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REVIEW ARTICLE

# A Comprehensive Approach to Hyperlipidemia Management for Cardiovascular Disease and Therapeutic Interventions: Integrating Lifestyle Modifications, Ayurveda, and Pharmaceutical Treatments

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## ABSTRACT

Hyperlipidemia refers to a metabolic disorder where plasma lipid levels are abnormal. It is marked by increased amounts of triglycerides, cholesterol, and lipoproteins (VLDL, LDL), and reduced HDL levels, which together, contribute to the development of cardiovascular diseases (CVD) and increase the risk thereof. It is classified into hypertriglyceridemia, hypercholesterolemia, mixed hyperlipidemia, and familial forms, depending on the predominant lipid abnormality. The condition arises due to genetic predisposition, dietary habits, sedentary lifestyle, obesity, diabetes, and certain medications. Often asymptomatic, severe cases may present with xanthomas or xanthelasmas. Diagnosis depends on lipid profile tests. Preventive measures mainly include change in diet, regular physical activity, keeping a healthy weight, and general lifestyle modifications. Therapeutic interventions consist of drug utilization such as statins, fibrates, niacin, ezetimibe, bile acid sequestrants, and omega, 3 fatty acids, PCSK9 inhibitors, lomitapide, and mipomersen. Comprehensive management through lifestyle and therapeutic approaches is crucial in reducing CVD risk and associated complications.

***KEYWORDS:*** *Ayurveda, Cardiovascular Disease, Herbal Remedies, Lipid Lowering Therapy, Lifestyle Modifications, Pharmaceutical Treatments.*

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## INTRODUCTION

Hyperlipidemia represents a state of elevating one or more of the chemicals, such as cholesterol or cholesterol esters, triglycerides, VLDL, LDL, and HDL. Imbalances in the blood plasma lipid levels can result in the atherosclerosis of peripheral blood vessels, coronary artery, heart, and cerebrovascular diseases.[1] Hyperlipidemia has been regarded as a disease, which is characterized by an increase in the concentration of lipoproteins that carry triglycerides or cholesterol in the blood plasma to levels higher than a predetermined normal range. The liver is the main organ responsible for cholesterol in the blood. It produces about 80% of the total cholesterol in the body, while only 20% are from cholesterol in diets rich in meat, fish, eggs, fried foods, and junk food, etc. Hyperlipidemia has been singled out as a significant contribution to the occurrence of cardiovascular diseases (CVDs).[2] These are the reason for one of every three deaths globally. Fatty acids might deposit on the arterial walls and thus, the arteries become less elastic. In effect, the chances of heart attack and stroke elevate significantly. There are three fundamental types of lipids in our blood.[3,4] The liver is the principal organ responsible for cholesterol in the blood. It generates nearly 80% of the total cholesterol in the body, whereas only 20% are from cholesterol in diets high in meat, fish, eggs, fried foods, and junk food, etc.[5,6] One of the major contributors to cardiovascular diseases (CVDs), which cause one out of every three deaths globally, is hyperlipidemia.

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Fatty acids may accumulate on artery walls, thereby making the arteries less flexible. Consequently, the chance of heart attack and stroke goes up significantly.[7]

There are three main types of lipids in our blood.

1. Cholesterol: necessary for the synthesis of bile acids.

2. Triglycerides: provide energy to the cell.

3. Phospholipids: major component of cell membrane

Because lipids are insoluble in blood plasma, they are wrapped in lipoproteins, which are then transported throughout the body via the blood stream.

**Plasma Lipoproteins Composition and Structure**

Lipoproteins are aggregates of proteins and lipids macromolecules; this configuration makes lipids compatible with aqueous body fluids. Lipoproteins consist of a specific protein called Apo lipoproteins, polar lipids such as phospholipids and unesterified cholesterol, and nonpolar lipids such as triglycerides and cholesteryl esters. Amphiphilic proteins, called Apo lipoproteins, can bind to plasma and lipids equally.[8] These lipoproteins differ in composition, size, and density.

**Chylomicron:** Chylomicrons are large, buoyant lipoprotein particles that are produced by intestinal cells (enterocytes) to transport dietary triglycerides, cholesterol, and fat, soluble vitamins from the intestines to body tissues via the lymphatic system and blood vessels. The size and density of these particles are an immediate indication of how many triglycerides were in the food consumed.

