JOURNAL OF APPLIED SCIENCE AND SOCIAL SCIENCE
eISSN 2229-3113 pISSN 2229-3205
Volume 15 Issue 11, November 2025
Impact factor: 2019: 4.679 2020: 5.015 2021: 5.436, 2022: 5.242, 2023: 6.995, 2024 7.75

THE EFFECT OF HYDROXYTYROSOL ON THE CARDIOVASCULAR SYSTEM: ITS ROLE IN LIPID PROFILE REGULATION, ENDOTHELIAL FUNCTION, AND INHIBITION OF ATHEROSCLEROSIS

Khakimov Muhammadi Khamidjon ugli,
Department of Biological Chemistry,
Andijan State Medical Institute, Uzbekistan, Andijan

ANNOTATION: This article analyzes the effects of hydroxytyrosol (3,4-dihydroxyphenyl ethanol) on the cardiovascular system, focusing on its role in modulating lipid profile, endothelial function, and the progression of atherosclerosis based on modern scientific sources and experimental findings. The study highlights the molecular mechanisms through which hydroxytyrosol restores cardiovascular homeostasis via its antioxidant, anti-inflammatory, anti-atherogenic, and antithrombotic properties. The results indicate that HT reduces LDL oxidation, enhances functional activity of HDL, increases endothelial NO synthesis, decreases the expression of inflammatory mediators, and improves atherosclerotic plaque stability. The obtained data provide a scientific basis for the use of hydroxytyrosol as a cardioprotective nutraceutical.

Keywords: Hydroxytyrosol; polyphenols; cardiovascular system; lipid profile; LDL oxidation; HDL; endothelial function; oxidative stress; atherosclerosis; NF-κB; eNOS; antioxidant; cardioprotective; anti-inflammatory activity.

INTRODUCTION

In the context of rapid advancements in modern biochemistry, cardiology, and nutraceutical sciences, the role of natural polyphenols in protecting the cardiovascular system has attracted significant scientific interest. In particular, hydroxytyrosol (3,4-dihydroxyphenylethanol), found in olives (Olea europaea L.) and their leaves, is currently recognized as one of the most potent natural antioxidants. The presence of ortho-dihydroxyl groups in its molecular structure determines its ability to rapidly and stably neutralize free radicals, protect cell membranes from oxidation, and modulate signaling pathways [1].

Cardiovascular diseases are the leading cause of mortality worldwide, and atherosclerosis, endothelial dysfunction, and lipid metabolism disorders represent the main pathogenic links of these conditions. Specifically, the oxidation of LDL cholesterol, activation of inflammatory mediators, increased platelet aggregation, and enhanced oxidative stress accelerate the formation of atherosclerotic plaques. From this perspective, studying natural molecules capable of reducing oxidative stress, restoring endothelial NO production, and normalizing the lipid profile is one of today's most urgent scientific tasks [2].
The antioxidant, anti-atherogenic, and endothelial-protective properties of hydroxytyrosol have been confirmed in numerous experimental and clinical studies in recent years. Research shows that it significantly reduces oxidation of LDL particles, improves HDL functionality, decreases

JOURNAL OF APPLIED SCIENCE AND SOCIAL SCIENCE
eISSN 2229-3113 pISSN 2229-3205
Volume 15 Issue 11, November 2025
Impact factor: 2019: 4.679 2020: 5.015 2021: 5.436, 2022: 5.242, 2023: 6.995, 2024 7.75

inflammatory markers in the vascular wall, and modulates key molecular pathways such as Nrf2/HO-1, eNOS, and NF-κB. In addition, hydroxytyrosol supports cardiovascular homeostasis by reducing platelet aggregation and enhancing the proliferative and regenerative activity of endothelial cells [3].

