# CLINICAL RESEARCH SCIENCE BINDER

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# 1
# The four working mechanisms of Bios Life™

An excerpt from a book by Peter J. Verdegem, Ph.D.

## Mechanisms of Bios Life™ for Cholesterol Management

Over the years, science has attempted to find different ways to lower or optimize cholesterol levels. Because cholesterol is part of a number of processes in the body, there are multiple biochemical pathways that may be used to achieve this goal. Pharmaceutical products tend to influence only one mechanism in the body. This is because most drugs on the market today contain only one active component that will have an effect on typically one area in the body. As explained before, statin medication blocks one enzyme in the body that is responsible for one reaction of the pathway to the synthesis of cholesterol. The result is that statins have only one predominant effect, which is the lowering of LDL cholesterol. Another drug, ezetimibe, utilizes the absorption mechanisms of cholesterol in the digestive tract and blocks efficient absorption into the bloodstream.

When the current formulation of Bios Life was being the developed, the scientists realized that in order to make a very effective natural product, a multitude of mechanisms had to be used to influence cholesterol levels. And that is exactly what happened. Carefully, all scientific data was assessed that dealt with natural or dietary components that had shown a proven effect on cholesterol levels. Next, the four most promising mechanisms were chosen and paired with natural ingredients. An important requirement for the products was that the ingredients should be part of common diets of people around the world. The result was the creating of a completely natural product that influenced cholesterol levels in the blood through four unique and different mechanisms. Those individual mechanisms are described in the following chapter.

## Mechanism 1: Bile Acid Sequestration

Bios Life's primary ingredient is soluble fiber. This macronutrient from the diet is a very well-known cholesterol-regulating ingredient, and medical associations advise to consume this nutrient in greater amounts. The key to the working mechanism of soluble fiber is called bile acid sequestration, or trapping the bile acids.

Fat from meals is digested in the intestinal system using bile and bile acids. Bile is elaborated by the liver. It contains bile acids, cholesterol, lecithin, and bile pigments, which are all synthesized by the liver cells. Bile is secreted into the bile duct that leads directly into the digestive tract. About 250 ml to 1,500 ml of bile is secreted per day into the digestive tract. In the periods between meals, bile is diverted to the gallbladder.

The gallbladder concentrates bile by removal of salt and water from the stored bile, resulting in a 5 to 20-fold concentration of the bile acids. Bile acids in the intestinal tract emulsify lipids, thereby increasing the surface area available to fat-digesting enzymes called lipases. After their function, bile acids are actively recycled by reabsorption in the terminal part of the small intestine. A small fraction of bile acids escapes absorption and is excreted. The returning bile acids are avidly taken up by the liver and are rapidly resecreted during the course of digestion.

The primary bile acid is cholic acid, which is synthesized in the liver using cholesterol as a building block. Therefore, the cholesterol pool that is available in the body is utilized to synthesize bile. Since most bile is reabsorbed and reutilized, the total amount of cholesterol is not changed due to the bile synthesis. In other words, if it would be possible to prevent the reabsorption of bile acids into the bloodstream from the intestinal tract, a mechanism to lower cholesterol in the body would be identified. This is exactly what soluble fiber accomplishes in the body.

Fiber is referred to as a mixture of polysaccharides present in the cells and skins of almost

all vegetables and fruits. It is also a part of the bark of trees. There are two kinds of fiber: soluble and insoluble. The soluble fraction of the fiber is known to have a cholesterol-lowering effect. Examples of soluble fibers are guar gum, pectin, and beta-glucans.

When the dissolved fibers reach the intestinal tract, they start to gel because of the acidic environment of the stomach. The gel is known to trap the bile acids in the intestinal tract, preventing them from being reabsorbed. When the gel matrix is being excreted from the intestines, the bile acids go along with it. Since bile acids are made from cholesterol, removal of bile acids from the body will reduce the total level of cholesterol.

Not every fiber mixture is equally effective in lowering cholesterol. Bios Life is comprised of a unique fiber mixture combined with calcium carbonate that has premium bile-acid sequestration properties. This combination is patented under the U.S. patents 4,883,788 and 4,824,672. These patents describe and protect the invention of combining soluble fiber with calcium carbonate.

Calcium carbonate generates carbon dioxide when it reaches the acids in the stomach. This bubbling of $CO_2$ promotes the dissolving and dispersion of the soluble fiber in the intestinal tract. This makes the BioSphere gel matrix larger and faster formed so that bile acid sequestration is more effective than by other fiber mixtures.

Bios Life includes a combination of different soluble fibers, namely guar gum, gum Arabic (also known as gum acacia), locust bean gum, pectin, and oat fiber. These fibers are harvested from different parts of the world.

Guar gum is extracted from the guar bean where it acts as a food and water store. Also called guaran, guar gum is primarily the ground endosperm of the seeds from Cyamopsis tetragonolobus. The guar seeds are dehusked, milled, and screened to obtain the guar gum. It is typically produced as a free-flowing, off-white, coarse-to-fine ground powder. The particle size of the guar gum determines the rate of solubility and gel formation. Locust bean gum is structurally very similar to guar gum but has some slight differences in solubility and gel-forming characteristics.

Gum arabic, or acacia, is a substance that is taken from two sub-Saharan species of the acacia tree, Acacia senegal and Acacia seyal. It is used primarily in the food industry as a stabilizer but has had more varied uses in the past, including viscosity control in inks. Gum arabic is a complex mixture of saccharides and glycoproteins. It serves as an important ingredient in soft drink syrups, firm gummy candies like gumdrops, and in marshmallows. As the name implies, gum arabic is also found in chewing gums, where it acts as one of the many factors that contribute to its texture.

Pectin is a soluble fiber that was first discovered in 1825. Today it is used in fillings, sweets, as a stabilizer in fruit juices and milk drinks, and as a source of dietary fiber in foods. The natural source of pectin is mainly apples and citrus fruits.

Finally, oat fiber is derived from the outer casing of the oat. It is also a source of beta-glucans that are naturally occurring in oat, and that are therefore also present in Bios Life. The source of the fibers in Bios Life is strictly controlled, and the manufacturer makes sure that the fibers are not contaminated with any herbicides or pesticides.

The American Heart Association recognizes the importance of soluble fiber as well. This institute has advised that every adult consume at least 30 grams of fiber per day. Sadly, the average American diet only contains about 12 grams of fiber. This is obviously the result of increasingly bad dietary habits. Most people are consuming more and more industrially made foods that have little to do with the way nature intended them to be. Processing foods tends to reduce the amount of intact and therefore functional fiber. Also, the consumption of fruits and vegetables has steadily decreased.

The cholesterol-lowering potential of soluble fiber has been proven many times in peer-reviewed publications. Table 13 provides a list of clinical trials that have investigated the potential of soluble fiber for cholesterol lowering. To limit the overview to the latest scientific work, only trials from the period 2000 to 2007 were included. This list was created using PubMed, with the search terms "fiber" and "cholesterol," with the search limits set on "clinical trial with humans." Not all information was obtainable from the abstracts listed at PubMed, therefore certain information is left blank.

Table 13. Overview of clinical trials with soluble fiber in the period 2000 – 2007.

| Author, Year | N | Amount of Fiber (g) | Study Duration | Δ TC (%) | Δ LDL (%) | Δ HDL (%) | Δ TG (%) |
|---|---|---|---|---|---|---|---|
| Theuwissen, 2007[41] | 40 | 5 | 4 wks | | -5% | 0 | |
| Poppitt, 2007[42] | 19 | 6.31 | | – | – | – | |
| Pittaway, 2006[43] | 47 | | 5 wks | -3.90% | -4.60% | | |
| Wood, 2007[44] | 15 | | 12 wks | | -14.1 | +10% | -34% |
| Roberts, 2007[45] | 19 | | 2 wks | – | – | | – |
| Grunberger, 2007[46] | 66 | | 3 mos | -8.20% | | | |
| Shrestha, 2006[47] | 33 | 7.68 | 4 wks | – | – | | |
| Roberts, 2006[48] | 22 | | 3 wks | – | – | + | |
| Naumann, 2006[49] | 47 | | 5 wks | -4.80% | -7.70% | | |
| Wood, 2006[50] | 29 | 3 | 12 wks | | -8.90% | +12% | -38.60% |
| Ziai, 2005[51] | 49 | 10 | 8 wks | – | – | + | |
| Martino, 2005[52] | 40 | | 8 wks | – | – | | |
| Karmally, 2005[53] | 152 | 3 | 11 wks | -4.50% | -5.30% | | |
| Robitaille, 2005[54] | 34 | 28 | 4 wks | – | | +11.20% | |
| Moreyra, 2005[55] | 68 | 15 | 8 wks | | -63mg/dL | 0 | 0 |
| Jenkins, 2005[56] | 34 | | 4 wks | | -29.60% | | |
| Behall, 2004[57] | 25 | 6 | 5 wks | – | | 0 | 0 |
| Hall, 2005[58] | 38 | 17 – 30 | 4 wks | -4.50% | -5.40% | 0 | 0 |
| Hoie, 2005[59] | 121 | | 8 wks | -8% | -9.70% | 0 | 0 |
| Trinidad, 2004[60] | 21 | | 8 wks | -10.80% | -9.20% | | – |
| Aller, 2004[61] | 53 | 30.5 | 3 mos | | -12.80% | 0 | 0 |
| Behall, 2004[62] | 18 | 9.4 | 5 wks | -20% | -24% | +18% | -16% |
| Jenkins, 2003[63] | 13 | 8.3 | 4 wks | | -35% | 0 | 0 |
| Zunft, 2003[64] | 29 | 15 | 6 wks | | -10.50% | | -11.30% |
| Jenkins, 2003[65] | 16 | 9.8 | 4 wks | | -28.60% | | |
| Beauchesne-Rondeau, 2003[66] | 3 groups | 29 | 26 days | -7% | -7% | + | – |
| Sprecher, 2002[67] | 119 | | 8 wks | | -7.10% | 0 | 0 |
| Davy, 2002[68] | 36 | 14 | 12 wks | -2.50% | -2.50% | 0 | -6.60% |
| Tonstad, 2002[69] | 130 | 10 – 16 | 24 wks | | – | | |
| Kris-Etherton, 2002[70] | 150 | | 7 wks | -5.60% | -7.10% | + | -14.20% |
| Jenkins, 2002[71] | 68 | 8 | 4 wks | -2.1 | – | 2.9 | |
| Saltzman, 2001[72] | 43 | 45 | 8 wks | – | – | | |
| Jenkins, 2001[73] | 10 | 55 | 2 wks | | -33 | | |
| Hermansen, 2001[74] | 20 | 20 | 6 wks | -8 | -10 | -22 | 0 |
| Vajifdar, 2000[75] | 114 | 10 | 6 mos | 0 | – | + | 0 |
| Anderson, 2000[76] | | 5.1 | 26 wks | -4.7 | -6.7 | | |
| Chandalia, 2000[77] | 13 | 50 | 6 wks | -6.7 | -12.5 | | -10.2 |
| Morgan, 2000[78] | 18 | 68 | 8 wks | - | - | | |
| Jenkins, 2000[79] | 20 | | 8 wks | | -8.5 | 6.4 | |

"0" indicates no significant change; "–" indicates a significant but unspecified decrease; "+" indicates a significant but unspecified increase.

## Mechanism 2: Inhibition of Absorption of Cholesterol from the Diet

The second mechanism by which Bios Life lowers cholesterol is by preventing the absorption of cholesterol from food in the digestive tract. Since this is the only entry point for cholesterol from sources outside the body, it has been studied widely by many research institutes and food manufacturers alike. The key components that take care of this mechanism are phytosterols from vegetable oils.

Phytosterols are biomolecules present in plants. The first part of the name originates from the Greek word "phuton" which means plant. The second part of the name, "sterol," refers to a chemical structure that is defined as a cyclopentanophenantrine ring structure of cholesterol plus an alcohol group. Because of this structural part of phytosterols, they are also known as cholesterol from plants.

Phytosterols have different functions in plants, but for us the most important aspect is that these molecules have a similar chemical structure to that of animal fat cholesterol. They are found mainly in vegetable oils, since like cholesterol, they are fat-soluble.

There are two main types of phytosterols: sterols and stanols. These two types differ only in the presence of a double carbon-carbon bond in the molecular structure. Some of the most common phytosterols are sitosterol, campesterol, and stigmasterol. The phytosterol content of some common foods is listed in Table 14.

Table 14. Phytosterol content in food. Data from reference [84].

| Food | Phytosterols (mg/100 g edible portion) |
|---|---|
| Corn oil | 952 |
| Sunflower oil | 725 |
| Safflower oil | 444 |
| Soybean oil | 221 |
| Olive oil | 176 |
| Almonds | 143 |
| Beans | 76 |
| Corn | 70 |
| Wheat | 69 |
| Palm oil | 49 |
| Lettuce | 38 |
| Banana | 16 |
| Apple | 12 |
| Tomato | 7 |

It was discovered several decades ago that when phytosterols from soy beans were added to the diet of chicks, the level of cholesterol in the blood was reduced [85]. Since then, many studies have been performed to find out the mechanism by which phytosterols lower cholesterol. This mechanism is most likely inhibition of cholesterol absorption in the intestinal tract. There are two sources of cholesterol in the digestive tract: diet and bile acids. The diet is responsible for roughly 300 mg per day of cholesterol, whereas biliary cholesterol adds about 1,000 mg per day to the intestinal mix [86]. Studies in people using test meals show that about 55 percent of cholesterol is absorbed from the intestinal tract into the bloodstream [87].

Cholesterol is poorly soluble in water [88, 89]. The transport of cholesterol in the digestive tract toward the small intestine, where actual absorption takes place, is therefore mediated by micelles [90, 91]. Micelles are spherical shapes of fatty acids and/or phospholipids that are hydrophilic (water-liking) on the outside, and lipophilic (fat-liking) on the inside. In this way, the micelles can travel through the water phase of the intestinal contents and transport fat-soluble molecules, such as cholesterol, in the inside of the sphere.

Micelles containing cholesterol are then transported down the intestinal tract until they reach the brush border membranes, where the cholesterol can be absorbed into the mucosa. The brush border membrane is a collective term for the surfaces of the epithelial cells lining the cavity of the small intestine, which is studded with long, flexible hair-like extremities known as microvilli. These microvilli enlarge the absorptive surface of the cells.

Once the cholesterol has reached the brush border membrane, it is absorbed by the mucosa. There are several theories describing the exact

mechanism by which this happens. One long-standing hypothesis suggests that cholesterol absorption is an energy-independent passive diffusion process in which micellar cholesterol is in equilibrium with free cholesterol in solution. This theory would mean that there is no active mechanism involved in cholesterol transport into the intestinal cells, but that the cholesterol simply travels through the cell membranes because there is a concentration gradient present [92, 93]. The uptake of cholesterol in this mechanism is regulated by ATP (adenosine triphosphate)-binding cassette transporters that return cholesterol back into the intestinal tract once too much cholesterol has been absorbed, thereby maintaining a balance in absorption and return of cholesterol [94].

The second theory for cholesterol uptake is through cholesterol transport proteins. These proteins serve as cholesterol receptors and actively shuttle cholesterol inside the intestinal cells. They are selective for cholesterol because the proteins have a domain (part of the protein structure) that recognizes the molecular structure of cholesterol [95-97]. After the cholesterol is absorbed by the intestinal cells it is converted into lipoproteins, such as HDL and LDL, before being released into blood circulation.

How do phytosterols lower cholesterol in the blood? They reduce the absorption of animal cholesterol in the digestive tract by 30 to 50 percent when the phytosterols are administered at maximum dosages [98-100]. The similar organic structure of phytosterols to cholesterol is the key to this effect. Phytosterols can take the place of cholesterol in the above-described mechanisms because they are able to fool the body and make it think it is dealing with bad animal fat cholesterol.

Phytosterols compete with cholesterol in incorporation in the micelles that transport cholesterol down the intestinal tract. The micelles are more likely to include phytosterols than cholesterol in the spheres [101-103] because this choice costs less energy [104]. If that is happening, the real cholesterol is left out and will not reach the brush border membrane where the actual absorption is taking place.

The second site for phytosterol interference is the transport proteins. The receptor part of the protein recognizing the molecular structure of cholesterol will also interact with phytosterols. The proteins, however, cannot absorb these phytosterols, and are therefore occupied dealing with phytosterols when the real cholesterol from food passes by. As such, the total absorption of cholesterol is lower.

Figure 26. The organic chemical structure of beta sitosterol and cholesterol.



beta sitosterol                    cholesterol
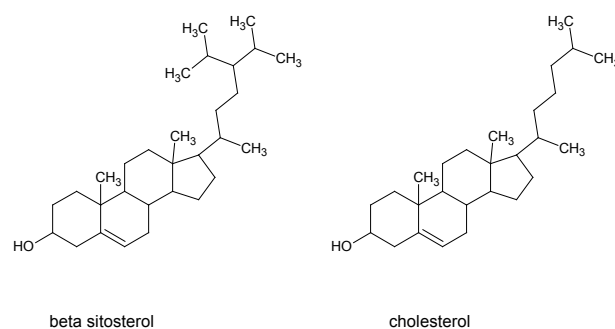
These mechanisms make dietary inhibition an interesting target for cholesterol lowering. In earlier times, this may well have been one of the reasons why our ancestors had no problem with high cholesterol. It is very likely that they consumed large amounts of phytosterols because their diet was mostly plant based [105].

Since the discovery of the cholesterol-lowering effects of phytosterols, many interventional studies have been performed to investigate to what extent they can lower cholesterol. Table 15 describes the trials that have been performed using phytosterols in monotherapy to lower cholesterol in the period 2000 to 2007. The search terms in PubMed were a combination of "phytosterols" and "cholesterol" with the limit set on "clinical trials in humans." This table of results does not discuss the difference between sterols and stanols and combines both types of sterols under the same group. Also, several studies evaluated the effect of multiple dosage levels of phytosterols on serum lipids. Of those studies only one representative dose was listed. Not all information was obtainable from the abstracts listed at PubMed, therefore certain information is left blank.

Table 15. Overview of trials with phytosterols to reduce cholesterol published in the period 2000 to 2007.

| Author, Year | n | Amount of Phyto-sterols (g) | Study Duration | Δ TC (%) | Δ LDL (%) |
|---|---|---|---|---|---|
| Jakulj, 2005[102] | 40 | 2 | 4 wks | | -4.7 |
| McPherson, 2005[103] | 52 | 1.26 | 6 wks | | -10.4 |
| Lau, 2005[104] | 14 | 1.8 | 3 wks | | -15.1 |
| Lau, 2005[104] | 15 | 1.8 | 3 wks | | -26.8 |
| Varady, 2004[105] | 21 | | 8 wks | -8.2 | |
| Noakes, 2005[106] | 39 | 2.0 | 3 wks | -7 | -9 |
| Amundsen, 2004[107] | 37 | 1.2 | 26 wks | -9.1 | -11.4 |
| Amundsen, 2004[107] | 20 | 1.5 | 26 wks | -9.1 | -11.0 |
| Thomson, 2004 [108] | 71 | 1.2 | 12 wks | | -7.1 |
| Thomson, 2004 [108] | 71 | 1.6 | 12 wks | | -9.6 |
| Clifton, 2004 [109] | 58 | 1.6 | 3 wks | -8.7 | -15.9 |
| Clifton, 2004 [109] | 58 | 1.6 | 3 wks | -5.6 | -8.6 |
| Clifton, 2004 [109] | 58 | 1.6 | 3 wks | | -6.5 |
| Clifton, 2004 [109] | 58 | 1.6 | 3 wks | | -5.4 |
| Devaraj, 2004[110] | 72 | 2.0 | 8 wks | -7.2 | -12.4 |
| Kozlowska, 2003[111] | 42 | | | | -11.0 |
| Quilez, 2003[112] | 28 | 3.2 | 8 wks | -8.9 | -14.7 |
| Seki, 2004[113] | 60 | 0.45 | 12 wks | -10.3 | |
| De Jong, 2003[114] | 41 | 2.3 | 4 wks | -11.0 | -14.0 |
| Hendriks, 2003[115] | 185 | 1.6 | 1 year | -4.0 | -6.0 |
| Ketomaki, 2003[116] | 23 | | 5 wks | -9.0 | -12.0 |
| Homma, 2003[117] | 34 | 2 | 4 wks | -6.5 | -9.6 |
| Homma, 2003[117] | 36 | 3 | 4 wks | -5.5 | -7.3 |
| Lee, 2003 [118] | 85 | 1.6 | 4 wks | -5.2 | -6.8 |
| Cleghorn, 2003[119] | 50 | 2.0 | 4 wks | -8.9 | -12.3 |
| Tammi, 2002[120] | 45 boys | | 3 mos | -6.0 | -9.0 |
| Tammi, 2002[120] | 36 | | 3 mos | -4.0 | -6.0 |
| Vanstone, 2002[121] | 15 | 1.8 | | -7.8 | -11.3 |
| De Graaf, 2002[122] | 70 | 1.8 | 4 wks | -6.4 | -10.3 |
| Geelen, 2002[123] | 31 | 3.2 | 3 wks | -7.4 | -12.2 |
| Lottenberg, 2002[124] | 60 | 1.68 | 4 wks | -10.0 | -12.0 |
| Amundsen, 2002[125] | 38 | 1.6 | 8 wks | -7.4 | -10.2 |
| Temme, 2002[126] | 42 | 1.6 | 4 wks | -7.0 | -10.0 |
| Judd, 2002[127] | 53 | 3.6 | wks | | -9.7 |
| Mussner, 2002[128] | 63 | 1.82 | 3 wks | -3.4 | -5.4 |
| Nestel, 2001[129] | 22 | 2.4 | 4 wks | | -13.6 |
| Mensink, 2002[130] | 60 | 3 | 3 wks | | -13.7 |
| Christiansen, 2001[131] | 155 | 1.5 | 6 mos | -7.5 | -11.6 |
| Maki, 2001[132] | 40 | 2.2 | 5 wks | -6.6 | -8.1 |
| Hallikainen, 2000[133] | 34 | 2.04 | 4 wks | -9.2 | -12.7 |
| Hallikainen, 2000[134] | 22 | 3.0 | 4 wks | -11.3 | -10.4 |
| Theuwissen, 2007[41] | 40 | 5 | 4 wks | | -9.60 |
| Varady, 2007[135] | 84 | | 8 wks | -7.70 | -18 |
| Polagruto, 2006[136] | 67 | 3 | 6 wks | | -6 |
| Devaraj, 2006[137] | 72 | 2 | 8 wks | -5 | -9.40 |
| Castro Cabezas, 2006[138] | 20 | | 3 days | | -15.60 |

| Shrestha, 2006[47] | 33 | 2.6 | 8 wks | | – |
|---|---|---|---|---|---|
| Goncalves, 2006[139] | 34 | 2 | 15 days | -9.20 | -12.20 |
| Jauhiainen, 2006[140] | 67 | 2 | 5 wks | -5.80 | -10.30 |
| Jakulj, 2006[141] | 42 | 2 | 4 wks | -7.50 | -9.20 |
| AbuMweiss, 2006[142] | 30 | 1.8 | 29 days | 0 | 0 |
| Alhassan, 2006[143] | 26 | 3 | 9 wks | -10 | -13 |
| Naumann, 2006[49] | 47 | | 5 wks | -4.80 | -7.70 |
| Saito, 2006[144] | | 0.5 | 4 wks | – | – |
| Lukaczer, 2006[145] | 59 | 4 | 12 wks | -15.8 | -14.80 |
| Goldberg, 2006[146] | 26 | 1.8 | 9 wks | – | – |
| Korpela, 2006[147] | 164 | 2 | 6 wks | -6.50 | -10.40 |
| Yoshida, 2006[148] | 34 | 1.8 | 3 wks | – | – |
| Hallikainen, 2006[149] | 76 | 1.9 | 10 wks | | - 6-9 |

"0" indicates no significant change; "–" indicates a significant but unspecified decrease; "+" indicates a significant but unspecified increase.

The results listed in Table 15 provide a clear case for the cholesterol-lowering effects of phytosterols. Although various dosages have been studied over various study periods, a fair conclusion is that phytosterols lower total cholesterol and LDL cholesterol by about 5 to 12 percent over a period of several weeks. These consistent positive results of phytosterols have led to the conclusion at the Food and Drug Administration (FDA) that products containing at least 1.3 grams of phytosterols per daily dose may carry a qualified health claim. Considering the fact that the FDA currently allows only a handful of those qualified health claims to be made, the case of phytosterols in cholesterol lowering is considered strong.

Bios Life features phytosterols that are derived from different sources; mainly sunflower and soybean oil, two very normal components of the typical diet.

## Mechanism 3: Inhibition of the Liver Synthesis of Cholesterol

Cholesterol in the blood has different sources. The most significant source of cholesterol in the body is the body's own production. In fact, about 75 percent of the cholesterol in the body comes from itself! The liver is the organ that biochemically synthesizes cholesterol in a multi-step process from nutrients in food. A critical step in the synthesis of cholesterol is the conversion of HMG CoA (3-hyroxy-3-methylglutaryl CoA), one of the intermediary products on the way to cholesterol, to mevalonate.

This step is mediated by an enzyme called HMG CoA reductase (see Chapter 3.2.1). Enzymes like this one typically work using the so-called key-lock principle. They have a cavity in the structure of the enzyme in which the substrate (the molecule the enzyme converts) fits. Once a fit is realized, the enzyme converts the substrate to the target molecule. In this case, HMG CoA is the substrate and mevalonate is the target molecule. This mechanism allows enzymes to be inhibited. Typically this is accomplished by administering a non-natural molecule that has a similar structure to the substrate. This molecule will somehow fit into the cavity of the enzyme, thereby preventing the enzyme from doing its usual normal conversion function. Statin medication is an example of this kind of inhibitor (see Chapter 3.2.1).

The working mechanism of statin medication is described in detail in Chapter 3.2.1. The third working mechanism of Bios Life works in a similar fashion to this principle. Bios Life includes a natural alternative to synthetic HMG CoA inhibition. The phytonutrient responsible for this action is policosanol. The term policosanol refers to a mixture of certain alcohols from sugar cane. Policosanol has been heavily researched in Cuba in several human populations for its cholesterol-lowering properties. In addition to improving serum lipids, policosanol reduces LDL oxidation, decreases platelet aggregation, decreases smooth muscle proliferation, and improves symptoms of cardiovascular disease. Side effects are virtually

non-existent. The mixture can vary based on the source, but typically it is comprised predominantly of octacosanol [154]. The mechanism by which policosanol inhibits cholesterol synthesis is similar to that of statin medication: it also inhibits HMG CoA reductase [155], but likely in a slightly different way [156, 157].

Many trials have been performed proving the efficacy of policosanol in reducing cholesterol in humans. Table 16 provides an overview of published clinical trials with policosanol as monotherapy up until May 2007. The search terms in PubMed were "policosanol" with "clinical trial in humans" as limit. Some studies looked at different dosing levels in the same study design, but the table only lists the most relevant dose used in the study. Not all information was obtainable from the abstracts listed at PubMed, therefore certain information is left blank.

Figure 28. Structure of octacosanol, the predominant alcohol in policosanol.
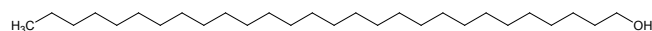


One may think that since policosanol uses the same mechanism to influence cholesterol synthesis as statin medication does, the ingredient will have the same side effect profile as statin molecules. This is not true. All studies that were performed with policosanol have shown that the liver parameters are not being elevated due to use of this component. This is likely due to the fact that the policosanol molecule, unlike statins, is not broken down by the liver to be removed from the body. The toxicity of statins is not due to the liver inhibition mechanism per se, but to the metabolites that are being created by the destruction process in the liver.

Table 16. Overview of studies with policosanol in reducing cholesterol in the period up to May 2007.

| Author, Year | n | Amount of Policosanol (mg) | Study Duration | Δ Total Cholesterol (%) |
|---|---|---|---|---|
| Castano 2005, [154] | | 5 | 8 wks | -13.5 |
| Castano 2005, [154] | | 10 | 8 wks | -16.0 |
| Mas, 2004 [155] | 129 | 5 | 3 yrs | -20.1 |
| Mas, 2004 [156] | 239 | 5 | 2 yrs | -21.9 |
| Castano, 2002[157] | 36 | 10 | 8 wks | -21.1 |
| Castano, 2003 [158] | 75 | 10 | 8 wks | -16.4 |
| Castano, 2002 [159] | 589 | 5 | 12 mos | -15.4 |
| Castano, 2001[160] | 29 | 20 | 6 mos | -15.6 |
| Castano, 2001[160] | 30 | 40 | 6 mos | -17.3 |
| Mirkin, 2001 [161] | 56 | 5 | 8 wks | -12.9 |
| Castano, 2001 [162] | 179 | 5 | 12 wks | -12.8 |
| Crespo, 1999 [163] | 53 | 10 | 12 wks | -14.2 |
| Castano, 1999 [164] | | 10 | 8 wks | -13.9 |
| Castano, 2000 [165] | 244 | 5 | 12 wks | -12.6 |
| Alcocer, 1999 [166] | 63 | 10 | 8 wks | -15.8 |
| Mas, 1999 [167] | 437 | 5 | 12 wks | -13.0 |
| Batista, 1996 [168] | 23 | 2 | 14 mos | -14.8 |
| Pons, 1994 [169] | 22 | 5 | 8 wks | -8.0 |
| Kassis, 2006[170] | 21 | 10 | 28 days | 0 |
| Cubeddu, 2006[171] | 99 | 20 | 12 wks | 0 |
| Berthold, 2006[172] | 143 | 80 | 6 wks, 12 wks | 0 |
| Greyling, 2006[173] | | 20 | 12 wks | 0 |
| Dulin, 2006[174] | 40 | 20 | 8 wks | 0 |

"0" indicates no significant change.

Bios Life features the policosanol that has been used in the studies that have shown benefit for cholesterol lowering. Some inferior products on the market today are using the cheaper rice bran wax source, but several studies have shown that this form of policosanol is not as effective or even completely lacks efficacy for cholesterol reduction.

## Mechanism 4: Enhancing the Conversion of Cholesterol into Bile Acids

Cholesterol serves many important functions in the body. As explained in Chapter 2.3.1, cholesterol is the building block for bile acids. As for all biomolecules, the body uses an array of enzymes to create bile acids from cholesterol. The rate-limiting step in this process is performed by an enzyme called $7\alpha$-hydroxylase. This enzyme converts cholesterol into $7\alpha$-hydroxycholesterol, which is an intermediairy molecule on the way to cholic acid, one of the bile acids. The research network of Unicity International has discovered a novel activator of this enzyme. An extract of Chrysanthemum morifolium has been shown to activate $7\alpha$-hydroxylase and thereby promote the removal of cholesterol by its conversion to $7\alpha$-hydroxycholesterol. By doing so, more bile acids are synthesized and excreted in the digestive tract.

This mechanism of Bios Life works in collaboration with the first mechanism that removes bile acids from the gut. Chrysanthemum increases the amount of bile acids made, and soluble fiber increases the removal of the bile acids from the body. This synergistic mechanism promotes cholesterol lowering even further. This discovery was made by Numico Research B.V. out of Wageningen in the Netherlands. They have proven this effect in in-vitro studies, but up to now, there have been no human clinical data that show this biological effect. Numico was able to patent this discovery in U.S. patent 6,933,291. Unicity has the sole rights to this patent.

Some readers may recall that the prerequisites for the development of Bios Life stated that the product had to contain only ingredients that were part of common diets. You may have never considered eating a chrysanthemum, but for many people this flower is consumed daily in the form of tea. Mainly in Asia, chrysanthemum tea is believed to have beneficial effects for immune strength and eye health, and is therefore a very common health tea.

Figure 29. Synthesis of cholic acid from cholesterol.
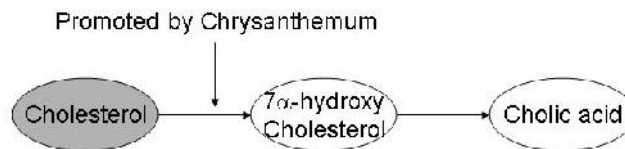


This fourth mechanism completes the unique cholesterol-lowering technology that is featured within the Bios Life formula. Of course, it was not Unicity that discovered the four biological mechanisms that can be utilized to optimize cholesterol, but it was Unicity's research network that realized that these four described mechanisms would work together in a highly synergistic way.

Today in the marketplace there are many products that claim to lower cholesterol, but typically they do this using one individual mechanism. This is true for most pharmaceuticals as well as for most nutritional products. The problem with mono-therapy approach is that typically the effect a dietary supplement has on one mechanism is not strong enough to make the product's effects on cholesterol and other lipids clinically relevant so that it can be used by doctors and patients. Unicity is the only company that has made a product that lowers cholesterol through a unique collection of four mechanisms. Because of the patents that protect this invention, there is no other product that may legally use this technology, not even should they use other ingredients in the product.

Also, unlike potential competitors on the market, Bios Life has many more beneficial effects, ranging from improved glucose control, increased nutrient utilization, immune stimulation, and craving control, as discussed in the next chapters.

