Advances in Research on Cellulose-based Drug Carriers

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Abstract: Traditional drug delivery methods are prone to large fluctuations in drug concentration and require multiple frequent doses. As a green material with excellent properties, cellulose has been widely used as a drug carrier for the development and preparation of drug controlled-release system. Based on the mechanisms of slow drug release, such as dissolution-diffusion release, degradation release, and nanochannel-controlled release, the preparation methods of cellulose-based drug carriers are introduced in this paper. The applications of cellulose-based drug carriers in the fields of antitumor therapy, antibacterial therapy, chronic disease treatment, and viral disease treatment are summarized with the aim of providing a useful reference for research on cellulose-based drug carriers.

Keywords: cellulose; drug carrier; drug controlled-release
Received: 22 July 2023; accepted: 12 September 2023; DOI: 10.26599/PBM.2023.9260026

1 Introduction

Traditional drug delivery methods such as oral, intravenous, and transdermal patches have several limitations. First, they can cause significant fluctuations of drug concentrations in patients, affecting their efficacy and safety [1–2]. Second, some drug exhibit low bioavailability in the body and require high or frequent multiple doses, resulting in inconvenience and increased patients' discomfort [3]. Additionally, traditional drug delivery methods cause drug accumulation in nontarget tissues, leading to side effects and toxic reactions [4], thereby endangering patient health.

Drug controlled-release system is a new type of drug delivery methods which using polymers as a carrier or medium for drug, and it can overcome the shortcomings of traditional drug delivery methods by maintaining stable drug concentrations and enhancing drug efficacy and safety [5–6]. Owing to the mechanism of different drug carriers with different drug dissolution and diffusion rates, the drug can be released in a slow, continuous, and steady stream after dissolution and hydrolysis of drug carriers. Drug controlled-release system can also achieve targeted drug delivery and reduce drug accumulation in non-target tissues [7–8]. In addition, the system can improve drug bioavailability, decrease invasiveness, and enhance patient compliance by reducing dosage frequency and improving patient experience [9]. However, drug controlled-release system still face challenges in practical application, including limitations of biocompatibility, drug loading capability, and release kinetics [10].

Polymer-based drug carrier materials, such as polylactic acid (PLA), polycaprolactone, polyethylene glycol (PEG), and chitosan, have been widely used in drug controlled-release system. Dhoke et al [11] introduced a PLA-based particle as drug carrier material for the delivery of the anticancer drug docetaxel to achieve efficient drug release control and endowed bioavailability, as shown in Fig. 1. Smith et al [12] employed polycaprolactone nanoparticles (NPs) for anticancer drug delivery, achieving precise control of drug release rates by modulating their size and shape. Kim et al [13] developed a PEG-based protein drug carrier with significantly enhanced stability and efficacy *in vivo*. Lee et al [14] devised chitosan microspheres for antibiotic delivery, successfully achieving sustained drug release and improved therapeutic efficacy. Among of them, petroleum-based polymers have limited sources and are potentially environmentally harmful in production processes; extraction and purification processes for chitosan are complex and high-cost, and its porosity and pore diameter are hard to control. By contrast, cellulose-based materials offer several advantages. As a natural polymer, cellulose is inexpensive and abundantly available from various sources, including plants (e. g., wood and cotton), marine organisms (e. g., seaweed), and bacteria [15–16]. The surface of cellulose is rich in hydroxyl groups, which makes it easy to react with modification agents, so that the molecular structure can be customized and adjusted according to the use needs to generate functionalized derivatives. Owing to the advantages of non-toxicity, hydrophilicity, biocompatibility, degradability and recyclability, the delivery of cellulose-based materials in organisms has better affinity and responsiveness, which has broad potential for application in the biomedical field [17–18].