**Very-low-density lipoprotein (VLDL):** VLDL are the major cholesterol carriers and are considered as high risk fats in blood. They create most of the cholesterol that is found in the blood. So most of the cholesterol measured in a blood sample will be the cholesterol that was "travelling" on VLDL. These are known as VLDL (very, low density lipoproteins), and they are smaller than chylomicrons with more cholesterol per triglyceride mole than the latter. VLDLs are the major carriers of sterol (primarily cholesterol) from liver to cells and tissues throughout the body. They are prepared from a mixture of lipids with predominance of triglycerides and cholesterol.[9]

**Intermediate density lipoproteins (IDL):** IDL are the result of lipase enzymes that hydrolyze very low-density lipoproteins (VLDL) in the adipose and muscle capillaries.

**Low-density lipoprotein (LDL):** LDL particles are more enriched in pure cholesterol as most of their triglycerides have been removed. Known as "bad" cholesterol, LDL is the main source of cholesterol that it delivers to body tissues and is, therefore, very close to the origin of plaque that can clog arteries.

**High-density lipoproteins (HDL):** HDL or "good cholesterol" are made by the liver. Their main function is to carry lipids, cholesterol included, from the tissues to the liver where they will be broken down. By doing this, HDL is the factor that prevents the formation of atherosclerosis and therefore can be considered an anti, atherogenic.[10]

**Lipoprotein Function:** Plasma lipoproteins are the vehicles that make lipids soluble, that is, they enable the transport of triglycerides an important energy source from the places where they are produced and absorbed to the areas where they are used or stored. In addition, they also carry cholesterol to and from different places that are involved in its absorption, production, breakdown, and excretion.[11]

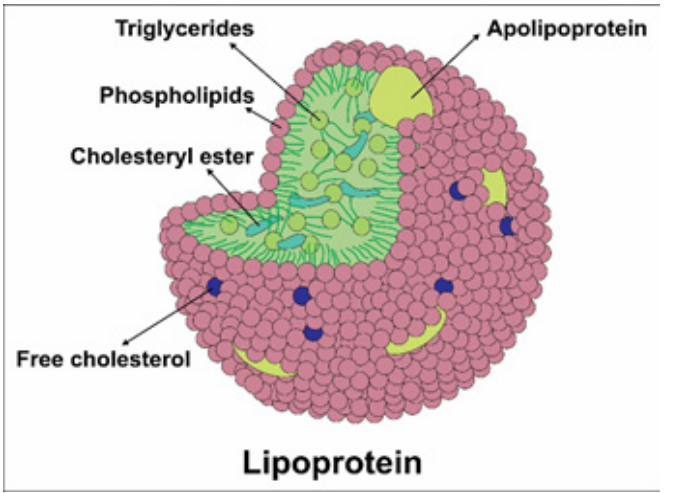


**Figure 1:** Showing the composition of lipoprotein.

**CLASSIFICATION OF HYPERLIPIDEMIA**

*Based on the Type of Lipid Involved:*

**Hypercholesterolemia:** A condition characterized by high levels of cholesterol in the blood.

**Hypertriglyceridemia:** A condition where there are high levels of triglycerides in the blood.

*Based on the Underlying Cause:*

Hyperlipidemia is classified into two main categories:

**1. Primary Hyperlipidemia (Inherited or Familial):**

This form of hyperlipidemia, commonly known as familial hyperlipidemia, is caused by

genetic mutations. It can arise from monogenic disorders, where a single gene is affected, or

from polygenic disorders, which involve alterations in multiple genes.[12]

Primary hyperlipidemia usually goes hand in hand with certain abnormal lipoprotein patterns,

which are classically considered:

Type I- Both cholesterol and triglycerides are elevated.

Type II- Increased cholesterol with triglycerides remaining at the normal level.

Type III- Both cholesterol and triglycerides are elevated.

Type IV- The TG are elevated, very often, atheromas and increased uric acid levels coexist.

Type V- The triglyceride level is extremely elevated.

