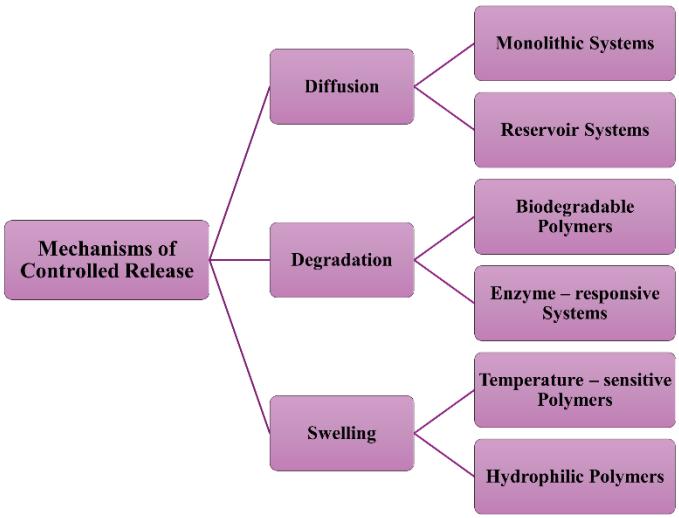


Fig. 3. Shows the mechanisms of controlled release**.**

are based on experimental data and are used to fit observed statement profiles. They provide a straightforward method for characterizing release kinetics without delving deeply into underlying devices. More, Mechanistic models are based on theoretical principles governing transport phenomena, such as diffusion and degradation processes [44]. They offer a more comprehensive understanding of how different factors influence drug release. Meanwhile, advanced computational techniques, including finite element analysis (FEA) and computational fluid dynamics (CFD), can simulate drug release from complex geometries and conditions, providing valuable insights into material behavior under various scenarios [45].

4.3 Importance of Release Kinetics and Modeling

The characterization of release kinetics and modeling is vital for Therapeutic Efficacy, Material Design, Regulatory Compliance. First, understanding how drugs are out from biomaterials helps optimize dosing regimens to achieve desired therapeutic products while minimizing side effects [46]. Furthermore, insights gained from kinetic studies inform the design of new biomaterials with tailored properties for specific applications, enhancing their effectiveness in clinical settings. Also, detailed knowledge of drug statement procedures is often required for regulatory approval processes, ensuring that new biomaterials meet safety and efficacy standards [47, 48].

5. Applications in Medicine

Smart biomaterial composites are increasingly recognized for their potential in various medical applications, particularly in cancer therapy and chronic disease management. These materials can be engineered to respond to specific physiological stimuli, allowing for controlled drug release and targeted treatment strategies that boost effectiveness while minimizing side effects [49].

5.1 Cancer Therapy

A growing number of cancer therapies are utilizing smart biomaterials to revolutionize treatment methods. Ghosh et al [49] reported that in cancer therapy, smart biomaterials present innovative solutions to improve the delivery of chemotherapeutic agents, addressing challenges such as systemic toxicity and inadequate targeting of tumor cells. For example, pH-sensitive hydrogels can release drugs specifically at tumor sites, exploiting the acidic microenvironment typical of tumors to activate drug release precisely where needed. This targeted approach can significantly reduce side effects associated with conventional chemotherapy [50]. Moreover, utilizing various stimuli such as temperature or light, smart biomaterials can provide organized release profiles that maintain therapeutic drug levels over extended periods. For example, thermosensitive hydrogels can transition from a sol to a gel state in response to body temperature changes, allowing for sustained drug release at the tumor site [51]. Likewise, Smart biomaterials can incorporate multiple therapeutic agents within a single system. This multifunctionality allows for synergistic effects, enhancing the overall efficacy of treatment regimens [52]. For instance, nanoparticles embedded in hydrogels can deliver both chemotherapy and immunotherapy agents simultaneously, transforming the immunosuppressive tumor environment into one that supports immune responses against cancer cells [53].

5.2 Chronic Disease Management

Chronic diseases such as diabetes, arthritis, and cardiovascular conditions require long-term management strategies that can benefit from smart biomaterial technologies [50]. In chronic disease management, maintaining consistent drug levels is crucial for effective treatment. Smart biomaterials can be engineered to relief medications gradually over time, tumbling the need for frequent dosing. For example, injectable hydrogels loaded with anti-inflammatory drugs have shown promise in managing conditions like rheumatoid arthritis by providing localized and sustained relief from symptoms [50]. However, some smart biomaterials are designed to respond to specific biomarkers associated with chronic diseases. For instance, glucose-responsive hydrogels can release insulin in response to elevated blood sugar levels in diabetic patients. This on-demand release mechanism helps maintain optimal glucose control while minimizing the risk of hypoglycemia [51]. Also, Wound Healing and Tissue Regeneration: Chronic conditions often lead to impaired healing methods. Smart biomaterials that mimic the extracellular matrix (ECM) can promote tissue regeneration by providing a supportive environment for cell growth and differentiation. Hydrogels with embedded growth factors or antibacterial agents are being developed for superior wound healing in diabetic patients [49].

6. Conclusion and Future Perspectives

The advancements in smart biomaterial composites signify a transformative step in drug delivery systems. As research continues to evolve, the integration of sophisticated stimuli-responsive mechanisms will likely lead to more effective therapies that are patient centric and adaptable to changing physiological conditions.

This strategic placement not only reinforces your discussion on future perspectives but also provides empirical data that supports your assertions about growth trends in the field of smart biomaterials. Future developments should focus on the creation of biomaterials that respond to multiple stimuli simultaneously could heightened the precision of drug delivery. By designing systems that can adapt to various internal and external triggers, researchers can develop more robust therapies capable of addressing complex medical conditions. Likewise, as the field progresses toward clinical applications, establishing standardized manufacturing processes and comprehensive toxicity assessments will be crucial. This will facilitate the translation of smart biomaterial technologies from the laboratory to clinical settings, ensuring safety and efficacy. In addition, the future of smart biomaterials lies in their potential for personalized medicine. By tailoring drug release profiles based on individual patient characteristics such as genetic makeup or specific disease states therapies can be optimized for maximum effectiveness. Moreover, integration with Advanced Technologies: Combining smart biomaterials with emerging technologies like nanotechnology, 3D printing, and artificial intelligence could revolutionize drug delivery systems. These integrations may lead to innovative solutions to complex health challenges through precise drug release control and improved patient compliance. Thorough, smart biomaterial composites hold great promise as controlled drug release systems. Continued research and development will not only improve our understanding of these materials but also pave the way for novel therapeutic strategies that improve patient results across a spectrum of medical conditions. As we advance into this new era of medicine, the potential for smart biomaterials to transform healthcare remains significant.

Authors' contribution

Amaneh Bakhtiari: Investigation, Writing—Original Draft Preparation, Writing—Review and Editing, **Lili Arabuli:** Conceptualization, Writing—Original Draft Preparation, Writing—Review and Editing, **Farnaz Sadeghi:** Writing—Original Draft Preparation, Writing—Review and Editing, **Neda Tamimi:** Writing—Original Draft Preparation, Writing—Review and Editing, **Jalaladdin Hosseinzadeh:** Writing—Original Draft Preparation, Writing—Review and Editing. **Azadeh Jafari Rad:** Writing—Original Draft Preparation, Writing—Review and Editing. **Omid Hamlehdari Najafabadi:** Writing—Original Draft Preparation, Writing—Review and Editing.

Declaration of competing interest

There are no known competing financial interests or personal relationships that could have influenced the authors' work.

Data availability

The article describes no data used in the research.

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