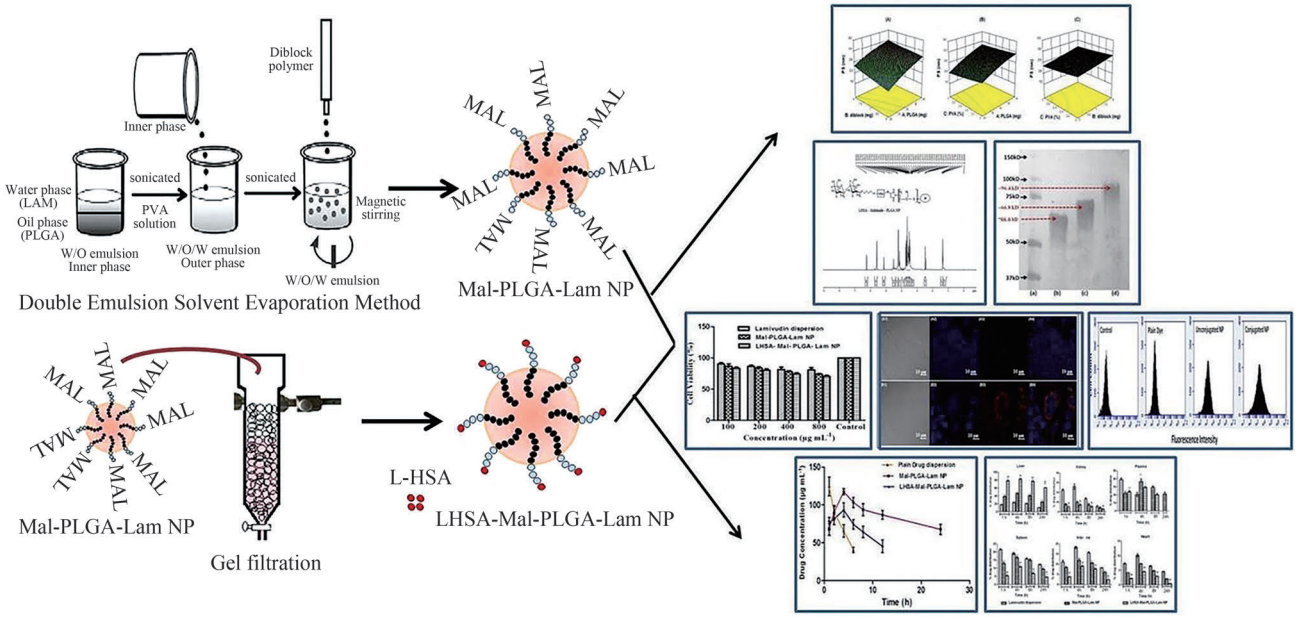

Fig. 1 Preparation of polymeric NPs conjugated with Lactosaminated-Human Serum Albumin (L-HSA) peptide [11]

In conclusion, the application of drug controlled-release system with cellulose-based materials provides certain advantages that can overcome the limitations of petroleum-based polymers, enhance efficacy and safety, and contribute to reducing environmental problems. These novel drug delivery system is expected to be widely used in the pharmaceutical industry.

In this paper, the drug retardation mechanism of cellulose-based drug carriers based on the properties of cellulose are reviewed. The preparation methods of cellulose-based drug carriers are also introduced, and the application of cellulose-based drug carriers in the fields of antitumor, antibacterial, chronic disease, and viral disease therapy are discussed, with the aim of providing useful references for the research and application of cellulose-based drug carriers.

2 Slow-release mechanism of cellulose-based drug carriers

Currently, the cellulose-based drug carriers achieving the slow-release of drug mainly include three types of slow-release mechanisms: dissolution-diffusion, cleavage release, and nanochannel release mechanisms. In this section, these three mechanisms and their influencing factors are described, and the research and development direction of cellulose-based drug carriers are summarized and prospected.

2.1 Dissolution-diffusion mechanism

The dissolution-diffusion mechanism refers to the slow-release of the drug from the carrier by dissolution and diffusion. The drug release rate of cellulose-based drug carriers is influenced by the dissolution and diffusion rates of the drug [19], which can be divided into two phases. The first stage is the dissolution of cellulose-based materials, which is influenced by the solubility of the cellulose-based materials, pore structure, and interaction force between the drug molecules and the cellulose-based materials; the faster the dissolution of cellulose-based materials, the faster the release rate of drug molecules [20]. The second stage is the diffusion of drug molecules, which is influenced by the size of the drug molecules, pore size of the cellulose-based materials, and environmental conditions [21].

The pore structure of cellulose-based materials significantly affects drug release rate. The larger the porosity, the faster the diffusion and release of drug molecules [22]. In addition, the surface properties of cellulose-based materials affect the drug release rate. Functional groups on the surface of cellulose-based materials, such as hydroxyl and carboxyl groups, can interact with drug molecules, thereby improving the diffusion rate of drug in cellulose-based materials [23]. Environmental conditions also influence the drug release rate. For instance, an increase in temperature increases the thermal movement of drug molecules, which in turn accelerates the diffusion rate of the drug. Moreover, changes in pH value affect the interaction between the drug and cellulose-based materials, thus affecting the release rate of the drug [24].