# References

1. Anderson, J.W., L.D. Allgood, J. Turner, P.R. Oeltgen, and B.P. Daggy (1999) Effects of psyllium on glucose and serum lipid responses in men with type 2 diabetes and hypercholesterolemia. Am J Clin Nutr 70, 466-73

2. Anderson, J.W., M.H. Davidson, L. Blonde, W.V. Brown, W.J. Howard, H. Ginsberg, L.D. Allgood, and K.W. Weingand (2000) Long-term cholesterol-lowering effects of psyllium as an adjunct to diet therapy in the treatment of hypercholesterolemia. Am J Clin Nutr 71, 1433-8

3. Chandalia, M., A. Garg, D. Lutjohann, K. von Bergmann, S.M. Grundy, and L.J. Brinkley (2000) Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. N Engl J Med 342, 1392-8

4. Eriksson, J., J. Lindstrom, T. Valle, S. Aunola, H. Hamalainen, P. Ilanne-Parikka, S. Keinanen-Kiukaanniemi, M. Laakso, M. Lauhkonen, P. Lehto, A. Lehtonen, A. Louheranta, M. Mannelin, V. Martikkala, M. Rastas, J. Sundvall, A. Turpeinen, T. Viljanen, M. Uusitupa, and J. Tuomilehto (1999) Prevention of Type II diabetes in subjects with impaired glucose tolerance: the Diabetes Prevention Study (DPS) in Finland. Study design and 1-year interim report on the feasibility of the lifestyle intervention programme. Diabetologia 42, 793-801

5. Jenkins, D.J., C.W. Kendall, V. Vuksan, E. Vidgen, T. Parker, D. Faulkner, C.C. Mehling, M. Garsetti, G. Testolin, S.C. Cunnane, M.A. Ryan, and P.N. Corey (2002) Soluble fiber intake at a dose approved by the US Food and Drug Administration for a claim of health benefits: serum lipid risk factors for cardiovascular disease assessed in a randomized controlled crossover trial. Am J Clin Nutr 75, 834-9

6. Knopp, R.H., H.R. Superko, M. Davidson, W. Insull, C.A. Dujovne, P.O. Kwiterovich, J.H. Zavoral, K. Graham, R.R. O'Connor, and D.A. Edelman (1999) Long-term blood cholesterol-lowering effects of a dietary fiber supplement. Am J Prev Med 17, 18-23

7. Neal, B., S. MacMahon, T. Ohkubo, A. Tonkin, and D. Wilcken (2002) Dose-dependent effects of folic acid on plasma homocysteine in a randomized trial conducted among 723 individuals with coronary heart disease. Eur Heart J 23, 1509-15

8. Sprecher, D.L. and G.L. Pearce (2002) Fiber-multivitamin combination therapy: a beneficial influence on low-density lipoprotein and homocysteine. Metabolism 51, 1166-70

9. Tai, E.S., A.C. Fok, R. Chu, and C.E. Tan (1999) A study to assess the effect of dietary supplementation with soluble fibre (Minolest) on lipid levels in normal subjects with hypercholesterolaemia. Ann Acad Med Singapore 28, 209-13

10. Tuomilehto, J., J. Lindstrom, J.G. Eriksson, T.T. Valle, H. Hamalainen, P. Ilanne-Parikka, S. Keinanen-Kiukaanniemi, M. Laakso, A. Louheranta, M. Rastas, V. Salminen, and M. Uusitupa (2001) Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 344, 1343-50

11. Vajifdar, B.U., V.S. Goyal, Y.Y. Lokhandwala, S.R. Mhamunkar, S.P. Mahadik, A.K. Gawad, S.A. Halankar, and H.L. Kulkarni (2000) Is dietary fiber beneficial in chronic ischemic heart disease? J Assoc Physicians India 48, 871-6

12. Weirauch, J. and G. JM (1978) Sterol content of foods of plant origin. J. Am. Diet. Assoc. 73, 39-47

13. Peterson, D.W. (1951) Effect of soybean sterols in the diet on plasma and liver cholesterol in chicks. Proc Soc Exp Biol Med 78, 143-7

14. Grundy, S.M. (1983) Absorption and metabolism of dietary cholesterol. Annu Rev Nutr 3, 71-96

15. Bosner, M.S., L.G. Lange, W.F. Stenson, and R.E. Ostlund, Jr. (1999) Percent cholesterol absorption in normal women and men quantified with dual stable isotopic tracers and negative ion mass spectrometry. J Lipid Res 40, 302-8

16. Swell, L., E.C. Trout, Jr., J.R. Hopper, H. Field, Jr., and C.R. Treadwell (1958) Specific function of bile salts in cholesterol absorption. Proc Soc Exp Biol Med 98, 174-6

17. Holt, P.R., B.M. Fairchild, and J. Weiss (1986) A liquid crystalline phase in human intestinal contents during fat digestion. Lipids 21, 444-6

18. Yao, L., J.E. Heubi, D.D. Buckley, H. Fierra, K.D. Setchell, N.A. Granholm, P. Tso, D.Y. Hui, and L.A. Woollett (2002) Separation of micelles and vesicles within lumenal aspirates from healthy humans: solubilization of cholesterol after a meal. J Lipid Res 43, 654-60

19. Hernell, O., J.E. Staggers, and M.C. Carey (1990) Physical-chemical behavior of dietary and biliary lipids during intestinal digestion and absorption. 2. Phase analysis and aggregation states of luminal lipids during duodenal fat digestion in healthy adult human beings. Biochemistry 29, 2041-56

20. Chijiiwa, K. and W.G. Linscheer (1987) Distribution and monomer activity of cholesterol in micellar bile salt: effect of cholesterol level. Am J Physiol 252, G309-14

21. Westergaard, H. and J.M. Dietschy (1976) The mechanism whereby bile acid micelles increase the rate of fatty acid and cholesterol uptake into the intestinal mucosal cell. J Clin Invest 58, 97-108

22. Repa, J.J., K.E. Berge, C. Pomajzl, J.A. Richardson, H. Hobbs, and D.J. Mangelsdorf (2002) Regulation of ATP-binding cassette sterol transporters ABCG5 and ABCG8 by the liver X receptors alpha and beta. J Biol Chem 277, 18793-800

23. Thurnhofer, H. and H. Hauser (1990) Uptake of cholesterol by small intestinal brush border membrane is protein-mediated. Biochemistry 29, 2142-8

24. Altmann, S.W., H.R. Davis, Jr., L.J. Zhu, X. Yao, L.M. Hoos, G. Tetzloff, S.P. Iyer, M. Maguire, A. Golovko, M. Zeng, L. Wang, N. Murgolo, and M.P. Graziano (2004) Niemann-Pick C1 Like 1 protein is critical for intestinal cholesterol absorption. Science 303, 1201-4

25. Davies, J.P., B. Levy, and Y.A. Ioannou (2000) Evidence for a Niemann-pick C (NPC) gene family: identification and characterization of NPC1L1. Genomics 65, 137-45

26. Lees, A.M., H.Y. Mok, R.S. Lees, M.A. McCluskey, and S.M. Grundy (1977) Plant sterols as cholesterol-lowering agents: clinical trials in patients with hypercholesterolemia and studies of sterol balance. Atherosclerosis 28, 325-38

27. Mattson, F.H., R.A. Volpenhein, and B.A. Erickson (1977)

Effect of plant sterol esters on the absorption of dietary cholesterol. J Nutr 107, 1139-46

28. Ostlund, R.E., Jr., C.A. Spilburg, and W.F. Stenson (1999) Sitostanol administered in lecithin micelles potently reduces cholesterol absorption in humans. Am J Clin Nutr 70, 826-31

29. Ikeda, I., Y. Tanabe, and M. Sugano (1989) Effects of sitosterol and sitostanol on micellar solubility of cholesterol. J Nutr Sci Vitaminol (Tokyo) 35, 361-9

30. Ikeda, I., K. Tanaka, M. Sugano, G.V. Vahouny, and L.L. Gallo (1988) Discrimination between cholesterol and sitosterol for absorption in rats. J Lipid Res 29, 1583-91

31. Ikeda, I., K. Tanaka, M. Sugano, G.V. Vahouny, and L.L. Gallo (1988) Inhibition of cholesterol absorption in rats by plant sterols. J Lipid Res 29, 1573-82

32. Armstrong, M.J. and M.C. Carey (1987) Thermodynamic and molecular determinants of sterol solubilities in bile salt micelles. J Lipid Res 28, 1144-55

33. Jenkins, D.J., C.W. Kendall, A. Marchie, A.L. Jenkins, P.W. Connelly, P.J. Jones, and V. Vuksan (2003) The Garden of Eden--plant based diets, the genetic drive to conserve cholesterol and its implications for heart disease in the 21st century. Comp Biochem Physiol A Mol Integr Physiol 136, 141-51

34. Jakulj, L., M.D. Trip, T. Sudhop, K. von Bergmann, J.J. Kastelein, and M.N. Vissers (2005) Inhibition of cholesterol absorption by the combination of dietary plant sterols and ezetimibe: effects on plasma lipid levels. J Lipid Res 46, 2692-8

35. O'Neill, F.H., T.A. Sanders, and G.R. Thompson (2005) Comparison of efficacy of plant stanol ester and sterol ester: short-term and longer-term studies. Am J Cardiol 96, 29D-36D

36. McPherson, T.B., R.E. Ostlund, A.C. Goldberg, J.H. Bateman, L. Schimmoeller, and C.A. Spilburg (2005) Phytostanol tablets reduce human LDL-cholesterol. J Pharm Pharmacol 57, 889-96

37. Lau, V.W., M. Journoud, and P.J. Jones (2005) Plant sterols are efficacious in lowering plasma LDL and non-HDL cholesterol in hypercholesterolemic type 2 diabetic and nondiabetic persons. Am J Clin Nutr 81, 1351-8

38. Varady, K.A., N. Ebine, C.A. Vanstone, W.E. Parsons, and P.J. Jones (2004) Plant sterols and endurance training combine to favorably alter plasma lipid profiles in previously sedentary hypercholesterolemic adults after 8 wk. Am J Clin Nutr 80, 1159-66

39. Noakes, M., P.M. Clifton, A.M. Doornbos, and E.A. Trautwein (2005) Plant sterol ester-enriched milk and yoghurt effectively reduce serum cholesterol in modestly hypercholesterolemic subjects. Eur J Nutr 44, 214-22

40. Amundsen, A.L., F. Ntanios, N. Put, and L. Ose (2004) Long-term compliance and changes in plasma lipids, plant sterols and carotenoids in children and parents with FH consuming plant sterol ester-enriched spread. Eur J Clin Nutr 58, 1612-20

41. Thomsen, A.B., H.B. Hansen, C. Christiansen, H. Green, and A. Berger (2004) Effect of free plant sterols in low-fat milk on serum lipid profile in hypercholesterolemic subjects. Eur J Clin Nutr 58, 860-70

42. Clifton, P.M., M. Noakes, D. Sullivan, N. Erichsen, D. Ross, G. Annison, A. Fassoulakis, M. Cehun, and P. Nestel (2004) Cholesterol-lowering effects of plant sterol esters differ in milk, yoghurt, bread and cereal. Eur J Clin Nutr 58, 503-9

43. Devaraj, S., I. Jialal, and S. Vega-Lopez (2004) Plant sterol-fortified orange juice effectively lowers cholesterol levels in mildly hypercholesterolemic healthy individuals. Arterioscler Thromb Vasc Biol 24, e25-8

44. Kozlowska-Wojciechowska, M., M. Jastrzebska, M. Naruszewicz, and A. Foltynska (2003) Impact of margarine enriched with plant sterols on blood lipids, platelet function, and fibrinogen level in young men. Metabolism 52, 1373-8

45. Quilez, J., M. Rafecas, G. Brufau, P. Garcia-Lorda, I. Megias, M. Bullo, J.A. Ruiz, and J. Salas-Salvado (2003) Bakery products enriched with phytosterol esters, alpha-tocopherol and beta-carotene decrease plasma LDL-cholesterol and maintain plasma beta-carotene concentrations in normocholesterolemic men and women. J Nutr 133, 3103-9

46. Seki, S., I. Hidaka, K. Kojima, H. Yoshino, T. Aoyama, M. Okazaki, and K. Kondo (2003) Effects of phytosterol ester-enriched vegetable oil on plasma lipoproteins in healthy men. Asia Pac J Clin Nutr 12, 282-91

47. de Jongh, S., M.N. Vissers, P. Rol, H.D. Bakker, J.J. Kastelein, and E.S. Stroes (2003) Plant sterols lower LDL cholesterol without improving endothelial function in prepubertal children with familial hypercholesterolaemia. J Inherit Metab Dis 26, 343-51

48. Hendriks, H.F., E.J. Brink, G.W. Meijer, H.M. Princen, and F.Y. Ntanios (2003) Safety of long-term consumption of plant sterol esters-enriched spread. Eur J Clin Nutr 57, 681-92

49. Ketomaki, A.M., H. Gylling, M. Antikainen, M.A. Siimes, and T.A. Miettinen (2003) Red cell and plasma plant sterols are related during consumption of plant stanol and sterol ester spreads in children with hypercholesterolemia. J Pediatr 142, 524-31

50. Homma, Y., I. Ikeda, T. Ishikawa, M. Tateno, M. Sugano, and H. Nakamura (2003) Decrease in plasma low-density lipoprotein cholesterol, apolipoprotein B, cholesteryl ester transfer protein, and oxidized low-density lipoprotein by plant stanol ester-containing spread: a randomized, placebo-controlled trial. Nutrition 19, 369-74

51. Lee, Y.M., B. Haastert, W. Scherbaum, and H. Hauner (2003) A phytosterol-enriched spread improves the lipid profile of subjects with type 2 diabetes mellitus--a randomized controlled trial under free-living conditions. Eur J Nutr 42, 111-7

52. Cleghorn, C.L., C.M. Skeaff, J. Mann, and A. Chisholm (2003) Plant sterol-enriched spread enhances the cholesterol-lowering potential of a fat-reduced diet. Eur J Clin Nutr 57, 170-6

53. Tammi, A., T. Ronnemaa, T.A. Miettinen, H. Gylling, L. Rask-Nissila, J. Viikari, J. Tuominen, J. Marniemi, and O. Simell (2002) Effects of gender, apolipoprotein E phenotype and cholesterol-lowering by plant stanol esters in children: the STRIP study. Special Turku Coronary Risk Factor Intervention Project. Acta Paediatr 91, 1155-62

54. Vanstone, C.A., M. Raeini-Sarjaz, W.E. Parsons, and P.J. Jones (2002) Unesterified plant sterols and stanols lower LDL-cholesterol concentrations equivalently in hypercholesterolemic persons. Am J Clin Nutr 76, 1272-8

55. De Graaf, J., P.R. De Sauvage Nolting, M. Van Dam, E.M. Belsey, J.J. Kastelein, P. Haydn Pritchard, and A.F. Stalenhoef (2002) Consumption of tall oil-derived phytosterols in a chocolate matrix significantly decreases plasma total and low-density lipoprotein-cholesterol levels. Br J Nutr 88, 479-88

56. Geelen, A., P.L. Zock, J.H. de Vries, and M.B. Katan (2002) Apolipoprotein E polymorphism and serum lipid response to plant sterols in humans. Eur J Clin Invest 32, 738-42

57. Lottenberg, A.M., V.S. Nunes, E.R. Nakandakare, M. Neves, M. Bernik, J.E. Santos, and E.C. Quintao (2002) [Food phytosterol ester efficiency on the plasma lipid reduction in moderate hypercholesterolemic subjects]. Arq Bras Cardiol 79, 139-42

58. Amundsen, A.L., L. Ose, M.S. Nenseter, and F.Y. Ntanios (2002) Plant sterol ester-enriched spread lowers plasma total and LDL cholesterol in children with familial hypercholesterolemia. Am J Clin Nutr 76, 338-44

59. Temme, E.H., P.G. Van Hoydonck, E.G. Schouten, and H. Kesteloot (2002) Effects of a plant sterol-enriched spread on serum lipids and lipoproteins in mildly hypercholesterolaemic subjects. Acta Cardiol 57, 111-5

60. Judd, J.T., D.J. Baer, S.C. Chen, B.A. Clevidence, R.A. Muesing, M. Kramer, and G.W. Meijer (2002) Plant sterol esters lower plasma lipids and most carotenoids in mildly hypercholesterolemic adults. Lipids 37, 33-42

61. Mussner, M.J., K.G. Parhofer, K. Von Bergmann, P. Schwandt, U. Broedl, and C. Otto (2002) Effects of phytosterol ester-enriched margarine on plasma lipoproteins in mild to moderate hypercholesterolemia are related to basal cholesterol and fat intake. Metabolism 51, 189-94

62. Nestel, P., M. Cehun, S. Pomeroy, M. Abbey, and G. Weldon (2001) Cholesterol-lowering effects of plant sterol esters and non-esterified stanols in margarine, butter and low-fat foods. Eur J Clin Nutr 55, 1084-90

63. Mensink, R.P., S. Ebbing, M. Lindhout, J. Plat, and M.M. van Heugten (2002) Effects of plant stanol esters supplied in low-fat yoghurt on serum lipids and lipoproteins, non-cholesterol sterols and fat soluble antioxidant concentrations. Atherosclerosis 160, 205-13

64. Christiansen, L.I., P.L. Lahteenmaki, M.R. Mannelin, T.E. Seppanen-Laakso, R.V. Hiltunen, and J.K. Yliruusi (2001) Cholesterol-lowering effect of spreads enriched with microcrystalline plant sterols in hypercholesterolemic subjects. Eur J Nutr 40, 66-73

65. Maki, K.C., M.H. Davidson, D.M. Umporowicz, E.J. Schaefer, M.R. Dicklin, K.A. Ingram, S. Chen, J.R. McNamara, B.W. Gebhart, J.D. Ribaya-Mercado, G. Perrone, S.J. Robins, and W.C. Franke (2001) Lipid responses to plant-sterol-enriched reduced-fat spreads incorporated into a National Cholesterol Education Program Step I diet. Am J Clin Nutr 74, 33-43

66. Hallikainen, M.A., E.S. Sarkkinen, H. Gylling, A.T. Erkkila, and M.I. Uusitupa (2000) Comparison of the effects of plant sterol ester and plant stanol ester-enriched margarines in lowering serum cholesterol concentrations in hypercholesterolaemic subjects on a low-fat diet. Eur J Clin Nutr 54, 715-25

67. Plat, J., E.N. van Onselen, M.M. van Heugten, and R.P. Mensink (2000) Effects on serum lipids, lipoproteins and fat soluble antioxidant concentrations of consumption frequency of margarines and shortenings enriched with plant stanol esters. Eur J Clin Nutr 54, 671-7

68. Hallikainen, M.A., E.S. Sarkkinen, and M.I. Uusitupa (2000) Plant stanol esters affect serum cholesterol concentrations of hypercholesterolemic men and women in a dose-dependent manner. J Nutr 130, 767-76

69. Roberts, W.C. (1997) The rule of 5 and the rule of 7 in lipid-lowering by statin drugs. Am J Cardiol 80, 106-7

70. Irmak, S. and N.T. Dunford (2005) Policosanol contents and compositions of wheat varieties. J Agric Food Chem 53, 5583-6

71. McCarty, M.F. (2002) Policosanol safely down-regulates HMG-CoA reductase - potential as a component of the Esselstyn regimen. Med Hypotheses 59, 268-79

72. Menendez, R., S.I. Fernandez, A. Del Rio, R.M. Gonzalez, V. Fraga, A.M. Amor, and R.M. Mas (1994) Policosanol inhibits cholesterol biosynthesis and enhances low density lipoprotein processing in cultured human fibroblasts. Biol Res 27, 199-203

73. Menendez, R., A.M. Amor, R.M. Gonzalez, V. Fraga, and R. Mas (1996) Effect of policosanol on the hepatic cholesterol biosynthesis of normocholesterolemic rats. Biol Res 29, 253-7

74. Castano, G., R. Mas, L. Fernandez, J. Illnait, S. Mendoza, R. Gamez, J. Fernandez, and M. Mesa (2005) A comparison of the effects of D-003 and policosanol (5 and 10 mg/day) in patients with type II hypercholesterolemia: a randomized, double-blinded study. Drugs Exp Clin Res 31 Suppl, 31-44

75. Mas, R., G. Castano, J. Fernandez, R. Gamez, J. Illnait, L. Fernandez, E. Lopez, M. Mesa, E. Alvarez, and S. Mendoza (2004) Long-term effects of policosanol on obese patients with Type II Hypercholesterolemia. Asia Pac J Clin Nutr 13, S102

76. Mas, R., G. Castano, J. Fernandez, R.R. Gamez, J. Illnait, L. Fernandez, E. Lopez, M. Mesa, E. Alvarez, and S. Mendoza (2004) Long- term effects of policosanol on older patients with Type 2 diabetes. Asia Pac J Clin Nutr 13, S101

77. Castano, G., R. Menendez, R. Mas, A. Amor, J.L. Fernandez, R.L. Gonzalez, M. Lezcay, and E. Alvarez (2002) Effects of policosanol and lovastatin on lipid profile and lipid peroxidation in patients with dyslipidemia associated with type 2 diabetes mellitus. Int J Clin Pharmacol Res 22, 89-99

78. Castano, G., R. Mas, L. Fernandez, J. Illnait, M. Mesa, E. Alvarez, and M. Lezcay (2003) Comparison of the efficacy and tolerability of policosanol with atorvastatin in elderly patients with type II hypercholesterolaemia. Drugs Aging 20, 153-63

79. Castano, G., R. Mas, J.C. Fernandez, L. Fernandez, J. Illnait, and E. Lopez (2002) Effects of policosanol

on older patients with hypertension and type II hypercholesterolaemia. Drugs R D 3, 159-72

80. Castano, G., R. Mas, L. Fernandez, J. Illnait, R. Gamez, and E. Alvarez (2001) Effects of policosanol 20 versus 40 mg/day in the treatment of patients with type II hypercholesterolemia: a 6-month double-blind study. Int J Clin Pharmacol Res 21, 43-57

81. Mirkin, A., R. Mas, M. Martinto, R. Boccanera, A. Robertis, R. Poudes, A. Fuster, E. Lastreto, M. Yanez, G. Irico, B. McCook, and A. Farre (2001) Efficacy and tolerability of policosanol in hypercholesterolemic postmenopausal women. Int J Clin Pharmacol Res 21, 31-41

82. Castano, G., R. Mas, J.C. Fernandez, J. Illnait, L. Fernandez, and E. Alvarez (2001) Effects of policosanol in older patients with type II hypercholesterolemia and high coronary risk. J Gerontol A Biol Sci Med Sci 56, M186-92

83. Crespo, N., J. Illnait, R. Mas, L. Fernandez, J. Fernandez, and G. Castano (1999) Comparative study of the efficacy and tolerability of policosanol and lovastatin in patients with hypercholesterolemia and noninsulin dependent diabetes mellitus. Int J Clin Pharmacol Res 19, 117-27

84. Castano, G., R. Mas, M.L. Arruzazabala, M. Noa, J. Illnait, J.C. Fernandez, V. Molina, and A. Menendez (1999) Effects of policosanol and pravastatin on lipid profile, platelet aggregation and endothelemia in older hypercholesterolemic patients. Int J Clin Pharmacol Res 19, 105-16

85. Castano, G., R. Mas, L. Fernandez, J.C. Fernandez, J. Illnait, L.E. Lopez, and E. Alvarez (2000) Effects of policosanol on postmenopausal women with type II hypercholesterolemia. Gynecol Endocrinol 14, 187-95

86. Alcocer, L., L. Fernandez, E. Campos, and R. Mas (1999) A comparative study of policosanol Versus acipimox in patients with type II hypercholesterolemia. Int J Tissue React 21, 85-92

87. Mas, R., G. Castano, J. Illnait, L. Fernandez, J. Fernandez, C. Aleman, V. Pontigas, and M. Lescay (1999) Effects of policosanol in patients with type II hypercholesterolemia and additional coronary risk factors. Clin Pharmacol Ther 65, 439-47

88. Batista, J., R. Stusser, F. Saez, and B. Perez (1996) Effect of policosanol on hyperlipidemia and coronary heart disease in middle-aged patients. A 14-month pilot study. Int J Clin Pharmacol Ther 34, 134-7

89. Pons, P., M. Rodriguez, C. Robaina, J. Illnait, R. Mas, L. Fernandez, and J.C. Fernandez (1994) Effects of successive dose increases of policosanol on the lipid profile of patients with type II hypercholesterolaemia and tolerability to treatment. Int J Clin Pharmacol Res 14, 27-33

# 6
# Physicians' Desk
# Reference Listing
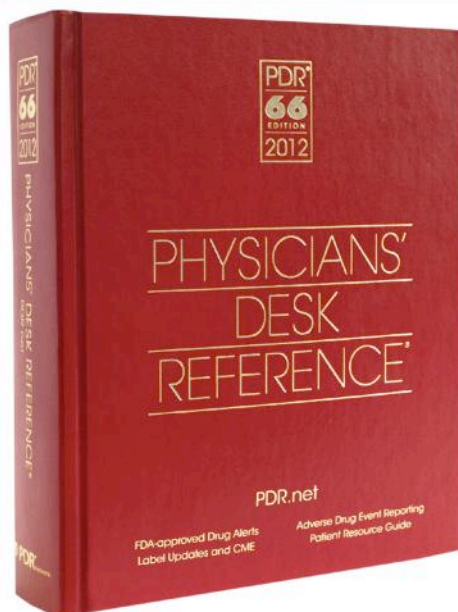
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Products of Unicity International are distributed through independent distributors.

BIO-C ™     DS
[bīo sē]

### DESCRIPTION
Bio-C™ is a vitamin C nutritional supplement.
Bio-C™ is a yellow, water-soluble, crystalline powder pressed into a tablet. Each Bio-C™ tablet consists of a proprietary blend of ascorbyl palmitate, calcium ascorbate, ascorbic acid, magnesium ascorbate and 75 mg of citrus bioflavonoids. In addition to the active ingredients, each 800 mg tablet contains dextrose, microcrystalline cellulose, silicon dioxide, magnesium stearate, and stearic acid.

### BENEFITS AND RESEARCH
Vitamin C (ascorbic acid) is a water-soluble vitamin that is used in the body to form cartilage, collagen, muscles and blood vessels. Vitamin C is a potent antioxidant that can protect small molecules such as proteins, carbohydrates, nucleic acids and lipids from damage caused by free radicals that are generated through the course of normal metabolism or through exposure to external toxins and pollutants (e.g. ultraviolet radiation from the sun or smoking). Vitamin C can also regenerate other antioxidants like vitamin E. Additionally, vitamin C is required for the synthesis of carnitine, a molecule involved in the transport of fats across the mitochondrial membrane, as well as the synthesis of norepinephrine, a neurotransmitter.[1]

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[1] THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT, CURE, OR PREVENT ANY DISEASE.

### USAGE
Take one tablet morning and night with a meal.

### SAFETY AND WARNINGS
Bio-C™ is well tolerated. Some gastrointestinal discomfort may be experienced as with any dietary supplement.

### HOW SUPPLIED
Available in tablets.

### REFERENCES
Carr, AC and Frei B. (1999), American Journal of Clinical Nutrition 96: 1086-1107.
Jacob, RA and Sotoudeh G. (2002), Nutrition in Clinical Care 5: 66-74.
Deruelle F, Baron B. (2008), Journal of Alternative and Complementary Medicine 14:1291-1298.
Levine M, Rumsey SC, Daruwala R, Park JB, Wang Y. (1999), The Journal of the American Medical Association 281: 1415-1423.

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BIOS LIFE® CARDIO     DS
[bī-o s līf kärd-e-ō]
**Advanced Fiber and Nutrient Drink**

### DESCRIPTION
Bios Life® Cardio is a fiber based, vitamin rich nutritional supplement. Bios Life® Cardio contains a blend of soluble and insoluble fibers, phytosterols, policosanol, an extract of *Chrysanthemum morifolium*, vitamins, and minerals that when combined with a healthy diet and exercise may lower total serum cholesterol, lower triglyceride levels and reduce the risk of heart disease.
Bios Life® Cardio is light orange in color. It is a hygroscopic crystalline powder that is generally soluble in water. Each serving of Bios Life® Cardio contains 3 g of fiber, 1 g of phytosterols, 6 mg of policosanol, and 12.5 mg of an extract of *Chrysanthemum morifolium*. In addition to these active ingredients, each serving of Bios Life® Cardio contains maltodextrin, citric acid, orange juice powder, sucralose and orange flavor.

### BENEFITS AND RESEARCH
It's estimated that Americans consume 10-12 g of total fiber per day, less than half the amount of the recommended daily intake. Epidemiological and clinical studies have correlated low daily fiber intake with higher incidences of hyperinsulinemia, hypercholesterolemia, and elevated risks of cardiovascular disease.
Bios Life® Cardio is a nutritional supplement designed to increased daily fiber intake. Each serving of Bios Life® Cardio contains three grams of dietary fiber. When taken three times a day this achieves nearly half of the recommended daily value of fiber. Fiber supplementation has been shown to decrease preprandial and postprandial glucose levels and lower LDL cholesterol and apolipoprotein B levels.
In addition to fiber supplementation, Bios Life® Cardio contains a patented blend of phytosterols, policosanol, *Chrysanthemum morifolium*, vitamins and minerals. This blend of ingredients optimizes cholesterol levels through a combination of four mechanisms. First, the soluble fiber matrix prevents cholesterol reabsorption in the gastrointestinal tract through bile-acid sequestration. Second, the phytosterols reduce dietary absorption of cholesterol. Third, policosanol inhibits hepatic synthesis of cholesterol mediated through HMG-CoA reductase. Fourth, *Chrysanthemum morifolium* provides phytonutrients that enhance conversion of cholesterol to 7-α-hydroxycholesterol. The four mechanisms provide a synergistic approach to optimizing cholesterol levels. Research has shown that this product may serve as a first line treatment option for mild hypercholesterolemia, as well as adjunct therapy for lipid lowering pharmaceutical intervention.

### SUGGESTED USAGE
Dissolve the contents of one packet or one scoop into 8 to 10 fl. oz. of liquid (water or juice) and stir vigorously. Drink immediately. Use 15-20 minutes prior to meals up to three times daily.

### SAFETY AND WARNINGS
Bios Life® Cardio is well tolerated. There may be mild gastrointestinal discomfort, such as increased flatulence or loose stools, during the first month of initial use due to the increased uptake of dietary fiber. This GI disturbance usually disappears within the first thirty days. If the GI discomfort persists, reduce the number of servings of Bios Life® Cardio. If the GI discomfort further persists, stop taking the product and consult your physician. Taking this product without adequate liquid can result in complications. If you are a diabetic, consult a physician for proper use of this product, as the chromium may reduce the need for medication.

### HOW SUPPLIED
Bios Life® Cardio is packaged in single-serving foil packets or in bulk canisters.

### REFERENCES
Sprecher, DL and Pearce GL (2002), Metabolism 51: 1166–70.
Verdegem, PJE; Freed, S and Joffe D (2005), American Diabetes Assocation 65th Scientific Sessions, San Diego, CA.
Duenas, V; Duenas, J; Burke, E and Verdegem, PJE (2006), 7th International Conference on Arteriosclerosis, Thrombosis, and Vascular Biology, American Heart Association, Denver, CO.
Verdegem, PJE (2007), Current Topics in Nutraceutical Research 5: 1-6
US Patent 6,933,291.
* THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT, CURE, OR PREVENT ANY DISEASE.
*Shown in Product Identification Guide, page 317*

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BIOS LIFE D     DS
[bī-o s līf dē]
**Advanced Fiber and Nutrient Drink**

### DESCRIPTION
Bios Life D is a nutrient-rich fiber drink mix that contains a patented complex of soluble and insoluble fibers, vitamins, and minerals. Each serving of Bios Life D comprising of one packet or scoop of Bios Life D contains 4.5 grams fiber, comprising of 90% of soluble fiber. Added to this fiber mix are optimal daily levels of several vitamins and minerals.

### BENEFITS AND RESEARCH
Bios Life—a good source of dietary fiber—when included as part of a healthy diet, may help lower your blood cholesterol levels and reduce your risk of heart disease. Research has shown that this product may serve as a first line treatment option for mild hypercholesterolemia, as well as adjunct therapy for lipid lowering pharmaceutical intervention.
In addition to supporting health cholesterol levels, there is considerable research that shows that the addition of viscous soluble fibers slows gastric emptying rates, digestion and the absorption of glucose. The immediate benefit is the

reduction in post-prandial glucose metabolism and over the course of time, significant reductions in glycated hemoglobin levels (HbA1c) are observed as well. Bios Life D supports healthy blood glucose levels.

## USAGE

First users: dissolve the contents of one packet or one scoop into 8 to 10 fl. oz. of water, mix vigorously and drink immediately 10 to 15 minutes before the two largest meals. After fiber adjustment, use as directed above up to three times daily before every meal.
For detailed dietary information, please see www.unicityscience.org

## SAFETY AND WARNINGS

Bios Life is well accepted. Some users report mild gastrointestinal discomfort after first use. This is a normal effect of increased fiber intake and normally disappears within 30 days. Taking this product without adequate liquid can result in complications.

## HOW SUPPLIED

Bios Life D is available in single serving sachets.

## REFERENCES

Sprecher, DL and Pearce GL (2002), Metabolism 51: 1166–70.
Verdegem, PJE; Freed, S and Joffe D (2005), American Diabetes Assocation 65th Scientific Sessions, San Diego, CA. Slavin, JL. (2005) Nutrition 21: 411-0418.
Delzenne NM, Cani PD, (2005) Current Opinion Clincal Nutrition & Metabolic Care 8: 636-640

## BIOS LIFE® SLIM ™                     DS
[bī-os līf slim]
### Advanced Fiber and Nutrient Drink

## DESCRIPTION

Bios Life® Slim™ is a fiber-based, vitamin-rich nutritional supplement. Bios Life® Slim™ contains a blend of soluble and insoluble fibers, Unicity® 7× technology, phytosterols, policosanol, an extract of *Chrysanthemum morifolium*, vitamins, and minerals that when combined with a healthy diet and exercise may lower total serum cholesterol, reduce the risk of heart disease and help achieve and maintain a healthy body weight.
Bios Life® Slim™ is light orange in color. It is a hygroscopic crystalline powder that is generally soluble in water. Each serving of Bios Life® Slim™ contains 4 g of fiber, 1 g of phytosterols, 750 mg of Unicity 7×, 6 mg of policosanol and 12.5 mg of an extract of *Chrysanthemum morifolium*. In addition to these active ingredients each serving of Bios Life® Slim™ contains maltodextrin, citric acid, orange juice powder, sucralose and orange flavor.

