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Evaluation of a Nutraceutical Containing Monacolin 2.94 Mg on Lipid Profile in Hypercholesterolemic Patients in Primary Prevention

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Abstract The aim of this study was to evaluate the changes in lipid profile, both at fasting and after an oral fat load (OFL), after 3 months of assumption of a nutraceutical containing monacolin K 2.94 mg, and other components as Cynara scolymus, Oryza sativa L., Brassica campestris L., folic acid, coenzyme Q10, and resveratrol compared to placebo in hypercholesterolemic patients in primary prevention. One hundred Caucasian patients were randomized to the nutraceutical or placebo for 3 months, an oral fat load was performed at baseline and at the trial end. Nutraceutical reduced total cholesterol (TC), triglycerides (Tg), and low-density lipoprotein-cholesterol (LDL-C), both compared to baseline, and to placebo. High sensitivity C-reactive protein decreased in the nutraceutical group both compared to baseline and to placebo. During the OFL performed after 3 months, there were lower levels of TC, and LDL-C compared to the OFL performed at baseline. TC, and LDL-C values were lowers also compared to placebo group at every time of OFL. Tg value recorded during the OFL at the end of the study was lower at 6 hours compared to baseline OFL, and placebo. The nutraceutical could be effective in improving lipid profile both at fasting and in a post-prandial condition.

Keywords: *monascus purpureus, brassica campestris l., cynara scolymus, oryza sativa l., polygenic hypercholesterolemia, lipid profile..*

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1. Introduction

Even if there is wide consensus that deducing LDL cholesterol (LDL-C) decreases the risk of developing cardiovascular disease, reaching the LDL suggested by European Society Cardiology/European Atherosclerosis Society guidelines is still a challenge for the physicians. Among hypocholesterolemic agents, statins [3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitors] are the most used: however, despite their effectiveness in reducing cholesterol [1], they also have some adverse effects, especially when they are used at high doses. Adverse events include muscle pain with creatine phosphokinase (CPK) elevation, fatigue and weakness, and liver transaminases increase with a decrease of patients' compliance [1]. For these reasons, in the latest years, nutraceutical have been largely used in the latest years. Nutraceuticals include fortified food or dietary supplements that provide health benefits in addition to their basic nutritional value [2], especially in patients in primary prevention, at low risk for cardiovascular disease. Among them, the most used one for the treatment of hypercholesterolemia is red yeast rice (RYR). RYR acts with a statin-like mechanism, inhibiting HMG-CoA reductase throughout monacolins, which represent the bioactive ingredient. In the latest years, several preparations of RYR have been marketed: according to their concentrations of monacolins, their effect in lowering TC and LDL-C levels change [3-6]. In particular, our group conducted several studies on monacolin, 10 mg, 5 mg or 3.3 mg, showing different effects on lipid profile. However, the long-term safety of the regular consumption of these nutraceuticals has not been fully documented and safety issues have been raised about the possible presence of contaminants in some preparations. At this regard, the Scientific Panel on Food Additives and Nutrient Sources added to Food (ANS) concluded that monacolin K in lactone form is identical to lovastatin, an active ingredient of several medicinal products and that the intake of monacolins from RYR via food supplements could lead to an exposure to monacolin K within the range of the therapeutic doses of lovastatin

[7]. To avoid safety concerns, the Panel concluded that intake levels of monacolins from RYR should not be higher than 3 mg/day [1]. Of course, at this point, if lower dose of RYR are allowed, we need to combine it with other substances acting on different cholesterol pathways to gain the same effect on lipid profile. At this regards β-sitosterol seems to decrease cholesterol and lipid metabolism both in rats and humans [8] inhibiting intestinal absorption of cholesterol, while resveratrol seems to have some effects on lipid profile activating sirtuins enzymes.

There is also evidence that artichoke leaf extract (*Cynara scolymus*) possesses, among others, hypocholesterolemic and antioxidant properties. The mechanisms of action suggested are a reduction in de novo cholesterol synthesis via the inhibition of HMG CoA reductase, an increase in cholesterol elimination in bile secretions, and an inhibition of LDL oxidation [9].

