VER
Vascular & Endovascular Review

Impact Of Flavonoid-Based Hypolipidemic Agents On Lipid Profile And Atherosclerosis Development In Hypercholesterolemic Rabbits

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ANNOTATION

The purpose of this research was to examine modifications in the lipid profiles of experimental rabbits with experimentally induced hypercholesterolemia and to explore the connection between these lipid variations and the onset of atherosclerosis. The investigation focused on analyzing the blood levels of total cholesterol, triglycerides, low-density lipoproteins (LDL), and high-density lipoproteins (HDL) in rabbits, highlighting their contribution to the pathophysiology of atherosclerosis. Rabbits with hypercholesterolemia demonstrated marked elevations in total cholesterol and triglyceride levels, accompanied by diminished HDL levels, factors that promote the formation of atherosclerotic lesions. The study established that flavonoid-rich formulations successfully restore lipid balance by suppressing atherogenic lipoprotein levels and enhancing HDL concentrations, thus offering potential applications in preventing and managing cardiovascular conditions.

KEYWORDS: Elevated Blood Cholesterol, Arterial Plaque Formation, Blood Fat Composition, Plant-Derived Polyphenols, Serum Cholesterol, Fatty Acid Esters, Heart And Vessel Disorders.

How to Cite: Kurbonova Z.Ch., Saidov A.B., Sayfutdinova Z.A., Akhmedova D.B., Tairova G.B., (2025) Impact Of Flavonoid-Based Hypolipidemic Agents On Lipid Profile And Atherosclerosis Development In Hypercholesterolemic Rabbits, Vascular and Endovascular Review, Vol.8, No.20s, 99-106

INTRODUCTION

Atherosclerosis, with its complications like coronary artery disease, stroke, and peripheral arterial disease, remains a leading cause of global mortality [1, 2]. These conditions are primarily driven by disturbances in lipid metabolism, particularly increased levels of atherogenic lipoproteins like LDL and VLDL, which contribute to plaque formation in arteries. As plaques accumulate, arteries narrow, lose elasticity, and blood flow to vital organs is impaired.

Hypercholesterolemia, characterized by elevated cholesterol levels, is a key risk factor for atherosclerosis, leading to plaque deposition and arteriosclerosis. This increases the risk of heart attacks and strokes. The World Health Organization highlights the growing global burden of cardiovascular diseases (CVD), driven by aging populations, unhealthy lifestyles, and rising rates of obesity and diabetes. Despite medical advances, CVD remains the leading cause of death worldwide.

In low- and middle-income countries, limited healthcare access exacerbates the situation. Lifestyle changes such as diet, physical activity, and smoking cessation, along with early intervention using statins and regular lipid monitoring, are essential for reducing atherosclerosis risk. In high-income countries, CVD causes millions of deaths each year, many linked to atherosclerosis. Russia faces a similar challenge, with tens of thousands of lives lost annually. Early diagnosis and treatment of hypercholesterolemia are crucial in combating atherosclerosis and improving public health outcomes [3, 4, 5].

Traditionally, hypercholesterolemia is treated with statins and other synthetic hypolipidemic drugs, but these medications can have side effects, such as liver dysfunction, muscle pain, and other unpleasant symptoms. This has led to growing interest in alternative, natural approaches, such as the use of flavonoid-based treatments, which have demonstrated significant antioxidant, anti-inflammatory, and hypolipidemic properties [6].

The connection between heart failure and kidney dysfunction is well-established and is referred to as the «cardiorenal syndrome». This pathophysiological condition involves a mutual exacerbation of heart and kidney diseases. In this syndrome, impaired heart function leads to inadequate blood supply to the kidneys, causing deterioration in renal function [4]. Conversely, renal dysfunction

contributes to worsening heart function due to fluid retention, disturbances in the electrolyte balance, and the accumulation of toxic metabolic byproducts [5].

In patients with CHF, renal dysfunction can present with a variety of symptoms, such as edema, elevated blood pressure, disturbances in fluid-electrolyte balance, and increased levels of creatinine and urea in the blood. Timely diagnosis of these changes is crucial for the early identification of renal failure, as early intervention can significantly improve disease prognosis and reduce the risk of more severe complications, such as chronic kidney disease (CKD) [6-8].

