Research Progress and Application of Nanotechnology in the Treatment of Atherosclerosis

Shenyu Zhao
China Medical University-The Queen's University of Belfast Joint College, China Medical University, Shenyang, Liaoning, 110122, China

Keywords: Nanomedicine, Atherosclerosis Treatment, Targeted Drug Delivery.

Abstract: Atherosclerosis has attracted much attention in the field of disease treatment around the world. Among them, improving the accuracy and efficiency of treating atherosclerosis is a common focus of the global community and a difficult problem that has been studied. With the rapid development of biotechnology today, the emergence of nanotechnology has become one of the excellent choices in the clinical field of medicine. In recent years, nanotechnology has been used to understand the characteristics of atherosclerosis better and effectively treat inflammatory sites and plaques in response to the complex pathology of atherosclerosis. This review collects experimental data and research results on the current cutting-edge and promising nanotechnology in treating atherosclerotic diseases and summarizes the development and application of this technology. The article focuses on the important components and properties of nanotechnology; discusses the mode of action and effective application of new nanotechnology in the field of atherosclerosis; combines biological factors for targeted treatment and achieves preventive monitoring through new technologies. The article also highlights the progress in the development of various types of nanotechnology and how they can help to treat atherosclerosis more efficiently and stably. Therefore, this review aims to demonstrate the profound impact of this technology on the treatment of atherosclerotic diseases, research in the field of vascular diseases, and even similar multifaceted clinical medicine in the future.

1 INTRODUCTION

In recent years, atherosclerosis (AS), as a chronic inflammatory disease, has been the main health burden of global society because of its complexity persistence, and diverse instability AS can cause a series of cardiovascular and cerebrovascular diseases, such as peripheral and carotid artery diseases and cardiovascular diseases. Furthermore, similar multi-disease complications can lead to the accumulation of thrombosis in the arteries, compressing the plaques and further exacerbating the disease. Serious medical events caused by AS cause 17.9 million deaths each year (Pan, et al.,2024). At present, traditional treatment methods that mainly use lipid-lowering and antihypertensive drugs can only solve early and basic problems and their treatment has limitations. Drug treatment has problems such as inaccurate administration routes and non-regression of plaques. At the same time, due to the systemic side effects of some drugs, they are clinically limited, and this similar basic treatment method cannot fill the gap in the transformation between the mechanism and the clinic.

Nowadays, with the rapid development of medical biotechnology, popular nanotechnology is considered to be one of the most promising emerging disciplines in the clinical treatment of AS. Nanotechnology is a new technology that combines knowledge from multiple interdisciplinary disciplines such as material science and physical chemistry. This technology has achieved many application achievements in biomedicine, environmental science, and other fields. In terms of biomaterials, the ultra-small size gives a larger specific surface area and more reaction sites, making it easier to penetrate biological barriers and having good biocompatibility. Secondly, the physicochemical properties of the material can be adjusted through controllable composition and structure, and it can be used as a carrier to carry cytokines for optimized treatment (Cheng, et al.,2023). In terms of technical properties, nanotechnology has a strong ability to deliver drugs in a targeted manner, effectively solving problems

Zhao, S.
Research Progress and Application of Nanotechnology in the Treatment of Atherosclerosis.
DOI: 10.5220/0014400400004933

In *Proceedings of the 1st International Conference on Biomedical Engineering and Food Science (BEFS 2025)*, pages 75-81
ISBN: 978-989-758-789-4

such as low water solubility of drugs and improving the efficiency of drug action. In addition, this process prolongs the circulation time of drug factors and reduces toxic side effects (Li, et al.,2022). Nanotechnology has achieved remarkable results in clinical treatment of different diseases.

Nanotechnology has been gradually applied to the clinical treatment of AS with experimentally proven feasibility and has even made relatively good progress. This research is large in scale and lacks a detailed and systematic review to guide development. This review will begin with the structural characteristics of different nanomaterials and the direction of their disease treatment. And more importantly, thus, this review will introduce the existing applications of nanotechnology in the treatment of AS from various perspectives of nanomedicine; the future development and challenges of nanotechnology in the clinical treatment of AS.