This trial aim was to the changes on lipid profile, both at fasting and after an oral fat load (OFL), after 3 months of treatment with a nutraceutical combination containing monacolin K 2.94 mg, artichoke (*Cynara scolymus)*, γ-orizanol *(Oryza sativa L.)*, colza (*Brassica campestris L. var Oleifera DC*), folic acid, coenzyme Q10, and resveratrol compared to placebo in hypercholesterolemic patients in primary prevention.

2. Material and Methods

2.1. Study Design

This randomised, double-blind, placebo-controlled study was conducted at the Department of Internal Medicine and Therapeutics, University of Pavia (Pavia, Italy). The study protocol was approved at the institutional review board (P-20160020534), and was conducted in accordance with the Declaration of Helsinki and its amendments.

2.2. Patients

One hundred Caucasian patients, aged ≥18 of either sex, at low cardiovascular risk (≤ 2%) according to Framingham Risk Score [10], with hypercholesterolemia [total cholesterol (TC) between 200-240 mg/dl), and with triglycerides (Tg) < 400 mg/dl] [11] were enrolled. For a full description of the study protocol, please see our previous paper [6].

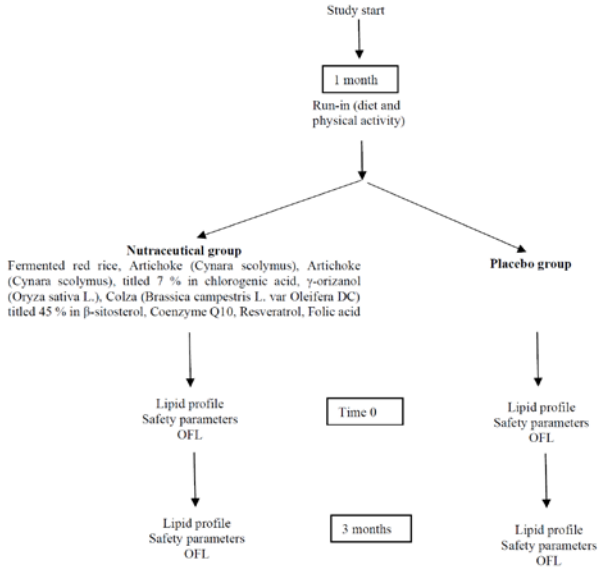
Table 1. Composition of the nutraceutical given in the Nutraceutical group

Substances	Each tablet
Folic acid	200 mcg
Monascus purpureus titled 3 % in K monacolin	2.94 mg
Artichoke (*Cynara scolymus*), titled 7 % in chlorogenic acid	50 mg
γ-orizanol *(Oryza sativa L.)*	20 mg
Colza (*Brassica campestris L. var Oleifera DC*) titled 45 % in β-sitosterol	23.7 mg
Coenzyme Q10	10 mg
Resveratrol	1 mg

The complete list of the drugs taken by patients was reported in Table 1; concomitant treatments were not changed during the trial.

2.3. Treatments

Patients were randomized, as addition to diet and physical activity, to take a botanicals combination containing fermented red rice titled at 3% in monacolin K (2.94 mg), artichoke (*Cynara scolymus*) titled 7 % in chlorogenic acid (50 mg), γ-orizanol (*Oryza sativa L.*) (20 mg), Colza (*Brassica campestris L. var Oleifera DC*) titled 45 % in β-sitosterol (23.7 mg), and food supplement as folic acid (200 µg), coenzyme Q10 (10 mg), and resveratrol (1 mg) [HDLGELAR® urto, marketed by Gelar Farma, Mori (TN), Italy] (Table 1) or placebo, once a day, for 3 months (Figure 1). Both treatments were supplied as identical, opaque, white capsules in coded bottles to ensure the blind status of the study.



OFL: Oral Fat Load

Figure 1. study design

2.4. Diet and Exercise

After the enrolment, all patients entered a one-month run-in period where they followed a controlled-energy diet (near 600 Kcal daily deficit) based on American Heart Association (AHA) recommendations [12]. Individuals were also encouraged to increase their physical activity by walking briskly for 20 to 30 min, 3 to 5 times per week, or by cycle.