The natural origin, high biological activity, low toxicity, and high bioavailability of hydroxytyrosol have brought this molecule to the scientific forefront as a promising compound for the development of functional foods, nutraceutical preparations, and cardioprotective agents. At the same time, it is necessary to thoroughly investigate its mechanisms of action on the pathophysiological processes associated with the cardiovascular system, particularly its role in modulating the lipid profile, endothelial function, and the inhibition of atherosclerosis. For this purpose, the present study is aimed at analyzing the molecular bases of hydroxytyrosol's protective effects on the cardiovascular system, evaluating its impact on atherosclerotic processes, and scientifically substantiating its potential as a cardioprotective bioactive compound [4].

Literature analysis shows that hydroxytyrosol (HT, 3,4-dihydroxyphenyl ethanol) is one of the most important bioactive polyphenols of olive (Olea europaea L.) fruits, leaves, and olive oil, distinguished by its strong antioxidant properties. Its molecular structure, containing ortho-dihydroxy groups, enhances the ability to stabilize phenoxyl radicals and rapidly neutralize free radicals. Scientific sources confirm the antioxidant (DPPH, ABTS, ORAC, FRAP), anti-inflammatory, anti-atherogenic, antimicrobial, antiglycation, and antithrombotic activities of hydroxytyrosol, and its efficacy in protecting the cardiovascular system has become one of the most extensively studied directions in recent years [5].

Studies on processes associated with dyslipidemia show that hydroxytyrosol significantly modulates the lipid profile. HT reduces the oxidation of LDL particles by 60–90%, slows down HDL degradation, and enhances its antioxidant function. Activation of the PPAR-α and LXR pathways leads to increased fatty acid oxidation, while elevated expression of LDL receptors in hepatocytes accelerates LDL clearance from the blood. Clinical studies show that oral doses of 5–25 mg of hydroxytyrosol administered for 15–60 days result in an 8–15% reduction in LDL levels, a 3–5% increase in HDL concentration, and a 10–20% decrease in triglycerides. These indicators provide grounds to consider hydroxytyrosol as a natural hypolipidemic component [6].

Endothelial dysfunction is the initial stage of atherosclerosis and is characterized by reduced nitric oxide (NO) production, increased oxidative stress, and elevated inflammatory mediators. Literature indicates that hydroxytyrosol possesses several endothelial-protective mechanisms. HT increases endothelial NO synthase (eNOS) activity and enhances NO biosynthesis, which supports vasodilation, improved microcirculation, and overall vascular relaxation. In addition, HT neutralizes superoxide radicals, reduces NO degradation, suppresses the activity of NADPH oxidase enzymes (NOX2/NOX4), and decreases the expression of inflammatory adhesion molecules such as ICAM-1, VCAM-1, and E-selectin by 20-40% in endothelial cells. These processes limit the adhesion of monocytes to the vascular wall and slow the formation of atherosclerotic plaque.

Sources that deeply investigate the pathogenesis of atherosclerosis emphasize hydroxytyrosol's inhibitory effects on this process at the molecular level. HT reduces ox-LDL formation by up to 70%, blocking a key oxidative step in plaque development. Decreasing the expression of CD36 and LOX-1 receptors in macrophages, it reduces foam cell formation and prevents cholesterol

JOURNAL OF APPLIED SCIENCE AND SOCIAL SCIENCE
eISSN 2229-3113 pISSN 2229-3205
Volume 15 Issue 11, November 2025
Impact factor: 2019: 4.679 2020: 5.015 2021: 5.436, 2022: 5.242, 2023: 6.995, 2024 7.75

accumulation. Inhibition of the NF-κB pathway significantly decreases the production of inflammatory mediators such as TNF-α, IL-1β, IL-6, COX-2, and iNOS. At the same time, hydroxytyrosol enhances collagen synthesis and reduces the activity of matrix metalloproteinases (MMP-2, MMP-9), thereby increasing the stability of atherosclerotic plaques and reducing the risk of plaque rupture [7].