### BENEFITS AND RESEARCH

It's estimated that Americans consume 10-12 g of total fiber per day, less than half the amount of the recommended daily intake. Epidemiological and clinical studies have correlated low daily fiber intake with higher incidences of obesity, hyperinsulinemia, hypercholesterolemia, and elevated risks of cardiovascular disease.
Bios Life® Slim™ is a nutritional supplement designed to increase fiber intake. Each serving of Bios Life® Slim™ contains four grams of fiber. When taken three times a day this achieves half of the recommended daily value of fiber. Fiber supplementation has been shown to decrease preprandial and postprandial glucose levels; lower LDL cholesterol and apolipoprotein B levels; increase satiety and facilitate weight loss.
In addition to fiber supplementation, Bios Life® Slim™ contains a patented blend of phytosterols, policosanol, *Chrysanthemum morifolium*, vitamins and minerals. Bios Life® Slim™ facilitates weight loss through five distinct mechanisms. First, the soluble fiber matrix promotes an increase in satiety. Second, Bios Life® Slim™ improves cholesterol levels. Reduction in LDL content removes a potent inhibitor of lipolysis. Third, Bios Life® Slim™ improves blood glucose levels. Maintaining appropriate serum glucose levels reduces hyperinsulinemia and promotes insulin sensitivity. Reducing insulin levels permits fatty acid oxidation to occur. Fourth, Bios Life® Slim™ restores appropriate leptin signaling. Lastly, Bios Life® Slim™, reduces triglyceride levels allowing for leptin to cross the blood-brain barrier and effect its mechanism of action. Research has shown that this product may serve as a first line treatment option for mild hypercholesterolemia, as well as adjunct therapy for lipid lowering pharmaceutical intervention.

## SUGGESTED USAGE

Dissolve the contents of one packet or one scoop into 8 to 10 fl. oz. of liquid (water or juice) and stir vigorously. Drink immediately. Use 15-20 minutes before meals up to three times daily.

## SAFETY AND WARNINGS

Bios Life® Slim™ is well tolerated. There may be mild gastrointestinal discomfort, such as increased flatulence or loose stools, during the first month of initial use due to the increased uptake of dietary fiber. This GI disturbance usually disappears within the first thirty days. If the GI discomfort persists, reduce the number of servings of Bios Life® Slim™. If the GI discomfort further persists, stop taking the product and consult your physician. Taking this product without adequate liquid can result in complications. If you are a diabetic, consult a physician for proper use of this product, as the chromium may reduce the need for medication.

## HOW SUPPLIED

Bios Life® Slim™ is packaged in single-serving foil packets or in bulk canisters.

## REFERENCES

Sprecher, DL and Pearce GL (2002), Metabolism 51: 1166-70.
Verdegem, PJE; Freed, S and Joffe D (2005), American Diabetes Assocation 65th Scientific Sessions, San Diego, CA. Slavin, JL, (2005) Nutrition 21: 411-418.
Delzenne NM, Cani PD, (2005) Current Opinion Clincal Nutrition & Metabolic Care 8: 636-640
Duenas, V; Duenas, J; Burke, E and Verdegem, PJE (2006), 7th International Conference on Arteriosclerosis, Thrombosis, and Vascular Biology, American Heart Association, Denver, CO.
Verdegem, PJE (2007), Current Topics in Nutraceutical Research 5: 1-6
US Patent 6,933,291.
* THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT, CURE, OR PREVENT ANY DISEASE.
*Shown in Product Identification Guide, page 318*

## BONEMATE® PLUS                     DS
[bōn-māt plŭs]
### Advanced Bone Health Formula

## DESCRIPTION

BoneMate® Plus is specially formulated to help maintain optimal bone health.[1] It contains three forms of calcium and vitamin D to maximize absorption and aid in the support of healthy bones, teeth, nerves, heart, and muscle tissue.
BoneMate® Plus is a light gray in color and is soluble in water. Each serving of BoneMate® Plus contains the following active ingredients 600mg of calcium, 300mg of magnesium, 30 mg of vitamin C, 2000 IU of vitamin D, 0.5mg of boron, 5 mg of zinc, 1mg of manganese, 1mg of copper, and 20mg of vitamin K. In addition, it also contains the inactive ingredients microcrystalline cellulose, croscarmellose sodium, and magnesium stearate.

### BENEFITS AND RESEARCH

Calcium is the most common mineral in the body. Almost 99% of the calcium in our body is found in the bones and teeth. Bone is a dynamic tissue that is constantly being remodeled throughout our lives. A chronically low calcium intake in growing individuals may prevent the attainment of optimal peak bone mass. Once peak bone mass has been achieved, inadequate calcium intake may contribute to accelerated bone loss and eventually to osteoporosis.
Vitamin D, a secosteroid that is produced by the body upon exposure to the sun, is required for optimal calcium absorption. To ensure that calcium absorption is not limited by inadequate vitamin D levels, BoneMate® Plus contains 2000 IU of vitamin D per serving. In addition to facilitating calcium absorption, Vitamin D has been shown to target over 2000 different genes in the body. Vitamin D deficiency has been associated with increased risks for heart disease, stroke, diabetes, depression, osteoarthritis, chronic pain, and osteoporosis.

[1] THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT, CURE, OR PREVENT ANY DISEASE.

## USAGE

Take two tablets twice daily with a meal.

## SAFETY AND WARNINGS

BoneMate® Plus is well tolerated. Some gastrointestinal discomfort may be experienced as with any dietary supplement. The Food and Nutrition Board of the Institute of Medicine has set the tolerable upper level (UL) of intake for calcium in adults at 2,500 milligrams (mg) of calcium/day.

## HOW SUPPLIED

Available as tablets or as a powder.

## REFERENCES

Weaver CM, Heaney RP. Calcium. In: Shils M, Olson JA, Shike M, Ross AC, eds. Modern Nutrition in Health and Disease, 9th ed. Baltimore: Williams & Wilkins; 1999:141-155.
Heaney RP. Calcium, dairy products and osteoporosis, J Am Coll Nutr. 2000;19(2 Suppl):83S-99S.
Food and Nutrition Board, Institute of Medicine. Calcium. Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington, D.C.: National Academy Press; 1997:71-145.
Reid IR. Therapy of osteoporosis: calcium, vitamin D, and exercise. Am J Med Sci 1996;312:278-86. Food and Nutrition Board, Institute of Medicine. Calcium. Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington, D.C.: National Academy Press; 1997:71-145.

## CARDIO-BASICS ™                     DS
### Caring for your heart*

## DESCRIPTION

Cardio-Basics™ is a nutritional supplement that combines multivitamins, minerals and antioxidants to support the cardiovascular system.
Cardio-Basics™ is a light orange, water-soluble powder pressed into tablets. Each tablet of Cardio-Basics™ contains the following vitamins, minerals, amino acids and antioxidants: beta-carotene (vitamin A), thiamine (vitamin B1), riboflavin (vitamin B2), niacin (vitamin B3), calcium d-pantothenate (vitamin B5), pyridoxine hydrochloride (vitamin B6), folate (vitamin B9), cyanocobalamin (vitamin B12), ascorbic acid and ascorbyl palmitate (vitamin C), cholecalciferol (vitamin D), d-alpha-tocopherol (vitamin E), biotin, calcium, chromium, copper, magnesium, manganese, molybdenum, phosphorus, potassium, selenium, sodium, zinc, L-arginine, L-carnitine, L-cysteine, L-lysine, L-proline, inositol, coenzyme Q10, and maritime pine extract. In addition to those active ingredients each tablet also contains microcrystalline cellulose, sucrose, fatty acid esters, silicon dioxide, magnesium stearate, and maltodextrin.

### BENEFITS AND RESEARCH

According to the Center for Disease Control and Prevention, one American will die every minute as a result of heart disease. Narrowing of the arterial walls can lead to blocked blood flow to the brain. A healthy lifestyle including being physically active, not smoking, and making good food choices can lead to a reduction of heart disease. Cardio-Basics™ provides the vitamins, minerals and antioxidants needed for a healthy heart. In clinical studies, participants using Cardio-Basics™ and Bio-C™ saw a significant reduction in arterial wall thickness, removal of calcification deposits and a reduced risk for cardiovascular disease when compared to the placebo group. Cardio-Basics™ provides the body with the necessary vitamins and minerals needed to support a healthy vascular system.[1]

[1] THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT, CURE, OR PREVENT ANY DISEASE.

## SUGGESTED USE

Take two tablets daily with food.

## SAFETY AND WARNINGS

Cardio-Basics™ is well tolerated. Some gastrointestinal discomfort may be experienced as with any dietary supplement.

## HOW SUPPLIED

Available in tablets.

## REFERENCES

Niedzwieckci, A, Rath, M. (1996) Journal of Applied Nutrition, 48: 67-78.
Jeejeebhoy, F, Keith, M, Freeman, M, Barr, A, McCall, M, Kurian, R, Mazer, D, Errett, L, (2002), American Heart Journal 143: 1092-1100.
Verdegem, PJE, Lonky, S, Curley, S. (2005) 7th Conference on Arteriosclerosis, Thrombosis and Vascular Biology.
Lloyd-Jones D, Adams R, Carnethon M, DeSimone G, Ferguson TB, Flegal K, Ford E, Furie K, Go A, Greenlund K, Haase N, Hailpern S, Ho M, Howard V, Kissela B, Kittner S, Lackland D, Lisabeth L, Marelli A, McDermott M, Meigs J, Mozaffarian D, Nichol G, O'Donnell C, Roger V, Rosamond W, Sacco R, Sorlie P, Stafford R, Steinberger J, Hong Y; (2009) Circulation, 119: 480-486.

# 7
# Overview of clinical studies with Bios Life™

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## Clinical Studies on Bios Life
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## 1  Cleveland Clinic, Cleveland Clinic Foundation, Cleveland, OH

| Year | N | Design | Intervention | Researchers |
|---|---|---|---|---|
| 2001 | 99 | DBPC | 8 weeks | Dennis L. Sprecher, Gregory L. Pearce |

| Outcomes | Inclusion | BL | EOT | % | % vs Placebo |
|---|---|---|---|---|---|
| TC | | 237 | 227 | -4.2% | -5.9% |
| LDL | >130 | 159 | 145 | -8.8% | -12.0% |
| HDL | | 48 | 51 | 6.3% | 0.0% |
| TG | | 146 | 119 | -18.5% | -5.6% |
| GLU | | 83 | 83 | 0.0% | -3.7% |
| ApoB | | 139 | 110 | -20.9% | -20.9% |
| Hcy | | 9.8 | 8.7 | -11.2% | -9.1% |
| Weight | | 85 | 84 | -1.2% | -2.4% |
| Placebo | | | | | |
| TC | | 242 | 246 | 1.7% | |
| LDL | >130 | 158 | 163 | 3.2% | |
| HDL | | 48 | 51 | 6.3% | |
| TG | | 140 | 122 | -12.9% | |
| GLU | | 82 | 85 | 3.7% | |
| ApoB | | 135 | 135 | 0.0% | |
| Hcy | | 9.4 | 9.2 | -2.1% | |
| Weight | | 80 | 81 | 1.3% | |

**Publications:**

Sprecher DL, Pearce GL (2002) Fiber-multivitamin combination therapy: a beneficial influence on low-density lipoprotein and homocysteine Metabolism 51, 1166-70.

## 2  Angeles University Foundation Medical Center, Angeles City, Philippines

| Year | N | Design | Intervention | Researchers |
|---|---|---|---|---|
| 2003 | 103 | Open label | 4 weeks | Edwin B. Balajadia, Amiel S Valerio, Norberto Yumul |

| Outcomes | Inclusion | BL | EOT | % |
|---|---|---|---|---|
| TC | | 267 | 222 | -16.9% |

**Publications:**

Balajadia E, Valerio A, Yumul N. Beneficial effects of Bios Life 2® (Dietary Fiber Supplement) in patients with dyslipidemia. in 34th Annual Convention of the Philippine College of Physicians. 2004.

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## 3  Diabetes in control #1, Deerfield, IL

| Year | N | Design | Intervention | Researchers |
|---|---|---|---|---|
| 1999 | 15 | Open label | 12 weeks | Steven H. Freed, David J. Joffe |

| Outcomes | Inclusion | BL | EOT | % |
|---|---|---|---|---|
| TC | | 210 | 185 | -12% |
| HDL | | 35 | 37 | 6% |
| TG | | 299 | 173 | -42% |
| GLU pre | | 150 | 125 | -17% |
| GLU post | | 250 | 160 | -36% |
| HbA1c | | 9.2 | 7.8 | -15.2% |
| Weight | | 208 | 202 | -2.9% |

**Publications:**

Freed S, Joffe D (2000) The Clinical Impact of Fiber Supplementation for the Reduction of Postprandial Blood Glucose and Risk Reduction of Complications from Diabetes Diabetes in Control 12-8.

| Year | N | Design | Intervention | Researchers |
|------|---|--------|--------------|-------------|
| 2004 | 78 | Open label | 90 days | Steven H. Freed, David J. Joffe |

| Outcomes | Inclusion | BL | EOT | % |
|----------|-----------|-----|-----|-----|
| TC | | 215 | 184 | -14.4% |
| LDL | | 129 | 92 | -28.7% |
| HDL | | 43 | 55 | 27.9% |
| TG | | 299 | 257 | -14.0% |
| GLU pre | | 173 | 156 | -9.8% |
| GLU post | | 278 | 237 | -14.7% |
| HbA1c | | 9 | 8.1 | -10.0% |
| Weight | | 182 | 176 | -3.3% |

**Publications:**

Freed S, Joffe D (2004) The Clinical Impact of Fiber Supplementation for the Reduction of Postprandial Blood Glucose and Risk Reduction of Complications from Diabetes II Diabetes in Control 212, 17.

Verdegem P, Freed S, Joffe D. The Clinical Impact of Fiber Supplementation on Cardio-Vascular Risk Parameters in type-2 Diabetes. in 6th International Conference on Atherosclerosis, Thrombosis and Vascular Biology. 2005. Washinton, DC, USA.

Verdegem P, Freed S, Joffe D. The Clinical Impact of Fiber Supplementation for the Reduction of Post-prandial Blood Glucose and Risk Reduction of Complications from Type-2 Diabetes. in 65th Scientific Session American Diabetes Association. 2005. San Diego, CA, USA.

Verdegem P, Freed S, Joffe D (2005) The clinical impact of fiber supplementation for the reduction of post-prandial blood blucose and reduction of complications from type-2 diabetes Diabetes 54, A425.

## 5  Utah #1, Orem, UT

| Year | N | Design | Intervention | Researchers |
|---|---|---|---|---|
| 2005 | 25 | Open label | 8 weeks | Peter J.E. Verdegem |

| Outcomes | Inclusion | BL | EOT | % |
|---|---|---|---|---|
| TC | | 214 | 196 | -8.2% |
| | > 200 | 237 | 211 | -10.7% |
| LDL | | 131 | 111 | -4.8% |
| | > 130 | 168 | 127 | -24.5% |
| | > 160 | 182 | 127 | -30.6% |
| HDL | | 48 | 52 | 8.3% |
| | < 40 | 32 | 37 | 12.0% |
| TG | | 176 | 166 | -5.7% |
| | > 150 | 228 | 194 | -14.9% |
| Ratio | | 4.89 | 4.14 | -5.3% |
| | > 5.0 | 6.51 | 5.04 | -24.2% |

**Publications:**

Verdegem P (2007) Viscous soluble fiber combined with phytosterols and policosanol reduces LDL-c and increases HDL-c in hypercholesterolemia Current Topics in Neutraceutical Research in press,

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## 6  Pacific Rim, The doctor's clinic, Tamuning, GU

| Year | N | Design | Intervention | Researchers |
|---|---|---|---|---|
| 2005 | 24 | Open label | 6 weeks | Vincent Duenas, Julie Duenas, Evelyn Burke, Peter Verdegem |

| Outcomes | Inclusion | BL | EOT | % |
|---|---|---|---|---|
| TC | >200 | 235 | 232 | -1.4% |
| LDL | >130 | 157 | 131 | -16.1% |
| LDL | >160 | 180 | 150 | -16.6% |
| HDL | <40 | 35 | 45 | 27.9% |
| Risk ratio | | 5.1 | 4.3 | -15.0% |
| TC | >200 | 232 | 229 | -1% |
| LDL | >130 | 150 | 118 | -21% |
| HDL | <40 | 34 | 42 | 23% |
| Risk ratio | | 5.2 | 4.4 | -15% |

**Publications:**

Duenas V, Duenas J, Burke E, Verdegem P (2006) A new fiber drink provides a natural first line treatment option in mild hypercholesterolemia Arterioscler Thromb Vasc Biol 26, e53-e107.

Duenas V, Duenas J, Burke E, Verdegem P. A new fiber drink can serve as an adjunct therapy to statin

medication in mild hypercholesterolemia. in 7th Annual Conference on Arteriosclerosis, Thrombosis and Vascular Biology. 2006. Denver.

Verdegem P, Duenas V, Duenas J, Burke E. LDL- and HLD-cholesterol optimization using phytonutrient combination therapy: first line intervention and adjunct therapy to statins. in 1st Asian Preventive Cardiology & Cardiac Rehabilitation Conference. 2006. Hong Kong.

Duenas V, Duenas J, Burke E, Verdegem P (2006) A new fiber drink can serve as an adjunct therapy to statin medication in mild hypercholesterolemia Arterioscler Thromb Vasc Biol 26, e53-e107.

Duenas V, Duenas J, Burke E, Verdegem P. A new fiber drink can serve as an adjunct therapy to statin medication in mild hypercholesterolemia. in 7th Annual Conference on Arteriosclerosis, Thrombosis and Vascular Biology. 2006. Denver.

Verdegem P, Duenas V, Duenas J, Burke E. LDL- and HLD-cholesterol optimization using phytonutrient combination therapy: first line intervention and adjunct therapy to statins. in 1st Asian Preventive Cardiology & Cardiac Rehabilitation Conference. 2006. Hong Kong.

## 7  Utah #2, Orem, UT

| Year | N | Design | Intervention | Researchers |
|------|-----|------------|----------|-------------------|
| 2006 | 39 | Open label | 8 weeks | Peter J.E. Verdegem |

| Outcomes | Inclusion | BL | EOT | % |
|----------|-----------|-----|-----|--------|
| TC | | 208 | 185 | -11.1% |
| TC | >200 | 235 | 206 | -12.3% |
| LDL | | 120 | 104 | -13.3% |
| LDL | >130 | 154 | 120 | -22.1% |
| LDL | >160 | 173 | 134 | -22.5% |
| HDL | <40 | 25 | 30 | 20.0% |
| TG | | 210 | 181 | -13.8% |
| TG | >150 | 310 | 237 | -23.5% |

**Publications:**

Verdegem P, Duenas V, Duenas J, Burke E. LDL- and HLD-cholesterol optimization using phytonutrient combination therapy: first line intervention and adjunct therapy to statins. in 1st Asian Preventive Cardiology & Cardiac Rehabilitation Conference. 2006. Hong Kong.

## 8  Texas, Katy, TX

| Year | N | Design | Intervention | Researchers |
|---|---|---|---|---|
| 2006 | 34 | Open label | 8 weeks | Bobbi Horne, Isabel Martinez, Peter J.E. Verdegem |

| Outcomes | Inclusion | BL | EOT | % |
|---|---|---|---|---|
| TC | | 208 | 178 | -14.2% |
| TC | >200 | 245 | 195 | -21.5% |
| LDL | | 127 | 104 | -18.3% |
| LDL | >160 | 197 | 141 | -28.9% |
| HDL | | 46 | 48 | 3.5% |
| HDL | <40 | 35 | 40 | 14.4% |
| TG | | 182 | 143 | -21.3% |
| TG | >150 | 242 | 163 | -32.5% |
| GLU pre | | 162 | 134 | -17.3% |
| GLU pre | >175 | 218 | 155 | -28.9% |
| HbA1c | | 7.2 | 6.6[a] | -9.4% |
| HbA1c | >8 | 9.2 | 7.8[a] | -15.8% |
| a | after 12 weeks | | | |

**Publications:**

Martinez I, Horne B, Verdegem P. Lipid and glucose optimization using phytonutrient combination therapy in diabetes. in 8th Annual Conference on Arteriosclerosis, Thrombosis and Vascular Biology. 2007. Chicago.

# 8
# Fiber-Multivitamin Combination Therapy: a Beneficial Influence on Low-density Lipoprotein and Homocysteine

by Dennis L. Sprecher,
and Gregory L. Pearce

Cleveland Clinic Foundation, Cleveland, OH, USA

# Fiber-Multivitamin Combination Therapy: A Beneficial Influence on Low-Density Lipoprotein and Homocysteine

Dennis L. Sprecher and Gregory L. Pearce

**Proven effective alternative and adjunctive therapies for lipid lowering could be beneficial for patients with hyperlipidemia. We evaluated a 90% soluble fiber for its ability to alter lipid, lipoprotein, and homocysteine levels in the setting of coadministered folate and B vitamins. Patients (n = 119) were randomized to either the fiber and vitamin combination, or placebo. Fasting lipid, glucose, and homocysteine concentrations, and body mass index (BMI) were obtained at baseline and weeks 4 and 8. Both between-group (Wilcoxon rank-sum test) and within-group (paired $t$ test) comparisons were used to evaluate treatment effects. After 6 weeks of a diet therapy (National Cholesterol Education Program [NECP] Step I) run-in period, subjects in both groups had similar low-density lipoprotein cholesterol (LDL-C) levels (159 mg/dL v 158 mg/dL). The treated group showed a 7.1% ± 11.6% reduction by 4 weeks, which was maintained at 8 weeks (7.9% ± 11.0%). Placebo patients had a slight increase in LDL-C values over the same period (+2.4% ± 11.7%), for a 10.3% difference between groups. The treatment effect was statistically significant both between groups ($P < .001$) and within the active-treatment group ($P < .001$) after the 8-week intervention. Apolipoprotein B (ApoB) levels in a representative subset of the treated group (n = 53) decreased by 20% ($P = .004$). The fiber blend neither raised triacylglycerol (TG) ($P = .95$) nor lowered high-density lipoprotein cholesterol (HDL-C) levels ($P = .54$), and lowered homocysteine (active, 9.8 to 8.7/$\mu$mol/L, $P = .02$; placebo, 9.4 to 9.2 /$\mu$mol/L, $P = .98$). Thus, a significant LDL-C lowering effect, with parallel Apo B reduction, was demonstrated for this fiber/vitamin combination. No adverse changes on TG or HDL-C levels were noted, and folate/B vitamin benefits attributed to homocysteine reduction were preserved. Concurrent administration of fiber and vitamins represents a preventive approach that may reduce the need for concomitant lipid-lowering therapies or serve as an adjunct therapy.**
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**P**RODUCTS ENRICHED with fiber have been reported to lower serum cholesterol levels and improve glucose concentrations in diabetics. Vitamins in addition to or incorporated with foods have resulted in the lowering of homocysteine serum concentrations. Given that the combination of various dietary supplements into one product could enhance benefits and overall compliance, it is important to establish the efficacy of their joint administration.

Fibers can reduce low-density lipoprotein cholesterol (LDL-C) concentrations by 5% to 10%; however, this often occurs with concurrent elevation in triacylglycerol (TG), reductions in serum high-density lipoprotein cholesterol (HDL-C) concentrations,[1] and frequent gastrointestinal side effects.[2] When provided separately or in combination, folic acid, vitamin $B_6$, and vitamin $B_{12}$ can reduce homocysteine plasma concentrations. However, fiber may modify $B_6$ bioavailability.[3,4] The influence of vitamin supplementation when coadministered with fiber has not been determined. Finally, it has been suggested that fiber products reduce glucose serum concentrations when provided to diabetic subjects, but it is not clear whether similar reductions occur in nondiabetic patients.

We chose to examine the potential of a combined fiber and vitamin preparation to lower LDL-C concentrations. Secondarily, we tested whether the supplementation of B vitamins in conjunction with fiber would provide the expected reduction in homocysteine levels. Finally, we examined HDL-C and TG changes, as well as possible glucose modification, that occur with daily fiber use.

## MATERIALS AND METHODS

### Subjects

Potential study subjects were eligible to participate if they were $\geq$ 18 years of age, had no known cardiovascular disease, and had a fasting LDL-C concentration $\geq$ 130 mg/dL. No concurrent lipid-lowering therapy or statin during the previous 30 days was permissible. Subjects were required to follow the National Cholesterol Education Program (NCEP) Step I diet for the duration of the investigation, and to avoid any intentional dramatic changes in diet. Female participants could not be pregnant (negative pregnancy test at screening) or breastfeeding, and agreed to use reliable contraception for the duration of the investigation.

Ineligibility criteria included established thyroid, liver, or renal disease; insulin-dependent diabetes mellitus; poorly controlled non–insulin-dependent daibetes mellitus (fasting blood glucose $\geq$ 200 mg/dL); vasculitis; human immunodeficiency virus infection; dysphagia or swallowing disorders; poorly controlled hypertension (systolic blood pressure $\geq$ 160 or diastolic blood pressure $\geq$ 105 mm Hg); and known cardiovascular or unstable cardiac disease. Persons with known allergies to any ingredients in either the active or placebo study compounds were also excluded. Subjects were not included in the study if fasting LDL-C concentration fell to less than 130 mg/dL after the NCEP Step I diet 6-week run-in period. Finally, if the LDL-C concentration did not stabilize (within 15% variance) between the week 3 and week 6 pre-randomization diet-only follow-up clinic visits, the individual was excused from the trial prior to randomization. Those subjects who remained eligible for the trial after the 6-week diet therapy run-in were randomized (n = 119) to receive either placebo or fiber blend in a double-blind parallel fashion. All randomized subjects continued to follow the NECP Step I diet for the next 8 weeks and add 2 servings per day of their assigned study compound.

Prospective subjects were recruited by advertisement in internal hospital communications and community newspapers. All subjects provided informed consent to participate in this investigation, which was approved by the Cleveland Clinic Foundation Institutional Review Board.

*Clinical Parameters Monitored*

Following screening for eligibility, a fasting blood sample was collected at defined intervals during the investigation. Blood parameters monitored included comprehensive lipid and metabolic panels, as well as blood counts and homocysteine concentrations. Subjects were also weighed and asked to report any adverse events or side effects at each visit, and underwent periodic physical examinations. Based on the LDL-C findings, a post-hoc analyses of apolipoprotein B (ApoB) was performed on archived samples, permitting a convenience sample of 55 patients (26 treatment, 29 placebo) at randomization, 8 weeks, and 16 weeks.

*Diet and Stool Studies*

Dietary intake was collected in a diet log completed by the subject and analyzed with The Food Processor software program, version 7.40 (ESHA Research, Salem, OR). Three-day stool records were collected for each subject on 4 occasions. Subjects recorded frequency and consistency for each entry over 3 days (no bowel movement, diarrhea/loose, soft, firm/normal, constipated, or no record).

*Fiber Blend Composition and Dosage*

The fiber tested was Bios Life 2 (Rexall Sundown, Boca Raton, FL), which provides 4.0 g of soluble fiber and 0.5 g of insoluble fiber per serving (guar gum, locust bean gum, pectin, oat fiber, gum acacia, and barley fiber), along with 1,000 IU vitamin A as $\beta$ carotene, 30 IU vitamin E, 60 mg vitamin C, 2.7 mg thiamine, 36 mg niacin, 3.1 mg riboflavin, 120 $\mu$g folic acid, 3.6 mg vitamin $B_6$, 9 $\mu$g vitamin $B_{12}$, 30 $\mu$g biotin, 100 mg calcium, 0.9 mg zinc, 54 $\mu$g chromium, and 4.2 $\mu$g selenium. The placebo consisted entirely of insoluble fiber, provided as a combination of purified cellulose and carboxymethylcellulose (Valentine Enterprises, Lawrenceville, GA). These powders were of identical appearance, color, odor, and flavor. Both were dispensed as identical single-serving packets of powder to be mixed with 8 oz of water and consumed within 30 minutes of a meal, twice per day. Subject compliance was estimated from the number of unused packets returned by the study subject at each scheduled study-related clinic visit. The participants attended the clinic 4 and 8 weeks after randomization for observation and follow-up.

*Sample Size Calculation*

Sample size estimates were calculated to provide 90% power at an $\alpha$ level of 0.05. With these assumptions, 50 patients were required in each group to detect a treatment effect of a 10% reduction in LDL (compared to no change in the placebo group) with a standard deviation of 15%. An additional 10 patients per group were recruited to allow for the probability that some patients would withdraw from the study.

*Statistical Methods*

Lipid, glucose, homocysteine, BMI, and dietary data are presented as median and interquartile ranges because distributions did not uniformly meet normality assumptions. The primary endpoint was LDL-C response from the start of the study to the end of the blinded phase. The starting concentration is calculated as the average LDL-C concentration from the screening and randomization visits because these 2 visits determined eligibility based on the LDL-C criterion. The response is described as percentage change from the start concentration to the concentration at the end of the blinded phase.

Differences between the treatment and placebo groups were evaluated first at each time period by univariate comparisons using Wilcoxon rank-sum tests.[5] Changes within groups over time were evaluated with paired *t* tests at each follow-up visit after randomization. This strategy was employed for the primary outcome (LDL-C) and secondary outcomes (total cholesterol [TC], ApoB, HDL, TG, glucose, and homo-

cysteine). In addition, for the primary outcome, a repeated-measures mixed model was developed using treatment group as a fixed effect and subjects as random effects.[6] The treatment and time main effects were adjusted for age and gender, and a time by treatment interaction was included.

Mean caloric intake, fiber and soluble fiber intake, calories from fat, protein, carbohydrate, and alcohol intake were calculated for each subject based on diet logs. Between-group comparisons were made at randomization and the end of the blinded phase with unpaired *t* tests. Changes in diet over time were evaluated within groups using paired *t* tests. As with dietary habits, stool consistency was compared between groups with unpaired *t* tests and within groups by paired *t* tests.

## RESULTS

A total of 137 subjects expressed interest in participating in the study at the time of the initial visit. Of these, 119 met all of the inclusion criteria and were randomized. Ninety-nine patients (50 treatment, 49 placebo) completed all visits through the end of the blinded phase. Of the 20 patients (10 treatment, 10 placebo) who dropped out of the study, gastrointestinal issues were the most commonly cited clinical reason (n = 7; 2 treatment, 5 placebo). Logistics issues accounted for 10 dropouts (6 treatment, 4 placebo). LDL-C at randomization was not different between those who finished the study (153 mg/dL) and those who did not (158 mg/dL). Baseline characteristics of the 99 patients who completed the study are listed in Table 1.

*LDL-C Response*

Patients randomized to the treatment group had a slightly lower (but not statistically significant) LDL-C concentration at the screening visit (159 mg/dL *v* 169 mg/dL). After the 6-week diet lead-in, the 2 groups showed virtually identical LDL concentrations (159 mg/dL *v* 158 mg/dL). By the time of the interim visit (4 weeks after randomization), the treatment group demonstrated significantly lower LDL-C than the placebo group (147 mg/dL *v* 162 mg/dL, *P* = .02). That trend continued through the next 4 weeks to the end of the blinded phase (145 mg/dL *v* 163 mg/dL, *P* = .003). Therefore, the LDL-C response at the end of the blinded phase was −7.9% ± 11.0% for the treatment group compared to +2.4% ± 11.7% for the placebo group (*P* < .001). Twelve percent (n = 6) of treatment subjects experienced an LDL reduction of greater than 20% compared to 2% (n = 1) in the placebo group (*P* = .05). The LDL:HDL ratio decreased 9.2% ± 11.9% in the treatment group (*P* < .001), but did not change significantly (-2.0% ± 12.7%, *P* = .27) in the placebo group. The mixed model confirmed that the treatment and time main effects were statistically significant (Fig 1). At the end of the labeled open retail treatment phase of the study, the 2 groups (n = 96, all on active treatment at this point) had begun to converge with regard to LDL-C concentrations (145 mg/dL *v* 156 mg/dL, *P* = .09).

*Secondary Endpoints*

TC, ApoB, HDL-C, TG, glucose, and homocysteine were secondary endpoints. Table 2 shows that TC mirrored the LDL-C response, with significant differences between the treatment and placebo groups appearing at the time of the interim visit, continuing through the end of the blinded phase, and converging by the end of the open treatment phase. The percent

**Table 1. Presentation Characteristics of Patients Who Completed the Study Through the End of the Blinded Phase**

| | Treatment | Placebo | PValue |
|---|---|---|---|
| n | 50 | 49 | — |
| Age (yr) | 49 (40-60) | 51(43-58) | .51 |
| Female | 16(32%) | 21(43%) | .26 |
| Non-white | 6(12%) | 1(2%) | .15 |
| TC (mg/dL) | 237 (221-262) | 242 (228-260) | .67 |
| LDL (mg/dL) | 159 (144-178) | 158 (148-178) | .83 |
| HDL (mg/dL) | 48 (42-62) | 48 (42-61) | .81 |
| TG(mg/dL) | 146(94-198) | 140(111-185) | .96 |
| LDL:HDL | 3.2 (2.6-3.8) | 3.3 (2.7-3.9) | .67 |
| Glucose (mg/dL) | 83(75-91) | 82(75-92) | .99 |
| BMI | 27.8 (25.3-30.7) | 27.3 (24.7-29.4) | .62 |
| Homocysteine | 9.8 (7.8-11.8) | 9.4 (8.4-10.4) | .49 |
| Systolic blood pressure (mm Hg) | 119(111-128) | 120(110-131) | .57 |
| Diastolic blood pressure (mm Hg) | 81(72-86) | 80 (75-89) | .82 |

NOTE. Continuous measures presented as median and interquartile range, categorical measures presented as number and percentage.

change in TC from randomization to the end of the blinded phase was −5.7% ± 8.8% for the treatment group compared to +3.1% ± 11.3% for the placebo group ($P < .001$).