2.5. Assessments

Before starting the study, all patients underwent an initial screening assessment that included a medical history, physical examination, vital signs, and a 12-lead electrocardiogram, measurements of height and body weight, calculation of BMI, abdominal circumference (AC), waist circumference (WC), hip circumference (HC). We evaluated also at the baseline, and after 3 months

these parameters: fasting plasma glucose (FPG), TC, Tg, high-density lipoprotein-cholesterol (HDL-C), LDL-C, and high sensitivity C-reactive protein (Hs-CRP), transaminases [aspartate aminotransferase (AST) and alanine aminotransferase (ALT)], and creatine phosphokinase (CPK). Furthermore, at the baseline and at the end of the study all patients underwent an oral fat load (OFL) (Figure 1).

In order to evaluate the tolerability assessments, all adverse events were recorded, and hepatic and renal function were evaluated.

For a description of how each parameter was evaluated see our previous paper [6].

2.6. Safety Measurements

Liver and muscle function were evaluated by measurement of transaminases [aspartate aminotransferase (AST), alanine aminotransferase (ALT), and CPK], and all adverse events were recorded.

2.7. Statistical Analysis

For a description of how statistical analysis was performed see our previous paper [6]. For all statistical analyses, $p < 0.05$ was considered statistically significant [13].

3. Results

3.1. General Characteristics of Patients

A total of 100 patients were enrolled in the study. Of these, all patients completed the study. The characteristics of the study population at study entry are shown in Table 2, where also concomitant medications are listed.

Table 2. General patient characteristics and concomitant therapy at baseline in the study.

	Patient characteristics
N	100
Sex (M/F), n	44/56
Age (years)	49.6 ± 10.2
Sm. st. (M/F), n	16/18
Height (m)	1.66 ± 0.09
Concomitant disease, n (M/F)	67 (35/32)
Hypertension	29 (15/14)
Concurrent medications, n (M/F)	28 (15/13)
ACE-I	15 (7/8)
ARBs	11 (6/5)
Calcium-antagonists	13 (7/6)
β-blockers	5 (2/3)
Diuretics	6 (3/3)
α-blockers	4 (3/1)

Data are expressed as means ± SD or n
Sm. st.: Smoking status; ACE-I: angiotensin-converting enzyme-inhibitors; ARBs: angiotensin receptor blockers

3.2. Effect of Nutraceutical Mixture on Anthropometric Parameters, Plasma Biochemistry and Inflammatory Markers Under Basal Conditions

We did not record any significant variations of BMI or circumferences during the trial (Table 3). Fasting plasma glucose did not change (Table 3) during the study.

High-density lipoprotein-cholesterol did not change with neither treatment, while there was a reduction of TC, Tg, and LDL-C, both compared to baseline ($p < 0.05$), and compared to placebo ($p < 0.05$).

No variations of hepatic or renal function were reported (Table 3).

