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Preliminary Evidence of Efficacy for Policol® One Cholesterol Lowering Effect from Week 4, Adapted to the Upcoming Restrictions for Monacolins in Food in the EU

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Abstract: Cholesterol is necessary for many cell functions but it can also be harmful if it is allowed to reach high blood concentrations, as the risk for premature atherosclerotic cardiovascular diseases increases. Many food supplements contain currently 10 mg of monacolin K in order to benefit of the approved claim to maintain normal blood LDL-cholesterol levels. However, the EFSA has considered that cases of adverse reactions have been reported for monacolins from red yeast rice at intake levels as low as 3 mg/day. That is the reason why the main aim of the present study was to show the effect of Policol® One new formula in patients with non-desirable lipidic profile levels. Policol® One new formula contains a wide range of plant extracts with not only a traditional use, but also a proven effect on plasma lipids. The consumption of one capsule of new Policol® One during dinner for only 4 weeks favorably affected plasma LDL-C (-39.52%) and TC (-40.52%) levels in healthy volunteers. No significant effect on TG and HDL-C was shown after 4 weeks. However, after 12 weeks TG biomarker exhibited a significant reduction (-19.91%) and HDL-C (+9.84%) also improved. No adverse effects were reported during the study. Lower lipid properties may be associated with a synergistic effect of the ingredients which allow us to formulate with a lower and safer dosage of monacolin K.

Keywords: Monascus Purpureus, Policosanol, Guggul, Cholesterol, Natural Therapies, Policol® One

1. Introduction

1.1. Cholesterol

Cholesterol is an organic substance essential for human life. It contains a bulky steroid nucleus with a 3β-hydroxyl group at one end and a flexible hydrocarbon tail at the other. As it is mostly lipophilic, it inserts into lipid bilayers and modulates the fluidity of these biological membranes. The fluidity can influence the ability of some small molecules to diffuse through the membrane, which changes the internal environment of the cell. All in all, cholesterol plays a role in intracellular transportation and regulates the membrane receptor function. Beyond its place in the cell membrane, it has many other roles: it acts as precursor of steroid hormones (e.g., cortisol, aldosterone and adrenal androgens), bile acids, vitamin D and prostaglandins [1, 2].

Cholesterol can be absorbed from diet and synthetized *de novo*. A primary location for most *de novo* synthesis process is the liver which uses Acetyl-CoA as precursor.

Typically, dietary cholesterol intake is approximately 300-450 mg/day and complements the 800-1400 mg of endogenous cholesterol stored in the bile. All cholesterol reaches the small intestine and can be absorbed. The dietary cholesterol must be hydrolyzed by intestinal pancreatic enzymes to form free fatty acids and non-esterified cholesterol. On the other hand, biliary cholesterol is already non-esterified and acts with other agents in order to form micelles during digestion [3].

Furthermore, a low dietary cholesterol intake is compensated by an increase in absorption, suggesting that the balance between absorption and synthesis is also modulated.

As cholesterol is mostly lipophilic, it is transported through the blood, along with triglycerides (TG) and inside

lipoprotein particles (low-density lipoprotein (LDL) and high-density lipoprotein (HDL)).

Plasma cholesterol level depends on many dietary and genetic factors at the same time. It is the net result of intestinal cholesterol absorption and hepatic cholesterol synthesis, on one hand, and biliary excretion and cellular use, on the other hand. Although cholesterol is necessary for many cell functions, it can also be harmful if it is allowed to reach high blood concentrations. In this situation, the risk for premature atherosclerotic cardiovascular diseases increases [1, 2].

1.2. Cardiovascular Diseases and Cholesterol

Cardiovascular diseases are the first cause of death in the developed world, every year more people die from cardiovascular events than from any other cause. It has been proved that high cholesterol levels increase the risks of heart disease and stroke. It has been calculated that one third of ischemic heart diseases are attributable to high cholesterol levels. Globally, raised cholesterol is estimated to cause 2.6 million deaths [4]. In Spain, the prevalence of metabolic cardiovascular risk factors are increasing since 1993. It has been estimated that 17.9% of the population suffer from hypercholesterolemia [5].

