# Cholesterol-Lowering Abilities of a Novel Proprietary Preparation (CholesLo™) - A Randomized, Double-Blind, Placebo-Controlled Study.

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## ABSTRACT

Cardiovascular diseases are a major cause of death in the United States and worldwide. Moreover, the annual cost of dealing with CVD and the resulting complications run in hundreds of billions of dollars every year. A major risk in the development of CVD is raised levels of plasma lipids – especially ischemic heart disease. In the backdrop of association of hypercholesterolemia (raised plasma cholesterol) with CVD and the high percentage of population with cholesterol problems – lowering blood cholesterol has assumed immense importance.

Owing to the adverse effects associated with use of lipid-lowering drugs, the onus in recent years has shifted to use of 'natural' supplements to normalize blood lipid chemistry. We decided to investigate the claims of one such lipid-lowering proprietary formulation – CholesLo™. We undertook a randomized, double-blind, placebo-controlled study to investigate the efficacy of CholesLo™ from CholesLo, Inc.[1], in reducing plasma cholesterol levels. Participants were randomly assigned to receive either 6 capsules of CholesLo™ or a placebo (dicalcium phosphate) (2 capsules, TID). The duration of the study was 20 weeks.

The results of our study showed that participants receiving CholesLo™ showed significant reductions in plasma total cholesterol, LDL and triglycerides levels. HDL levels, on the other hand, rose markedly. Similar findings were observed with homocysteine levels; dramatic reduction in the homocysteine level was observed in those that received CholesLo™. We therefore conclude that CholesLo™ effectively reduces plasma cholesterol and homocysteine levels and therefore the risk of subsequent development of cardiovascular disease. Also, participants in our study did not report any major adverse effects. Therefore, we opine that CholesLo™ may be totally safe for use in the general population.

## BACKGROUND

Cardiovascular diseases (CVD) are a major cause of death in the United States (*Kenneth et al., 2009*) and worldwide (*Deaton et al., 2007*).

Out of 58 million deaths in 2008, CVD were responsible for 17.5 million deaths (*Gaziano, 2008; World Health Organisation, 2009*); CVD as a cause of death was 3 times commoner than major infectious diseases – tuberculosis, malaria and HIV-AIDS – put together! It is estimated that by 2030, CVD will be responsible for 75% of all deaths (*Deaton et al., 2007*)! Moreover, the annual costs of dealing with CVD and complications arising out of CVD run in hundreds of billions of dollars; in 2005, the US spent a whopping $349 billion and Europe, a staggering €169 billion (*Leal, Luengo-Fernandez, Gray, Petersen, & Rayner, 2006; American Heart Association, 2005)*.

Needless to say, it makes more sense in preventing CVD rather than managing them.

## Pathogenetic link between hypercholesterolemia and cardiovascular disease.

A major risk in the development of CVD is raised levels of plasma lipids – total cholesterol, low density lipoprotein (LDL) and triglycerides (TGs)(de Bekker-Grob, van, van den Berg, Verheij, & Slobbe, 2007; Lloyd-Jones et al., 2006; Pischon et al., 2005; Qinna et al., 2008; Yusuf, Reddy, Ounpuu, & Anand, 2001). Hypercholesterolemia is conspicuously present as a causal factor in most vascular diseases – especially ischemic heart disease (Barzi et al., 2005; Critchley, Liu, Zhao, Wei, & Capewell, 2004).

Currently, according to an estimate, over a third of men (34%) and almost half of all women (42%) in the US have elevated blood cholesterol (Feuerstein & Bjerke, 2008) and therefore an elevated risk of developing cardiovascular disease.

In light of such findings –association of hypercholesterolemia (raised plasma cholesterol) with CVD and the high percentage of population with cholesterol problems – lowering blood cholesterol has assumed immense importance. That lowering plasma cholesterol will reduce the risk of developing CVD is backed up by research (Pasternak et al., 1996; Sacks et al., 1996; Shepherd et al., 1995).

Regulation of plasma cholesterol levels within normal ranges thus forms the basis of managing CVD; pharmacological (use of statins) and dietary interventions (low hydrogenated fat foods) are the most often used approaches. Drugs, although effective, are more likely to have adverse effects. Strict diets to reduce cholesterol, on the other hand, are not always practical and do not enjoy long term patient compliance.

