Review Article

Nanomedicine Based on Natural Products: Improving Clinical Application Potential

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Natural products have antitumor, anti-inflammatory, antioxidant, and other pharmacological activities and are an important source of drugs for prevention and treatment of various diseases. However, the inherent defects of natural products in physiological media such as poor solubility and stability and short biological half-life limit their clinical application. In recent years, more and more attention has been paid to the science of drug delivery by nanoscale materials. A large number of in vitro and in vivo studies have further confirmed the efficacy and safety of nanomedicine based on natural products in preclinical models of various diseases. In this review, we summarized the achievements of nanomaterials in improving the efficacy of natural products, introduced the research progress in several key fields of natural product-based nanomedicine in medical application, and discussed the challenges and prospects of clinical transformation of nanomedicine.

1. Introduction

In discovering lead compounds to treat various human diseases, natural products from plants, animals, and microorganisms provide rich sources for novel compound identification [1]. It is generally believed that compared with synthetic compounds, the structure of natural products is diverse [2]. In addition, most natural products show strong biological activity, optimal adsorption, good distribution, adequate metabolism, and elimination characteristics, which are more similar to drugs compared with synthetic compounds [3]. For multifactorial and complex diseases, different natural products activate a variety of signal transduction pathways to treat diseases by regulating multiple targets, which has more therapeutic potential than drugs aimed at a single site [4]. Therefore, natural products not only contain excellent precursor structure but also provide direct treatment. At present, there are 2 million species of plants, animals, microorganisms, and fungi, of which 95% have not been evaluated for biological activities [5]. Due to the high costs and development associated with synthetic compounds and a wide range of natural products, additional valuable and bioactive natural products need to be uncovered. Thus, natural products are worthy of attention since they exhibit great potential for the discovery, development, and application of drugs.

Although the pharmacological activity and therapeutic potential of natural products for human diseases are recognized, the application and development of natural products are limited by their susceptibility to physiological media and low bioavailability. The emergence of nanotechnology provides an effective strategy for efficient delivery of natural products to adapt to valuable clinical applications by improving bioavailability, targeting, and controlled release [6](Figure 1).
2. Historical Review of Drugs Derived from Natural Products

Plant-derived natural products have played a leading role in drug development since plants are easy to obtain. Early humans recognized the therapeutic role of plants when trying to treat diseases. These plants have proven to have medicinal value in practice, as they are present in a number of recorded documents [7–9]. So far, about 60% of the pharmaceutical preparations in the market are derived from botanical natural products and about 80% of the world’s population depends on traditional botanical drugs [10]. “Hot” drugs attracting international attention include the anticancer drug paclitaxel and its derivatives, the antimalarial drug artemisinin, and the cardio-cerebrovascular drug ginkgolide.

As a substance inhibiting the proliferation of microbial competitors and other pathogenic microbes in the environment, antibiotics are widely used to fight infectious diseases [11]. Natural products from microbes play an important role in the discovery and development of antibiotics. Most antibiotics with therapeutic activity are natural products derived from microbes [12]. Since the British bacteriologist Alexander Fleming discovered penicillin, the world’s first antibiotic, in 1928, it has ushered in a golden age of natural products derived from microorganisms to treat human diseases. Of course, microbial products are not limited to antibiotics, as a single microbe can produce up to 50 secondary metabolites that can be used to develop antiviral drugs, anticancer agents, and immunosuppressants [13].

