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Review Article

Lipoprotein Nanoparticles and Their Role in Cardiovascular Disease Management – A Review

Prashant D Sawant*

Intraceuticals Pty Ltd, Melbourne, Australia

Abstract

Two key lipoprotein nanoparticles, high density lipoproteins (HDL) and low density lipoproteins (LDL), are associated with cardiovascular diseases (CVD). HDL is smallest lipoprotein (~10nm) and considered as good cholesterol where as LDL (20-27nm) is considered as bad cholesterol.

60-80% of the cholesterol in the blood is transported by LDL from liver to human tissues and only 15-20 percent is transported by HDL from human tissues back to liver for the processing. A small amount of cholesterol is transported by other lipoproteins.

Both LDL and HDL particles are made up of aggregates of (apo) proteins and cholesterol in different ratios. However, both low-density lipoprotein cholesterol (LDL-C) and HDL cholesterol (HDL-C) are not cholesterol in reality. Despite being termed as bad cholesterol, LDL nanoparticles in reality perform vital functions in the human body. However, excess of oxidised LDL nanoparticles are responsible for cardiovascular diseases.

Some literature of the CVD management suggests that antioxidants such as vitamin E can reduce the LDL oxidation whereas niacin (vitamin B3) can increase HLD in addition to statin regime and a healthy diet and lifestyle.

Keywords: Lipoproteins; nanoparticles; HDL; LDL; CVD; CHD; Vitamins

Introduction

Cardiovascular disease (CVD) is one of the leading causes of mortality globally. In 2010, CVD was accounted for 31.9% and 31.4% of US deaths in 2010 and 2012, respectively [1], However, between 1980 to 2000, coronary heart

disease (CHD) deaths due to cholesterol are found to decreased by 33% in USA [2]. Also, in other developed countries, age-adjusted CVD mortality rates are declining by 19%–46% [2]. Despite the reduction in the CVD mortality rates, CVD still remains the leading cause of mortality in the rapidly aging population in the developed countries. On the contrary, both age-adjusted CVD mortality rates and aging of populations are contributing to a rapid increase in CVD mortality in low-income to middle-income countries [3].In 2010 the resultant direct and indirect annual costs in USA are estimated as $240.9 billion [4,5] and the global cost of CVD is estimated as $863 billion. This cost is expected to increase by 22% by 2030 [6].

Cholesterol

Cholesterol is essential for human life and is abundantly found in the brain, nervous tissue, skin and adrenal glands. It performs three key functions within the body: (i) a structural component of all cell membranes; (ii) manufactures steroid hormones and Vitamin D; and (iii) produces bile acids, which facilitate the digestion and absorption of fats in the diet. The human body produces cholesterol mainly in the liver. The amount of cholesterol synthesised by the body is influenced by the food intake. Excess amount of saturated fat elevates cholesterol level in the human body. Cholesterol is removed as either cholesterol or bile salts through the bile synthesis pathway. Through the enterohepatic circulation, around 98% of bile salts excreted from the gall bladder are reabsorbed by the large intestine. Bile salts are then taken up by the liver, and re-excreted as bile. Bile salts which are not reabsorbed are excreted in the faeces. Moreover, maximum one gram of cholesterol (healthy and unhealthy) is excreted each day in this manner only whereas total normal human body contained 2g cholesterol per kg total weight. It shows that better to control diet to keep the cholesterol in healthy range.

Lipoprotein Nanoparticles

Lipids are insoluble in water and hence are transported through the circulation as complexes with proteins to form lipoproteins. Lipoprotein nanoparticles transport cholesterol from the liver to different parts of the body and back from body parts to liver. LDL nanoparticles are less dense than HDL, transport cholesterol from liver to body tissues whereas HDL more dense particles that help transport cholesterol from body tissues (including arterial walls) to liver (opposite action).

***Corresponding author:** Prashant D Sawant, Intraceuticals Pty Ltd, Melbourne, Australia, E-mail: pdsawant@yahoo.com

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Cholesterol is taken up into cells when lipoprotein binds to LDL receptors on the cell surface. Then LDL is taken into the cell and broken down into free cholesterol and amino acids.

