

Review Article

Biobased Nanomaterials in Drug Delivery System: Current Trends and Future Prospectives

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Abstract

Biobased nanomaterials have emerged as a transformative platform in drug delivery systems, offering significant advantages such as biocompatibility, biodegradability, and reduced toxicity compared to conventional synthetic nanocarriers. This review comprehensively explores current trends in the synthesis, functionalization, and application of biobased nanomaterials including polysaccharides, proteins, lipid-based carriers, dendrimers, and green-synthesized metallic nanoparticles in enhancing targeted and controlled drug delivery. Advances in surface modification techniques and stimuli-responsive designs have improved site-specific drug release and therapeutic efficacy, while combination therapies leveraging biobased nanocarriers address challenges like multidrug resistance. Pulmonary and personalized medicine applications highlight their versatility in achieving localized delivery and tailoring treatments to individual patient profiles. Despite challenges in large-scale production, stability, and regulatory approval, ongoing innovations in green synthesis, multifunctionality, and nanocarrier optimization position biobased nanomaterials to revolutionize drug delivery. Their integration into next-generation therapeutics promises improved clinical outcomes and a sustainable approach to precision medicine. This review emphasizes the eco-friendly, biocompatible, and biodegradable nature of biobased nanomaterials, addressing the urgent need for safer and more sustainable drug delivery platforms in modern medicine.

Keywords

Biobased Nanomaterials, Drug Delivery System, Biopolymers, Dendrimers, Biocompatibility

1. Introduction

Traditional drug delivery methods primarily include oral and parenteral administration. Oral delivery is the most common and convenient route which involves as a tablets, capsules, and solutions, offering high patient compliance and ease of use [1]. However, it faces limitations such as poor bioavailability due to degradation in the gastrointestinal tract, first-pass metabolism in the liver, and potential gastrointestinal irritation [1, 2]. Traditional drug delivery methods, such as oral and parenteral administration, have been widely used

but come with several significant limitations. Oral delivery is convenient and preferred for its ease of use and high patient compliance, often suffers from poor bioavailability due to drug degradation in the gastrointestinal tract and first-pass metabolism in the liver, which reduces the amount of active drug reaching systemic circulation [3]. Additionally, oral drugs can cause gastrointestinal irritation and may have limited drug loading capacity and stability issues. Parenteral routes bypass the gastrointestinal tract and provide rapid drug

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action but are invasive, can cause pain and risk of infection, and typically require trained healthcare professionals for administration [4]. Moreover, traditional methods generally lack precise control over drug release, leading to fluctuating drug levels that can compromise therapeutic efficacy and increase side effects [5]. They also suffer from non-specific distribution, causing systemic toxicity by affecting healthy tissues alongside target sites. Other challenges include poor solubility and permeability of drugs, instability under environmental conditions, and difficulties in targeting drugs to specific tissues or cells, especially across biological barriers like the blood-brain barrier [6]. These limitations have driven the development of novel drug delivery systems aimed at improving bioavailability, targeting, controlled release, and patient compliance [2].

Nanomaterials in drug delivery systems (NDDS) represent a most advanced approach that leverages nanoparticles (engineered materials) typically sized between 1 and 100 nanometers to improve the delivery and efficacy of therapeutic agents [7]. These nanomaterials possess unique physico-chemical properties, such as a high surface-area-to-volume ratio and tunable chemical and geometric features, which enable enhanced drug loading, stability, and controlled release [8]. One of the key advantages of NDDS is their ability to improve bioavailability by protecting drugs from degradation and facilitating their uptake across cellular membranes [9]. Additionally, nanomaterials enable targeted delivery by functionalizing their surfaces with ligands or antibodies that recognize specific receptors on diseased cells, thus concentrating the drug at the site of action while minimizing exposure to healthy tissues [10, 11]. This targeted approach not only increases therapeutic efficacy but also significantly reduces side effects and toxicity. Furthermore, NDDS can prolong drug circulation time and allow for controlled and sustained release, addressing limitations of traditional drug delivery methods [1]. Overall, nanomaterial-based drug delivery systems offer a promising strategy to overcome challenges such as poor solubility, nonspecific distribution, and rapid clearance, thereby enhancing safety and treatment outcomes in various diseases [12, 13].