It is known that the ocean covers more than 70% of the earth’s surface, representing 90% of the biosphere volume. Due to the limitations in science, technology, and human cognition, drug discoveries based on natural products mainly depended on terrestrial organisms. Therefore, natural products derived from marine organisms are a neglected treasure [14, 15]. In the late 1980s, improved science, technology, and modern bioengineering, individuals began to pay more attention to marine organisms [16]. The marine environment is quite different from the terrestrial environment, since these organisms face high pressure, high salt concentrations, low temperatures, and low oxygen levels. During the course of long-term evolution, marine organisms formed different metabolic modes and adaptation mechanisms from terrestrial organisms. Some secondary metabolites with novel structures and significant pharmacological and toxicological effects were produced. Presently, many breakthrough achievements have been made in the development of marine drugs. Scientists have isolated a series of new compounds with antibacterial, antiviral, anti-inflammatory, antitumor, and other biological activities from marine organisms such as algae, sponges, starfish, and echinoderms [17–20]. The chemical structure novelty and pharmacological activity of marine bioactive natural products are unmatched by terrestrial organisms, and it has become one of the main directions in the development of new drugs [21].

3. Nanostrategy of Drugs from Natural Products

Nanometer-sized particles exhibit unique properties and functions. Clinical experience shows that the application of nanoparticles increases the accumulation of active ingredients in lesion sites, weakens the systemic toxicity of drugs, promotes the solubility of insoluble drugs, improves the
The application of nanodrugs derived from natural products pose serious challenges to global health. This article reviews generative diseases, cardiovascular diseases, and other diseases. Without a doubt, the combination of natural products and nanotechnology will have great advantages in natural products. The synthesis and design of nanodrugs are particularly important. The development and application of nanodrugs are particularly important.

Many isolated natural products show strong pharmacological activities including antitumor, anti-inflammatory, antioxidant, and other beneficial effects as proven in vitro [24–26]. However, most natural products show limitations such as low hydrophilicity, instability, quick metabolism, low bioavailability, or poor permeability. As a consequence, the in vivo effects of these drugs are not ideal and require repeated dose administration beyond the safe range, which is unfavorable in the cases of long-term treatment for chronic diseases [4]. Nanotechnology represents a new method to overcome these challenges. The development and application of nanotechnology have greatly promoted the therapeutic efficacy, safety, and patient compliance for drugs derived from natural products. Without a doubt, the combination of natural products and nanotechnology will have great advantages in health care in the future. At present, cancer, diabetes, neurodegenerative diseases, cardiovascular diseases, and other diseases pose serious challenges to global health. This article reviews the application of nanodrugs derived from natural products and their use to treat human diseases.

4. Application of Nanodrugs Derived from Natural Products

4.1. Application of Nanodrugs Derived from Natural Products Used to Treat Cancer. The incidence and mortality rates for cancer are increasing yearly worldwide. According to the International Agency for Research on Cancer, about 18 million new cancer cases and 9.6 million cancer-related deaths were reported worldwide in 2018. It is expected that the number of new cancer cases and related deaths will increase to 20.3 million and 13.2 million, respectively, by 2030 [27, 28]. Therefore, cancer is expected to become a major threat to human health in countries around the world and is a block on the road to long life expectancy [28].

Even though cancer has been effectively treated using surgery, radiotherapy, and chemotherapy, the systemic side effects caused by chemical drugs cannot be ignored. Obvious side effects include hair loss, vomiting, hypertension, heart disease, and arterial thromboembolism [29]. The advantage of natural products lies in their multitarget and multimechanism antitumor effects, which can modulate the cancer microenvironment and diverse cell signal cascades. Some natural products have the ability to can induce apoptosis and autophagy in tumor cells such as quercetin, silymarin, taurine, melatonin, and astaxanthin. Others, such as curcumin, lycopene, piperine, epigallocatechin-3-gallate, and vitamin D, treat cancer by regulating embryonic developmental pathways (Notch pathway, Wnt pathway, and Hedgehog pathway) [30]. At present, a variety of in vitro and in vivo experiments show that compared with other synthetic chemotherapy drugs, natural products have comparable anticancer efficiency and lower side effects [31, 32].

Even more surprising, natural products can reverse or bypass drug resistance in tumor cells by regulating drug-resistant proteins and targeting nonapoptotic cell death [33]. In addition, the size and surface modifications of nanoparticles also play an important role in tumor therapy. On one hand, due to the existence of enhanced permeability and retention effects (EPR), nanoscale drugs tend to gather in tumor tissues. On the other hand, the surface functionalization of nanoparticles can target specific cancer cells and improve the localization and efficacy of drugs [34](Figure 3).

