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Review article

Status of cholesterol in our diets: A review

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ABSTRACT

Cardiovascular disease (CVD) is the leading cause of death in the world. Hypercholesterolemia, characterized by elevated blood low-density lipoprotein cholesterol (LDL-C) concentrations, is a risk factor for CVD. A growing body of research suggests that LDL-C levels and CV risk are linked. Despite the fact that the majority of current epidemiologic studies show no substantial link between eating one egg per day and blood cholesterol levels or cardiovascular risk, proponents of a positive link remain. The goal was to look at intervention trials that looked at the impact of cholesterol on LDL levels in people. In addition, eggs and dietary cholesterol affect serum cholesterol in many ways. The importance of decreasing cholesterol levels with probiotics, dietary fiber, plant sterols, and nutraceuticals was also discussed.

Keywords: Saturated fatty acids; Low density lipoproteins; High density lipoproteins; Cholesterol; Cardiovascular disease

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1. Introduction

Cholesterol is a sterol produced by animal cells and found in animal-based foods. Its principal job is to keep cell membranes intact and increase fluidity, as well as to act as a precursor for the creation of essential compounds like steroid hormones, bile acids, and vitamin D (Zampelas & Magriplis, 2019).

Cholesterol is a necessary chemical that has pleiotropic effects. Although cholesterol is necessary for cellular function, too much of it can be detrimental. In addition, a lack of cholesterol in the bloodstream can prevent Vitamins K and E from reaching essential organs, which can have catastrophic implications (Soliman, 2018); therefore maintaining cholesterol homeostasis is critical (Afonso et al., 2018).

The link between blood cholesterol and heart disease is well-established, with the major goal of preventative medication being to lower serum low-density lipoprotein (LDL) cholesterol. Furthermore, higher levels of high-density lipoprotein (HDL) cholesterol have been linked to a lower risk of heart disease in epidemiological studies (Blesso & Fernandez, 2018).

The association between dietary cholesterol intake and the risk of heart disease has also piqued researchers' curiosity. Eggs are one of the highest dietary sources of cholesterol. Large-scale epidemiological studies, on the other hand, have identified only shaky links between egg consumption and the risk of cardiovascular disease (Blesso & Fernandez, 2018).

The question of whether dietary cholesterol contributes considerably to high blood cholesterol and atherosclerotic disease is still debated in the nutrition field. High-cholesterol diets generate mild increases in blood cholesterol levels, according to carefully controlled metabolic studies. Because of complicating considerations, it has been difficult to validate this in population research (Grundy, 2016).

It is important to note that dietary cholesterol is just one of many dietary components that influence blood cholesterol levels. Saturated fatty acids, trans fatty acids, soluble fiber, and total caloric consumption are among the others (Grundy, 2016).

According to Barnard et al. (2019), if eggs had no influence on plasma lipid concentrations, the results would be evenly split between those showing lipid rises and those showing lipid reductions. In particular, if an infinite number of studies with identical research design and sample size were done and the results were normally distributed, mean elevations and reductions would be expected to fall uniformly.

Cardiovascular disease (CVD) is the leading cause of death in the world (WHO, 2019). It has been claimed that substituting monounsaturated and polyunsaturated fatty acids for saturated fatty

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acids reduces the risk of cardiovascular disease (Sacks et al., 2017). However, some studies contradict this statement, finding that saturated fatty acid consumption did not raise the risk of CVD, cardiovascular events, or mortality. Furthermore, saturated fat consumption has been shown to increase big, buoyant LDL particles, which may explain, in part, the disparities in the effects of fat consumption on CVD risk (Froyen, 2021). The objective of this review is to compare evidences regarding relationship between cholesterol and cardiovascular diseases.

2. Relationship between dietary cholesterol and serum cholesterol and CVD

2.1. *Effect of dietary cholesterol on CVD*

The effect of eggs and of dietary cholesterol on blood cholesterol concentrations has been examined in several reviews and meta-analyses (Vincent et al., 2019; Rouhani et al., 2018).

