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Prevention of Atherosclerosis Through Targeted Delivery of Nanoparticles

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ABSTRACT: Atherosclerosis signifies the buildup of plaque in the arteries. Plaque cells are not engulfed by macrophages, causing buildup in the arterial lining. This research aims to prevent atherosclerosis and plaque progression in the arteries through nanoparticle delivery targeting macrophages. The author used qualitative data collection to narrow down the most efficient nanoparticles for the prevention processes of atherosclerosis. Nanoparticles include: HDL-like nanoparticles, liposomal alendronate, dendrimers, micelles, polymeric nanoparticles, nanogels, and inorganic nanoparticles. The research process was a collection of data through secondary sources and did not use any testing. HDL-like nanoparticle variants serve for homeostasis and prevention through reduced oxidative damage in the endothelial barrier, and slowing the progression of plaque—nanogels as a great alternative to stenting, along with minimization of DNA damage. Cerium-zirconium oxide (CZALO and CZ) nanoparticles offer potential strategies for future prevention through the minimization of DNA damage and maintenance of homeostasis. Silver, iron oxide, and cerium oxide nanoparticles also serve as antioxidative nanoparticles for the arteries and have antibacterial properties. For future research, the author strongly recommends understanding the genetic components that contribute most to atherosclerosis. With this, researchers can potentially safely alter DNA using nanoparticles to reduce the risk of atherosclerosis in the future.

KEYWORDS: Materials Science, Nanomaterials, Atherosclerosis, HDL-like Nanoparticles, Arterial Plaque.

Introduction

People who are diagnosed with atherosclerosis only have symptoms after 70 percent of their arteries are blocked, and then they will be able to reverse it before symptoms appear with earlier identification. Also, if plaque is built due to a combination of habits and genetics or one of the two, then a possibility lies in tracing the habits or the genetics that are most prominent and leading to atherosclerosis before symptoms. The research aims to find the initial causes and factors for the onset of atherosclerosis and how the application of nanoparticle-based prevention can be safely targeted with the highest efficiency.

The American Heart Association shares evidence pointing to the idea that people with plasma LDL levels <40 mg/dL are more often nonpermissive to the "progression of atherosclerotic heart disease in subjects with preexisting disease and perhaps <70 mg/dL if maintained throughout the entire lifetime."[1] This research, along with research on regressing the condition, will also aim at finding ways through which different factors, such as plasma levels of patients, can be improved.

Approximately 931,578 people died from Cardiovascular disease in 2021 in America alone. It is also found that 48.6% of adults between 2017 and 2020 had some form of cardiovascular disease.[2] Atherosclerosis is a big contributor to cardiovascular disease-related fatality. Atherosclerosis is the buildup of plaque (made up of fats, cholesterol, calcium, and other substances, which are considered cellular waste) in the inner lining of arteries, causing them to harden and narrow, restricting blood flow to vital tissues and organs. As lipoproteins accumulate in specific regions of the arterial tree, they draw monocytes, which differentiate into macrophages that promote inflammation, which in turn intensifies the inflammatory response locally. Early atherosclerotic lesions are initiated at arterial sites submitted to hemodynamic and mechanical forces, modifying shear stress. In these lesion-prone areas, the endothelium (inner lining of blood vessels) loses its protective properties and allows low-density lipoproteins through. Once exposed to different factors such as oxidation by enzymes and other sources, they become inflammatory molecules. Plaque tends to target the cell walls in the arteries due to high LDL (low-density lipoprotein) cholesterol levels, as it deposits in such areas. As the body sends macrophages to engulf the plaque, inflammation occurs, which attracts more macrophages and initiates the process of plaque formation. If plaque ruptures, it could also cause blood clotting and blockage of blood flow.

Millard emphasizes that half of all people aged 45 to 84 in America aren't aware that they have atherosclerosis.[3] Cleveland Clinic states that symptoms of atherosclerosis occur only when arteries are 70% blocked.[4] This addresses a huge problem, as almost 3 quarters of the arteries are blocked until the cause is noticed. Millions of people every year learn that they have Atherosclerosis, which is almost irreversible when in advanced stages.