Not surprisingly then, the onus in recent years has shifted to use of 'natural' supplements to normalize blood lipid chemistry. Fish oils, flaxseed oil, beta-sitosterols, sitostanol (in Benecol®), garlic extract and green tea extract are some of the ingredients that are typically present in cholesterol-lowering supplements (Mayo Clinic Staff, 2008).

Such herbal cholesterol-lowering supplements abound on the market. The authors of this study decided to investigate the claims of a proprietary formulation – CholesLo™ – that promises to naturally help lower total cholesterol, LDL and triglycerides effectively and in a safe manner. Additionally, it helps reduces plasma homocysteine levels as well.

## STUDY DESIGN

We undertook a randomized, double-blind, placebo-controlled study to investigate the efficacy of CholesLo™ from CholesLo, Inc.[1] in reducing plasma cholesterol levels.

Ethical approval was sought from and granted by the Kawasaki Medical University.[2]

## PARTICIPANTS

Selection criterion for participants in the study was elevated plasma cholesterol with/without CVD and presence/absence of other risk factors to develop CVD.

50 overweight adults (28 men and 22 women), with elevated parameters of cardiovascular disease – namely total cholesterol, LDL and triglycerides (TGs) – were selected for the study. These participants also had subnormal to low HDL levels.

## SCREENING METHODS

Prior to commencement of the study, the 50 selected participants attended screening sessions. Blood samples were collected and appropriate tests used to record total plasma cholesterol, LDL cholesterol, HDL cholesterol and TGs levels.

Test indicated the following level in participants' plasma: total cholesterol was 250 ± 25 mg/dL, LDL cholesterol was 150 ± 10 mg/dL, HDL cholesterol 40 ± 8 and triglycerides were 230 ± 20 mg/dL (see table 1).

Since homocysteine is an independent predictor of subsequent development of heart disease (*Vizzardi et al., 2009*), we conducted methionine load test to record participants' plasma homocysteine levels as well. The results of the test suggested homocysteine levels of 150 ± 7 µg/dL (see table 1).

Table 1- Baseline levels of blood lipids and homocysteine

| Plasma Levels | Pre-participation |
|---|---|
| **Total Cholesterol** | 250 ± 25 mg/dL |
| **LDL** | 150 ± 10 mg/dL |
| **HDL** | 40 ± 8 mg/dL |
| **Triglycerides** | 230 ± 20 mg/dL |
| **Homocysteine** | 150 ± 7 µg/dL |

## METHODOLOGY

Participants were randomly assigned to receive either 6 capsules of CholesLo™ or a placebo – dicalcium phosphate (2 capsules, TID). Participants were instructed to take the capsules with food (beginning of meal) and a minimum of 8 oz. of water. No other changes were made or instructed to the participants (CholesLo™ or placebo group). However, appropriated improvements in diet and exercise should be considered and utilized as part of a total heart-healthy life-style.

CholesLo's™ all-natural formula **c**ontains ingredients such as Policosanal, d-Pantethine, Red Yeast Rice Extract, Coenzyme Q10, Artichoke Leaf Extract, Guggulsterones, Phytosterols Complex and additional herbs and vitamins. All of these ingredients supposedly exert a synergistic action to lower atherogenic blood lipids (see 'discussion'). The duration of the study was 20 weeks.

## RESULTS

Participants receiving CholesLo™ showed significant reductions in plasma cholesterol, LDL and triglycerides levels. HDL levels, on the other hand, rose markedly – Please refer to table 2a and 2b.

In contrast, tests conducted on control subjects showed very little changes – Please refer to table 3a and 3b.

Similar findings were observed with homocysteine levels; dramatic reduction in the homocysteine level was observed in those that received CholesLo™ – Please refer to table 2a and 2b.

