

# Beneficial effects of multicomponent functional foods in patients with metabolic syndrome

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**Abstract:** The ANTIATERO-ALIM study was a randomized, parallel design nutritional trial testing functional food (FF) diets against the usual diet recommended in the metabolic syndrome. Functional meals included balsamic vinegar from apples and honey and grape juice enriched with polyphenols from seeds of red grapes. 300 patients with metabolic syndrome were randomized into 4 groups: gr.1: FF +  $\Omega$ -3 supplements, gr.2: FF, gr.3:  $\Omega$ -3 supplements, gr.4: control. IRHOMA insulin resistance, plasma lipids and oxidative stress were assessed at inclusion and at 6 months. After 6 months there was a very significant decrease of oxidative stress in group 3, followed by a significant decrease in groups 1 and 2.

**Keywords:** metabolic syndrome, multicomponent functional foods, antioxidant bioactive ingredients, polyphenols

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## 1. Introduction

Metabolic syndrome has long been recognized as the common denominator for a set of five features: abdominal obesity, high glucose and insulin levels, low HDL, high triglycerides and high blood pressure [1]. Oxidative stress is thought to be linked to cardiovascular diseases, since oxidation of LDL in the vascular endothelium is a precursor to atherosclerotic plaque formation [2]. It is well known that atherosclerosis is associated with an increased production of reactive oxygen species and a reduction in antioxidant defences. Antioxidant micronutrients have been shown to significantly contribute to reduction or prevention of diabetic complications and atherosclerosis [3]. The Dietary

Approaches to Stop Hypertension (DASH) trials featured controlled nutrient intake and repeated measurements, allowing for longitudinal analyses of biomarkers and traditional CVD risk factors [4]. The participants following the DASH diet had increases in serum antioxidants and oxygen radical absorbance capacity (ORAC) levels, and reduced breath ethane levels. Similarly in the DASH Sodium Trial, those on the DASH diet had increases in serum antioxidant and ORAC levels, lowered F<sub>2</sub>-isoprostane levels and increased antibodies to oxidized LDL [5].

The importance of efficient interventions to reduce obesity-linked risk has increased in recent decades because of the epidemic proportions of this condition. This seems to be particularly important for early intervention in high-risk individuals with metabolic syndrome, the cornerstone for cardiovascular diseases (CVD) and diabetes. Population-based strategies for healthy eating are being developed, among them recommendations for consumption of functional and novel foods with proven effects on biomarkers [6].

Functional foods typically contain small quantities of extra-nutritional constituents named bioactive compounds. These compounds vary widely in chemical structure and function and are grouped accordingly. Phenolic compounds, including their subcategory, flavonoids, are present in all plants and have been studied extensively in cereals, legumes, nuts, olive oil, vegetables, fruits, tea, and red wine. Many phenolic compounds have antioxidant properties, and some epidemiologic studies have reported protective associations between flavonoids or other phenolics and CVD, while other studies have not found these associations [7][8][9]. Studies with beta-carotene have led to similar results [10].

Antioxidant research has also involved extensive animal dietary trials. These trials are used to document effects in functional food development. Resveratrol (3,4',5 trihydroxystilbene), a naturally-occurring phenolic antioxidant, is synthesized by plants in response to attacks by fungi or bacteria; it is also known to possess an array of cardioprotective effects [11][12]. A recent study has shown resveratrol to protect against the metabolic changes associated with hypercaloric diets in mice with induced insulin resistance, hyperglycemia, and dyslipidemia [13]. In diabetic mice, resveratrol restored endothelial function in type 2 diabetes by inhibiting TNF $\alpha$ -induced activation of NAD(P)H oxidase and preserving eNOS phosphorylation, suggesting the potential for new treatment approaches to promote vascular health in metabolic diseases [14].

A recent study in a rat model with myocardial infarction indicates that salvianolic acid B, a water-soluble polyphenolic antioxidant from sage (*Salvia miltiorrhiza*) has a protective potential against myocardial infarction injury and that protective effects may be due to its scavenging lipid peroxidation products, increasing endogenous antioxidant defence enzymes [15]. It has also been demonstrated that oral administration of salvianolic acid A can significantly improve glucose metabolism and inhibit oxidative injury as well as protect against impaired vascular responsiveness in streptozocin-induced diabetic rats [16].