To help prevent atherosclerosis, targeting plaque at a lower amount of buildup than 70% blockage, preferably 20% or less, which is considered mild or acceptable, is needed. Once plaque buildup reaches over 50%, it is considered severe and requires critical treatment. However, it is not simple to target

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plaque with regular procedures this way without nanoparticles due to the low presence of plaque cells. Researcher Mandy Erickson of Stanford Medicine shares the inability of macrophages to influence the plaque due to their avoidance of plaque cells themselves.[5] However, there is a clear solution to this; nanoparticles will help target the movement of plaque-eating cells more efficiently than regular procedures. They serve as a means of enhancing the drug loading abilities, along with stability and controlled release. Nanoparticles also contain factors of precision in medicinal treatments.

Methodology

This research is a study of the most prominent causes of habits that result in atherosclerosis. This was followed by studying the carbon nanoparticles on the regression of plaque and the safest way to regress the condition without harm. The researcher dove further into the nanoparticles used in prevention: HDL-like variants, dendrimers, liposomal alendronate, micelles, polymeric nanoparticles, nanogels, and inorganic nanoparticles. Limitations to this study include clinical trials due to unethicality. Theoretical proposals are not considered in this study, but any research that has been proven before. This study aims to improve the research on the regression of atherosclerosis by connecting what has been proven to cause and treat atherosclerosis and proposing a methodical approach to the regression of plaque at an earlier stage of atherosclerosis before symptoms. Sources and databases such as those from Stanford, BMC, ScienceDirect, NIH, AHA Journals, Tadfonline, and the Cleveland Clinic published from 2003 to 2025 were used for this research. Resources relevant to the drug-carrying ability of nanoparticles on the endothelial area and the arteries were gathered as part of this research. Keywords used for identifying the data from the sources included: Statins, lipids, lipid carriers, foam cells, nanoparticle drug delivery systems (NDDSs), Nitric Oxide (NO), macrophages, and arteries. An example of screening is from the Journal of Nanobiotechnology. This source was relevant to the research topic as it addresses the many different anti-atherosclerosis drugs and their beneficial physiological abilities. This research paper gives a breakdown of multiple drugs, including Statins (of the keywords), SPIO (nanoparticles), and multiple other drugs. Keywords mentioned above were searched in the abstract of each article reviewed, along with the gaps in research of the area, and the overall findings and contribution of the solution to atherosclerosis-related problems. Initially, 64 articles were retrieved and were screened down to 36 articles. Further analysis of the data collected from sources with information about the drugs used for the drug delivery system in atherosclerosis, liposomes, dendrimers, micelles, polymeric nanoparticles, nanogels, and inorganic nanoparticles was conducted. With these sources, the results of each data set were compared and filtered further for the most efficient drug and method of delivery. Finally, the most efficient outcome was determined by comparing the best strengths and weaknesses of the nanoparticles with categorization of processes involved in the author's methodical approach to prevention strategies, along with treatment. The author uses this methodology as a proposal for future research and testing. Limitations of this study, including the inability to test the analyzed data and the genetic factors at play, are involved. Due to such limitations, the author sets this study as one of comparative analysis with current data on functioning nanoparticles as discussed and their influence on macrophage reactions and the interaction with plaque in the endothelial bilayer.