In a study, led by a team in the Department of Preventive Medicine at Northwestern University Feinberg School of Medicine, included data from 29,615 adults with results showing that those who consumed 300 mg of dietary cholesterol a day had a 17% higher risk of cardiovascular disease and 18% higher risk of all-cause death, independent of saturated fat or other dietary fats (Zhong et al., 2019).

In a 2018 meta-analysis based on 28 randomized controlled intervention studies, egg eating increased total cholesterol and LDL cholesterol by 5.6 mg/dL and HDL cholesterol by 2.1 mg/dL ($P < .0001$), respectively, when compared to control groups (Rouhani et al., 2018).

MacDonald et al. (2020) investigated the associations between consumption of egg and cholesterol, and hypertension risk (HR) in a cohort of French women. Higher cholesterol consumption was associated with an increased risk of hypertension: HRQ1-Q5 = 1.22 [1.14:1.30], with associations similar regarding egg consumption up to seven eggs per week: HR4–7 eggs = 1.14 [1.06:1.18]. They concluded that egg and cholesterol intakes were associated with a higher risk of hypertension in French women.

A 2019 meta-analysis of intervention studies looked at the dose-response relationship between dietary and circulating cholesterol, finding that a 100 mg/day increase in dietary cholesterol was associated with increases in circulating LDL cholesterol concentrations ranging from 1.90 to 4.58 mg/dL, depending on the model used. The relationship varied based on the cholesterol level at the start. A 100 mg/day increase in dietary cholesterol was anticipated to raise LDL cholesterol concentration by 2.7, 3.6, 4.6, and 5.5 mg/dL, respectively, at baseline LDL cholesterol concentrations of 100, 125, 150, and 175 mg/dL (Vincent et al., 2019).

In hyper-responders, chronic daily egg consumption raises LDL-C to some extent. When eggs are consumed during weight loss, however, LDL-C reactions are often minor. However, egg consumption moves LDL particles to the less harmful big LDL subtype while having no effect on oxidized LDL levels. In addition to increasing HDL-C and the concentration of large HDL, egg consumption has been shown to raise HDL-C and the concentration of large HDL in those who have lost weight (Blesso & Fernandez, 2018).

According to available evidence from demographic and genetic research, a 5% reduction in blood cholesterol throughout a lifetime results in a 15% reduction in the risk of atherosclerotic cardiovascular disease (ASCVD) (Grundy, 2016).

Theoretically, this lower risk might be accomplished by lowering dietary cholesterol. As a result, a low-cholesterol diet should be a part of any plan for preventing atherosclerosis. Adding plant sterols or stanols, which limit cholesterol absorption, can lower your risk even more.

Whole egg and cholesterol intakes were both positively associated with all-cause, CVD, and cancer mortality. In multivariable-adjusted models, the hazard ratios (95% CI (confidence intervals)) associated with each intake of an additional half of a whole egg per day were 1.07 (1.06-1.08) for all-cause mortality, 1.07 (1.06-1.09) for CVD mortality, and 1.07 (1.06-1.09) for cancer mortality. Each intake of an additional 300 mg of dietary cholesterol per day was associated with 19%, 16%, and 24% higher all-cause, CVD, and cancer mortality, respectively (Zhuang et al., 2021).

Barnard et al. (2019) conducted a research about percentage of researches that concluded that there was a relationship between diet cholesterol and serum cholesterol. The percentage of studies supported by industry has climbed from 0% in the 1950s to 60% in 2010 to 2019 ($p > 0.001$). Net cholesterol increases were found in 88 (93%) of the 94 non-industry-funded intervention studies for which the effect of egg eating on cholesterol concentrations could be evaluated (51 % statistically significant, 21% not significant, 21% significance not reported). Net cholesterol rises were found in 51 (86%) of the 59 industry-funded intervention studies (34% statistically significant, 39% not significant, and 14% significance not reported). There have been no trials that show significant reductions in cholesterol levels.