**Secondary Hyperlipidemia (Acquired or Drug-induced):**

This kind of hyperlipidemia arises from other diseases or is influenced by external factors. It is possible to have it as a side effect of glomerular disease, diabetes, chronic alcohol

consumption, hypothyroidism, or taking some drugs like beta, blockers, corticosteroids, and oral contraceptives. When secondary hyperlipidemia is accompanied by significantly elevated triglyceride levels, it can lead to pancreatitis.[13]

**Involved Enzymes in the Metabolism of Lipoproteins**

**Lipoprotein lipase (LPL):** LPL is a pleiotropic enzyme, which is endothelial cell-surface localized in heart, muscle, adipose tissue, macrophage and lactating mammary gland. Free-fatty acids and monoacylglycerol results from hydrolyzation of TG, which is catalyzed by LPL. In addition, LPL also allows cells to take up free fatty acids, cholesterol, and lipoproteins through receptor, mediated endocytosis of lipoproteins.[14]

**Hepatic lipase (HL):** HL is a protein that aids in regulating the metabolism of

Hepatocytes create lipoproteins, which are present in the ovary and adrenal glands.

HL hydrolyzes phospholipids and triglycerides in plasma lipoproteins. Furthermore,

HL modifies intracellular lipid transport via promoting the absorption of lipoproteins by

cell surface receptors and proteoglycans.[15]

**Lecithin cholesterol acyl transferase (LCAT):**

LCAT is an enzyme critical to HDL metabolism as it esterifies free cholesterol that then becomes associated with the core of the lipoprotein to mature HDL particles.[16]

**Cholesteryl ester transfer protein (CETP):** The primary lipids that are transferred from HDLs to chylomicrons, VLDL, and LDL at a far quicker pace than triglycerides are the esterified cholesterol esters (CE).The process is facilitated by a hydrophobic plasma glycoprotein called cholesterol ester transfer protein (CETP). The plasma lipid transfer protein is another name for it. An ACETP deficiency is associated with lower LDL and higher HDL levels.[17]

**Microsomal triglyceride protein (MTP):** MTP is a phospholipid transferring protein that facilitates the movement of neutral lipids, including TG and cholesterol esters, across the liver and isolated microsomes and lumen mucosa membranes. MTP is closely associated with the assembly of lipoproteins, which are apo B, containing. At present, MTP is considered to be the main factor in the regulation of the production of cholesterol ester and glycolipid, presenting molecules.[18]

**Acyl CoA Transferase (ACAT):** The enzyme acyl CoA transferase (ACAT), a membrane, bound protein, takes the lead in the production of cholesterol esters by combining long-chain fatty acyl CoA and cholesterol. ACAT has significant roles in many processes, primarily it works to prevent the excessive and thus harmful buildup of cholesterol in cells, as well as being a part of the mechanism that keeps the cellular cholesterol balance steady in various tissues. The significance of ACAT is also due to its pivotal role in the liver and intestines in the production and release of lipoproteins containing apolipoprotein B.[19]

**Metabolization of Lipids**

Most of the dietary fats are absorbed by the intestinal lymph after which they are repacked into chylomicrons by the intestinal lymph. These lipoproteins pass through the bloodstream where they are hydrolyzed by lipoprotein lipase located on the surface of endothelial cells. This enzyme cleaves the triglycerides to free fatty acids and glycerol. Later on, the liver cells take up the remaining chylomicron and mix it with cholesteryl esters, cholesterol, and ApoB100 to produce VLDL. On their way to the blood, hepatic lipase and lipoprotein lipase convert VLDL into IDL. Furthermore, phospholipids and apolipoproteins are removed from HDL during that operation. Besides that, IDL by hydrolysis with hepatic lipase will be converted into LDL and will lose some more apolipoproteins.[20] The reverse cholesterol transport pathway is carried out by HDLs that are formed by the liver and released into the bloodstream. They are used for the transport of cholesterol from the periphery to the liver. In this process, LCAT converts HDL cholesterol in plasma to cholesteryl ester, which is then transferred to VLDL and chylomicrons and reaches the liver via the LDL receptor. CETP transfers cholesterol ester to LDL particles that are then internalized by endocytosis mediated by LDL receptors. Finally, the body eliminates bile acid that originates from the process in which cholesteryl esters are hydrolyzed to cholesterol.[21]

