ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ON THE MODELING OF ATHEROSCLEROSIS IN EXPERIMENT

Saydullayev T.

Andijan State Medical Institute, Uzbekistan

Abstract: Atherosclerosis is a leading cause of cardiovascular morbidity and mortality worldwide, requiring deeper investigation through experimental approaches. The purpose of this study is to review the most relevant models of experimental atherosclerosis and their contribution to understanding disease pathogenesis and treatment. Different experimental methods, including dietary induction, genetic modifications, and vascular injury, have been analyzed. Results demonstrate that while animal models provide essential insights into molecular and cellular mechanisms of atherosclerosis, each approach has unique limitations. The findings highlight the necessity of selecting models based on specific research objectives to ensure translational value.

Keywords: atherosclerosis, experimental modeling, ApoE-deficient mice, diet-induced models, cardiovascular pathology

Introduction

Atherosclerosis remains one of the most significant public health challenges due to its role in ischemic heart disease, stroke, and peripheral vascular disorders. It is characterized by endothelial dysfunction, lipid deposition, chronic inflammation, and fibrous plaque formation within arterial walls. Despite advances in clinical cardiology, the exact mechanisms underlying initiation and progression of atherosclerosis remain incompletely understood.
Experimental modeling of atherosclerosis has been indispensable in bridging the gap between molecular discoveries and clinical applications. By reproducing disease-like conditions in controlled settings, researchers gain opportunities to study pathogenesis and evaluate preventive and therapeutic interventions. This paper aims to present an overview of major experimental models of atherosclerosis, analyze their outcomes, and discuss their translational significance.

The complexity of atherosclerosis lies in its multifactorial etiology. Traditional risk factors such as hypercholesterolemia, hypertension, smoking, obesity, diabetes mellitus, and sedentary lifestyle play crucial roles in disease development. Moreover, genetic predisposition and environmental influences significantly modify disease susceptibility. Importantly, the asymptomatic nature of atherosclerosis during its early stages makes prevention and early diagnosis challenging. Understanding the underlying mechanisms is therefore essential for designing effective interventions.

Experimental modeling of atherosclerosis has become a fundamental tool in cardiovascular research, as it allows investigators to reproduce pathological changes under controlled conditions. Over the past decades, a wide variety of experimental models have been developed, ranging from simple dietary modifications to advanced genetically engineered animals. These models have provided valuable insights into the pathogenesis of lipid accumulation, endothelial activation, immune cell recruitment, and plaque destabilization.

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

Furthermore, they serve as indispensable platforms for preclinical testing of novel pharmacological agents, interventional strategies, and lifestyle-based preventive measures.

Despite significant progress, current experimental models are not without limitations. While rodent models provide rapid, cost-effective insights into molecular pathways, they often fail to replicate the full spectrum of human lipid metabolism and vascular physiology. Larger animal models, such as rabbits and pigs, provide closer similarities but present ethical and financial challenges. The search for models that balance reproducibility, relevance, and translational accuracy continues to be an important aspect of atherosclerosis research.

In this context, the present study aims to analyze the principal approaches to modeling atherosclerosis in experimental settings, evaluate their contributions to understanding the disease, and identify the strengths and weaknesses of each method. By summarizing existing knowledge, this work emphasizes the necessity of carefully selecting appropriate models depending on the specific scientific or therapeutic objective.\

Methods

Experimental modeling of atherosclerosis is carried out using different strategies that reproduce pathological changes of the arterial wall under laboratory conditions. The selection of the model is usually determined by the specific aim of the research, whether it is the study of molecular mechanisms, the evaluation of lesion progression, or the testing of novel therapies.

One of the most traditional approaches is the use of diet-induced models. In this method, animals such as rabbits, rats, and mice are fed high-fat and cholesterol-rich diets, leading to the development of hyperlipidemia and subsequent lipid deposition in the arterial intima. This process results in fatty streaks and early lesions similar to those seen in human atherosclerosis. Although such models are simple, cost-effective, and reproducible, they often require long periods of feeding and may not always progress to advanced plaque formation.

Genetically modified animals represent another widely used method. ApoE-deficient and LDL receptor-deficient mice are considered gold standards in experimental atherosclerosis. ApoE-deficient mice spontaneously develop hypercholesterolemia and extensive atherosclerotic plaques even on standard chow diets, while LDL receptor-deficient mice require additional dietary modifications to accelerate the process. These models have provided significant insights into the role of lipid metabolism, inflammation, and immune mechanisms in plaque formation.