Results

Breaking Down Atherosclerosis:

The reason atherosclerosis is prominent is due to what researcher Mandy Erickson of Stanford Medicine refers to as the "don't eat me" signal given off by dead cells in plaque, as a message to immune cells. This means the dead cells are able to pass by immune cells and spread without being eaten. Fighting off atherosclerosis is done by targeting the immune cells in the plaque and regressing the buildup of dead cells in order to clear the arteries. More specifically, these immune cells (which are avoided by plaque cells) are the macrophages (white blood cells), which are in charge of clearing cellular waste and harmful particles. Erickson reports, "The same signal is found on the surface of many types of cancer cells, allowing them to escape detection and multiply."[5] This signifies atherosclerosis is most notably a disease that needs more attention to not just treat, but to prevent, for plaque to stop as early as possible. The American Heart Association shares that "Lipoprotein entry and retention within the subendothelium and hence atherogenesis depend on sustained plasma levels of apoB lipoproteins."[1] Lack of certainty is cited in the areas discussing the contributing factors of lipoprotein entry, such as Lipoprotein size, charge, and composition, along with endothelial permeability. Peter Libby shares that "Non-traditional drivers of atherosclerosis—such as disturbed sleep, physical inactivity, the microbiome, air pollution and environmental stress—have also gained attention."[6] Researchers Christopher K. Glass and Joseph L. Witzdum explain, "Analysis of human atherosclerosis suggests that the evolution of advanced plaques may involve repetitive cycles of microhemorrhage and thrombosis. Plaque ruptures associated with acute myocardial infarction generally occur at the shoulder regions of the plaque and are more likely to occur in lesions with thin fibrous caps, a relatively high concentration of lipid-filled macrophages within the shoulder region, and large necrotic cores."[7] This shows how the buildup of plaque may start in the shoulder region and transfer to the arteries as the lower-concentration lipids flow through. Endothelial cells (ECs) are very susceptible to stresses provided by blood flow, as explained before. This results in a change in their morphology and triggers many signaling cascades. Lee *et al.* state that a moderate intensity statin (cholesterol-reducing drug) with ezetimibe combination therapy is suitable to be an alternative to high intensity monotherapy "if high-intensity statins cannot be tolerated or further reduction in LDL cholesterol levels is required, as recommended by the current guidelines for managing dyslipidaemia among patients with DM and ASCVD."[8] clinical data prove that plaque can be regressed through cholesterol-reducing drugs and do not point out a way to target the plaque or substances before they can

cause symptoms. Lowering of apoB-containing lipoproteins to extremely low levels as a treatment to eliminate the risk of plaque build-up, as a treatment after Atherosclerosis is discovered in patients, is also part of the treatment process.

Research has focused mostly on reactionary measures such as slowing down plaque build-up through drugs and habitual changes once Atherosclerosis is diagnosed, but not on the inflammatory concept. There are currently no studies or reviews showing the prevention of atherosclerosis before the arteries are blocked to 70%, proving there is a lack of research in this area. Studies such as those of Healthline only explain the process of slowing it down through drugs or habits.

Atherosclerosis Prevention:

Early interaction can drastically reduce the number of people with atherosclerosis by preventing plaque buildup before any symptoms occur. Doing so, providing a healthy life for millions of people and thereby reducing the number of cardiovascular disease-related fatalities by millions is the vision. Neda Naseri *et al.* have shown that the use of Nanoparticles in treatment enhances the fighting ability of the disease.[9] She acknowledged the excellent drug-carrying abilities of solid lipid NPs (SLNs) and nanostructured lipid carriers (NLCs). The best approach to treatment is by using carbon nanoparticles. Carbon nanoparticles are loaded with a drug that activates the immune cells to target dead cells rather than letting them pass and spread. This process is known as efferocytosis. It is proven safe after being tested on mice and shows no side effects. In fact, studies on efferocytosis show that treating macrophages with anti-miR-33 nanoparticles enhances efferocytosis.[10] So far, nanoparticle-based treatments to counter plaque buildup after symptoms have been identified. Research on measures to prevent Atherosclerosis before symptoms are revealed is lacking. Further research is needed to understand the effectiveness of various nanoparticle-based treatments available and their effectiveness in use as preventive measures. This study will be a stepping stone for future cardiologists and researchers aiming to reduce cases of Atherosclerosis and also to educate people on potential preventative options. It is important to note the possibility of genetic interference, which sets a limitation on this study; however could be maneuvered as a basis for further, more accurate, and developed research for Atherosclerosis and macrophage behavior.