Laboratory diagnostics play a central role in the management of CHF patients, allowing not only for the evaluation of renal function but also for the detection of potential hidden changes at early stages of the disease [9]. Modern laboratory methods, such as measuring creatinine and urea levels, albuminuria, assessing the albumin-to-creatinine ratio in urine, and testing for electrolytes and acid-base balance, provide the opportunity to confirm renal impairment, monitor disease progression, assess treatment efficacy, and prevent the development of renal failure [10].

It is also crucial to emphasize that, as time progresses, renal dysfunction can become a significant factor in worsening the course of chronic heart failure (CHF). This creates a harmful and self-perpetuating cycle where the decline in the function of one organ directly contributes to the worsening of the other. The kidneys, which play a vital role in maintaining fluid balance, blood pressure regulation, and the elimination of waste products, are often negatively impacted in patients with heart failure. As heart failure progresses, decreased blood flow to the kidneys can lead to renal impairment, further exacerbating heart failure symptoms. This interdependent relationship between the heart and kidneys significantly complicates the management of both conditions.

Addressing renal dysfunction can have a profound impact on improving the overall health status of patients, alleviating symptoms, and potentially slowing the progression of both heart and kidney disease. Furthermore, by managing these conditions appropriately, healthcare providers can enhance the patient's quality of life and significantly extend their life expectancy. The goal should always be to break this vicious cycle and offer patients the best possible outcome through integrated care approaches that target both heart and kidney health simultaneously.

RESEARCH METHODS

Experimental Animals

In this study, male rabbits were randomly allocated into either a control (intact) group (n=6) or a hypercholesterolemic group (n=18). The animals were housed in a controlled environment with a 12-hour light/dark cycle, ensuring optimal welfare standards. Unrestricted access to food and water was provided throughout the duration of the experiment. The study protocol strictly adhered to ethical principles governing animal research and obtained prior approval from the institutional ethics review board.
Induction of Hypercholesterolemia

Hypercholesterolemia was induced in the experimental group through a high-cholesterol diet. The rabbits were fed a diet containing 1.5% cholesterol (w/w) for 8 weeks. The control group was fed a regular diet without added cholesterol.

Lipid Profile Analysis

At the conclusion of the experimental period, the rabbits were humanely euthanized, and blood samples were obtained via cardiac puncture. Plasma was isolated by centrifugation and stored at −80°C until subsequent analyses. The following lipid parameters were then determined:

Total cholesterol (TC) levels were assessed using enzymatic colorimetric assays.
Triglyceride (TG) levels were measured employing a standard enzymatic methodLDL and HDL levels were measured with an ELISA kit, while VLDL concentrations were calculated using the Friedewald equation.

Statistical Analysis

Data were processed using statistical software. Differences between the control group and the hypercholesterolemic group were evaluated using a two-sample t-test. Significance was set at $p < 0.05$.

RESULTS OF THE STUDY

General Cholesterol (Total Cholesterol)

Total cholesterol (TC) is a crucial biomarker that provides valuable insight into the overall status of lipid metabolism in the body. It serves as an important indicator of an individual's lipid balance and is considered one of the primary markers for the development of atherosclerosis. The total cholesterol level reflects the sum of all cholesterol molecules present in the blood, including both high-density lipoprotein (HDL) and low-density lipoprotein (LDL), and it plays a central role in assessing cardiovascular risk. Given its significance, TC is often used in clinical settings to monitor and diagnose lipid abnormalities, which are commonly associated with the development of cardiovascular diseases (CVD), especially atherosclerosis.

In the context of this research, a notable difference was observed in the total cholesterol levels between two distinct groups of rabbits: the intact group (n=6) and the hypercholesterolemic group (n=18). The intact group, which served as a control and consisted of healthy rabbits with normal lipid profiles, exhibited a total cholesterol level of 5.6 mmol/l. This value falls within the accepted reference range for healthy animals, indicating that the cholesterol metabolism in these rabbits was functioning

optimally. Under normal metabolic conditions, cholesterol maintains a delicate balance between the plasma and cellular compartments.