According to an analysis of individual participant data collected from six prospective cohorts in the United States, higher consumption of dietary cholesterol or eggs is related with an elevated risk of incident cardiovascular disease (CVD) and all-cause death in a dose–response relationship. The study comprised 29,615 people (44.9% men, 31.1 percent black, and a mean age of 51.6 years at the start), with a median follow-up period of 17.5 years. Each additional 300 mg of dietary cholesterol intake per day was linked to a higher risk of CVD (adjusted HR 1.17) and mortality from any cause (adjusted HR 1.17). (adjusted HR 1.18) (Lim, 2019).

2.2. *Effect of dietary cholesterol on serum cholesterol*

A study was performed to systematically quantify the association between egg consumption and stroke risk. A dose-response analysis revealed a virtually J-shaped relationship between egg consumption and stroke risk. The intake of one to four eggs per week was associated with a lower risk, while the intake of more than six eggs per week was associated with a higher risk. At a weekly intake of 10 eggs, the results were substantial. According to the findings of this meta-analysis, there is a J-shaped relationship between egg consumption and stroke risk (Tang et al., 2020).

Egg consumption elevated serum total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C), according to new research. Moderate egg eating (one egg per day) reduced the TC/HDL-C and LDL-C/HDL-C ratios, whereas excessive egg consumption (>1 egg per day) resulted in a greater TC/HDL-C and LDL-C/HDL-C ratio (Sikaroudi et al., 2020).

In a cohort study carried out by Xia et al. (2020), associations between dietary intakes of eggs and cholesterol and all-cause and heart disease mortality in a US population were identified. They found out that an additional daily consumption of half an egg had no significant connection with all-cause mortality (multivariable-adjusted hazard ratio, 1.04; 95% CI, 0.96–1.13) or heart disease mortality (0.96; 0.80–1.14). All-cause mortality was inversely linked with each 50-mg/day increase in cholesterol consumption among people with daily intake 250 mg (0.87; 0.77–0.98), but positively associated with all-cause mortality among patients with daily intake 250 mg (1.07; 1.01–1.12). There was no evidence of a link between dietary cholesterol intake and mortality from heart disease (Xia et al., 2020).

Available epidemiologic research in healthy Japanese adults, according to Sugano and Matsuoka (2021), demonstrated no link between daily egg consumption and blood cholesterol levels, which is congruent with findings in the US population. However, when compared to the US population in terms of major nutrients and cholesterol-rich foods, Japanese individuals may have a buffer against the impact of eggs on cardiovascular risk factors, despite eating more eggs.

Although, for the reduction of chronic disease risk blood cholesterol levels should be low, there are organs in the human body where cholesterol is of major importance, such as the eye (Zampelas & Magriplis, 2019). The human lens fiber cell's plasma membranes are saturated with cholesterol, which not only saturates the phospholipid bilayer but also causes the creation of pure cholesterol bilayer domains. Cholesterol levels rise with age, and in older people, they exceed the cholesterol solubility threshold, causing cholesterol crystals to develop. All of these alterations take place in a standard lens without compromising lens transparency. A serious disease develops when cholesterol levels in other organs' cell membranes rise to the point where cholesterol crystals form. inflammasomes are activated by minute cholesterol crystals in vascular cells leading to atherosclerosis development (Widomska & Subczynski, 2019).

In Nigeria, a cross-sectional survey to determine consumption pattern was carried out on 400 respondents using food frequency questionnaire (FFQ) and 24-hour dietary recall. The results of correlations between dietary cholesterol intake (DCI) and lipid profile measures revealed a negative connection (at p =.01) in both males and females. Furthermore, the group who ate more than 5 eggs per week had the lowest TC and LDL-c levels (4.230.19 mmol/L and 2.380.10 mmol/L, respectively). According to the respondents' consumption patterns, eggs (boiled and fried) contributed 34.8% to total DCI, followed by milk (15.9%), and salad cream (0.3%) to total DCI. In normocholesterolemic adults, increased DCI from cholesterol-containing foods (such as eggs) did not result in an increase in blood cholesterol levels (Onyenweaku et al., 2019).