Basil (*Ocimum* spp., Lamiaceae) contains a wide range of essential oils rich in phenolic compounds and a wide array of other natural products including polyphenols such as flavonoids and anthocyanins [17][18]. Aqueous extracts of basil have been shown to exert antithrombotic and

antioxidant properties in rats [19]. Rosmarinic acid has been shown to prevent atherosclerosis by endothelial nitric oxide synthase activation [20].

The Coronary Artery Risk Development in Young Adults (CARDIA) study and its ancillary study, Young Adult Longitudinal Trends in Antioxidants (YALTA) observational studies utilised a young American cohort, aged 18–30 years, in a bi-ethnic, multi-centre, prospective, longitudinal design. Serum carotenoid concentrations including alfa- and betacarotene, zeaxanthin, lutein and betacryptoxanthin, blood markers of inflammation, oxidative stress and endothelial dysfunction – all potential risk factors for disease development – were analysed. Serum carotenoids were found to be inversely related to markers of inflammation, oxidative stress and endothelial dysfunction [21].

The aim of our study was to test multi-component functional foods with bioactive ingredients from the plants mentioned above, with proven antioxidant, anti-inflammatory and antiatherosclerotic properties in patients with metabolic syndrome.

## **2. Materials and methods**

### **2.1 Functional foods**

The functional foods tested in the study, created by the Biotechnology Laboratories SC Proplanta SA Cluj Napoca Romania, were: 1. balsamic vinegar from apples with honey, buckthorn berry (*Hyppophae rhamnoides*) juice and extracts from herbs with proven antioxidant activity - sage, basil and rosemary; 2. the already marketed VITIS product, a hydro-alcoholic extract from skins and seeds of red grapes. The balsamic vinegar was obtained from common apple vinegar, to which 5% buckthornberry juice and hydro-alcoholic extracts from sage, basil and rosemary in a proportion according to the standardized recipe have been added. The product contains antocyanins (pelargonidin, malvidin), phenolic acids (cafeic, cumaric, ferulic, galic), flavonoids (kaemferol and quercetin), free aminoacids, peptides, 15 oligoelements (Mg, K, Zn, Ca, Fe) in bioavailable form and provitamin A (carotenoids). The concentration of polyphenols in 100 ml of standardized product was 42 mg expressed in galic acid equivalents, according to the Folin-Ciocalteu method and that of beta-carotene was 17 micrograms, determined by HPLC analysis with saponification of samples according to a method described elsewhere [22][23].

The VITIS product is a monomeric, dimeric and polymeric polyphenolic compound obtained by sparing extraction from seeds, ramifications and skins of grapes, all sub-products of winemaking. High performance liquid chromatography (HPLC) revealed 6 classes of phenolic compounds: phenolic acids, proantocyanidins, tanins, catechines, antocyanins, flavonoids. The Folin-Ciocalteu method for polyphenol quantitation revealed a concentration of 33 mg/100 ml product, expressed in galic acid equivalents [22].

### **2.2. Nutritional trial protocol**

300 patients with metabolic syndrome were randomized for intervention or non-intervention in a prospective, randomized, parallel design nutritional trial at the University of Medicine and Pharmacy Victor Babes Timisoara, Romania. All patients had at least 3 criteria for metabolic syndrome according

to the National Cholesterol Education Program Adult Treatment Panel III guidelines in managing dyslipidemia. (ATP III) criteria [24]. The study was approved by the local Ethics Committee.

All participants were instructed to respect the usual diet for metabolic syndrome according to guidelines [24]. In prescribing the caloric intake we took into account the resting metabolic rate (Kcal), determined by bioimpedance on the InBody 720 body composition analyser, to which we added an extra 400 Kcal for medium level of work and another 200-400 kcal daily if they were exercising regularly. The recommended diet was low fat (15% of calories) with a polyunsaturated-to-saturated fatty acid ratio of 2.4 to 1, moderate protein (20% of calories), unrefined carbohydrates with low glycemic index (65% of calories) and fiber (more than 40 grams daily). The consumption of 30 ml olive oil to prepare salads was recommended to all participants. Compliance to the diet was monitored by an adapted version of the National Health and Nutrition Examination Survey (NHANES) Questionnaire [25].