At 8 weeks, the treatment group had dropped to a median ApoB of 110 mg/dL, while the placebo group remained at 135 mg/dL ($P = .005$). The correlation between change in LDL-C and change in ApoB (end of blinded phase) was 0.27 ($P = .006$). The correlation for the changes between the end of the blinded phase and the end of the open-label phase was not significant ($r = 0.14$, $P = .30$). Because ApoB was only measured in a subsample, a bias could have been incorporated. However, lipid concentrations (TC, LDL-C, HDL-C, TG) and homocysteine were similar for those with and without ApoB measures at each visit. Further, baseline ApoB measures were similar between the treatment (139 mg/dL) and placebo (135 mg/dL) groups ($P = .75$).

Plasma homocysteine was measured at randomization and at



**Fig 1. LDL response (mean ± SEM) by median and interquartile range by placebo (P) and treatment (T) groups.**

**Table 2. Median and Interquartile Range (IQR) for Outcomes at Each Time Period**

| | Treatment (n = 50) | | Placebo (n = 49) | |
|---|---|---|---|---|
| | Median | IQR | Median | IQR |
| **LDL (mg/dL)** | 26) | | 29) | |
| Screening | 159 | 144-182 | 169 | 148-184 |
| Randomization | 159 | 144-178 | 158 | 148-178 |
| Interim | 147 | 127-163 | 162 | 143-178 |
| EOB | 145 | 134-165 | 163 | 143-181 |
| EOO | 145 | 130-166 | 156 | 138-178 |
| **TC (mg/dL)** | | | | |
| Screening | 238 | 222-268 | 247 | 229-271 |
| Randomization | 237 | 221 -262 | 242 | 228-260 |
| Interim | 225*† | 210-238 | 245 | 227-259 |
| EOB | 227*† | 202-251 | 246 | 230-279 |
| EOO | 233† | 211-261 | 237 | 217-264 |
| **HDL (mg/dL)** | | | | |
| Screening | 50 | 44-60 | 51 | 42-61 |
| Randomization | 48 | 42-62 | 48 | 42-61 |
| Interim | 51 | 43-58 | 49 | 42-60 |
| EOB | 51 | 45-59 | 51† | 43-63 |
| EOO | 53 | 44-59 | 51† | 45-64 |
| **TG (mg/dL)** | | | | |
| Weeks | 122 | 88-174 | 137 | 100-171 |
| Randomization | 146 | 94-198 | 140 | 111-185 |
| Interim | 123 | 103-160 | 127 | 96-176 |
| EOB | 119 | 89-177 | 122 | 104-162 |
| EOO | 130 | 102-205 | 132 | 102-159 |
| **Weight (kg)** | | | | |
| Weeks | 85 | 74-93 | 80 | 72-89 |
| Randomization | 85 | 75-93 | 80 | 71-89 |
| Interim | 84 | 70-92 | 80 | 72-90 |
| EOB | 84 | 72-93 | 81 | 72-88 |
| EOO | 83 | 72-92 | 79 | 71-90 |
| **GLU (mg/dL)** | | | | |
| Randomization | 83 | 75-91 | 82 | 75-92 |
| Interim | 83 | 75-89 | 86 | 80-92 |
| EOB | 83 | 76-90 | 85 | 77-91 |
| EOO | 85 | 77-91 | 82 | 77-90 |
| **ApoB (mg/dL)** | | | | |
| Randomization | 139 (n = | 123-150 | 135 (n = | 130-152 |
| EOB | 110*† | 89-121 | 135 | 114-153 |
| EOO | 134 | 115-138 | 133 | 117-155 |
| **HCY (mmol/L)** | | | | |
| Randomization | 9.8 | 7.8-11.8 | 9.4 | 8.4-10.4 |
| EOB | 8.7† | 7.6-1 0.0 | 9.2 | 8.3-1 0.9 |

NOTE. Data are shown for the screening visit, randomization (which is the combined data for visits 2 and 3), the interim visit (4 weeks after randomization), the end of the blind phase (8 weeks after randomization), and the end of the open phase (16 weeks after randomization).

Abbreviations: IQR, interquartile range; EOB, end of blinded phase; EOO, end of open-label phase; GLU, glucose; HCY, homocysteine.

*$P < .05$ for between-group difference.

†$P < .05$ for within-group difference ($v$value at randomization).

the end of the blinded phase. Both the treatment and placebo groups were similar at randomization (9.8 mg/ⱼ.mol/L $v$ 9.4 mg/ⱼ.mol/L, $P = .49$). The treatment group showed a significant reduction over 8 weeks, with the median plasma homocysteine dropping to 8.7 mg/j.mol/L ($P = .02$). The placebo group showed no change (8-week plasma homocysteine, 9.2 mg/ⱼ.mol/L; $P = .98$).

Between-group differences never exhibited statistical significance for HDL-C or TG (Table 2). HDL-C increased modestly for both groups (treatment group, $+2.3\% \pm 11.3\%$; placebo group, $+5.1\% \pm 9.9\%$; $P = .19$) as did glucose (treatment, $+2.7\% \pm 15.0\%$; placebo, $+4.0\% \pm 18.2\%$; $P = .70$). TG concentrations decreased somewhat in the treatment group ($-5.3\% \pm 23.7\%$), while increasing slightly in the placebo group ($+4.3\% \pm 42.5\%$), but the difference was not statistically significant ($P = .17$).

The treatment and placebo groups showed similar baseline dietary habits for soluble fiber, fat calories, saturated fat, protein, and alcohol (Table 3). However, total caloric intake, total fiber, and carbohydrate intake were different at randomization. The only statistically significant change in dietary pattern from randomization to the end of the blinded phase was a decrease in soluble fiber intake for the treatment group ($P = .04$). A similar, though not statistically significant, tendency was seen in the placebo group ($P = .09$). This result precludes fiber being associated with the test product itself.

Including baseline dietary fiber intake (ie, not associated with test product) in the mixed models for LDL-C response does not dampen the observed treatment effect. Similarly, incorporating the change in soluble fiber intake does not affect the primary conclusions that LDL-C concentrations were significantly reduced in the treatment group. Neither fiber intake ($P = .49$) nor change in soluble fiber intake ($P = .61$) from the diet alone were significantly related to LDL-C reduction in these models. Stool consistency was not different between groups at randomization ($P = .98$) or at the end of the blinded phase ($P = .54$). Moreover, there was no change over time within the treatment ($P = .99$) or placebo groups ($P = .86$).

## DISCUSSION

In this preliminary, double-blind randomized clinical trial, we found a high soluble fiber mixture, supplemented with a full

**Table 3. Median and Interquartile Range for Diet Parameters at Baseline (1) and End of Blind Visit (2) With Between-Group *P* Values**

|  | Treatment | Placebo | P Value* |
|---|---|---|---|
| Calories1 | 1,952 (1,696-2,462) | 1,855 (1,372-2,189) | 0.06 |
| Calories2 | 2,047 (1,575-2,607) | 1,741 (1,415-2,114) | 0.13 |
| Fiber1 | 23 (17-32) | 19 (14-24) | 0.03 |
| Fiber2 | 20 (16-27) | 16 (13-24) | 0.05 |
| Soluble fiber1 | 3.3 (2.1-4.9) | 3.4 (2.0-4.4) | 0.60 |
| Soluble fiber2 | 3.0 (1.9-4.9) | 2.9 (1.8-4.9) | 0.94 |
| Fat calories1 | 596 (439-802) | 468 (362-668) | 0.10 |
| Fat calories2 | 644 (435-804) | 563 (438-695) | 0.36 |
| Saturated fat1 | 166 (129-258) | 143 (98-222) | 0.14 |
| Saturated fat2 | 195 (111-288) | 163 (131-217) | 0.53 |
| Protein1 | 83 (69-110) | 78 (62-89) | 0.15 |
| Protein2 | 81 (61-108) | 73 (66-90) | 0.30 |
| Carbohydrate1 | 270 (205-329) | 217 (169-300) | 0.03 |
| Carbohydrate2 | 258 (213-329) | 222 (172-279) | 0.04 |
| Alcohol1 | 0 (0-10) | 0 (0-11) | 0.99 |
| Alcohol2 | 0 (0-13) | 0 (0-13) | 0.89 |

NOTE. Calories, fat calories and saturated fat are reported as calories, while the remaining parameters are reported as grams.

*Wilcoxon rank-sum tests.

complement of vitamins, to reduce LDL-C by 10% compared to placebo, without adverse effects on HDL-C or TG concentrations. The LDL:HDL ratio significantly improved, and ApoB levels decreased in a representative subsample. The expected modest reduction in homocysteine was observed. Such a supplement could represent a valuable agent in the growing demand for nonsystemic cardiovascular prevention therapies.

In the 49 subjects of the treatment group, this fiber supplement produced an average 7.9% reduction in LDL-C from baseline, during a concurrent 8-week period in which the placebo group LDL-C increased 2.4%. The observed 17-mg/dL LDL-C reduction was consistent with the 1-g soluble fiber per 2.2 mg/dL LDL-C decrease expected based on a recent meta-analysis.[7] The reduction was already observed at the mid 4-week point, which was then subsequently maintained for the additional 4 weeks. Twelve percent of the treatment group achieved 20% or better LDL-C reduction, and the patients appeared to tolerate the supplement without a change in gastrointestinal activity. ApoB decreased coordinately ($r = .27$) with the LDL-C concentrations. In fact, there was a suggestion that ApoB decreased more than LDL-C, leading perhaps to a less dense LDL-C particle and thereby less cardiovascular toxicity.[8] Hunninghake et al[9] recently reported a fiber product that similarly demonstrated an overall 9% LDL-C decrease from placebo, with a companion article[10] indicating an ApoB decrease that evaporated by the 15th week. In addition, the observed LDL-C lowering diminished by the 9th week of fiber intake, all consistent with our own data. We found ApoB and LDL-C lowering markedly diminished if not lost by the 16th week. Compliance appears to be the most likely basis for these outcomes, but it remains possible that some biologic tolerance is a contributing factor. The specific type of fiber is potentially relevant in this regard, as psyllium has only modest effects on ApoB.[11]

Multiple fiber products[1] have provided LDL-C lowering, and mild HDL-C/TG changes. Meta-analyses of 8 controlled trials related to psyllium suggested a 7% average reduction in LDL-C, along with subtle 1% to 3% increases in TG and decreases in HDL-C. Guar gum/pectin combination therapy provided 7% to 8% reductions in LDL, with LDL-C:HDL-C ratio reductions of 6% to 9%[10] and no clear change in HDL-C or TG. This is consistent with the 9% reduction in the LDL-C:HDL-C ratio we observed. While there was no clear tendency for a reduced HDL-C or increased TG in our current study, a downward trend in TG was observed during the blinded phase. Bile acid sequestrants, which target bile acid absorption and are thought to parallel the physiologic action of fiber products, do produce significant increases in TG concentrations.[12] The basis for relatively little change in TG concentrations with fiber compared to bile-absorbing resins remains unclear.

The incorporation of 240 $\mu$g of daily folic acid, along with 18 $\mu$g of vitamin $B_{12}$ and 7.2 mg vitamin $B_6$, into the fiber preparation resulted in a modest but anticipated reduction in homocysteine. Given the reported influence of fiber on the absorption of $Ca^{2+}$,[13] beta-carotenoids,[14] and fat-soluble vitamins,[15] as well as vitamin $B_6$[3,4] via the intestinal system, we thought it prudent to address this issue. At low baseline concentrations of homocysteine with an average 500 $\mu$g folate

dose, we might have expected a nearly 20% decrease, rather than the 10% decrease observed.[16] However, we can still reasonably conclude that supplementation with these B vitamins modestly promotes homocysteine changes, even in the setting of fiber coadministration, consistent with reports suggesting fiber does not alter vitamin $B_6$.[17,18] Given the supplemental folic acid included today in many typical fortified food items, it is noteworthy that a modest trend was still observed. In addition, serum glucose concentrations did not change, suggesting little influence on glucose intestinal uptake and metabolism in nondiabetic subjects.

The recent NCEP Adult Treatment Program guidelines strongly support the use of fiber to lower elevated LDL concentrations.[19] We demonstrate that this fiber-vitamin mixture attains the LDL reduction anticipated, while permitting the homocysteine-related benefit of B vitamins. Long-term studies should be undertaken to preclude ultimate tolerance to this agent. Such a product, if taken regularly, could reduce cardiovascular risk on a population basis and potentially decrease the need and/or dose for lipid-lowering prescription drugs.

## ACKNOWLEDGMENT

## REFERENCES

1. Anderson JW, Allgood LD, Lawrence A, et al: Cholesterol-lowering effects of psyllium intake adjunctive to diet therapy in men and women with hypercholesterolemia: Meta-analysis of 8 controlled trials. Am J Clin Nutr 71:472-479, 2000

2. Sprecher DL, Harris BV, Goldberg AC, et al: Efficacy of psyllium in reducing serum cholesterol levels in hypercholesterolemic patients on high- or low-fat diets. Ann Intern Med 119:545-54, 1993

3. Reynolds RD:Bioavailability of vitamin B-6 from plant foods. Am J Clin Nutr 48:863-86 1988

4. Keagy PM, Shane B, Oace SM: Folate bioavailability in humans: Effects of wheat bran and beans. Am J Clin Nutr 47:80-88, 1988

5. Conover W: Practical Nonparametric Statistics (ed 2). New York, NY, Wiley, 1980, p 493

6. Littell R, Milliken G, Stroup W, et al: SAS System for Mixed Models. Cary, NC, SAS Institute, 1996, p 633

7. Brown L, Rosner B, Willett WW, et al: Cholesterol-lowering effects of dietary fiber: A meta-analysis. Am J Clin Nutr 69:30-42, 1999

8. Superko HR, Krauss RM: Coronary artery disease regression. Convincing evidence for the benefit of aggressive lipoprotein management. Circulation 90:1056-1069, 1994

9. Hunninghake DB, Miller VT, LaRosa JC, et al: Long-term treatment of hypercholesterolemia with dietary fiber. Am J Med 97:504-508, 1994

10. Hunninghake DB, Miller VT, La Rosa JC, et al: Hypocholesterolemic effects of a dietary fiber supplement. Am J Clin Nutr 59:1050-1054, 1994

11. Anderson JW, Garrity TF, Wood CL, et al: Prospective, randomized, controlled comparison of the effects of low-fat and low-fat plus high-fiber diets on serum lipid concentrations. Am J Clin Nutr 56:887-894, 1992

12. Sprecher DL, Abrams J, Allen JW, et al: Low-dose combined therapy with fluvastatin and cholestyramine in hyperlipidemic patients. Ann Intern Med 120:537-543, 1994

13. Wolf RL, Cauley JA, Baker CE, et al: Factors associated with calcium absorption efficiency in pre- and perimenopausal women. Am J Clin Nutr 72:466-471, 2000

14. Riedl J, Linseisen J, Hoffmann J, et al: Some dietary fibers reduce the absorption of carotenoids in women. J Nutr 129:2170-2176, 1999

15. Khokhar S, Kapoor AC: Effect of dietary fibres on bioavailability of vitamin A and thiamine. Plant Foods Hum Nutr 40:259-265, 1990

16. Homocysteine Lowering Trialists' Collaboration: Lowering blood homocysteine with folic acid based supplements: Meta-analysis of randomised trials. BMJ 316:894-898, 1998

17. Shultz TD, Leklem JE: Vitamin B-6 status and bioavailability in vegetarian women. Am J Clin Nutr 46:647-651, 1987

18. Hudson CA, Betschart AA, Oace SM: Bioavailability of vitamin B-6 from rat diets containing wheat bran or cellulose. J Nutr 118:65-71, 1988

19. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 285:2486-2497, 2001

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# Beneficial effects of Bios Life 2® (Dietary Fiber Supplement) in patients with dyslipidemia

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## ABSTRACT

The importance of dietary fibers in lowering cholesterol levels is not well recognized by the general public and medical practitioners. The lipid and sugar-lowering effects of dietary fibers, particularly the BioSphere fiber matrix, have been investigated in the Caucasian population but not in Asians. This study was done to determine the cholesterol-lowering effect of dietary fibers in adult patients.

This is an experimental, uncontrolled study involving a total of 103 patients. Baseline total cholesterol determination was done after which subjects were given six grams of the BioSphere fiber blend for four weeks and were advised to follow a low fat diet. A repeat total cholesterol determination was done after four weeks.

Most patients who are dyslipidemic are hypertensive, which comprised 68.9 percent of the study population. Hypercholesterolemia is more common in the female group compared with males. Sex has a relation on the levels of baseline total cholesterol with computed X2 value of 9.94 compared to the tabular value at five percent with two degrees of freedom (df), of 5.99. Female response to the treatment is significantly greater than male, with a computed X2 of 9.92 and tabular X2 value at five percent with 2 df of 5.99.

Analysis of treatment effect using the Student T-test yielded a computed T value of 10.040 and tabular T value of 1.986 at five percent with 102 df, which is a significant result.

The percentage decrease in the baseline total cholesterol of all the subjects combined is 15.9 percent.

## Introduction

Hypercholesterolemia is the elevation of fasting plasma total cholesterol in the presence of normal levels of triglycerides and is associated with increased concentrations of plasma LDL cholesterol. LDL carries about 65 to 75 percent of total plasma cholesterol [207]. The normal range for total blood cholesterol is less than 200 mg/dL. For higher levels, the risk of heart disease begins to rise. Given the high-stake consequences of high cholesterol being heart attacks and strokes, estimates are that 102.3 million American adults have total blood cholesterol values of 200 mg/dL and higher, and about 41.3 million American adults have levels of 240 mg/dL or higher. In adults, total cholesterol levels of 240 mg/dL or higher are considered high, and levels from 200 to 239 mg/dL are considered borderline-high [208].

In May of 2001, the National Cholesterol Education Program revised its statin drug recommendations. As a result, the number of patients qualifying for prescription drug treatment went as high as 36 million as compared to a previous 13 million patients. Statin drugs are often associated with side effects such as nausea, headaches, dizziness, sleep disturbances, liver problems, muscle weakness, and pain. One statin drug, cerivastatin (Baycol®), was recalled by the manufacturer in August 2001 after it was found to be linked to more than 50 deaths. In addition

to these risks, the average cost of statin drugs is more than $100 a month. Since the revised guidelines mean big business for pharmaceutical companies, it's no wonder that news of the natural alternatives to these drugs has remained unknown to the general public [209].

The search for alternative medicines or dietary supplements should be done in order to reduce the risk of cardiovascular diseases with the benefit of minimizing the side effects of lipid-lowering agents.

## Objectives of the study:

### Significance of the Study

The inclusion of fibers in the diet of persons at risk of developing cardiovascular disease is normally not emphasized by clinicians. Focus has been on the prescription of synthetically manufactured medicines like lipid-lowering agents, antihypertensive medicines, and sugar-lowering agents. The general public is not aware of the beneficial effects of fibers, thus consumption of more fiber is not advocated by most physicians. Most studies on fibers have been done on Caucasians. No study has been done on Asians to evaluate cholesterol-lowering effects of dietary fibers.

There is growing awareness of risk of having elevated cholesterol levels among Filipinos and the high prices of lipid-lowering agents, coupled with their side effects. This study was done to evaluate if dietary fiber will be effective among other race groups than Caucasians in lowering the serum cholesterol level since a reduction would prevent complications like diabetes, hypertension, and coronary artery disease.

### Review of Related Literature

A study has been performed by the Cleveland Clinic Foundation using the BioSphere fiber blend of Bios Life which is a unique, fiber-rich nutrient drink mix that can support healthy cholesterol and blood sugar levels when combined with a healthy lifestyle. A total of 119 patients was randomized for the trial. All of the patients were required to eat the same low-fat diet for the six weeks leading up to the trial and then continue on a controlled diet throughout the trial. This isolated the variable of diet. In other words, the patients' diets could not have been the cause of any difference in serum cholesterol as all of the patients had been following the same diet. Ninety-nine patients completed the trial (50 on Bios Life and 49 on placebo). Blood work was done at the fourth and the eighth week of the trial. Significant LDL- and ApoB-lowering effects were demonstrated. No adverse effects on triglyceride or HDL-c levels were noted, and folate/B vitamin-derived benefits toward homocysteine reduction were preserved. This combination product could be used to reduce the need for concomitant lipid-lowering prescription therapy as well as for advancing self-styled primary prevention strategies [210].

The randomized controlled trial done at Cleveland Clinic using Bios Life has yielded significant recommendations for the beneficial effects of the fiber supplement. Bios Life is one of the fiber products that seems superior to other fiber supplements because it contains a mixture of different kinds of dietary fibers such as guar gum, locust bean gum, pectin, oat fiber, gum acacia, barley, and stevia.

Lipoprotein substances (combination of a fat and a protein) act as carriers for cholesterol and fats in the bloodstream. High levels of low density lipoprotein (LDL) are considered a positive risk factor for the development of coronary artery disease. Blood levels of less than 130 mg/dL are desirable, 130 to 159 mg/dL are borderline high, over 160 mg/dL are considered high.

The mechanism of action of statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) is different from fibers, but their effects are comparable. This was demonstrated by a study done in July 2003 where a portfolio of cholesterol-lowering foods versus lovastatin showed comparable reduction in the lipid levels of the study subjects [211].

### Materials and Methods

### Study Design

The study followed the experimental uncontrolled design. This involves one group of intervention users that was evaluated pre- and post-intervention.

## Subjects

### Inclusion Criteria

Adult patients, age 18 years and above, diagnosed of dyslipidemia who are not taking any lipid-lowering agent were included in the study. Patients who have stopped taking lipid-lowering agent for at least one month were also included in the study.

### Exclusion Criteria

Patients who are azotemic, have active liver disease, or are patients with malabsorption syndrome were excluded from participating.

### Scope and Limitation of the Study

The study is an uncontrolled experimental study. The compliance of patients was monitored through telephone calls. They were advised regarding their diet and intake of the fiber supplement.

### Patient Follow-up and Instructions

The patients were given six grams of Bios Life daily for four weeks. They were advised to remain on their usual low-fat diet. Baseline serum total cholesterol was determined prior to the administration of Bios Life. After four weeks, the serum total cholesterol measurement was repeated. No attempt was made to blind the subjects or the study personnel. Patients were classified according to age, sex, and the presence of hypertension, diabetes, and coronary artery disease and/or myocardial infarction was noted.

### Definition of Terms

*Hypercholesterolemia* – total cholesterol level of 200 mg/dL or greater.

*Desirable cholesterol* – total cholesterol level of less than 200 mg/dL.

*Borderline cholesterol* – total cholesterol between 200 to 239 mg/dL.

*Undesirable cholesterol* – total cholesterol level of 240 mg/dL or greater.

### Time and Place of Study

The study was conducted at Angeles University Foundation Medical Center from May 1, 2003, to October 30, 2003, on an out-patient basis; 103 patients were included in the study.

## Statistical Analysis

Patients' levels of total cholesterol were classified as desirable, borderline, and undesirable. The mean, percentage, and frequency were used in describing the age, sex, and clinical profile of the patients while the pre- and post-treatment total cholesterol levels were analyzed by using the students' T-test (two-tailed) and expressed as means +/- standard error of the mean. To test the correlation between age and sex and the baseline and post-treatment total cholesterol levels, the Chi square test was used.

## Results

Included in the study were 103 patients who had their baseline cholesterol determined and were followed up until four weeks of treatment with Bios Life.

Figure 37 shows the age distribution of the subjects. Patients' ages ranged from 25 to 84 years. There is an increase in frequency among age group 65 to 74 years, which totaled 28 patients, and the smallest age group was the 25 to 34 group, which accounted for three subjects. Twenty-seven percent of the subjects were male, and 73 percent were female.

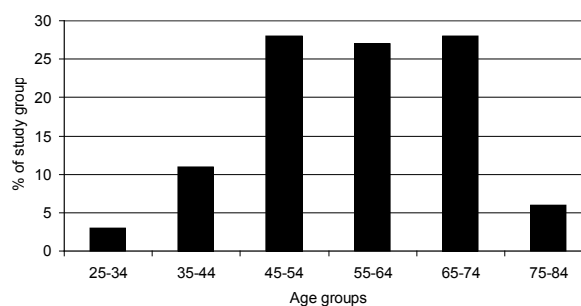Figure 37. Age distribution of the included subjects.



Figure 38 shows that about 68 percent of the patients are hypertensive, of whom most are in the age group of 65 to 74 years.

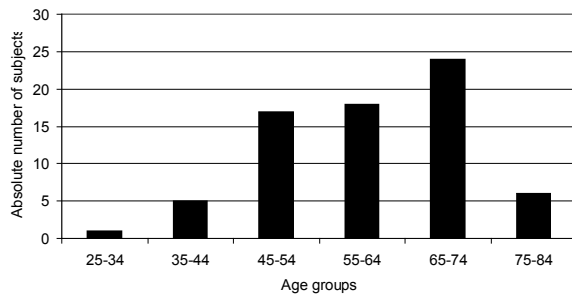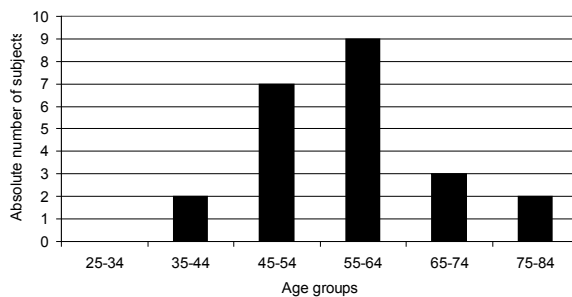Figure 38. Absolute number of hypertensive subjects.



Figure 39 shows that 22 percent of the patients are diabetic. Most are in the age group of 55 to 64 years.

Figure 39. Absolute incidence of diabetes in the subject group.



In Figure 40, it was shown that most patients with CAD (coronary artery disease) or previous myocardial infarction are in the age group of 65 to 74 years, comprising approximately 10 percent of the patient population.

Figure 40. Absolute incidence of CAD or previous MI in the subject group.
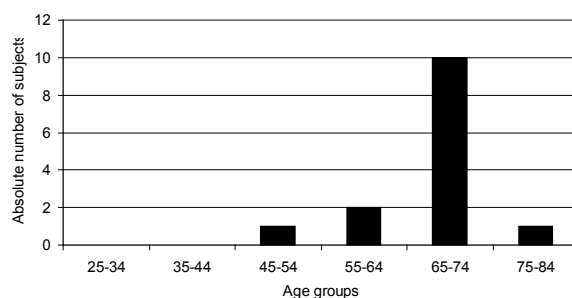


Most of the hypertensive patients are female, comprising 48 percent of the study group. Also most of the diabetics (14 percent) and those with CAD (12 percent) or previous myocardial infarction are female.

The incidence of hypertension is high in patients who have dyslipidemia. Of the study population 68.9 percent are hypertensive, 22.3 percent are diabetic, and 13.59 percent have a history of myocardial infarction or coronary artery disease.

Figure 41 shows that the frequency of having undesirable cholesterol levels is highest in the age group of 65 to 74 years with 23 patients, and smallest in the 25 to 34 age group, accounting for two patients. Statistical analysis using chi-square was then applied to determine if age affects cholesterol levels. Analysis revealed a computed $X2$ of 8.89 which is not statistically significant as compared to the tabular $X2$ value at five percent with 10 degrees of freedom, which equals to 18.31. This shows that although there is an increasing trend noted among the age group of 65 to 74, age has no correlation with the levels of cholesterol. Also after four weeks of intervention, this correlation did not exist.

Figure 41. Baseline LDL level distribution among the study subjects, according to the NCEP guidelines.
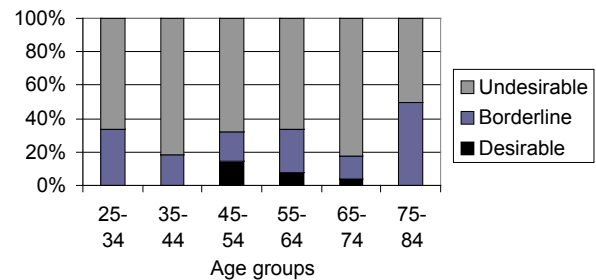


Figure 42. LDL cholesterol levels post treatment in the subject group according to NCEP guidelines.
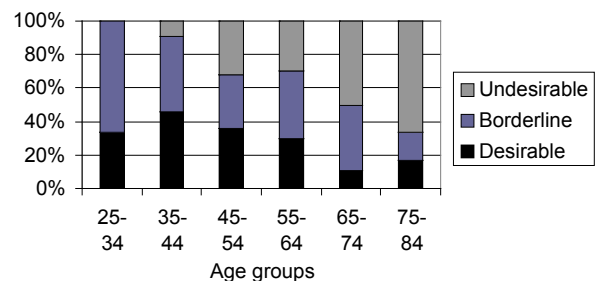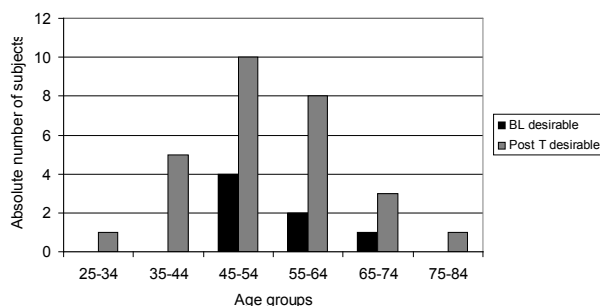
Figure 43. Baseline desirable versus post-treatment desirable LDL.



Sex has a significant effect on the levels of cholesterol, both in the baseline and post-treatment phase with computed X2 value of 9.94 compared to the tabular value at five percent with 2 df, of 5.99. Treatment applied among all age groups revealed a computed X2 of 9.92 as compared with tabular X2 value at five percent with 2 df of 5.99. In conclusion, there is a statistical significant greater reduction in the total cholesterol levels in the female population compared to the male population.

Statistical analysis using student T test revealed a significant effect of Bios Life in lowering total cholesterol with a computed T value of 10.040 and tabular T value of 1.986 at five percent with 102 degrees of freedom. In summary, the percentage decrease in the baseline total cholesterol of all the subjects combined is 15.9 percent.

## Discussion

Hypercholesterolemia has shown to be one of the major risk factors for atherosclerosis. Over the past three decades a variety of epidemiological, animal, and human trials has demonstrated the preventive and therapeutic benefits of dietary fibers on hypercholesterolemia and reduction of the mortality rate of CAD.

The mechanism of the reduction of plasma cholesterol by dietary fibers is controversial. The increase in the bile acid excretion among patients increasing fiber intake probably explains most of the reduction, and a reduction in cholesterol absorption may have contributed to this finding [212].

In our study we were able to demonstrate the cholesterol-lowering effect of the BioSphere fiber matrix of Bios Life in four weeks' time. Most likely our patients also have increased excretion of bile acids in their stools, but we did not determine this.

Diversifying the content of a cholesterol-lowering diet is the key in obtaining significant reduction of lipid levels since the various types of fibers have different functions. Some absorb water, making the stool softer and increasing the transit time of feces in the colon, and this is particularly true for the non water-soluble dietary fibers.

A high intake of dietary fiber, particularly the soluble type, above the level of the recommendations of the American Diabetic Association (25 to 30 g), improves glycemic control, decreases hyperinsulinemia, and lowers plasma lipid concentration in patients with type II diabetes. Among patients with established coronary artery disease and who are post-myocardial infarction, dietary fibers could reduce the serum total and LDL cholesterol levels and delay the progression and increase the overall regression of coronary artery disease [213].

Non water-soluble fibers increase stool bulk by absorbing water and making the stool softer, which prevents constipation and possibly diverticulosis.

The combination of soluble and insoluble fibers as in Bios Life works in the intestinal tract by binding fats ingested during a meal and by "pulling" cholesterol, especially LDL cholesterol, from the circulatory system into the bowel. These two functions lower blood cholesterol, LDL cholesterol, and serum triglyceride levels simultaneously.

In our study there is increased frequency of females with elevated cholesterol with hypertension, diabetes, and coronary artery disease. There is ample evidence that women with coronary heart disease and hypercholesterolemia should be treated as aggressively as men. An elevated serum cholesterol level in women is as predictive of later CHD events as it is in men. The prognosis for women with CHD (coronary heart disease) is similar to or worse than that of men. Therefore, the old idea of women being at lower risk vanishes when CHD is documented. It is not surprising that trials of lipid-lowering agents

Bios Life Science

show similar levels of effectiveness.

There is a great deal of evidence that people with high blood pressure and/or blood cholesterol levels have a greater risk of developing cardio-vascular diseases. The higher the blood pressure and/or cholesterol level, the greater the risk.

## Conclusions

In our study group, hypertension was most prevalent, followed by diabetes and coronary artery disease. An increase in the incidence of dyslipidemia was noted in the elderly subjects, but statistical analysis revealed this is not significant. Young and elderly patients can develop hypercholesterolemia just as effectively.