HDL-like Nanoparticles:

HDL-like lipoproteins range from 7 to 13 nanometers in diameter.[11] McMahon also states HDL-like nanoparticles (High Density Lipoproteins) "are diverse natural nanoparticles that carry cholesterol and are best known for the role that they play in cardiovascular disease. However, due to their unique targeting capabilities, diverse molecular cargo, and natural functions beyond cholesterol transport, it is becoming increasingly appreciated that HDLs are critical to cancer development and progression."[11] This quote indicates the ability to transport such molecular cargo, in this case, of drug-carrying particles, in the prevention process. Although it is shown to have great ability in transportation, the primary factor to consider is the amount of usage, as it correlates with cancer development, as stated. HDL-like nanoparticles show their benefit by reducing oxidative damage to blood vessel walls, maintaining or restoring the integrity and function of the vascular endothelium, reducing plaque formation and development, and slowing or stopping the progression of atherosclerosis. Statins improve the water solubility of drugs and decrease the side effects.[12]

The table below (Table 1) represents the various drugs and their uses in the drug delivery system to the arteries. The table links multiple parts of the drug-carrying system contributing to atherosclerosis treatment. The information comes from the author and researcher Tu *et al.*[12]

Table 1: HDL-like Nanoparticles Contributing to Arterial Integrity and Health.

Zr-labelled CER-001	More accurate tracking of nanoparticle distribution and activity
ETC-216	Reduces plaque formation and development
CER-001	Reduces plaque formation and development
CSL112	Maintains or restores the integrity and function of vascular endothelium
MDCO-216	Reduces oxidative damage to blood vessel walls

Table 1 shows five different HDL-like nanoparticles that have various properties in maintaining arterial stability. Each HDL-like nanoparticle helps arterial health through either unique or shared properties. Overall, they contribute to the arterial integrity through slowing development and reducing damage with a focus on tracking abilities. Created by Hari.

Liposomal Alendronate:

Liposomal alendronate is a formulation of the biophosphate known as alendronate, which is then encapsulated into liposomes. This enhances drug delivery efficiency and is effective in various medical applications. It also helps with immunity.

Danenberg *et al.*[13] conducted a test on rabbits with hypercholesterolemia. This test had rabbits undergoing a hypercholesterolemic diet, which led to stent deployment and bilateral iliac artery balloon denudation. After injection of liposomal alendronate, monocyte counts lowered by over 90% over a course of 24-48 hours after the injection. The findings indicate "This treatment significantly reduced intimal area at 28 days, from 3.88±0.93 to 2.08±0.58 and 2.16±0.62 mm2. Lumen area was increased from 2.87±0.44 to 3.57±0.65 and 3.45±0.58 mm2. Arterial stenosis was reduced from 58±11% to 37±8% and 38±7% in controls, rabbits treated with 3 mg/kg, and rabbits treated with 6 mg/kg, respectively (mean±SD, n=8 rabbits/group, $P<0.01$ for all 3 parameters)".[13] Overall, they concluded that the injections concurrent with injury reduce in-stent neointimal formation and arterial stenosis in hypercholesterolemic rabbits.

Dendrimers:

Researcher Rout *et al.*[14] explain the nanoparticle: dendrimers, as "repetitively branched, globular, and macromolecular struc-

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tures having size ranges from 2.5 to 10 nm."[14] They also emphasize their three main units, consisting of a central core, branching units which carry the drug, and the internal cavity composed of a variety of natural or synthetic factors such as sugars, amino acids, peptides, etc. They continue by noting that a "Dendrimer can either be loaded with drugs within the internal cavities or in their central core through hydrophobic interaction, hydrogen bonding, or by a chemical bond."[14]