For example, camptothecin (CPT) is a cytotoxic quinoline alkaloid isolated from bark and branches of Camptotheca acuminata grown in China. Its anticancer activity was approved by the U.S. Food and Drug Administration.
(FDA) and is widely used for the treatment of a variety of tumors [35].

Research on the anticancer mechanisms of CPT has promoted the emergence of a large number of CPT derivatives and analogues, including irinotecan, topotecan, and 10-hydroxycamptothecin [36]. Even though this has greatly improved the inherent defects of maternal drugs with good antitumor activity, there are still many problems in their clinical application, such as systemic toxicity and low tolerance. In order to overcome these problems, scientists try to combine nanotechnology with traditional medicine to improve therapeutic effects. In designing camptothecin-based nanodrugs, most are based on nanocarrier-assisted drug delivery, carrier-free nanodrugs, and prodrugs coupled with nanodrug delivery. Among these, the typical nanopharmaceutical is CRLX101, which is a type of CPT nanoparticle based on cyclodextrin. Gaur et al. [37] reported the therapeutic effects of CRLX101 in phase 1/2a clinical trials on patient samples with advanced solid malignancies. Results showed that CRLX101 significantly inhibited tumor cell proliferation and angiogenesis, but also decreased the expression of topoisomerase-1, Ki-67, CaIX, CD31, and VEGF. Compared with CPT and its derivatives, CRLX101 showed better tolerance, safety, efficacy, and pharmacokinetic characteristics [38]. To understand the nanosizing of anticancer drugs, Zhao et al. [39] combined the two different anticancer drugs 10-hydroxycamptothecin (HCPT) and doxorubicin (DOX) into a single drug delivery system through a self-assembly method to understand the combination therapy of carrier-free pure nanodrugs. The preparation of this dual-drug nanoparticle is not only simple and convenient but also the water solubility of the HCPT is increased 50 times after self-assembly, and the intracellular DOX retention is increased 2 times, showing higher chemosensitivity and inhibition of drug-resistant cancer cells. In addition, conventional wisdom emphasizes that cells are not able to fully uptake fibrillar structures. Both in vitro and in vivo studies have proven that nanofibers formed by coupling the anticancer drug CPT with poly-peptides can effectively inhibit the growth of tumor cells by overexpressing integrin. This new prodrug delivery system provides a novel research direction for tumor-targeting drug delivery [40].

Berberine (BBR) shows antiaacute myeloid leukemia activity in vitro. To improve the solubility of BBR, researchers designed a self-nanoemulsifying system containing BBR (BBR SNE). This system helps enhance penetration and prevents outflow of BBR, which significantly improves relative oral bioavailability of BBR and greatly improves the efficacy against acute myeloid leukemia. The particle size of this system is approximately 23.50 ± 1.67 nm [41].

Phycocyanin (C-PC) is a water-soluble phycobiliprotein that can be used as food. It is believed that phycocyanin prevents the development of cancer through multiple mechanisms and has potential as an antitumor drug with high efficiency and low toxicity [42]. However, poor stability limits the development and application of the molecule. Yang et al. [43] constructed PH-sensitive carboxymethyl chitosan-CD59-specific ligand peptide nanoparticles to deliver C-PC, which can effectively target HeLa cells and slow-release drugs for anticancer effects.