Characteristics of Lipoproteins Nanoparticles

The properties of lipoproteins are summarised in Table 1. As seen from Table 1 that HDL lipoproteins are smaller as compared to LDL and other lipoproteins. Also, HDL particles contained 40% less cholesterol than LDL. Because of more cholesterol connected with LDL, LDL lipoproteins are blamed for CVD in the public domain.

Proteins Associated Lipoprotein Nanoparticles

Each LDL nanoparticle contained a single apolipoprotein B-100 molecule (Apo B-100). It has 4536 amino acid residues and a mass of 514kDa, and 80-100 additional ancillary proteins. Each LDL nanoprotein exhibits a highly hydrophobic core consisting of polyunsaturated fatty acid, linoleate, and hundreds to thousands (average ~ 1500) esterified and unesterified cholesterol molecules. This core also carries varying numbers of triglycerides (TG) and other fats. The core is surrounded by a shell of phospholipids and unesterified cholesterol, as well as the single copy of Apo B-100. Since LDL particles (LDL-P) contain a variable and changing number of fatty acid molecules, there is a distribution of LDL-P mass and size [7].

Table 1: Characteristics of Lipoprotein Nanoparticles.

Lipoproteins	Diameter (nm)	Protein (%)	Cholesterol (%)	Phospholipids (%)	Triacylglycerol & Cholesterol Ester (%)	Density (g/mL)	Function
HDL	5–15	33	30	29	4	>1.063	Transport surplus cholesterol from tissues back to liver
LDL	18–28	25	50	21	8	1.019–1.063	Transport cholesterol from liver to tissues
VLDL	30–80	10	22	18	50	0.95–1.006	Transport triglycerides (TG) from liver to adipose tissue and muscle
Chylomicrons	100-1000	<2	8	7	84	<0.95	Transport TG from intestine to tissues

HDL nanoparticles are densest particles because it contains the highest proportion of proteins to lipids. 80% HDL proteins are comprised of apolipoproteins: apo A-I and apo A-II [8]. A-II proteins in humans is encoded by the APOA2 gene [9] and defects in this gene or deficiency may result in hypercholesterolemia [10].

Morphological Study of LDL and HDL Nanoparticles

Lipoproteins's structural heterogeneity makes their morphological analysis challenging. Despite difficulties, several attempts have been made to gain detailed information of the LDL nanaoparticles using several techniques such as electron microscopies [11-18].

Figure 1 is a set of consecutive sections through the final 3D map developed by Orlova *et al* [19]. It shows a clear division of shell and core of LDL. The shell has a higher density as compared to its core and is ≈20–30 Å in thickness. Three vertical "walls" in the core can be followed through the whole map.

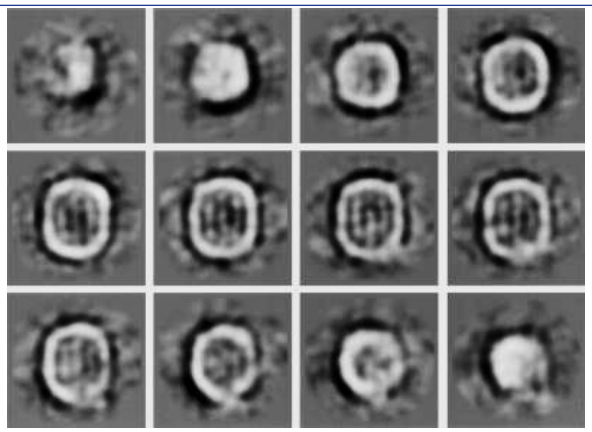

Figure 1: Set of consecutive sections through the final 3D map. Source: Orlova *et al.* (1999) Proc Natl Acad Sci USA. 96:8420–8425. Copyright © 1999, The National Academy of Sciences.

Figure 2 is a 3D map of the LDL. Figures 2 (*a* and *c*) depict the overall shape of LDL in two orthogonal orientations and (*b* and *d*) are corresponding cutaway views of the particle which reveals the 30 Å thick outer shell (orange) and inner core structure (yellow). The yellow layers are projected as striations in this orientation. Figures 2 (*f* and *g*) are the variance map of the reconstruction with Blue colour representing the low variance and red representing higher variance of the 3D map. Both the shell and the core are mostly blue representing the stability of the LDL structure.