Participants were randomized into 4 groups:

Group 1 = multi-component functional foods + omega3 supplements

Group 2 = functional foods alone

Group 3 = omega 3 supplements alone

Group 4 = control

Participants in group 1 and 2 were instructed to add 2 tablespoons of balsamic vinegar and 1 tablespoon of VITIS to either a salad of raw, fresh vegetables or a vegetable soup daily, 5 days per week. Omega3 supplements were added in the form of gelatinous capsules of 500 mg, 1 daily, to participants in gr 1 and 3 in order to compare the effect of functional foods with that of omega3 supplementation, alone or in combination, on oxidative stress and metabolic parameters using group 4 randomized to usual diet as control.

The effects of nutritional intervention in the 4 groups were assessed at inclusion and at 6 months by parameters of metabolic effect: HOMA IR score for insulin-resistance, lipid profile and parameters of oxidative stress: total radicalic activity of whole blood measured by FORMox, total liposoluble antioxidants from serum (ACL) and total hidrosoluble antioxidants from serum (ACW) measured by photochemoluminometry.

The level of circulating insulin was determined by ELISA, using the kit DSL-10-1600 ACTIVE Insulin, DRG Diagnostics GmbH, Marburg, Germany. Blood glucose was determined by the colorimetric method with glucooxidase-peroxidase, kit-Clinical Lab. Diagnosticum, Budapest; for serial cholesterol the enzymatic colorimetric method was used, kit-Clinical Lab. Diagnosticum, Budapest; serum triglycerides were determined by enzymatic colorimetric method using the kits-Clinical Lab. Diagnosticum, Budapest. To determine HDL-cholesterol we used the Vitalab-Flex-PC analyser.

The radicalic activity of whole blood was measured using the FORT test based on the ability of colorimetric transition of metals such as iron to catalyze the transformation of hidroperoxide radicals in derivatives under the Fenton reaction. The test was performed on capillary blood collected from the tip of the finger on the FORMox analyzer, Callegari, Italy. Values > FORT 310 units were considered suggestive for increased oxidative stress.

Total hydrosoluble antioxidants from serum (ACW) and total liposoluble antioxidants from serum (ACL) were measured by photochemoluminometry (Photochem, Analytik Jena, Germany), at inclusion and after 6 months of functional diet.

### 3. Results

The study sample consisted of 300 patients (158 males, 142 females). In these patients, the parameters of metabolic syndrome were measured i.e. waist circumference, triglycerides (TG), HDL cholesterol, systolic and diastolic blood pressure and fasting glucose. The general characteristics of all patients are represented in Table 1.

**Table 1.** Characteristics of patients at inclusion (n=300)

	Variable	n=300
1	Age (yrs)	54.25 ± 11.08
2	Sex	158M, 142F
3	Glycemia ( mg/dl)	101.66 ± 33.9
4	Systolic BP (mmHg)	145.83 ± 20.25
5	Diastolic BP (mmHg)	88.91 ± 10.85
6	TC (mg/dl)	219.52±51.37
7	HDL (mg/dl)	49.57 ± 12.26
8	TG (mg/dl)	185.97 ± 86.58
9	Waist Circumference (cm)	M: 114.78 ± 3.21 F: 110.17 ± 2.57
10	Body Mass Index(kg/m <sup>2</sup> )	M: 35.65 ± 9.96 F: 35.13 ± 0.78
11	FORM ox( uFORT)	327.89 ± 85.32
12	IR HOMA	4.82 ± 3.32

Main characteristics were compared within the four groups at inclusion and after six months. 280 patients were compliant to the end of the study, there were 20 drop-outs. Evolution of metabolic syndrome parameters in patients on functional foods and omega 3 supplements (group 1, n=70) are presented in Table 2. Total cholesterol registered a significant decrease after 6 months from 217.92±50.93 to 208.12±40.71 mg/dl (p = 0.01), TG decreased significantly from 192.61±97.08 to 160.58±125.51 mg/dl (p = 0.01) and HDL increased from 45.57±18.34 to 52.59±11.81 mg/dl (p= 0.003). Group 1 showed a significant decrease in IRHOMA after 6 months from 5.34±3.93 to 4.38±2.38 (p=0.01) and a very significant decrease in Form-ox after 6 months from 315.11±85.94 to 275.41±84.34 UFORT (p = 0.001).