**Hyperlipidemia Symptoms:** Usually, hyperlipidemia is a silent case as it doesn't show any symptoms, where the symptoms are mostly explored on regular testing or when the condition gets very close to the point of a heart attack or stroke. In this case, patients with a genetic form of the disease or high blood cholesterol may see the development of xanthomas, or cholesterol deposits under the eye skin, mainly. Also, patients with high triglycerides may have multiple pimples, like lesions at different locations of the body.[22]

**HYPERLIPIDEMIA COMPLICATIONS**

**Atherosclerosis:** It starts with hyperlipidemia as the primary cause of atherosclerosis, which becomes the first significant cardiovascular disease risk factor. The buildup of calcium, cholesterol, and lipids as well as the development of fibrous plaques in big and medium-sized artery walls are the hallmarks of atherosclerosis, a degenerative process.[23]

**Coronary Artery Disease (CAD):** The major culprit for coronary artery disease is the buildup of fatty and fibrous plaques in the walls of arteries, which is known as

atherosclerosis. The blood flow is compromised as the arteries of the myocardium become narrow, thus resulting in oxygen deficiency in the heart. Coronary atherosclerosis has been associated with elevated lipid levels.[24]

**Myocardial Infarction (MI):** MI is an acute disorder that occurs when one or more cardiac arteries are fully or partially blocked from getting blood and oxygen, which damages or kills heart cells. The blockage could result from the rupture of plaque that is atherosclerotic. The researchers found that around one, fourth of the patients who survived myocardial infarction were having high blood cholesterol.[25]

**Ischemic stroke:** Stroke is the second among the top four leading causes of death. A majority of the time, stroke takes place when a clump of blood or a tiny fragment of a Plaque with atherosclerosis impedes an artery in the brain. A vast number of clinical studies have shown that a 15% reduction in total cholesterol and low, density lipoprotein dramatically decreases the risk of the first stroke.[26]

**CAUSES**

The following foods contain trans-fat, fatty acids, and cholesterol that may raise blood lipid levels:

• Products made from dairy.

• Pastries with ice cream.

• Junk food and fried foods.

• Meat, etc.[27]

Major causes of hyperlipidemia include obesity, diabetes mellitus, and hypothyroidism. Low levels of exercise and smoking can cause hyperlipidemia.[28] Hyperlipidemia risk is also increased by excessive alcohol consumption. B-blockers and steroids are two medications that can lead to hyperlipidemia because of mutations in lipoprotein lipase.[29]

**Additional Reasons for Hyperlipidemia**

• Genetics or inheritance

• Obesity

• Smoking

• Various medications, including oestrogen, corticosteroids, Hypertriglyceridemia are a risk factor for beta blockers.

• Steroids, alcohol, hypothyroidism, kidney failure, and others.

• Little exercise.[30]

**The Hyperlipidemia Pathogenesis**

Coronary arteriosclerosis develops following the first interaction between platelets and monocytes with the endothelium and the subendothelium of the artery, at the site of endothelial injury in hyperlipidemia. The mediators' release among them Growth factor produced from platelets, triggers collagen production, cholesterol uptake, smooth cell proliferation in the vessel's medial and intimal layers and the very first hyperlipidemic plaque. The immediate symptoms of myocardial infarction, unstable angina, and abrupt heart failure are caused by low activity plaque ruptures.[31]

**Importance**

After the one, to, one relationships between lipid concentrations and risk were established, healthcare practitioners have been particularly concerned about hyperlipidemia, i.e., the major cause of death in the US is cardiovascular disease (CVD).[32-34] The Lipid Research Clinics Coronary Primary Prevention Trial, the most important study, which was published in two parts in 1984 (each with a different statistical analysis), firmly contributed to the understanding that treatments intended to reduce cholesterol levels result in a decreased risk of cardiovascular morbidity or mortality.[35,36] A multipart review published by The Journal of Lipid Research over three years and available online, gives a comprehensive account of the cholesterol controversy.[37-43]

**Diagnosis:** There are no additional specific hyperlipidemia symptoms. The only way to identify it is through a blood test. A blood test based on lipid profiles is used to screen for hyperlipidemia.[44] A routine blood test for cholesterol, triglycerides, HDL, VLDL, and LDL can identify hyperlipidemia.[45]

**Prevention of Hyperlipidemia**

It is advised to follow a low-fat, low-cholesterol diet. Include in your diet fruits, beans, and oats which are rich in soluble fiber. Keep your weight in check through regular exercise.

