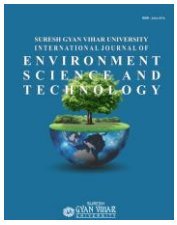

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Review article

Overviewing the Progress of Self-Assembled Organic Nanoparticles towards Effective Therapeutic Delivery

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Abstract

Nanotechnology has significantly influenced therapeutic delivery in recent years, with self-assembled organic nanoparticles (SAONs) gaining prominence due to their unique physicochemical properties. These nanocarriers spontaneously organize through non-covalent interactions, forming highly structured and biocompatible assemblies from organic constituents such as polymers, lipids, and peptides. Compared to conventional drug delivery vehicles, SAONs offer enhanced flexibility in encapsulating diverse therapeutic agents including chemotherapeutics and nucleic acids while enabling controlled release and site-specific targeting. This review elucidates the fundamental principles of nanoparticle self-assembly, the materials utilized in their synthesis, and the current methodologies for functionalization. It further explores their application across therapeutic domains, such as in oncology and gene therapy, where promising preclinical outcomes have been observed. This overview provides a comprehensive perspective on optimizing SAONs for safe and effective therapeutic delivery.

INTRODUCTION

The intersection of chemistry, nanotechnology, and medicine has led to transformative advancements in therapeutic delivery systems. At the forefront of these innovations are self-assembled organic nanoparticles (SAONs), which are a class of nanoscale carriers that spontaneously form well-defined structures through non-covalent interactions. These systems are highly tunable and have garnered significant attention for their potential in addressing the limitations of conventional drug delivery, especially in the treatment of complex diseases

such as cancer, infections, and genetic disorders. Traditional drug administration methods are often hindered by poor solubility, rapid clearance, non-specific distribution, and dose-limiting toxicity. These drawbacks necessitate the development of advanced delivery platforms capable of enhancing bioavailability, prolonging systemic circulation, and enabling controlled, site-specific drug release.

Nanoparticles have emerged as one of the most promising solutions, with various inorganic and organic formulations under extensive investigation. Among these, SAONs offer distinct advantages due to their biocompatibility, biodegradability, and structural versatility. (Joseph et al., 2023) These nanoparticles are assembled under physiological or near-physiological conditions via weak intermolecular forces such as hydrogen bonding, π–π stacking, electrostatic interactions, and hydrophobic effects. (Caputo et al., 2013) The resulting structures exhibit dynamic behavior and can respond to environmental stimuli, making them ideal candidates for intelligent drug delivery applications. In particular, the incorporation of stimuli-responsive elements is one of the most powerful features of SAONs. These elements allow nanoparticles to undergo physicochemical changes such as swelling, disassembly, or surface charge reversal in response to specific endogenous triggers (e.g., acidic pH in tumors, high glutathione concentration in cancer cells, or disease-associated enzymatic activity) or external triggers (such as heat, magnetic fields, ultrasound, or light irradiation). Such responsiveness ensures that therapeutic payloads are released only at the desired site, thereby minimizing systemic toxicity and enhancing therapeutic efficacy. (Joseph et al., 2023; Caputo et al., 2013) For example, pH-sensitive polymeric micelles disassemble in acidic tumor microenvironments to release anticancer drugs, while redox-responsive vesicles exploit intracellular glutathione gradients to enable selective cytoplasmic drug release. Similarly, enzyme-cleavable peptide linkages in SAONs facilitate the release of payloads in tissues overexpressing disease-related proteases, thereby achieving a high degree of spatiotemporal precision.

Organic materials such as lipids, peptides, amphiphilic block copolymers, and polysaccharides serve as foundational components for SAON construction. (Bodratti et al., 2018) These materials offer tunable physicochemical characteristics and facilitate the encapsulation of a wide range of therapeutic agents, including small-molecule drugs, proteins, RNA, and genome-editing systems like CRISPR.(Kim et al., 2024) Furthermore, their structures can be engineered to enable stimuli-responsive release triggered by pH change, redox gradients, enzymatic activity, or external stimuli such as heat or light.(El-Husseiny et al., 2022) This adaptability provides an added advantage in tailoring delivery vehicles for specific diseases, where the biological environment can be exploited as a natural switch for drug release. For instance, thermoresponsive liposomes have been designed to release their content when exposed to mild hyperthermia at tumor sites, and light-sensitive nanoparticles enable on-demand drug release with spatiotemporal precision when illuminated with near-infrared (NIR) radiation. These examples

highlight how stimuli-responsive elements transform SAONs from passive carriers into "smart" systems that actively participate in therapeutic delivery.