On the other hand, the hypercholesterolemic group, which was induced with high cholesterol levels through diet, displayed a total cholesterol concentration of 11.4 mmol/l. This value was more than double that of the intact group, highlighting a clear disruption in lipid metabolism. The substantial rise in total cholesterol levels in the hypercholesterolemic group can be largely attributed to the high cholesterol intake provided in their diet. Excess cholesterol, mainly LDL, accelerates atherosclerosis and cardiovascular disease. Elevated cholesterol in hypercholesterolemic rabbits indicates lipid imbalances and early atherosclerosis, helping develop management strategies.

In conclusion, the findings from this research underscore the significance of total cholesterol levels as a reliable and informative marker for lipid metabolism disorders. By identifying and understanding the mechanisms behind cholesterol dysregulation, particularly in hypercholesterolemic conditions, healthcare professionals can better assess the risk of atherosclerosis and other cardiovascular diseases. Furthermore, the data from this study can contribute to the development of more effective treatments and interventions aimed at controlling cholesterol levels and preventing the onset of cardiovascular disease in individuals with lipid metabolism abnormalities.

Triglycerides

Triglycerides are a type of lipid that play a central role in energy storage and production within the body. As the primary form of fat circulating in the bloodstream, triglycerides serve as a vital energy reserve, providing fuel for various physiological processes, particularly during periods of fasting or increased physical activity. Triglycerides are formed by the combination of glycerol and three fatty acid molecules, and they are stored in adipose tissue, where they can be mobilized when the body needs extra energy. Given their essential role in metabolism, maintaining appropriate triglyceride levels is crucial for overall health.

In the current study, triglyceride levels were analyzed in two distinct groups of rabbits: the intact group (n=6), which served as the control with normal lipid metabolism, and the hypercholesterolemic group (n=18), which had been induced with elevated cholesterol levels. In the intact group, the triglyceride levels were measured at 1.91 mmol/l. This value falls within the expected range for healthy animals with optimal metabolic function. It reflects the normal balance between energy storage and utilization, indicating that the body is efficiently managing its lipid reserves without excessive accumulation of fat in the bloodstream. In this group, lipid metabolism appears to be functioning effectively, with triglycerides being stored in adipose tissue for future energy needs while not leading to any harmful excess in circulation.

However, in the hypercholesterolemic group, the triglyceride levels were found to be significantly elevated, reaching 5.72 mmol/l. This value is more than three times higher than the level observed in the intact group, highlighting a profound disruption in lipid metabolism. Such an excessive level of triglycerides is a strong indication of metabolic abnormalities, particularly those associated with a high intake of dietary fats. This process obstructs blood flow, raising the risk of heart attacks, strokes, and complications.

The significant rise in triglyceride levels in the hypercholesterolemic rabbits is likely attributable to the high-fat diet they were subjected to during the experimental period. Such a diet leads to the overproduction and accumulation of triglycerides in the liver, which are subsequently released into the bloodstream.

This excessive triglyceride accumulation not only contributes to the development of atherosclerosis but also promotes inflammatory processes within the blood vessels. In conclusion, the findings from this study underscore the importance of maintaining normal triglyceride levels for cardiovascular health. The marked elevation of triglycerides in the hypercholesterolemic group serves as a key indicator of lipid metabolism disorders and highlights the detrimental effects of a high-fat diet on the cardiovascular system. By understanding the mechanisms that drive elevated triglyceride levels and their association with atherosclerosis, it is possible to develop targeted strategies for managing lipid disorders and preventing the onset of cardiovascular diseases. Further research is needed to explore the specific pathways through which triglycerides contribute to atherosclerosis, as well as to identify effective interventions that can mitigate their harmful effects on vascular health.

High-Density Lipoproteins (HDL)

HDL removes excess cholesterol and transports it to the liver for excretion. This process is critical for maintaining a healthy balance of cholesterol within the body, as well as for protecting the blood vessels from the harmful effects of cholesterol accumulation. By facilitating the clearance of cholesterol from the arteries, HDL helps to prevent the formation of atherosclerotic plaques, which can lead to the narrowing and hardening of the arteries, a hallmark of atherosclerosis.

In this study, HDL levels were measured in two distinct groups of rabbits: the intact group (n=6), which represented a healthy control group with normal lipid metabolism, and the hypercholesterolemic group (n=18), which was induced with elevated cholesterol levelsIn the intact group, HDL levels were 1.11 mmol/l, indicating healthy lipid metabolism and helping prevent cholesterol accumulation in the arteries, thus reducing the risk of atherosclerosis.