Findings of Spyropoulos-Antonakakis *et al.*[15] analyze the aggregation of PAMAM zero-generation dendrimers (G0) that serve as drug delivery vehicles and conjugated G0 PAMAM dendrimers with a ZnPc photosensitizer to symptomatic and asymptomatic human carotid tissues. The Atomic force microscopy (AFM) was used in this study to examine this. The study's findings demonstrate that adding G0 PAMAM dendrimers or G0 PAMAM/ZnPc conjugates to either healthy or atheromatous carotid tissue dramatically changes the local texture properties of human carotids at the nanoscale, suggesting that the G0 NPs have various agglomerating responses. However, along with these, penetration of dendrimers across the endothelial barrier (inner lining of arteries) depends on important features such as concentration, incubation time, efflux transport, surface charge modification, local thermodynamic conditions, and polar-entropic competition.[15]

Micelles:

Researcher Anne Helmenstine explains micelles as "spherically shaped, consisting of surfactant molecules arranged so that their hydrophobic tails are shielded from the surrounding liquid by the hydrophilic heads".[16] She also reports key features including their ability to dissolve in water (micelles are soluble), ability to alter size and shape depending on temperature and sufficient concentration, and their continuous exchanging with their outside solution rather than being static.

Chin *et al.* researched mice with atherosclerosis. They have found that one dose of miR-145 (microRNA-145: a regulator of vascular smooth muscle tissue phenotypic switching) micelles prevented 49% of the formation of lesions in early-stage atherosclerotic ApoE-/- (apolipoprotein E) mice, and two weeks after therapy, the level of miR-145 expression remained elevated. Furthermore, in mid-stage atherosclerotic ApoE-/-mice, miR-145 micelles decreased plaque development by 35% and 43%, respectively, in comparison to free miR-145 and PBS. Together, they offer a new treatment approach and cell target for atherosclerosis. They introduced miR-145 micelles as a promising nanotherapeutic that can stop the evolution of atherosclerosis in both its early and late phases.[17]

Polymeric Nanoparticles:

Polymeric nanoparticles are engineered materials made from polymers, anywhere from 1 to 1000 nanometers in size. They also tend to have a higher surface area to volume ratio, allowing for more efficiency in interactions with the surrounding environment. They can encapsulate a variety of compounds within their core.

A study from Leal *et al.* uses nanometer-sized polymeric PLGA nanoparticles (NPs) capable of simultaneously encapsulating and delivering miRNA-124a (miRNA variant) and the statin atorvastatin (ATOR) in order to target inflamed cells from atherosclerosis. They found that the dual-loaded NPs effectively bound overexpressed VCAM receptors, released the payloads inside cells in a sustainable way, and were non-toxic to cells over a wide range of doses. In LPS-activated macrophages and vascular endothelial cells, the combination of ATOR and miRNA significantly decreased the levels of reactive oxygen species (ROS) and proinflammatory cytokines like IL-6 and TNF-α. Furthermore, dual-loaded NPs prevented morphological alterations and the buildup of low-density lipoproteins (LDL) inside macrophages more than single-loaded NPs did.[18]

Nanogels:

Nanogels are three-dimensional hydrogel materials that are "formed by crosslinked swellable polymer networks with a high capacity to hold water, without actually dissolving into the aqueous medium,"[19] according to researcher Kruti S Soni. Soni *et al.* also explain that nanogels are mostly spherical in shape, and their characteristics can be altered by varying the chemical composition of the nanogels.[19]

Results of the studies from Maram K. Reddy from research on nanogels (Rapamycin-loaded gel-like nanoparticles) were targeted at a group of rats with a carotid artery injury. Intima/media ratio: 1.5‘0.02 versus 2.7‘0.6; P<0.01) showed significant inhibition of hyperplasia; localized delivery of nanoparticles maintained the drug level in the target artery for more than two weeks; and, most significantly, reendothelialized the injured artery (endothelium coverage: treated 82% versus control 28%). Additionally, they showed that the treated artery's caspase-3/7 enzyme activation was inhibited, which stopped VSMCs from going through apoptosis and allowed macrophages to infiltrate. They concluded that localized delivery of rapamycin inhibited apoptosis of VSMCs, which helped with the process of re-endothelialization. They found it to be a great alternative to stenting as it did not include the risk factors of thrombosis or in-stent restenosis. This is due to it being a natural process of reendothelialization.[20]