In addition to cancer and genetic disorders, SAONs have also been explored for antimicrobial and antiviral therapies. For instance, peptide- and polymer-based SAONs have been engineered to encapsulate antimicrobial peptides or antibiotics, improving their stability and enabling controlled release at infection sites. Similarly, lipid- and polymeric-SAONs have been investigated as carriers for antiviral agents, including nucleoside analogues and RNA-based therapeutics, where stimuli-responsiveness can enhance drug penetration into infected cells while reducing systemic toxicity. (Bodratti et al., 2018; Kim et al., 2024)

Despite considerable progress, challenges remain. The reproducibility of the self-assembly process is highly sensitive to environmental conditions, which complicates manufacturing scalability and clinical translation. Biological safety and immunogenicity also require thorough evaluation, as accumulation in organs and immune interactions may pose risks. Additionally, intracellular delivery barriers such as endosomal entrapment necessitate advanced strategies to ensure effective cytosolic release. Finally, the path to clinical application is further hindered by the need for scalable manufacturing techniques, regulatory approval frameworks, and standardized characterization protocols. Addressing these limitations is critical to advancing SAONs from preclinical research to practical, patient-ready therapeutics. (Kim et al., 2024; El-Husseiny et al., 2022)

This review aims to provide a comprehensive overview of SAONs, including their design principles, material selection, self-assembly mechanisms, surface functionalization strategies, and therapeutic applications. It further discusses how nanoparticle architecture influences biological performance, identifies translational bottlenecks, and outlines potential pathways to overcome existing challenges.

*1. **Mechanistic Insights into Self-Assembly***

Self-assembly is a foundational concept in nanotechnology and supramolecular chemistry, referring to the spontaneous organization of molecular components into ordered structures through non-covalent interactions. This process is driven by the natural tendency of molecules to attain a thermodynamically favorable configuration, thereby minimizing free energy. In the context of therapeutic delivery, the ability of organic molecules to form self assembled nanoparticles allows for the construction of dynamic, functional carriers capable of encapsulating and delivering therapeutic agents with high precision.

*1.1 **Fundamental Driving Forces***

The formation of self-assembled nanoparticles is primarily governed by weak, reversible interactions such as hydrogen bonding, hydrophobic interactions, electrostatic interactions, and π–π stacking. These molecular forces collectively determine the initiation, stability, and final morphology of the nanoparticles.

Hydrogen bonding is widely observed in peptide- and nucleic acid-based systems, where it stabilizes secondary structures such as β-sheets and helices, thereby influencing nanoparticle shape and rigidity. (Delfi et al., 2021) DNA nanostructures and peptide amphiphiles represent typical examples in which directional hydrogen bonding guides ordered assembly.

Hydrophobic interactions occur in amphiphilic molecules that contain both hydrophilic and hydrophobic domains. In aqueous environments, these molecules spontaneously organize to reduce contact of the hydrophobic moieties with water, leading to the formation of core–shell structures such as micelles and bilayered vesicles. (Chen et al., 2021) Polymeric micelles formed from block copolymers like PEG–PLA and lipid-based vesicles are common examples. The structural properties of micelles include a hydrophobic inner core that can solubilize poorly water-soluble drugs and a hydrophilic corona that ensures aqueous stability and prolonged circulation. Vesicles, on the other hand, exhibit a bilayer membrane enclosing an aqueous core, which allows simultaneous encapsulation of both hydrophobic agents (within the bilayer) and hydrophilic molecules (within the core). This dual-loading capacity makes vesicles versatile platforms for diverse therapeutics. In practical applications, micelles are often preferred for solubilizing small hydrophobic drugs, whereas vesicles are selected when both hydrophilic and hydrophobic cargos need to be delivered together, offering greater formulation flexibility.

Electrostatic interactions arise from attractions between oppositely charged groups, enabling the formation of polyelectrolyte complexes. (Insua et al., 2016) For example, cationic polymers such as polyethyleneimine (PEI) or chitosan interact with negatively charged nucleic acids to form stable nanoparticles for gene delivery. The balance of charge density strongly influences particle stability and release kinetics, making electrostatics a powerful but tunable driving force.