As to gender, there is a greater number of females who have increased cholesterol levels but when treatment was applied using Bios Life, they showed greater reduction in cholesterol levels compared to males. There was a 15.9 percent reduction in the total cholesterol of the subject group, showing that Bios Life is beneficial in patients with dyslipidemia in lowering total cholesterol levels. Bios Life, therefore, prevents atherosclerosis, which leads to a decrease in prevalence of hypertension, diabetes mellitus, and coronary artery disease and/or angina pectoris.

### Recommendations

It is recommended that further studies be conducted, preferably randomized controlled trials, and that the clinical outcomes like mortality, morbidity, and other co-morbid factors will be evaluated in patients receiving Bios Life.

Patients with elevated total cholesterol should take Bios Life if their diet is not sufficient to meet the daily intake of 20 to 35 grams of fiber as recommended by the American Dietetic Association.

# 10

# The Clinical Impact of Fiber Supplementation for the Reduction of Postprandial Blood Glucose and Risk Reduction of Complications from Diabetes

by Steven H. Freed
and David J. Joffe

**The Clinical Impact of Fiber Supplementation for the Reduction of Postprandial Blood Glucose and Risk Reduction of Complications from Diabetes**

**Abstract**:

**OBJECTIVE**: The prevalence of diabetes has increased dramatically in recent years[1].  However, the role of dietary fiber in blood glucose regulation remains unclear.  The purpose  of this work was to investigate the acute effects of supplementing the diet with soluble fiber   in regards to it's glucose and cholesterol lowering thereby reducing the HbA1c and therefore the complications from diabetes.   By reducing the HbA1c (Average Blood Glucose) 1%, the DCCT[2] study showed Type 1 diabetics could reduce the complications of  Retinopathy by 38%, Nephropathy by 28% Neuropathy by 35%.  The UKPDS[3] showed that by reducing the HbA1c in Type 2 diabetics by 0.9% you could reduce any diabetic end point by 12%, reduce any Microvascular end point by 25%, reduce MI by 16%, reduce Retinopathy by 21% and reduce microalbuminurea at 12 years by 34%.

The UKPDS also showed that Postprandial (blood glucose 1-2 hours after eating) glucose is a better indicator of glycemic control than fasting glucose levels[4].  Treatment of postprandial hyperglycemia is critical to achieving optimal outcomes in type 2 diabetes[5].

The New England JM[6] 5/2000 showed that a high intake of dietary fiber 50 gms particularly  of the soluble type, improves glycemic control, decreases hyperinsulinemia, and lowers plasma lipid concentrations in patients with type 2 diabetes.

**METHODS**: After 30 days of monitoring fasting and postprandial blood glucose, a base HbA1c (9.2%), cholesterol screen-total cholesterol (210), Triglycerides (299), HDL (35), weight (208lbs.)and blood pressure(145/82), Average Postprandial blood glucose(250mg/dl.), average fasting blood glucose (150mg/dl.) were taken.  Fifteen patients (7male/8 female), average age 65, were given 10grams of soluble fiber to be added to their diet of 15-20 grams.  Fiber consisted of Guar Gum, Gum Arabic, Locust Bean Gum, Pectin, Oat Fiber (Source of Beta Glucans), and Stevia dispersed in Calcium Carbonate.  Five grams were taken twice daily 5-10 minutes prior to eating for 90 days.  They continued to monitor fasting and postprandial blood glucose through the study period.  At the conclusion  of the 90 day period, their levels were measured.

**RESULTS**: Compliance with the fiber diet and supplementation was excellent. During the   12 weeks of the high-fiber diet and supplementation, mean daily preprandial plasma glucose concentrations were 17 percent lower (95 percent confidence interval).   The high-fiber diet and supplementation also lowered the area under the curve for 2-hour plasma glucose concentrations, by 36 percent. The high-fiber diet and supplementation reduced plasma total cholesterol concentrations by 12 percent, triglyceride concentrations by 42 percent, raised high-density lipoprotein cholesterol concentrations by 6 percent, reduced body weight by an average of 6 pounds, lowered blood pressure from 145/82 to 131/77 and lowered HbA1c from 9.2% to 7.8%(1.4 decrease).

**CONCLUSIONS**: A high intake of dietary fiber, particularly of the soluble type, above the level recommended by the ADA (25-30grm.), improves glycemic control, decreases hyperinsulinemia, and lowers plasma lipid concentrations in patients with type 2 diabetes. Reducing postprandial blood glucose significantly caused a decrease of HbA1c by 1.4%, therefore reducing the complications from diabetes.[2-5-6]

1-Beckles GLA et al. Diabetes Care. 1998;21:1432-1438.American Diabetes Association. Diabetes Care. 1998;21(Suppl 1).Colwell JA. Ann Intern Med. 1996;124(1pt2):131-135.Abraira C et al. Diabetes Care. 1992;15:1560-1571.Klein R et al. Am J Epidemiol. 1987;126:415-428.Cowie CC et al. Diabetes in America. 2nd ed. vol. 44, November ol. 44, November, 1995.
2- The New England Journal of Medicine -- September 30, 1993 -- Vol. 329, No. 14-DCCT research group, Diabetes 95;44:969-983;
3- Hawaii Med J 2000 Jul;59(7):295-8, 313; BMJ. 2000 Aug 12;321(7258):405-12.
4- Harris et al. Diabetes Care. 1994.
5- De Veciana et al. N Engl J Med. 1995;333:1239
6- NEJM May 11, 2000 - Vol. 342, No. 19; Klein, R, Diabetes Care. 1996:18:258-268

Source Information. Can J Physiol Pharmacol June 1988; J Am Coll Nutr Aug 1996; Jama 1999;282; Am J Clin Nut 1993;58:513-8; Ann Intern Med April 1978; Va Med Nov 1979;  Vopr Pitan 1994; Am Fam Physician Apr. 1989; Am J Clin Nutr Nov 1991; Can J Physiol Pharmacol June 1988

# 11

# The Clinical Impact of Fiber Supplementation for the Reduction of Postprandial Blood Glucose and Risk Reduction of Complications from Diabetes II

by Steven H. Freed
and David J. Joffe

Diabetes in Control published in *Diabetes In Control* Newsletter, Issue 212 (1) : 17 2004 June

## OBJECTIVE

The prevalence of diabetes has increased dramatically in recent years[1]. However, the role of dietary fiber in blood glucose regulation remains unclear. The purpose of this work was to reaffirm the acute effects of supplementing the diet with soluble fiber in regards to it's glucose and cholesterol as indicated in the first study.

By reducing the HbA1c (Average Blood Glucose) 1%, the DCCT[2] study showed Type 1 diabetics could reduce the complications of Retinopathy by 38%, Nephropathy by 28% Neuropathy by 35%. The UKPDS[3] showed that by reducing the HbA1c in Type 2 diabetics by 0.9% you could reduce any diabetic end point by 12%, reduce any Microvascular end point by 25%, reduce MI by 16%, reduce Retinopathy by 21% and reduce microalbuminurea at 12 years by 34%.

The UKPDS also showed that Postprandial (blood glucose 1-2 hours after eating) glucose is a better indicator of glycemic control than fasting glucose levels[4]. Treatment of postprandial hyperglycemia is critical to achieving optimal outcomes in type 2 diabetes[5].

The New England JM[6] 5/2000 showed that a high intake of dietary fiber 50 gms particularly of the soluble type, improves glycemic control, decreases hyperinsulinemia, and lowers plasma lipid concentrations in patients with type 2 diabetes.

## METHODS

After 30 days of monitoring fasting and postprandial blood glucose, the following base values were gathered  HbA1c (9.03%), total cholesterol (215), Triglycerides (299), LDL(129), HDL (43), weight (182lbs.) and blood pressure(141/83). Average Postprandial blood glucose(278mg/dl.), average fasting blood glucose (173mg/dl.) were also taken. 78 patients (42male/36 female), average age 59, were given 10-15 grams of soluble fiber to be added to their diet. Fiber consisted of Guar Gum, Gum Arabic, Locust Bean Gum, Pectin, Oat Fiber (Source of Beta Glucans), and Stevia dispersed in Calcium Carbonate. In addition this product contained chromium polynicotinate, and B-vitamins. Five grams were taken twice to 3 times daily 5-10 minutes prior to eating for 90 days. They continued to monitor fasting and postprandial blood glucose through the study period. At the conclusion of the 90 day period, their levels were remeasured.

## RESULTS

As with the first study compliance with the fiber supplementation was excellent. During the 12 weeks of the high-fiber supplementation, mean daily preprandial plasma glucose concentrations were 17mg/dl lower (95 percent confidence interval). The high-fiber supplementation also lowered the 2-hour plasma glucose concentrations, by 41 mg/dl. The high-fiber supplementation reduced plasma total cholesterol concentrations by 31 mg/dl, triglyceride concentrations by 42 mg/dl, raised high-density lipoprotein cholesterol concentrations by 12 mg/dl, lowered LDL by 37 mg/dl, reduced body weight by an average of 6 pounds, lowered blood pressure from 130/84 to 127/82 and lowered HbA1c from 9.0% to 8.1%(0.9 decrease).

## CONCLUSIONS

As indicated in the first study and reaffirmed in this new study, high intake of dietary fiber, particularly of the soluble type, above the level recommended by the ADA (25-30grm.), improves glycemic control, decreases hyperinsulinemia, and lowers plasma lipid concentrations in patients with type 2 diabetes. Reducing postprandial blood glucose significantly caused a decrease of HbA1c by 0.9%, therefore reducing the risk of complications from diabetes. [2-5-6]

### References

1-Beckles GLA et al. Diabetes Care. 1998;21:1432-1438.American Diabetes Association. Diabetes Care. 1998;21(Suppl 1).Colwell JA. Ann Intern Med. 1996;124(1pt2):131-135.Abraira C et al. Diabetes Care. 1992;15:1560-1571.Klein R et al. Am J Epidemiol. 1987;126:415-428.Cowie CC et al. Diabetes in America. 2nd ed. vol. 44, November ol. 44, November, 1995.

2- The New England Journal of Medicine - - September 30, 1993 -- Vol. 329, No. 14-DCCT research group, Diabetes 95;44:969-983;

3- *Hawaii Med J* 2000 Jul;59(7):295-8, 313; BMJ. 2000 Aug 12;321(7258):405-12.

4. Harris et al. *Diabetes Care*. 1994.

5- De Veciana et al. *N Engl J Med.* 1995;333:1239

6- NEJM May 11, 2000 - Vol. 342, No. 19; Klein, R, Diabetes Care. 1996:18:258-268

Source Information. Can J Physiol Pharmacol June 1988; J Am Coll Nutr Aug 1996; Jama 1999;282; Am J Clin Nut 1993;58:513-8; Ann Intern Med April 1978; Va Med Nov 1979; Vopr Pitan 1994; Am Fam Physician Apr. 1989; Am J Clin Nutr Nov 1991; Can J Physiol Pharmacol June 1988

# 12
# The clinical impact of fiber supplementation on cardio-vascular risk parameters in type 2 diabetes

by Peter J.E. Verdegem, Ph.D., Steven H. Freed, R.Ph., and David J. Joffe, R.Ph.,CDE, FACA

Diabetes In Control.com, and Unicity International, Orem, UT

## Introduction

Fiber supplementation, in particular of the soluble kind, has known beneficial effects in lowering the cardio-vascular risk profile by lowering serum cholesterol. It is thought that bile-acid sequestration of cholesterol in the digestive system is the main mechanism for cholesterol reduction. This study investigates the efficacy of Bios Life 2®, a fiber supplement combining soluble and insoluble fiber, that has been specifically designed for cholesterol lowering.

## Methods

This study included 78 type 2 diabetes patients with an average age of 59. At baseline, total cholesterol, triglycerides, LDL, and HDL were assessed. The subjects then added 10–15 gram of the fiber supplement to their diet for 90 days. At the final visit, the parameters were re-assessed. The fiber supplement is taken as a drink, and consists of guar gum, gum arabic, locust bean gum, pectin, and oat fiber dispersed in calcium carbonate. In addition this product contained chromium, and B-vitamins. Five grams were taken 2–3 times daily 5–10 minutes prior to eating.

## Results

The compliance with the fiber supplementation was excellent. The supplementation with fiber resulted in beneficial changes to the assessed parameters. The changes are listed in the table.

## Conclusion

Supplementing the diet with this fiber drink to a level as recommended by the American Heart Association has clear beneficial effects on the lipid profile of type 2 diabetics. This specially designed fiber supplement has promising effects as an alternative treatment to pharmaceutical intervention for hyperlipidemia.

| Parameter | Baseline average | 90-day average | % change |
|---|---|---|---|
| Total cholesterol | 215 mg/dL | 184 | -14.4 |
| Triglycerides | 299 mg/dL | 257 | -14.0 |
| LDL | 129 mg/dL | 92 | -28.7 |
| HDL | 43 mg/dL | 55 | +21.8 |

# 13
# The clinical impact of fiber supplementation on cardio-vascular risk parameters in type 2 diabetes

by Peter J.E. Verdegem, Ph.D.,
Steven H. Freed, R.Ph., and
David J. Joffe, R.Ph.,CDE, FACA

DiabetesInControl.com, and Unicity International, Orem, UT

# THE CLINICAL IMPACT OF FIBER SUPPLEMENTATION FOR THE REDUCTION OF POSTPRANDIAL BLOOD GLUCOSE AND RISK REDUCTION OF COMPLICATIONS FROM TYPE 2 DIABETES

Peter J.E. Verdegem, Ph.D.[a]; Steven H. Freed, R.Ph.[b]; David J. Joffe, R.Ph.[b]

## Introduction

- Diets high in soluble fiber may interfere with glucose uptake from the diet.
- The advised level of fiber, 30 grams per day, is difficult to achieve through diet alone.
- Bios Life 2 is a patented fiber drink mix, designed to lower cholesterol, but case reports also indicate benefits for diabetics.
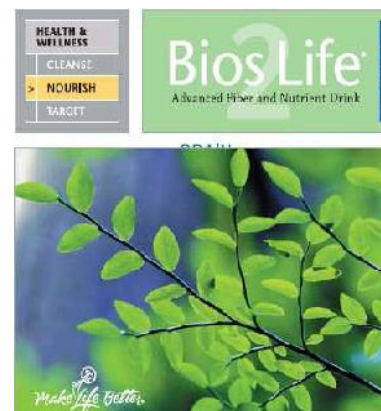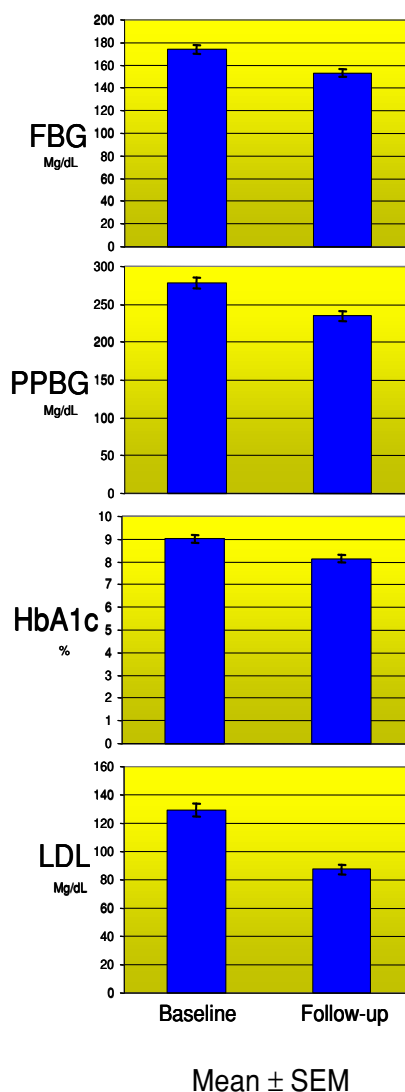
## Objectives

- To study the effect of BiosLife 2 on glycemic and lipid parameters in Type-2 diabetics.

## Study design

- Open label study with 78 Type-2 Diabetics (42 male, 36 female) with average age 59 years.
- Subjects took 10 – 15 grams of Bios Life 2, in 5 grams portions 10 minutes prior to a meal.
- Baseline and follow-up (90 days) measurements of HbA1c, FBG, PPBG, Tot.Chol., LDL, HDL, TG, and weight.
- Statistical analysis with paired Student's T-test.

## Results



Mean ± SEM

| Parameter | Unit | t=0 ± SEM | t=90 ± SEM | Δ | p-value |
|---|---|---|---|---|---|
| Total Chol | mg/dL | 215.5 | 179.5 | − 36.0 | p < 0.000001 |
| LDL | mg/dL | 129.2 | 87.4 | − 41.8 | p < 0.000001 |
| HDL | mg/dL | 43.3 | 59.3 | + 16.0 | p < 0.000001 |
| Triglycerides | mg/dL | 214.8 | 164.1 | − 50.7 | p < 0.000001 |
| Fasting BG | mg/dL | 173.7 | 153.3 | − 20.4 | p < 0.001 |
| Post-prandial BG | mg/dL | 278.1 | 234.4 | − 43.7 | p < 0.0001 |
| HbA1c | % | 9.03 | 8.15 | − 0.88 | p < 0.001 |
| Systolic BP | mmHg | 131.3 | 127.2 | − 4.1 | p < 0.000001 |
| Diastolic BP | mmHg | 82.7 | 81.2 | − 1.5 | p < 0.05 |
| Weight | lb | 182.1 | 175.4 | − 6.7 | ns |

## Discussion

- Increasing soluble fiber intake with Bios Life 2 significantly reduces pre- and post prandial glucose, and HbA1c levels.
- Mechanism is through interaction of carbohydrates with gel matrix formed by soluble fiber.
- Same mechanism reduces lipid and cholesterol levels.

## Conclusion

- **Bios Life 2 is a very beneficial fiber drink mix for Type-2 diabetics, who want to control their glycemic parameters and cholesterol in a natural side-effect free way.**

## References

- Sprecher, *et al*, Metabolism (2002), **51**, 1166.

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www.makelifebetter.com
[b]Diabetes in Control
www.diabetesincontrol.com

# 14
# The clinical impact of fiber supplementation on cardio-vascular risk parameters in type 2 diabetes

by Peter J.E. Verdegem, Ph.D.,
Steven H. Freed, R.Ph., and
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Diabetes In Control.com, and Unicity
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Press release of the American Heart Association

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**Abstract P 284**

**Fiber supplements may lower cardiovascular risk in type 2 diabetes**

WASHINGTON, D.C., April 30 – Fiber supplements lowered "bad" low-density lipoprotein (LDL cholesterol) and increased "good" high-density lipoprotein (HDL cholesterol) in people with type 2 diabetes, according to a study presented at the Sixth Annual Conference on Arteriosclerosis, Thrombosis and Vascular Biology.

Type 2 diabetes occurs when the body is unable to produce or properly use insulin to turn food into energy. Heart disease is the leading cause of diabetes-related deaths. According to the most recent statistics published by the American Heart Association, half of all diabetics have high cholesterol, which is a major risk factor for heart disease.

Supplements that increase dietary fiber have been shown to reduce blood cholesterol levels, which led researchers at Unicity International in Orem, Utah to study its effect on type 2 diabetes.

"The remarkable observation is that this works on two sides: it decreased LDL and increased HDL by significant amounts at 90 days," said the study's lead author, Peter J. Verdegem, Ph.D., chief science officer at Unicity International. "This approach is virtually free of side effects. It opens up an alternative treatment option."

The study is one of the first to examine the effect of fiber in heart disease risk reduction for type 2 diabetes, said Verdegem.

The 78 participants in the open label trial had type 2 diabetes and an average age of 59 years. Total blood cholesterol, triglycerides, LDL and HDL were measured at baseline and again at 90 days.

Cholesterol is a soft, waxy fat that is used by the body to form cell membranes and perform other important functions. Lipoproteins transport cholesterol through the body. LDL escorts cholesterol through the circulatory system; HDL carries it to the liver where it it can be eliminated.

Elevated cholesterol levels can raise the risk of hard deposits called plaques forming in the arteries, which likewise increases the risk of heart attack and stroke. LDL levels of 160 milligrams per deciliter (mg/dL) and above are considered high.

Soluble fiber has been shown to help lower blood cholesterol levels. However, most adults in the United States do not consume enough dietary fiber. According to the American Heart Association, average daily intake for adults is 15 grams, whereas 25 to 30 grams of fiber is recommended.

"The product was designed to fill that gap between the real intake and the advised intake," Verdegem said.

Study participants received 10 to 15 grams of a fiber supplement called Bios Life 2®, an over-the-counter product manufactured by Unicity International. The drink contains both soluble and insoluble fiber from guar gum, gum arabic, locust bean gum, pectin and oat fiber dispersed in calcium carbonate. It was administered in five-gram doses two to three times daily five to 10 minutes before eating.

"When it is in the intestines, the fiber decreases reabsorption of cholesterol from a meal," said Verdegem.

At the end of the study period, total cholesterol had dropped from 215 mg/dL to 184 mg/dL, a decrease of 14.4 percent. Triglycercides also improved. Levels dropped from 299 mg/dL to 257 mg/dL, a decrease of 14.0 percent.

LDL decreased from 129 mg/dL to 92 mg/dL--a 28.7 percent improvement. HDL rose from 43 mg/dL to 55 mg/dL--a 21.8 percent increase.

"With a normal pharmaceutical intervention you see a decrease in LDL but not an increase in HDL to these levels," Verdegem said. "It is usually only a one-sided effect."

Statin drugs are among the most commonly used cholesterol-lowering medications. Verdegem said the study demonstrates that dietary fiber supplements are an alternative to statins for people with moderately high cholesterol who are unable or unwilling to take statins.

Co-authors are Steven H. Freed and David J. Joffe.

# 15
# The Clinical Impact of Fiber Supplementation for the Reduction of Postprandial Blood Glucose and Risk Reduction of Complications from Type 2 Diabetes

by Peter J.E. Verdegem, Ph.D.,
Steven H. Freed, R.Ph., and

David J. Joffe, R.Ph.,CDE, FACA

DiabetesInControl.com, and Unicity International, Orem, UT

*Objective*

The prevalence of diabetes has increased dramatically in recent years. However, the role of dietary fiber in blood glucose regulation remains unclear. The purpose of this work was to establish the effects of supplementing the diet with Bios Life 2®, a specifically designed fiber drink, on glucose and cholesterol.

*Methods*

After 30 days of monitoring fasting and postprandial blood glucose, baseline values for HbA1c, total cholesterol, Triglycerides, LDL, and HDL were measured. 78 patients with average age 59, were given 5 grams of fiber as a drink, 2 – 3 times daily, 5 – 10 minutes prior to a meal. Fiber consisted of guar gum, gum arabic, locust bean gum, pectin, and oat fiber dispersed in calcium carbonate. In addition this product contained chromium, and B-vitamins. At the conclusion of the 90 day period, all levels were remeasured.

*Results and discussion*

Compliance with the fiber supplementation was excellent. The changes in assessed parameters are listed in the table. The mechanism by which this fiber supplement reduces the glucose levels is thought to be due to delayed gastric emptying. Cholesterol is thought to be lowered through bile-acid sequestration in the digestive tract.

*Conclusions*

As indicated in this study, high intake of dietary fiber, particularly of the soluble type, improves glycemic control, decreases hyperinsulinemia, and lowers plasma lipid concentrations in patients with type 2 diabetes. Reducing postprandial blood glucose significantly caused a decrease of HbA1c by 0.9 % points, thereby reducing the risk of complications from diabetes.

| Parameter | Baseline average | 90-day average | % change |
|---|---|---|---|
| Preprandial gluc. | 173 mg/dL | 156 | -9.8 |
| Postprandial gluc | 278 mg/dL | 237 | -14.7 |
| HbA1c | 9.0 % | 8.1 % | -10 |
| Total cholesterol | 215 mg/dL | 184 | -14.4 |
| Triglycerides | 299 mg/dL | 257 | -14.0 |
| LDL | 129 mg/dL | 92 | -28.7 |
| HDL | 43 mg/dL | 55 | +27.9 |

# 16
# The Clinical Impact of Fiber Supplementation for the Reduction of Postprandial Blood Glucose and Risk Reduction of Complications from Type 2 Diabetes

by Peter J.E. Verdegem, Ph.D.,
Steven H. Freed, R.Ph., and
David J. Joffe, R.Ph., CDE, FACA

DiabetesInControl.com, and Unicity International, Orem, UT

# THE CLINICAL IMPACT OF FIBER SUPPLEMENTATION FOR THE REDUCTION OF POSTPRANDIAL BLOOD GLUCOSE AND RISK REDUCTION OF COMPLICATIONS FROM TYPE 2 DIABETES

Peter J.E. Verdegem, Ph.D.[a]; Steven H. Freed, R.Ph.[b]; David J. Joffe, R.Ph.[b]

## Introduction

- Diets high in soluble fiber may interfere with glucose uptake from the diet.
- The advised level of fiber, 30 grams per day, is difficult to achieve through diet alone.
- Bios Life 2 is a patented fiber drink mix, designed to lower cholesterol, but case reports also indicate benefits for diabetics.
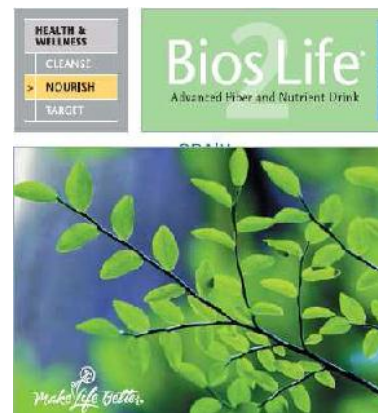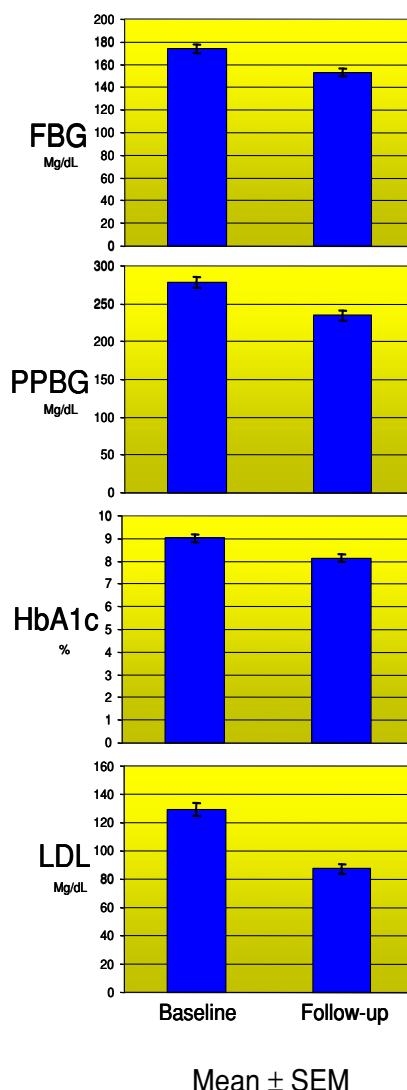
## Objectives

- To study the effect of BiosLife 2 on glycemic and lipid parameters in Type-2 diabetics.

## Study design

- Open label study with 78 Type-2 Diabetics (42 male, 36 female) with average age 59 years.
- Subjects took 10 – 15 grams of Bios Life 2, in 5 grams portions 10 minutes prior to a meal.
- Baseline and follow-up (90 days) measurements of HbA1c, FBG, PPBG, Tot.Chol., LDL, HDL, TG, and weight.
- Statistical analysis with paired Student's T-test.

## Results

| Parameter | Unit | t=0 ± SEM | t=90 ± SEM | Δ | p-value |
|---|---|---|---|---|---|
| Total Chol | mg/dL | 215.5 | 179.5 | − 36.0 | p < 0.000001 |
| LDL | mg/dL | 129.2 | 87.4 | − 41.8 | p < 0.000001 |
| HDL | mg/dL | 43.3 | 59.3 | + 16.0 | p < 0.000001 |
| Triglycerides | mg/dL | 214.8 | 164.1 | − 50.7 | p < 0.000001 |
| Fasting BG | mg/dL | 173.7 | 153.3 | − 20.4 | p < 0.001 |
| Post-prandial BG | mg/dL | 278.1 | 234.4 | − 43.7 | p < 0.0001 |
| HbA1c | % | 9.03 | 8.15 | − 0.88 | p < 0.001 |
| Systolic BP | mmHg | 131.3 | 127.2 | − 4.1 | p < 0.000001 |
| Diastolic BP | mmHg | 82.7 | 81.2 | − 1.5 | p < 0.05 |
| Weight | lb | 182.1 | 175.4 | − 6.7 | ns |

FBG Mg/dL

PPBG Mg/dL

HbA1c %

LDL Mg/dL

Baseline    Follow-up

Mean ± SEM

## Discussion

- Increasing soluble fiber intake with Bios Life 2 significantly reduces pre- and post prandial glucose, and HbA1c levels.
- Mechanism is through interaction of carbohydrates with gel matrix formed by soluble fiber.
- Same mechanism reduces lipid and cholesterol levels.

## Conclusion

- **Bios Life 2 is a very beneficial fiber drink mix for Type-2 diabetics, who want to control their glycemic parameters and cholesterol in a natural side-effect free way.**

## References

- Sprecher, *et al*, Metabolism (2002), **51**, 1166.

[a]Unicity Int. Orem, UT, USA.
www.makelifebetter.com
[b]Diabetes in Control

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# 17

# Bios Life™ Complete, a new viscous soluble fiber drink improves lipid profiles in mild hypercholesterolemia

By Peter J.E. Verdegem, Ph.D.

Research and Development, Unicity International, Orem, UT

## LDL- and HLD-cholesterol optimization using phytonutrient combination therapy: first line intervention and adjunct to statins

**Introduction:** Framingham risk analysis showed that simultaneous decreasing of LDL-c and increasing of HDL-c has a strong correlation with risk reduction for development of cardio vascular disease. Current prescription lipid lowering therapy has shown excellent results in reducing LDL-c, but limited results for HDL-c increase. Our research focuses on using phytonutrient combinations (soluble fiber, phytosterols, policosanol, etc.) in optimizing both lipoprotein fractions. We present our results of phytonutrient combination therapy are a first line treatment for hypercholesterolemia, as well as adjunct therapy to statin medication.

**Methods:** A group of 25 subjects with optimal to mildly elevated LDL-c levels added the fiber drink to their diet. The drink was taken at least twice daily 15-20 minutes before meals. The lipid panel was measured at baseline and 4 and 8 weeks. The fiber drink consists of viscous soluble fiber, minerals, vitamins, policosanol, phytosterols, and an aqueous *Chrysanthemum morifolium* extract.

**Discussion:** Bios Life™ Complete, a new fiber drink that combines ingredients that are known to lower cholesterol through 4 different mechanisms is very effective in lowering LDL-c, and increasing HDL-c. The TC levels have not changed dramatically, mainly due to the significant increase in HDL-c. Compared to statin medication, this product has similar efficacy in reducing LDL-c, but has a much better effect on HDL-c.

**Conclusion:** Bios Life Complete offers an effective alternative for patients with mild hypercholesterolemia, that can't or won't take statin medication.

## Results

| Parameter | Inclusion criteria at BL (mg(dL) | B.L. (mg/dL) | t=8 weeks (mg/dL) | Δ % | p-value |
|---|---|---|---|---|---|
| TC | All | 214 | 196 | -8.2 | 0.011 |
| TC | >200 | 237 | 211 | -10.7 | 0.007 |
| LDL-c | All | 131 | 111 | -4.8 | 0.0037 |
| LDL-c | >130 | 168 | 127 | -24.5 | 0.0001 |
| LDL-c | >160 | 182 | 127 | -30.6 | 0.000001 |
| HDL-c | All | 48 | 52 | +8.3 | 0.037 |
| HDL-c | <40 | 32 | 37 | +12.0 | n.s. |
| HDL-c (responders) | <40 | 32 | 42 | +28.6 | 0.017 |
| Risk ratio | All | 4.89 | 4.14 | -5.3 | 0.017 |
| Risk ratio | >5.00 | 6.51 | 5.04 | -24.2 | 0.026 |

# 18

# A new fiber drink provides a natural first line treatment option in mild hypercholesterolemia

By Vincent Duenas, M.D.[1], Julie Duenas[1], Evelyn Burke[1], and Peter J. Verdegem, Ph.D.[2]

[1]The Doctors Clinic, Tamuning, GU; [2]Research and Development, Unicity International, Orem, UT

## Introduction

There is increasing interest in natural, non-pharmaceutical, intervention therapies for altering the lipid profile in hypercholesterolemia. This study investigates the efficacy of a novel fiber drink (Bios Life™ Complete) as a first line treatment for mild hypercholesterolemia.

## Methods

A group of 24 subjects with mild hypercholesterolemia and LDL-c levels > 130 mg/dL added the fiber drink to their diet. The drink was taken at least twice daily 15-20 minutes before meals. The lipid panel was measured at baseline and 6 weeks. The fiber drink consists of soluble fiber, minerals, vitamins, policosanol, phytosterols, and Chrysanthemum morifolium extract.

## Discussion

Bios Life Complete, a novel fiber drink that combines ingredients that are known to lower cholesterol through 4 different mechanisms is very effective in lowering LDL-c, and increasing HDL-c. The TC levels have not changed dramatically, mainly due to the significant increase in HDL-c. Compared to statin medication, this product has similar efficacy in reducing LDL-c, but has a much better effect on HDL-c. More than 80% of the subjects reacted positively to the fiber drink, in relation to LDL, and HDL.

## Conclusion

Bios Life™ Complete offers an effective alternative for patients with mild hypercholesterolemia, that can't or won't take statin medication.

