NUTRACEUTICAL PLATFORMS

Lowering Cholesterol: A Careful Balancing Act

It is important to consider more than just numbers when wishing to lower cholesterol levels – impact on disease should remain the number one factor.

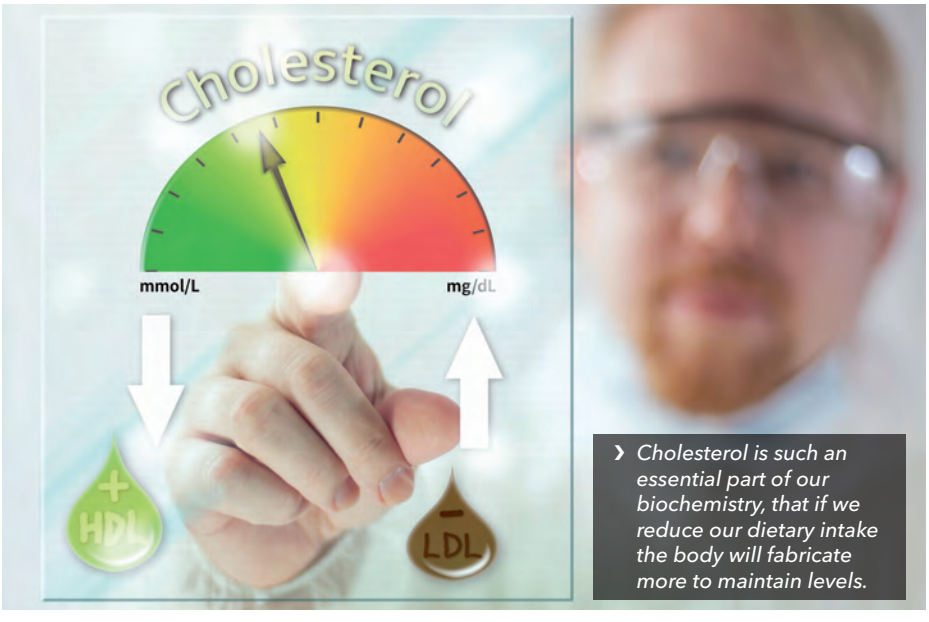
by Coriander Stone

What constitutes high cholesterol? Who sets the guidelines and where do the numbers for the ideal reference ranges come from? When considering the use of nutraceuticals to lower cholesterol, these are questions worth considering. The current UK recommendations for low-density lipoprotein count (LDL-c) in healthy adults is ≤3mmol/L (US ≤3.7mmol/L) and for at risk adults is ≤2mmol/L. High-density lipoprotein (HDL) should be >1mmol/L and triglycerides over 1.7 mmol/L. However, no distinction is made between male and female recommended ranges, which could be considered somewhat of an oversight, as oestrogen has quite an impact on levels.

Where's the Evidence?

Since April 2014, the American Heart Association and the American College of Cardiology have, however, issued new guidelines stating that doctors need no longer focus on numbers of LDL and should concentrate rather on whether cholesterol-lowering drugs (i.e. statins), reduce the risk of heart disease and stroke. In fact, it is now becoming more widely recognized that improving LDL-c targets does not reduce the risk of cardiovascular disease (CVD) and in the words of influential cardiologist Steven Nissen on the effect of LDL targets on disease: "the evidence was never there." Regarding where the numbers for the ideal targets came from and what research they were based on, he says committees "made them up out of thin air."

Clearly, it is important to consider more than just numbers when wishing to lower cholesterol levels – impact on disease should remain the number one factor. In order to make a clear decision as to whether cholesterol levels need to be reduced, it is vital to understand what cholesterol is and its' role in the body.



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The Role of Cholesterol

Cholesterol is fabricated in the body not from fats as popular belief has it, but from sugars. The metabolism of carbohydrates to glucose within the body creates the building blocks for cholesterol and the reason that altering cholesterol intake via diet has little or no impact on serum levels is due to the complex bio-feedback mechanism, which responds to external intake by limiting or increasing internal production. The liver produces around 700mg of cholesterol per day and only 20-25% of serum cholesterol comes from dietary intake. In short, to control and lower cholesterol levels, we need to concentrate on reducing carbohydrate intake rather than fat. In fact, cholesterol is such an essential part of our biochemistry, that if we reduce our dietary intake the body will fabricate more to maintain levels.

Cholesterol forms the basis for all steroid hormones and is also essential for the stability of animal cell membrane structure. Figure 1 shows how cholesterol is responsible for the synthesis of all other steroid hormones.

A False Indicator?

In fact, there are more deaths from suicides related to mental health problems due to cholesterol being too low, than there are from CVD related to high cholesterol. Statins have been shown to increase risk of CVD by 9% and of diabetes by a massive 71% in post-menopausal women. In short, not only is low cholesterol a false indicator of low disease risk, it can also have devastating impacts on other body functions.