Biobased nanomaterials are nanoscale materials derived from natural biological sources such as polysaccharides (cellulose, chitosan), proteins (albumin, silk fibroin), lipids, and other biomolecules [14, 15]. These materials are engineered to interact with biological systems, making them inherently biocompatible and often biodegradable, which reduces the risk of toxicity and adverse immune responses when used in drug delivery [14]. Their significance in enhancing biocompatibility lies in their natural origin and structural similarity to biological components, which allows them to be well tolerated by the body and to avoid triggering significant immune reactions [14]. Additionally, biobased nanomaterials can be finely tuned to control drug release kinetics, improve drug stability, and enable targeted delivery to specific tissues or cells by minimizing systemic side effects and enhancing

therapeutic efficacy [8]. Their biodegradability further ensures that they break down into non-toxic byproducts, reducing long-term accumulation and toxicity risks [16].

Generally, biobased nanomaterials offer a safer and more effective platform for drug delivery by combining natural biocompatibility with the ability to precisely control drug release and targeting, ultimately improving patient outcomes while reducing toxicity [17-19]. This review aims to provide a comprehensive overview of biobased nanomaterials and their role in advancing drug delivery systems, highlighting their biocompatibility, biodegradability, and targeted delivery capabilities.

2. Types of Biobased Nanomaterials

Biobased nanomaterials have emerged as promising candidates in drug delivery systems due to their biocompatibility, biodegradability, and ability to be derived from natural sources, minimizing toxicity and environmental impact [8]. Various types of biobased nanomaterials are extensively studied and utilized for targeted and controlled drug delivery, such as Protein-Based Nanomaterials, Biodegradable polymer, Polysaccharide-Based Nanomaterials, Dendrimers, Lipid-Based Nanostructures and Green-Synthesized Metallic Nanoparticles [15, 20].

2.1. Protein Based Nanomaterials

Protein based nanomaterials for drug delivery are synthesized through several methods, which primarily categorized into chemical, physical, and self-assembly approaches [21]. Chemical methods include emulsion and complex coacervation techniques, which allow control over nanoparticle size and shape and achieve high encapsulation efficiency though they may require surfactants and stabilizers and can produce relatively larger particles [22]. Physical methods such as electrospray and nano spray drying generate small, stable nanoparticles under mild conditions suitable for heat sensitive drugs; electrospray is scalable but may cause some macromolecule degradation due to operational stresses, while nano spray drying is cost-effective but limited to small scale production and less suited for hydrophobic drugs [23]. The self-assembly method, including desolvation, involves proteins forming nanoparticles spontaneously in response to changes in solvent conditions, producing highly stable and small particles with excellent drug loading, though it is applicable only to proteins tolerant of the process conditions [21].

These protein nanoparticles exhibit crucial properties such as biocompatibility, biodegradability, and the ability to protect encapsulated drugs from enzymatic degradation and renal clearance, thereby improving drug stability, activity, and half-life [24]. Their size, surface characteristics, and morphology can be finely tuned through synthesis parameters, enabling controlled and sustained drug release. Additionally,

surface modification allows targeted delivery, enhancing therapeutic efficacy while minimizing side effects. Protein-based nanomaterials have been successfully applied in delivering a variety of therapeutics including anticancer drugs, proteins, peptides, and nucleic acids [25]. They facilitate cellular uptake via endocytosis and are used in targeted therapies for cancer, lung diseases, and vaccines. Overall, protein-based nanomaterials offer a versatile, safe, and effective platform for drug delivery, overcoming many limitations of traditional methods through improved bioavailability, targeted delivery and reduced toxicity [26].

2.2. Biodegradable Polymer

Biodegradable polymers used in drug delivery systems are synthesized through various methods that allow precise control over their properties to achieve efficient, targeted, and sustained drug release [27]. Common synthesis techniques include emulsion-based methods (single and double emulsion), nanoprecipitation, solvent evaporation, and polymerization, which enable the fabrication of nanoparticles, micro-particles, hydrogels, and implantable devices tailored for specific therapeutic needs [28]. These polymers, both natural (chitosan, alginate, collagen) and synthetic (polylactic acid [PLA] and polyglycolic acid [PGA], which degraded in the body into non-toxic metabolites such as carbon dioxide and water, which is used to eliminate the need for surgical removal [29]. Their degradation rate can be finely tuned by modifying chemical composition, crystallinity, and hydrophilicity, allowing controlled and predictable drug release profiles [30].