Top of Form

Bottom of Form

The electron microscopy images of HDL nanoparticles shows discoidal and spherical morphologies that contain the incorporated signalling chain homo-oligomerization triggering receptor (expressed on myeloid cells-1) (TREM-1 SCHOOL) peptide GF9 [20]. Similar to LDL, shape, size and size distribution are observed for HDL with oxidized apo A-I or its unmodified and oxidized peptides. It is worth noting that Apolipoprotein A-I [21,22] is the major protein component of HDL in plasma.

Benefits of LDL for Cardiovascular Repairs

The LDL nanoparticles carry more cholesterol than other lipoproteins. Their role is to deliver cholesterol to tissues throughout the human body. LDL nanoparticles actually serve an important function because the human body needs cholesterol to make vitamin D and steroid hormones.

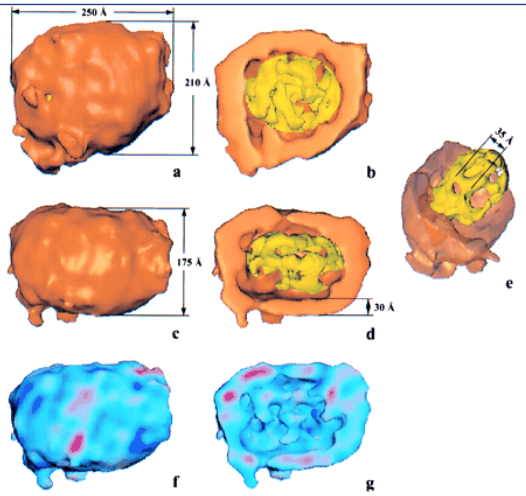

Figure 2: 3D map of the LDL. (*a* and *c*) Overall shape of LDL in two orthogonal orientations. (*b* and *d*) Corresponding cutaway views of the particle revealing the 30-Å-thick outer shell (orange) and inner core structure (yellow). (*e*) The shell is made semitransparent to reveal the inner core structure. The yellow layers are projected as striations in this orientation. (*f* and *g*) In the 3D variance map of the reconstruction, blue colour represents low variance and red represents higher variance. Both the shell and the core are mostly blue, suggesting the stability of the LDL structure.Source: Orlova *et al.* (1999) Proc Natl Acad Sci USA. 96:8420–8425. Copyright © 1999, The National Academy of Sciences.

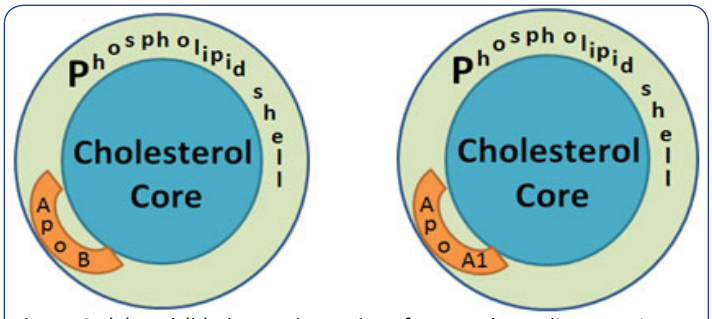

Figure 3: (a) and (b) show schematics of LDL and HDL lipoproteins. As seen in Figure 3 the cholesterol core is covered by bilayers of phospholipids. The phospholipid layer contained Apo-B proteins in LDL lipoproteins and Apo-A1 in HDL lipoproteins.

LDL nanoparticles are often termed as a "bad cholesterol" when their concentration is exceeded and hence carrying excessive cholesterol in blood. During the circulation LDL lipoproteins can break down to release the cholesterol in the blood that was actually intended for cells. The released cholesterol can attached to (faulty) blood vessel walls for repairing of the wall but unfortunately attract blood clots as deposits and cause cardiovascular disease.

HDL carries cholesterol from tissues to back to the liver for reprocessing. Therefore, the ratio of HDL to LDL is vital because high levels of HDL and low levels of LDL can reduce cholesterol deposits of the artery walls and reduce CHD events.