Dyslipidemias can be categorized into high total cholesterol (TC), high LDL-cholesterol (LDL-C), high TG and low HDL-cholesterol (HDL-C). The guideline with standard levels is as follows [6]:

Table 1. *Definition and reference values for total cholesterol (mg/dl).*

TC value (mg/dl)	Definition
< 200	Desirable
200-239	Upper limit
≥ 240	High

Table 2. *Definition and reference values for low-density lipoprotein cholesterol (mg/dl).*

LDL-C value (mg/dl)	Definition
< 100	Desirable
100-129	Almost optimal
130-159	Upper limit
160-189	High
≥ 190	Very high

Table 3. *Definition and reference values for triglycerides (mg/dl).*

TG value (mg/dl)	Definition
< 150	Normal
150-199	Upper limit
200-499	High
≥ 500	Very high

Table 4. *Definition and reference values for high-density lipoprotein cholesterol (mg/dl).*

HDL-C value (mg/dl)	Definition
< 40	Low
≥ 60	High

Hypercholesterolemia (high LDL-C) is one of the major risk factors contributing to the formation of atherosclerotic plaques. Also, it has been shown that an elevated HDL-C blood concentration is correlated with a decreased cardiovascular risk in epidemiological studies.

The total cardiovascular risk factors determine which will be the therapeutic approach for high LDL-C. Alternatives include a healthier lifestyle and pharmacological treatment if it is needed [7].

Raised cholesterol is mainly treated with statin drugs which act by decreasing the cellular cholesterol content by selectively inhibiting 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMG-CoA reductase), thus limiting cholesterol biosynthesis and lowering hepatic cholesterol concentrations. This results in a higher expression of low-density lipoprotein receptors (LDL-receptors) in liver cell membranes, enhancing clearance of the circulating LDL particles from blood [8]. Supplementation should be also considered as a preventive action before taking pharmacological treatment [9].

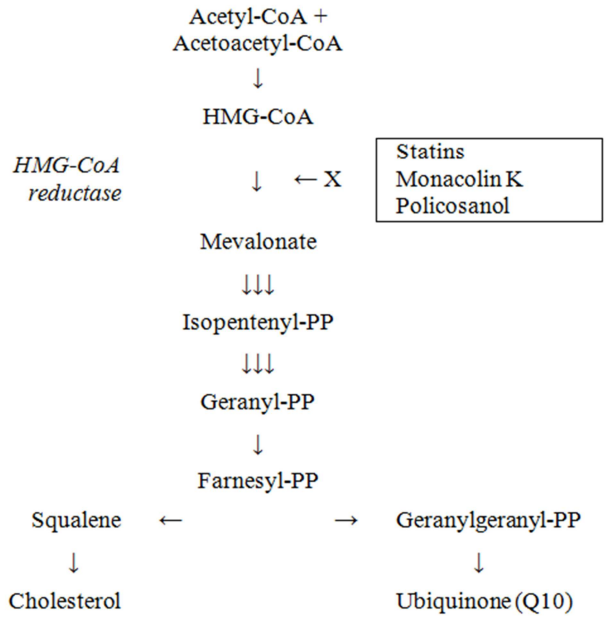

Figure 1. *Branched pathway of mevalonate metabolism.*

It is well known that cardiovascular diseases and coronary hearth diseases are related to higher values of TC and in particular, LDL-C. That is why a preventive supplementation should be considered before taking pharmacological treatment [9].

1.3. Policol® One: A Supplement with Lipid Lowering Properties

Policol® One (*Plameca*) (Table 1) is a food supplement based on red yeast rice, rich in monacolin K with lowering lipid properties, as it has been proved in a previous study [10] and acknowledged by the European Commission with the health claim for red yeast rice at a daily dose of 10 mg of monacolin K. But nevertheless, a recent statement suggested that a 10 mg/day dosage in these products cannot be regarded as safe when used without medical supervision [11]. Our updated formula contains 2,95 mg of monacolins and is complemented with other natural ingredients traditionally

used for its cardio and hepatoprotective properties to reinforce the action of a lower dose of monacolins. It has been proved that combinations of nutraceuticals with different lipid-lowering activities and mechanisms of action, particularly when associated with an appropriate lifestyle, might have essential synergistic effect [9]. All things considered, we want to prove the efficacy for Policol One novel cholesterol lowering formula from 4 weeks.