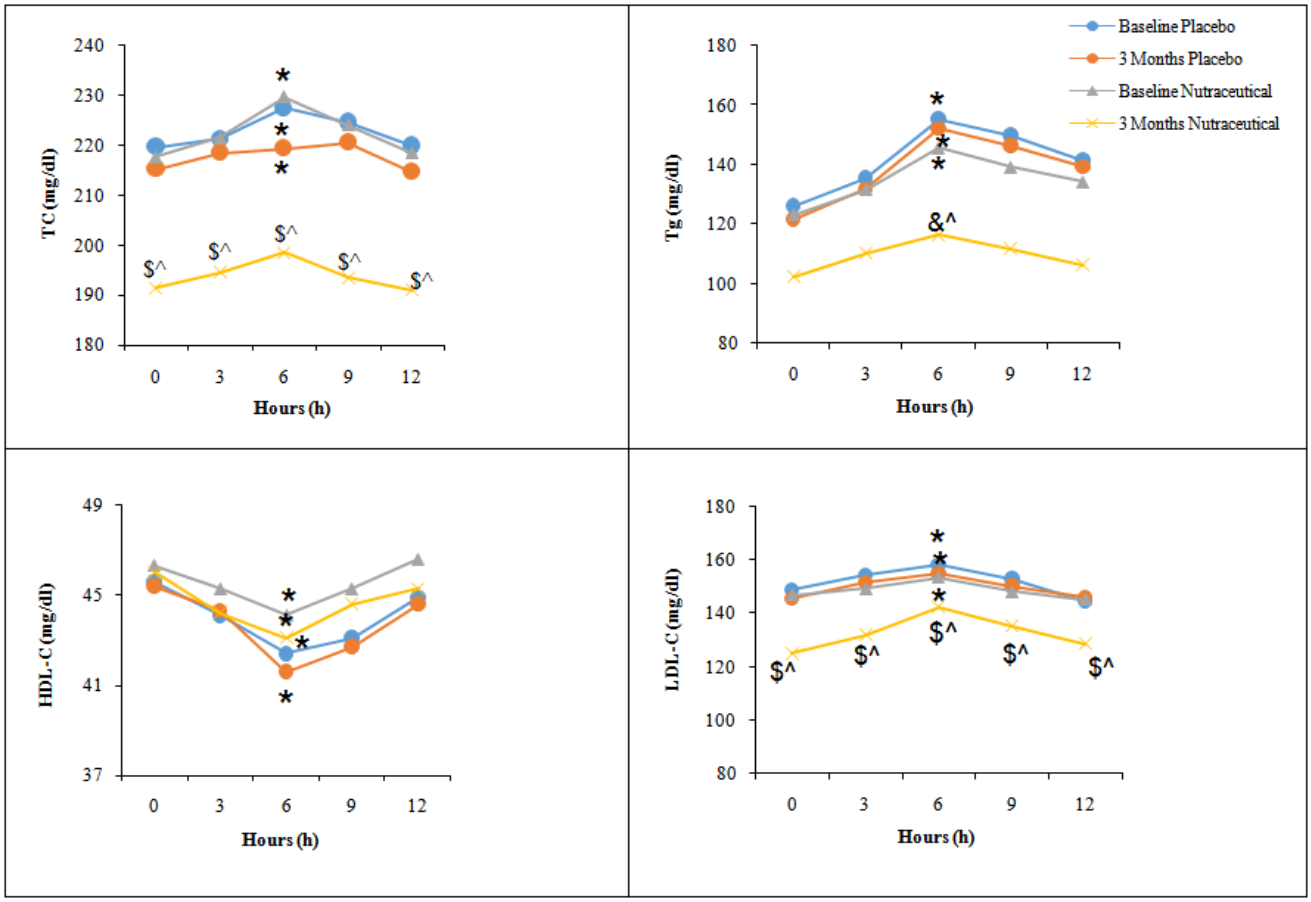
High sensitivity C-reactive protein decreased in the group treated with nutraceutical both compared to baseline and to placebo ($p < 0.05$ for both) (Table 3).

Table 3. Patient parameters in Placebo and Nutraceutical group during the study

	Placebo group		Nutraceutical group	
	Baseline	**3 months**	**Baseline**	**3 months**
N	50	50	50	50
sex (M/F)	21/29	21/29	23/27	23/27
Age (years)	48.3 ± 7.6	-	50.1 ± 8.4	-
Sm. st. (M/F)	9/8	9/8	7/10	7/10
Weight (Kg)	79.1 ± 8.8	78.8 ± 8.6	78.6 ± 8.3	78.4 ± 8.2
Height (m)	1.65 ± 0.08	1.65 ± 0.08	1.67 ± 0.09	1.67 ± 0.09
BMI (Kg/m^2)	29.1 ± 0.8	28.9 ± 0.7	28.2 ± 0.6	28.1± 0.5
WC (cm)	84.8 ± 7.1	84.4± 7.0	83.9 ± 6.8	83.6 ± 6.5
HC (cm)	110.2 ± 9.3	109.6 ± 9.1	109.5 ± 8.9	109.4 ± 8.6
AC (cm)	97.8 ± 8.4	96.9 ± 8.1	97.1 ± 8.2	96.7 ± 7.9
FPG (mg/dl)	89.6 ± 7.9	88.5 ± 7.2	88.3 ± 7.0	87.6 ± 6.8
TC (mg/dl)	211.4 ± 10.2	209.6 ± 9.5	210.3 ± 9.8	186.8 ± 7.8*^
LDL-C (mg/dl)	140.9 ± 8.6	140.1 ± 8.3	140.2 ± 8.4	118.7 ± 5.9*^
HDL-C (mg/dl)	44.2 ± 7.3	43.8 ± 7.1	44.0 ± 7.2	44.9 ± 7.6
Tg (mg/dl)	131.9 ± 18.6	128.3 ± 17.2	130.4 ± 18.1	116.2 ± 15.8*^
TC/HDL ratio	4.78 ± 0.36	4.78 ± 0.38	4.78 ± 0.36	4.16 ± 0.25
AST (UI/l)	25.1 ± 7.9	26.3 ± 8.8	24.2 ± 7.1	24.4 ± 7.2
ALT (UI/l)	29.8 ± 11.6	30.5 ± 12.2	28.3 ± 11.1	28.9 ± 11.7
CPK (UI/l)	141.6 ± 28.2	135.1 ± 25.8	139.7 ± 26.4	143.3 ± 30.2
Hs-CRP (mg/l)	1.0 ± 0.5	1.0 ± 0.5	1.1 ± 0.7	0.8 ± 0.3*^