4.2. Application of Nanodrugs Derived from Natural Products Used to Treat Diabetes Mellitus. Diabetes is a chronic metabolic disease caused by defective insulin secretion or impaired biological effects. Long-term high blood glucose levels may damage macrovessels and microvessels and endanger the heart, brain, kidney, eyes, and feet, leading to other diseases such as cardiovascular diseases, chronic kidney disease, retinopathy, and lower limb necrosis [44]. Diabetes cannot be cured and long-term use of synthetic antidiabetic drugs increases the risk of adverse reactions. In addition, the increased prevalence of diabetes and the threat of related complications prompt the discovery of new safe drugs. A study found that some natural products show great potential in treating diabetes and its complications, and the application of nanotechnology enhances the benefits of natural products in the treatment of disease. The nanocarrier
protects loaded natural hypoglycemic agents from rapid clearance in vivo, thus, optimizing the hypoglycemic effect.

The occurrence and development of diabetes are related to mitochondrial dysfunction and malfunctioning of the glucose uptake signaling cascade [45, 46]. In vitro experiments have shown that compared with free pelargonidin, pelargonidin encapsulated in poly (lactic-co-glycolic acid) (PLGA) produces nanopelargonidin (~12 nm) with an extremely small size. Even when the dose was reduced by 10-fold, the nanopelargonidin showed a greater protective effect of mitochondrial function and the glucose uptake signal cascade, which is expected to be used to prevent diabetes or delay its progression [47]. Similarly, PLGA nanoparticles for curcumin effectively prevent the initiation of inflammation and pancreatic islets/β-cell apoptosis, improve islet β-cell function, and prevent type 1 diabetes mellitus. This formulation increases the oral availability of curcumin by at least 9-fold, improving the curative effects of the diabetic model [48]. Diabetes affects wound healing. Bairagi et al. [49] found that ferulic acid-poly (lactic-co-glycolic acid) (FA-PLGA) nanoparticles not only reduced the levels of blood glucose but local application and oral administration of ferulic acid nanoparticles promote wound healing in diabetic rats better than free ferulic acid.

To enhance the antiabetic effects of quercetin (Qu), Singh et al. [50] prepared Soluplus ®micellar (SMs) supported on quercetin using the cosolvent evaporation method. Moreover, the in vitro release study demonstrated that Qu-SMs sustained release characteristics. Pharmacokinetic studies performed in vivo showed that the relative bioavailability of Qu reached 1676% by encapsulating the drug into SMs. To study the efficacy of QU-SMs in vivo, diabetic rats induced by streptozotocin were orally administered with QU-SMs and free QU solution. Blood glucose levels in the rats were measured and compared with pure drugs. Qu-SMs-treated animals showed lower blood glucose levels. Therefore, the application of nanocarriers improved the antiabetic performance of Qu. Oleanolic acid (OA) shows antiabetic activity against both type 1 and type 2 diabetes. It has been proven that the nanocrystallization of OA improves the bioavailability and pharmacodynamic properties of OA. At the same time, it can enhance the pharmacological efficacy of preventing and treating diabetes and its related metabolic diseases [51].

4.3. Application of Nanodrugs Derived from Natural Products to Treat Neurodegenerative Diseases. So far, nanoparticles have attracted attention for the treatment of psychiatric diseases due to their unique structural advantages, high stability, easy surface functionalization, and modifications, as well as their access across the easy blood-brain barrier (BBB).

4.3.1. Alzheimer’s Disease. The biocompatibility and biodegradability of PLGA are recognized but limited by shortcomings of poor water solubility and easy first-pass metabolism of quercetin. Sun et al. [52] prepared PLGA functionalized quercetin nanoparticles (PLGA@QT) to study their effects and safety in treating AD. The prepared nanomedicine shows synergism and detoxification. Most importantly, the effects of PLGA@QT nanoparticles on improving spatial memory increase with increased dose, which is expected to be used in the treatment of AD. Ginsenoside Rg3 has been extensively studied as the main active ingredient of ginseng, and studies have shown its strong antioxidant capacity is beneficial to Alzheimer’s disease [53]. To prevent rapid clearance of ginsenoside Rg3 from the blood and increase drug accumulation at the disease site, researchers developed PLGA-Rg3 nanoparticles that can specifically target amyloid plaques/amyloid fibers and determined that PLGA-Rg3 nanoparticles effectively pass through BBB, continuously release ginsenoside Rg3 and reduce the formation of AD plaques. In addition, this nanotherapy results in less side effects and has potential benefits for delaying AD development [54].