The possibility of implementing a non-pharmacological nutraceutical based treatment for lowering lipid concentrations is getting increasing attention, and is considered to be an important preventive action to take when hypercholesterolemia is mild or moderate.

Table 5. *Policol® One new formula.*

Ingredients	Quantity per one serving
Ceremyces® (heat treated *Saccharomyces cerevisiae*)	175 mg
Guggul dry extract	80 mg
Sterol content	*1.6 mg*
Red yeast rice	65.55 mg
Monacolins content	*2.95 mg*
Birdseed	50 mg
Nicotinamide (Vitamin B3)	21.6 mg (135% NRV*)
Artichoke dry extract	25 mg
Cynarine content	*0.6 mg*
Dandelion dry extract	25 mg
Inulin content	*4 mg*
Policosanol	16.6 mg
Octacosanol content	*10 mg*
Coenzyme Q10	10 mg

*NRV is nutrient reference value.

1.3.1. Red yeast Rice (RYR) and Monacolin K

Monascus purpureus is a mold fungus that ferments white rice to produce red yeast rice (RYR). It contains sterols, isoflavones, mono unsaturated fatty acids and monacolins [8, 12]. In particular, monacolin K represents between 70-83% of the total active components [13]. Monacolin K has been evaluated in previous studies for its cholesterol-lowering effect. Their mechanism of action has been correlated to its ability to inhibit HMG-CoA reductase, as a result, the endogenous synthesis of cholesterol is reduced and elevated cholesterol levels decrease. Previous studies demonstrated that monacolin K has an identical structure to lovastatin, however human studies have reported that the bioavailability is different for each substance. Patients receiving RYR have a higher bioavailability value than in those taking lovastatin in the same pharmaceutical form. These results have been correlated to a higher dissolution rate and lower degree of crystallinity in monacolin K supplements [14, 15]. Monacolin K is able to reduce LDL-C concentrations by up to 20-25% when given at doses of 3-10 mg/day, consequently it is one of the most typical and effective cholesterol-lowering substances sold as food supplement [13].

1.3.2. Saccharomyces Cerevisiae

Ceremyces® is a group of specific *Saccharomyces cerevisiae* yeast strains used as a dietary source of chromium, B-complex vitamins and selenium. Ceremyces® contains selected yeasts that are heat-activated and dried at a temperature sufficient to inactivate the yeast, but low enough to retain its nutritional properties. Several clinical studies suggest the use of brewer's yeast to lower TC levels and increase HDL-C levels due to its chromium content [16]. A more recent study, showed lower concentration in plasma total cholesterol levels between baseline and week 8 but it also resulted in a significant reduction in plasma TG and LDL-C levels after 4 and 8 weeks. There was also a significant increase in plasma HDL-C levels after 4 and 8 weeks compared with baseline [17].

1.3.3. Coenzyme Q10

Coenzyme Q10 is an isoprenoid that participates in many cellular functions and it is produced by the mevalonate pathway, the same biochemical pathway as cholesterol. Statins, the most common and effective medicines to reduce cholesterol, act as inhibitors of HMG-CoA reductase, the rate-controlling enzyme of the mevalonate pathway. As a consequence, coenzyme Q10 levels can be reduced during statin treatment, which might be associated with statin-induced myopathy [18]. One meta-analysis concluded that coenzyme Q10 supplementation could ameliorate statin-induced myopathy [19].

1.3.4. Nicotinamide

Niacin or vitamin B3 is a water soluble vitamin whose major role is being a precursor for nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADH). These coenzymes participate in oxidation-reduction reactions. Niacin is a widely used agent in the treatment of dyslipidemia as it reduces concentrations of TC, TG, and LDL-C levels. It has been proved that the treatment with niacin significantly reduces mortality, coronary events and retards the progression of coronary atherosclerosis [20].