Data are expressed as means ± standard deviation
*$p < 0.05$ vs Baseline; ^$p < 0.05$ vs Placebo group
Sm. st.: Smoking status; BMI: body mass index; WC: waist circumference; HC: hip circumference; AC: abdominal circumference; FPG: fasting plasma glucose; TC: total cholesterol; LDL-C: low- density lipoprotein-cholesterol; HDL-C: high-density lipoprotein-cholesterol; Tg: triglycerides; AST: alanine aminotransferase; AST: aspartate aminotransferase; CPK: creatinine phosphokinase; Hs-CRP: high-sensitivity C-reactive protein.

Figure 2. Lipid profile variations during OFL in Placebo and Nutraceutical group at baseline and at the study end



*p < 0.05 vs time 0; ^p < 0.05 vs Baseline; &p < 0.05 vs Placebo group; $p < 0.01 vs Placebo group
TC: total cholesterol; LDL-C: low-density lipoprotein-cholesterol; HDL-C: high-density lipoprotein-cholesterol; Tg: triglycerides.

Table 4. AUC (x 12 h) values at baseline and after 3 months in both groups

	Placebo group		Nutraceutical group	
	Baseline	3 months	Baseline	3 months
TC (mg/dl)	116,241.76 ± 24,288.76	114,815.29 ± 21,749.11	115,377.91 ± 22,418.32	111,476.94 ± 17,248.36*^
LDL-C (mg/dl)	74,263.99 ± 4,217.41	73,993.24 ± 3,922.83	74,038.46 ± 3,991.28	56,426.28 ± 2,855.71*^
HDL-C (mg/dl)	22,751.33 ± 4,503.69	22,136.45 ± 4,012.58	22,512.82 ± 4,289.56	23,953.19 ± 4,963.16
Tg (mg/dl)	98,992.76 ± 8,215.12	96,447.88 ± 7,849.52	98,068.35 ± 8,006.13	74,391.48 ± 6,831.58*^

Data are means ± S.D.; AUC: are under the curve
*p < 0.05 vs Baseline; ^p < 0.05 vs Placebo group
TC: total cholesterol; LDL-C: low-density lipoprotein-cholesterol; HDL-C: high-density lipoprotein-cholesterol; Tg: triglycerides.

3.3. Effect of Nutraceutical Mixture on Lipid Profile Under Post-Prandial Conditions

The variation of each parameter during the OFL is showed in Figure 2, the area under the curve value is showed in Table 4.

During the OFL performed at the end of the study, values of TC, and LDL-C in the group treated with the nutraceutical combination were lower compared to the ones recorded during the baseline OFL ($p < 0.05$), and also compared to the ones in placebo group ($p< 0.01$) at every time of OFL.

Regarding Tg, the value recorded during the OFL at the end of the study was lower at 6 hours compared to baseline OFL ($p < 0.05$ vs baseline), and to placebo ($p < 0.05$).

High-density lipoprotein-cholesterol trend did not change during OFL, there was a decrease of HDL after 6 hours ($p < 0.05$ vs time 0) since the meal ingestion, both at baseline and at the end of the study, in both groups.