Inorganic Nanoparticles:

Inorganic nanoparticles are composed of various inorganic materials. They range from 1 to 100 nanometers in size. Alexandru Scafa Udriște *et al.* researched osteopontin (OPN)-modified nanoliposomes (CZALO) that encapsulate L-arginine (L-Arg) and cerium-zirconium oxide nanoparticles (CZ NPs), which exhibit enzyme-like activities for targeted atherosclerosis treatment. Findings show that by controlling the secretion of senescence-associated secretory phenotype factors, improving lysosomal function, easing cell cycle arrest, and minimizing DNA damage, NOS, which is overexpressed in macrophages, catalyzes L-Arg to produce NO, which is subsequently selectively released in situ and diffuses into endothelial cells. Together, CZALO nanoliposomes' anti-aging and antioxidant properties reduce the atherosclerotic burden in vitro and in vivo with negligible toxicity. This "two-birds-one-stone"[21] nanotherapeutic provides a new method for controlling the homeostasis of the vascular milieu and enhancing the effec-

tiveness of treatment for atherosclerosis. It is also found that CZ NPs released from CZALO nanoliposomes scavenge the reactive oxygen species, inhibiting the cholesterol buildup and promoting macrophage phenotypic transformation, resulting in both antioxidant and anti-inflammatory effects Udriste *et al.*[21] Figure 1 below, adapted from the International Journal of Molecular Sciences, evaluates three distinct inorganic nanoparticles that are used generally for cardiovascular disases.

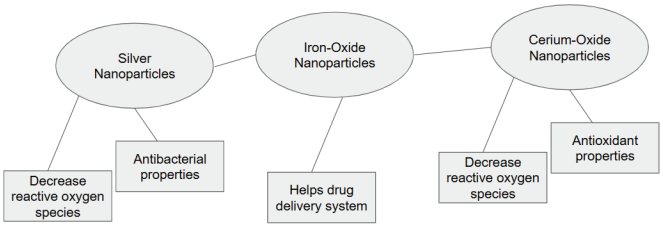

Figure 1: Inorganic Nanoparticles. The figure shows the properties of metals used in cardiovascular diseases. These are three of many inorganic nanoparticles; Silver nanoparticles and Cerium-Oxide nanoparticles share properties of antioxidants. Iron oxide nanoparticles also help with the drug delivery system. These three work together to help reduce damage and keep stability and arterial health in the long run. Created by Hari, adapted from the International Journal of Molecular Sciences.

■ Discussion

The research shows that HDL-like nanoparticle variants seem very efficient. This certain nanoparticle shows many great features that contribute well to the arteries and drug-carrying system. The author's suggestion from this finding is to implement this nanoparticle in the different designations for each type of HDL-like nanoparticles before symptoms, which would be able to counter plaque, along with restoring the arteries, therefore reducing the chance of symptoms occurring and plaque progressing.

Using other nanoparticles, such as Silica-Gold nanoparticles, platelet-derived extracellular vesicles, and cyclodextrin-based polysaccharide nanoparticles,[12] can help with the process of curing atherosclerosis after prevention to ensure the safety of vessels and prevent plaque from building up. With Danenberg *et al.*[13] of the American Heart Association study of hypercholesterolemic rabbits and the injection of liposomal alendronate, it is seen that the injection proves useful when having high amounts of cholesterol, as it deploys stents during atherosclerosis, which can be an option to back up the prevention of nanoparticles. It could be used if blood tests, cardiac catheterization, echocardiograms, or other tests indicating plaque in the arteries show a heightened amount from prior tests.

A good plaque reducer is miR-145 micelles. Shown in results,[17] they have proven to be efficient as they helped with reducing plaque buildup in mid-stage atherosclerotic ApoE-/-mice by over 35%. They also used early-stage atherosclerotic ApoE-/-mice for this, and results showed similar, signifying miR-145 micelles are a good nanoparticle in terms of security after administration of the preventing nanoparticles.