Gold nanoparticle-based drug delivery methods have also achieved better intracerebral administration in neurotherapy. This is because gold nanoparticles can easily pass through brain endothelial cells and promote effective drug delivery to the brain [55]. As a result, an anthocyanin-loaded gold nanoparticle coated with PEG used to treat AD was designed, hoping to improve the neuroprotective effects of anthocyanin. It has been confirmed that anthocyanin-loaded PEG-gold nanoparticles have successfully penetrated the brain and showed more significant anti-AD and anti-inflammatory effects compared with anthocyanins alone, with no significant cytotoxic effect on neuronal cells, suggesting that this nanoparticle may be a potential drug for AD treatment [56]. To explore the potential of hesperetin in the treatment of AD and the advantages of nanodrug delivery, Kheradmard et al. [57] used Alzheimer’s disease animal models to compare the effects of hesperetin and nanohesperetin on neurobehavioral activity and antioxidant parameters. The experimental results showed that both hesperetin and nanohesperetin improved memory and learning and increased the antioxidation index of the hippocampus. However, it was obvious that nanohesperetin showed better neuroprotective effects than hesperetin and had more therapeutic value.

4.3.2. Parkinson’s Disease. In the past few decades, individuals explored the antioxidant properties of flavonoids and discussed their neuroprotective mechanisms. Rutin is a flavonoid that can activate a variety of endogenous antioxidant enzymes and suppress lipid peroxidation, which is considered as a potential drug for the prevention or treatment of PD [58]. Its application is mainly limited to poor water solubility, which leads to less intestinal absorption and low oral availability. Self-nanoemulsifying drug delivery systems are an effective method to improve this defect. Compared with rutin suspension, the optimized formulation increased the relative oral bioavailability of rutin by 2.3-fold. In addition, increased levels of rutin in the brain suggest that self-emulsification improves the permeability of rutin [59]. Schizandrin A (SA) is a promising natural product for anti-Parkinson’s disease. It can significantly inhibit SH-SY5Y cytotoxicity induced by 6-hydroxydopamine (6-OHDA) or 1-methyl-4-phenylpyridinium ion (MPP+) in vitro. In zebrafish and PD mouse models, it has significant
protective effects on dopaminergic neuron loss induced by 6-OHDA and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), respectively [60–62]. To increase uptake of SA by the brain and extend the circulation time of SA in the blood-stream, Chen et al. [62] used the flash nanoprecipitation method to encapsulate SA into methoxy poly(ethylene glycol)-block-poly(D,L)-lactic-co-glycolic acid nanoparticles (SA-NPs) with high encapsulation efficiency and high drug loading and is in a sustained release mode. Pharmacokinetic studies showed that SA content in the brain tissue and plasma of rats in the SA-NPs group increased significantly. The SA-NPs exerted strong neuroprotective effects on zebrafish and PD cell models, demonstrating the advantages of the nanodrug in cross-barrier transportation and bioavailability.

4.3.3. Huntington’s Disease. Protein misfolding and aggregation into fibrillar deposits are one of the causes of neurodegenerative diseases [63]. It is believed that the abnormal expansion of the polyglutamine (polyQ) repeats in the huntingtin (htt) protein causes mutant huntingtin to form amyloid aggregates, further triggering Huntington’s disease (HD) [64]. Trehalose, known as the “sugar of life,” is found in many plants, insects, and microorganisms and acts as an important autophagy modulator and antioxidant [65, 66]. The neuroprotective effects of trehalose have been demonstrated in various neurodegeneration models, and the general hypothesis is that trehalose promotes the elimination of protein aggregates by inducing autophagy [67]. Nanosized trehalose has been shown to further enhance this property. Mandal et al. designed a trehalose-functionalized gold nanoparticle that enhanced cell uptake in the form of endocytosis. This improved the inhibitory effects on the aggregation of polyglutamine-containing mutant proteins in neuronal cells [68]. Others synthesized trehalose-functionalized zwitterionic nanoparticles with a size between 20 and 30 nm. Results show that this type of nanotrehalose is safe and efficient and is 1000 times more efficient than molecular trehalose when it comes to inhibiting the accumulation of polyglutamine under extra/intracellular conditions or in HD model mouse brain. In addition, ideal effects could be achieved at the micromolar concentration [69].