In summary, the dissolution-diffusion mechanism in cellulose-based drug carriers is influenced by various factors such as the pore structure of cellulose-based materials, size of drug molecules, interaction between the drug and cellulose-based materials, and environmental conditions. Through an in-depth study of these influencing factors, the design of cellulose-based drug carriers can be optimized to achieve precise control of drug release rate and release time. In addition, according to the therapeutic needs of different diseases, drug carriers with specific release characteristics can be constructed by adjusting parameters such as the pore structure, surface properties, and interaction forces of cellulose-based materials to improve therapeutic effects and reduce side effects [25–26].

2.2 Cleavage release mechanism

The cleavage release mechanism refers to the slow-release of the drug through degradation or rupture of the carrier material. The biodegradability of cellulose-based drug carriers allows for its gradual degradation in the organism and consequent release of the drug [27]. The rate of carrier degradation depends on the type and structure of the cellulose material, the crosslinking density, pH value, and temperature [28]. In addition, the presence of enzymes or microorganisms capable of degrading cellulosic material

may also affect the degradation rate of cellulose-based drug carriers, and thus, the drug release rate [29].

Controlled degradation rates matching the desired drug release rate can be achieved by changing the structure and properties of cellulose-based drug carriers. For example, the introduction of pH- or temperature-sensitive functional groups into the cellulose backbone enables the prepared cellulose-based carriers to degrade under specific trigger conditions to achieve more precisely targeted drug release [30]. In addition, combining cellulose materials with other biodegradable polymers can result in composite carriers with tunable degradation rates and enhanced mechanical properties, which can increase drug loading, prolong drug release time, and achieve specific drug release patterns [31].

2.3 Nanochannel release mechanism

The nanochannel release mechanism refers to the control of drug release through a nanoscale channel structure within cellulose-based drug carriers. Nanochannel can effectively regulate the diffusion rate of drug in cellulose-based drug carriers to achieve slow-release of drug [32]. The size, shape, and surface properties of the nanochannel can be modified to control the drug release rate and improve the selectivity and targeting ability of drug delivery [33].

Researchers have created nanochannel in cellulose-based carriers by using self-assembly methods or introducing porous inorganic nanoparticles with adjustable pore sizes and shapes, such as mesoporous silica nanoparticles [34–35]. In addition, targeted changes in the surface properties of nanochannel, such as surface charge, hydrophobicity, and chemical structure, can be achieved by modifying the cellulose material to affect drug release [36]. For example, by changing the surface hydrophilicity and hydrophobicity of the cellulose material, the affinity of the drug to the nanochannel is affected and its release rate is altered. Furthermore, through introducing the stimuli-responsive functional groups, the drug carrier changes its physical behavior or chemical structure when specific triggers (e. g., pH value and temperature) are changed, to achieve a fixed-point, quantitative, and timed drug release with a highly efficiency [37].

In addition to controlling drug release, the construction of nanochannel within cellulose-based drug carriers can improve their biocompatibility. By optimizing the size and surface properties of nanochannel, the interaction of the carrier with biological components can be weakened, potential immune resistance can be reduced, and the circulation time of the drug in the body can be increased [38].

Cellulose-based drug carriers based on these three mechanisms can be explored further in the following ways. A more in-depth study of the factors affecting drug release, such as pore structure, surface properties, and interaction forces of cellulose-based materials, is required to optimize the design of cellulose-based drug carriers. Novel cellulose-based materials and composites can be developed to enhance drug loading, prolong drug release time, and achieve specific drug release patterns. Novel nanochannel structures and surface modification methods should be explored to achieve high therapeutic efficacy and specific drug delivery. Efforts should be made to investigate the *in vivo* biodistribution and drug release kinetics of cellulose-based drug carriers to better understand their potential applications for sustained drug release.

3 Preparation of cellulose-based drug carriers

Cellulose-based drug carriers have received considerable attention in the field of drug delivery because of their good biocompatibility and tunable structural properties. In addition to the aforementioned drug release mechanisms, the preparation method plays a key role in the performance and application of cellulose-based drug carriers. Cellulose-based drug carriers based on the dissolution-diffusion mechanism are usually prepared by a physical modification method, which dissolves and releases the drug through the porous cellulose material without changing the cellulose backbone. Cellulose-based drug carriers based on the cleavage release mechanism are usually prepared by chemical and biomodification methods, in which insoluble cellulose macromolecules are converted into stable materials with high drug-loading capacity and good solubility by chemical/biological