The concentration of LDL and HDL nanoparticles in blood can be influenced by the type of foods intake. Saturated and Trans fats can increase the concentration of bad cholesterol in blood whereas soluble fibres from beans, fruits and vegetables can help reduce the concentration of the bad cholesterol in blood. Monounsaturated and polyunsaturated fats from nuts, seeds, vegetable oils and fatty fish, such as salmon and tuna helps boost good cholesterol levels and lowers the bad cholesterol level in blood.

The Metabolism of Human Plasma Lipoprotein Nanoparticles

The primary pathways for the metabolism of human plasma lipoproteins have been reviewed recently by Aldons *et al.* [23]

TG rich lipoproteins and VLDL are secreted by intestine and liver, respectively. These lipoproteins undergo lipolysis in the blood circulation to deliver fatty acids to tissues. Then Chylomicron remnants and about half of the VLDL remnants are taken up by the liver and rest of the VLDL remnants is further metabolized to cholesterol-rich LDL. Therefore, LDL nanoparticles are the main cholesterol carrying particles in humans.

HDL is formed in the circulation from lipid-poor apolipoproteins secreted by liver and intestine, and from surface components sloughed during the lipolysis of TG-rich lipoproteins.

The liver synthesizes these lipoproteins as complexes of apolipoproteins and phospholipids. These complexes form cholesterol-free flattened spherical lipoprotein particles. These complexes are capable of picking up cholesterol, carried internally, from cells by interaction with the ATP-binding cassette transporter A1 (ABCA1) [24].

A plasma enzyme, Lecithin-cholesterol acyltransferase, converts the free cholesterol into cholesteryl ester (a more hydrophobic form of cholesterol) [25]. Cholesteryl ester is then sequestered into the core of the lipoprotein particle (LDL-P). The newly synthesized HDL nanoparticles are converted into a spherical shape. HDL particles increase in size as and absorb more cholesterol and phospholipids from cells and other lipoproteins while circulate through the bloodstream. HDL transports cholesterol mostly to the liver and steroidogenic organs such as adrenals, ovary and testes by both direct and indirect pathways to help the synthesis of steroid hormones. HDL is then removed by HDL receptors such as scavenger receptor BI (SR-BI), which mediate the selective uptake of cholesterol from HDL. In humans, indirect pathway is mostly a relevant pathway which is mediated by cholesteryl ester transfer protein (CETP). The CETP protein exchanges TG of VLDL against cholesteryl esters of HDL because of which VLDLs are processed to LDL and finally, LDL are removed by the LDL receptor pathway from the blood circulation. The TG, not stable in HDL, get degraded by hepatic lipase so that small HDL particles are left behind. Small HDL particles then restart the uptake of cholesterol from cells. The cholesterol is delivered to the liver and excreted into the bile and finally to intestine after its conversion into bile acids.

Relationship between LDL Apoproteins and Cardiovascular Disease

Apoproteins are involved in the receptor recognition at cell surfaces and enzyme regulation [26]. LDL and apoprotein (a) are assembled in liver to form lipoprotein (a) or Lp(a). Lp(a) may increase CHD risk [27] by interfering with clotting mechanisms and promoting thrombosis at the endothelial surface which may lead to an accumulation of cholesterol in the blood vessels walls. The concentration of Lp(a) in the plasma is genetically determined [28]. A high level of Lp(a) in the presence of raised LDL levels becomes a risk factor for heart disease [29] and therefore, it is important to reduce elevated LDL levels.

Recently, low-density lipoprotein cholesterol (LDL-C) is selected as a risk marker and the primary treatment target for hyperlipidemia instead of total cholesterol. Additionally, the reduction in LDL-C levels due to statin-based therapies has proven to reduce the risk of nonfatal CVD events and mortality in a continuous and graded manner over a wide range of baseline risk and LDL-C levels [30]. Plasma LDL cholesterol concentrations are related to changes in coronary artery stenosis and cardiovascular events in patients with coronary artery disease and low HDL-cholesterol [30].