**Treatment**

**Healthy Diet:** Reduce your intake of cholesterol and saturated fats. Incorporate fruits like bananas, apples, and pears, which are rich in fiber and nutrients.

**Low-Fat Foods:** Choose foods that are low in fat to support a healthy diet and lower cholesterol levels.

**Weight Management:** It's critical to keep a healthy weight. Less weight on the body can help in managing cholesterol levels effectively.

**Regular Exercise:** In addition to helping with weight management, regular exercise also raises HDL (good cholesterol) levels.

**Fish Consumption:** Include fish in your diet regularly, aiming for at least once every two

days, as it provides beneficial omega-3 fatty acids that contribute to lowering cholesterol.

**Medication Adherence:** In some cases, medication such as statins or fibrates (like

fenofibrate) may be prescribed. It's important to follow the prescribed dosage and continue

the treatment plan as recommended by healthcare professionals.

**Lifelong Treatment:** Depending on individual health conditions, lifelong measures may be necessary. Adhering to prescribed treatment plans is crucial for effectively managing cholesterol levels and reducing associated health risks.

**Triglyceride Management:** Statins and fibrates, like fenofibrate, are known to help reduce triglyceride levels, which are also important to monitor for overall heart health.46 These points encompass lifestyle changes and potential medical interventions that can effectively lower cholesterol levels and mitigate associated health risks. Always seek the counsel of medical specialists for individualized guidance and needs-based treatment programs.

**Therapeutic lifestyle changes:** The first line of treatment should consist of diet modifications, consistent exercise, stopping smoking, and weight loss, especially when there is mild hyperlipidemia, when there are two risk factors, and when the person does not have heart disease or its risk equivalent. It is important to remember that dieting lowers the amount of cholesterol consumed. Meanwhile, the liver is producing a significant amount of cholesterol. Don't consume more than 7% of your energy from saturated fats. A maximum of 25% to 35% of total energy should come from fat consumption. Less than 200 mg of cholesterol should be consumed per day. Plant sterol esters and soluble fiber consumption is strongly recommended. One of the first medical systems in human history is Ayurvedic medicine. The basis of Ayurvedic medicine is the "laws" of nature. Its healthcare philosophy is based on the understanding of the interrelationships of the physical, mental, and spiritual individuals. In order to prevent disease and promote health, ayurvedic medicine combines and balances various elements through yoga, meditation, herbs, diet, and seasonal everyday activities.[47]

**Home medications:** Certainly, here's a revised and concise version of the information regarding home remedies and various items that are believed to assist in managing cholesterol levels

**Nuts:** Almonds are known to potentially reduce LDL (bad cholesterol) by about 4.4%, while walnuts may lower LDL by around 16%.

**Oatmeal:** Consumption of oatmeal is linked to a notable reduced in LDL cholesterol levels of ranging from 12-24%.

**Orange Juice:** Some studies suggest that orange juice consumption might contribute to reducing overall blood cholesterol levels.

**Corriander Seeds:** Coriander seeds are thought to possess properties that can reduce both cholesterol and triglyceride levels.

**Fish Oil:** Rich in omega-3 fatty acids, fish oil is used to reduce blood triglyceride levels.

**Honey:** Consumption of honey may potentially help in reducing cholesterol levels.

**Soybeans:** Compounds found in soybeans might inhibit the production of new cholesterol, aiding in lowering overall cholesterol levels.

**Indian Gooseberry (Amla):** Indian Gooseberry is believed to assist in decreasing excess cholesterol buildup.

**Brown Rice:** Consumption of brown rice is associated with lower cholesterol levels due to its higher fiber content compared to white rice.

**Turmeric:** Turmeric consumption is thought to lower LDL cholesterol levels.

**Brinjal (Eggplant):** Brinjal consumption is believed to contribute to reducing LDL cholesterol levels.

**Coconut Oil:** While controversial, some sources suggest that coconut oil might increase raise HDL (good cholesterol) levels and enhance the LDL to HDL cholesterol ratio.