Biodegradable polymers exhibit key properties including biocompatibility, biodegradability, mechanical strength, and the ability to protect encapsulated drugs from premature degradation, thereby enhancing drug stability and bioavailability [31]. They facilitate localized delivery, reducing systemic side effects and enable sustained drug release, which improves patient compliance by decreasing dosing frequency [32]. Moreover, their surfaces can be modified to improve muco-adhesion or target specific tissues with optimizing therapeutic outcomes. Applications of biodegradable polymers span a wide range of drug delivery fields, notably ocular drug delivery which overcome anatomical barriers to provide sustained release for conditions like glaucoma and retinal diseases as well as colon-specific delivery, cancer therapy, and vaccine administration [33]. Their versatility is demonstrated by their use in nanoparticles, hydrogels, microspheres, and implantable devices, making them a cornerstone in advanced, safe, and effective drug delivery systems [34].

2.3. Polysaccharide Based Nanomaterials

Polysaccharide based nanomaterials are widely employed in drug delivery systems due to their biocompatibility, biodegradability, and abundance from natural sources [35]. They are synthesized using various methods such as nanoprecipitation,

complex coacervation, emulsification, and advanced techniques like microfluidics, which allow precise control over particle size, morphology, and drug loading capacity. These methods exploit the chemical functionality of polysaccharides mainly their free carboxyl and hydroxyl groups to form stable nanoparticles that can encapsulate a variety of drugs efficiently [36]. Polysaccharide nanoparticles exhibit favorable properties including high drug loading efficiency, fast and controlled drug release rates, good targeting ability, and low toxicity in physiological environments. Their surfaces can be chemically modified to enhance stability, targeting specificity, and interaction with biological systems [37]. Applications of polysaccharide-based nanomaterials in drug delivery are diverse, which ranging from oral and intestinal targeted delivery to anticancer therapy [38]. For example, polysaccharide-gold nanocomplexes have been developed to improve drug stability and enable controlled release, while functionalized nanoparticles have shown effective delivery of poorly water-soluble drugs and enhanced tumor targeting. Generally, polysaccharide-based nanomaterials offer a sustainable, versatile, and effective platform for improving drug bioavailability, reducing side effects, and achieving precise delivery to target tissues [39].

2.4. Dendrimers

Dendrimers are highly branched, monodisperse, and radially symmetric nanoscale polymers synthesized mainly via two approaches: the divergent and convergent methods [40]. The divergent synthesis was developed by Tomalia in the 1980s, begins from a multifunctional core molecule and grows outward by successive addition of monomer units, generating dendrimers with increasing generations and surface functional groups. This method allows rapid growth and high payload capacity, making it suitable for drug delivery and imaging applications, but it can produce structural defects due to side reactions and requires excess monomer to minimize by-products [41, 42]. The convergent approach was introduced by Hawker and Fréchet in 1990, which involves first synthesizing dendritic branches (dendrons) which are then attached to a core, offering better control over structure, fewer impurities, and precise surface functionalization. However, it is more labor-intensive, limited in dendrimer size due to steric hindrance, and less suited for large-scale production. Dendrimers possess unique properties including a well-defined architecture, high degree of branching, tunable surface chemistry, internal cavities for drug encapsulation, and excellent water solubility [43]. These features enable high drug loading capacity through covalent or non-covalent interactions, enhanced bioavailability, controlled and targeted drug release, and improved cellular penetration [40]. In drug delivery, dendrimers are used as carriers for anticancer drugs, gene delivery vectors, and imaging agents, facilitating targeted delivery and reducing systemic toxicity. Their ability to conjugate drugs or encapsulate them within their structure

prolongs drug half-life and allows for stimuli-responsive release [44]. Despite challenges like potential toxicity and synthesis complexity, dendrimers remain a promising platform for multifunctional, efficient, and safe drug delivery systems [45].