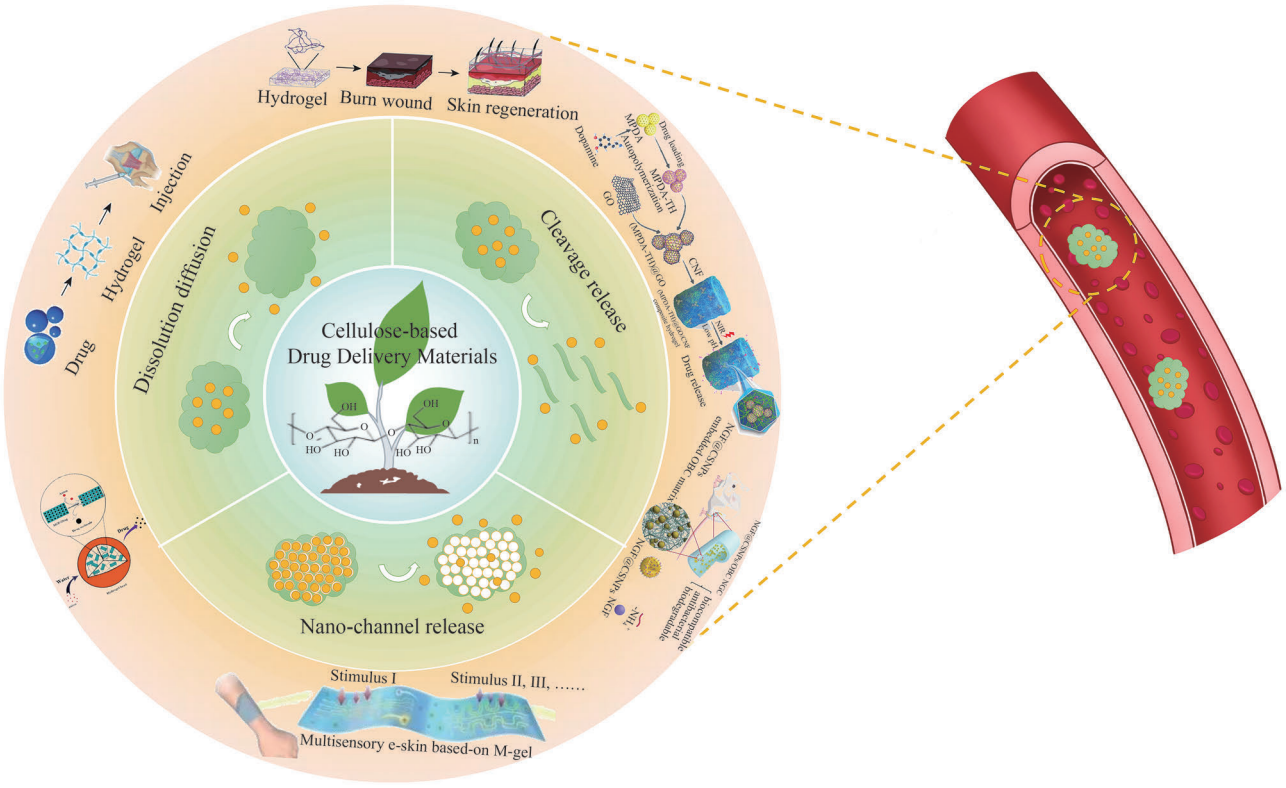

Fig. 2 Schematic diagram of drug release mechanisms and application of cellulose-based drug delivery materials [17-18, 25-26]

modification. Cellulose-based drug carriers based on the nanochannel release mechanism are usually prepared using nano-means to improve the biocompatibility and selectivity of cellulose carriers. This chapter focuses on these four common methods for the preparation of cellulose-based drug carriers.

3.1 Physical modification method

Physical modification method changes the structure and properties of cellulose by physical means, including heating, UV irradiation, and mechanical treatment. These methods can be used to prepare different types of cellulose-based drug carriers, including hydrogels, membrane materials, and other porous materials [39]. Compared with chemical modification method, physical modification method has higher biocompatibility and produces fewer side effects; however, they may affect the mechanical properties and stability of cellulose-based drug carriers to some extent.

3.1.1 Cellulose-based hydrogels

Cellulose-based hydrogels are three-dimensional polymer networks that can absorb and retain large amounts of water and biofluid [40]. Cellulose-based hydrogels can be prepared using different physical methods such as solvent exchange, freeze-thaw cycles, and radiation [41]. Owing to their good biocompatibility, adjustable mechanical properties, and ability to control drug release, cellulose-based hydrogels have been widely studied and used in drug delivery [42].

3.1.2 Cellulose-based film materials

Cellulose-based membrane materials can be prepared by casting, solvent evaporation, or electrospinning [43]. Cellulose-based membrane materials can be used as drug delivery vehicles with the potential for transdermal, buccal mucosal, or ocular drug delivery, offering the advantages of controlled drug release, reduced side effects, and improved patient compliance [44].