2 STRUCTURAL PROPERTIES OF DIFFERENT NANOMATERIALS AND THEIR DIRECTION OF DISEASE TREATMENT

Nanomaterials are a new class of materials with particle structures defined in sizes from 1 to 100 nanometers. The properties of nanomaterials, such as thermal conductivity and thermal stability, quantum size effect and surface effect, and even molecular loading delivery of biological drugs, make nanomaterials bring many new opportunities for the development of medical technology. Not only that, many nanomaterials have structures and properties that have great potential in the treatment of different diseases, and some of them have been well used in clinical treatment (Zhu, et al., 2023). Therefore, the next article selects the core commonly used nanomaterials in both the organic and inorganic nanomaterials sections to provide a detailed description of their important functional properties and disease treatment modalities.

2.1 Organic Nanomaterials

Organic nanomaterials, mainly composed of carbon skeletons and biomolecules, have good degradability and biocompatibility, and are widely used in nanotechnology for drug delivery and imaging therapy.

2.1.1 Lipid-Based Nanomaterials

Lipid-based nanomaterials contain liposomes, lipid nanoparticles (LNPs), and solid lipid nanoparticles (SLNs). These representative materials are of interest for their lipid bilayer structure and tiny lipid cholesterol molecules. Among them, liposomes are composed of phospholipid bilayers wrapped around an aqueous core, while SLNs are composed of lipid monolayers wrapped around a solid lipid core. The two most important representative materials are structurally different, but they can be effectively used in targeted drug delivery systems because they can be surface-modified for good prolongation of blood circulation. Both are used in inhalation therapy for chronic lung diseases because they are very stable during aerosolisation. Meanwhile, SLNs can utilise a solid lipid core to achieve slow and controlled drug release. SLNs loaded with berberine show good bioavailability and produce an enhanced response to antidiabetic effects (Chenthamara, et al., 2019).

2.1.2 Polymer-Based Nanomaterials

Polymer-based nanomaterials are divided into nanomaterials based on natural polymers and nanomaterials based on synthetic polymers (including biosynthetic polymers and chemically synthesised polymers). Natural polymers are a renewable resource, such as chitosan, which has good biocompatibility and degradability, allowing the formation of polymer composites that are suitable for delivery vehicles. At the same time, its adsorption and humectancy can be chemically modified to produce derivatives with properties superior to those of chitosan, becoming a non-viral carrier with non-immunogenicity and a large specific surface area, which can be used as a delivery vehicle for vaccines. For example, Newcastle disease virus (NVD) encapsulated in N-2-hydroxypropyl trimethylammonium chloride chitosan nanoparticles (NDV/La Sota-N-2-HACC-NPs), which are low in toxicity and safety, and which can sustainably trigger stronger immune responses, can produce effective results in immunomodulation. In addition to this, synthetic polymers such as polylactic acid-hydroxyacetic acid copolymers (PLGA), which can control the rate of degradation by the ratio of lactic acid to hydroxyacetic acid. Drug delivery encapsulated in PLGA nanoparticles or microspheres can effectively grow the duration of action of

chemotherapeutic drugs at the tumor site and reduce adverse effects.PLGA improves the pharmacokinetic properties of drugs and has become an excellent material for controlled drug release worldwide (Han, et al., 2018).

2.2 Inorganic Nanomaterials

Inorganic nanomaterials are mainly composed of non-carbon-based inorganic elements or compounds with unique magnetic and catalytic activities, which are widely used in microenvironmental modulation and targeted therapy.