π–π stacking interactions are characteristic of aromatic systems such as polyphenols and porphyrins, where delocalized electron clouds promote stacking and improve nanoparticle stability. (Zhao et al., 2016) This interaction is particularly useful for the incorporation of aromatic drugs such as doxorubicin or for engineering porphyrin-based nanostructures in photodynamic therapy.

Together, these driving forces act in combination to stabilize SAONs and dictate key parameters such as size, shape, assembly kinetics, and drug-loading efficiency. Importantly, the interplay of hydrophobic interactions with micelle and vesicle formation highlights how fundamental forces not only drive self-assembly but also directly shape the structural and functional properties of the resulting nanocarriers.

1.2 ***Thermodynamics and Kinetics of Assembly***

Self-assembly is predominantly a thermodynamically driven process that requires a negative change in Gibbs free energy (ΔG). Favorable enthalpic contributions from noncovalent interactions and entropic gains such as the displacement of structured water molecules during hydrophobic assembly facilitate spontaneous nanoparticle formation. (Schauperl et al., 2016) However, kinetic parameters also play a

critical role. Variables such as temperature, pH, solvent polarity, and mixing speed can influence the rate and pathway of assembly. (Homocianu et al., 2020) In some cases, systems may traverse metastable intermediate states before reaching a stable thermodynamic minimum. Controlling both kinetic and thermodynamic aspects is vital for achieving reproducible nanoparticle formulations with desirable functional attributes.

1.3 ***Role of Amphiphilicity in Nanostructure Formation***

The amphiphilic molecules, containing distinct hydrophobic and hydrophilic regions, are particularly effective in forming a wide range of nanostructures. These include micelles, vesicles, and bilayers, all of which are instrumental in therapeutic delivery applications. For instance, block copolymers such as poly(ethylene glycol)-b-poly(lactic acid) (PEG-PLA) and poly(ethylene glycol)-b-poly(caprolactone) (PEG-PCL) self-assemble into core-shell micelles in aqueous environments. (Negut et al., 2023) The hydrophobic core encapsulates lipophilic drugs, while the hydrophilic corona provides steric stabilization and prolongs circulation time. Similarly, lipid-based molecules naturally form liposomes and solid lipid nanoparticles, which have been successfully employed in multiple FDA approved therapies. Peptide amphiphiles further expand the design space by forming nanofibers and hydrogels with inherent bioactivity. (Homocianu et al., 2020)

1.4 ***Morphological Control and Environmental Responsiveness***

The morphology and functionality of SAONs can be finely tuned by adjusting molecular design parameters and environmental conditions. Factors such as block copolymer composition, chain length, and the hydrophilic-to hydrophobic ratio directly impact the resulting particle's size, shape, and internal structure. The incorporation of stimuli-responsive elements into the nanoparticle design enhances their functional adaptability. For example, pH-sensitive linkers that are cleaved in acidic environments (e.g., tumor tissues or endosomes/lysosomes) and redox-responsive disulfide bonds that degrade in the presence of intracellular glutathione serve as notable elements in this category. (Liu et al., 2020) Similarly, thermosensitive polymers have also been known to alter solubility based on temperature changes. Such strategies enable "smart" delivery systems capable of releasing their therapeutic payloads in response to specific biological cues, thereby minimizing systemic toxicity and improving therapeutic index.

2. ***Materials and Nanoparticle Architectures***

The design of self-assembled organic nanoparticles (SAONs) is fundamentally influenced by the selection of constituent materials and the architecture they form. These materials not only dictate the stability, morphology, and functionality of the nanoparticles but also determine their interactions with biological systems, encapsulation efficiency, release profile, and biodegradation behavior. This section outlines the major classes of organic building blocks used in SAON construction namely polymers, lipids, peptides, and polysaccharides and explores the diverse nanoparticle architectures derived from these materials (Figure 1).