In the literature, the cardioprotective and antithrombotic properties of hydroxytyrosol also occupy a distinct place. HT reduces platelet aggregation by 20-40%, decreases blood viscosity, and restores the prostacyclin/thromboxane ratio to physiological levels, thereby reducing the risk of thrombosis. This is an important protective factor, particularly for individuals with a predisposition to ischemic heart disease, hypertension, and metabolic syndrome. Clinical trial results also confirm the cardioprotective efficacy of hydroxytyrosol. When administered for 30–60 days, arterial elasticity improved, functional activity of HDL increased, and oxidative stress biomarkers-MDA and 8-iso-PGF2α-decreased significantly. In patients with mild and moderate hypertension, a reduction of 5-8 mmHg in systolic blood pressure was recorded.

Overall, the literature emphasizes that hydroxytyrosol exerts strong cardioprotective effects by regulating lipid metabolism, reducing LDL oxidation, restoring endothelial function, inhibiting atherosclerosis at the molecular level, and decreasing inflammation and oxidative stress. In this regard, it has great scientific and practical significance as a natural nutraceutical compound targeting metabolic, inflammatory, and oxidative processes.

The research findings demonstrated that the effects of hydroxytyrosol on the cardiovascular system are governed by multifaceted and complex molecular mechanisms. Based on the obtained experimental data and available clinical and biochemical literature, the effects of hydroxytyrosol on lipid metabolism, endothelial function, and the development of atherosclerosis were evaluated in an integrated manner.

First of all, the antioxidant properties of hydroxytyrosol were identified as the most stable and strongest indicator throughout the experiment. The marked decrease in oxidative stress markers, particularly MDA, diene conjugates, and 8-iso-PGF2α levels, confirms the ability of HT to directly neutralize free radicals. At the same time, the reduction in NADPH oxidase activity and the increase in antioxidant enzyme activities (SOD, catalase, GPx) show that hydroxytyrosol also strengthens the endogenous antioxidant defense system. These results are associated with decreased endothelial NO degradation and increased NO bioavailability, which subsequently contributed to improved vascular function.

One of the most important findings observed during the study was the significant normalization of the lipid profile. When hydroxytyrosol was administered, LDL oxidation was reduced by 60–80%, which is a highly relevant parameter considering the key pathogenic role of oxidized LDL in the early stages of atherosclerosis. The increased resistance of LDL particles to oxidation limits their uptake by macrophages, thereby reducing foam cell formation and markedly slowing plaque development. At the same time, the enhanced biochemical activity of the HDL fraction and the strengthening of its antioxidant properties, along with a 10–20% reduction in triglycerides, demonstrate that hydroxytyrosol plays a key role in restoring metabolic stability. These findings are consistent with clinical data, as reductions in LDL and increases in HDL have been consistently reported in patients treated with HT.

Data obtained from the assessment of endothelial function demonstrated that hydroxytyrosol exerts both direct and indirect effects in improving the condition of the vascular wall. The

JOURNAL OF APPLIED SCIENCE AND SOCIAL SCIENCE
eISSN 2229-3113 pISSN 2229-3205
Volume 15 Issue 11, November 2025
Impact factor: 2019: 4.679 2020: 5.015 2021: 5.436, 2022: 5.242, 2023: 6.995, 2024 7.75

increase in eNOS activity, the enhancement of NO production, and the restoration of vascular vasodilation capacity were the main factors contributing to improved microcirculation. In addition, the 20-40% reduction in the expression of inflammatory mediators such as ICAM-1, VCAM-1, and E-selectin indicates a reduction in endothelial inflammation. This, in turn, plays a decisive role in the adhesion and migration of monocytes to the vascular wall and subsequent plaque formation. The results once again confirm the significance of hydroxytyrosol as a molecule that strengthens endothelial stability.
The results obtained on processes related to atherosclerosis were also positive, showing a decrease in the number of foam cells, a reduction in the level of inflammation in plaque tissue, and an increase in collagen synthesis during hydroxytyrosol therapy. The reduced activity of plaque-associated metalloproteinases—MMP-2 and MMP-9—contributes to increased mechanical stability of the plaque, thereby helping to reduce the risk of myocardial infarction and stroke. These mechanisms are directly associated with clinically observed reductions in plaque progression rate and increased arterial elasticity.
The results of platelet activity assessment confirmed the antithrombotic properties of hydroxytyrosol. The reduction of platelet aggregation by up to 20–40%, the decrease in platelet activation markers, and the restoration of the prostacyclin/thromboxane balance demonstrate that hydroxytyrosol is an important factor in reducing the risk of ischemic heart disease. This is consistent with its effects on reducing vascular smooth muscle spasms and improving overall hemodynamic stability.
Overall, the research findings showed that the beneficial effects of hydroxytyrosol on the cardiovascular system are achieved not through a single mechanism, but through several molecular and physiological mechanisms acting simultaneously. It reduces oxidative stress, attenuates inflammation, normalizes lipid metabolism, restores endothelial function, inhibits the development of atherosclerosis, and decreases the risk of thrombosis. This multi-vector effect makes hydroxytyrosol a natural cardioprotective nutraceutical of high scientific and practical relevance.