2.2.1 Noble Metal Nanomaterials

Noble metal nanomaterials have many representative materials, such as gold nanoparticles (Au NPs) and silver nanoparticles (Ag NPs). They have been prepared in a well-established method with good surface modification, strong biocompatibility, and excellent antimicrobial properties. One of the more rapid developments is Au NPs, which, given their excellent light absorption, can generate localized surface plasmon resonance at specific wavelengths for use in photothermal therapy (PTT) to treat bacterial infections. Meanwhile, Ag NPs used in combination with PTT and hydrogel under near-infrared light and heat will induce heating of the hydrogel on the wound surface and denaturation of the proteins in the bacterial cells, which will promote the release of Ag NPs. Such nanoparticles with a large surface area and small size are more likely to enter into the cell and chemically bond, leading to the complete death of the bacteria. Both have great potential in the biomedical field and co-processing with other biotechnologies has led to an effective increase in therapeutic efficacy (Wang, et al., 2022).

2.2.2 Silica-Based Nanomaterials

Silicon dioxide-based nanomaterials have achieved success in a variety of disease treatment areas. Among them, mesoporous silica nanoparticles (MSNs) are the best-known and have many advantages. Firstly, with very high flexible structural properties, they have a huge range of pore sizes and specific surface area, with a strong drug-carrying capacity. Secondly, their hydrophilic surfaces have a large amount of Si-OH, making them more susceptible to functionalized modifications of internal and external porous surfaces, which significantly improves bioavailability, and biocompatibility and enables a precise drug delivery process, making them excellent bases for the construction of various nanocomposites. MSNs have a large number of biomedical applications, such as MSN therapy itself, where Si ions released during bone disease treatment can activate bone-related gene expression, thereby stimulating cartilage differentiation and bone recovery. For example, MSNs are combined with polytherapy, which means that multiple treatment modalities, such as photodynamic therapy and enzyme-like catalysis, are integrated into MSNs as an emerging targeted therapy, which can lead to more stable and effective targeted therapeutic outcomes. For example, the desired material is combined in MSNs, and upconversion NPs/MSNs nanocomposites are inorganic nanomaterials containing lanthanide ions with high biological tissue penetration. This material can produce effective synergistic thrombolytic and anticoagulant therapy in thrombolytic therapy, which successfully promotes the efficiency of energy conversion through different activators and sensitizers (Xu, et al., 2023).

3 MULTIFACETED DEVELOPMENT AND APPLICATION OF NANOTECHNOLOGY IN THE FIELD OF ATHEROSCLEROSIS

The mature development and diversification of nanomaterials have made nanotechnology treatments more and more perfect, and gradually applied in the clinical treatment of many different disease areas. This technology has been well developed and applied to the AS treatment process, from targeted delivery systems, diagnostic imaging tests, anti-inflammatory and anti-oxidant interventions, plaque stabilisation and elimination, and clinical combination therapy. Nanotechnology solves the problem of AS disease in many ways and is one of the excellent technologies of modern medicine to solve AS through biotechnology.

3.1 Diagnostic and Therapeutic Imaging

AS can monitor the degree of lesioning of plaques by imaging, thus assessing the level of risk of the disease, and providing diagnostic information and corresponding treatment. The different characteristic

molecules will serve as markers for determining that AS is not in the same disease level stage, and therefore can be combined with nanotechnology for detection and regulation, as well as accurate treatment.

3.1.1 Fe_3O_4@M Biomimetic Nanoparticles for Accurate Monitoring of Symptoms of Early AS

In the early stages of AS, the adhesion molecule VCAM-1, which is expressed on the surface of activated endothelial cells, becomes a targeted biomolecule for monitoring abnormalities in endothelial cell production because it promotes leukocyte recruitment to endothelial cell interactions. Leukocytes do this by binding to the glycoprotein α4β1 integrin, which is highly expressed on macrophage membranes, and both can specifically recognise and link VCAM-1. Based on the above principles, Huang et al. synthesised bionic nanoparticles, a technique in which Fe_3O_4 nanoparticles are coated with macrophage membranes (Fe_3O_4@M）containing a large amount of α4β1, which can be used to monitor VCAM-1 on endothelial cells. This molecule is observed and magnetic resonance imaging (MRI) is performed to further understand and monitor changes in early AS. Huang et al. performed pre-experiments in which Fe_3O_4@M (targeted nanoparticles) and Fe_3O_4@P (control nanoparticles) were injected intravenously in an early atherosclerosis rat model. It was found that the MRI signal intensity of the aortic root was significantly reduced in atherosclerotic rats injected with Fe_3O_4@M and there was no change in the signal in the control group. This experiment demonstrated that the bionanoparticles Fe_3O_4@M have the ability to target early lesions of AS plaques, as well as the ability to accurately monitor and with inspection (Zhang, et al., 2023). Nowadays, different nanoparticles for different periods of marker molecules can effectively regulate the different stages of disease that AS is in, and effectively diagnose and prevent the risk of the disease.