4. Discussion

Our trial showed that the nutraceutical combination is effective in reducing lipid profile compared to placebo. There was a reduction of TC (-23.5 mg/dl, -11.2 %), Tg (-21.5 mg/dl, -10.9 %), and LDL-C (-14.2 mg/dl, -15.3 %), respectively. Moreover, there was not any significant variation of HDL-C (-0.9 mg/dl, -0.6 %), however, there are very few drugs acting on HDL-C, several clinical trials for several drugs specifically designed to increase HDL levels were halted early because they didn't reduce the risk of heart attacks. The effects obtained with the nutraceutical containing monacolin K 2.94 mg was similar to the ones obtained in a previous study conducted by our group where we evaluated a similar nutraceutical, but containing monacolin K 3.3 mg [6]. In that case, we recorded a

reduction of TC of -26.2 mg/dl, -12.0 %, Tg of -20.7 mg/dl, -16.8 %, and LDL-C of -21.8 mg/dl, -14.9 %, respectively. Moreover, there was not any significant variation of HDL-C (-0.3 mg/dl, -0.6 %). Considering the different components of the nutraceutical, monacolin K is still the main actor in reducing cholesterol; however, its presence is limited to 2.94 mg in this nutraceutical. Given that monacolin efficacy is directly related to its concentration, we need other components to help monacolin to reduce lipid profile. At this regard, β-sitosterol seems to decrease cholesterol and lipid metabolism both in rats and humans [8] inhibiting intestinal absorption of cholesterol. A possible hypothesis is that β-sitosterol competes with cholesterol for available fatty acids, bile salts, and the enzyme used in cholesterol esterification, thereby interfering with cholesterol absorption [14]. Also resveratrol seems to have some effects on lipid profile activating sirtuins enzymes. In a study by Batista-Jorge et al., resveratrol showed a reduction of Tg of about 36%, it decreased TC, VLDL, and increased HDL-C levels compared to placebo. In the study by Batista-Jorge (2020) resveratrol was administered at the dose of 250 mg/day vs 1 mg/day of our study, suggesting that a higher dose is requested to obtain a significant hypocholesterolemic effect [15]. Coenzyme Q10 could contribute to decrease asthenia, myalgia and muscle pain related to monacolin K assumption like previously reported by our group [16]. Another important finding of this study is the reduction of Hs-CRP with the nutraceutical: this is a possible evidence of the anti-inflammatory role of the nutraceutical under study. Inflammation has a pivotal role in the post-prandial phase, as showed in experimental model using OFL [17]. Regarding OFL data, the nutraceutical used in this study has similar effect of a similar nutraceutical containing 3.3 mg of monacolin K as previously published by our group [6].

These results are important, because there is evidence that the load of lipids leads to a reduction in HDL-C, evidence of an endothelial suffering that the load can give. The nutraceutical in study seems to mitigate the HDL reduction after the load.

Study limitations included the short duration of the trial and the fact that we evaluated only some inflammatory markers, focusing our attention on a few of them. Finally, we did not observe if the effects of the nutraceutical agent were reversible after the interruption of the study.

5. Conclusion

A nutraceutical containing monacolin K 2.94 mg, and other components as artichoke (*Cynara scolymus*), Asian rice (*Oryza sativa L.*), Brassica campestris L., folic acid, coenzyme Q10, and resveratrol could be helpful in improving lipid profile in hypercholesterolemic patients with low cardiovascular risk, both at fasting and in post-prandial phase.

Conflict of Interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. No writing assistance was utilized in the production of this manuscript.

Contributions Section

Design and conduction of the study: Giuseppe Derosa, Pamela Maffioli and Giovanni Gaudio; data collection: all Authors; data interpretation and manuscript writing: Giuseppe Derosa, Pamela Maffioli and Giovanni Gaudio. All authors read and approved the final version of the manuscript.

References

[1] Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, Chapman MJ, De Backer GG, Delgado V, Ference BA, Graham IM, Halliday A, Landmesser U, Mihaylova B, Pedersen TR, Riccardi G, Richter DJ, Sabatine MS, Taskinen MR, Tokgozoglu L, Wiklund O, ESC Scientific Document Group. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur. Heart. J. 2020; 41(1): 111-188.