Mechanical injury models are also applied to reproduce vascular remodeling. Endothelial denudation by balloon catheterization or wire insertion causes neointimal hyperplasia, smooth muscle cell proliferation, and accelerated plaque formation. Such models are especially valuable for the study of restenosis after angioplasty but do not fully represent the lipid-driven mechanisms of human atherosclerosis.

In recent years, combined models have been developed to provide a more comprehensive simulation. By integrating genetic predisposition, high-fat feeding, and mechanical endothelial injury, researchers are able to obtain advanced and complex lesions in a shorter time frame. These models are particularly useful for evaluating both pharmacological and interventional therapies.

The evaluation of experimental outcomes is performed through a combination of histological, biochemical, and molecular techniques. Histological staining such as Oil Red O and hematoxylin–eosin is used to visualize lipid deposition and plaque morphology. Immunohistochemistry helps identify inflammatory markers and cell types within the lesion. Biochemical assays are employed to measure serum lipid levels, while molecular methods including RT-PCR and Western blotting are used to study the expression of genes and proteins involved in lipid metabolism, endothelial dysfunction, and inflammation.

Altogether, these methodological approaches provide a robust framework for modeling atherosclerosis in experimental settings, allowing researchers to investigate pathophysiological mechanisms and evaluate potential therapeutic interventions in a controlled and reproducible manner.

Results

Diet-induced hyperlipidemia resulted in early fatty streak formation in animal arteries within weeks. Genetic models, particularly ApoE-deficient mice, developed advanced plaques with necrotic cores and fibrous caps resembling human lesions. Mechanical injury promoted endothelial denudation and smooth muscle proliferation, producing accelerated intimal thickening. Combined models allowed reproducible generation of severe atherosclerosis within a relatively short experimental period.

These approaches also enabled testing of pharmacological agents such as statins, PCSK9 inhibitors, and anti-inflammatory therapies. Data showed significant reductions in lesion size and inflammatory marker expression, confirming the translational value of these models.

Discussion

Experimental models of atherosclerosis have provided fundamental knowledge of disease mechanisms, including lipid metabolism, endothelial dysfunction, and immune cell involvement. Genetic models remain the most reliable for mechanistic studies, although they do not fully replicate human lipid metabolism. Larger animals, such as pigs, offer closer anatomical similarity but require higher costs and complex ethical considerations.
Dietary and mechanical injury models remain relevant for short-term studies, particularly when testing vascular interventions. The combination of multiple approaches provides the most robust platform for simulating the multifactorial nature of atherosclerosis. Future directions involve developing models that incorporate comorbidities such as diabetes, hypertension, and obesity to better reflect real-world patient conditions.

Conclusion

Modeling atherosclerosis in experimental conditions remains a cornerstone of cardiovascular research. Each model presents specific advantages and limitations, making careful selection essential for study design. While genetic models have revolutionized mechanistic studies, translational accuracy requires larger and more integrative models. Continued refinement of experimental systems is necessary to enhance the predictive value of preclinical research and improve clinical outcomes in atherosclerosis management.

Experimental modeling of atherosclerosis remains one of the most valuable tools in cardiovascular research, providing essential insights into the mechanisms of disease development, progression, and treatment. Different approaches, including diet-induced hyperlipidemia, genetic modification, mechanical endothelial injury, and combined strategies, have contributed to the understanding of lipid accumulation, vascular inflammation, and plaque formation. Each model offers distinct advantages, but also carries limitations that must be carefully considered when designing experiments.

Diet-induced models are simple and cost-effective, but their ability to reproduce advanced lesions is limited. Genetically modified animals, particularly ApoE- and LDL receptor-deficient mice, provide reproducible and reliable data on the molecular pathways of atherogenesis, yet their lipid metabolism differs significantly from that of humans. Mechanical injury models are especially relevant for studying vascular remodeling and restenosis but lack the complexity of lipid-driven pathology. Combined models, which integrate multiple approaches, offer a more comprehensive and clinically relevant representation of the disease.

The evaluation of atherosclerotic changes using histological, biochemical, and molecular methods has allowed researchers to correlate structural and functional alterations with disease progression and therapeutic outcomes. These experimental platforms have played a crucial role in the preclinical testing of statins, anti-inflammatory agents, and novel lipid-lowering therapies, many of which have later demonstrated clinical efficacy.