3.1.2 LFP/PCDPD Multifunctional Nanoparticles Targeted to Detect and Treat AS

To further image the detection of AS and target therapy for this disease, the research group of Xu et al. constructed a multifunctional nanoparticle (LFP/PCDPD) with reactive oxygen species (ROS) corresponding to drug release, lipid removal, and lipid-specific AIE fluorescence imaging. This nanoparticle, which releases LFP at the lesion to bind to the lipid to emit green fluorescence, enables lipid-specific imaging. At the same time, this nanoparticle has good imaging ability to monitor the extent and location of the lesion more accurately. More importantly than monitoring, in vitro experiments by this group demonstrated that LFP/PCDPD can target damaged endothelial cells, effectively enrich at the site of plaque sclerosis, inhibit plaque formation, and reduce the degree of inflammation. In terms of experimental assurances, this nanotechnology is low in toxicity and generates a ROS response and controlled drug release, more comprehensively targeted to address the clinical aspects of AS disease (Xu, et al., 2022).

3.2 Targeted Delivery of Cytokines

In the treatment of AS, the targeted delivery system can precisely regulate the plaque microenvironment and accurately act on the lesions, improving the therapeutic effect and reducing the side effects. Similarly, nanomedicine targeted delivery of cytokines brings more possibilities for the clinical treatment of AS, both in the middle and end stages of treatment.

3.2.1 Novel Targeted and Efficient MM/RAPNPs Mimetic Nanoparticles

Wang and his group developed a biomimetic nanoparticle designed to target AS, but conventional targeted delivery systems suffer from problems such as susceptibility to clearance by the immune system. Therefore, the group developed a bionic nanoparticle called MM/RAPNPs, which is a rapamycin (RAP)-loaded PLGA nanoparticles (RAPNPs) combined with a macrophage membrane (MM) coating. The structure of this nanoparticle not only contributes to a slow and long-lasting release of the drug, but also successfully preserves macrophage membrane functional proteins. More importantly, it enhances the uptake of activated endothelial cells in vivo and inhibits the proliferation of macrophages and vascular smooth muscle cells, thereby reducing plaque inflammation. In vitro, MM/RAPNPs treatment significantly inhibited the course of AS lesions, reduced lipid deposition and necrotic area, and maintained vascular integrity. This technology passed the characterisation test and safety assessment of nanoparticles, which are potentially excellent carriers

and can effectively inhibit the progression of AS plaque inflammation, providing a new strategy for a targeted drug delivery system for AS (Wang, et al., 2021).

3.3 Nucleic Acid Nanostructures that Accurately Connect Gene Pathways: miR-146a-SPIONs

Bai and his group prepared a polyethylene glycol (PEG)-coated superparamagnetic iron oxide nanoparticle core (SPION) with non-cationic nucleic acid nanostructures miR-146a-SPIONs attached to phosphorothioate (PS)-modified miR-146a oligonucleotides. This approach advances a boost in the efficiency of gene therapy for AS, in which miR-146a inhibits the activation of signalling pathways associated with vascular inflammation and the PS modification protects it from degradation by nuclease. Firstly, multiple in vivo injections of miR-146a-SPIONs significantly reduced plaque area and stabilised plaques by enhancing collagen content in the plaques. Secondly, this nanotechnology inhibits the development of AS at the genetic level by regulating genes related to lipid metabolism, immune response, and signalling pathways. Finally, in vitro tests have shown this efficacy to be effective in accessing macrophages and endothelial cells, leading to a reduction in plaque inflammation without inducing severe toxicity. This nanotechnology is safe and effective, revealing excellent prospects for nucleic acid nanomedicine in AS (Bai, et al., 2022).