[2] Wildman REC, Bruno RS. Handbook of Nutraceuticals and Functional Foods. 2020. CRC Press. ISBN 9781498703727.

[3] Derosa G, D'Angelo A, Romano D, Maffioli P. Effects of a combination of Berberis aristata, Silybum marianum and Monacolin on lipid profile in subjects at low cardiovascular risk; a double-blind, randomized, placebo-controlled trial. Int. J. Mol. Sci. 2017; 18(2): 343.

[4] Cicero AF, Derosa G, Parini A, Maffioli P, D'Addato S, Reggi A, Giovannini M, Borghi C. Red yeast rice improves lipid pattern, high-sensitivity C-reactive protein, and vascular remodeling parameters in moderately hypercholesterolemic Italian subjects. Nutr. Res. 2013; 33(8): 622-628.

[5] D'Addato S, Scandiani L, Mombelli G, Focanti F, Pelacchi F, Salvatori E, Di Loreto G, Comandini A, Maffioli P, Derosa G. Effect of a food supplement containing berberine, monacolin K, hydroxytyrosol and coenzyme Q(10) on lipid levels: a randomized, double-blind, placebo controlled study. Drug Des. Devel. Ther. 2017; 11, 1585-1592.

[6] Derosa G, Gaudio G, D'Angelo A, Maffioli P. Botanicals and food supplement combination in patients with polygenic hypercholesterolemia: evaluation at fasting and after oral fat load test. J. Food Nutr. Res. 2020; 8(12): 700-706.

[7] https://efsa.onlinelibrary.wiley.com.

[8] Feng S, Dai Z, Liu AB, Huang J, Narsipur N, Guo G, Kong B, Reuhl K, Lu W, Luo Z, Yang CS. Intake of stigmasterol and β-sitosterol alters lipid metabolism and alleviates NAFLD in mice fed a high-fat western-style diet. Biochim. Biophys. Acta Mol. Cell. Biol. Lipids 2018; 1863(10): 1274-1284.

[9] Bundy R, Walker AF, Middleton RW, Wallis C, Simpson HCR. Artichoke leaf extract (Cynara scolymus) reduces plasma cholesterol in otherwise healthy hypercholesterolemic adults: a randomized, double blind placebo-controlled trial. Phytomedicine 2008; 15(9): 668-675.

[10] Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European guidelines on cardiovascular disease prevention in clinical practice: the sixth joint task force of the European Society of Cardiology and Other Societies on cardiovascular disease prevention in clinical practice (constituted by representatives of 10 societies and by invited experts) developed with the special contribution of the European Association for Cardiovascular Prevention & amp; rehabilitation (EACPR). Eur. Heart J. 2016; 37: 2315-2381.

[11] 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). J.A.M.A. 2001; 285(19): 2486-2497.

[12] World Health Organization, 1997. Obesity: Preventing and Managing the Global Epidemic. Report of WHO Consultation on Obesity. Geneva: WHO.

[13] Winer BJ. 1971. Statistical Principles in Experimental Design. 2nd ed, McGraw-Hill, New York.

[14] Best MM, Duncan CH, Van Loon EJ, Wathen JD. The effects of sitosterol on serum lipids. Am. J. Med. 1955; 19(1): 61-70.

[15] Batista-Jorge GC, Barcala-Jorge AS, Silveira MF, Lelis DF, Andrade JMO, de Paula AMB, Guimarães ALS, Santos SHS. Oral resveratrol supplementation improves Metabolic syndrome features in obese patients submitted to a lifestyle-changing program. Life Sci. 2020; 256: 117962.

[16] Derosa G, D'Angelo A, Maffioli P. Coenzyme q10 liquid supplementation in dyslipidemic subjects with statin-related clinical symptoms: a double-blind, randomized, placebo-controlled study. Drug Des. Devel. Ther. 2019; 13: 3647-3655.

[17] Derosa G, Ferrari I, D'Angelo A, Salvadeo SA, Fogari E, Gravina A, Mereu R, Palumbo I, Maffioli P, Randazzo S, Cicero AF. Oral fat load effects on inflammation and endothelial stress markers in healthy subjects. Heart Vessels 2009; 24(3): 204-210.