**Table 2.** Evolution of metabolic syndrome in patients on FF and Ω3 supplements (Group 1, n = 70)

Variables	Inclusion	6 months	p value
Total cholesterol (mg/dl)	217.92±50.93	208.12±40.71	0.01

<b>Triglycerides(mg/dl)</b>	192.61±97.08	160.58±125.51	0.01
<b>HDL (mg/dl)</b>	45.57±18.34	52.59±11.81	0.003
<b>IRHOMA</b>	5.34±3.93	4.38±2.38	0.01
<b>Form-ox (UFORT)</b>	315.11±85.94	275.41±84.34	0.001
<b>BMI</b>	34.53±2.86	32.86±1.97	0.02

Evolution of metabolic syndrome parameters in patients on functional foods only (group 2, n=65) are presented in Table 3. TC showed a significant decrease after 6 months from 216.1±42.41 to 205.74±34.59 mg/dl ( $p = 0.02$ ), of TG from 177.34±92.20 to 163.05±112.48mg/dl ( $p = 0.02$ ) and a very significant increase in HDL from 45.45±13.62 to 51.97±9.41 mg/dl ( $p = 0.001$ ). Group 2 showed a significant decrease in IRHOMA after 6 months from 4.72±3.73 to 4.01±2.69 ( $p = 0.02$ ) and also a significant decrease in Form-ox after 6 months from 317.93±91.91 to 290.04±82.86 UFORT ( $p = 0.01$ ).

**Table 3.** Evolution of metabolic syndrome in patients on FF (Group 2, n = 65)

<b>Variables</b>	<b>Inclusion</b>	<b>6 months</b>	<b>p value</b>
<b>Total cholesterol (mg/dl)</b>	216.1±42.41	205.74±34.59	0.02
<b>Triglycerides(mg/dl)</b>	177.34±92.20	163.05±112.48	0.02
<b>HDL (mg/dl)</b>	45.45±13.62	51.97±9.41	0.001
<b>IRHOMA</b>	4.72±3.73	4.01±2.69	0.02
<b>Form-ox(UFORT)</b>	317.93±91.91	290.04±82.86	0.01
<b>BMI</b>	34.16±3.23	32.19±2.78	<0.01

Evolution of metabolic syndrome parameters in patients on omega 3 supplements (group 3, n = 75) are presented in Table 4. TC showed a significant decrease after 6 months from 228.5±49.72 to 214.56±39.61 mg/dl ( $p = 0.03$ ), a very significant decrease in TG from 203.06±103.63 to 166.45±80.45 mg/dl ( $p = 0.001$ ). Group 3 showed a very significant increase in HDL after 6 months from 44.03±12.85 to 49.86±8.88 mg/dl ( $p = 0.004$ ) and also a very significant decrease in Form-ox after 6 months from 327.36±73.73 to 265.95±82.23 UFORT ( $p = 0.0001$ ). Group 3 did not show any significant change in IRHOMA after 6 months ( $p=NS$ ).

Evolution of metabolic syndrome in the control group (group 4, n = 70) showed an insignificant decrease in TC after 6 months from 215.68±48.10 to 208.65±44.06 mg/dl ( $p = NS$ ) and in TG from 158.73±68.17 to 152.79±43.30 mg/dl ( $p = NS$ ). HDL increased significantly after 6 months from 41.94±11.51 to 44.47±13.77 mg/dl ( $p = 0.02$ ). IRHOMA and Form-ox remained unchanged ( $p = NS$ ), as shown in Table 5.