In previous studies, curcumin has been reported to show strong antioxidant, anti-inflammatory, and antiprotein aggregation effects, which can improve mitochondrial dysfunction, polyQ-induced compromised neuronal function, cytotoxicity, and cell death [64, 70]. Hickey et al. reported beneficial effects of dietary curcumin on the HD mouse, especially on Huntington aggregates [71]. The most important aspect is that curcumin passes through the BBB making it an ideal neuroprotective compound [72]. However, the clinical application of curcumin is limited due to its poor water solubility, unstable in vivo properties, less absorption in the gastrointestinal tract, and rapid metabolism [73, 74]. The nanoparticle drug delivery system protects the stability of curcumin in vivo and prevents its enzymatic and PH degradation [75]. Based on these shortcomings of the drug and the advantages of nanoparticles, researchers developed curcumin solid lipid nanoparticles (C-SLN) to enhance oral bioavailability and their neuroprotective effects on HD induced by 3-nitropipionic acid (3-NPD) [76]. The experimental results showed that C-SLN improved the 3-NP-induced oxidative stress by activating the Nrf2 antioxidant pathway. The animal model treated with C-SLN showed reduced mitochondrial swelling, increased cytochrome levels, and improved neuromotor coordination. It is certain that C-SLN has an advantage over curcumin alone.

4.4. Application of Nanodrugs Derived from Natural Products in the Treatment of Cardiovascular Diseases. Cardiovascular diseases (CVD) are recognized as the leading cause of death worldwide [77]. Atherosclerosis and hypertension are risk factors for cardiovascular disease [78]. Many natural products have great potential and bright prospects in the treatment and prevention of cardiovascular diseases, such as curcumin, resveratrol, and epigallocatechin-3-gallate [78].

So far, the development of nanodrugs is mostly focused on tumor-targeted drug delivery and bypassing the BBB to treat brain diseases. The development of nanodrugs related to the treatment of cardiovascular diseases is still in initial stages, especially when it comes to targeted drug delivery. Presently, a variety of nanocarriers such as liposomes, solid lipid nanoparticles, and polymer nanoparticles have been developed to improve the bioavailability of drugs and the targeted treatment of cardiovascular diseases [79]. Therefore, nanotechnology is a promising strategy for the treatment of cardiovascular diseases and has broad application prospects in drug delivery.

The antioxidant and anti-inflammatory properties of resveratrol (Res) and the ability to upregulate endothelial NO synthase (eNOS) have potential beneficial effects on CVD [80]. The low bioavailability and high photosensitivity of the compound are the main issues researchers are trying to overcome with the use of a nanodelivery system.

Lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) (particle sizes between 160-190 nm) can protect resveratrol from degradation and enhance intestinal permeability. SLNs and NLCs can be used for oral administration of resveratrol, which is expected to enhance its efficacy in vivo [81]. Epigallocatechin-3-gallate (EGCG) is a powerful natural antioxidant with both hypolipidemic activity and antiinflammatory effects. Several studies support the view that EGCG has many benefits in the treatment of cardiovascular diseases [82–84]. However, the low bioavailability and instability of EGCG limit its effectiveness in the prevention and treatment of human cardiovascular diseases. Therefore, the application of nanocarriers can be used as a strategy to enhance its stability and effectiveness [85]. Compared with the same concentration of free EGCG, EGCG conjugated gold nanoparticles showed significant selective affinity and low toxicity to human smooth muscle cells and endothelial cells [86]. The L-Enano (composed of PC, kolliphor HS15, (+)-α-tocopherol acetate, EGCG, and KOdiA-PC), a type of CD36-targeted EGCG-loaded nanoparticles with a particle size of 108 nm that can enhance the stability and sustained release of EGCG, promotes the targeted delivery of EGCG to intimatal macrophages, improves the efficacy, and reduces side effects [87].
Hyaluronic acid (HA) is a targeted bioactive molecule associated with inflammation [88]. Thanks to nanotechnology, the uptake efficiency of hyaluronic acid nanoparticles by proinflammatory macrophages in vitro is increased by 6-40 times. Hyaluronic acid can target atherosclerotic plaque-associated macrophages in animal models and show strong anti-inflammatory effects. At the same time, hyaluronic acid mediates the targeted delivery of diagnostic agents to specific lesions and performs PET/MRI imaging, which represents a new method for the diagnosis of atherosclerosis [89]. Recombinant high-density lipoprotein (rHDL) can promote cholesterol efflux. Use of HA- (C)-PLGA-rHDL nanoparticles with a particle size of 138 nm enhances cellular cholesterol efflux (2.43 times), and drug loading can achieve a more effective antiatherosclerotic effect [90]. Chitosan is a natural product with strong hypolipidemic activity and shown to have significant benefits in blood lipids and lipoproteins when used alone and is a potential therapeutic agent to reduce the risk of CVD [91, 92]. Due to its good biocompatibility, biodegradability, and nontoxicity, it has become an ideal drug loading system when used alone and is a potential therapeutic agent to reduce the risk of CVD [91, 92]. Due to its good biocompatibility, biodegradability, and nontoxicity, it has become an ideal drug loading system that can improve the bioavailability of anticardiovascular drugs and increase the sustained release of drugs. In short, the combination of these natural product nanocarriers and related disease drugs not only reduces the dose of these drugs but also reduces side effects and achieves stronger therapeutics effects.

5. Conclusions and Future Prospects

The application of nanotechnology in drug delivery has had a positive impact on the treatment of a variety of human diseases. This method is especially essential for the development of appropriate drug delivery methods for hydrophobic drugs that are easily affected by the environment. Researchers are aware of the great potential of pharmacologically active natural products in the prevention and treatment of human diseases and are currently conducting research on natural products. Investigators are trying to use a nanodrug delivery system to improve the limitations of its application and improve efficacy. Nanodrugs containing paclitaxel, camptothecin, curcumin, or resveratrol have been on the market or are used in clinical research, showing very promising results. Some polysaccharide natural products show nice pharmacological activities and can be used as excellent nanocarrier materials, which highlight the advantages and potential of natural products in the nanodrug field. So far, results of natural product-based nanopreparations in animal models show better stability and sustained release ability, as well as exhibit ideal therapeutics effects at low doses. In turn, this increases the safety of long-term use of this system (Figure 4).

However, the clinical transformation of these nanodrugs is still a challenge. One of the main reasons may be inconsistencies between the occurrence and development of human
and animal diseases. Long-term treatment of diseases is inevitable, which requires that designed nanodrugs must meet many criteria, such as stability in systemic circulation and release effective concentrations of drugs in the desired areas without affecting healthy tissues. It is worth noting that nanoparticles that deliver drugs can stimulate or inhibit the immune response and may remain in the body, which requires researchers to design appropriate nanodrugs and modify according to disease characteristics and drugs and carry out extensive immunotoxicology research before translating to the clinical. In the future, it is necessary to establish a complete clinical evaluation and detection system to achieve the transition from basic to clinical research.

In summary, we have entered a nanomedicine era of natural products. Even though there is still some way to go before this system is truly optimized, it is obvious that nanobased drugs on natural products show broad application prospects in modern medicine.

Data Availability

No data were used to support this study.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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