Oxidation of LDL Nanoparticles

The liver regulates the concentration of circulating lipoproteins by their clearance through LDL receptors on the hepatic surface [31]. LDL-P penetrates the endothelium of arterial walls where it may oxidized through a complex set of biochemical reactions and promote inflammation and drive injury to the overlying endothelium and surrounding smooth muscle cells [32].Authors [32] have found that persistent elevations in circulating LDL-C are responsible for the progression of early-stage fatty streaks to advanced-stage lipid-rich plaques. LDL receptor deficient mice (which are unable to clear LDL from the circulation) have elevated LDL-C and develop severe atherosclerosis [33] whereas mice with virtually no LDL-C in the circulation have not developed atherosclerosis irrespective of diet and other CHD risk factors [34]. Additionally, epidemiologic investigations have validated LDL-C as an independent predictor of CVD risk. Furthermore, the Framingham Heart Study demonstrated that men and women are 1.5 times more likely to develop clinically significant CHD if their LDL-C is 160 mg/dL compared to a reference population with LDL-C 130 mg/dL [35].In the Atherosclerosis Risk in Communities study, the risk of an incident CHD event was elevated by approximately 40% for every 39 mg/dL incremental increase in LDL-C [36]. Therefore, a low concentration of LDL-C in circulation can reduce the risk of CHD or CVD.

Number of Circulating LDL Nanoparticles

The estimation of the number of circulating LDL-P can be used as an important prognostic tool for a given LDL-C level. It is found that a high number of small sizes LDL-P may pose high CVD risk [36].

A study involving around 7000 participants without CVD at baseline found that the LDL-attributable atherosclerotic risk can be better indicated by LDL-P number when LDL-C and LDL-Pare discordant [36] due to the enhanced delivery of cholesterol to an atheroma by greater numbers of smaller LDL-P [37]. Furthermore, small dense LDL-P are more susceptible to oxidation and experience-decreased uptake by LDL receptors [38].Other laboratory markers of atherogenic lipoproteins correlate with LDL-C and CVD risk. Both apo-B and non–HDL-C help-measure the contribution to atherogenic risk from the total number of atherogenic particles, including LDL, VLDL, IDL, chylomicrons, and lipoprotein(a) [39]. The total number of apoB particles represents the total number of atherogenic lipoproteins, whereas non-HDL-C measures the total cholesterol content carried by these particles. These assays can be used for patients with elevated TG and susceptible for greater CVD risk from TG-rich particles than those with lower TG levels. In a meta-analysis of epidemiologic studies of three atherogenic biomarkers, apoB was found to be the best CVD risk predictor, followed by non-HDL-C and LDL-C [40]. In an analysis of statin-treated patients, non HDL-C was found to be the best predictor of CVD risk when compared to apoB and LDL-C [41]. These findings have led to the incorporation of non-HDL-C and apoB as primary or secondary treatment targets in recent guidelines.

Although the roles of LDL-P number, apoB, non-HDL-C, or other measures such as the ratio of apoB/apoA1 for CVD risk assessment are increasing, LDL-C still remains the most commonly used measure for clinical trials and in clinical care.

In addition to the analysis of LDL-C, the assessment of the size and the number of LDL-P can be a more reliable method of atherogenicity [42]. Each LDL particle has one apoprotein B-100 measure attached; therefore, determination of whole plasma apoprotein B can be considered the best measure of LDL-P number. Because the cholesterol content per LDL-P exhibits large inter-individual variation, the information provided by LDL-C and LDL-P is not equivalent. Individuals with the same level of LDL-C may have higher or lower numbers of LDL-P and, as a result, may differ in terms of absolute CVD risk [43]. Therefore, the size and number of LDL-P provide independent measures of atherogenicity and can be strong predictors of CVD [43]. Also LDL-P can be used to monitor the effectiveness of treatment in decreasing the number of small-dense LDL-P. Furthermore, the LDL-P test may be helpful for an overall evaluation of cardiac risk for patients with a personal or family history of early CVD, particularly in absence of typical cardiac risk factors such as highcholesterol, high LDL-C, high TG, low HDL-C, smoking, obesity, inactivity, diabetes, and/or hypertension. The LDL lipoprotein sub fraction test along with other lipid tests can be used to monitor the treatment effectiveness for patients with an increased LDL-P and/or a large proportion of small, dense LDL-P undergoing the lipid-lowering treatment or lifestyle changes. However, it is worth to note that the presence of exclusively large, fluffy LDL and a lower LDL-P will add no additional risk.