2.5. Lipid-based Nanostructures

Lipid-based nanostructures, including solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), are synthesized using a variety of methods that enable efficient drug encapsulation and controlled release [46]. The most widely used synthesis techniques include high-pressure homogenization (HPH), microemulsion, ultrasonic homogenization, thin-film hydration, and nanoprecipitation [12]. High-pressure homogenization, a top-down approach, involves forcing molten lipids and surfactants through narrow orifices at high pressure, creating fine emulsions that solidify into nanoparticles upon cooling. This method supports large-scale production and yields particles with controlled size and stability. The microemulsion method forms lipid nanoparticles by dispersing a warm lipid phase into an aqueous surfactant solution, followed by rapid cooling, though it requires high surfactant concentrations and dilution steps [47]. Ultrasonic homogenization uses cavitation energy to break down lipid particles but may cause lipid degradation and low encapsulation efficiency [48]. Bottom-up methods like thin-film hydration dissolve lipids in organic solvents to form thin films that upon hydration, self-assemble into nanoparticles. However, this method often suffers from poor size control and batch variability [49, 50]. Nanoprecipitation, a solvent-based self-assembly technique, mixes lipid-containing organic solvents with aqueous phases, triggering nanoparticle formation through rapid solvent diffusion; this method offers excellent size control and high encapsulation efficiency and is favored in advanced formulations such as mRNA vaccines [51]. Lipid-based nanostructures exhibit key properties including biocompatibility, biodegradability, high drug loading capacity, protection of labile drugs, and the ability to encapsulate both hydrophilic and hydrophobic molecules [52]. Their amphiphilic nature allows for controlled and targeted drug release, improved bioavailability, and reduced systemic toxicity [48]. Applications span a wide range of therapeutic areas, including cancer treatment, gene therapy, vaccine delivery, and neurological disorders, where they facilitate crossing biological barriers and enhance cellular uptake [53]. Generally, lipid-based nanostructures represent a versatile and effective platform for modern drug delivery systems, combining scalable synthesis methods with favorable physicochemical and biological properties [54].

2.6. Green Synthesized Metallic Nanoparticles

Green synthesized metallic nanoparticles (MNPs) are produced using eco-friendly, cost-effective and sustainable

methods that utilize biological resources such as plants, bacteria, fungi, and algae as reducing and stabilizing agents [55]. Unlike conventional chemical and physical synthesis methods that often involve toxic chemicals and high energy consumption, green synthesis leverages natural biomolecules like phytochemicals in plant extracts to reduce metal ions to their zero valent nanoparticle form under mild conditions, minimizing environmental impact and toxicity [56]. Commonly used biological sources include leaf, bark, fruit, and root extracts, which contain compounds such as polyphenols, flavonoids, and proteins that act as both reducing and capping agents, controlling nanoparticle size and shape [57]. The synthesis process typically involves mixing metal salt solutions with the biological extract, leading to nucleation, growth, and stabilization phases that yield stable nanoparticles with tunable physicochemical properties [58]. Characterization techniques such as UV-Vis spectroscopy, TEM, and XRD confirm nanoparticle formation and morphology [59]. Green synthesized MNPs, including silver, gold, copper, and iron nanoparticles, exhibit excellent biocompatibility, enhanced antimicrobial and anticancer activities, and reduced side effects compared to chemically synthesized counterparts [60]. Their unique optical, electronic, and surface properties make them effective carriers for drug delivery, enabling targeted therapy, controlled drug release, and improved bioavailability [57]. Due to their biocompatibility and environmentally benign synthesis, green MNPs hold great promise for applications in nanomedicine, including cancer treatment, antimicrobial therapies, and diagnostic imaging, while addressing sustainability concerns in nanotechnology [61].

3. Current Trends in Biobased Nanomaterials for Drug Delivery

Current trends in biobased nanomaterials for drug delivery emphasize the integration of sustainability, biocompatibility, and advanced targeting capabilities to overcome limitations of traditional therapies [62]. Innovations focus on developing multifunctional nanocarriers derived from natural polymers and biomolecules that offer improved bioavailability, controlled release and reduced systemic toxicity [63]. Biobased nanomaterials such as polysaccharides, proteins, and biodegradable polymers are being engineered with surface modifications and ligand attachments to enhance targeted delivery and cellular uptake [57]. The use of lipid nanoparticles (LNPs), notably demonstrated by mRNA COVID-19 vaccines, exemplifies how biobased carriers protect sensitive biologics and enable precise delivery to target cells, driving a surge in RNA-based therapeutics and vaccines [64]. Additionally, green-synthesized metallic nanoparticles using plant extracts and microbial processes are gaining attention for their eco-friendly production and enhanced safety profiles [1].