1.3.5. Guggul

The guggul tree (*Commiphora mukul*) found in India, Bangladesh and Pakistan has been used in the ancient Ayurveda to treat various diseases including hypercholesterolemia [21]. The gugulipid contains pregnane and cholestane steroids (guggulsterones), as well as diterpenes and lignans such as sesamin [10]. The hypolipidemic effects may be due to steroids, Z-guggulsterone and E-guggulsterone which are antagonists at farnesoid x receptor (FXR). This factor is a key transcriptional regulator for the maintenance of cholesterol and bile acid homeostasis. These guggulsterones upregulate the bile salt export pump (BSEP), an efflux transporter responsible for removal of cholesterol metabolites, bile acids from the liver. This favors cholesterol metabolism into bile acids, and thus represents another possible mechanism for its hypolipidemic activity. [21, 22] The hypolipidemic effect of gugulipid and guggulsterone has been consistently demonstrated in various animal species. In various clinical studies, guggul demonstrated hypolipidemic activity with an average of 10-30% and 10-20% decrease in TC and TG,

respectively. However, it has been noted some individual variations in hypolipidemic response [21].

1.3.6. Birdseed

The birdseed (*Phalaris canariensis)*, typically found around the Mediterranean area, has been widely used to reduce high cholesterol levels in Spain. Its seeds contain starch, lipids, resin, salicylic and oxalic acids, but also a huge amount of proteins and enzymes. In view of the tradition of use in this country, the effect of birdseed on cholesterol and TG was studied showing that every participant reduced TC and TG levels after only 3 weeks of treatment [23].

1.3.7. Policosanol

It is a sugar cane (*Saccharum officinarum*) extract which contains a mixture of alcohols but mainly it is formed by octacosanol, 12% triacontanol and 7% hexacosanol. Policosanol has been researched in human population for its cholesterol-lowering properties. It seems to cause decreased synthesis and increased degradation of 3-hydroxy-3-methylglutaryl Coenzyme A (HMG-CoA), which is the rate-limiting step in cholesterol synthesis. An increase of binding, uptake and degradation of LDL-C has been demonstrated, which results in an improvement in LDL-C metabolism [24]. There are several clinical studies demonstrating the efficacy of combinations containing policosanol in association with other active ingredients like monacolin K [15].

1.3.8. Artichoke

Artichoke (*Cynara scolymus*) is a plant native to the Mediterranean region whose leaves are used medicinally. Its main active components are not only phenolic acids such as caffeylquinic acids, but also flavonoids and sesquiterpene lactones [25]. It is known that artichoke has a potential hypolipidemic and hepatoprotective effects due to its antioxidant action. Luteolin, one of its active molecules, interacts with HMG-CoA reductase enzyme and the pathways of regulation in the liver of sterol regulatory element-binding proteins. One meta-analysis concluded that artichoke extract supplementation was associated with a significant reduction in both TC and LDL-C levels. Artichoke has been combined with red yeast rice and other extracts to reach hypolipidemic and anti-inflammatory properties [15, 17].

1.3.9. Dandelion

Dandelion (*Taraxacum officinale)* is indigenous to the northern hemisphere [26]. Its root and leaves have been traditionally used due to its active molecules. The root contains abundant potassium salts, inulin and sesquiterpene lactones and the leaves contain sesquiterpene lactones, triterpenes, phytosterols and flavonoids [27]. Medicinal uses described in pharmacopoeias include diuresis stimulation, bile flow increase, appetite stimulant and treatment of dyspepsia [26].

1.4. Regulatory Landscape

The General Food Law Regulation [Regulation (EC) No. 178/2002 of the European Parliament and of the Council 2002] established an independent organization called the European Food Safety Authority (EFSA) with the specific task of giving scientific advice based on the health benefits and risks related to food intake. Health claims for food referring to the reduction of disease risk and to children's development and health are regulated by Commission Regulation the Commission Regulation (EU) No. 432/2012 of 16 May 2012. In fact, that health claims refer to an exact nutrient, food or substance with an specific conditions of use [14].

The EFSA considered that there is a relationship established between the daily intake of 10 mg of monacolin K and the maintenance of normal blood LDL-C levels but a recent EFSA statement suggested that at 10 mg/day dosage, these products cannot be regarded as safe when used without medical supervision [28].

2. Methods and Materials

2.1. Participants and Study Design

A 12-week long intervention period was initiated with three examinations: baseline examination (t_0), intermediate examination at 4-week (t_4) and final examination at 12-week (t_{12}). It started during December 2019 but unfortunately, we could not collect the final data (t_{12}) as COVID-19 pandemic started just during these weeks and people in Spain were locked down. We could only collect intermediate data (t_4).