3.1.3 Cellulose-based porous materials

Cellulose-based porous materials, which have highly interconnected porous structures that enable controlled drug release, tissue growth, and angiogenesis, can be prepared by physical method, such as lyophilization, particle drenching, or bubble foaming [45], and they have been extensively studied in the fields of tissue engineering,

wound healing, and drug delivery.

3.2 Chemical modification method

Chemical modification method is used to improve the drug loading and sustained release performance of prepared cellulose-based drug carriers by introducing new functional groups into the macromolecular backbone of cellulose through chemical reactions, such as esterification, acylation, and sulfation of cellulose molecules [46]. Recently, researchers have developed new chemical modification methods to broaden the scope of application of cellulose-based drug carriers. For example, polymers with different properties, such as polyvinyl alcohol and polyamides, can be grafted onto cellulose molecules through grafting reactions to improve their solubility, stability, and biocompatibility in specific environments [47]. In addition, the preparation of drug carriers with drug-cellulose covalent bonds by directly binding drug molecules to cellulose can achieve controlled release of drug *in vivo* while avoiding the accumulation of drug in non-target tissues and reducing side effects and toxic reactions.

However, some byproducts may be generated during the chemical modification process, which may potentially affect the biological activity and safety of the drug. Therefore, when developing new chemical modification methods, the effects on drug properties and biosafety must be considered to ensure that the prepared cellulose-based drug carriers have good efficacy and safety.

For practical application, suitable chemical modification method can be selected to modulate the performance of cellulose-based drug carriers according to the nature of the drug, the therapeutic targets, and the clinical requirements. By optimizing the chemical modification conditions, precise control of key performance indicators, such as drug loading, release rate, and biocompatibility, can be achieved, providing more efficient and safe drug delivery solutions for clinical treatment.

3.3 Biomodification method

Biomodification method is the enzymatic digestion and modification of cellulose using biological enzymes, which include cellulases, pectinases, and xylanases. Johnson et al [48] demonstrated that cellulase treatment improves the biocompatibility of cellulose-based drug carriers, thus enhancing drug efficacy. Lee [49] improved the surface properties of cellulose-based drug carriers using pectinase, enabling them to load and release drug more efficiently. Williams [50] improved the mechanical properties and porosity of cellulose-based drug carriers using xylanase enzymes, resulting in improved drug loading and release ability. Biomodification method is environmentally friendly, mild, and controllable, which can achieve changes in cellulose structure and properties without altering the basic cellulose skeleton. However, biomodification method may be limited by enzyme activity, selectivity, and stability, which may affect the effectiveness and application scope of drug carriers.

3.4 Nanotechnology

In recent years, nanotechnology has become an important means of preparing cellulose-based drug carriers at the nanoscale such as nanocellulose hydrogels, membranes, and aerogels. Nanoscale cellulose-based drug carriers have received widespread attention because of their high drug loading, good slow-release performance, and targeted delivery capability, enabling a wide range of applications in the fields of tumor therapy and gene therapy. For example, it is used as a targeted drug delivery system to precisely deliver drug to the site of the disease to improve the therapeutic effect and reduce side effects [51–54].

3.4.1 Nanocellulose hydrogel

Nanocellulose hydrogels exhibit good biocompatibility, degradability, and plasticity [55], and their preparation methods include free-radical polymerization, cold coagulation, thermal coagulation, and ionic coagulation. The free-radical polymerization method [56] introduces a free-radical initiator to induce free-radical polymerization between the nanocellulose molecular chains and form nanocellulose hydrogels. It has the advantages of fast reaction rate and better controllability; however, toxic free-radical initiators may be introduced. The cold condensation method [57] and hot condensation method [58] use the formation of hydrogen bonds between cellulose molecular chains at low and high temperatures,

respectively, to induce nanocellulose to form hydrogel structures. The preparation process is simple, but the temperature control is more stringent and may affect drug stability. The ionic coagulation method [59] induces an ionic crosslinking reaction between the nanocellulose molecular chains by adding an ionic crosslinking agent to form a nanocellulose hydrogel. The advantages are a fast reaction rate and mild preparation conditions, while the disadvantage is that it may be limited by the ionic crosslinking agents.

Nanocellulose hydrogels are widely used as drug carriers in tissue engineering and trauma repair. Their application in the field of tissue engineering as a biological scaffold material can promote tissue repair and regeneration [60]; they can also be used in slow-release drug delivery system to improve drug efficacy and reduce side effects.