3.4 Plaque Elimination and Inflammation Prevention in the later Stages of Treatment

In clinical practice, the above nanotechnology treatment options have good efficacy for AS and can even reverse the progression of the disease. However, after treatment by these nanotechnologies, residual plaque elimination and inflammation prevention become existential pitfalls that still have the chance to lead to the recurrence of acute AS, even life-threatening. In recent years, nanotechnology has been developed while observing the structural changes of advanced AS plaques to find new target site opportunities for further thorough treatment. Inflammatory response and plaque elimination is one of the important issues in the end stage of AS treatment, and the CANTOS study has shown that methotrexate (MTX) combined with lipid core nanoparticles (LDE) in combination with paclitaxel (PTX) not only reduces the risk of cardiovascular disease due to chronic inflammation, but also, by choosing different nanoparticles, such as hyaluronic acid nanoparticles (HA- NPs), it could produce plaque stabilisation and anti-inflammatory effects. It was found that its bionic NP white vesicles can mimic the distribution of leukocytes accumulating at the site of vascular injury, inhibit the release of inflammatory factors and shrink the necrotic core of plaques by delivering drugs to the inflammatory site of plaques, resolving the destabilising factors arising at the later stages of AS, so that the whole course of treatment of AS can achieve the optimal expected results (Ou, et al., 2021).

4 CONCLUSION

In this review, the article mainly summarizes the existing development and therapeutic applications of different types of nanotechnology in the clinical treatment of AS diseases. In the process of collating data and literature, this paper ensures that the topic is related to nanotechnology, nanomedicine, and nanomaterials. This article not only observes the treatment directions of different nanomaterials for different diseases but also connects and analyzes atherosclerosis, which is the main focus of this article, to obtain valuable research results of existing nanotechnology from all aspects. In fact, nanotechnology has become one of the important technologies in clinical medicine today. Due to its good biocompatibility, small size, large specific area, controllable and adjustable structure, excellent targeted drug delivery, and relatively mature development level, it can undoubtedly be applied to various diseases. At the same time, this article also found that nanotechnology research in the field of AS treatment has made significant progress. Among them, the precisely targeted delivery system improves the ability to eliminate inflammation and plaques, the multifunctional integrated diagnosis and treatment design, the controllable structural changes of nanomaterials, and the rate and dosage of drug release. All of the above advantages reflect the advanced development of modern nanomedicine, which almost surpasses the inefficiency, toxicity, and recurrence produced by the traditional treatment of AS in clinical practice. Therefore, within the novel biotechnology, nanotechnology offers reliable and innovative strategies for the treatment of AS in the clinical field and also has very excellent prospects.

Focusing first on the structural properties of different nanomaterials and the various directions for the treatment of diseases, the article presents examples of materials that are mainly used in modern nanotechnology, in two separate sections: organic nanomaterials and inorganic nanomaterials. Examples include lipid-based nanomaterials and polymer-based nanomaterials in organic materials, and noble metal nanomaterials and silica nanomaterials in inorganic materials. All of these nanoparticles are important representatives of nanomaterials, which are widely used in the fields of environmental regulation and targeted therapy in nanomedicine. Of course, different nanomaterials have unique advantages and are suitable for use in different diseases, and these nanomaterials are used in combination with modern biotechnology to address complex clinical medical diseases in a multifaceted way. More importantly, understanding the general principles of these nanomaterials can help connect to the atherosclerotic diseases that the article focuses on. Therefore, the authors focus on the existing applications of nanotechnology in the treatment of AS from several main aspects. From the beginning of the diagnostic and therapeutic aspects of imaging, we introduce Fe_3O_4@M nanoparticles, which can accurately monitor the symptoms of early AS, and LFP/PCDPD multifunctional nanoparticles, which can detect and treat AS, with a focus on the diagnosis and treatment of AS from an imaging perspective. Then to the critical therapeutic period of targeted drug delivery, introducing novel targeted and highly efficient MM/RAPNPs mimetic nanoparticles and miR-146a-SPIONs nucleic acid nanostructures that accurately link genes. Finally focusing on the elimination of plaque and inflammation in the later stages of treatment, there are also many optional nanomedicine strategies to prevent disease recurrence. Thus, the data and applications demonstrate that nanotechnology can address AS disease and make a significant contribution to cardiovascular disease.