However, in the hypercholesterolemic group, the HDL levels were significantly reduced, with a measurement of just 0.36 mmol/l. This value is markedly lower than the level observed in the intact group, indicating a serious disturbance in lipid metabolism. A reduction in HDL levels is a key indicator of impaired cholesterol clearance and reflects a heightened risk of atherosclerosis.

When HDL levels are low, the body's ability to remove excess cholesterol from the bloodstream is compromised, allowing cholesterol to accumulate in the arteries.

The imbalance between low HDL and high LDL levels is a well-established risk factor for the development and progression of atherosclerosis, as it promotes both the accumulation of cholesterol and the inflammatory processes that destabilize atherosclerotic plaques, increasing the risk of plaque rupture and subsequent cardiovascular events.

The findings of this study underscore the importance of maintaining a healthy balance between HDL and LDL levels to prevent cardiovascular diseases. The significant reduction in HDL levels in the hypercholesterolemic group serves as a strong indicator of lipid metabolism dysfunction and highlights the critical role of HDL in protecting the cardiovascular system.

Low-Density Lipoproteins (LDL)

While cholesterol is essential for various physiological functions, such as membrane structure and hormone production, an excessive accumulation of cholesterol in the arterial walls can lead to the formation of atherosclerotic plaques. These plaques can progressively narrow the arteries, reducing blood flow and increasing the risk of cardiovascular diseases, including heart attacks, strokes, and peripheral artery disease. Elevated LDL levels are widely recognized as one of the primary risk factors for the development and progression of atherosclerosis.

In this study, LDL levels were measured in two distinct groups of rabbits: the intact group (n=6), which served as a healthy control with normal lipid metabolism, and the hypercholesterolemic group (n=18), which was induced with elevated cholesterol levels to model a lipid metabolism disorder. In the intact group, the LDL levels were found to be 2.77 mmol/l, which falls within the normal reference range for healthy rabbits. This level of LDL indicates a well-balanced lipid profile, with cholesterol levels being efficiently transported and distributed to cells as needed, without excess accumulation in the arterial walls. As a result, the risk of developing atherosclerosis remains low in the intact group, as cholesterol is utilized appropriately without contributing to plaque formation or arterial damage.

However, in the hypercholesterolemic group, the LDL levels were significantly elevated, measuring 5.1 mmol/l. This value is nearly double the level observed in the intact group, which suggests that the elevated LDL levels in these animals contribute to an imbalance in lipid metabolism. The higher LDL concentration in the hypercholesterolemic rabbits promotes the deposition of cholesterol within the walls of the arteries, a process known as atherosclerosis. Over time, this accumulation of cholesterol leads to the formation of fatty streaks and plaques, narrowing the arteries and reducing their elasticity. As a result, blood flow is impeded, and the risk of cardiovascular diseases significantly increases.

The elevated LDL levels in the hypercholesterolemic group are indicative of a disruption in lipid homeostasis, where the excessive supply of cholesterol to the arterial walls exacerbates the development of atherosclerotic lesions. These plaques not only restrict blood flow but also promote inflammation within the arteries, further destabilizing the plaques and increasing the likelihood of plaque rupture. When these plaques rupture, they can lead to blood clot formation, which may result in a heart attack or stroke.
Overall, the findings from this study emphasize the critical role of LDL in the development of atherosclerosis and cardiovascular diseases. Therapeutic interventions such as statins, dietary modifications, and lifestyle changes aimed at reducing LDL cholesterol may be crucial in preventing the progression of atherosclerosis and reducing the associated cardiovascular risks.

Very Low-Density Lipoproteins (VLDL)

VLDL transports triglycerides from the liver to tissues for energy, similar to LDL's role in cholesterol transport. However, elevated VLDL levels are commonly linked to metabolic disorders, such as insulin resistance and obesity, and they represent a significant risk factor for the development of atherosclerosis. Just like LDL, VLDL can contribute to the accumulation of fatty deposits in the arterial walls, leading to narrowing of the arteries, impaired blood flow, and an increased likelihood of cardiovascular events, such as heart attacks and strokes.