3.4.2 Nanocellulose membrane

Nanocellulose membranes can be prepared as drug carriers by wet spin-coating, solution casting, or electrospinning. Wet spin-coating disperses the nanocellulose solution on a rotating substrate to form a uniform film by controlling the spin speed and time [61], which has the advantages that the film thickness can be controlled and the structure is uniform. However, solvent residue may be generated during the process. Solution casting [62] is the uniform application of the formation of a nanocellulose film by evaporation or curing of a nanocellulose solution on a flat surface, which is a simple operation; however, the film thickness and uniformity are difficult to control. Electrospinning [63] is carried out by applying a high voltage between two electrodes, and the nanocellulose solution is sprayed and stretched into nanoscale fibers to form a film after collected. The advantage is that nanoscale fibers can be obtained to improve drug loading and control drug release; the disadvantage is that the equipment is complicated, and the cost is high.

Nanocellulose membranes are increasingly used in the medical field, especially in drug delivery systems, where they exhibit excellent performance. Researchers have incorporated the non-steroidal anti-inflammatory drug pyridine sulfonate into nanocellulose membranes. Because of the good biocompatibility and excellent controlled release properties of nanocellulose membranes, the drug is released slowly and continuously in body, greatly improving the efficacy of the drug and reducing side effects [64]. In addition, nanocellulose membranes play a key role in the development of drug delivery system, such as insulin delivery system based on nanocellulose membranes. In this system, insulin is embedded in nanocellulose membranes and administered transdermally through the skin to achieve continuous and stable insulin release.[65]

3.4.3 Nanocellulose aerogel

The preparation of nanocellulose aerogels typically involves two methods: freeze-drying and supercritical drying. Freeze-drying involves freezing the nanocellulose dispersions and sublimating it under vacuum to remove the ice crystals and form aerogels with a porous structure [66]. This method is simple and can produce large porosity and high drug-loading capacity; however, the freeze-drying process may cause partial loss and structural changes of nanocellulose. Supercritical drying is a method of drying nanocellulose dispersions under supercritical conditions [67]. The advantage is that a more detailed and uniform porous structure can be obtained, which is conducive to the uniform distribution and continuous release of drug; however, the equipment is complex, costly, and requires a strict operating environment.

Nanocellulose aerogels have also shown a high potential for use in drug delivery system. For example, studies have shown that nanocellulose aerogels can be used as effective carriers for anticancer drug. Nanocellulose aerogels loaded with anticancer drug have been prepared using the freeze-drying method. Owing to the high porosity and good biocompatibility of the aerogel, the drug is continuously released into tumor cells, thus improving its efficacy and reducing its side effects [68]. Additionally, innovative drug delivery system can be developed using nanocellulose aerogels. The drug is uniformly distributed in the nanocellulose aerogels by ultrasound and delivered through the intestine after

controlled drug release. This new drug delivery system can automatically adjust the drug release rate according to the internal environment of the body, such as pH value changes, to achieve more effective therapeutic effects [69].

Moreover, nanocellulose aerogels have shown great potential in the field of tissue engineering, such as bone repair and regeneration. This material not only acts as a drug carrier, gradually releasing drugs such as bone formation-promoting factors, but also acts as a scaffold for cells, promoting the growth of bone cells and thus enabling bone repair [70], which was demonstrated that nanocellulose aerogel had a promising application in the field of drug delivery and tissue engineering.

Nanotechnology has significant advantages in the preparation of cellulose-based drug carriers, providing an effective way to prepare cellulose-based drug carriers with high drug loading, good slow-release performance, and targeted delivery capability. However, current nanotechnology preparation methods still need to be further optimized, such as improving biocompatibility of materials with a high drug loading capacity, and optimizing preparation conditions for saving cost. Future research should continue to focus on the improvement of nanotechnology preparation methods to meet different drug delivery needs and application scenarios. Researchers should also explore in depth the application of nanocellulose-based drug carriers in specific disease areas to improve therapeutic effects and reduce side effects.

In addition, to broaden the application of cellulose-based drug carriers for clinical field, further studies on their biocompatibility, drug loading, and drug release properties through bionic design, high-throughput screening, and computer simulations are needed to improve the design accuracy and performance of cellulose-based drug carriers.

4 Application of cellulose-based drug carriers

The design of cellulose-based drug carriers can be optimized according to the therapeutic needs of different diseases, and construct a circumferential drug system by adjusting the pore structure and surface properties of cellulose-based materials. Additionally, cellulose-based materials have good biocompatibility, which is expected to reduce the side effects of drug delivery system and improve their therapeutic efficacy [71]. Currently, cellulose-based drug carriers used to treat chronic and viral diseases have gained progress in antitumor and antibacterial applications, and are expected to be clinically implemented.