## Table 2a - Participants receiving CholesLo™

| Plasma Levels | Pre-participation | After 20 weeks on CholesLo™ |
|---|---|---|
| **Total Cholesterol** | 250 ± 25 mg/dL | 190 ± 5 mg/dL |
| **LDL** | 150 ± 10 mg/dL | 60 ± 9 mg/dL |
| **HDL** | 40 ± 8 mg/dL | 65 ± 3 mg/dL |
| **Triglycerides** | 230 ± 20 mg/dL | 160 ± 9 mg/dL |
| **Homocysteine** | 150 ± 7 µg/dL | 80 ± 5 µg/dL |

## Table 2b - Participants receiving CholesLo™

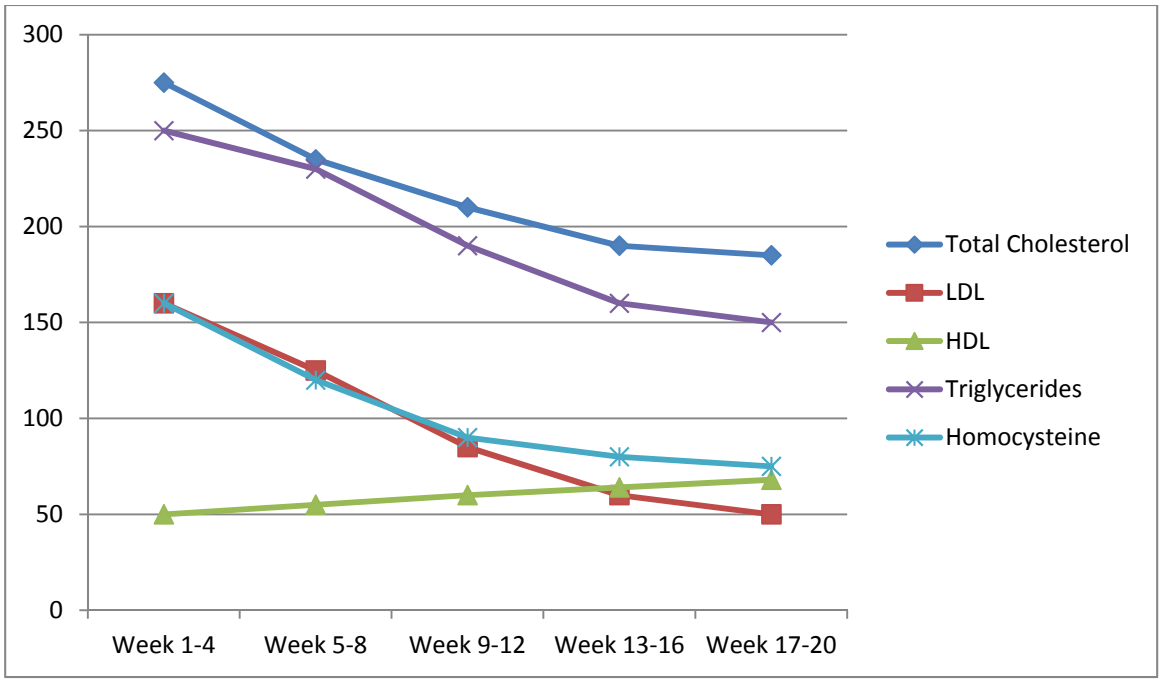
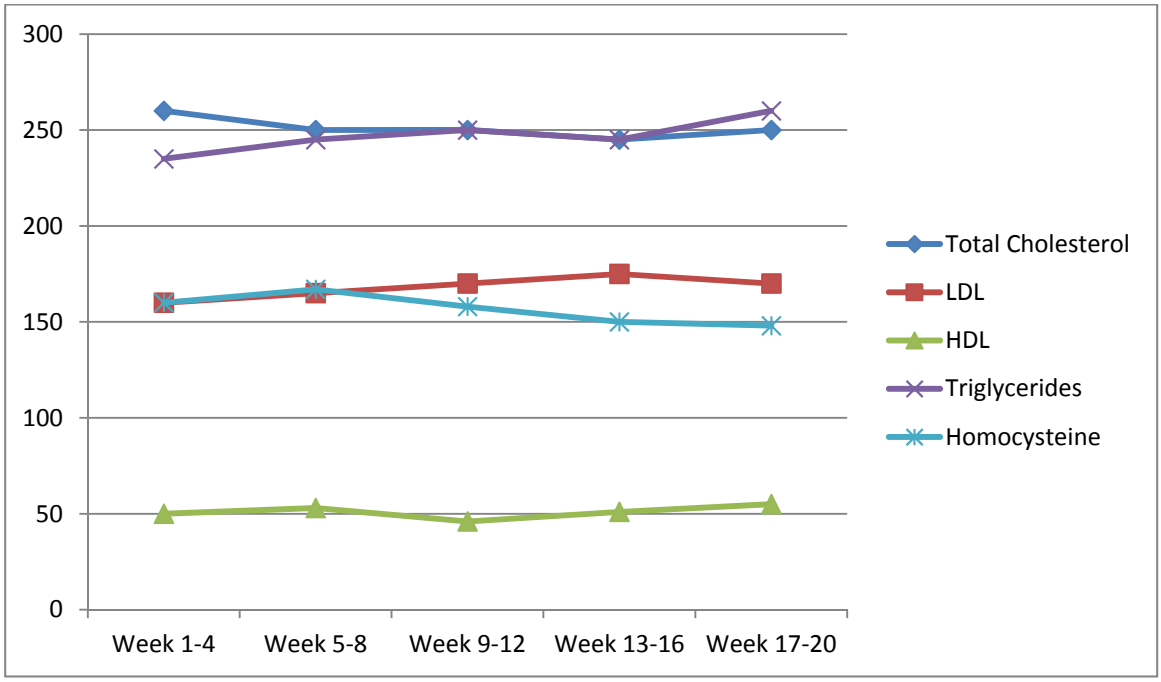