Recently epidemiological studies have demonstrated that patients with predominantly small LDL-P (also termed as pattern B) have

greater CVD risk than those with predominantly large LDL-P (also termed as pattern A) [44-46] in addition to large LDL size [47, 48]. This is because small LDL particles may be more atherogenic than large LDL-P due to the greater oxidation potential of small LDL particles and their relationship to other metabolic abnormalities, particularly high levels of TG-rich lipoproteins and low serum concentration of HDL-C.

Analysis Methods of Lipoprotein Numbers

The gradient gel electrophoresis is a most used method which determines only the distribution of LDL subclasses or average LDL size phenotype (large or small) but it does not count individual number of small and large lipoprotein particles. A decrease in average LDL size measured by gradient gel electrophoresis does not necessarily translate into greater number of small LDL particles, since it could also be due to fewer large LDL particles. Also similar previous studies where gradient gel electrophoresis was used also could not directly compare the risk associated with small versus large LDL particles. This is an important factor as small LDL particles contained substantially less cholesterol than large LDL particles [43]. Additionally, previous studies did not adequately control for the inverse correlation between small and large LDL-p concentrations and potential confounding due to their differing associations with other lipoproteins, lipids, and traditional cardiovascular risk factors [49-51]. Compared to the gradient gel electrophoresis and traditional methods of quantifying cholesterol in lipoproteins classified by density, the nuclear magnetic resonance (NMR) spectroscopy enables quantification of the concentrations in terms of number of lipoprotein particles of varying size and composition [52]. Subclasses of different sizes and compositions of LDL particles are individually detected and quantified by NMR based on the distinct lipid methyl group signal that each subclass emits [49].

Mora *et al.* [53] have studied a multi-ethnic cohort (38% white Americans, 28% African Americans, 22% Hispanic, and 12% Chinese, with 53% women) of 5,538 asymptomatic individuals in the age-group of 45-84 years who are free from CVD at the time of enrolment (2000-2002) and directly compare the associations of small and large LDL particles with carotid intima-media thickness (IMT) (which is a direct and non-invasive measure of subclinical atherosclerosis). Authors [53] hypothesized that NMR-measured small and large LDL particles were both associated with IMT and the concentration of LDL particles, but not LDL-P size, was associated with IMT. Authors further showed that small and large LDL-P concentrations are inversely correlated with each other (Spearman correlation coefficient - 0.64) and they correlated in opposite directions with LDL-P size. Additionally, authors also statistically demonstrated that without accounting for LDL subclass correlation, LDL-P size and small LDL-P separately are associated with IMT (- 20.9 and 31.7 micron change in IMT per 1-SD, respectively, both $p< 0.001$), but not large LDL-P (4.9 microns, P = 0.27). Authors further found that after accounting for their inverse correlation, both LDL subclasses showed highly significant and independent associations with IMT (36.6 and 52.2 micron higher IMT per 1-SD of large and small LDL-P respectively, both $p< 0.001$). Authors also found that there was a greater difference in IMT per large LDL-P compared with small LDL-P when compared on a per particle basis (17.7 and 11.6 microns per 100 nmol/L of large and small LDL-P respectively, both $p< 0.001$). Smaller LDL size was not found to be significant after consideration of the particle concentrations of the two LDL subclasses and risk factors. Therefore, small LDL-P has strong affinity to large LDL-P with carotid atherosclerosis and adjusting for small LDL-P revealed the true association of large LDL-P with IMT. Small LDL-P size is found to have a strong confounder for the association of LDL-P particle number with IMT.

In analyses where authors did not adjust for small LDL-P found that large LDL-P was only weakly associated with atherosclerosis which was consistent with results from earlier published reports [49-51,54]. There are several mechanisms that can explain the atherosclerotic effect of both large and small LDL-P [55]. Also, at both extremes of LDL-P size, receptor-binding affinity for LDL receptors is reduced [56]. Small LDL-P is susceptible to rapid oxidation and has been associated with endothelial dysfunction and metabolic dyslipidemia [57]. Large LDL-P is predominant in patients with familial hypercholesterolemia and those consuming high saturated fat diets [58]. Large LDL-P has higher core cholesterol ester content therefore, potentially delivering more cholesterol per particle to arterial walls [59].