Participants were recruited by several physicians based on Barcelona area (Spain) according to inclusion criteria: both male or female patients at age of 25 – 85, with LDL-C between 130 – 159 mg/dl, HDL-C lower than 60 mg/dL and TC between 200 – 239 mg/dl. Finally, 23 volunteers, 8 men and 15 women between 40 and 85 years were selected. Recruited participants were informed, filled in the admission questionnaire, including their lifestyle habits and the results of the analysis of their lipidic profile, which could not be older than one month at the beginning of the intervention. Anthropometric data like height, body weight and blood pressure were measured at t_0 and t_4. Participants filled the same questionnaire at t_4 to check whether any lifestyle changes had been stablished during the study. Adverse events, if any, had to be recorded in the report.

The lifestyle questionnaire is described below:

"What do you usually eat? – Options: Mediterranean diet; Fast food; High carbohydrates diet; Other diet.

Do you drink alcoholic beverages regularly? twice wineglass a week, 1 wineglass a day, 2-3 wineglass a day; +3 wineglass a day.

Do you practice sports usually? If yes, how many times a week? Less than once a week, once a week, twice a week, more than twice a week.

Do you smoke regularly? No smoker, only occasionally, less than a packet of cigarettes a day, a packet of cigarettes a day, two or more packets of cigarettes a day."

Exclusion criteria were defined as follows: pregnant women, being allergic to gluten and/or sulfites, individuals

who have significantly modified their lifestyle during the study, participants who have taken any medication or other food supplement for the control of hyperlipidemia during the trial or 30 days before the trial, participants who have not completed the two lifestyle questionnaires or who have not had their lipid and blood pressure parameters analyzed at the end of the study.

At the end of 2020, a new study was designed with the same inclusion and exclusion criteria to collect data with 12 weeks treatment.

Participants were recruited by some physicians based on Barcelona (Spain). This new study was a 12-week long intervention period with two examinations: baseline examination (t_0) and final examination after 12 weeks (t_{12}). 22 volunteers, 9 men and 13 women between 42 and 76 years were selected. Recruited participants were informed, filled in admission questionnaire, including their lifestyle habits and lipidic fractions profile not older than one month at the beginning of the intervention. Anthropometric data like height, body weight and blood pressure were measured at t_0 and t_{12}. Participants filled the same questionnaire at t_{12} to check whether any lifestyle changes had been stablished during the study. Adverse events, if any, had to be recorded in the report.

All patients were provided with new Policol® One and they were asked to take one capsule a day with dinner during 12 weeks to evaluate the efficacy of new Policol® One. Its formula is shown in Table 1.

2.2. Plasma Analyses

Blood samples were taken at t_4 or t_{12} from each participant by a qualified physician. The blood samples were analyzed by an external laboratory and plasma lipids (LDL-C, HDL-C, TG, TC) were quantified.

2.3. Statistical Analyses

On the first intervention (4 weeks), all the patients finished the treatment course and were included for the statistical analyses. On the second one (12 weeks), all participants finished the treatment, but only 19 volunteers out of 22 were included in final statistical analyses because one participant reported changes in diet and the others were rejected by medical recommendation because of suspecting an analytical error in the determination of blood lipids concentrations. All clinical data were collected and descriptive statistics as mean, standard deviation were calculated for age, height, weight, body mass index (BMI), sex, blood pressure and lipidic fractions. Independent and paired t-tests were performed to analyze the data and normal distribution of the scores. Significance level was set at 0.05.

Both population samples were analyzed in order to confirm if there were any statistically significative differences between them.

The population samples at both interventions were compared and found there were no significant differences between them.

3. Results

3.1. Study Population

For the first intervention the mean age was 54.478±20.801 and the mean BMI was 28.037±5.613. Regarding the lipidic parameters in the baseline, mean TC was 233.826±16.634, mean LDL-C was 151.609±14.761 and mean TG was 119.826±54.865, which corresponds with the upper recommended limit. The mean HDL-C was 59.148±10.880, which is considered acceptable.