**Fenugreek Seeds:** Fenugreek seeds are believed to potentially lower cholesterol levels by approximately 14%.

**Phytotherapeutic Agents for Lipid Control:** Medicinal plants, with their abundant therapeutic qualities and pure natural the nation, responsibility have long been regarded is a nutritious source of life for everyone. Herbal medicine has gained international attention during the past ten years, affecting both international trade and global health. The excessive cost of Western medical care and pharmaceuticals contributes significantly to the widespread use of herbal medicine by a substantial portion of the population live in developing nations.[48]

**Treatment through Pharmaceuticals:** A wide range of hypolipidemic drugs are on the market for the treatment of hyperlipidemia. However, various studies indicate that these drugs have limited effectiveness in the prevention of heart attacks (myocardial infarction) in individuals suffering from coronary heart disease.[49]

**Drug-based Therapeutic Approach:** Based on the fact that LDL is the major atherogenic lipoprotein, lowering it is projected to reduce atherosclerosis and the associated negative effects on the cardiovascular system. Along with having high LDL, risk factors for CHD should be taken into consideration before starting medication therapy and making lifestyle changes. Immunotherapy has exhibited a high degree of efficacy in the treatment of hyperlipidemia. However, to achieve a more comprehensive effect, it may

be necessary to employ combination therapy. Currently, the pharmacological arsenal against hyperlipidemia encompasses five principal drug classes: statins, bile acid binding resins, nicotinic acid and fabric acid derivatives, and cholesterol absorption inhibitors.

### Statins

Statins operate by inhibiting the enzyme HMG, CoA reductase, a major contributor to cholesterol synthesis. This enzyme is in charge of the initial and rate-limiting step in the biosynthesis of cholesterol, which is the conversion of HMG and CoA to mevalonate. Consequently, statins block this enzyme and prevent the liver from making cholesterol on its own.

The liver is where statins mainly work. As a result of diminished cholesterol production in liver cells, the number of LDL receptors on the liver surface is increased dramatically by the body. In other words, the liver takes up more LDL cholesterol from your blood, and as a result, the level of LDL, cholesterol in your blood decreases.

Typically, statins lower cholesterol levels very well; the reduction is between 20 and 50 percent. Not only that, but also the statins administrations can considerably increase HDL-C and decrease TG and VLDL-C. As a result, they are the first line of treatment for hypercholesterolemia and have been linked to a decreased incidence of cardiovascular disease and a decrease in cardiovascular mortality in high-risk patients (Martin and Blumenthal).[50,51] Myopathy, myositis, and elevated liver enzymes are the three main side effects of statins. The most popular statins are atorvastatin (10–80 mg), rosuvastatin (5–40 mg), simvastatin (10–40 mg), pravastatin (10–80 mg), fluvastatin (20–80 mg), and lovastatin (20–80 mg).[52]

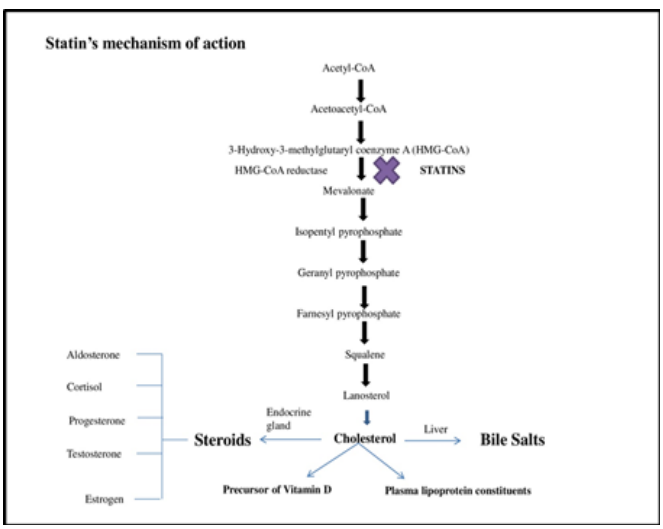


**Figure 2:** Depicting the biosynthesis of cholesterol and the mechanism of action of statins.

### Ezetimibe

Ezetimibe works by selectively inhibiting the absorption of cholesterol, thus providing a mechanism that complements the action of statins by preventing the intestines from absorbing cholesterol. Ezetimibe, when merged with statins, yields synergistic impacts via two biologically intertwined routes, one entails lessening of the intracellular cholesterol concentration along with intensified LDL uptake by hepatocytes; the other one involves the decline of intestinal cholesterol absorption. The joint use of these two agents manifests additive effects in lowering plasma LDL cholesterol levels and, indeed, has become a source of great utility to patients with statin intolerance and those who, despite statin monotherapy, fail to achieve lipid targets.[53] When statin dosage is doubled, LDL cholesterol levels can be reduced by 6%, but ezetimibe plus statins can reduce LDL cholesterol levels by 25%.[54]