The size of LDL particles is predominantly affected by high-fat and low-fat diets, as well as high and low saturated fatty acids (SFA) intakes. These findings highlight the need of eating enough fat to limit the development of sdLDL particles and hence reduce the risk of CVD (Froyen, 2021).

A total of 146,011 individuals from 21 countries were used in the Prospective Urban Rural Epidemiology (PURE) study. In the PURE study, after excluding those with history of CVD, higher intake of egg (≥ 7 egg/wk compared with < 1 egg/wk intake) was not significantly associated with blood lipids, composite outcome (HR: 0.96; 95% CI: 0.89, 1.04; P-trend = 0.74), total mortality (HR: 1.04; 95% CI: 0.94, 1.15; P-trend = 0.38), or major CVD (HR: 0.92; 95% CI: 0.83, 1.01; P-trend = 0.20). In three large international prospective studies including ~177,000 individuals, 12,701 deaths, and 13,658 CVD events from 50 countries in six continents, no significant associations between egg intake and blood lipids, mortality, or major CVD events was found (Dehghan et al., 2020).

Kim and Campbell (2018) assessed the effect of co-consuming cooked whole egg (CWE) on dietary cholesterol absorption from two randomized-crossover studies. Whole egg ingestion had no effect on plasma total-cholesterol (areas under the curve) AUC_{0-10h} in either study, but raised triacylglycerol AUC_{0-10h}. These findings imply that the dietary cholesterol in whole eggs is poorly absorbed, which could explain why it has no immediate effect on plasma total cholesterol levels and is not linked to long-term plasma cholesterol control.

According to Rhee et al. (2020), dietary cholesterol intake did not have an association with LDL-C level or with risk for coronary artery calcification in apparently healthy Korean adult. The odds ratio for coronary artery calcification was not significantly higher in either gender when dietary cholesterol levels were higher (as assessed by quartile). The risk of coronary artery calcification was not substantially higher in participants with LDL-C 70–129 mg/dL compared to those with LDL-C 70 mg/dL, but it was considerably higher in subjects with LDL-C 130 mg/dL compared to those with LDL-C 70 mg/dL.

According to mediation analysis conducted by Cha and Park (2019), dietary cholesterol had no direct impacts on serum levels of total cholesterol (TC) and LDL-C; however, SFA had significant indirect effects on the link between dietary cholesterol and serum levels of TC and LDL-C. Furthermore, processed meats were strongly linked with the likelihood of abnormalities in both TC (OR: 1.220, 95% CI: 1.083–1.374; p = 0.001) and LDL-C (OR: 1.193, 95% CI: 1.052–1.354; p = 0.004) levels, but not eggs or other meats. The current investigation found that increased intake of processed meats with high SFA, but not dietary cholesterol, was linked to a higher risk of TC and LDL-C abnormalities.

Xu et al. (2019) carried out a prospective study of 409,885 men and women in nine European countries. Their results showed that consuming 7+ eggs/week was not associated with all-cause mortality (HR 1.09, 95% confidence interval (CI) 0.997–1.200) or ishemic heart disease (IHD) (HR 0.97, 95% CI 0.90–1.05), but associated with a small reduction in stroke (HR 0.91. 95% CI 0.85–0.98). Hence eating one egg daily is not associated with increase in CVD or all-cause mortality.