For the second one, the mean age was 62.000±14.241 and the mean BMI was 28.608±4.906. The mean lipidic parameters in the baseline were 233.421±21.544 for TC, 154.000±16.770 for LDL-C and 145.489±16.770 for TG. Those values correspond to the upper limit. On the other hand the mean HDL-C was 51.895±12.552, which is considered adequate.

Results showed that both population samples were considered not statistically different one from the other in age (p=0.161), gender (p=0.637), height (p=0.251), weight (p=0.747), BMI (p=0.730), systolic pressure (p=0.239), diastolic pressure (p=0.606) and lipidic profile (TC (p=0.946), LDL-C (p=0.629), TG (p=0.175), HDL-C (p=0.052)) before intervention. This coincidence allows us to compare the results (t_4 and t_{12}) after the treatment.

Table 6. *Age, gender distribution, weight, height, BMI, lipidic profile, blood pressure – 4 and 12 week intervention.*

Parameters	4 week intervention – Baseline t_0 (n=23)	12 weeks intervention – Baseline t_0 (n=19)	P
Men | Women	8 | 15	8 | 11	0.637
Age	57.478±20.801	62.000±14.241	0.161
Weight (kg)	78.113±20.801	76.289±14.241	0.747
Height (cm)	165.891±7.714	163.211±7.070	0.251
BMI (kg/m^2)	28.037±5.613	28.608±4.906	0.730
TC (mg/dl)	233.826±16.634	233.421±21.544	0.946
LDL-C (mg/dl)	151.609±14.761	154.000±16.770	0.629
TG (mg/dl)	119.826±54.865	145.489±65.696	0.175
HDL-C (mg/dl)	59.148±10.880	51.895±12.552	0.052
Systolic pressure (mmHg)	124.913±14.647	130.632±16.317	0.239
Diastolic pressure (mmHg)	75.957±14.647	77.474±10.142	0.606

Data are mean ± SD. P-values are for comparisons to independent *t* test.

3.2. Lipid Metabolism

First of all, the data collected were analyzed separately for week 4 and week 12.

In the first trial, according to the aforementioned clinical guidelines and the results, TC levels improved significatively after 4 weeks of new Policol® One treatment from 233.826±16.634, which is within the upper limit to 193.304±20.485, a desirable value. A 17,3% TC difference was experienced compared to baseline after 4 weeks of treatment (p=0.000). The outcome for LDL-C levels showed a decreasing tendency from 151.609±14.76, an upper limit value, to 112.087±23.285, which is considered an almost optimal value in accordance to the clinical guidelines. In conclusion, 26,1% LDL-C difference was shown compared to baseline after 4 weeks of treatment (p=0.000). Unfortunately, HDL-C and TG levels did not show any significant improvement between the baseline and after taking Policol® One in the 4 weeks intervention.

Table 7. *Lipidic parameters (mg/dl) – 4 week intervention.*

Parameters	Baseline, t_0 (n=23)	After 4 weeks, t_4 (n=23)	P
TC (mg/dl)	233.826±16.634	193.304±20.482	0.000
LDL-C (mg/dl)	151.609±14.761	112.087±23.285	0.000
TG (mg/dl)	119.826±54.865	117.826±37.548	0.420
HDL-C (mg/dl)	59.148±10.880	59.261±9.780	0.459

Data are mean ± SD. P-values are for comparisons to paired *t* test.