Emerging technologies include stimuli-responsive nanocarriers that release drugs in response to pH, temperature,

or enzymatic triggers, enabling smart and localized therapy particularly in oncology and chronic diseases [65, 66]. The convergence of nanobiotechnology with materials engineering and micro-robotics is also opening new avenues for highly controlled and personalized drug delivery, where biobased nanomaterials serve as biocompatible platforms for these innovations [67]. Furthermore, advances in scalable and reproducible synthesis methods are facilitating the translation of biobased nanomaterials from laboratory research to clinical applications. Generally, the trend is toward environmentally sustainable, patient-centric drug delivery systems that combine the natural advantages of biobased materials with cutting-edge nanotechnology to enhance therapeutic efficacy and safety [68].

3.1. Targeted Drug Delivery

Targeted drug delivery using biobased nanomaterials often involves surface modification of nanoparticles with targeting ligands such as antibodies, peptides, and aptamers to achieve tumor-specific recognition [69, 70]. These ligands bind selectively to receptors overexpressed on cancer cells, enhancing cellular uptake and minimizing off-target effects. Additionally, stimuli-responsive nanoparticles are designed to release their drug payload in response to specific environmental triggers found in diseased tissues, such as the acidic pH, elevated enzyme levels, redox conditions, or temperature variations characteristic of tumor microenvironments [62]. For example, pH-responsive nanoparticles exploit the slightly acidic tumor milieu to trigger drug release, while redox-responsive systems utilize higher intracellular glutathione concentrations in cancer cells to cleave disulfide bonds and release drugs intracellularly. Multi-stimuli responsive systems combining pH, redox, and enzymatic triggers enable precise, on-demand drug release, improving therapeutic efficacy and reducing systemic toxicity [71, 65].

For instance, biobased nanomaterials used for targeted delivery include polysaccharide-based nanoparticles functionalized with ligands for cancer therapy, protein-based nanocarriers engineered for receptor-mediated uptake, and lipid-based nanostructures such as liposomes modified with targeting moieties for cardiovascular and infectious diseases [72, 73]. Stimuli responsive biobased nanocarriers have been applied in cancer, infections, and cardiovascular diseases, where controlled drug release enhances treatment outcomes [74]. For instance, keratin-based nanoparticles have been developed for triple stimuli responsive delivery (pH, glutathione, enzyme) of anticancer drugs, demonstrating improved release profiles and targeting [71]. Generally, combining surface ligand modification with stimuli responsive mechanisms in biobased nanomaterials offers a powerful strategy for precise, efficient, and safe targeted drug delivery across various diseases [75].

3.2. Combination Therapies

Combination therapies using nanodrug delivery systems (NDDS) have become a pivotal strategy to overcome drug resistance and improve therapeutic efficacy, particularly in cancer treatment [76, 77]. Biobased nanocarriers enable the co-delivery of multiple drugs with different physicochemical properties within a single nanoparticle, maintaining optimized synergistic drug ratios and ensuring simultaneous intracellular uptake by target cells [58]. This approach addresses challenges such as multidrug resistance (MDR), narrow therapeutic windows, and systemic toxicity associated with monotherapies [78, 79]. Integration of chemotherapy, immunotherapy, and targeted therapies using biobased nanomaterials, such as polymeric nanoparticles, liposomes, dendrimers, and hybrid nanocarriers has shown enhanced tumor targeting, reduced side effects, and improved pharmacokinetics [80].

For instance, polymeric nanoparticles co-encapsulating paclitaxel and the P-glycoprotein modulator tariquidar, surface-functionalized with biotin for tumor targeting, demonstrated significantly higher cytotoxicity and tumor growth inhibition compared to single drug formulations, effectively overcoming MDR [49]. Similarly, curcumin loaded chitosan nanoparticles enhanced cellular uptake and cytotoxicity in cervical cancer cells versus free curcumin. Another notable example is a biodegradable triple block nanocarrier combining polyethylene glycol (PEG), polycaprolactone (PCL), and a carboxyl functionalized core to co-deliver doxorubicin and cisplatin, achieving synergistic cell killing in breast cancer cells even when free drugs were antagonistic [81]. Micellar nanoparticles functionalized with phage proteins have also been used to selectively deliver paclitaxel to breast cancer cells, showing extensive tumor reduction and necrosis in preclinical models [77]. Additionally, dual-drug co-delivery systems using amphiphilic diblock copolymers have successfully delivered doxorubicin and platinum-based drugs simultaneously, enhancing cellular uptake and therapeutic outcomes [82]. Basically, biobased nanomaterial mediated combination therapies offer a promising platform for synergistic, targeted, and controlled delivery of multiple therapeutics, thereby enhancing efficacy, reducing drug resistance and minimizing adverse effects in cancer and other diseases [83].