Table 3a - Control participants receiving placebo.

| Plasma Levels | Pre-participation | After 20 weeks on CholesLo™ |
|---|---|---|
| **Total Cholesterol** | 250 ± 25 mg/dL | 248 ± 8 mg/dL |
| **LDL** | 150 ± 10 mg/dL | 160 ± 9 mg/dL |
| **HDL** | 40 ± 8 mg/dL | 48 ± 6 mg/dL |
| **Triglycerides** | 230 ± 20 mg/dL | 250 ± 9 mg/dL |
| **Homocysteine** | 150 ± 7 µg/dL | 144 ± 8 µg/dL |

Table 3b - Control participants receiving placebo.




Also, none of the participants receiving CholesLo™ reported any long-term or unpleasant effects. On the contrary, majority reported a sense of well-being and 'buzz'. Improvements in glucose levels, as well as blood pressure were also reported in the CholesLo™ group as a "side-benefit".** These findings were not consistent with the control group receiving placebo. – Please refer to table 4.

## Table 4 - Adverse Events* Reported Over A 20-Week Period

| Adverse Events*<br>CholesLo (n)<br>Placebo (n) | Week 1-4<br>(n = 35)<br>(n = 15) | Week 5-8<br>(n = 35)<br>(n = 15) | Week 9-12<br>(n = 35)<br>(n = 15) | Week 13-16<br>(n = 35)<br>(n = 15) | Week 17-20<br>(n = 35)<br>(n = 15) |
|---|---|---|---|---|---|
| Upset Stomach†<br>CholesLo (n)<br>Placebo (n) | <br>3.0% (1)<br>9.0% (1) | <br>0.0% (0)<br>0.0% (0) | <br>0.0% (0)<br>0.0% (0) | <br>0.0% (0)<br>0.0% (0) | <br>0.0% (0)<br>0.0% (0) |
| Constipation††<br>CholesLo (n)<br>Placebo (n) | <br>3.0% (1)<br>9.0% (1) | <br>0.0% (0)<br>0.0% (0) | <br>0.0% (0)<br>0.0% (0) | <br>0.0% (0)<br>0.0% (0) | <br>0.0% (0)<br>0.0% (0) |
| Increase Energy†††<br>CholesLo (n)<br>Placebo (n) | <br>10.0% (4)<br>0.0% (0) | <br>8% (3)<br>0.0% (0) | <br>8% (3)<br>0.0% (0) | <br>4.0% (1)<br>0.0% (0) | <br>4.0% (1)<br>0.0% (0) |

* Due to the low number of participants in the study (50), adverse events were recorded by both percentage and total numbers. [% (n)]

† Upset stomach was rectified when taken with a 8-12 oz. of purified water, immediately before a meal.

†† Constipation for both groups was transitory and lasted a maximum of 48 hours, on the initial start of the trial.

††† Increase in energy levels was a welcomed "side-effect" by participants. Though not typically viewed as an "adverse event", we felt it was best to note it anyway.

** Improvements in glucose levels and blood pressure were noted in the CholesLo™ group, but were outside the scope of this study and were not recorded in statistical details for this report.