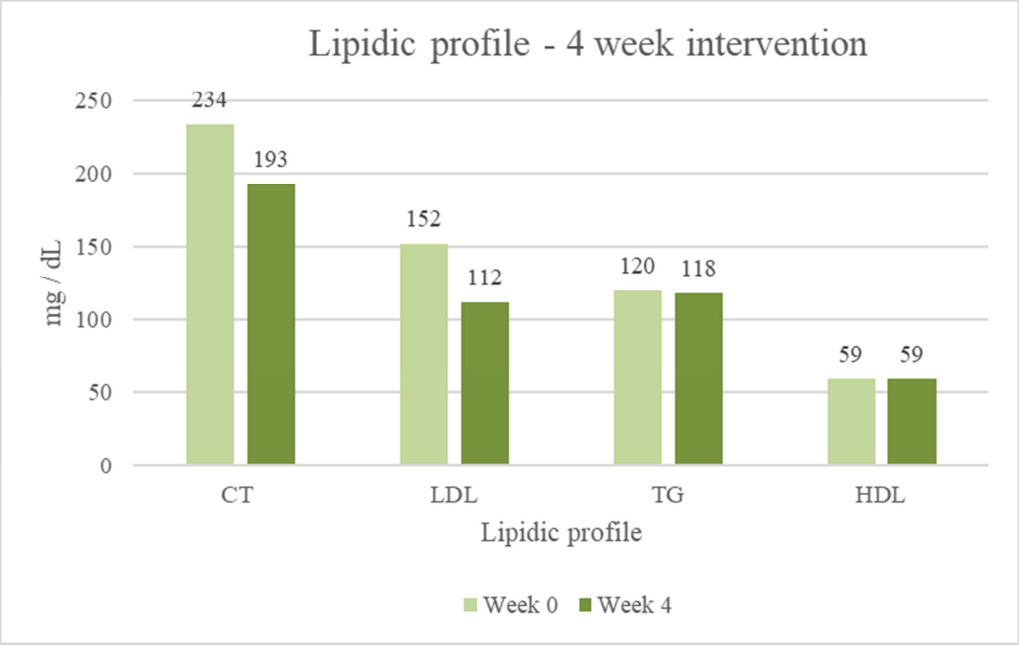

Figure 2. *Lipidic parameters (mg/dl) – 4 week intervention. Data are mean.*

In the second trial, the results showed that TC, LDL-C, TG and HDL-C levels had a tendency to improve significatively after 12 week of Policol® One treatment. In accordance with the clinical guidelines, TC turned from 233.421±21.544, an upper limit value to 198.737±13.564 (p=0.000), which is considered as a desirable value. LDL-C levels were reduced from 154.000±16.770 to 122.842±15.703 (p=0.000). TG parameter changed from 145.489±54.865 to 125.579±37.548 (p=0.007). A 13.7% TG reduction was experienced compared to baseline after 12 weeks of treatment. HDL-C improved from 51.895±12.552, a low value, to 61.737±10.614 which is an optimal value (p=0.001). 19.0% HDL-C increment was shown compared to baseline after 12 weeks of treatment.

Table 8. *Lipidic parameters (mg/dl) – 12 week intervention.*

Parameters	Baseline, t_0 (n=19)	After 12 weeks, t_{12} (n=19)	P
TC (mg/dl)	233.421±21.544	198.737±13.564	0.000
LDL-C (mg/dl)	154.000±16.770	122.842±15.703	0.000
TG (mg/dl)	145.489±54.865	125.579±37.548	0.007
HDL-C (mg/dl)	51.895±12.552	61.737±10.614	0.001

Data are mean ± SD. P-values are for comparisons to paired *t* test.