In this study, a comparison was made between the lipid profiles of rabbits with induced hypercholesterolemia and those of healthy controls. VLDL were observed, which points to significant disturbances in lipid metabolism. These findings are indicative of the early stages of atherosclerosis development, as the accumulation of atherogenic lipoproteins leads to lipid deposition in the arterial walls, resulting in plaque formation and an elevated risk of cardiovascular diseases.

Regular lipid profile assessments can help in identifying early metabolic disturbances, enabling timely intervention to prevent the progression of atherosclerosis and associated cardiovascular complications.

In addition to conventional therapeutic approaches, plant-based preparations, particularly those rich in flavonoids, have been increasingly recognized as potential tools for improving lipid metabolism and enhancing vascular health. By modulating lipid metabolism, flavonoid-rich preparations can potentially reduce the levels of atherogenic lipoproteins (such as LDL and VLDL) and promote a healthier lipid profile, thus mitigating the risk of atherosclerosis. Moreover, flavonoids possess antioxidant and anti-inflammatory properties, which can help protect the blood vessels from oxidative stress and inflammation, further contributing to vascular health.

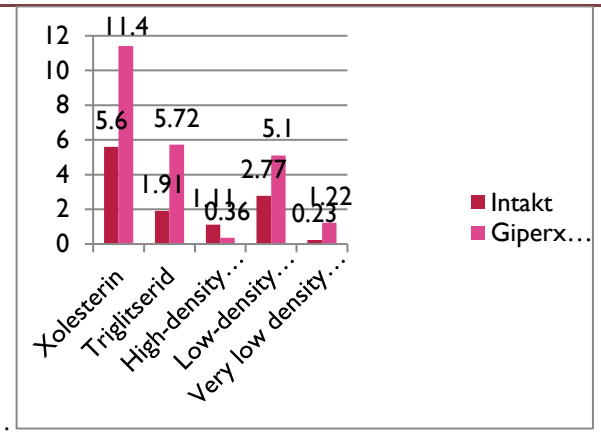

Figure 1. Changes in lipid spectrum parameters in experimental animals with hypercholesterolemia

This section of the study focuses on the effects of flavonoid-based hypolipidemic agents on the lipid profile and the alterations induced by hypercholesterolemia. By examining the impact of these natural compounds, the research aims to explore their potential role in restoring lipid balance, reducing atherogenic lipoproteins, and ultimately preventing or slowing the progression of atherosclerosis. Given the promising results from previous studies, flavonoid-based interventions could serve as an adjunct to traditional lipid-lowering therapies, offering a more holistic approach to the management of hypercholesterolemia and the prevention of cardiovascular diseases. Further research is necessary to fully understand the mechanisms through which flavonoids exert their beneficial effects on lipid metabolism and their potential applications in cardiovascular medicine

Lipid Profile Alterations in Flavonoid-Treated Groups

After treatment with flavonoid-based agents, a significant reduction in cholesterol levels was observed in the experimental group, with the total cholesterol dropping to 7.8 mmol/L. This outcome highlights the effectiveness of flavonoids in improving lipid metabolism and mitigating the hypercholesterolemic state. Flavonoids appear to exert their beneficial effects by primarily targeting atherogenic lipoproteins. This balanced adjustment of lipid levels—reducing harmful LDL and VLDL while boosting protective HDL—results in an overall decrease in total cholesterol levels, thereby decreasing the risk of atherosclerosis and other cardiovascular diseases.

The antioxidant properties of flavonoids further contribute to their efficacy in cardiovascular health. By neutralizing reactive oxygen species (ROS) and preventing the oxidation of LDL cholesterol, flavonoids help reduce oxidative damage to the blood vessels. Oxidized LDL is particularly atherogenic, as it accelerates the formation of plaques in the arteries. Flavonoids, through their antioxidant effects, help curb this process, thereby offering additional protection against the development of atherosclerosis and the associated cardiovascular complications, such as coronary artery disease, stroke, and heart attack.