## Results

| Parameter | Inclusion criteria | B.L. | t=6 weeks | Δ % | p-value |
|---|---|---|---|---|---|
| TC | >200 | 235 | 232 | -1.4 | n.s. |
| TC (responders, 60%) | >200 | 229 | 203 | -11.0 | < 0.000001 |
| LDL-c | >130 | 157 | 131 | -16.1 | <0.001 |
| LDL-c (responders, 88%) | >130 | 155 | 123 | -20.4 | < 0.000001 |
| LDL-c | >160 | 180 | 150 | -16.6 | <0.05 |
| LDL-c (responders, 89%) | >160 | 175 | 140 | -20.2 | <0.05 |
| HDL-c | <40 | 35 | 45 | +27.9 | <0.01 |
| HDL-c (responders, 82%) | <40 | 35 | 47 | +34.7 | <0.01 |
| Risk ratio | | 5.1 | 4.3 | -15.0 | <0.0001 |
| Risk ratio (responders, 79%) | | 5.3 | 4.2 | -20.8 | <0.000001 |

# 19
# A new fiber drink provides a natural first line treatment option in mild hypercholesterolemia

By Vincent Duenas, M.D.[1],
Julie Duenas[1], Evelyn Burke[1],
and Peter J. Verdegem, Ph.D.[2]

[1]The Doctors Clinic, Tamuning, GU; [2]Research and Development, Unicity International, Orem, UT

# A NEW FIBER DRINK PROVIDES A NATURAL FIRST LINE TREATMENT OPTION IN MILD HYPERCHOLESTEROLEMIA

Vincent Duenas, M.D.[a]; Julie Duenas[a]; Evelyn Burke[a]; Peter J.E. Verdegem, Ph.D.[b]

## Introduction

- There is an increasing demand for natural treatment options to lower cholesterol, because of fear of side-effects of statins.
- BiosLife combines 4 unique mechanisms to lower cholesterol: viscous soluble fiber, phytosterols, policosanol, and chrysanthemum.

## Objectives

- To study the lipid lowering potential of Bios Life in mildly elevated lipid levels.

## Study design

- Open label study with 41 subjects (11 male, 30 female) with average age 52.3 ± 1.3 years, and with LDL values > 110 mg/dl.
- Subjects took 13 – 19.5 grams of Bios Life, in 6.5 grams portions 10 minutes prior the meal.
- Baseline and follow-up (6 weeks) measurements of TC, LDL, HDL, and risk ratio. Safety: liver panel
- Statistical analysis with paired Student's T-test.

## Results



LDL (mg/dL)



HDL (mg/dL)



Ratio

BL          6 wk

Mean ± SEM

| Parameter | Group | t=0 ± SEM | t=6 ± SEM | %Δ | p-value |
|---|---|---|---|---|---|
| TC | >200 | 235 | 232 | -1.4 | n.s. |
| TC (resp, 60%) | >200 | 229 | 203 | -11.0 | < 0.000001 |
| LDL | >130 | 157 | 131 | -16.1 | <0.001 |
| LDL (resp, 88%) | >130 | 155 | 123 | -20.4 | < 0.000001 |
| LDL | >160 | 180 | 150 | -16.6 | <0.05 |
| LDL (resp, 89%) | >160 | 175 | 140 | -20.2 | <0.05 |
| HDL | <40 | 35 | 45 | +27.9 | <0.01 |
| HDL (resp, 82%) | <40 | 35 | 47 | +34.7 | <0.01 |
| Risk ratio | | 5.1 | 4.3 | -15.0 | <0.0001 |
| Risk ratio (resp, 79%) | | 5.3 | 4.2 | -20.8 | <0.000001 |
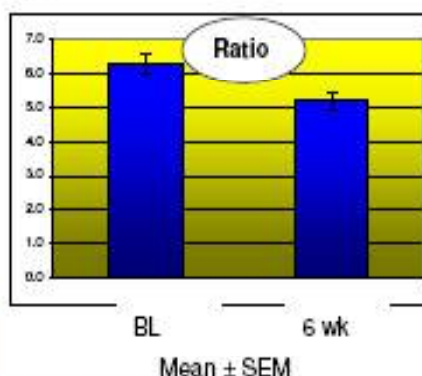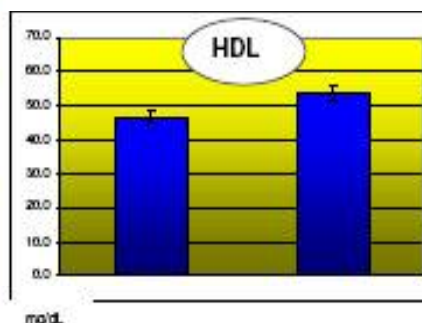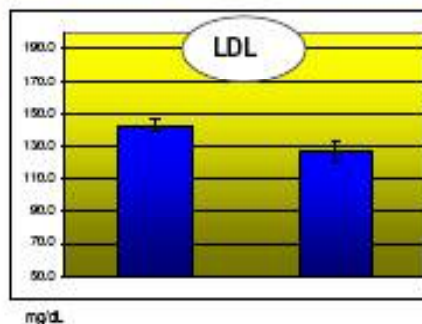
## Discussion

- Four synergistic mechanisms lower lipids effectively.
- Large response rate to intervention.
- Clinical significant reduction in LDL, and raise in HDL.
- Compared to statins, BiosLife is equally effective in lowering LDL, but outperforms in raising HDL.
- No elevated liver enzymes.

## Conclusion

- BiosLife, a new patented drink that lowers cholesterol in 4 distinct ways, serves as a natural first line intervention option to manage hyperlipidemia.

## References

- Sprecher, et al, Metabolism (2002), 51, 1166.

[a]The Doctors' Clinic, Tamuning, Guam
[b]Unicity International, Orem, Utah
www.unicity.net

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# 20
# A new fiber drink can serve as an adjunct therapy to statin medication in mild hypercholesterolemia

by Vincent Duenas, M.D.[1],

Julie Duenas[1], Evelyn Burke[1],

and Peter J.E. Verdegem, Ph.D.[2]


[1]The Doctors Clinic, Tamuning, GU; [2]Unicity International, Orem, UT

## Introduction

Statin medication is widely used as a first line intervention for hypercholesterolemia. Not all patients get their LDL-c levels in optimal ranges with statins, and statins typically do not increase HDL-c levels adequately. This study investigates the efficacy of a novel fiber drink (Bios Life Complete) as an adjunct therapy to statin medication.

## Methods

A group of 11 subjects with mild hypercholesterolemia and LDL-c levels > 130 mg/dL and current statin use added the fiber drink to their diet. The drink was taken at least twice daily 15-20 minutes before meals. The lipid panel was measured at baseline and 6 weeks. The fiber drink consists of soluble fiber, minerals, vitamins, policosanol, phytosterols, and Chrysanthemum morifolium extract.

## Discussion

Statin users that have not changed their lipid profile over 6 months (Pre-B.L. vs. B.L.) have a significant impressive additional decrease in LDL-c of 21.1%. The HDL-c levels have increased by 23.2% in this group, which is significantly higher than the average effect of statin medication. The TC levels have not changed dramatically, mainly due to the significant increase in HDL-c. More than 80% of the subjects reacted positively to the fiber drink.

## Conclusion

Bios Life™ Complete is a promising adjunct therapy option for patients with hypercholesterolemia that are currently using statins, and for whom the statin effects have reached a maximum.

## Results

| Parameter | | Pre-B.L. | B.L. | t=6 weeks | Δ % | p-value |
|---|---|---|---|---|---|---|
| TC | >200 | 232 | 229 | 211 | -8.1 | n.s. |
| TC (responders, 82%) | >200 | 225 | 228 | 199 | -12.8 | <0.001 |
| LDL-c | >130 | 146 | 150 | 118 | -21.1 | <0.05 |
| LDL-c (responders, 83%) | >130 | 145 | 151 | 108 | -28.4 | <0.001 |
| HDL-c | <40 | 35 | 34 | 42 | +23.2 | <0.05 |
| HDL-c (responders, 88%) | <40 | 36 | 34 | 43 | +26.3 | <0.05 |
| Risk ratio | | 5.3 | 5.2 | 4.4 | -15.2 | <0.01 |
| Risk ratio (responders, 85%) | | 5.0 | 5.4 | 4.3 | -18.9 | <0.001 |

# 21
# A new fiber drink can serve as an adjunct therapy to statin medication in mild hypercholesterolemia

By Vincent Duenas, M.D.[1],
Julie Duenas[1], Evelyn Burke[1],
and Peter J.E. Verdegem, Ph.D.[2]

[1]The Doctors Clinic, Tamuning, GU; [2]Unicity
International, Orem, UT

# A NEW FIBER DRINK CAN SERVE AS AN ADJUNCT THERAPY TO STATIN MEDICATION IN MILD HYPERCHOLESTEROLEMIA

Vincent Duenas, M.D.[a]; Julie Duenas[a]; Evelyn Burke[a]; Peter J.E. Verdegem, Ph.D.[b]

## Introduction

- There is an increasing demand for natural treatment options to lower cholesterol, and HDL raising strategies alongside statins.
- BiosLife combines 4 unique mechanisms to improve lipids: viscous soluble fiber, phytosterols, policosanol, and chrysanthemum.
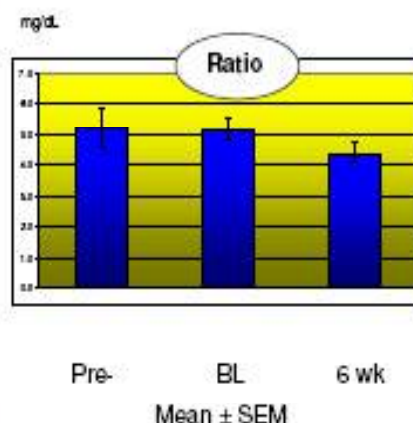
## Objectives

- To study the lipid lowering potential of Bios Life in statin users that have not reached goal.

## Study design

- Open label study with 11 subjects (2 male, 9 female) with average age 54.9 ± 2.5 years, and with LDL values > 110 mg/dl.
- Subjects took 13 – 19.5 grams of Bios Life, in 6.5 grams portions 10 minutes prior the meal, and statins.
- Two last LDL levels no more than 10% apart.
- Baseline and follow-up (6 weeks) measurements of TC, LDL, HDL, and risk ratio. Safety: liver panel
- Statistical analysis with paired Student's T-test.



LDL

mg/dl



HDL

mg/dl



Ratio

Pre-    BL    6 wk

Mean ± SEM

## Discussion

- Four synergistic mechanisms lower lipids effectively.
- Large response rate to intervention.
- Clinical significant reduction in LDL, and raise in HDL.
- Effects found on top of already realized lipid lowering due to statin use.
- No elevated liver enzymes.

## Conclusion

- BiosLife, a new patented drink that lowers cholesterol in 4 distinct ways, can be used as adjunct therapy to statin use, providing an additional LDL reduction combined with a substantial HDL increase.

## References

- Sprecher, et al, Metabolism (2002), 51, 1166.

[a]The Doctors' Clinic, Tamuning, Guam
[b]Unicity International, Orem, Utah
www.unicity.net

## Results

| Parameter | Group | t=pre-BL± SEM | t=0 ± SEM | t=6 ± SEM | %Δ | p-value |
|---|---|---|---|---|---|---|
| TC | >200 | 232 | 229 | 211 | -8.1 | n.s. |
| TC (resp, 82%) | >200 | 225 | 228 | 199 | -12.8 | <0.001 |
| LDL | >130 | 146 | 150 | 118 | -21.1 | <0.05 |
| LDL (resp, 83%) | >130 | 145 | 151 | 108 | -28.4 | <0.001 |
| HDL | <40 | 35 | 34 | 42 | +23.2 | <0.05 |
| HDL (resp, 88%) | <40 | 36 | 34 | 43 | +26.3 | <0.05 |
| Risk ratio | | 5.3 | 5.2 | 4.4 | -15.2 | <0.01 |
| Risk ratio (resp, 85%) | | 5.0 | 5.4 | 4.3 | -18.9 | <0.001 |

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# 22
# Viscous soluble fiber combined with three other phytonutrients benefits lipid profiles in hypercholesterolemia

By Peter J.E. Verdegem, Ph.D.

Manuscript for publication

Highly Confidential

## Abstract

*Introduction.* This pilot study investigates the efficacy of a combination of neutraceuticals in improving lipid levels. The tested product combines viscous soluble fiber with phytosterols, policosanol, and an extract of *Chrysanthemum morifolium*. All four ingredients have been shown to have cholesterol lowering potential, but all through different biological mechanisms. The test product is the first to combine these four cholesterol lowering mechanisms in one product.

*Materials and methods.* Twenty five subjects completed an 8-week open label study design. The product was taken twice daily before the main meals. Fasting lipid panels were measured at baseline, 4, and 8 weeks.

*Results.* The total cholesterol levels were reduced 8.2 % ($p<0.05$) after 8 weeks, and 10.7% ($p<0.01$) in a subgroup of subjects with TC levels > 200 mg/dL at baseline. LDL-c was reduced 4.8% ($p<0.01$) and 24.5 % ($p<0.001$), and 30.6 % ($p<0.00001$) in sub groups of subjects having baseline LDL-c levels > 130 and > 160 mg/dL, respectively. HDL-c levels were increased 8.3% ($p<0.05$).

*Conclusion*: This neutraceutical combination therapy is promising as a first line intervention,
and may serve as an adjunct therapy to pharmaceutical lipid lowering prescription therapy.

1. Introduction

Elevated total cholesterol (TC), LDL-cholesterol (LDL-c), and reduced HDL-cholesterol (HDL-c) levels have been determined a major risk factor for the development of cardio vascular disease, and the formation of atherosclerotic plaques. (Yusuf *et al.* , 2004) Improving these lipid levels has been effective in lowering the risk for the development of heart disease and stroke. (Corvol *et al.* , 2003; Huxley *et al.* , 2002) Conventional first line treatment for hypercholesterolemia is focused on dietary changes and life style, and if not adequately successful, followed by pharmaceutical interventions, such as statins, fibrates, and bile-acid sequestrants. In the last decades, an increasing number of non-pharmaceutical intervention therapies has been developed, and tested in randomized clinical trials. Examples are viscous soluble fiber, (Anderson *et al.* , 1999; Anderson *et al.* , 2000; Chandalia, 2000; Jenkins *et al.* , 2002; Knopp *et al.* , 1999; Sprecher and Pearce, 2002) phytosterols, and phytostanols, (Jenkins *et al.* , 2005; McPherson *et al.* , 2005; Plat and Mensink, 2005; Thompson, 2005; von Bergmann *et al.* , 2005) and policosanol. (Castano *et al.* , 2002; Crespo *et al.* , 1999) These nutritional intervention therapies have generally shown moderate lipid lowering success, and are therefore not always an intervention option for immediate hypercholesterolemia. Nevertheless, there is a growing awareness among the public about potential side-effects of pharmaceutical compounds in general and of statin lipid lowering prescription therapy in particular. This has resulted in an increasing demand for dietary or phytotherapeutical approaches to lowering cholesterol.

Traditionally, interventional therapies, both pharmaceutical and dietary, influence only one mechanism to lower cholesterol. While effective for pharmaceuticals, the one-mechanism approach for dietary intervention has shown limited success. At least theoretically, a product combining different mechanisms to lower cholesterol, should have an enhanced efficacy, when compared to a mono-mechanism approach. An increasing number of pharmaceutical

intervention therapies has also adopted this concept, (Vasudevan and Jones, 2005) such as using the combination of statins and ezetimibe. (Davidson, 2003; Kosoglou *et al.*, 2005)

In this study, we investigated the lipid lowering efficacy of a neutraceuticals combination product, based on a viscous soluble fiber drink, combined with three other phytonutrients: phytosterols, policosanol, and *Chrysanthemum morifolium*. All four individual ingredients have independent data about their lipid-lowering potential. This product therefore approaches lipid lowering through a potentially synergistic combination of 4 different mechanisms.

## 2. Materials and Methods

### Subjects

The study used a protocol which was approved by an outside institutional review board, and deemed in compliance with the Declaration of Helsinki V. (World Medical Association, 2000) Subjects were invited from a pool of 125 office staff of the research institute. Subjects were informed about the study through a mass communication, to exclude pressure to participate. The identity of the subjects was kept confidential at all times. Subjects were eligible to participate in the trial if they were between 18 and 75 years old, and if the baseline (BL) value for LDL-c was 110 mg/dL or higher. Subjects were not eligible to participate if they suffered from type-1 diabetes, severe hypertension, defined as at least 180/100 mmHg, or had any other health condition that may interfere with the study results, as judged by the principle investigator. The subjects were also excluded if they suffered from an allergy against any of the ingredients in the tested product, or if they had any medical condition in which fiber consumption is contra-indicated, *e.g.* Chron's disease. Subjects were allowed to use vitamin or mineral supplements, provided they did not contain any of the tested ingredients. Pregnant women or breast feeding women were excluded. If subjects had only one regular meal per day, they were also excluded. Finally, a history of alcohol or drug abuse, psychological or other mental issues that are likely to invalidate the informed consent, or

limit the ability of the patient to comply with the protocol requirements resulted in exclusion from this trial. Subjects were not compensated for their participation in the trial. The recruitment was spread out over a period of 2 weeks.

### Study procedures

All potential subjects for this study were screened to evaluate their eligibility to participate by an interview with the principle investigator. After signing informed-consent forms, the participants in this study used the test product prior to lunch and dinner for a period of 8 weeks. The product was supplied as a powder in a canister that included 60 dosages, and subjects were instructed to mix one dosage (6.5 grams, measured with a scoop) at a time with about 230 ml of water, and drink the product about 10 – 15 minutes before the meal. A lipid panel, including TC, LDL-c, HDL-c, TG, and cardio vascular risk ratio was measured at baseline (BL), 4 weeks, and 8 weeks. The cholesterol measurements were performed on-site using a Cholestech LDX system (Cholestech Corp. Hayward, CA). The subjects were instructed to come in fasted before each measuring day. Fasted was defined as having no food or drinks other than water since going to bed the previous night. Visit windows were set at plus or minus 2 days. The subjects were instructed to continue with normal daily activities during their participation in the trial, and not make any changes to normal diet, and physical activities. Compliance with the protocol was promoted by a weekly phone call with all participants. Side effects of the product were evaluated during these weekly phone calls, and at the end of the trial using a questionnaire. Compliance was assessed using a questionnaire and an interview with the subjects at the end of the trial.

### Composition of the test product

The tested product is marketed under the brand name Bios Life™ (Unicity International, Orem, UT). A unitary dose of the product comprises of 3.3 grams of dietary fiber consisting of guar gum (1.2 grams), gum Arabic (0.65 grams), locust bean gum (0.61 grams), pectin (0.42 grams), and oat fiber (0.35 grams). This fiber mix comprises of more than 90 % soluble fiber. The product

further contains a vitamin and mineral mix, including vitamins A, B1, B2, B6, B11, B12, C, E, and minerals selenium, chromium, zinc, and calcium. All vitamins and minerals are added at or close to their respective RDAs. The test product further comprises 1.0 gram of esterified phytosterols (including sitosterol, stigmasterol, and campesterol), 6 mg of policosanol (standardized to 60 % octocosanol), and 12.5 mg aqueous extract of *Chrysanthemum morifolium.* All subjects used two packets per day of this formula. All individual ingredients of the tested product have demonstrated safety records for long-term use, and therefore we decided not to collect safety data for the test product. (Carabin and Flamm, 1999; Chen *et al.* , 2005; Plat and Mensink, 2005)

### Data analysis and statistical methods

The results were analyzed as means in the group. Within-group differences over time were analyzed using 2-tailed paired *t* tests for dependent groups, after the normality of the data was determined. These procedures were used for all measured parameters. Statistical significance was defined as a p-value of 0.05 or lower. Variations in measurements are indicated as standard errors of the mean (± SEM).

## 3. Results

Thirty seven subjects expressed interest in participating in the trial. Twenty five subjects completed the 8 week protocol. Reasons for discontinuation were all related to lack of time or further interest in participation. Of this group 13 subjects were male, and 12 female. The age of the group varied between 61, and 25, with an mean age of 40.2 ± 1.8 years. Four subjects were post-menopausal. The BL lipid levels of this group were: TC 213.6 ± 7.8 mg/dL; LDL-c 130.6 ± 8.1 mg/dL; HDL-c 47.8 ± 3.0 mg/dL; TG 175.8 ± 15.5 mg/dL, and cardio vascular risk ratio (defined as TC/HDL-c) 4.9 ± 0.3.

Compliance was estimated to be at least 60 %. In this small-scale pilot trial, however, no one was excluded based on low compliance. Side-effects reported were generally mild, and included gastro-intestinal discomfort, flatulence, and diarrhea, but the side effects reported were

not a reason to discontinue with participation in the trial, and typically disappeared after several days. The side effects reported were in line with previous studies that tested fiber supplementation. (Sprecher and Pearce, 2002)

### Total Cholesterol

The TC levels in the whole group were significantly reduced by 8.2 %. The subgroup of subjects having TC levels of 200 mg/dL or more at BL showed a statistically significant reduction of 10.7 % after 8 weeks.

### LDL cholesterol

The mean change in LDL cholesterol for the total group amounted to 1.6 % after 4 weeks and 4.8 % after eight weeks. The reduction after 8 weeks was significant. LDL-c reductions for subgroups of subjects having LDL values at BL of more than 130 mg/dL and 160 mg/dL amounted to 24.5 % and 30.6 %, after 8 weeks, respectively. Both reductions were statistically significant.

### HDL cholesterol

HDL-c was increased in the total group amounted to a significant 8.3 %. For the subgroup of subjects with HDL-c levels of 40 mg/dL or lower at BL, the mean change in HDL-c was 12.0 %, but not significant.

### Triglycerides

After 8 weeks, triglyceride levels were changed by 5.7 % for the whole group, and 14.9 % for the sub group of subjects having TG levels of 150 mg/dL or more at BL. Both changes did not reach statistical significance. The differences after 4 weeks of intervention did reach significance, and were reductions of 16.4% for the total group and 21.4% for the subgroup having TG levels of 150 mg/dL or more at BL.

### Cardio vascular risk ratio

The risk ratio for the whole group was significantly reduced by 5.3 %, and by 24.2 % for the subgroup of subjects having risk ratio levels higher than 5.0 at BL.

The detailed results for all parameters are listed in Table 1.

## 4. Discussion

The tested product in this study is a fiber drink, based on 3.3 grams mostly soluble fiber combined with vitamins, minerals, esterified phytosterols, policosanol, and an aqueous extract of *Chrysanthemum morifolium*. The product has been designed to lower cholesterol using four different biological mechanisms. These four mechanisms are:

1. *Bile-acid sequestration*. Bile acids are needed to digest fat, and they are being synthesized using the cholesterol pool in the body. After aiding in fat digestion, the bile acids, along with the cholesterol are re-absorbed in the system and re-utilized by the liver. The total size of the cholesterol pool is largely unchanged by this mechanism, since the gross amount of cholesterol used from the pool to synthesize bile acids is returning back into our body. When the soluble fiber present in the test product enters the digestive tract before the meal, the fiber forms a gel matrix due to the acidic condition in the stomach. This matrix sequesters the bile acids and prevents them from being re-absorbed, but rather excreted. Fibers are also fermented in the colon by bacteria to yield short-chain fatty acids, such as acetates, propionates, and butyrates that may inhibit cholesterol synthesis. This mechanism alone is known to lower LDL cholesterol by 5 – 15 % after 8 weeks. (Anderson *et al.* , 1999; Jenkins *et al.* , 2002; Knopp *et al.* , 1999; Sprecher and Pearce, 2002) A randomized placebo-controlled study with the fiber mixture present in the tested product was published by Sprecher and Pearce in 2002. (Sprecher and Pearce, 2002)

2. *Dietary absorption inhibition*. Cholesterol is actively absorbed from the small intestine into the blood by transporter proteins. (Thurnhofer and Hauser, 1990) Phytosterols are plant components that have a similar chemical structure to cholesterol. When phytosterols are present in the digestive tract before the meal, they displace real cholesterol in the absorption processes. (Ikeda *et al.* , 1989; Ikeda *et al.* , 1988a; Ikeda *et al.* , 1988b) In this way serum cholesterol is lowered. This mechanism alone has been shown to lower LDL-cholesterol by 5 – 15 % after about 8 weeks. (Ostlund, 2004)

3. *Cholesterol synthesis inhibition*. A critical step in the cholesterol biosynthetic route is the conversion of HMG-CoA into mevalonate, performed by HMG-CoA reductase. Policosanol is a sugar cane extract that has been shown to inhibit this enzyme.(McCarty, 2002) This mechanism alone has been shown to lower LDL-cholesterol 15 – 30 % after 8 weeks. (Castano *et al.* , 2002; Castano *et al.* , 2001; Castano *et al.* , 2003; Castano *et al.* , 1999; Varady *et al.* , 2003) Two recently published studies, however, failed to show an effect of policosanol. (Berthold *et al.* , 2006; Greyling *et al.* , 2006)

4. *Enhancement of cholesterol metabolism*. Cholesterol is converted into several other biomolecules in our body. One process that uses cholesterol is the synthesis of cholic acid, the most predominant member of the bile acids. The enzyme responsible for the conversion of cholesterol to 7 -cholesterol, which is the first metabolite on the pathway to cholic acid, is 7 -hydroxylase.(Lathe, 2002) Chen *et al.* published that an aqueous extract of *Chrysanthemum morifolium* enhances the function this enzyme, thereby promoting the metabolism and removal of serum cholesterol. (Chen *et al.* , 2000)

This neutraceuticals combination product has been designed to optimize lipoprotein levels, and as a result, to reduce the risk for developing cardio vascular health concerns. Total cholesterol levels in this study did not change with impressive numbers. Since TC is derived from the sum of LDL-c and HDL-c (and others), and most study participants showed considerable HDL-c increases, the overall reduction in TC is smaller than would be observed in statin intervention studies. (Edwards and Moore, 2003)

The test product reduces LDL cholesterol in the total study group significantly with 4.8 % after 8 weeks. This small overall reduction may be explained by the relative healthy dietary habits of the study population, limiting the effect

of dietary intervention to optimize cholesterol levels in the total group. The reductions are greater in subgroups of subjects that have higher LDL cholesterol levels at BL, which is in line with expectations. For a subgroup with "borderline high" LDL-c levels, as defined by the Adult Treatment Panel III of the National Cholesterol Education Program (NCEP), (National Institute of Health, 2001) the reduction after 8 weeks amounts to 24.5 %. For "high" BL levels, (National Institute of Health, 2001) LDL cholesterol was reduced with 30.6 %. These reductions are clinically relevant, and may be compared with reductions reached by average dosages of statin lipid lowering medication, for hyperlipidemic subjects.(Edwards and Moore, 2003) It is evident that the tested product is more effective in subjects with higher BL LDL-c levels. Higher LDL-c levels are generally associated with less healthy dietary habits, (Hata and Nakajima, 2000) and this may explain why dietary intervention may be more effective for this group. The test product is likely to have a direct mechanistic effect on indigenous cholesterol production (policosanol) and clearance (*Chrysanthemum morifolium*), and a change on dietary factors influencing cholesterol absorption (fiber, phytosterols). Because this study did not evaluate baseline diet characteristics of the subjects, we are unable to discriminate the serum lipid effects between the different mechanisms. Follow-up studies performed by our laboratory focus on this research question.

The relative low increase in HDL in the total group is likely a result of the high mean BL value for HDL. This hypothesis is supported by the observation that for people having HDL baseline levels of 40 mg/dL or lower, the mean change is higher (although not significant in our small sample size). Analyzing only the responders in this group (7 out of 9), gives a statistically significant increase of 28.6 %. The two individuals in this group that did not respond to the treatment may be subjects with low compliance, or subjects that have a biochemical reason for not responding, since these subjects were also non-responders in LDL reduction.

It is known that statin prescription therapy has limited efficacy in increasing high-density lipoprotein levels in clinically relevant amounts.(Edwards and Moore, 2003) Clinicians are increasingly aware of the need of reducing LDL-c, while at the same time increasing HDL-c. (Kuvin *et al.*, 2006) The Framingham heart study revealed that increasing HDL-c may equally important as decreasing LDL-c. (Nam *et al.*, 2006) Our HDL-c results for the responder group may open up an alternative, or adjunct therapy to lipid-lowering prescription therapy. The data suggest that responding patients with with mild to moderate hypercholesterolemia can reduce their LDL-c adequately using neutraceutical combination therapy, and at the same time increase HDL-c.

There is increasing concern among patients about the safety of prescription medication, in particular statins, because of existing side-effects, such as muscle weakness, and liver damage. (Silva *et al.*, 2006) Although the prevalence of these side-effects is rather low, (Law and Rudnicka, 2006) patients are exploring the availability of natural therapies as a first line intervention to lower their cholesterol levels. Our preliminary data warrant the further exploration of this neutraceutical combination as a first line treatment for hyperlipidemia. According the NCEP guidelines, the first intervention for high cholesterol should be the so-called Therapeutic Lifestyle Change Diet. (National Institute of Health, 2001) Part of this dietary guideline is the intake of fiber at minimum daily levels of 25 – 30 grams. The average dietary consumption of adults in the USA is well below this level. (Liu *et al.*, 2002) Two servings of the test product provide 6.6 grams of dietary fiber, and can therefore serve to partly fill the gap between actual and advised dietary consumption of fiber.

The cardio vascular risk ratio is defined as TC divided by HDL. Although ATP III does not define this ratio as a therapy target, many studies show that the TC/HDL cholesterol ratio is a powerful predictor of CHD risk. (National Institute of Health, 2001) The American Heart Association defines a risk ratio of lower than 5.0 as preferential, if there are no other risk factors present. The combined results on the lipid fractions have significantly benefited the ratio values for our study participants.

We limited the study period to 8 weeks for practical reasons. It is unknown if the observed

improvements in lipid profiles persist for longer times. Some reports indicate that results of intervention trials with phytosterols over longer periods (up to 1 year) may be less pronounced than for shorter periods. (Ostlund, 2004) To our knowledge, similar findings have not been reported for the other ingredients in this tested product. Future studies should therefore study the test product during longer follow-up periods.

## 5. Conclusion

Viscous soluble fiber combined with phytosterols, policosanol, and an aqueous extract of *Chrysanthemum morifolium* is a promising natural dietary intervention to lower LDL cholesterol, and to increase HDL cholesterol, simultaneously. These changes result in an improved risk profile for heart disease among otherwise healthy young individuals. The changes observed in LDL-c for subjects with "borderline high" and "high" cholesterol levels may be compared to the treatment effects reached for average dosages of statin medication. This combination product is promising in providing a natural dietary approach to successfully improving lipid profiles. This pilot study warrants further study with this ingredient combination in larger groups, for longer follow-up periods, and with better compliance.

## Tables

Table 1. Lipid level and cardiovascular risk ratio changes after t=4 and t=8 weeks using the neutraceutical combination product. All lipid concentrations are in mg/dL. The changes refer to changes from baseline (BL).

* p<0.05; ** p<0.01; *** p<0.001, [a]defined as TC/HDL.

## References

Anderson JW, Allgood LD, Turner J, Oeltgen PR, Daggy BP (1999) Effects of psyllium on glucose and serum lipid responses in men with type 2 diabetes and hypercholesterolemia *Am J Clin Nutr* **70**, 466-73.

Anderson JW, Davidson MH, Blonde L, Brown WV, Howard WJ, Ginsberg H, Allgood LD, Weingand KW (2000) Long-term cholesterol-lowering effects of psyllium as an adjunct to diet therapy in the treatment of hypercholesterolemia *Am J Clin Nutr* **71**, 1433-8.

Berthold HK, Unverdorben S, Degenhardt R, Bulitta M, Gouni-Berthold I (2006) Effect of policosanol on lipid levels among patients with hypercholesterolemia or combined hyperlipidemia: a randomized controlled trial *Jama* **295**, 2262-9.

Carabin IG, Flamm WG (1999) Evaluation of safety of inulin and oligofructose as dietary fiber *Regul Toxicol Pharmacol.* **30**, 268-82.

**Table 1**

|  | Group | N | # Men | Age | BL | t=4 | Δ (%) | p | t=8 | Δ (%) | p |
|---|---|---|---|---|---|---|---|---|---|---|---|
| TC | Total | 25 | 13 | 40.2 | 214 | 208 | -2.7 | n.s. | 196 | -8.2 | * |
|  | > 200 | 16 | 8 | 40.6 | 237 | 224 | -5.2 | n.s. | 211 | -10.7 | ** |
| LDL | Total | 25 | 13 | 40.2 | 131 | 129 | -1.6 | n.s. | 111 | -4.8 | ** |
|  | > 130 | 11 | 6 | 36.0 | 168 | 159 | -5.6 | n.s. | 127 | -24.5 | *** |
|  | > 160 | 7 | 2 | 38.7 | 182 | 166 | -8.9 | n.s. | 127 | -30.6 | *** |
| HDL | Total | 25 | 13 | 40.2 | 48 | 50 | +4.7 | n.s. | 52 | +8.3 | * |
|  | < 40 | 9 | 7 | 38.1 | 32 | 35 | +9.1 | n.s. | 37 | +12.0 | n.s. |
| TG | Total | 25 | 13 | 40.2 | 176 | 147 | -16.4 | * | 166 | -5.7 | n.s. |
|  | > 150 | 14 | 8 | 44.6 | 228 | 179 | -21.4 | ** | 194 | -14.9 | n.s. |
| Ratio[a] | Total | 25 | 13 | 40.2 | 4.89 | 4.71 | -3.7 | n.s. | 4.14 | -5.3 | * |
|  | > 5.0 | 11 | 7 | 37.0 | 6.51 | 6.27 | -3.6 | n.s. | 5.04 | -24.2 | * |

Castano G, Mas R, Fernandez JC, Fernandez L, Illnait J, Lopez E (2002) Effects of policosanol on older patients with hypertension and type II hypercholesterolaemia *Drugs R D* **3**, 159-72.

