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Nanoparticle-Mediated Delivery of Natural Anti-Inflammatories for Cardiovascular Disease [Letter]

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Dear editor

I am delighted to express my keen interest in the comprehensive and insightful review titled "Nanoparticles as a Novel Platform for Cardiovascular Disease Diagnosis and Therapy" authored by Tang et al.[1] This review not only encapsulates the breadth and depth of the current landscape of nanoparticles in the diagnosis and management of cardiovascular diseases (CVDs) but also underscores their invaluable contribution to advancing the field. In particular, the discussion on the progress and prospects of nanomedicines in CVDs is truly intriguing. However, there exists an intriguing avenue worth exploring within the framework of this review: the recent advancements in the development of natural drug monomers as targeted anti-inflammatory agents for intervening in CVDs. This emerging field holds promise for novel therapeutic strategies that harness the power of nature to combat the complex pathophysiology of these conditions.

Systemic suppression of inflammation, while effective in mitigating the progression of atherosclerosis, carries the risk of immunosuppression and heightened susceptibility to infections. This underscores the importance of developing therapies that can specifically target the atherosclerotic plaque while minimizing the impact on systemic immune function. As highlighted in the CANTOS trial,[2] even modest reductions in inflammation were shown to confer significant benefits, albeit accompanied by an increased risk of infections. To address these challenges, researchers have ventured into innovative nanotechnology-based approaches for targeted delivery of anti-inflammatory agents directly to atherosclerotic plaques. Curcumin is chosen as the anti-inflammatory payload model. One prominent example is the study by Luo et al[3] which introduced LLC nanoparticles (LLC NPs) utilizing an amphiphilic low molecular weight heparin-lipoic acid conjugate (LMWH-LA) as a reactive oxygen species (ROS)-sensitive carrier. This innovative carrier material addresses safety concerns associated with chemically synthesized alternatives and incorporates clinically approved injectable drug molecules, thereby minimizing the risk of unknown side effects. Concurrently, another promising strategy involves the development of biomimetic platelet-cloaked nanoparticles for the delivery of curcumin.[4] These nanoparticles are coated with a tannic acid (TA)-Fe(III) complex and further cloaked with fragments derived from platelet cell membranes, enhancing their interaction with endothelial and macrophage cells in steady-state and inflamed conditions. Importantly, these nanoparticles exhibit cytocompatibility towards various cell types crucial in atherosclerosis pathogenesis without eliciting immune activation.

The curcumin-loaded nanoparticles demonstrate their anti-inflammatory efficacy by reducing the expression of key pro-inflammatory markers, including Nf-κb, TGF-β1, IL-6, and IL-1β, in lipopolysaccharide-inflamed endothelial cells. Similarly, the LLC NPs designed by Luo et al[3] leverage the LMWH shell to target P-selectin on plaque endothelial cells, blocking monocyte migration and inhibiting the initiation of ROS and inflammatory factors. Upon encountering the plaque's ROS-rich microenvironment, the lipoic acid component undergoes oxidation, facilitating the release of curcumin into the plaque. Curcumin then exerts its potent anti-inflammatory and antioxidant effects, further suppressing ROS production and mitigating inflammatory responses.

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Anti-inflammatory therapies hold promise in reducing cardiovascular events beyond lipid-lowering interventions.[5] Targeting inflammation at the plaque level and individualizing therapies based on inflammatory profiles improves cardiovascular outcomes and reduces the global burden of atherosclerotic cardiovascular disease.

Disclosure

The author declares no conflict of interest in this communication.

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