In comparison, the group that received the comparative treatment showed a more modest reduction in cholesterol levels, with an average of 9.2 mmol/L. While this reduction still reflects some degree of efficacy, it is clear that the flavonoid-based treatment had a significantly greater impact on cholesterol normalization. The comparative treatment, although effective to some extent, appeared to have a more limited influence on lipid metabolism, as evidenced by the higher final cholesterol levels observed in this group compared to the flavonoid-treated group. This suggests that the comparative agent may have a less potent effect in terms of managing lipid profiles and addressing the underlying lipid metabolism disorder.

Further studies and clinical trials are warranted to explore the full potential of flavonoids in cardiovascular disease management, and to better understand their mechanisms of action in lipid metabolism and vascular health.

Flavonoid Effects on Triglycerides

The flavonoid-treated group also exhibited a notable decrease in triglyceride levels, with the average concentration dropping to 3.2 mmol/L. This marked reduction highlights the effectiveness of flavonoids in normalizing lipid metabolism, particularly in terms of triglyceride regulation.

The decrease in triglyceride levels observed in the flavonoid-treated group suggests that flavonoids play a key role in regulating lipid metabolism by not only reducing the levels of harmful lipids but also by improving the overall efficiency of lipid processing within the body. One of the mechanisms behind this effect is likely the antioxidant properties of flavonoids, which help reduce oxidative stress and prevent the overproduction of triglycerides in the liver. By curbing excessive triglyceride synthesis, flavonoids help protect the liver from conditions such as fatty liver disease and improve the overall lipid profile, which is essential for reducing the risk of atherosclerosis and related cardiovascular complications.

In contrast, the comparative treatment led to a more modest reduction in triglyceride levels, with concentrations dropping only to 4.5 mmol/L. Although this reduction indicates some therapeutic effect, it is clear that the comparative agent has a less significant impact on lipid metabolism, particularly regarding triglyceride regulation. The slower and less pronounced effect of the comparative treatment suggests that it may not address the root causes of lipid metabolism disturbances as effectively as

flavonoids. This comparison underscores the superior efficacy of flavonoids in regulating triglyceride levels and their potential as a more potent option for managing lipid disorders associated with cardiovascular diseases.

The results of this study further emphasize the potential of flavonoid-based treatments in the management of lipid metabolism These findings encourage further exploration of flavonoid-based therapies as part of a comprehensive approach to cardiovascular health and disease prevention.

Flavonoids and High-Density Lipoprotein (HDL) Levels

Flavonoid treatment led to a significant increase in high-density lipoprotein (HDL) levels, reaching 0.75 mmol/L. HDL is commonly referred to as "good" cholesterol due to its crucial role in transporting excess cholesterol from the bloodstream to the liver, where it is processed and excreted. This process helps to prevent the buildup of cholesterol in the arterial walls, thereby reducing the risk of atherosclerosis and related cardiovascular diseases. The observed increase in HDL levels following flavonoid treatment suggests that these compounds enhance the body's natural protective mechanisms against cholesterol accumulation. Flavonoids exert this effect through their antioxidant and anti-inflammatory properties, which help to improve the function of the vascular system and maintain a healthy balance of lipid molecules. By promoting the synthesis or activity of HDL, flavonoids contribute significantly to reducing the risks associated with lipid imbalances and cardiovascular disorders.

The study results provide compelling evidence that flavonoids are effective in boosting HDL levels, thereby playing a key role in improving the overall lipid profile and supporting cardiovascular health. This finding further highlights the potential of flavonoid-based treatments as a therapeutic strategy for managing hypercholesterolemia and preventing the progression of atherosclerosis, a leading cause of cardiovascular morbidity and mortality worldwide.

In contrast, the comparative treatment group demonstrated a less pronounced increase in HDL levels, with a final measurement of 0.56 mmol/L. Although this increase still reflects some degree of efficacy, it is significantly lower than the effect seen with flavonoid treatment.

These findings underscore the superior cardioprotective effects of flavonoids, particularly in their ability to increase HDL levels more efficiently. By improving HDL cholesterol, flavonoids not only help maintain a healthier lipid profile but also contribute to a reduced risk of atherosclerosis and other related cardiovascular conditions. Given their multiple beneficial effects on lipid metabolism and cardiovascular health, flavonoids present a promising natural alternative for the prevention and treatment of lipid disorders and cardiovascular diseases.