3. Relationship between dietary cholesterol and serum cholesterol and CVD

A high-sugar diet has been linked to a three-fold greater risk of death from cardiovascular disease, but sugars, like saturated fats, are a diverse group of chemicals. Monosaccharide, fructose, and fructose-containing sweeteners (e.g., sucrose) cause more metabolic irregularities than glucose (either as a monomer or in chains as starch) and may increase the risk of coronary artery disease (DiNicolantonio et al., 2015).

Some SFA-rich foods may have no risk of coronary heart disease (CHD) and may even be beneficial. Advice to cut saturated fat from the diet without taking into account the intricacies of LDL, SFAs, or dietary sources may actually raise people's risk of heart disease. When saturated fats are replaced with refined carbohydrates, particularly added sugars (such as sucrose or high fructose corn syrup), and the outcome is not good for heart health. Changes in LDL, HDL, and triglycerides occur as a result of this substitution, which may raise the risk of CHD. Additionally, high-sugar diets may cause a variety of additional irregularities linked to an increased risk of CHD, such as higher glucose and insulin levels (DiNicolantonio et al., 2015).

The evidence linking carbohydrate-rich meals to coronary heart disease has been progressively growing. Refined carbohydrates, particularly sugar-sweetened beverages, raise the risk of coronary artery disease (Temple, 2018). To support this, several researches and meta-analyses have elucidated on links between sugars and CVD.

4. Functions

Cholesterol offers a diverse range of biological roles and is required for cellular homeostasis. It is a precursor to bile acids, aids in the manufacture of steroid and vitamin D, and is essential for the rigidity and fluidity of cellular membranes (Luo et al., 2020).

Another key feature of this cholesterol issue was the link between cardiovascular disease and bone metabolism (Yin et al., 2019). A link between cardiovascular disease and the risk of osteoporosis has been proposed, implying a close interaction between hyperlipidemia and/or hypercholesterolemia and bone metabolism. Cholesterol and its metabolites affect bone homeostasis through influencing osteoblast and osteoclast differentiation and activity. Furthermore, hematopoietic cells and bone marrow adipocytes occupy the majority of the space in the bone cavity, and the effects of cholesterol on hematopoietic stem cells, such as proliferation, migration, and differentiation, are well-known.

5. Lowering of LDL-cholesterol

For many years, dietary guidelines have recommended lowering cholesterol intake to reduce the risk of coronary heart disease. CHD is the leading cause of death worldwide. One of the key risk factors for CHD is hypercholesterolemia, which is defined as a high level of cholesterol in the blood. Government officials have long advised people to avoid high-cholesterol meals in order to maintain a healthy blood cholesterol level, but those days may be coming to an end. The American Dietary Guidelines and the Japanese Dietary Guidelines both withdrew the dietary cholesterol limit suggestion in 2015. The Chinese Dietary Guidelines also removed the cholesterol intake limit suggestion in 2016. The public and scientific communities are both concerned about the removal of the dietary cholesterol limit (Zhu & Chen, 2017).

The liver, as well as the intestine, manage cholesterol homeostasis in human bodies. The liver regulates cholesterol de novo synthesis, bile salt production, which is the primary form of cholesterol excretion, lipid secretion in the bloodstream in the form of VLDL, cholesterol synthesis and storage, as well as modulating the expression of the cellular receptor responsible for the liver's uptake of blood lipoproteins (LDL receptor) (Reis et al., 2016). However, achieving an LDL-C of 40-50 mg/dl seems to be safe, and importantly might offer CV beneficial effects (Faselis et al., 2018).

Because of the negative side effects of standard medications (statins), there has been a surge in demand for functional foods to minimize the risk of cardiovascular illnesses, particularly hypercholesterolemia (Moumita et al., 2018).

5.1. Probiotics

According to Reis et al. (2016), deconjugation of bile salts; co-precipitation of intestinal cholesterol with the deconjugated bile salts; integration and assimilation of cholesterol in the cell membrane; and prevention of hepatic cholesterol synthesis are all possible reasons for probiotic yeasts' hypocholesterolaemic impact. According to the favorable hypocholesterolaemic effects seen here, frequent ingestion of probiotic bacteria and yeast as a non-pharmaceutical method to help reduce cardiovascular risk offers promise. The hypocholesterolaemic effects, on the other hand, vary according on the strains utilized, the host's physiological state, and the type of food to which the probiotics are added.