4.1 Antitumor therapy

To improve the selectivity and bioavailability of anticancer drug, cellulose-based drug carriers can be functionalized with various targeting ligands or molecules such as antibodies, peptides, and oligonucleotides. These targeting ligands or molecules can recognize and specifically bind cancer cells, leading to more effective drug delivery to the tumor site. For example, the coupling of monoclonal antibodies targeting tumor-specific antigens with a cellulose-based carrier can direct drug loading onto tumor cells [72]. In addition, the surface of cellulose-based carriers can be modified with hydrophilic macromolecules such as PEG, which can enhance the circulation time of the carrier in the bloodstream and increase the affinity to tumor site [73].

One way that cellulose-based drug carriers reduce side effects is to protect the carrier drug from premature degradation and non-specific interactions with healthy cells [74]. Another approach is to design carriers that respond to specific stimuli (such as pH value, temperature, or enzyme activity) in the tumor microenvironment, which allows the controlled release of the drug at the tumor site and reduces systemic toxicity [75].

Cellulose-based drug carriers can improve therapeutic efficacy by enhancing drug entry into tumor tissues and promoting intracellular phagocytosis. For example, surface-modified nanoparticles with additional cell-penetrating peptides can more effectively penetrate the dense tumor extracellular matrix and promote intracellular uptake [76]. In addition, the use of stimulus-responsive drug release mechanisms can enable intracellular drug release, allowing the drug to bypass the extracellular pump and reduce the risk of drug resistance development [77].

Furthermore, cellulose-based drug carriers can be

used to co-deliver multiple therapeutic agents such as chemotherapy, gene therapy, and immunotherapy agents. Such combinatorial therapeutic approaches can provide synergistic effects to overcome drug resistance and enhance the overall therapeutic effects. For example, designing a cellulose-based drug carrier that encapsulates chemotherapeutic drugs and small interfering RNA (siRNA) molecules targeting specific oncogenes provides chemotherapy and gene-silencing effects simultaneously [78].

In summary, cellulose-based drug carriers can enhance the selectivity and bioavailability of anticancer drug, reduce side effects, and improve therapeutic efficacy by utilizing strategies such as ligand functionalization, controlled drug release, stimulus-responsive drug release, and combination therapies. Further research is required to optimize the design and fabrication of cellulose-based carriers for clinical application.

4.2 Antimicrobial therapy

Sustained drug release can be achieved by designing cellulose-based drug carriers with specific physical and chemical properties. By controlling the drug loading, drug encapsulation efficiency, and drug release kinetics, cellulose-based carriers can improve patient compliance [79]. For example, the incorporation of hydrophobic or hydrophilic polymers into cellulose-based carriers can modulate the drug release rate according to the intended application [80].

The development of drug resistance is a difficult challenge for the treatment of infectious diseases. Cellulose-based drug carriers can help reduce the emergence of drug-resistant strains by maintaining effective drug concentrations at the infection site and reducing sub-therapeutic drug levels that contributes to resistance [81]. In addition, cellulose-based carriers allow for the co-delivery of multiple anti-infective agents with different mechanisms of action and can provide synergistic effects on drug anti-resistance development [82], and improve the overall therapeutic efficacy of combination therapies [83].

Cellulose-based drug carriers can improve therapeutic efficacy by enhancing drug bioavailability, targeting, and penetrating the infection site. For example, the modification of marker-specific targeting ligands on the surface of cellulose-based carriers, such as antibodies or peptides, can increase drug delivery to the infection site and reduce non-targeting effects [84]. In addition, cellulose-based carriers can be designed to overcome biological barriers, such as the mucus layer in the respiratory or gastrointestinal tract, to increase drug penetration and improve therapeutic efficacy [85]. For example, a cellulose-based carrier can be designed to encapsulate both antibiotics and immunomodulators to provide antibacterial and immunomodulatory effects [86].

In summary, cellulose-based drug carriers can achieve sustained release of anti-infective drug, reduce drug resistance, and improve therapeutic efficacy by utilizing various strategies, such as controlled drug release, multi-dose co-delivery, targeting, and enhanced drug penetration.

4.3 Chronic disease treatment

Cellulose-based drug carriers have a wide range of applications for the treatment of chronic diseases. Chronic disease treatment usually requires long-term drug delivery, and cellulose-based drug carriers are ideal controlled material for drug release system owing to their biocompatibility and reproducibility [87].