2.1 ***Polymeric Nanoparticles***

The polymers are among the most adaptable materials for self assembled nanoparticles due to their tunable chemical structures, which allow precise control over molecular weight, hydrophilic-hydrophobic balance, degradability, and functionalization. Amphiphilic block copolymers spontaneously form micelles or vesicles in aqueous environments, where the hydrophobic core encapsulates lipophilic drugs and the hydrophilic corona imparts colloidal stability and prolonged circulation. The biodegradable polymers such as poly(lactic acid) (PLA), poly(glycolic acid) (PGA), and their copolymer PLGA are extensively used due to their regulatory approval and favorable degradation profiles. (Makadia et al., 2011) Conjugation with poly(ethylene glycol) (PEG) enhances biocompatibility and minimizes recognition by the mononuclear phagocyte system. (Knop et al., 2010) Additionally, stimuli-responsive polymers that react to pH, temperature, or enzymatic activity enable spatially and temporally controlled drug release.

2.2 ***Lipid-Based Architectures***

The lipid-based nanoparticles, including liposomes and solid lipid nanoparticles (SLNs), have garnered significant attention for their structural similarity to biological membranes and excellent biocompatibility. (Akbarzadeh et al., 2013) Liposomes comprising one or more phospholipid bilayers can encapsulate both hydrophilic and hydrophobic agents, making them highly versatile for drug delivery applications. Their ease of functionalization, stability, and capacity for large-scale production have contributed to their clinical success. Notably, the use of lipid nanoparticles in mRNA vaccine delivery has underscored their potential in immunotherapy and gene delivery. Current research also explores hybrid lipid-polymer systems that integrate the benefits of both material types.

2.3 ***Peptide-Based Nanostructures***

The peptides are attractive building blocks for nanoparticle design due to their inherent biocompatibility, biodegradability, and sequence programmability. (Habibi et al., 2016) The short peptide chains can self-assemble into nanofibers, nanotubes, or hydrogels under physiological conditions, driven by hydrogen bonding, π-π stacking, and hydrophobic interactions. These materials offer the advantage of incorporating biological motifs that promote cell adhesion, internalization, or enzyme-triggered release. These peptide-based nanostructures are particularly suitable for applications in regenerative medicine, tissue engineering, and targeted drug delivery.

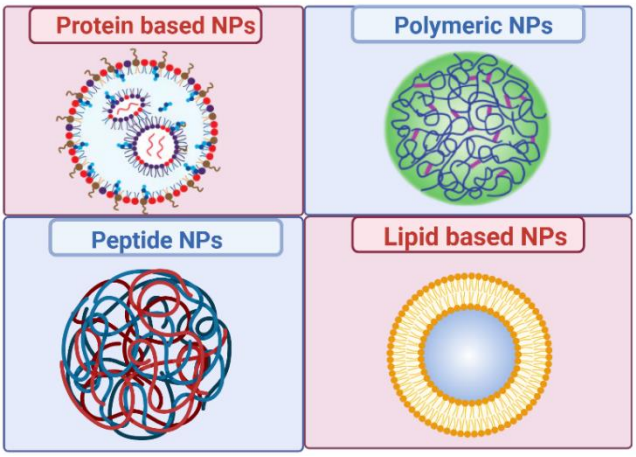

Figure 1. The widely explored self-assembled organic nanoparticles (SAONs) derived from polymers, lipids, peptides and proteins for different biomedical applications.

2.4 ***Polysaccharide-Based Carriers***

The polysaccharides such as chitosan, alginate, dextran, and hyaluronic acid are widely employed in SAON formulations due to their natural abundance, low toxicity, and ease of chemical modification. (Liu et al., 2008; Fonte et al., 2016; Maiti et al., 2015) These materials possess functional groups that facilitate crosslinking, drug conjugation, and responsiveness to physiological triggers such as pH and enzymes. Amongst many, chitosan-based nanoparticles are known for their mucoadhesive properties and ability to enhance oral bioavailability, while hyaluronic acid targets CD44 receptors overexpressed in certain tumors, enabling site specific drug delivery. (Maiti et al., 2015)

3. ***Functionalization and Surface Engineering***

Functionalization is a critical step in enhancing the performance of self-assembled organic nanoparticles (SAONs), transforming them from passive carriers into dynamic, and intelligent delivery systems. The surface engineering techniques are employed to improve biocompatibility, extend circulation time, promote site-specific targeting, and enable stimulus-responsive behavior. This section outlines key functionalization strategies that have significantly advanced the biomedical utility of SAONs.