So while there are some effective cholesterol-lowering nutraceuticals on the market which may be useful for people with, for example, familial hypercholesterolaemia or high levels of inflammation, they may not reduce disease risk in the vast majority of people. In fact, the reason that statins reduce the risk of CVD in a small minority is because they reduce inflammation as an unseen side-effect, as well as lowering LDL-c and this is one of the real keys in reducing disease risk alongside minimizing LDL oxidation. Lowering the LDL particles (LDL-p) is also important and may be the true indicator of risk, rather than LDL-c. People with higher LDL-c but low LDL-p have actually been shown to be better protected against CVD than people with low LDL-c.

The Real Causes

One of the most common reasons for elevated LDL-c is poor thyroid function. Depletion of thyroid hormone leads to lowered LDL receptors in the liver, resulting in raised LDL serum cholesterol. In most cases, once thyroid function is improved, cholesterol reduces to normal levels.

Liver function must also be considered as a potential mechanism for raised LDL cholesterol and so all of these factors should be taken into account before targeting LDL levels directly. The most effective nutraceuticals act on the liver, affecting lipid metabolism in the same way as steroids do, but not many have adequate human studies.

The following ingredients may be useful in reducing serum LDL-c and/or CVD risk:

Phytosterols: These include both sterols and stanols, both of which are steroid compounds – the only difference being that stanols are saturated sterols. As the name suggests, their molecular structure is very similar to cholesterol and they are found naturally in nuts, berries, fruits and seeds. They work by blocking the absorption of cholesterol in the small intestine, thereby lowering serum LDL. They are EFSA and FDA approved, although the FDA is currently reviewing the health claims.

Phytosterols have been shown to reduce serum cholesterol but not CVD risk and one meta-analysis showed that 3g of phytosterols daily led to up to a 15% reduction in LDL, but no reduction in CVD risk. In fact, high levels of phytosterols have actually been linked to an increased risk of CVD rather than a lowered one. Another meta-analysis showed no relationship between low LDL cholesterol levels and CVD.

Soluble Fiber: Found in beans, grains, some fruits and vegetables, oats, nuts, seeds and psyllium, soluble fiber has been shown to reduce LDL-c. A large epidemiological study found a 20-40% reduction in CVD risk among people who consumed wholegrains. It works by reducing the amount of bile reabsorbed in the intestines, forcing the body to make more bile salts – for which cholesterol is necessary. The recommendation is minimum 5-10g daily for reducing LDL cholesterol and a meta-analysis of 67 controlled trials found that between 2-10g per day led to a decrease of 0.3g LDL and could reduce LDL by around 0.13mmol/L. The source of the soluble fiber doesn't seem

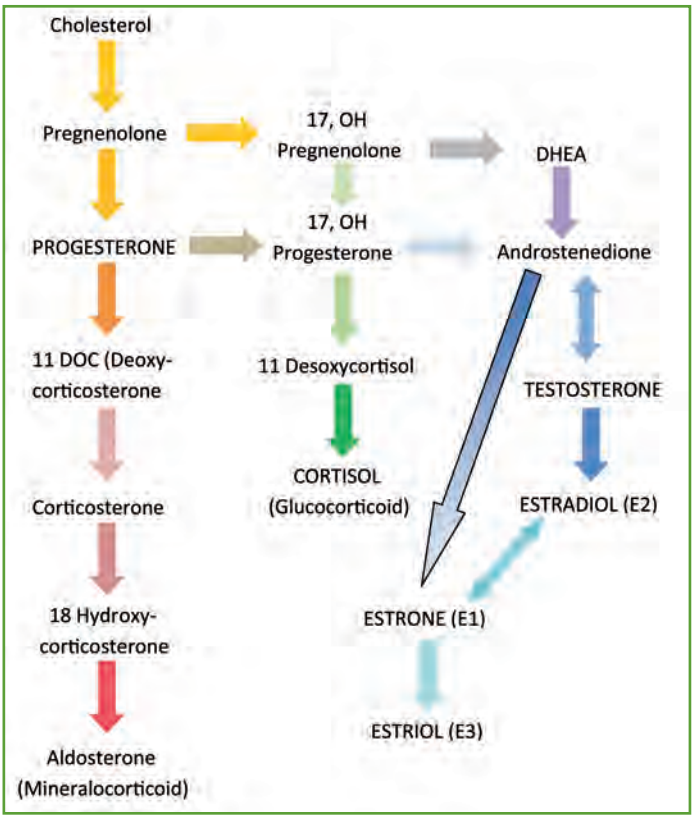

Figure 1: Synthesis of Steroid Hormones From Cholesterol

to matter – any will have a similar effect.