## DISCUSSION

The current basis of pharmacological management of hypercholesterolemia is through use of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (i.e. statins); these have the potential to lower total cholesterol and LDL by 20% to 28%.

Use of statins however, is characterized by severe side-effects. Thus, therapies other than statins are always sought after.

As stated earlier, the 'lipid optimizing system' of CholesLo™ contains natural ingredients like Policosanal, d-Pantethine, Red Yeast Rice Extract, Coenzyme Q10, Artichoke Leaf Extract, Guggulsterones, Phytosterols Complex and additional herbs and vitamins. In combination with the other vital ingredients, it has been show to reduced LDL, total cholesterol and triglycerides. Additionally, it is a powerful antioxidant. CQ10 is also hypolipidemic and an antioxidant– supplementation with CQ10 has been shown to cause reduction of circulating markers of inflammation as well (*Wang, Rainwater, Mahaney, & Stocker, 2004)*.

Guggulsterone is a phytosterol possessing hypolipidemic properties (*Yang et al., 2008*). Similarly, red yeast rice extract (*from Monascus purpureus*) and phytosterols have been shown to reduce LDL cholesterol markedly – 33% as compared to 28% by statins (*Feuerstein & Bjerke, 2008*). Turmeric containing curcumin as

the active principle and artichoke extracts (from *Cynara scolymus*) have cholesterol-lowering abilities (*Qinna et al., 2008*) – turmeric is present as a 95% curcuminoid extract in CholesLo™. In addition to lipid-lowering properties (*Englisch, Beckers, Unkauf, Ruepp, & Zinserling, 2000; Pittler, Thompson, & Ernst, 2002*), artichoke extract possess strong antioxidant properties (*Lupattelli et al., 2004*).

Milk thistle (flavonoids) and N-acetyl L-cysteine have antioxidant and hepatoprotective properties (*Loguercio & Festi, 2007*); these are contained in the 'liver cleansing formula' of CholesLo™.

### Importance of reducing homocysteine levels:

Traditionally, the risk of developing CVD has been accessed by measuring a multitude of factors – low physical activity levels, dyslipidemia, smoking, hypertension and presence of diabetes mellitus (*Anonymous, 2001; Hamer & Stamatakis, 2009; Wilson et al., 1998*). However, more recently, newer markers of CVD have been defined; these are – elevated levels of homocysteine, C-reactive protein (CRP) and presence of metabolic syndrome (*Wang et al., 2006; Gami et al., 2007*). Notwithstanding the importance of high plasma cholesterol in predicting CVD, some believe that elevated level of homocysteine is an independent predictor (and may even be a causal factor) of CVD (independent of the classic risk factors enumerated previously) (*Luhmann, Schramm, & Raspe, 2007*). Furthermore, there is some evidence to suggest that homocysteine levels can be reduced by intake of folic acid and vitamin of the B-complex group (*Perna et al., 2008; Jung et al., 2007; Luhmann et al., 2007*).

The 'homocysteine reducing formula' of CholesLo™ contains cyanocobalmine folic acid, (Vit.$B_{12}$) and pyridoxine (Vit.$B_6$). CholesLo™ contains the correct ratios and amounts of these key vitamins, as proven in clinically studies for homocysteine reduction *(Dr. Kilmer S. McCully, 1969, 1998).*

## CONCLUSION

CholesLo™ shows clinical significance in helping reduce plasma cholesterol and homocysteine levels and therefore affects favorably the risk of subsequent development of cardiovascular disease. Furthermore, our findings suggest that the dose required to cause such improvements in plasma lipid profile is safe enough to be considered for use in general population.

## FURTHER RESEARCH

Although, we concluded that most ingredients of CholesLo™ were effective in lowering blood cholesterol and safe for use, the safety profile of each of these individual herbs on long term use has not been established in literature (*Liu et al., 2007*). Further research in that direction is warranted.

We also intend to undertake in the near future, investigation/s to ascertain if CholesLo™ could be prescribed routinely to everyone – with or without elevated plasma lipids and presence of CVD risk factors – as a preventive measure against CVD.

Lastly, the importance of a "healthy life-style" should always be emphasized. An attempt should be made to control hypercholesterolemia with appropriate diet, exercise, and weight reduction in obese patients.

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