Low-Density Lipoprotein (LDL) Reduction with Flavonoid Treatment

In the flavonoid-treated group, low-density lipoprotein (LDL) levels were significantly reduced to 3.1 mmol/L. LDL is often referred to as "bad" cholesterol due to its role in transporting cholesterol to various tissues, including the arterial walls. The marked reduction in LDL levels following flavonoid treatment demonstrates their powerful effect on lipid metabolism and their ability to improve cholesterol balance within the body. This underscores the essential role of flavonoids in managing cholesterol metabolism and maintaining optimal vascular health.

Flavonoids achieve this reduction in LDL levels through their multifaceted mechanisms, including their antioxidant, anti-inflammatory, and lipid-modulating properties. These compounds not only help decrease the synthesis and release of LDL but also enhance the body's ability to remove excess cholesterol from the bloodstream, contributing to a healthier lipid profile overall. The ability of flavonoids to regulate LDL levels effectively highlights their potential as a therapeutic strategy for preventing and managing atherosclerosis and other cardiovascular diseases that result from lipid metabolism disturbances.

In contrast, the comparative treatment group demonstrated a higher LDL level, measuring at 4.2 mmol/L. Although this is a reduction compared to baseline levels in hypercholesterolemic rabbits, it is significantly higher than the LDL levels observed in the flavonoid-treated group. This indicates that the comparative treatment, while still showing some effect, is less effective at reducing LDL levels compared to flavonoid treatment. The modest impact of the comparative agent on LDL reduction suggests that it may not target the underlying mechanisms of cholesterol metabolism as efficiently as flavonoids, ultimately offering less protection against cardiovascular disease.

These findings highlight the superior ability of flavonoids to lower LDL levels and manage cholesterol metabolism, making them a more potent option for reducing the risk of atherosclerosis and improving overall cardiovascular health. By significantly decreasing LDL cholesterol, flavonoid-based treatments offer a promising approach for addressing lipid imbalances and preventing the progression of cardiovascular diseases associated with high cholesterol levels.

Very Low-Density Lipoprotein (VLDL) Reduction

The flavonoid treatment group also demonstrated a significant reduction in very low-density lipoprotein (VLDL) levels, which decreased to 0.4 mmol/L. VLDL particles are primarily responsible for carrying triglycerides and cholesterol through the bloodstream. When VLDL levels are elevated, they can contribute to the buildup of plaque in the arterial walls, leading to atherosclerosis and increasing the risk of cardiovascular diseases. The reduction in VLDL levels observed in the flavonoid-treated rabbits suggests that flavonoids are effective in reducing the accumulation of both cholesterol and triglycerides in the arteries, thus mitigating the progression of atherosclerosis. Furthermore, flavonoids, particularly polyphenolic compounds, have well-

documented antioxidant and anti-inflammatory properties that help improve lipoprotein metabolism, reduce oxidative stress, and minimize the inflammatory processes associated with lipid accumulation in the blood vessels.

In contrast, the comparative treatment group exhibited a higher VLDL level (0.85 mmol/L), indicating that the comparative agent was less effective in reducing VLDL levels. This higher VLDL concentration suggests that the comparative treatment had a more limited impact on lipid metabolism, resulting in a less significant reduction in the risk of plaque formation in the arteries. The relatively modest reduction in VLDL levels in the comparative treatment group highlights the superior efficacy of flavonoid-based treatment in improving lipid profiles and preventing the pathogenesis of cardiovascular diseases.

The results of this study underscore the positive impact of flavonoid-based hypolipidemic agents on the lipid spectrum in hypercholesterolemic conditions. Flavonoid treatment by effectively improving the lipid profile and reducing the risk factors associated with atherosclerosis, flavonoids offer a promising therapeutic approach for managing hypercholesterolemia. Compared to the comparative treatment, flavonoids exhibited significantly higher efficacy, suggesting they may be a more potent and recommended alternative in the prevention and treatment of cardiovascular diseases related to lipid metabolism disturbances.