3.3. Pulmonary Drug Delivery

Pulmonary drug delivery using inhalable nanodrug delivery systems (NDDS) offers a promising strategy for direct administration of therapeutics to lung tumors, thereby minimizing systemic side effects common in conventional chemotherapy [84, 85]. These biobased nanomaterials, such as biodegradable polymeric nanoparticles, lipid-based carriers, and ligand-functionalized nanocomplexes, facilitate localized drug delivery by enhancing drug retention and permeability within lung tissues while overcoming physiological barriers like the mucus layer and mucociliary clearance [86]. Strategies to improve drug retention include engineering nanopar-

ticles with mucoadhesive properties, optimizing particle size and surface charge to enhance mucus penetration, and employing stimuli responsive materials that release drugs in response to the lung's microenvironment (pH or enzymes) [87, 88]. For instance, gelatin-based nanoparticles conjugated with epidermal growth factor ligands have demonstrated increased localized drug concentration and therapeutic efficacy in metastatic lung cancer models, while inhalable doxorubicin nanoparticles decorated with tumor necrosis factor related apoptosis inducing ligand (TRAIL) showed synergistic tumor targeting and apoptosis induction [89, 85].

Despite these advances, pulmonary drug delivery faces challenges such as variability in lung function among patients affecting drug deposition, difficulties in quantifying drug release specifically at tumor sites, and potential local toxicity from high drug concentrations [44]. Furthermore, aerosolization technology requires refinement to improve dose control, reproducibility, and patient compliance [90]. Future directions emphasize the development of multifunctional biobased nanocarriers capable of precise tumor targeting, controlled and sustained release and immune system modulation, including nano-based vaccines delivered via the pulmonary route to enhance anti-tumor immunity [91]. Generally, biobased nanomaterials for pulmonary drug delivery hold significant potential to revolutionize lung cancer treatment by maximizing local drug efficacy while reducing systemic toxicity and improving patient quality of life [92].

3.4. Advances in Nanocarriers

Advances in nanocarriers have focused on optimizing their size, shape, and surface properties to enhance biocompatibility, prolong circulation time and improve targeting efficiency [93]. Techniques such as controlling synthesis parameters and employing surface modification strategies enable precise tuning of these characteristics [94]. For instance, NLCs composed of a mixture of solid and liquid lipids offer superior drug loading capacity, enhanced physical stability and biocompatibility compared to earlier lipid-based systems like SLNs [95, 96]. Their small size and occlusive nature improve drug permeation and retention, making them ideal for delivering drugs through challenging routes while reducing side effects [97]. Polymer based nanoparticles also contribute to improved drug solubility and controlled release, though they may face challenges like immune response; hybrid lipid-polymer nanoparticles combine the advantages of both enhancing encapsulation efficiency and stability [73, 98].

Surface modification techniques such as PEGylation (attachment of polyethylene glycol chains), ligand conjugation (antibodies, peptides) and charge modulation are widely used to improve nanoparticle stability, reduce recognition and clearance by the immune system and enhance cellular uptake and targeting specificity [62, 99, 100]. PEGylation increases circulation time by providing a hydrophilic stealth coating, while ligand conjugation facilitates receptor mediated endo-

cytosis for targeted delivery [101, 102]. Charge modulation can improve interaction with cell membranes or mucus barriers depending on the therapeutic context. These advances in nanocarrier design and surface engineering enable the development of safe, effective, and targeted drug delivery systems with broad applications in cancer, infections, neurodegenerative diseases, and more [103-105].