Monacolins: Monacolin K is the active component of red yeast rice and has a very similar molecular structure to statins, particularly lovastatin. In fact, the FDA ruling is that any product containing monacolin K is the same as a statin and as such, must be subject to the same regulations – essentially classifying it as a drug. At least 10mg of monacolin K is necessary to have any effect, yet most red yeast rice products contain almost none at all in order to escape FDA regulations. Just like statins, monacolins work on the liver, limiting the synthesis of cholesterol.

A meta-analysis of 93 controlled trials found that monacolins reduced LDL by 0.7mmol/L and raised HDL by 0.15Mmol/L and EFSA concluded a cause and effect relationship between 10mg monacolin K per day from red yeast rice and the maintenance of normal LDL concentrations, capable of reducing LDL by 20%.

Where monacolins may be really interesting is in their capacity to reduce C-reactive proteins – inflammatory markers – just as statins do.

Garlic: The phytochemical allyl sulphides in garlic, interferes with squalene monooxygenase – responsible for the regulation of cholesterol biosynthesis – thus lowering cholesterol and improving cardiovascular function.

A meta-analysis of five randomized controlled studies in people with a total net cholesterol of >5.17mmol/L found a net reduction of 0.59mmol/L, with intake of 0.5-1 clove per day, reducing cholesterol by 9% in total and another study showed that 800mg per day of aged garlic extract for 5 months reduced LDL by 10% in hypercholesterolemic men.

Omega 3: Omega 3 is found in fish, chia seeds, flax seeds, walnuts and some leaves and has been well studied for its cardioprotective effects. ≈4g per day has been shown to lead to a 25-30% decrease in triglycerides and the FDA has stated that doses of ≤3g are safe. However, care must be taken that the ratio of omega 3:6 is correct, as this also seems important for CVD. Ratios of between 1:1 and about 3:1 are generally perceived as healthy.

The interesting aspect of omega 3 is that it actually increases LDL-c but lowers LDL-p and therefore may be a good cardioprotective agent. Omega 3 has been shown to be effective in reducing CVD incidents, even though it increases LDL-c and this strongly suggests that our focus should be shifting from LDL-c to other markers.

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In a meta-analysis of 21 trials, 3g fish oil consumption lowered triglycerides by 0.30mmol/L, raised HDL by 0.04mmol/L and increased LDL by 0.155mmol/L.

Niacin: Also known as vitamin B3 or nicotinic acid, niacin has been shown to not only lower total cholesterol but also lower LDL cholesterol, triglycerides, and fibrinogen levels while simultaneously raising HDL levels. Niacin has also been shown to be the only lipid-lowering agent to actually reduce overall mortality.

However, it is needed in very high doses of 1-3g daily to have this effect which in some people may cause unpleasant side-effects, particularly flushing and a tingling sensation in extremities.

The Coronary Drug Project – an epidemiological study conducted between 1966 and 1975 – looked at five lipid-lowering drugs including niacin and found that niacin reduced mortality by ≤11% compared to both the other drugs and the placebo groups. It is often used in conjunction with statins for an improved cholesterol-lowering effect.

Key Considerations

When wishing to implement the use of nutraceuticals to lower cholesterol, the question "what is the aim of lowering LDL" must be considered. Is it to reduce the risk of CVD or because inflammation is also high or due to familial hypercholesterolemia?

If there are other reasons besides reducing CVD risk then some of these nutraceuticals may be worth considering.

If reducing the risk of CVD in people with no history of heart attack or stroke is the aim, then it may be wiser to choose a nutraceutical which targets triglycerides and inflammation rather than LDL-c cholesterol – shown to be far greater indicators of risk.▼

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Table 1: The Effect of Lipid-Lowering Nutraceuticals on CVD Outcomes

Nutraceutical	Trial Design	Result	Reduce CVD Risk?
Phytosterols	Meta-analysis	3g daily led to an LDL decrease of ≈15%	No
	Meta-analysis using 17 studies and a total of 11,182 subjects	No relationship found between cholesterol levels and CVD	No
Soluble fiber	Overweight pre-menopausal women given 28g oat bran for 4 weeks	↓ LDL-c and ↑ HDL	No
Monacolins	Meta-analysis of 93 controlled trials	↓ LDL by 0.7mmol/L and ↑ HDL by 0.15 mmol/L	In a select group
Garlic	Meta-analysis of 5 RCT	≥ 0.5 clove per day resulted in 9% reduction in total cholesterol	Yes
	RCT using 800mg/day aged garlic extract for 5 months	↓ LDL by 10%	–
Omega 3	Meta-analysis of 21 trials using 3g fish oil daily	↑ LDL by 0.155mmol/L, ↑ HDL by 0.04mmol/L and ↓ triglycerides by 0.30mmol/L	Yes
Niacin	Coronary Drug Project studying effect of 5 lipid-lowering drugs including niacin on mortality	Niacin ↓ total mortality from all causes by 11% compared to placebo and other drugs	Yes