From polymeric nanoparticles, the researcher found that dual-loaded nanoparticles with the combination of ATOR and miRNA reacted with LPS-activated macrophages and vascular endothelial cells in a more effective way than single-loaded NPs. The researcher saw that it decreases ROS levels and proinflammatory cytokines, and also prevents the buildup of LDLs in macrophages better than single-loaded NPs.[18] With polymeric nanoparticles, their use is in the process of prevention, as they work much better than single-loaded nanoparticles in terms of both prevention and decrease in ROS. Using this in the prevention phase and treatments following seems most efficient as it can provide a thorough prevention of harmful lipids while treating ROS if it rises as an issue.

Nanogels serve as a great therapeutic nanoparticle and a potential nanoparticle that can help in prevention. The author found it to be a great property as it undergoes reendothelialization in arteries, essentially rebuilding the inner lining, as a natural solution. It is also able to maintain such a status in the arteries, along with avoiding thrombosis and in-stent restenosis. It serves as a much better alternative to nanoparticles, which may cause stenting.[20]

Inorganic nanoparticles NOS highlight the ability to minimize DNA damage, along with many factors in reducing inflammation that lead to the production of NO to infuse with endothelial cells to clear blockage. The CZALO and CZ NPs (cerium-zirconium oxide containing nanoparticles) give antioxidant and anti-inflammatory effects.[21] This overall may be able to contribute to prevention solely through DNA protection. As it is a far reach, future scientists may be able to uncover what genetic factors play a role in the plaque buildup of atherosclerosis and how nanoparticle drug delivery can alter DNA safely for potential prevention of plaque buildup. Inorganic nanoparticles may be a sufficient part of prevention as they indicate minimization of DNA damage along with homeostasis. The standpoint of the inorganic nanoparticles, including silver nanoparticles, iron-oxide nanoparticles, and cerium oxide nanoparticles, and their effectiveness are shown in Figure 1. Silver nanoparticles can be used in processes during prevention to ensure less potential of disease due to their antibacterial properties. Silver nanoparticles, along with cerium oxide nanoparticles, both decrease reactive oxygen species. Cerium oxide nanoparticles also have antioxidant properties. Iron oxide nanoparticles help the drug delivery system, which can serve to transport drugs during treatment and prevention of atherosclerosis, such as Atorvastatin (for cardiovascular health) and Fluvastatin (reduces cholesterol).[21]

With the help of future studies, researchers can understand not only the nanoparticles' involvement in arteries, but also possibly through genetic alteration, in hopes of a safe prevention.

■ Conclusion

This study evaluated potential prevention strategies using nanoparticles capable of treating atherosclerosis and preventing various causes. This study reviewed many key nanoparticles, such as HDL-like nanoparticle variants (for homeostasis and prevention), nanogels as a great alternative to stenting, along with minimization of DNA damage, and CZALO and CZ NP nanoparticles, which highlight a potential strategy for future prevention through DNA damage minimization and

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homeostasis. Other inorganic nanoparticles, such as silver nanoparticles, iron-oxide nanoparticles, and cerium-oxide nanoparticles, can be used for prevention through properties of drug delivery and reactive oxygen species depletion. With the antibacterial properties, future researchers will be able to ensure a safer process of prevention. This study was not able to fully prevent atherosclerosis, as genetic factors should also be useful to be taken into consideration.

As a final takeaway, this study sets a basis for prevention strategies using nanoparticles, including HDL-like nanoparticles, Liposomal Alendronate, Dendrimers, Micelles, Polymeric nanoparticles, Nanogels, and Inorganic nanoparticles, and their known capabilities. This study suggests safe targeted delivery of these nanoparticles to macrophages in the arteries to target plaque in the endothelial barrier. It opens a new perspective for future research through gene alteration to restrict the main genetic factors that contribute to such a disease.

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