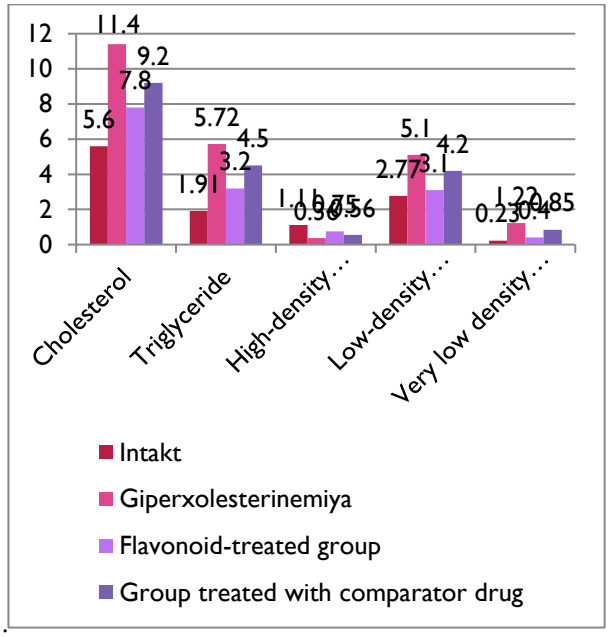

Figure 2. Changes in lipid profile during correction of hypercholesterolemia

These findings highlight the therapeutic potential of flavonoids in addressing lipid imbalances and reducing the burden of cardiovascular diseases, emphasizing their role as a valuable addition to the arsenal of treatments for hypercholesterolemia and its associated complications

CONCLUSION

The findings of this study strongly support the use of flavonoid-based hypolipidemic agents as highly effective treatments for improving lipid profiles and mitigating the effects of hypercholesterolemia.

Furthermore, the results revealed that flavonoid treatments were markedly more effective than the comparative agent in improving the lipid profile, emphasizing the superior potential of flavonoids in the management of hypercholesterolemia. The efficacy of flavonoids in reducing key lipid parameters such as LDL and VLDL, which are directly linked to the development of atherosclerosis, highlights their therapeutic promise in addressing the underlying causes of cardiovascular diseases.

In addition to their lipid-regulating effects, flavonoids possess powerful antioxidant and anti-inflammatory properties. The antioxidant effect of flavonoids helps neutralize harmful free radicals in the bloodstream, while their anti-inflammatory properties work to reduce the inflammation that contributes to plaque formation in the arteries.

In conclusion, the study underscores flavonoids as a promising therapeutic strategy for managing lipid disorders and promoting cardiovascular health. By regulating cholesterol and triglyceride levels, improving lipoprotein balance, and offering protective benefits through their antioxidant and anti-inflammatory actions, flavonoids represent a comprehensive approach to reducing the risk of cardiovascular diseases. Their superior efficacy, as compared to the comparative treatment, further highlights their potential as a valuable tool in preventing and treating conditions related to lipid metabolism disorders, such as hypercholesterolemia and atherosclerosis.

PRACTICAL RECOMMENDATIONS:

Based on the findings of this study, the following practical recommendations can be made:

1. Flavonoid-based Therapies for Hypercholesterolemia:

Flavonoid-rich preparations should be considered as part of the treatment regimen for individuals with hypercholesterolemia and related cardiovascular risks.

2. Dietary Recommendations:

In addition to pharmacological treatments, incorporating flavonoid-rich foods (such as fruits, vegetables, tea, and dark chocolate) into the diet may help enhance lipid metabolism and improve cardiovascular health. Regular consumption of these foods can complement medical treatment and help prevent or manage hypercholesterolemia.

3. Personalized Treatment Plans:

Given the strong effects of flavonoids on lipid metabolism, they should be incorporated into personalized treatment plans based on an individual's lipid profile, lifestyle, and overall health status. Healthcare providers should monitor lipid levels regularly to assess the efficacy of flavonoid-based therapies and adjust doses or combine them with other lipid-lowering agents if necessary.

4. Further Research:

Additional clinical trials and long-term studies are needed to better understand the full scope of flavonoid effects on lipid metabolism, particularly in human populations. Research on the optimal dosages, specific flavonoid compounds, and potential side effects will be crucial for refining treatment protocols.

5. Integration into Public Health Strategies:

Public health campaigns promoting the inclusion of flavonoid-rich foods in the diet, alongside other measures to control blood lipid levels, should be encouraged. Governments and health organizations can integrate this approach into preventive healthcare strategies to reduce the burden of cardiovascular diseases on the population.

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