Cellulose-based drug carriers can achieve slow drug release for chronic disease treatment by adjusting the degree of crosslinking of cellulose molecular chains, cellulose microstructure, and drug-carrier interactions [66]. For example, nanocellulose and microsphere carriers can effectively control the release rate of drug during the treatment of chronic diseases, thereby reducing the number of doses required and improving patient compliance [88]. In addition, cellulose-based drug carriers can be used to improve the hydrophilic and lipophilic properties of drug through surface modification techniques, such as graft polymerization and covalent binding, to optimize drug release behavior [89].

Slow-release system for chronic disease treatment using cellulose-based drug carriers can reduce the treatment burden and improve the quality of life for patients. For example, in the treatment of diabetes, cellulose-based drug carriers can achieve a slow-release of insulin,

reduce the number of injections and the stress on patients' lives [90]. In cardiovascular disease treatment, cellulose-based drug carriers can achieve slow-release of anticoagulant and hypotensive drugs, thus reducing side effects in patients and improving the therapeutic effect [91].

With the continuous development of cellulose-based drug carrier technology, its application in chronic disease treatment is expected to become more extensive in the future.

4.4 Treatment of viral diseases

Cellulose-based drug carriers have several important applications in the treatment of viral diseases. Through nanotechnology, cellulose-based drug carriers can achieve the precise targeting and progressive release of antiviral drug [92], and major application include treatment for HIV, hepatitis B, hepatitis C, and other diseases [93].

As carriers, cellulose nanocrystals can increase the bioavailability of antiviral drug and improve their pharmacokinetic properties, thus enhancing their therapeutic effect [94]. Additionally, cellulose-based drug carriers can further increase drug bioavailability by improving drug solubility *in vivo*. Cellulose-based drug carriers can also improve drug targeting through the specific binding of drug to target cells, thereby reducing their impact on normal cells, and decreasing side effects [95].

The application of cellulose-based drug carriers in the treatment of viral diseases also includes the design of targeted nanocarriers to enhance drug aggregation at the sites of viral infection. Such targeting can be achieved by modifying functional groups on the surface of cellulose-based carriers, for example, using receptor-ligand interactions to enhance the selectivity of drug against viruses [52]. In addition, cellulose-based drug carriers can improve the therapeutic efficacy against viral diseases by enhancing the immune response. For example, cellulose-based carriers can be used as vaccine adjuvants to enhance the immune efficacy of vaccines, thereby enabling more effective virus control [28].

The use of cellulose-based drug carriers for the treatment of viral diseases also benefits from their biocompatibility and environmental friendliness. These properties allow cellulose-based drug carriers to be used with a minimal impact on patients and the environment during treatment, thereby reducing the risk of potential toxicity [96].

5 Conclusion and outlook

As green materials with excellent properties, cellulose-based drug carriers have wide potential for application in drug controlled-release system. In this paper, the research progress on cellulose-based drug carriers is reviewed, including the mechanisms of the slow-release of cellulose-based materials, preparation methods, and their application in various fields. However, cellulose-based drug carriers still face challenges in practical application, such as optimization of the preparation process, biosafety evaluation, and regulation of drug loading and release performance. Future research should focus on these challenges and further develop novel cellulose-based drug carriers, including multiple modes of administration, such as injection and oral administration, in combination with clinical needs to promote the wide application of drug controlled-release system in biomedical fields.

Currently, cellulose-based drug carriers have not been fully validated in cytotoxicity and biosafety studies compared to commercially available mature drug carriers. It is traditionally recognized that non-degradable cellulose is excreted in feces and other excretions. However, there are still few studies in which cellulose-based carriers can be excreted through such channels without posing health hazards to organisms. The future studies should focus on mechanistic studies of the degradation of surface chemistry, interfacial properties, and other physicochemical properties of cellulose-based drug carriers in living organisms. In addition, the side effects of cellulose as a carrier material on organisms at the cellular and genetic levels need to be further explored.

Interdisciplinary collaboration will play an important role in the future of cellulose-based drug carrier research in the fields of materials science, drug formulation, biomedicine, and clinical research. Through interdisciplinary collaboration, researchers can better

understand the role of cellulose-based drug carriers in disease treatment and conduct a more in-depth investigation of the interactions between cellulosic materials and the cells or tissues of organisms. Thus, more efficient and safe drug delivery systems can be designed, enabling cellulose-based drug carriers to realize more biomedical applications, and providing more possibilities for disease treatment.

Foundation

Shaanxi Province College Student Innovation and Entrepreneurship Training Program Project (Project Number: S202310708098).

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