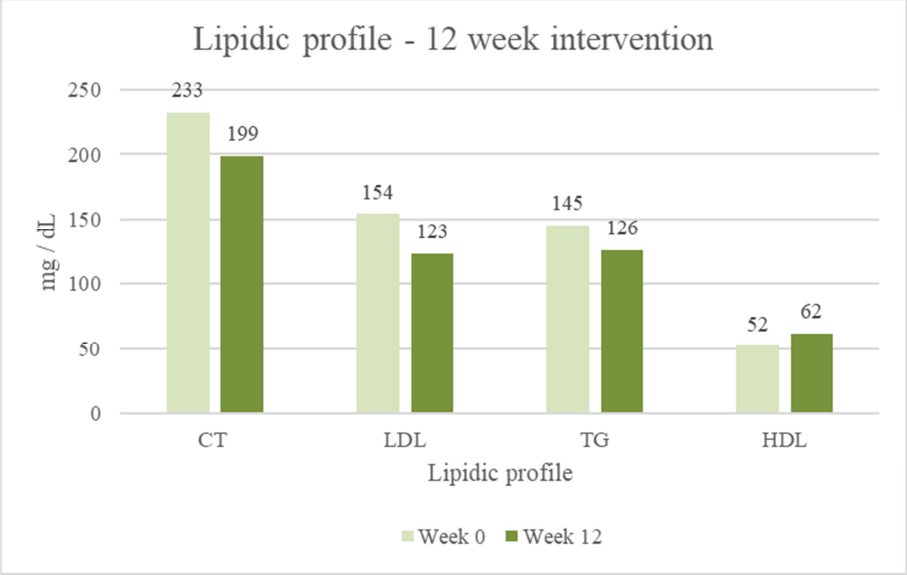

Figure 3. *Lipidic parameters (mg/dl) – 12 week intervention. Data are mean.*

The results at week 4 and 12 of both trials were also compared in order to check whether that the reduction for TC and LDL-C levels in 12 months can be achievable in only 4 weeks. TC reduction did not show any significant difference (p=0.398) between both interventions (t_4 and t_{12}). LDL-C reduction is considered significantly equitable (p=0.201) between the results obtained at t_4 and t_{12}. In view of these results, we can presume that the reduction for TC and LDL-C levels can be reached in only 4 weeks. On the other hand, TG showed a significant difference (p=0.001) between 4 and 12 week. That means that TG parameter showed an improvement in week 12 compared to week 4. Although HDL-C increase did not show any significative difference (p=0.164) between both interventions, it was noteworthy.

Table 9. *Lipidic parameters reduction (mg/dl) – 4 and 12 week intervention.*

Parameters	Change t_4-t_0 (n=23)	Change t_{12}-t_0 (n=19)	P
TC (mg/dl)	-40.521	-34.684	0.398
LDL-C (mg/dl)	-39.521	-31.168	0.201
TG (mg/dl)	-2.000	-19.910	0.001
HDL-C (mg/dl)	+0.113	+9.842	0.164

Data are mean differences.

4. Discussion

The aim of the present pilot study was to show the effect of Policol® One new formula in patients with TC levels above 200 mg/dl. The study found that the consumption of one capsule of new Policol® One during dinner for 4 weeks favorably affected plasma LDL-C and TC levels in volunteers. These beneficial effects of new Policol® One may be attributed to its unique formula which contains a wide range of plant extracts with not only a traditional use, but also some published studies about their effect on plasma lipids. Most of the published evidence of efficacy supporting beneficial effects lies on single active ingredients formulas. However, few studies have been published for some ingredients, as for birdseed. More studies should be run to confirm the results of the current study in order to have stronger evidence of efficacy on the new formula of Policol® One.

In the present study, the consumption of Policol® One for 4 weeks had no significant effect on TG and HDL-C; however, after 12 weeks TG biomarker exhibited a significant reduction and HDL-C also improved. It was concluded that in only 4 weeks it seem to be possible to reach the same results as in 12 weeks for TC and LDL-C parameters because the results were statistically equal between week 4 and week 12 collected data. Therefore, the reduction on TC and LDL-C values achieved in 4 weeks was maintained after 12 weeks. The fact that there were no changes in BMI and diet throughout the duration of the present study presumes that the aforementioned changes in biochemical lipidic parameters are the result of the new unique Policol® One ingredients combination.

The results allowed volunteers to achieve a better lipidic profile: mean CT after the treatment turned into a desirable value (CT<200 mg/dl) and LDL-C mean after taking Policol® One improved to an almost optimal value (LDL-C=100-129 mg/dl) according to the medical guidelines referenced in the introduction.

Some studies have concluded that there is an inverse association between the HDL-C concentration and the prevalence of cardiovascular disease, even at normal HDL-C

concentrations [29]. A significative improvement for HDL-C parameter was observed, it experimented a 9.84% increase at 12 weeks. This enhancement is similar to the observed in several relevant epidemiological studies with statins treatment. In those studies, it has been shown that statins can increase HDL-C levels by approximately 5 to 7% [30].

It was not reported any variation in blood pressure values or lifestyle. No adverse effects were recorded in none of the two interventions.

5. Conclusion

In conclusion, the new Policol® One formula demonstrated a significant cholesterol lowering effect and was well tolerated in all volunteers with no adverse effects detected. Its lipid profile improving capacity properties may be associated with a synergic effect of the ingredients which allow us to formulate with a lower and safer dosage of monacolin K complying with the expected new regulation of the EU. This study had some limitations, including recruiting a reduced group of volunteers. This limitation reduces our ability to generalize conclusions about the effects of Policol® One on every single person. It is important to note that further trials should be done to confirm the results reported here.

Conflict of Interest

The authors declare that they have no competing interests.

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