3.1 ***PEGylation: The Gold Standard for Stealth***

The polyethylene glycol (PEG) modification-commonly referred to as PEGylation is one of the most established strategies for extending nanoparticle circulation. (Suk et al., 2016) The PEG chains form a hydrophilic, flexible corona that reduces protein adsorption and recognition by the mononuclear phagocyte system (MPS), thereby minimizing immune clearance and enhancing systemic stability. Despite its widespread use, PEGylation has limitations, including the potential for immunogenicity and the accelerated blood clearance (ABC) phenomenon upon repeated administration. As a result, alternative stealth polymers such as poly(zwitterions), poly(oxazolines), and polysaccharides are under investigation.

3.2 ***Ligand Conjugation for Active Targeting***

The nanoparticles can be tailored with specific targeting ligands that attach to receptors found in excess on diseased cells. This customization boosts both the precision and absorption of the nanoparticles. (Bazak et al., 2015) These ligands include some small molecules (e.g., folic acid), Peptides (e.g., RGD motifs), antibodies or antibody fragments and aptamers. (Bertrand et al., 2014) The ligand-receptor interactions facilitate receptor-mediated endocytosis, increasing intracellular accumulation of therapeutics. The folic acid-conjugated nanoparticles have shown enhanced targeting of folate receptor-positive tumors, while transferrin and EGFR ligands are used for brain and breast cancer targeting, respectively.

3.3 ***Surface Charge Modulation and Zeta Potential Tuning***

The surface charge of nanoparticles plays a crucial role in how they interact with cell membranes, blood components, and various biological barriers. (Fröhlich et al., 2012) Typically, positively charged nanoparticles show improved cellular uptake because they are attracted to the negatively charged surfaces of cells. However, they are also more prone to rapid clearance and cytotoxicity. To

optimize performance, the zeta potential can be modulated by incorporating neutral or zwitterionic groups, striking a balance between uptake efficiency and systemic stability. The charge modification is also essential for maintaining colloidal stability in physiological fluids.

3.4 ***Stimuli-Responsive Surface Engineering***

Incorporating stimuli-responsive moieties into the nanoparticle surface enables selective drug release in response to specific environmental triggers, enhancing treatment efficacy while reducing off-target effects. The common strategies include the application of acid (pH responsive) sensitive linkers that degrade in the acidic tumor microenvironment or endosomes as it can be seen in Figure 2. The disulfide bonds (redox potential responsive) cleave in the presence of high intracellular glutathione concentrations. Protease-sensitive (enzymes responsive) linkers release drugs in response to overexpressed enzymes such as matrix metalloproteinases (MMPs). The external triggers (temperature or light) can initiate controlled drug release or particle disassembly. These systems offer precise spatial and temporal control over therapeutic action.

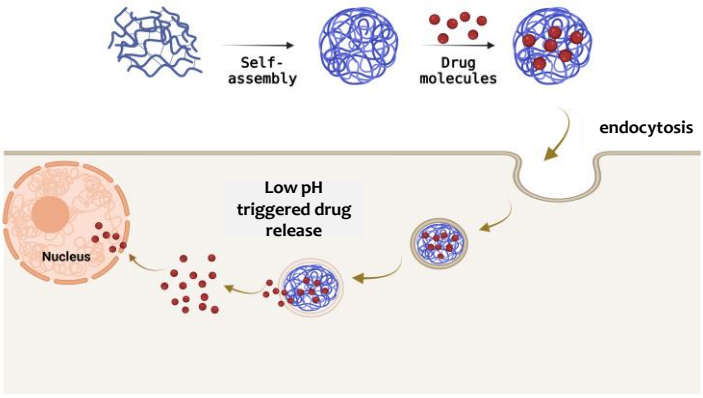

Figure 2. The schematic diagram representative of stimuli (low pH) responsive dug delivery to intracellular space upon endocytosis using self-assembled polymeric nanoparticles.

4. ***Therapeutic Applications and Delivery Strategies***

The versatility of self-assembled organic nanoparticles (SAONs) has led to their application across a broad range of therapeutic fields. These nanoparticles enhance drug stability, improve pharmacokinetics, and enable controlled, site-specific delivery. This section highlights major application areas where SAONs have demonstrated considerable promise, including oncology, gene therapy, infectious diseases, cardiovascular and neurological disorders, and vaccine delivery.