In a study carried out by Moumita et al. (2018) in the isolation and characterization of microbes for probiotic attributes, from locally made curd, the best isolate was used for the production of soy-fortified green tea curd (GTC). Among the 15 isolates, CI1 (*Enterococcus faecium*) had the best probiotic potential. In comparison to unfortified GTC, soy-fortified GTC had better probiotic viability for a longer period under refrigerated storage and stronger angiotensin-converting enzyme inhibitors (ACEI) activity.

Lactobacillus fermentum MJM60397 could be turned into a probiotic for lowering cholesterol levels in the blood. In vitro safety testing and in vivo probiotic characterization were performed on *Lactobacillus fermentum* MJM60397. In high-fat diet-induced hypercholesterolemic male ICR mice, the hypocholesterolemic effects of strain MJM60397 were investigated. The mice were placed into three experimental groups and fed a high-cholesterol diet (HCD). The total cholesterol and low-density lipoprotein (LDL) cholesterol levels in the livers of the HCD-MJM60397 mice were considerably lower after 7 weeks (Palaniyandi et al., 2020).

Lactobacillus helveticus strains KII13 and KHI1 isolated from fermented cow milk by in vitro and in vivo studies were characterized for their probiotic properties. KII13 showed higher in vitro cholesterol-lowering activity (47%) compared with KHI1 (28%) and *L. helveticus* ATCC 15009 (22%), and hence, it was selected for in vivo study of cholesterol-lowering activity in atherogenic diet-fed hypercholesterolemic mice. The serum total cholesterol level was significantly decreased by 8.6% and 7.78% in the high cholesterol diets (HCD) HCD-KII13 and HCD-*L.ac* (*Lactobacillus acidophilus*) groups ($p < 0.05$), respectively, compared with the HCD group. Low-density lipoprotein cholesterol levels in both HCD-KII13 and HCD-*L.ac* groups were decreased by 13% and 11%, respectively, compared with the HCD group (both, $p < 0.05$). Analysis of cholesterol metabolism-related gene expression in mice liver showed increased expression of LDL receptor (LDLR) and sterol regulatory elements binding protein-2 (SREBF2) genes in mice fed with KII13 (Damodharan et al., 2016).

5.2. Dietary fiber

The edible sections of plants and similar carbohydrates that are resistant to digestion and absorption in the human intestine are referred to as fibers. They can be soluble or insoluble, and their postulated mechanism of action is to reduce cholesterol absorption while increasing bile acid reabsorption, resulting in increased bile acid excretion and subsequent conversion of cholesterol to bile acids (Hunter & Hegele, 2017).

Dietary fiber can be used to supplement statin monotherapy in decreasing total and LDL-Cholesterol, as well as to reduce the statin dose, reduce adverse effects, and improve drug acceptability.

Dietary fibers, both soluble and insoluble, in whole foods have a variety of non-nutritive health effects that assist enhance lipoprotein profiles and have no caloric value, so they can be incorporated into a balanced eating pattern. Whole grains, protein foods, fruits, and vegetables have a lot of dietary fiber, which makes them good candidates for disease prevention and lowering the risk of atherosclerosis and cardiovascular disease (Soliman, 2019).

A vast number of research have been undertaken to determine the effects of oats on cholesterol levels, particularly LDL-cholesterol, in order to reduce the risk of cardiovascular disease. Several countries have currently accepted health claims for oat-glucan and its LDL-cholesterol-lowering impact or CVD risk reduction based on significant research relating an inverse relationship between -glucan intake and LDL cholesterol (FDHP, 2010).