Castano G, Mas R, Fernandez JC, Illnait J, Fernandez L, Alvarez E (2001) Effects of policosanol in older patients with type II hypercholesterolemia and high coronary risk *J Gerontol A Biol Sci Med Sci* **56**, M186-92.

Castano G, Mas R, Fernandez L, Illnait J, Mesa M, Alvarez E, Lezcay M (2003) Comparison of the efficacy and tolerability of policosanol with atorvastatin in elderly patients with type II hypercholesterolaemia *Drugs Aging* **20**, 153-63.

Castano G, Mas R, Roca J, Fernandez L, Illnait J, Fernandez JC, Selman E (1999) A double-blind, placebo-controlled study of the effects of policosanol in patients with intermittent claudication *Angiology* **50**, 123-30.

Chandalia M (2000) Beneficial Effects of High Density Fiber Intake In Patients with Type II Diabetes mellitus *New England Journal of Medicine* **342**, 1392-8.

Chen JT, Wesley R, Shamburek RD, Pucino F, Csako G, Carabin IG, Flamm WG (2005) Meta-analysis of natural therapies for hyperlipidemia: plant sterols and stanols versus policosanol *Pharmacotherapy.* **25**, 171-83.

Chen Q, de Bont H, Van der Zee L, Lansink M, Van Norren K (2000) Cholesterol lowering supplement, US Patent 6,933,291.

Corvol JC, Bouzamondo A, Sirol M, Hulot JS, Sanchez P, Lechat P (2003) Differential effects of lipid-lowering therapies on stroke prevention: a meta-analysis of randomized trials *Arch Intern Med* **163**, 669-76.

Crespo N, Illnait J, Mas R, Fernandez L, Fernandez J, Castano G (1999) Comparative study of the efficacy and tolerability of policosanol and lovastatin in patients with hypercholesterolemia and noninsulin dependent diabetes mellitus *Int J Clin Pharmacol Res* **19**, 117-27.

Davidson MH (2003) Ezetimibe: a novel option for lowering cholesterol *Expert Rev Cardiovasc Ther* **1**, 11-21.

Edwards J, Moore R (2003) Statins in

hypercholeterolaemia: A dose-specific meta-analysis of lipid changes in randomised, double blind trials *BMC Family Practice* **4**, 1-19.

Greyling A, De Witt C, Oosthuizen W, Jerling JC (2006) Effects of a policosanol supplement on serum lipid concentrations in hypercholesterolaemic and heterozygous familial hypercholesterolaemic subjects *Br J Nutr* **95**, 968-75.

Hata Y, Nakajima K (2000) Life-style and serum lipids and lipoproteins *J Atheroscler Thromb* **7**, 177-97.

Huxley R, Lewington S, Clarke R (2002) Cholesterol, coronary heart disease and stroke: a review of published evidence from observational studies and randomized controlled trials *Semin Vasc Med* **2**, 315-23.

Ikeda I, Tanabe Y, Sugano M (1989) Effects of sitosterol and sitostanol on micellar solubility of cholesterol *J Nutr Sci Vitaminol (Tokyo)* **35**, 361-9.

Ikeda I, Tanaka K, Sugano M, Vahouny GV, Gallo LL (1988a) Discrimination between cholesterol and sitosterol for absorption in rats *J Lipid Res* **29**, 1583-91.

Ikeda I, Tanaka K, Sugano M, Vahouny GV, Gallo LL (1988b) Inhibition of cholesterol absorption in rats by plant sterols *J Lipid Res* **29**, 1573-82.

Jenkins DJ, Kendall CW, Marchie A, Faulkner DA, Wong JM, de Souza R, Emam A, Parker TL, Vidgen E, Trautwein EA, Lapsley KG, Josse RG, Leiter LA, Singer W, Connelly PW (2005) Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants *Am J Clin Nutr* **81**, 380-7.

Jenkins DJ, Kendall CW, Vuksan V, Vidgen E, Parker T, Faulkner D, Mehling CC, Garsetti M, Testolin G, Cunnane SC, Ryan MA, Corey PN (2002) Soluble fiber intake at a dose approved by the US Food and Drug Administration for a claim of health benefits: serum lipid risk factors for cardiovascular disease assessed in a randomized controlled crossover trial *Am J Clin Nutr* **75**, 834-9.

Knopp RH, Superko HR, Davidson M, Insull W, Dujovne CA, Kwiterovich PO, Zavoral JH, Graham K, O'Connor RR, Edelman DA (1999) Long-term blood cholesterol-lowering effects of

a dietary fiber supplement *Am J Prev Med* **17**, 18-23.

Kosoglou T, Statkevich P, Johnson-Levonas AO, Paolini JF, Bergman AJ, Alton KB (2005) Ezetimibe: a review of its metabolism, pharmacokinetics and drug interactions *Clin Pharmacokinet* **44**, 467-94.

Kuvin JT, Alsheikh-Ali AA, Karas RH (2006) High-density lipoprotein cholesterol-raising strategies *J Cardiovasc Pharmacol* **47**, 196-204.

Lathe R (2002) Steroid and sterol 7-hydroxylation: ancient pathways *Steroids* **67**, 967-77.

Law M, Rudnicka AR (2006) Statin safety: a systematic review *Am J Cardiol* **97**, 52C-60C.

Liu S, Buring JE, Sesso HD, Rimm EB, Willett WC, Manson JE (2002) A prospective study of dietary fiber intake and risk of cardiovascular disease among women *J Am Coll Cardiol* **39**, 49-56.

McCarty MF (2002) Policosanol safely down-regulates HMG-CoA reductase - potential as a component of the Esselstyn regimen *Med Hypotheses* **59**, 268-79.

McPherson TB, Ostlund RE, Goldberg AC, Bateman JH, Schimmoeller L, Spilburg CA (2005) Phytostanol tablets reduce human LDL-cholesterol *J Pharm Pharmacol* **57**, 889-96.

Nam BH, Kannel WB, D'Agostino RB (2006) Search for an optimal atherogenic lipid risk profile: from the Framingham Study *Am J Cardiol* **97**, 372-5.

National Institute of Health (2001) Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III) *Jama* **285**, 2486-97.

Ostlund RE, Jr. (2004) Phytosterols and cholesterol metabolism *Curr Opin Lipidol* **15**, 37-41.

Plat J, Mensink RP (2005) Plant stanol and sterol esters in the control of blood cholesterol levels: mechanism and safety aspects *Am J Cardiol* **96**, 15D-22D.

Silva MA, Swanson AC, Gandhi PJ, Tataronis GR (2006) Statin-related adverse events: a meta-analysis *Clin Ther* **28**, 26-35.

Sprecher DL, Pearce GL (2002) Fiber-multivitamin combination therapy: a beneficial influence on low-density lipoprotein and homocysteine *Metabolism* **51**, 1166-70.

Thompson GR (2005) Additive effects of plant sterol and stanol esters to statin therapy *Am J Cardiol* **96**, 37D-9D.

Thurnhofer H, Hauser H (1990) Uptake of cholesterol by small intestinal brush border membrane is protein-mediated *Biochemistry* **29**, 2142-8.

Varady KA, Wang Y, Jones PJ (2003) Role of policosanols in the prevention and treatment of cardiovascular disease *Nutr Rev* **61**, 376-83.

Vasudevan AR, Jones PH (2005) Effective use of combination lipid therapy *Curr Cardiol Rep* **7**, 471-9.

von Bergmann K, Sudhop T, Lutjohann D (2005) Cholesterol and plant sterol absorption: recent insights *Am J Cardiol* **96**, 10D-4D.

World Medical Association (2000) Declaration of Helsinki V: ethical principles for medical research involving human subjects.

Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L (2004) Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study *Lancet* **364**, 937-52.

# 23

# Viscous soluble fiber combined with three other phytonutrients is effective as first line treatment or adjunct therapy to statins in hypercholesterolemia

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## Abstract

***Introduction.*** This preliminary pilot study investigates the efficacy of a fiber drink in improving lipid levels. The product combines viscous soluble fiber with phytosterols, policosanol, and an aqueous extract of *Chrysanthemum morifolium*. All four ingredient groups have been shown to have cholesterol lowering potential, but all through different biological mechanisms. The test product is the first to combine these four cholesterol lowering mechanisms in one product.

***Materials and methods.*** Forty-one subjects with mild hypercholesterolemia (LDL-c > 110 mg/dL) completed a 6-week open label study design. The product was taken twice daily before the main meals. Fasting lipid panels were measured at baseline and 6 weeks. The study also analyzed the effects of the product in a subgroup of statin prescription medication users.

***Results.*** For the total group, LDL-c was reduced 11.4% (p<0.01) in the whole group and 16.1 % (p<0.001), and 16.6 % (p<0.05) in sub groups of subjects having LDL levels > 130 and > 160 mg/dL, respectively. HDL levels were increased 14.8% (p<0.001) in the whole group, and 27.9% (p<0.01) in a sub group of subjects having HDL levels < 40 mg/dL at baseline. Total cholesterol levels were reduced 1.1 % (n.s.) after 6 weeks, and 1.4% (n.s.) in a subgroup of subjects with TC levels > 200 mg/dL at baseline. TG and Risk Ratio were also positively influenced. For the subgroup of statin users, that had reached the maximum efficacy of their prescription medication, the LDL-c dropped by an additional 14.3 % (p<0.05) and 21.1% (p<0.05) for subjects having LDL-c levels > 130 mg/dL at baseline. HDL-c levels increased 13.7% (p<0.05) and 23.2% (p<0.05) for HDL-c levels < 40 mg/dl at baseline.

***Conclusion.*** This fiber drink combining viscous soluble fiber with three other phytonutrients is a promising natural therapy as a first line intervention, and may serve as an adjunct therapy to pharmaceutical lipid lowering prescription therapy.
Introduction

Elevated total cholesterol (TC), LDL-cholesterol (LDL-c), and reduced HDL-cholesterol (HDL-c) levels have been determined a major risk factor for the development of cardio vascular disease, and the formation of atherosclerotic plaques. [1] Improving these lipid levels has been effective in lowering the risk for the development of heart disease and stroke. [2, 3] Conventional first line treatment for hypercholesterolemia comprises of pharmaceutical interventions, such as statin medication, fibrates, and bile-acid sequestrants.[4] In the last decades an increasing number of non-pharmaceutical intervention therapies has been developed, and tested in randomized clinical trials. Examples of these intervention therapies are viscous soluble fiber, [5, 6] phytosterols, and phytostanols, [10-14] and policosanol. [15, 16] These natural non-pharmaceutical intervention therapies have shown moderate lipid lowering success, and are therefore not always an intervention option for immediate hypercholesterolemia. Nevertheless, there is a growing awareness among the public about potential side-effects of pharmaceutical compounds in general and of statin lipid lowering prescription therapy in particular. This has resulted in an increasing demand for dietary or phytotherapeutical approaches to lowering cholesterol. The test product has been developed in an attempt to provide a true alternative to cholesterol lowering prescription.

Traditionally, interventional therapies, both

pharmaceutical and natural, influence only one mechanism to lower cholesterol. While effective for pharmaceuticals, the one-mechanism approach for dietary intervention has shown limited success. At least theoretically, a product combining different mechanisms to lower cholesterol, should have an enhanced efficacy, when compared to a mono-mechanism approach. An increasing number of pharmaceutical interventional therapies are also exploring this concept, [17] for example by using a combination of statin lipid lowering therapy and ezetimibe. [18, 19]

In this study, we investigated the lipid lowering efficacy of a soluble fiber drink, combined with three other phytonutrients, that all have independent data about their lipid-lowering potential. This product therefore approaches lipid lowering through a potentially synergistic combination of 4 different mechanisms. The efficacy will be evaluated as a stand-alone product and as an adjunct therapy to statin medication.

## Materials and Methods

### Subjects

The subjects participating in this study were all residents from Guam, a pacific island that is part of the USA. The subject group consisted of males and females with hypercholesterolemia, and was either currently using lipid lowering prescription medication (statins), or not. The subjects that already were on prescription medication were contacted through the clinic. The subjects that were newly diagnosed with hypercholesterolemia were invited to join in this trial when they visited the clinic. All included subjects signed informed-consents. Subjects were not compensated for their participation in the trial. The recruitment was spread out over a period of 4 weeks. The identity of the subjects was only known to the primary investigator of this study (VD).

### In- and exclusion criteria

Subjects were eligible to participate in the trial if they were between 18 and 75 years old, and if the baseline (BL) value for LDL-c was 110 mg/dL or higher. For the group of statin users in this trial, the last two measured LDL-c levels (not further than 6 months apart) must differ less than 10% from each other, both ways. This ensured that the maximum effect of the current dose of lipid lowering prescription therapy has been reached. Furthermore, they could not have changed their statin dose in the last 6 months.

Subjects were not eligible to participate if they suffered from type-1 diabetes, severe hypertension, defined as at least 100/180 mmHg, or had any other health condition that may interfere with the study results, as judged by the principle investigator. The subjects were also excluded if they suffered from an allergy against any of the ingredients in the tested product, or if they had any medical condition in which fiber consumption is contra-indicated, e.g. Chron's disease. Subjects were allowed to use vitamin or mineral supplements, provided they did not contain fiber, phytosterols, policosanol or *Chrysanthemum morifolium*. Pregnant women or breast feeding women were excluded. If subjects had only one regular meal per day, they were also excluded. Finally, a history of alcohol or drug abuse, psychological or other mental issues that are likely to invalidate the informed consent, or limit the ability the ability of the patient to comply with the protocol requirements resulted in exclusion from this trial.

### Study procedures

This preliminary pilot study used the open-label design, of which the protocol was approved by an external institutional review board. After signing informed consent, the height, and weight were measured, and a lab order was given to the subject to measure the BL lipid levels. The participants were instructed to use the fiber drink prior to at least lunch and dinner for a period of 6 weeks. Using the product before breakfast was also allowed. The fiber drink was supplied as a powder in a canister that included 60 dosages, and subjects were instructed to mix one dosage (6.5 grams, measured with a scoop) at a time with 8 ounces of water, and drink the product about 10 – 15 minutes before the meal. A lipid panel, including TC, LDL, HDL, TG, and cardio vascular risk ratio was measured at BL, and at 6 weeks. The BL measurements were performed by the local laboratory, and the 6 week cholesterol data was performed on-site using a Cholestech LDX system (Cholestech Corp. Hayward, CA). The subjects were instructed to come in fasted before each measuring day. Fasted was defined as having no food or drink other than water since

going to bed the previous night. Visit windows were set at plus or minus 2 days. The subjects were instructed to continue with normal daily activities during their participation in the trial, and not make any changes to normal diet, physical activities, and medication use. Compliance with the protocol was promoted by a weekly phone call with all participants. Compliance was assessed using a questionnaire and an interview with the subjects at the end of the trial.

If the patients changed their use in lipid lowering medication, such as starting a statin drug during the study, or altering the dose, they were discontinued from the trial.

### Composition of the test product

The tested product is marketed under the brand name Bios Life Complete (Unicity International, Orem, UT). A unitary dose of the product comprises of 3.3 grams of dietary fiber consisting of guar gum, gum Arabic, locust bean gum, pectin, and oat fiber. This fiber mix comprises of more than 90 % soluble fiber. The product further contains a vitamin and mineral mix, including vitamins A, B1, B2, B6, B11, B12, C, E, and minerals selenium, chromium, zinc, and calcium, at or near RDA levels. The other phytonutrients to this products are 1.0 grams of phytosterols (including sitosterol, stigmasterol, and campesterol), 6 mg of policosanol (standardized to 60 % octocosanol), and 12.5 mg extract of *Chrysanthemum morifolium*, per unitary dosage.

### Data analysis and statistical methods

The results were analyzed as means in the group. Within-group differences over time were analyzed using 2-tailed paired *t* tests for dependent groups using Microsoft Excel. These procedures were used for all measured parameters. Statistical significance was defined as having a p-value of 0.05 or lower. Variations in measurements are indicated as standard errors of the mean (± SEM).

### Results

Ninety nine subjects were contacted to participate in the trial. Forty-one subjects were eligible to participate, and finalized the 6-week protocol. The age of the group varied between 61,

and 25, with an average age of $52.3 \pm 1.3$ years. The group consisted of 30 females and 11 males. The BL lipid levels of this group were for total cholesterol (TC) $224.0 \pm 4.2$ mg/dL; LDL-c $142.6 \pm 4.2$ mg/dL; HDL-c $46.9 \pm 1.8$ mg/dL; triglycerides (TG) $166.7 \pm 14.0$ mg/dL; and cardio vascular risk ratio $5.1 \pm 0.2$. The cardio vascular risk ration is defined as TC / HDL-c, according to the American Heart Association. Compliance was estimated to be > 60 % on average. In this small-scale pilot trial, however, no one was excluded based on low compliance. Side-effects reported were generally mild, and included gastro-intestinal discomfort, flatulence, and diarrhea, but the side effects reported were not a reason to discontinue with participation in the trial, and typically disappeared after several days. The side effects reported were in line with previous studies that tested fiber supplementation. [9] Of this 41 subject group, 15 subjects were currently using statin medication. The types of statins varied among the group.

### Total Cholesterol

TC levels were slightly reduced in the total group (1.1%), but not significantly. In the subgroup of responders (25/41), the levels were reduced with a mean of 10.1% (p<0.001). The subgroup of responders that had BL levels > 200 mg/dl (18/41) saw an mean reduction of 11.0 % (p<0.001).

For the statin user sub group, the TC levels did not change significantly from the pre-BL to BL time point, but decreased 6.4% after 6 weeks (n.s.). Pre-BL levels are defined as the lipid level measured prior to the BL measurement, typically 6 months before BL. The responder group with BL levels > 200 mg/dl (9/15) had a mean additional decrease of 12.8% (p < 0.001).

### LDL cholesterol

The total group saw a mean reduction of 11.4 % in LDL-c levels (p<0.01). For the subgroups of subjects that had BL levels > 130 mg/dl (24/41) and > 160 mg/dl (9/41), the mean reductions increased to 16.1 % (<0.001) and 16.6% (p<0.05), respectively. For the group of responders that had BL levels > 130 mg/dl (21/41) the mean reduction was 20.4% (p<0.001).

The reduction in LDL-c for the total group of statin users was 14.3% (p<0.05) after six weeks.

The group of statin users that had BL levels > 130 mg/dl reduced LDL-c by a mean of 21.1% (p<0.05), and the responders of that group (5/6) with an additional 28.2% (p<0.001).

### HDL cholesterol

For the good cholesterol, HDL-c, increases in the overall group amounted to a significant 14.8 % (p<0.001). For the subgroup of subjects with HDL-c levels of 40 mg/dL or lower at BL, the mean increase in HDL-c was 27.9 % (p<0.01), and the responders in this group (9 out of 11 subjects) increased their good cholesterol significantly by 34.7 % (p<0.01). For the subgroup of statin users, the average HDL-c levels from pre-BL to BL did not change significantly. After 6 weeks, the average additional increase in HDL-c was 13.7% (p<0.05) for the whole group. The subgroup of BL levels < 40 mg/dl (8/15) increased their HDL-c levels by an average of 23.2% (p<0.05). The responders in this group (7/8) increased their levels by an additional 26.3% (p<0.05).

### Triglycerides

After 6 weeks, triglyceride levels were increased by 12.8 % for the whole group (n.s.) and decreased 13.9% for the subgroup of subjects having TG levels > 200 mg/dl at BL (p<0.05). The subgroup of responders with BL levels > 200 mg/dL (8/10) had a mean reduction of 19.1% (p<0.01). The subgroup of statin users saw a mean reduction of 11.5% (n.s.) in 6 weeks. Subjects on statins and with a BL level > 200 mg/dl (6/15) reduced their TG levels by a mean of 31.4%, but not significantly.

### Cardio vascular risk ratio

The risk ratio for the whole group was significantly reduced by 15.0 % (p<0.001), and by 17.7 % (p<0.01) for the subgroup of subjects having risk ratio levels higher than 5.0 at BL. The responding subgroup (14/17) reduced their risk ratio by an average of 23.5% (p<0.001)

The detailed results for all parameters can be found in Table 1 and 2.

## Table 1

| Parameter | Group | n | BL | t=6 weeks | Δ % | p |
|---|---|---|---|---|---|---|
| TC | All | 41 | 224.0 ± 4.2 | 221.5 ± 6.7 | -1.1 | n.s. |
| | > 200 | 30 | 235.0 ± 4.1 | 231.7 ± 8.0 | -1.4 | n.s. |
| | All, responders | 25 | 218.7 ± 4.9 | 196.6 ± 5.2 | -10.1 | *** |
| | > 200, responders | 18 | 228.5 ± 5.2 | 203.4 ± 6.2 | -11.0 | *** |
| LDL | All | 38 | 142.6 ± 4.2 | 126.4 ± 5.7 | -11.4 | ** |
| | > 130 | 24 | 156.7 ± 4.5 | 131.4 ± 7.0 | -16.1 | *** |
| | > 160 | 9 | 179.8 ± 6.0 | 149.9 ± 13.3 | -16.6 | * |
| | All, responders | 30 | 143.9 ± 4.2 | 116.1 ± 4.4 | -19.3 | *** |
| | > 130, responders | 21 | 154.6 ± 4.0 | 123.1 ± 5.4 | -20.4 | *** |
| | > 160, responders | 8 | 174.8 ± 3.7 | 139.5 ± 9.4 | -20.2 | * |
| HDL | All | 41 | 46.9 ± 1.8 | 53.8 ± 2.1 | 14.8 | *** |
| | < 40 | 11 | 34.8 ± 0.9 | 44.5 ± 2.7 | 27.9 | ** |
| | All, responders | 31 | 45.3 ± 1.9 | 55.9 ± 2.4 | 23.4 | *** |
| | < 40, responders | 9 | 34.9 ± 0.9 | 47.0 ± 2.5 | 34.7 | ** |
| TG | All | 41 | 166.7 ± 14.0 | 188.0 ± 12.1 | 12.8 | n.s. |
| | > 200 | 10 | 300.9 ± 20.8 | 259.1 ± 21.3 | -13.9 | * |
| | All, responders | 15 | 219.1 ± 28.5 | 177.5 ± 23.8 | -19.0 | *** |
| | > 200, responders | 8 | 303.6 ± 26.2 | 245.6 ± 23.9 | -19.1 | ** |
| Risk Ratio | All | 38 | 5.1 ± 0.2 | 4.3 ± 0.2 | -15.0 | *** |
| | > 5 | 17 | 6.3 ± 0.3 | 5.2 ± 0.3 | -17.7 | ** |
| | All, responders | 30 | 5.3 ± 0.3 | 4.2 ± 0.2 | -20.8 | *** |
| | > 5, responders | 14 | 6.5 ± 0.3 | 5.0 ± 0.3 | -23.5 | *** |

Table 1. Lipid level results for subjects with baseline LDL-c > 110 mg/dL.

Table 2, Lipid level results for the subgroup of current statin prescription medication users with baseline LDL-c > 110 mg/dl.

## Discussion

Bios Life™ Complete, the tested product in this study, is a currently marketed fiber drink, comprising of 3.3 grams mostly soluble fiber combined with vitamins, minerals, phytosterols, policosanol, and an aqueous extract of *Chrysanthemum morifolium*. The product has been designed to lower cholesterol utilizing four different biological mechanisms. The four mechanisms have been reviewed in detail elsewhere [20], but in short they are: 1) Bile-acid sequestration by the soluble fiber matrix; 2) Dietary absorption inhibition by the phytosterols; 3) Cholesterol synthesis inhibition by policosanol; and 4) Enhancement of cholesterol metabolism by *Chrysanthemum morifolium*. Some of us [20] have recently investigated this combination of ingredients in a group of subjects with mild hypercholesterolemia. The results of the present study are well in line with the earlier findings, that showed moderate to good LDL-c reductions and good to very good HLD-c increases.[20]

Soluble dietary fiber taken before meals forms a gel-matrix that binds bile acids, and takes them out of the body, as opposed to re-absorption of the bile acids into the blood stream. Since bile acids are derived from cholesterol, the cholesterol pool will be reduced. Studies with soluble fiber alone in relation to lowering lipid levels have shown variable reductions in LDL-c. [5, 6] A recent meta-analysis by Castro *et al.*[22] concluded from 19 studies that soluble fiber lowers LDL-c, TC, and TG, while increasing HDL-c.

Phytosterols are plant components that have a similar organic chemical structure to cholesterol, and when taken before a meal, they interfere with the absorption of cholesterol. [10] These components have an established use as additives to margarines, to lower the cholesterol levels. Supplementation studies with phytosterols in hypercholesterolemia suggest LDL-c lowering in the 5 – 20 % range, over 12-week periods. [12, 13, 23-28]

Policosanol is a poly-alcohol derived from a

| Parameter | Group | n | Pre-BL | BL | Δ % | p | t=6 weeks | Δ % | p |
|---|---|---|---|---|---|---|---|---|---|
| TC | All | 15 | 224.6 ± 7.4 | 218.1 ± 5.9 | -2.9 | n.s | 204.1 ± 8.6 | -6.4 | n.s. |
| | > 200 | 11 | 231.5 ± 9.3 | 228.9 ± 4.5 | -1.1 | n.s | 210.5 ± 10.9 | -8.1 | n.s |
| | All, responders | 11 | 221.5 ± 8.3 | 221.3 ± 6.3 | -0.1 | n.s | 194.9 ± 8.1 | -11.9 | *** |
| | > 200, responders | 9 | 225.3 ± 9.7 | 227.9 ± 5.5 | 1.1 | n.s | 198.7 ± 9.2 | -12.8 | *** |
| | | | | | | | | | |
| LDL | All | 12 | 140.0 ± 4.8 | 133.5 ± 5.6 | -4.6 | n.s | 114.5 ± 6.0 | -14.3 | * |
| | > 130 | 6 | 145.7 ± 5.6 | 149.5 ± 5.5 | 2.6 | n.s | 118.0 ± 10.8 | -21.1 | * |
| | All, responders | 10 | 136.5 ± 5.0 | 134.2 ± 6.5 | -1.7 | n.s | 106.9 ± 3.2 | -20.4 | *** |
| | > 130, responders | 5 | 144.8 ± 6.8 | 151.0 ± 6.4 | 4.3 | n.s | 108.4 ± 6.0 | -28.2 | *** |
| | > 160, responders | | | | | | | | |
| | | | | | | | | | |
| HDL | All | 15 | 40.5 ± 3.1 | 43.3 ± 3.5 | 6.9 | n.s | 49.2 ± 3.9 | 13.7 | * |
| | < 40 | 8 | 35.1 ± 3.3 | 33.9 ± 1.3 | -3.6 | n.s | 41.8 ± 3.8 | 23.2 | * |
| | All, responders | 10 | 40.4 ± 3.8 | 40.4 ± 3.5 | 0.0 | n.s | 50.1 ± 4.7 | 24.0 | ** |
| | < 40, responders | 7 | 36.4 ± 3.5 | 34.3 ± 1.4 | -5.9 | n.s | 43.3 ± 4.0 | 26.3 | * |
| | | | | | | | | | |
| TG | All | 15 | 247.1 ± 29.1 | 266.1 ± 58.8 | 7.7 | n.s | 235.5 ± 24.5 | -11.5 | n.s. |
| | > 200 | 6 | 346.5 ± 44.6 | 465.3 ± 102.9 | 34.3 | n.s | 319.3 ± 32.7 | -31.4 | n.s |
| | All, responders | 6 | 304.2 ± 45.0 | 403.0 ± 123.8 | 32.5 | n.s | 227.5 ± 42.3 | -43.5 | n.s |
| | > 200, responders | 4 | 363.0 ± 39.4 | 532.3 ± 147.0 | 46.6 | n.s | 290.5 ± 20.7 | -45.4 | n.s. |
| | | | | | | | | | |
| Risk Ratio | All | 13 | 5.3 ± 0.6 | 5.2 ± 0.3 | -1.4 | n.s | 4.4 ± 0.3 | -15.2 | ** |
| | > 5 | 7 | 6.4 ± 0.6 | 6.0 ± 0.3 | -6.0 | n.s | 5.0 ± 0.4 | -17.5 | * |
| | All, responders | 11 | 5.0 ± 0.7 | 5.4 ± 0.4 | 6.2 | n.s | 4.3 ± 0.3 | -18.9 | ** |
| | > 5, responders | 6 | 6.1 ± 0.7 | 6.1 ± 0.3 | 0.6 | n.s | 4.8 ± 0.5 | -21.2 | ** |

waxy substance from the sugar cane plant. The active component from this mixture is thought to be octocosanol. Mechanistic studies have suggested that this phytonutrient works similar to statin medication in inhibiting HMGCoA reductase, and thereby lowering cholesterol levels. [29] The majority of interventional studies with policosanol have been performed by Castano, [15, 30-34] but other groups have investigated this phytonutrient as well. [35, 36] Most studies indicate a solid reduction of LDL-c with policosanol, and a moderate HDL-c increase. Two recently published studies, however, failed to show an effect of policosanol. [36, 37]

Finally, *Chrysanthemum morifolium* is a flower that has been used in Asia as a health promoting tea for centuries.[38] Recently, an extract of this flower was shown to stimulate 7-alpha hydroxylase in vitro. [39] This enzyme converts cholesterol into 7-alpha hydroxyl cholesterol, a precursor to cholic acid, one of the major bile acids. [40] The investigators suggest that this plant extract may therefore help in lowering serum cholesterol levels, [39] but, as to our knowledge, such an effect has not been established in a human study.

This combination of neutraceuticals lowers LDL cholesterol with a mean of 11.4 % in a six week period. For subjects that have higher BL LDL-c levels, the reductions are more profound: 16.1 % and 16.6 % on average after 6 weeks, well in line with expectations, and earlier findings. [20] As with all studies, not all subjects respond to the intervention. In our group 30 subjects out of a total 41 responded to the treatment, which amounts to 73%. Not responding may have different reasons. First, lack of perfect compliance is a problem for all interventional studies, and since dietary interventions for cholesterol lowering are generally requiring a longer treatment period, it is of particular importance in this trial. Another potential explanation is the relative inconvenient delivery method of the product, compared to capsules or tablets. We have used a questionnaire to evaluate the compliance in our group, and concluded it was more than 60% on average. It is likely, however, that some subjects have over-reported compliance. A third possible confounding factor may be changes in dietary habits during the 6 week trial period. Although only about 25% of cholesterol levels in the

body are influenced by dietary intake, differences in fat composition of the meal may well influence the lipid levels in the subject group. We have not monitored the dietary habits of the subjects in this trial, because we wanted to observe the effects this product may have in a real world setting, were dietary changes are a normal part of life.

HDL-c was increased dramatically in this study. It has been reported that dietary interventions may have a remarkable effect on HDL-c levels, which may be partly caused by general positive health effects of better nutrition.[41] For subjects that have levels lower than the advised minimum level, the mean increase was almost 28%.

Statin medication is known to lower LDL-c significantly. A recent review by Edwards and Moore[42] concluded that the average LDL-c reduction of the most common dosage forms of statins amounts to 32% after a minimum of 12 weeks intervention. The average results for HDL-c increase, however, were only 7% for the same time period.

In this study we report an average LDL-c reduction which is clinically relevant in a period of six weeks. For subjects having higher BL LDL-c levels, the reductions in the six-week period were about 16%. We anticipate that for longer study periods and better compliance the reductions will be more pronounced, because in our previous work, an LDL-c reduction of 30% was reached after 8 weeks in subjects with BL LDL-c levels of higher than 160 mg/dl. [20]

The results from this work indicate that the tested product may serve as a first line treatment option for people with mildly elevated lipid levels. The results for HDL-c, however, are much stronger than for statin medication. The recent study with rosuvastatin[43] reported a mean HDL-c increase of 14.7% after an intervention period of 24 months, and according to the authors this was the best results ever reported for statin medication. Our mean results are an increase of 14.8%, but already obtained in a period of six weeks. For the subgroup of subjects that had BL levels < 40 mg/dl, the results are almost double.

Total cholesterol levels in this study did not improve with impressive numbers. This can be explained by the combined reduction in LDL cholesterol and increase in HDL cholesterol. Since TC is derived from the sum of these two

values (and others), the overall reduction in TC is smaller than would be observed in statin intervention studies, that typically do not show a large HDL-c increase. [42]

The cardio vascular risk ratio is defined as TC divided by HDL. Although ATP III does not define this ratio as a therapy target, many studies show that the total cholesterol/HDL cholesterol ratio is a powerful predictor of CHD risk. [44] The American Heart Association defines a risk ratio of lower than 5.0 as preferential, if there are no other risk factors present. The effect of the test product on this ratio in our pilot study is significant for the total group and the sub group that has a BL level of 5.0 or more. The major contributor to this reduction in the risk ratio is the increase in HDL.

The levels of triglycerides were negatively influenced by the tested product in the whole group after 6 weeks, but positively in the subgroup of TC levels > 200 mg/dL at BL. This is contrary to earlier obtained results with this product. [20] A possible explanation for this phenomenon may be that subjects increased their fat consumption during the trial, but that the people that were used to having a higher fat content in their diet (the subgroup), were experiencing a positive change in this dietary habit, due to the increased fiber content in their diet. This has been observed by more fiber intervention studies. [9] Although all subjects were fasted before coming in to have the lipid panels measured, the fasting time (from going to bed), may have been too short to reduce diet-related fluctuations of this level.