The medication ezetimibe targets the human sterol transport protein Niemann, Pick C1, like 1 (NPC1L1), which is a protein mainly responsible for the small intestine to absorb cholesterol. Thus, the quantity of cholesterol absorbed from the intestine and sent to the liver is lowered. Therefore, cholesterol removal from the blood increases.[55] A single daily dose of 10 mg is recommended for adults. The common side effects are diarrhea, headaches, and stomachaches, and so on.[56]

### Bile Acid Sequestrants

Bile acid sequestrants represent one of the older lipid-lowering drug classes, working by binding bile acids in the intestines and promoting their fecal excretion.[57] While they have shown modest LDL-cholesterol reduction of approximately 15-20%, they are now rarely used as first-line agents due to gastrointestinal side effects and the availability of more potent alternatives.[58] However, they remain useful options for select patient populations, particularly those with mild hyperlipidemia or specific contraindications to other agents.[59,60]

### Fibrates

The primary mechanism by which fibrates (fenofibrate, bezafibrate, ciprofibrate, as well as gemfibrozil) function is via the peroxisome proliferation activating receptor alpha (PPARalpha). By activating this receptor, fibrates raise high density and lower triglycerides (TGs). Lipoprotein cholesterol (HDL,C). Several factors influence LDL, C levels. The kidneys are primarily responsible for excreting the active metabolite of fenofibrate. Gemfibrozil and statins together are not advised.[61] Bezafibrate three times a day, 200 mg recommended dosage for adults, or 400 mg taken with meals as a modified-release tablets.[62] If necessary, fenofibrate can be taken as four 67-mg capsules or as a single 200-mg dose each day. Nonetheless, some fenofibrate formulations (48and 145 mg) with Nano Crystal technology remove the need to take the medication with

a meal, and other formulations (67, 134, and 200 mg) with micronized capsules offer increased solubility and enhanced bioavailability. The suggested daily intake of gemfribozil is 900 1200 mg.Fibrates are almost entirely absorbed through the mouth; however, fenofibrates.[63]

### Niacin

Niacin, often known as nicotinic acid or vitamin B3, dramatically increases HDL levels while lowers VLDL and LDL levels. Inhibiting hormone, sensitive lipase, niacin mainly functions by halting adipose tissue lipolysis. The usual side effects of niacin are skin vasodilation resulting in flushing and itching, and a temporary increase of AST and ALT plasma levels. It can, along with statins, elevate the risk of rhabdomyolysis and myopathy.[64]

### Omega, 3 fatty acids

Omega-3 fatty acids, another name for polyunsaturated fatty acids, has impacts on metabolism and physiology. They reduce serum total cholesterol through the process of fatty acid oxidation. The pharmaceutical form of each soft capsule of 1000 mg, which is taken twice a day, comprises 375, 380 mg of docosahexaenoic acid (DHA) and 460, 465 mg of eicosapentaenoic acid (EPA). Gastrointestinal side effects are typical.[65]

**Table 1:** Demonstrated the list of medication and mechanism of action used for the pharmacological treatment of hyperlipidemia.