4.1 ***Cancer Therapy***

Cancer remains one of the most extensively explored areas for SAON-based delivery systems. These nanoparticles overcome the limitations of conventional chemotherapy such as poor solubility, systemic toxicity, and multidrug resistance by facilitating targeted and responsive drug delivery. The passive targeting is achieved through the enhanced permeability and retention (EPR) effect, which is the tendency of nanoparticles to accumulate in tumors because their blood vessels are abnormally leaky and their lymphatic drainage is poor, leading to longer retention. This property enables nanoparticles to deliver higher drug concentrations to tumors compared with normal tissues. In addition to passive accumulation, active targeting is enabled via ligand-receptor interactions. (Shi et al., 2017) The nanoparticles incorporating doxorubicin, paclitaxel, cisplatin, and other chemotherapeutics have shown improved pharmacokinetics and

therapeutic indices in preclinical models. Furthermore, stimuli-responsive SAONs enable precise drug release at tumor sites, reducing off-target effects and enhancing treatment efficacy.

On the other hand, delivering nucleic acids such as siRNA, mRNA, and CRISPR components poses unique challenges due to their instability and susceptibility to degradation. SAONs composed of cationic polymers and lipids effectively encapsulate and protect these molecules, facilitating cellular uptake and promoting endosomal escape. The lipid nanoparticles have demonstrated notable success in delivering mRNA vaccines. Ongoing innovations are focused on improving transfection efficiency, minimizing cytotoxicity, and enhancing tissue-specific delivery. The SAONs are revolutionizing immunotherapy by enabling precise delivery of antigens, adjuvants, and immune modulators. These platforms can simultaneously present multiple immune signals, enhancing both innate and adaptive responses. In cancer immunotherapy, SAONs deliver tumor antigens and immune stimulants to dendritic cells to promote T-cell activation. (Irvine et al., 2015)

4.2 ***Antimicrobial and Antiviral Applications***

In the face of rising antimicrobial resistance, SAONs offer promising strategies to enhance the delivery and efficacy of antibiotics and antiviral agents. These systems improve solubility, protect labile compounds from enzymatic degradation, and facilitate targeted accumulation at infection sites. The peptide-based nanoparticles are particularly advantageous due to their dual role as carriers and intrinsic antimicrobial agents, reducing the potential for resistance development. The applications in antiviral therapy include nanoparticles delivering agents like acyclovir and tenofovir to mucosal tissues for chronic infections. (Carmona-Ribeiro et al., 2013) In infectious disease contexts, SAON-based vaccines offer controlled antigen presentation and improved lymph node targeting. The success of lipid-based mRNA vaccines has reinforced the clinical relevance of this approach.

4.3 ***Cardiovascular and Neurological Disorders***

The SAONs are increasingly utilized in treating cardiovascular diseases by enabling targeted delivery of anti-inflammatory agents, statins, and thrombolytics to inflamed or thrombosed vasculature. Functionalized nanoparticles can home in on damaged endothelial tissues, improving therapeutic precision. (Kamaly et al., 2016) In neurology, overcoming the blood-brain barrier (BBB) remains a major obstacle. The BBB is a highly selective physiological barrier formed by tightly connected endothelial cells, pericytes, and astrocytic end-feet, which together regulate the passage of substances between the bloodstream and the brain. While this barrier is essential for maintaining central nervous system homeostasis and protecting against toxins, it also severely restricts the entry of most therapeutic molecules, including large proteins and nucleic acids. (Carmona-Ribeiro et al., 2013) To address this, surface-modified SAONs employing ligands like transferrin or lactoferrin have shown promise in delivering therapeutics across the BBB for the treatment of neurodegenerative diseases such as Parkinson's and Alzheimer's. (Kreuter et al., 2002)

5. ***Challenges***

Despite significant advancements in the design and application of self-assembled organic nanoparticles (SAONs), several scientific, technical, and translational challenges persist. Overcoming these limitations is essential for realizing the full clinical potential of SAON-based therapeutics. This section discusses key barriers related to physicochemical reproducibility, biological interactions, safety, regulatory issues, and manufacturing, while also highlighting emerging strategies and future directions.