The author aims to summarize the importance of nanotechnology to AS and the entire medical field. The importance of "nano" can be seen from the fact that it has penetrated every aspect of life, and nanomedicine has led to the prosperity of biotechnology. This technology has good prospects in terms of materials and technology, but it also brings difficulties and challenges. For example, the in vivo metabolic pathways and potential organ accumulation risks of nanomaterials have not been clarified; differences in plaque composition and endothelial barrier penetration at different levels of AS disease will weaken the universality of nanocarriers; even if nanomedicine can prevent AS, residual inflammation The possibility of recurrence still exists; the cost of large-scale production and the integrity of integrated diagnosis and treatment need to be further improved. Therefore, this field should focus on the joint research of "materials science-molecular biology-clinical diseases" and combine advanced artificial intelligence to produce personalized treatment plans for patients. Finally, the author hopes that people all over the world will work together to overcome these existing medical problems so that nanomedicine will play an increasingly revolutionary role in the treatment of cardiovascular diseases. Therefore, biotechnology will bring methods and results, progress and breakthroughs, and a great future to many medical fields in the future.

REFERENCES

Bai Q, et al. 2022. Scavenger receptor-targeted plaque delivery of microRNA-coated nanoparticles for alleviating atherosclerosis. Proceedings of the National Academy of Sciences of the United States of America, 119(39), e2201443119.

Cheng J, et al. 2023. Nanomedicine for diagnosis and treatment of atherosclerosis. Advanced Science (Weinh), 10(36), 2302337.

Chenthamara D, et al. 2019. Therapeutic efficacy of nanoparticles and routes of administration. Biomaterials Research, 23, 20.

Han J, et al. 2018. Polymer-based nanomaterials and applications for vaccines and drugs. Polymers (Basel), 10(1), 31.

Li W, et al. 2022. Surface-modified nanotherapeutics targeting atherosclerosis. Biomaterials Science, 10(19), 5459-5471.

Ou LC, et al. 2021. Application of targeted therapy strategies with nanomedicine delivery for atherosclerosis. Acta Pharmacologica Sinica, 42(1), 10-17.

Pan Q, et al. 2024. Top five stories of the cellular landscape and therapies of atherosclerosis: Current knowledge and future perspectives. Current Medical Science, 44(1), 1-27.

Wang Y, et al. 2021. Macrophage membrane functionalized biomimetic nanoparticles for targeted anti-atherosclerosis applications. Theranostics, 11(1), 164-180.

Wang B, et al. 2022. Inorganic nanomaterials for intelligent photothermal antibacterial applications. Frontiers in Bioengineering and Biotechnology, 10, 1047598.

Xu H, et al. 2022. ROS responsive nanoparticles loaded with lipid-specific AIEgen for atherosclerosis-targeted

diagnosis and bifunctional therapy. Biomaterials, 288, 121734.

Xu B, et al. 2023. Multifunctional mesoporous silica nanoparticles for biomedical applications. Signal Transduction and Targeted Therapy, 8(1), 435.

Zhang X, et al. 2023. Molecularly targeted nanomedicine enabled by inorganic nanoparticles for atherosclerosis diagnosis and treatment. Advanced Drug Delivery Reviews, 194, 114709.

Zhu X, & Li S. 2023. Nanomaterials in tumor immunotherapy: New strategies and challenges. Molecular Cancer, 22(1), 94.