**Table 4.** Evolution of metabolic syndrome in patients on  $\Omega$ 3 supplements (Group 3, n = 75)

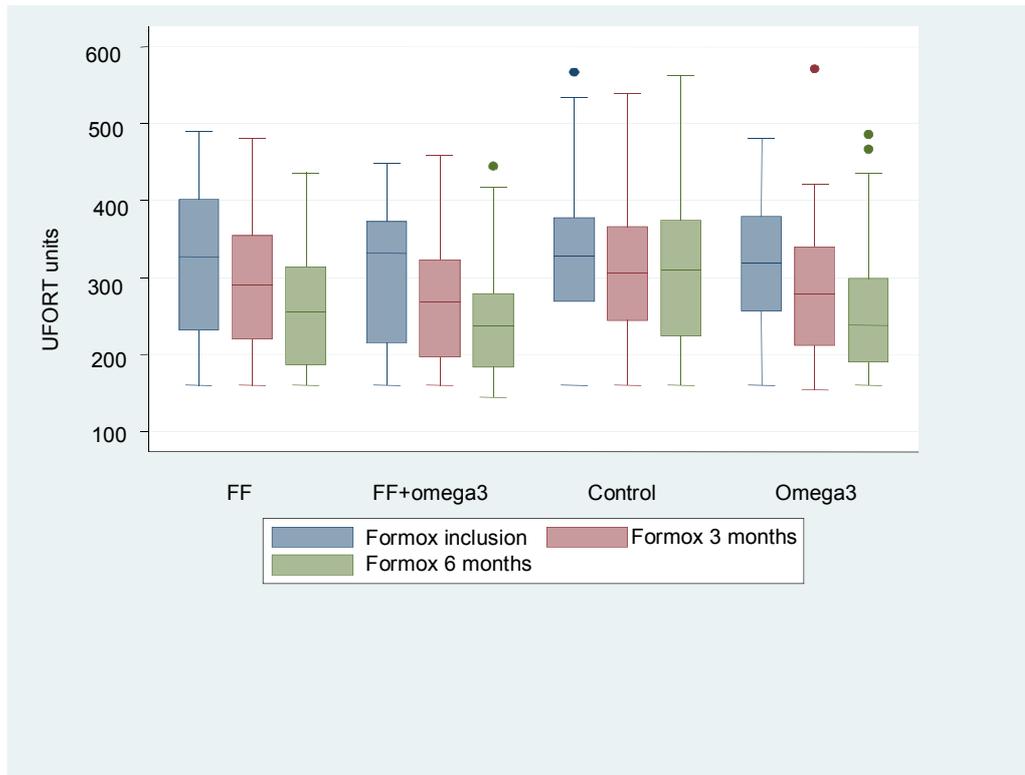
<b>Variables</b>	<b>Inclusion</b>	<b>6 months</b>	<b>p value</b>
<b>Total cholesterol(mg/dl)</b>	228.5±49.72	214.56±39.61	0.03
<b>Triglycerides(mg/dl)</b>	203.06±103.63	166.45±80.45	0.001

<b>HDL(mg/dl)</b>	44.03±12.85	49.86±8.88	0.004
<b>IRHOMA</b>	4.94±3.06	4.65±2.20	NS
<b>Form-ox(UFORT)</b>	327.36±73.73	265.95±82.23	0.0001
<b>BMI</b>	33.46±3.42	32.87±1.54	0.001

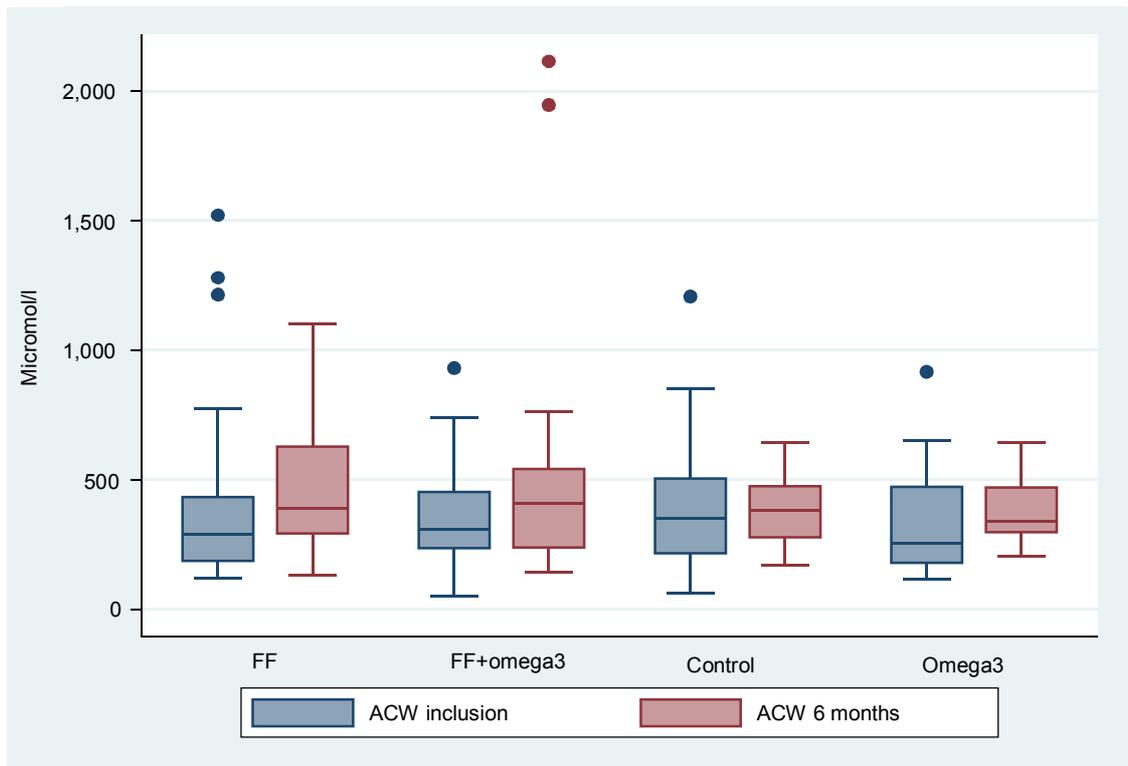
**Table 5.** Evolution of metabolic syndrome in the control group (Group 4, n = 70)

