**Graphene-Based Nanomaterials as Novel Modulators of Lipid Metabolism and Inflammation in Atherosclerosis**

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**Abstract**

Atherosclerosis, a chronic inflammatory disease marked by lipid accumulation and macrophage-driven foam cell formation, remains a leading cause of cardiovascular morbidity. Graphene oxide (GO) and reduced graphene oxide (rGO), synthesized from oil palm biomass, offer tunable surface chemistries enabling therapeutic modulation of lipid metabolism and immune pathways. This study integrates computational and experimental approaches to elucidate their mechanisms of action. Molecular docking and dynamics simulations revealed that rGO interacts with lipid-associated proteins (CD36, LOX1, ApoB) predominantly via hydrophobic forces, while GO forms more stable hydrogen-bonded complexes, modulating lipid uptake and inflammatory signaling. Characterization (Raman, FTIR, XRD, AFM) confirmed GO’s higher oxygen functionalization (hydrophilicity) and rGO’s partial hydrophobicity. In macrophages, neither material induced foam cell formation, yet both inhibited oxidized LDL (oxLDL)-driven lipid accumulation, with GO showing greater efficacy. GO enhanced cholesterol efflux via ABCA1 upregulation while suppressing scavenger receptors (CD36, SRA1) and pro-inflammatory cytokines (IL-1β, TNF-α, NF-κB). rGO also promoted ABCA1 but increased IL-1β and SRA1, reflecting divergent immunometabolic effects. Metabolomics revealed that GO influenced glucosinolate and estrogenic pathways, while rGO modulated phenylalanine metabolism. These results highlight surface functionalization as a determinant of graphene bioactivity. GO, with its oxygen-rich chemistry, exhibits superior anti-atherogenic potential by enhancing cholesterol clearance and mitigating inflammation, underscoring its promise as a nanotherapeutic platform for atherosclerosis.

Keywords: Graphene Oxide, Reduced Graphene Oxide, Atherosclerosis, Foam Cells, Inflammation.