In a systematic review and meta analyses conducted by Ho et al. (2016), a total of 58 trials (n 3974) were included in the study. When compared to control interventions, a median dose of 35 g/d of oat-glucan significantly reduced LDL cholesterol (-019; 95% CI -023, -014 mmol/l, P000001), non-HDL cholesterol (-020; 95% CI -026, -015 mmol/l, P000001), and apoB (-003; 95 percent CI -005, -0. In the evaluation of LDL-cholesterol (I 2=79%) and non-HDL-cholesterol (I2=99%), there was evidence of significant unexplained heterogeneity. Oat-glucan had a decreasing effect on LDL cholesterol, non-HDL cholesterol, and apoB, according to pooled analyses.

A meta-analysis on the comparative effects of different whole grains and bran on blood lipid profile was conducted by Hui et al. (2018). There were fifty-five trials that were eligible, with 3900 participants. Oat bran was the most effective intervention method for lowering TC and LDL-C, with significant reductions of - 0.35 mmol/L (95% CI - 0.47, - 0.23 mmol/L) and - 0.32 mmol/L (95% CI - 0.44, - 0.19 mmol/L) in TC and LDL-C, respectively, when compared to control.

Hypercholesterolemic adults were randomly assigned to a 4-week daily ingestion of oat or rice porridge in a randomized crossover study. A daily ingestion of 70 g of oat porridge with 3 g of β-glucan for 4 weeks helped lower markers of inflammation and oxidation as compared to rice porridge (Pavadhgul et al., 2019).

5.3. Plant sterols and stanols

Plant sterols or phytosterols and their saturated derivatives are naturally occurring steroid-like substances that are structurally similar to cholesterol but poorly absorbed in the intestinal tract (Sahebkar et al., 2016; Mannarino & Pirro, 2014; Chen et al., 2008). They act by decreasing the intestinal absorption of cholesterol by reducing the cholesterol content in micelles. Some plant sterols may also increase the activity of transmembrane proteins responsible for the excretion of cholesterol in the intestine and liver (Barbagallo et al., 2015) and reduce ApoB secretion from enterocytes and hepatocytes (Sahebkar et al., 2016).

According to Schoeneck and Iggman (2021), there was strong evidence that foods fortified with plant sterols and stanols reduced LDL cholesterol in a modest way (approximate weighted mean dose 2.2 g per day compared with diets without foods enriched with plant sterols and stanols, in 58 of 59 Register of Controlled Trials (RCTs) which reported units as g per day).

5.4. Nutraceuticals

Nutraceuticals are food ingredients that can be utilized to treat a variety of ailments. An active ingredient, a refined supplement, a functional food, or therapeutic herbs are among the many compounds accessible (Barbagallo et al., 2015). In the literature, over 40 nutraceuticals have been described as having promising benefits on improving lipid profiles and reducing CVD risk (Sahebkar *et al*., 2016; Mannarino & Pirro, 2014).

6. Effect of processing on cholesterol

An important aspect of food processing that changes cholesterol concentration is the loss of moisture. Cooking or any heat application usually increases cholesterol content because moisture is lost, whereas cholesterol is retained. However, some cholesterol can be lost during cooking because of oxidation or fat drip. Oxidation occurs more easily to free cholesterol, for example, cholesterol in eggs or lean tissues, whereas cholesterol esters in fat droplet are more likely to be lost through cooking, for example, chicken skin or fat tissues.

Cholesterol is primarily diluted or concentrated through food processing because of changes in protein, lipid, and moisture contents. Therefore, cholesterol reducing strategies for foods normally involve protein and fat replacement by those from plant sources and the development of further processes that compensate for the loss of texture and flavor, such as extrusion or restructuring of protein, lipid hydrogenation, and flavor addition (natural or synthetic) (Dinh & Thompson, 2016). By lowering the activation energy for hydrogen abstraction, high temperatures can cause lipid oxidation and the generation of radicals (Barriuso et al., 2017).