<b>Variables</b>	<b>Inclusion</b>	<b>6 months</b>	<b>p value</b>
<b>Total cholesterol (mg/dl)</b>	215.68±48.10	208.65±44.06	NS
<b>Triglycerides(mg/dl)</b>	158.73±68.17	152.79±43.30	NS
<b>HDL(mg/dl)</b>	41.94±11.51	44.47±13.77	0.02
<b>IRHOMA</b>	4.57±2.90	4.76±3.71	NS
<b>Form-ox(UFORT)</b>	327.79±86.62	310.61±85.46	NS
<b>BMI</b>	33.64±2.93	31.87±2.74	0.05

The decrease of BMI was significant in all groups, in the following order: gr.3<gr.2<gr.1<gr.4. The comparative evolution of oxidative stress between groups is presented in Figure 1. Measurements were made at inclusion, at 3 months and at 6 months. There was a constant very significant decrease of oxidative stress in group 3 (Omega 3, p<0.0001), followed by a significant decrease in group 1 (FF+Omega 3, p<0.001) and group 2 (FF, p<0.01). There was an insignificant decrease of oxidative stress in Group 4 (control, p=NS), placing the effect of interventions on oxidative stress in the following order Omega3>FF+Omega3>FF>Control (Fig 1).

**Figure 1** : Comparison of Form-ox between the four groups

As shown in Figure 2, there was a significant increase of hydrosoluble antioxidants determined by photochemoluminometry in patients in group 1 on functional foods and omega 3 fatty acid supplements, from  $339.49 \pm 41.49$  to  $585.59 \pm 138.42$  micromoles/l ( $p < 0.05$ ) and in group 2 on functional foods only from  $354.53 \pm 32.25$  to  $456.42 \pm 89.37$  micromoles/l ( $p = 0.02$ ).

**Figure 2:** Comparison of hydrosoluble antioxidants between the four groups

#### 4. Discussion

Epidemiological studies have suggested positive associations between the consumption of phenolic-rich foods or beverages and the prevention of diseases [26]. These effects have been attributed to antioxidant components such as plant phenolics, including flavonoids and phenylpropanoids among others [27]. In our nutritional trial, designed to study the level of oxidative stress in response to a functional diet in patients with metabolic syndrome (n=280), we demonstrated the functionality of the foods tested, balsamic vinegar from apples with honey, buckthorn berry juice (*Hyppophae rhamnoides*) and herbs with proven antioxidant activity - sage, basil and rosemary and the VITIS product, an extract from skins and seeds of red grapes.

The diet used was very simple, patients were asked to have one functional meal a day but only for 5 days (Monday – Friday) in a week in a randomized open trial. The 5/7 regimen was chosen to allow a better compliance and to imitate normal life conditions, where the same products cannot be eaten daily for six months. The products were easily available to the patients, some being already marketed products like the VITIS or the omega3 supplements. All other supplements were strictly forbidden during the trial. The decrease of oxidative stress was significantly enhanced by  $\Omega 3$  supplements, that contributed also to significant decreases of TG levels. After 6 months of functional meals in the diet, group 1 showed the most significant decrease in the levels of glycemia, triglycerides, IRHOMA, insulin, Formox, compared to the diet recommended in the metabolic syndrome alone. So far, most of

the cardio-protective effect of olive oil in the context of the Mediterranean diet has been attributed to its high MUFA content. In 2003, the Food and Drug Administration permitted a claim on olive oil labels concerning: “the benefits on the risk of coronary heart disease (CHD) of eating about 2 tablespoons (23 grams) of olive oil daily, due to the monounsaturated fat (MUFA) in olive oil” [28]. In our study, olive oil was also used in small amounts daily (max 30 ml) to prepare salads and the functional meals and its effect may also have contributed to our results, especially in the control group.