4. Applications in Personalized Medicine

Biobased nanoparticles play a crucial role in personalized medicine by enabling the tailoring of medical therapies to individual patients based on their specific disease profiles [106-108]. Nanodrug delivery systems (NDDS) can be engineered to improve drug bioavailability and absorption rates, allowing for more precise control over drug release timing and enhanced solubility of poorly water-soluble drugs [109]. This customization ensures that therapeutic agents are delivered efficiently at optimal doses, reducing side effects and improving treatment outcomes [110, 111]. By adjusting nanoparticle composition, size, and surface characteristics, NDDS can address patient-specific factors such as genetic variations, disease stage, and tissue environment, ultimately supporting more effective and individualized treatment regimens [112, 113]. This approach is particularly valuable in complex diseases like cancer and infections, where targeted delivery and controlled release are essential for maximizing therapeutic efficacy while minimizing systemic toxicity [72, 106, 114].

5. Challenges and Future Perspectives

Biobased nanomaterials in drug delivery systems hold tremendous promise due to their biocompatibility, biodegradability and potential for targeted and controlled drug release [14, 115]. However, several challenges continue to limit their widespread clinical translation. Key difficulties include ensuring consistent biocompatibility and minimizing toxicity, as some nanomaterials may induce unintended immune responses or accumulate in organs causing adverse effects [116-119]. Stability of biobased nanoparticles during storage and in physiological environments is another concern, as degradation or aggregation can impair drug delivery efficiency [1, 120, 121]. Achieving high targeting efficiency remains difficult due to biological barriers such as the blood-brain barrier, tumor microenvironment heterogeneity and mucus layers, which restrict nanoparticle penetration and accumulation at disease sites [122-124]. Additionally, large scale, reproducible and cost-effective manufacturing of biobased nanomaterials with precise control over size, shape, and surface properties is still challenging [125]. Regulatory hurdles and the need for comprehensive safety evaluation protocols further slow clinical adoption [125, 126].

Future perspectives focus on innovative nanoparticle de-

signs incorporating stimuli-responsive and multifunctional features to enhance site-specific drug release and reduce side effects [127, 128]. Surface modification techniques like PEGylation, ligand conjugation, and charge modulation are being refined to improve circulation time and targeting specificity [126]. Advances in green synthesis and scalable production methods aim to address environmental and economic concerns. Integration of biobased nanomaterials with personalized medicine approaches promises tailored therapies with improved efficacy and safety [126, 129]. Furthermore, combining drug delivery with diagnostic capabilities (theranostics) is an emerging trend. Continued interdisciplinary research and collaboration among material scientists, biologists, and clinicians will be crucial to overcoming current limitations and realizing the full potential of biobased nanomaterials in next-generation drug delivery systems [130].

6. Conclusion

Biobased nanomaterials have significantly advanced drug delivery by offering enhanced bioavailability, targeted delivery, controlled release and reduced toxicity compared to conventional (traditional) systems. Their natural origin ensures biocompatibility and biodegradability, while surface functionalization with ligands improves targeting specificity and therapeutic efficacy. These nanomaterials enable precise drug delivery to diseased sites, minimizing systemic side effects and improving patient outcomes. Innovations such as polymer-lipid hybrid nanoparticles combine the strengths of multiple materials to achieve high stability, sustained release and efficient encapsulation for further enhancing treatment effectiveness. Moreover, biobased nanocarriers facilitate the integration of combination therapies and personalized medicine, tailoring treatments to individual patient profiles and disease characteristics. This versatility positions biobased nanomaterials as transformative tools in modern medicine, promising to revolutionize personalized therapies and significantly improve therapeutic outcomes across a broad spectrum of diseases. Addressing challenges in achieving scalable manufacturing, demonstrating long-term biosafety and meeting regulatory standards for clinical adoption will require interdisciplinary collaboration to unlock the full potential of biobased nanomaterials, ultimately paving the way for safer, more efficient therapeutic interventions across diverse medical applications.

Abbreviations

HPH	High Pressure Homogenization
MDR	Multidrug Resistance
MNP	Metallic Nanoparticles
NDDS	Nanomaterial In Drug Delivery System
NLC	Nanostructured Lipid Carriers

PCL	Polycaprolactone
PEG	Polyethylene Glycol
PGA	Polyglycolic Acid
PLA	Polylactic Acid
SLN	Solid Lipid Nanomaterials
TEM	Transmission Electron Microscope
TRAIL	Tumor Necrosis Factor Related Apoptosis Inducing Ligand
XRD	X-Ray Diffraction

Author Contributions

Alebachew Molla is the sole author. The author read and approved the final manuscript.

Conflicts of Interest

The author declares no conflicts of interest.

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