| Drug Class | Drug name | Drug dose | Mechanism of action | Side effects | Ref. |
|---|---|---|---|---|---|
| Statins | Lovastatin | 20–80 mg | Inhibits HMG-CoA reductase, reducing cholesterol synthesis in the liver and upregulating LDL receptors to increase LDL clearance | Elevation of liver enzymes, myopathy, myositis | (52) |
| | Simvastatin | 10–40 mg | | | |
| | Pravastatin | 10–80 mg | | | |
| | Fluvastatin | 20–80 mg | | | |
| | Atorvastatin | 10–80 mg | | | |
| | Rosuvastatin | 5–40 mg | | | |
| Cholesterol Absorption Inhibitor | Ezetimibe | 10 mg once daily | Inhibits the Niemann-Pick C1-like 1 (NPC1L1) protein, reducing intestinal absorption of cholesterol | Headache, abdominal pain, diarrhea | (56) |
| Bile Acid Sequestrants | Cholestyramine | Variable | Binds bile acids in the intestine, preventing their reabsorption and increasing conversion of cholesterol to bile acids | Flatulence, bloating, indigestion, nausea, constipation, potential osteoporosis, exacerbation of hypertriglyceridemia, vitamin/mineral deficit | (58), (59), (60) |
| | Colestipol | | | | |
| Fibrates | Bezafibrate | 200 mg three times a day or 400 mg as a modified-release tablet taken with meals | Activates peroxisome proliferator-activated receptor alpha (PPAR-alpha), increasing lipolysis and elimination of triglyceride-rich particles, and increasing HDL production | Variable | (62, 63) |
| | Fenofibrate | 48–200 mg | | | |
| | Gemfibrozil | 900–1200 mg | | | |
| Niacin | Nicotinic Acid (Vitamin B3) | Variable | Inhibits hormone-sensitive lipase, reducing lipolysis in adipose tissue, thereby decreasing production of VLDL and LDL, and increasing HDL levels | Flushing, itching, transient rise in AST and ALT plasma levels, increased risk of rhabdomyolysis and myopathy when combined with statins | (64) |
| Omega-3 Fatty Acids | EPA/DHA | 1000 mg capsules (taken twice daily) | Increases fatty acid oxidation, reducing serum triglycerides, and modestly increasing HDL levels | Gastrointestinal side effects | (65) |
| PCSK9 Inhibitors | Evolocumab | Variable | Binds to PCSK9, preventing it from degrading LDL receptors, thereby increasing the number of LDL receptors available to clear LDL from the blood | Variable | (66) |
| | Alirocumab | | | | |
| Other | Lomitapide | Variable | Inhibits microsomal triglyceride transfer protein (MTP), reducing the production of chylomicrons and VLDL | Variable | (67) |
| | Mipomersen | | Antisense oligonucleotide that binds to and degrades apoB-100 mRNA, reducing apoB-100 production and thus lowering LDL levels | | |
| | Nexletol (bempedoic acid) | | Inhibits ATP-citrate lyase, reducing cholesterol synthesis | Side effects differ from statins | (68) |
| | Nexlizet (bempedoic acid and ezetimibe) | | Combination of ATP-citrate lyase inhibition and NPC1L1 inhibition | | |

**PCSK9 Inhibitors**

PCSK9 inhibitors are human monoclonal IgG antibodies that bind with selectivity to PCSK9 and stop it from binding to LDL receptors, lowering levels of LDL-C, TC, ApoB, and non-HDL-C. Thus, LDL-C is reduced by 60%. At present, only two PCSK9 inhibitors are on the market, namely, evolocumab and alirocumab.[66]

**Lomitapide and Mipomersen:** Lomitapide, a specific inhibitor of the microsomal MTP lowers LDL and C levels by around 40%. An antisense oligonucleotide called Mipomersen reduces LDL-C by about 37% and prevents the synthesis of apoB, 100. For patients with homozygous FH who are unable to meet LDL objectives with statins, both provide novel treatment options.[67]

The Two new non-statin medications have received FDA (Food and Drug Administration) approval. After they demonstrated significant results in clinical trials for reducing high cholesterol. Nexletol and nexlizet, which are associated with mild or moderate side effects, may be used in combination with statins. A few side effects of the two novel medications are different from those of statins.[68]

## CONCLUSION

Managing hyperlipidemia to reduce cardiovascular disease risk requires a comprehensive approach that combines lifestyle changes, Ayurveda, and medication. A diet reduced in cholesterol and saturated fat, frequent exercise, and weight management and smoking cessation can significantly improve lipid profiles and heart health in general. Ayurvedic interventions, such as using medicinal herbs like Guggul and garlic and practices like yoga and detoxification, provide extra natural support. Medicines such as statins, PCSK9 inhibitors, and fibrates are good choices for controlling blood lipids. Using these methods together is a holistic and effective way to keep hyperlipidemia under control and reduce the risk of cardiovascular disease, thus improving general health and promoting heart wellness.

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