Vitamins and Antioxidants as Supplements in Addition to Statin Based Therapies

Recently several randomised placebo-controlled studies showed that niacin or nicotinic acid (NA) or vitamin B3helps increase HDL particles and its ability to positively influence both angiographic and clinical outcomes [60-66]. Niacin can be used in large quantities (gram doses) to positively modify pathogenetically relevant lipid disorders like elevated LDL-C, elevated non-HDL-C, elevated TG, elevated lipo(a), and reduced HDL-C. Julius [66] reviewed the latest findings of niacin's mechanisms on lipids and its anti-inflammatory and anti-atherosclerotic effects. Niacin can play an important role either as an additive to a statin or as a substitute for a statin in statin-intolerant patients. Moreover, patients with elevated TG and low HDL-C levels and patients with elevated lipoprotein (a) concentrations will possibly benefit from niacin. Liu *et al.* [67] have showed that the pharmacological dose of NA (500-2000 mg/day) decreases LDL increases HDL and inhibits the progression of atherosclerosis and cardiovascular morbidity. Some effects of NA may be mediated through lipid-independent pathways. Authors [67] have suggested that NA participates in the regulation of glucose metabolism and the NAD-sirtuin pathway, which may relate to the altered mitochondrial biogenesis. NA exerts its anti-atherosclerotic or side effects via binding to GPR109A and receptor TRPV1. It may regulate lipid metabolism via adipokines, especially TNFa and adiponectin. NA participates in several cellular pathways, including fork head transcription factors, sirtuins, and

protein kinase B. Despite much progress on the regulatory effect of NA has been obtained, the exact cellular signal pathways on the regulatory mechanism needed more studies. Further investigations of signalling pathways by which NA controls lipid metabolism in the muscle, liver, and adipose tissue require more research.

On the other hand, Masana *et al.* [68] showed that fenofibrate and niacin (HDL-increasing drugs) have failed to decrease the cardiovascular risk in patients with type 2 diabetes. Therefore, more studies needed to prove the effect of niacin to improve HDL nanoparticles further. Additionally, possible side effects of niacin such as flushing and liver damage, and contraindications need to be considered before prescribing the niacin therapy.

One of the solutions to reduce the side-effects of niacin is to use extended release niacin (ERN) [68] In addition to its lipid profile effects, ERN has beneficial effects on endothelial function as well as on inflammatory markers [70, 71]. ERN may also be useful to alter LDL particle numbers, thereby potentially reducing cardiovascular risk [72-75]. Niacin therapy may also works well with fenofibrate [79].

Oxidised LDL can be reverted back to its original form by the reduction process using anti-oxidants. Antioxidants such as vitamin C and E, carotenoids, liposomal glutathione and red wine polyphenols in addition to a healthy diet and lifestyle can help to selectively reduce oxidized LDL [76-77].

Fuller *et al.* [78] demonstrated that RRR-alpha-tocopheryl acetate supplementation at pharmacologic doses decreases low-density-lipoprotein oxidative susceptibility.

However, further epidemiological studies about the effectiveness of supplements for the cholesterol or CVD management are needed to understand the extent of applications of vitamins and other supplement for CVD or CHD management.

Conclusions

The present review discussed structure-function relationship of two key lipoprotein nanoparticles, high density lipoproteins and low density lipoproteins and their role in cardiovascular diseases. HDL is smallest lipoprotein (~10nm) and transports only 15-20% of cholesterol from tissues to liver and hence considered as good cholesterol. LDL nanoparticles (20-27nm) transport 60-80% of cholesterol from liver to human tissues and are considered as bad cholesterol. A small amount of cholesterol is transported by other lipoproteins.

Both LDL and HDL nanoparticles are made up of aggregates of (apo) proteins and cholesterol in different ratios. Despite being termed as bad cholesterol, LDL nanoparticles in reality perform vital functions in the human body. However, excess of LDL nanoparticles which oxidised in endothelium cells through complex biochemical pathways are responsible for CVD and the oxidised LDL can be reversed back to normal LDL using vitamins.

The latest literature of the CVD management suggests that antioxidants such as vitamin E can reduce the LDL oxidation whereas niacin (vitamin B3) can increase HLD in blood in addition to statin regime. These two therapies in combination with statin therapy and a healthy diet and lifestyle may help to reduce CVD significantly.

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