5.1 Physicochemical Variability and Reproducibility

The achievement of consistent physicochemical characteristics such as size, surface charge, morphology, and drug-loading efficiency is a persistent challenge in SAON development. These properties profoundly influence biodistribution, pharmacokinetics, cellular uptake, and therapeutic outcomes. However, because SAONs are formed via non-covalent interactions, the self-assembly process is highly sensitive to environmental factors like pH, temperature, and ionic strength. Only a small variation in preparation protocols can lead to batch to-batch inconsistencies, complicating quality control and regulatory approval (Leong et al., 2019). Moreover, reproducibility at larger scales remains difficult, as self-assembly may introduce structural defects and inconsistencies across batches, limiting translational potential (Choo et al., 2025).Therefore, the establishment of standardized fabrication methods and robust quality assurance protocols is critical for clinical translation.

5.2 Biological Barriers and Pharmacokinetics

Once administered, SAONs must navigate multiple biological barriers, including opsonization by serum proteins, phagocytic clearance by the mononuclear phagocyte system (MPS), renal and hepatic elimination, and transport across cellular membranes. Delivery to immune-privileged or poorly accessible sites such as ocular tissues or the central nervous system (CNS) further complicates therapeutic efficacy, as noted in ocular oncology applications (Tsoplaktsoglou et al. 2025). While stealth strategies such as PEGylation extend circulation time, they may also trigger immunogenic responses or the accelerated blood clearance (ABC) effect upon repeated dosing. The advanced targeting strategies and stimuli-responsive designs are being investigated to enhance tissue penetration and improve intracellular delivery. Additionally, vaccine formulations exploiting self-assembled nanoparticles have demonstrated improved lymph node trafficking and dose stability, showing promise in infectious disease management (Yang et al., 2024)

5.3 Immunogenicity and Long-Term Safety

Although SAONs are typically composed of biocompatible materials, their long-term safety remains insufficiently characterized. The chronic exposure or repeated administration may provoke immune activation, complement activation, or cytokine release. For instance, some lipid-based or cationic constructs have been reported to activate innate immunity, raising toxicity concerns (Zhao et al., 2024). Self-assembled nanovaccines can induce immunogenic cell death effectively but require careful evaluation to avoid off-target immune reactions (Ma et al., 2024). The lipid-

based systems, in particular, can elicit hypersensitivity reactions or accumulate in organs like the liver and spleen, potentially causing toxicity. Therefore, understanding the in vivo fate, biodegradation pathways, and clearance mechanisms of these nanoparticles is essential. The comprehensive toxicological studies, including long-term animal studies and pharmacovigilance in clinical settings, are required to ensure safety.

CONCLUSION

The emergence of self-assembled organic nanoparticles (SAONs) has revolutionized the field of nanomedicine, establishing them as highly adaptable and customizable carriers for therapeutic delivery. These nanosystems offer several distinct advantages over traditional delivery methods, such as improved biocompatibility, targeted delivery, controlled drug release, and minimized systemic toxicity. By utilizing a range of organic building blocks such as lipids, polymers, peptides, and amphiphilic molecules, SAONs can respond dynamically to physiological stimuli and adjust to complex biological environments. This flexibility makes them especially valuable for addressing critical challenges in cancer therapy, gene delivery, infectious disease treatment, and neurological disorders. In this review, we have delved into the core principles behind nanoparticle self-assembly, exploring thermodynamic and kinetic factors, structural considerations, and supramolecular interactions. We also examined key points that influence essential properties like particle size, morphology, and encapsulation efficiency. The wide range of therapeutic applications highlighted in this review underscores the vast potential of SAONs across various medical fields, as well as their promise in advancing personalized, precision-based therapies. However, despite their significant potential, several challenges still hinder the widespread clinical adoption of SAONs. The issues related to reproducibility, long-term safety, immune responses, pharmacokinetics, and large-scale production need to be addressed through rigorous, interdisciplinary research. Moreover, regulatory uncertainties and the lack of standardized guidelines continue to slow the translation of SAON-based therapeutics from the laboratory to clinical settings. Looking ahead, the future of SAONs will likely be shaped by innovations in smart, multifunctional nanoparticle systems, deeper integration with artificial intelligence and computational modeling, and the development of sustainable green synthesis techniques. As the field progresses, collaboration among chemists, material scientists, biomedical engineers, clinicians, and regulatory agencies will be essential to the design of next-generation nanoparticle platforms that are safer, more effective, and clinically viable. In conclusion, self-assembled organic nanoparticles represent one of the most promising frontiers in therapeutic delivery. While challenges remain, ongoing advancements in design and translational approaches offer a clear path forward to overcome current limitations and fully unlock the potential of these nanostructures in modern medicine.

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