Processing including cooking, deep frying, and dehydrating is one of the main factors causing cholesterol oxidation in animal origin foods (Asmaa & Tajul, 2017; Khan et al., 2015). The effect of cooking and their combinations with re-heating methods on the formation of cholesterol oxidation products (COPs) have been studied by many researchers (Choe et al., 2018; Guizellini et al., 2020).

Guizellini et al. (2020) observed that storing and grilling increased cholesterol oxidation products in a study to identify the antioxidant capacity of garlic (*Allium sativum* L.) and leek (*Allium ampeloprasum* L.) and evaluate their anticholesterol oxidation potential in fish burgers. After 90 days, however, samples containing 3% leek + 0.5% garlic were the most effective in suppressing the production of cholesterol oxides during storage and had the least rise in cholesterol oxidation products concentration (21.16 %).

Choe et al. (2018) investigated the effect of cooking and their combinations with re-heating methods on the formation of cholesterol oxidation products (COPs) in stored chicken thigh meat. The high amount ($p < 0.05$) of 25-hydroxycholesterol or α-epoxide was detected in meat samples reheated by steaming or microwaving at 3 or 6 d of storage after steamed cooking, respectively.

In a recent study conducted by Hashari et al. (2020), the effects of cooking methods (boiling and frying) on the production levels of COPs in processed foods were investigated. Compared to boiling, frying generated significantly more COPs, specifically triol (0.001–0.004 mg/kg) and 7-keto (0.001–0.200 mg/kg), in all samples.

The high temperatures required to fry fish may cause cholesterol thermo-oxidization, resulting in cholesterol oxidation products (COPs). According to Ferreira et al. (2017), herbs as natural antioxidants, on the other hand, were found to be beneficial in lowering COP levels in the majority of samples. The strongest protection against lipid oxidation was found when 4% cheiro-verde was added to air-fried sardines. In the control samples, air frying reduced the concentration of essential polyunsaturated fatty acids (PUFAs) and increased the levels of COPs from 61.2 (raw) to 283 μ/g ($p < 0.05$).

Microwaving and oven grilling resulted in higher production of COPs in processed meat as compared with other cooking methods especially. In addition, refrigerated storage tended to significantly increase the COPs content especially 7β-hydroxycholesterol and α-epoxides (Khan et al., 2015).

7. Cholesterol homeostasis

Cholesterol homeostasis is essential for cellular and systemic activities to function effectively. Cardiovascular illness, as well as a growing number of other diseases such as neurological diseases and cancers, is caused by a disruption in cholesterol homeostasis. The dynamic balance between biosynthesis, absorption, export, and esterification - a process in which cholesterol is transformed to neutral cholesteryl esters for storage in lipid droplets or secretion as elements of lipoproteins - is reflected in the cellular cholesterol level (Luo et al., 2020).

Dietary intake, endogenous production, use, and excretion all play a role in cholesterol homeostasis. The effects of egg eating on cholesterol homeostasis via intestinal cholesterol absorption have recently attracted researchers' interest. Phospholipids, a nutrient found in eggs, may have a role in this process (Kuang et al., 2018).

8. Conclusion

Dietary cholesterol and serum cholesterol, as well as LDL-cholesterol, have been linked in several clinical investigations, meta-analyses, and randomized crossover studies. As a result, a low-cholesterol diet should be a part of any plan for preventing atherosclerosis. Adding probiotics, dietary fiber, nutraceuticals, and plant sterols or stanols that prevent cholesterol absorption will reduce your risk even more. The impact of processing and storage conditions on cholesterol oxidation products is numerous. Overall, recent egg intervention studies show that extra dietary cholesterol has no deleterious effect on blood lipids and, in some circumstances, appears to improve lipoprotein particle profiles and HDL functionality; nonetheless, cholesterol homoeostasis is critical.

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Conflict of interest

The authors declare that they have no competing interests.

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