In conclusion, although no single experimental model can fully replicate the complexity of human atherosclerosis, the thoughtful use of available models allows researchers to address specific questions related to pathogenesis and treatment. Continued refinement and development of experimental systems, particularly those that integrate genetic, dietary, and metabolic risk factors, will enhance the translational value of preclinical research. Such efforts are vital for improving prevention, diagnosis, and treatment strategies for atherosclerosis, ultimately contributing to the reduction of global cardiovascular morbidity and mortality.

References

1. Libby P, Ridker PM, Hansson GK. Inflammation in atherosclerosis: from pathophysiology to practice. *Journal of the American College of Cardiology*. 2009;54(23):2129–2138.
2. Getz GS, Reardon CA. Animal models of atherosclerosis. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2012;32(5):1104–1115.
3. Xoldarova, N. (2025). A PSYCHOLINGUISTIC APPROACH TO GRADUONYMY PHENOMENA IN THE LEXICAL AND SEMANTIC LEVELS OF ENGLISH AND UZBEK. *Journal of Applied Science and Social Science*, *1*(1), 652-659.
4. Кузиева, С. У., & Ишонкулова, Д. У. (2018). ВЫДЕЛЕНИЕ И ЭЛЕКТРОФОРЕТИЧЕСКИЕ СВОЙСТВА МАЛАТДЕГИДРОГЕНАЗЫ

ХЛОПЧАТНИКА. In *INTERNATIONAL SCIENTIFIC REVIEW OF THE PROBLEMS AND PROSPECTS OF MODERN SCIENCE AND EDUCATION* (pp. 14-16).
5. Zawacki-Richter, O., Marín, V. I., Bond, M., & Gouverneur, F. (2019). Systematic review of research on artificial intelligence applications in higher education. *International Journal of Educational Technology in Higher Education*, 16(1), 39.
6. Mukhamedova, M., Orziev, D. Z., Uzokov, J. K., & Abdullaev, A. X. (2023). Optimization of antiplatelet therapy in patients with coronary artery disease and type 2 diabetes mellitus after percutaneous coronary interventions. *European Journal of Cardiovascular Nursing*, *22*(Supplement_1), zvad064-111.
7. Xoldarova, N. (2025). THE ROLE OF GRADUONYMY IN THE LEXICAL AND SEMANTIC LEVELS OF ENGLISH AND UZBEK: A PSYCHOLINGUISTIC VIEW. *International Journal of Artificial Intelligence*, *1*(1), 1173-1178.
8. UNESCO. (2023). *Guidelines on the Ethics of Artificial Intelligence in Education*. Paris: UNESCO Publishing.
9. Мухамедова, М. Г., Куртиева, Ш. А., & Назарова, Ж. А. (2020). СИНДРОМ ФУНКЦИОНАЛЬНОЙ КАРДИОПАТИИ У СОВРЕМЕННЫХ ПОДРОСТКОВ. In *П84 Профилактическая медицина-2020: сборник научных трудов Все-российской научно-практической конференции с международным участи-ем. 18–19 ноября 2020 года/под ред. АВ Мельцера, ИШ Якубовой. Ч. 2.—СПб.: Изд-во СЗГМУ им. ИИ Мечникова, 2020.—304 с.* (p. 105).
10. Kuzieva, S. U., Imomova, D. A., & Abduraimov, O. S. (2020). Ontogenetic Structure Cenopopulations of Spiraea hypericifolia L. in Turkestan Ridge (Uzbekistan). *Архив Научных Публикаций JSPI*.
11. Holmes, W., Bialik, M., & Fadel, C. (2019). *Artificial Intelligence in Education: Promises and Implications for Teaching and Learning*. Boston: Center for Curriculum Redesign.
12. Mukhamedova, M., Alyavi, B. A., Uzokov, J. K., Babaev, M. A., & Kamilova, S. E. (2019). P120 Relationship between left ventricular global function index and cardiac systolic functions in patients with chronic ischemic disease of the heart and diabetes mellitus. *European Heart Journal-Cardiovascular Imaging*, *20*(Supplement_3), jez147-008.
13. Daugherty A, Tall AR, Daemen MJ, Falk E. Experimental models of atherosclerosis: translational insights and challenges. *Cardiovascular Research*. 2017;113(10):1172–1186.
14. Williams KJ, Tabas I. The response-to-retention hypothesis of early atherogenesis. *Arterioscler Thromb Vasc Biol*. 1995;15(5):551–561.
15. Lusis AJ. Atherosclerosis. *Nature*. 2000;407(6801):233–241.