CONCLUSION

The research results confirmed that hydroxytyrosol is a highly effective, multi-directional bioactive compound in protecting the cardiovascular system. According to the obtained data, hydroxytyrosol exerts cardioprotective effects by reducing oxidative stress, normalizing lipid metabolism, restoring endothelial function, and inhibiting the molecular stages of atherosclerosis. Its ability to markedly reduce LDL oxidation, enhance HDL activity, and decrease the expression of inflammatory mediators and adhesion molecules strengthens the structural and functional stability of the vascular wall. In addition, increased plaque stability, reduced metalloproteinase activity, and decreased platelet aggregation help reduce the risk of ischemic heart disease, hypertension, and thrombotic complications. Overall, the strong antioxidant and anti-atherogenic properties of hydroxytyrosol allow it to be proposed as a promising nutraceutical for the prevention and complex treatment of cardiovascular diseases. In the future, large-scale clinical studies are needed to further substantiate its dosing, safety profile, and long-term efficacy.

References

JOURNAL OF APPLIED SCIENCE AND SOCIAL SCIENCE
eISSN 2229-3113 pISSN 2229-3205
Volume 15 Issue 11, November 2025
Impact factor: 2019: 4.679 2020: 5.015 2021: 5.436, 2022: 5.242, 2023: 6.995, 2024 7.75

1. 1. Sokurenko M. S., Bessonov V. V., Solovieva N. L. Hydroxytyrosol - a natural antioxidant of olive oil // Nutrition Issues. - 2015. - Vol. 84. - No. S5. - Pp. 75-75.
2. 2. Yashin Ya. I., Vedenin A. N., Yashin A. Ya. Powerful natural polyphenolic antioxidants, their food sources and their impact on human health // Phenolic compounds: properties, activity, innovations. - 2018. - Pp. 571-576.
3. 3. KRYSIN A. P. et al. Cardioprotective effect of p-tyrosol in the acute period of cardiovascular and cerebral ischemia // Chemistry for Sustainable Development. - 2019. - Vol. 27. - No. 4. – P. 365-372.
4. 4. Kholshin S. V. et al. 630126, Novosibirsk, Vilyuyskaya St., 28, Novosibirsk State //Communications. – 2007. – Vol. 37. – No. 23. – P. 4245-4252.
5. 5. Storozhok N. M. et al. Antioxidant effect of structural analogs of tyrosol, the active substance of Rhodiola rosea //Butlerov Communications. – 2011. – Vol. 24. – No. 3. – P. 105-108.
6. 6. Shilov V. et al. Anti-ischemic effect of isoliquiritigenin and a combination of hydroxytyrosol with cis-aconitate, cytosine and amino acids // Science and Innovations. – 2016. – V. 5. – No. 159. – P. 64-66.
7. 7. Zaporozhsky A. A., Mohammad A. T. Towards the creation of gerodietetic nutrition products with immunoprotective properties // Modern problems of food safety. Proceedings of the international scientific conference. Editorial board: Stekolnikov A. A. – 2020. – P. 37.