Because we expected an important effect of the test product for HDL-c levels, we decided to include a number of current statin medication users in the trial. Due to logistic reasons, we were unable to include only patients with identical treatment regimens, but in stead chose to include a variety of statin types, and dosages in our study group. We assumed that the individual types of statins and their dosages had been chosen as an optimal treatment for the individual subject. Because our inclusion criteria ensured that the subjects on statins did not have significant changes in LDL-c levels over the last six months, we were sure that the maximum lipid

improvement effect of the statin medication had been reached, at that particular dose.

We were surprised to find that the mean reduction in LDL-c in this group after six weeks of intervention with the test product was 14.3%. This reduction was realized *on top of the already reduced values* due to the statin use. The additional reduction in LDL-c levels was likely possible because the test product and statins have different biological mechanisms to lower cholesterol. Also in this sub group, higher BL levels result in higher reductions. The statin users that were not able to reduce their LDL-c to values to under 130 mg/dL even realized an additional 21.1% reduction using the test product in 6 weeks.

For the good cholesterol, HDL-c, the mean increase during the study period was 13.7% and 23.2% for subjects having BL levels < 40 mg/dL. Given the very modest results of statins in increasing HDL-c, this result suggests that the test product can serve as a very valuable adjunct therapy to statin medication: the LDL-c values will be further reduced, while the HDL-c levels are expected to improve dramatically. Clinicians are increasingly aware of the need of reducing LDL-c, while at the same time increasing HDL-c. [41] The Framingham heart study revealed that increasing HDL-c may be even more important than decreasing LDL-c. [45] This is leading to increased pharmaceutical research to find complimentary intervention therapies to increase HDL-c. [46] This reported result of a combined use of statin and the test product may provide exactly that option. Future research in this area is therefore needed.

TC, TG, and Risk Ratio were also positively influenced by the combination of the test product and statins. All pre-BL vs. BL changes were not statistically significant for this group, but after 6 weeks of co-treatment the parameters changed beneficially in statistically significant ways.

There is increasing concern among patients about the safety of prescription medication, in particular statins, because of existing side-effects, such as muscle weakness, and liver damage. [47] Although these side-effects are rather rare in users of these medications, patients are exploring the availability of natural side-effect free therapies as a first line intervention to lower their cholesterol levels. The preliminary data obtained in this study

warrant the exploration of this fiber drink as a first line treatment for hyperlipidemia. According the NCEP guidelines, the first intervention for high cholesterol should be the so-called Therapeutic Lifestyle Change Diet. [44] Part of this dietary guideline is the intake of fiber at minimum daily levels of 25 – 30 grams. The average dietary consumptions of adults in the USA are well below this level. [21] Two servings of the test product provide 6.6 grams of dietary fiber, and can therefore serve to partly fill the gap between actual and advised dietary consumption of fiber.

Although the results in this preliminary pilot study are impressive, the overall average effect of the tested product is likely to have been reduced because of lower than optimal compliance. Compliance is of utmost importance in all studies, but even more in dietary intervention trials that rely on typically milder effects of the ingredients. In our continued studies with this product we are currently using methods to improve the compliance with the test product.

We limited the study period to 6 weeks for practical reasons. It is unknown if the observed improvements in lipid profiles persist for longer times. Some reports indicate that results of intervention trials with phytosterols over longer periods (up to 1 year) may be less pronounced than for shorter periods. [48] To our knowledge, similar findings have not been reported for the other ingredients in this tested product. Future studies should therefore study the test product during longer follow-up periods.

**Conclusion**

Viscous soluble fiber combined with phytosterols, policosanol, and an aqueous extract of *Chrysanthemum morifolium* is a promising natural dietary supplement to lower LDL cholesterol, and to increase HDL cholesterol with clinically relevant numbers. The reported effects are found in a group of subjects with mild hypercholesterolemia, and also in a subgroup of subjects that have used statin medication to treat these high cholesterol levels. The test product Bios Life can serve as a primary intervention therapy for high cholesterol. Because the effects on both LDL-c and HDL-c are also found when combining the product with statin prescription

medication, the product is promising as an adjunct therapy to lipid lowering therapy. This pilot study warrants further study with this product in larger groups, for longer follow-up periods, and with better compliance.

**References**

1. Yusuf, S., S. Hawken, S. Ounpuu, T. Dans, A. Avezum, F. Lanas, M. McQueen, A. Budaj, P. Pais, J. Varigos, and L. Lisheng (2004) Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 364, 937-52

2. Switzer, J.A. and D.C. Hess (2006) Statins in stroke: prevention, protection and recovery. Expert Rev Neurother 6, 195-202

3. Amarenco, P., P.C. Lavallee, J. Labreuche, and P.J. Touboul (2005) Stroke prevention, blood cholesterol and statins. Acta Neurol Taiwan 14, 96-112

4. Edwards, J.E. and R.A. Moore (2003) Statins in hypercholesterolaemia: a dose-specific meta-analysis of lipid changes in randomised, double blind trials. BMC Fam Pract 4, 18

5. Anderson, J.W., L.D. Allgood, J. Turner, P.R. Oeltgen, and B.P. Daggy (1999) Effects of psyllium on glucose and serum lipid responses in men with type 2 diabetes and hypercholesterolemia. Am J Clin Nutr 70, 466-73

6. Anderson, J.W., M.H. Davidson, L. Blonde, W.V. Brown, W.J. Howard, H. Ginsberg, L.D. Allgood, and K.W. Weingand (2000) Long-term cholesterol-lowering effects of psyllium as an adjunct to diet therapy in the treatment of hypercholesterolemia. Am J Clin Nutr 71, 1433-8

7. Jenkins, D.J., C.W. Kendall, V. Vuksan, E. Vidgen, T. Parker, D. Faulkner, C.C. Mehling, M. Garsetti, G. Testolin, S.C. Cunnane, M.A. Ryan, and P.N. Corey (2002) Soluble fiber intake at a dose approved by the US Food and Drug Administration for a claim of health benefits: serum lipid risk factors for cardiovascular disease assessed in a randomized controlled crossover trial. Am J Clin Nutr 75, 834-9

8. Knopp, R.H., H.R. Superko, M. Davidson,

W. Insull, C.A. Dujovne, P.O. Kwiterovich, J.H. Zavoral, K. Graham, R.R. O'Connor, and D.A. Edelman (1999) Long-term blood cholesterol-lowering effects of a dietary fiber supplement. Am J Prev Med 17, 18-23

9. Sprecher, D.L. and G.L. Pearce (2002) Fiber-multivitamin combination therapy: a beneficial influence on low-density lipoprotein and homocysteine. Metabolism 51, 1166-70

10. von Bergmann, K., T. Sudhop, and D. Lutjohann (2005) Cholesterol and plant sterol absorption: recent insights. Am J Cardiol 96, 10D-14D

11. Thompson, G.R. (2005) Additive effects of plant sterol and stanol esters to statin therapy. Am J Cardiol 96, 37D-39D

12. Plat, J. and R.P. Mensink (2005) Plant stanol and sterol esters in the control of blood cholesterol levels: mechanism and safety aspects. Am J Cardiol 96, 15D-22D

13. McPherson, T.B., R.E. Ostlund, A.C. Goldberg, J.H. Bateman, L. Schimmoeller, and C.A. Spilburg (2005) Phytostanol tablets reduce human LDL-cholesterol. J Pharm Pharmacol 57, 889-96

14. Jenkins, D.J., C.W. Kendall, A. Marchie, D.A. Faulkner, J.M. Wong, R. de Souza, A. Emam, T.L. Parker, E. Vidgen, E.A. Trautwein, K.G. Lapsley, R.G. Josse, L.A. Leiter, W. Singer, and P.W. Connelly (2005) Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants. Am J Clin Nutr 81, 380-7

15. Castano, G., R. Mas, J.C. Fernandez, L. Fernandez, J. Illnait, and E. Lopez (2002) Effects of policosanol on older patients with hypertension and type II hypercholesterolaemia. Drugs R D 3, 159-72

16. Crespo, N., J. Illnait, R. Mas, L. Fernandez, J. Fernandez, and G. Castano (1999) Comparative study of the efficacy and tolerability of policosanol and lovastatin in patients with hypercholesterolemia and noninsulin dependent diabetes mellitus. Int J Clin Pharmacol Res 19, 117-27

17. Vasudevan, A.R. and P.H. Jones (2005) Effective use of combination lipid therapy. Curr Cardiol Rep 7, 471-9

18. Kosoglou, T., P. Statkevich, A.O. Johnson-Levonas, J.F. Paolini, A.J. Bergman, and K.B. Alton (2005) Ezetimibe: a review of its metabolism, pharmacokinetics and drug interactions. Clin Pharmacokinet 44, 467-94

19. Davidson, M.H. (2003) Ezetimibe: a novel option for lowering cholesterol. Expert Rev Cardiovasc Ther 1, 11-21

20. Verdegem, P. (2006) Viscous soluble fiber combined with three other phytonutrients benefits lipid profiles in hypercholesterolemia. Submitted

21. Liu, S., J.E. Buring, H.D. Sesso, E.B. Rimm, W.C. Willett, and J.E. Manson (2002) A prospective study of dietary fiber intake and risk of cardiovascular disease among women. J Am Coll Cardiol 39, 49-56

22. Castro, I.A., L.P. Barroso, and P. Sinnecker (2005) Functional foods for coronary heart disease risk reduction: a meta-analysis using a multivariate approach. Am J Clin Nutr 82, 32-40

23. Goldberg, A.C., R.E. Ostlund, Jr., J.H. Bateman, L. Schimmoeller, T.B. McPherson, and C.A. Spilburg (2006) Effect of plant stanol tablets on low-density lipoprotein cholesterol lowering in patients on statin drugs. Am J Cardiol 97, 376-9

24. Varady, K.A., A.C. St-Pierre, B. Lamarche, and P.J. Jones (2005) Effect of plant sterols and endurance training on LDL particle size and distribution in previously sedentary hypercholesterolemic adults. Eur J Clin Nutr 59, 518-25

25. Lau, V.W., M. Journoud, and P.J. Jones (2005) Plant sterols are efficacious in lowering plasma LDL and non-HDL cholesterol in hypercholesterolemic type 2 diabetic and nondiabetic persons. Am J Clin Nutr 81, 1351-8

26. Jakulj, L., M.D. Trip, T. Sudhop, K. von Bergmann, J.J. Kastelein, and M.N. Vissers (2005) Inhibition of cholesterol absorption by the combination of dietary plant sterols and ezetimibe: effects on plasma lipid levels. J Lipid Res 46, 2692-8

27. Fernandez, M.L. and S. Vega-Lopez (2005) Efficacy and safety of sitosterol in the management of blood cholesterol levels. Cardiovasc Drug Rev 23, 57-70

28. Cater, N.B., A.B. Garcia-Garcia, G.L. Vega, and S.M. Grundy (2005) Responsiveness of plasma lipids and lipoproteins to plant stanol esters. Am J Cardiol 96, 23D-28D

29. Singh, D.K., L. Li, and T.D. Porter (2006) Policosanol Inhibits Cholesterol Synthesis in Hepatoma Cells by Activation of AMP-kinase. J Pharmacol Exp Ther

30. Castano, G., R. Mas, L. Fernandez, J.C. Fernandez, J. Illnait, L.E. Lopez, and E. Alvarez (2000) Effects of policosanol on postmenopausal women with type II hypercholesterolemia. Gynecol Endocrinol 14, 187-95

31. Castano, G., R. Mas, L. Fernandez, J. Illnait, R. Gamez, and E. Alvarez (2001) Effects of policosanol 20 versus 40 mg/day in the treatment of patients with type II hypercholesterolemia: a 6-month double-blind study. Int J Clin Pharmacol Res 21, 43-57

32. Castano, G., R. Mas, J.C. Fernandez, J. Illnait, L. Fernandez, and E. Alvarez (2001) Effects of policosanol in older patients with type II hypercholesterolemia and high coronary risk. J Gerontol A Biol Sci Med Sci 56, M186-92

33. Castano, G., R. Menendez, R. Mas, A. Amor, J.L. Fernandez, R.L. Gonzalez, M. Lezcay, and E. Alvarez (2002) Effects of policosanol and lovastatin on lipid profile and lipid peroxidation in patients with dyslipidemia associated with type 2 diabetes mellitus. Int J Clin Pharmacol Res 22, 89-99

34. Castano, G., R. Mas, L. Fernandez, J. Illnait, M. Mesa, E. Alvarez, and M. Lezcay (2003) Comparison of the efficacy and tolerability of policosanol with atorvastatin in elderly patients with type II hypercholesterolaemia. Drugs Aging 20, 153-63

35. Gamez, R., R. Maz, M.L. Arruzazabala, S. Mendoza, and G. Castano (2005) Effects of concurrent therapy with policosanol and omega-3 fatty acids on lipid profile and platelet aggregation in rabbits. Drugs R D 6, 11-9

36. Greyling, A., C. De Witt, W. Oosthuizen, and J.C. Jerling (2006) Effects of a policosanol supplement on serum lipid concentrations in hypercholesterolaemic and heterozygous familial hypercholesterolaemic subjects. Br J Nutr 95, 968-75

37. Berthold, H.K., S. Unverdorben, R. Degenhardt, M. Bulitta, and I. Gouni-Berthold (2006) Effect of policosanol on lipid levels among patients with hypercholesterolemia or combined hyperlipidemia: a randomized controlled trial. Jama 295, 2262-9

38. Kim, H.J. and Y.S. Lee (2005) Identification of new dicaffeoylquinic acids from Chrysanthemum morifolium and their antioxidant activities. Planta Med 71, 871-6

39. Chen, Q., H. de Bont, L. Van der Zee, M. Lansink, and K. Van Norren (2000) Cholesterol lowering supplement.

40. Salway, J., *Metabolism at a Glance*. 2004, Malden, MA: Blackwell Publishing Ltd.

41. Kuvin, J.T., A.A. Alsheikh-Ali, and R.H. Karas (2006) High-density lipoprotein cholesterol-raising strategies. J Cardiovasc Pharmacol 47, 196-204

42. Edwards, J. and R. Moore (2003) Statins in hypercholeterolaemia: A dose-specific meta-analysis of lipid changes in randomised, double blind trials. BMC Family Practice 4, 1-19

43. Nissen, S.E., S.J. Nicholls, I. Sipahi, P. Libby, J.S. Raichlen, C.M. Ballantyne, J. Davignon, R. Erbel, J.C. Fruchart, J.C. Tardif, P. Schoenhagen, T. Crowe, V. Cain, K. Wolski, M. Goormastic, and E.M. Tuzcu (2006) Effect of very high-intensity statin therapy on regression of coronary atherosclerosis: the ASTEROID trial. Jama 295, 1556-65

44. Health, N.I.o. (2001) Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). Jama 285, 2486-97

45. Nam, B.H., W.B. Kannel, and R.B. D'Agostino (2006) Search for an optimal atherogenic lipid risk profile: from the

Framingham Study. Am J Cardiol 97, 372-5

46. Lee, J.M. and R.P. Choudhury (2006) Prospects for atherosclerosis regression: HDL elevation and other emerging therapeutic technologies. Heart

47. Silva, M.A., A.C. Swanson, P.J. Gandhi, and G.R. Tataronis (2006) Statin-related adverse events: a meta-analysis. Clin Ther 28, 26-35

48. Ostlund, R.E., Jr. (2004) Phytosterols and cholesterol metabolism. Curr Opin Lipidol 15, 37-41

# 24
# LDL- and HLD-cholesterol optimization using phytonutrient combination therapy: first line intervention and adjunct therapy to statins

By Peter J.E. Verdegem, Ph.D.[2], Vincent Duenas, M.D.[1], Julie Duenas[1], Evelyn Burke[1]

[1]The Doctors Clinic, Tamuning, GU; [2]Unicity International, Orem, UT

Abstract presented at the 1st Asian Preventive Cardiology and Cardiac Rehabilitation Conference 2006, Hong Kong

Research and Development Department, Unicity International, Orem, UT, USA; The Doctor's Clinic, Tamuning, Guam.

## Introduction

Framingham risk analysis shows that simultaneous decreasing LDL-c and increasing HDL-c has a strong correlation with risk reduction for development of cardio vascular disease. Current prescription lipid lowering therapy has shown excellent results in reducing LDL-c, but limited results for HDL-c increase. Our research focuses on using phytonutrient combinations in optimizing both lipoprotein fractions. We present our results of phytonutrient combination therapy as a first line treatment for hypercholesterolemia, as well as adjunct therapy to statin medication.

## Methods

Three studies were performed at three locations in subjects with elevated LDL-c levels (130 – 200 mg/dl at baseline), that used phytonutrient combination therapy (viscous soluble fiber, policosanol, phytosterols, and *Chrysanthemum morifolium*) as stand-alone or along with statins for a period of 8 weeks.

## Conclusion

The intervention product, that lowers cholesterol through 4 different mechanisms, is effective in lowering LDL-c, and increasing HDL-c, making it an effective alternative for patients with mild hypercholesterolemia, also in combination with statin medication.

## Results:

| | Parameter | BL level (mg(dL) | BL (mg/dL) | t=8 weeks (mg/dL) | Δ % | p-value |
|---|---|---|---|---|---|---|
| **Study 1** | LDL-c | >130 | 168 | 127 | -24.5 | <0.0001 |
| | HDL-c | <40 | 32 | 37 | +12.0 | n.s. |
| **Study 2 (adjunct to statins)** | LDL-c | >130 | 150 | 118 | -21.1 | <0.05 |
| | HDL-c | <40 | 34 | 42 | +23.2 | <0.05. |
| **Study 3** | LDL-c | >130 | 154 | 119 | -22.5 | <0.05 |
| | HDL-c | <40 | 25 | 30 | +20.2 | n.s. |

# 25
# Lipid and glucose optimization using phytonutrient combination therapy in diabetes

By Isabel Martinez, MD.[1],

Bobbi Horne[1], Peter J.E. Verdegem, Ph.D., MBA[2]

[1]Blue Mesa Medical Associates, Katy, TX,
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Poster presented at the 8th Annual Conference on Arteriosclerosis, Thrombosis and Vascular Biology

2007, Chicago, IL

**Introduction:** Dietary approaches to management of lipid and glucose parameters in diabetes is gaining popularity among patients. Monotherapy with dietary ingredients has shown positive effects, but with limited clinical relevance. Our research focuses on using a phytonutrient combination in optimizing lipid and glucose parameters. All four ingredients have individual data supporting their use for optimizing lipoprotein fractions in hypercholesterolemia. This pilot study evaluates their combined efficacy in type-II diabetes.

**Methods:** A group of 34 subjects with established type-II diabetes and hypercholesterolemia added the product to their diet. The drink was taken twice daily 15-20 minutes before meals. The fiber drink consists of viscous soluble fiber, minerals, vitamins, policosanol, phytosterols, and an aqueous *Chrysanthemum morifolium* extract. Lipid and glucose parameters were measured at baseline, 4 and 8 weeks.

**Conclusion:** Bios Life™, a phytonutrient combination drink, shows potential in optimizing parameters associated with cardio vascular disease risk in type-II diabetes. These findings are well in line with previously reported clinical results. The fiber component has reduced the post-prandial glucose levels and the resulting lower HbA1c levels indicate that Bios Life provides a natural option to improve diabetes management.

## Results:

| Parameter | Inclusion criteria at BL (mg(dL) | B.L. (mg/dL) | t=8 weeks (mg/dL) | Δ % | p-value |
|---|---|---|---|---|---|
| TC | All | 208 | 178 | -14.2 | <0.01 |
| TC | >200 | 245 | 195 | -21.5 | <0.001 |
| LDL-c | All | 127 | 104 | -18.3 | <0.05 |
| LDL-c | >160 | 197 | 141 | -28.9 | <0.005 |
| HDL-c | All | 46 | 48 | +3.5 | n.s. |
| HDL-c | <40 | 35 | 40 | +14.4 | n.s. |
| TG | All | 182 | 143 | -21.3 | n.s. |
| TG | >150 | 242 | 163 | -32.5 | <0.05 |
| Glu | All | 162 | 134 | -17.3 | <0.05 |
| Glu | >175 | 218 | 155 | -28.9 | <0.05 |
| HbA1c | All | 7.2[a] | 6.6[a,b] | -9.4 | <0.05 |
| HbA1c | >8[a] | 9.2[a] | 7.8[a,b] | -15.8 | <0.05 |

[a]in %; [b]measurement at 12 weeks.

# The effects of a fiber-rich nutritional supplement, Bios Life® Slim, on the glycemic index of three starchy foods

**Background:**
Glycemia is defined as the presence of glucose or sugar in the blood. Research has shown that glycemic control, or blood sugar management, is an accurate indicator for overall health and wellness. Further research has shown that long term consumption of high glycemic index diets lead continual surges in blood sugar and insulin levels which have been correlated to increased risks for diabetes, cardiovascular disease and most recently, obesity.

**Objective:**
The objective of this study was to quantitatively measure the impact of a fiber-rich nutritional supplement on the glycemic index of three common foods, white bread, white rice and instant mashed potatoes.

**Design:**
Lean, healthy subjects (n=10) consumed 50 grams of glucose in water and three starchy foods (white bread, white rice and instant mashed potatoes) along with 7.25 g of Bios Life Slim or 14.5 g of Bios Life Slim dissolved in 250 ml of water. Using standardized methods for determining glycemic indices, plasma samples were collected and analyzed for glucose and insulin levels.

The data were plotted, curves were generated and areas under the curves (AUC) were calculated. Glycemic and insulinemic indices were calculated by dividing the two-hour plasma glucose or insulin AUC by the two-hour plasma glucose reference AUC and multiplying that value by 100 to obtain a percentage.

**Results:**
One dose of Bios Life Slim reduces the glycemic index of white rice, instant mashed potatoes, white bread and by 16.0%, 16.9% and 20.5% respectively. Two doses of Bios Life Slim reduces the glycemic index instant mashed potatoes, white rice and white bread by
20.4%, 24.7%, and 27.7% respectively. One dose of Bios Life Slim reduces the insulinemic index of instant mashed potatoes, white rice and white bread by 10.4%, 16.9% and 21.3% respectively. Two doses of Bios Life Slim reduces the insulinemic index of instant mashed potatoes, white bread and white rice by 15.1%, 27.0% and 27.3% respectively.

# The effects of a fiber-rich nutritional supplement, Bios Life® Slim, on the glycemic index of three starchy foods.

Jennie Brand-Miller [1], Fiona Atkinson [1], and Thomas Cutler [2]

Continued

# The effects of a fiber-rich nutritional supplement, Bios Life® Slim, on the glycemic index of three starchy foods.

Jennie Brand-Miller [1], Fiona Atkinson [1], and Thomas Cutler [2]
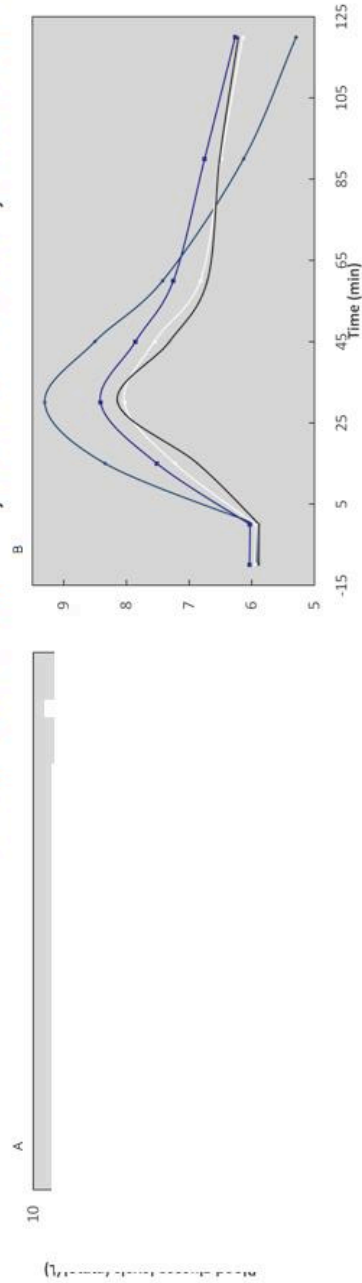


Figure 2. Average plasma glucose response curves of equal carbohydrate portions of a glucose reference shown in blue diamonds, a food (Figure 2A – White Bread, 2B – White Rice, and 2C – Instant Mashed Potatoes) show in red squares and the meals plus one dose (7.25 g) of Bios Life Slim, shown in the green triangles, or the meal plus two doses (14.50 g) of Bios Life Slim shown
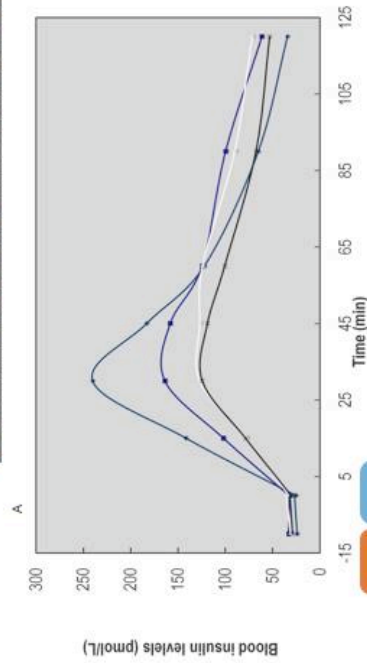


Figure 3. Average plasma insulin response curves of equal carbohydrate portions of a glucose reference shown in blue diamonds, a food (Figure 3A – White Bread, 3B – White Rice, and 3C – Instant Mashed Potatoes) show in red squares and the meals plus one dose (7.25 g) of Bios Life Slim, shown in the green triangles, or the meal plus two doses (14.50 g) of Bios Life Slim shown

# The effects of a fiber-rich nutritional supplement, Bios Life® Slim, on the glycemic index of three starchy foods.

Jennie Brand-Miller [1], Fiona Atkinson [1], and Thomas Cutler [2]

## Abstract

Background: Glycemia is defined as the presence of glucose or sugar in the blood. Research has shown that glycemic control, or blood sugar management, is an accurate indicator for overall health and wellness. Further research has shown that long term consumption of high glycemic index diets lead continual surges in blood sugar and insulin levels which have been correlated to increased risks for diabetes, cardiovascular disease and most recently, obesity.

Objective: The objective of this study was to quantitatively measure the impact of a fiber-rich nutritional supplement on the glycemic index of three common foods, white bread, white rice and instant mashed potatoes.

Design: Lean, healthy subjects (n=10) consumed 50 grams of glucose in water and three starchy foods (white bread, white rice and instant mashed potatoes) along with 7.25 g of Bios Life Slim or 14.5 g of Bios Life Slim dissolved in 250 ml of water. Using standardized methods for determining glycemic indices, plasma samples were collected and analyzed for glucose and insulin levels. The data were plotted, curves were generated and areas under the curves (AUC) were calculated. Glycemic and insulinemic indices were calculated by dividing the two-hour plasma glucose or insulin AUC by the two-hour plasma glucose reference AUC and multiplying that value by 100 to obtain a percentage.

Results: One dose of Bios Life Slim reduces the glycemic index of white rice, instant mashed potatoes, white bread and by 16.0%, 16.9% and 20.5% respectively. Two doses of Bios Life Slim reduces the glycemic index instant mashed potatoes, white rice and white bread by 20.4%, 24.7%, and 27.7% respectively. One dose of Bios Life Slim reduces the insulinemic index of instant mashed potatoes, white rice and white bread by 10.4%, 16.9% and 21.3% respectively. Two doses of Bios Life Slim reduces the insulinemic index of instant mashed potatoes, white bread and white rice by 15.1%, 27.0% and 27.3% respectively.

## Supplement Facts

Serving Size: 1 Packet (7.25 g)
Servings Per Container: 60

| Amount Per Serving | | % Daily Value** |
|---|---|---|
| Calories 10 | Calories from Fat 0 | |
| Total Fat | 0 g | 0% |
| Saturated Fat | 0 g | 0% |
| Trans Fat | 0 g | |
| Cholesterol | 0 mg | 0% |
| Total Carbohydrate | 5 g | 2% |
| Dietary Fiber | 4 g | 16% |
| Soluble Fiber | 4 g | |
| Insoluble Fiber | 0 g | |
| Sugars | 0 g | |
| Other Carbohydrates | 1 g | |
| Protein | 0 g | |
| Vitamin A (100% as Beta-Carotene) | | 15% |
| Vitamin C | | 70% |
| Vitamin E | | 60% |
| Thiamin | | 100% |
| Riboflavin | | 100% |
| Niacin | | 100% |
| Vitamin B-6 | | 90% |
| Folate | | 100% |
| Vitamin B-12 | | 60% |
| Biotin | | 35% |
| Zinc | | 10% |
| Calcium | | 15% |
| | | 10% |

**Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs.
† Percent Daily Value is not established.

Ingredients: Biosphere Fiber® (guar gum, gum arabic, locust bean gum, citrus pectin, oat fiber, maltodextrin, beta glucan), Nutri-fiber™ (plant-derived polysaccharides, orange juice powder flavor blend, calcium carbonate, stevia, citric acid), Bios Vitamin Complex™ (vitamin C (ascorbic acid), vitamin A (as beta-carotene), vitamin E (d-alpha-tocopheryl acetate), niacin (niacinamide), zinc (zinc gluconate), folic acid, biotin, vitamin B1 (thiamine HCl), vitamin B6 (pyridoxine HCl), vitamin B2 (riboflavin), vitamin B12 (cyanocobalamin), orange juice powder, citric acid).

Figure 1. A – Carton image of the fiber-rich nutritional supplement, Bios Life Slim. B – Contents of Bios Life Slim. C – Calculated supplemental facts of Bios Life Slim.

# The effects of a fiber-rich nutritional supplement, Bios Life® Slim, on the glycemic index of three starchy foods.

Jennie Brand-Miller [1], Fiona Atkinson [1], and Thomas Cutler [2]

**Table 1.** The composition, carbohydrate content and weights of the glucose reference and three starchy foods calculated using the manufacturers' data.

| Test Food | Portion Size (g) | Energy (kJ) | Protein (g) | Fat (g) | Available Carbohydrate (g) | Sugar (g) | Fiber (g) |
|---|---|---|---|---|---|---|---|
| Reference Food (glucose sugar) | 51.4 g glucose 250 g water | 800 | 0 | 0 | 50 | 50 | 0 |
| White Bread | 119.0 g | 1195 | 10.5 | 3 | 50 | 4.5 | 7.1 |
| White Rice Instant | 63.0 g (dry) | 932 | 4.6 | 0.3 | 50 | 0.3 | 0.4 |
| Mashed Potatoes | 67.3 g (dry) | 1206 | 6.5 | 5.8 | 50 | 3.6 | 5.7* |

* Estimated based on food composition tables

**Table 2.** The mean ± standard error of the mean (SEM) of the glycemic index (GI) and insulinemic index (II) values for the glucose reference and the three starchy foods.'
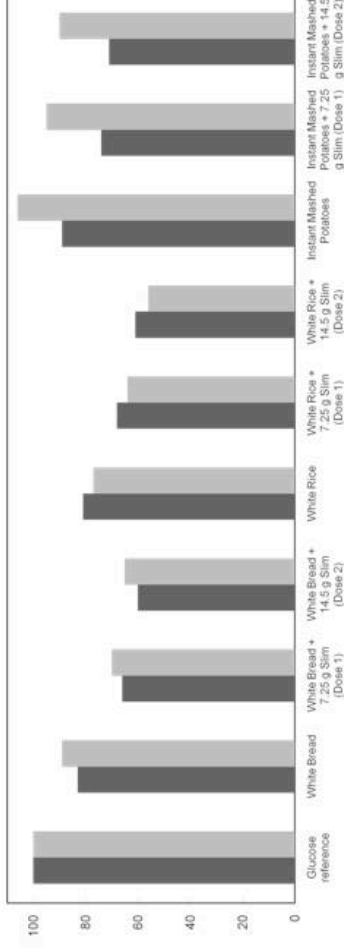
| Test Food | GI value | GI category | II value |
|---|---|---|---|
| Glucose reference | 100 ± 0 | High GI | 100 ± 0 |
| White Bread | 83 ± 6 | High GI | 89 ± 5 |
| White Bread + 7.25 g Slim (Dose 1) | 66 ± 5 | Medium GI | 70 ± 5 |
| White Bread + 14.5 g Slim (Dose 2) | 60 ± 4 | Medium GI | 65 ± 7 |
| White Rice | 81 ± 5 | High GI | 77 ± 4 |
| White Rice + 7.25 g Slim (Dose 1) | 68 ± 6 | Medium GI | 64 ± 5 |
| White Rice + 14.5 g Slim (Dose 2) | 61 ± 5 | Medium GI | 56 ± 5 |
| Instant Mashed Potatoes | 89 ± 6 | High GI | 106 ± 3 |
| Instant Mashed Potatoes + 7.25 g Slim (Dose 1) | 74 ± 5 | High GI | 95 ± 6 |
| Instant Mashed Potatoes + 14.5 g Slim (Dose 2) | 71 ± 6 | High GI | 90 ± 3 |



**Figure 4.** The mean glycemic index (show in blue) and the insulin index (shown in green) values for the glucose reference and the three starchy

## Conclusions

The fiber-rich supplement, Bios Life Slim, decreased the glycemic index of three common, starchy foods in a dose dependent manner. In two of the three cases, white bread and white rice, it reduced their glycemic indices from high glycemic foods to medium glycemic foods. Furthermore, Bios Life Slim, reduced the insulinemic index for all three test foods. Bios Life Slim was most effective in reducing the glycemic and insulinemic indices of white bread and white rice. Further research is needed to measure the effects of supplementation long-term. Additional research is needed to measure the effects of Bios Life Slim with a population that is insulin resistant or that has type 2 diabetes. At the present, Bios Life Slim does provide a means for modulating post-prandial glucose and insulin