The oxidative stress induced by the metabolic syndrome is important in developing its complications, like diabetes mellitus, hypertension and cardiovascular diseases. Antioxidant micronutrients may thus significantly contribute to reduction or prevention of complications and atherosclerosis [29]. As antioxidants, polyphenols and carotenoids regulate the redox potential within the cells and activate signal transduction, important effects in disease prevention. Recent literature emphasizes potential therapeutic effects of micronutrients found in natural products, indicating positive applications for controlling the pathogenesis of chronic diseases. It is relevant that purified micronutrients isolated from natural products may be less effective than a combination seen in the natural product due to synergistic effects of interacting agents [30].

The use of herbal remedies has been on the rise worldwide. The safety of the plants used in the present study is evident by their use in folk medicine through time. Scientific evidence obtained so far is indicating antioxidant, properties of each of the plants. The main active ingredient in the grape skin extract VITIS, resveratrol, was recently reported to reduce endothelial oxidative stress by modulating the gene expression of superoxide dismutase 1 (SOD1), glutathione peroxidase 1 (GPx1) and NADPH oxidase subunit (Nox4), besides inhibition of LDL oxidation and suppression of platelet aggregation [31]. Rosemary (*Rosmarinus officinalis L.*) added to the balsamic vinegar is a very important medicinal and aromatic plant, which belongs to the Lamiaceae family and has been cultivated for a long time. Rosmarinic acid has antibacterial, antioxidant and antiphlogistic effect [32]. SMND-309, a novel derivative of salvianolic acid B, has been shown to significantly increased the activities of superoxide dismutase, catalase and glutathione peroxidase in a rat model of acute myocardial infarction [15]. These effects may account for decrease of oxidative stress in our study, added to the noted increase of ACW.

A recent review of current literature suggests that fruits and vegetables in combination have synergistic antioxidant effects leading to greater reduction in risk of chronic disease, specifically for cancer and heart disease, as established by the European Prospective Investigation into Cancer and Nutrition Study (EPIC) [33]. In our study, this synergistic antioxidant effect seems to have been achieved by the combination within the foods tested of the most important classes of antioxidants – carotenoids and polyphenols, an effect suggested in Groups 1 and 2 by the constant and significant decrease of FORMox and by the increase of serum ACW.

There is a significant lack of understanding of the precise biological mechanisms of how plant-based bioactive food components impart health-promoting benefits. It is clear that bioactive food components act simultaneously at different or identical target sites. Bioactive food components have health-promoting roles at various stages of diseases that are associated with multiple progressive steps, from initiation to development. Isoflavones may reduce circulating oxidized low-density lipoproteins

in the plasma, bind cholesterol in the intestinal tract, thereby reducing absorption of dietary cholesterol, enhance bile excretion reducing endogenous cholesterol levels, and modulate arterial elasticity improving blood vessel dilation and constriction response. [34]

Although there has been an increased emphasis on antioxidants and health in the literature, no ‘gold-standard’ method exists for assessing the health effects of antioxidants, and as such many methodologies have been developed. Results are therefore difficult to compare, and because of this are often conflicting. While more research is needed to define the ‘best’ study design for antioxidant studies, collaboration between the different scientific disciplines undertaking this research is needed to limit gaps in the literature and to ensure efficiency.

## 5. Conclusion

1. The functional products studied were well tolerated by all patients
2. The functional products studied decreased oxidative stress and contributed to an increase of water-soluble antioxidants in patients with metabolic syndrome
3. The decrease of oxidative stress was enhanced by omega-3 supplements, that also contributed to significant decreases of TG levels and increase of HDL
4. The functional products added to the diet brought lipid parameters closer to target and lowered IRHOMA, although a better control is needed
5. Long-term effects of functional diets seem promising for the control of metabolic syndrome parameters

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## Abbreviations

FF	Functional food
IRHOMA	Homeostasis Model Assessment of Insulin Resistance
HDL	High Density Lipoprotein

LDL	Low Density Lipoprotein
BMI	Body Mass Index
DASH	Dietary Approaches to Stop Hypertension
CVD	CardioVascular Disease
ORAC	Oxygen Radical Absorbance Capacity
TNF-alpha	Tumor Necrosis Factor-alpha
NADPH	Nicotinamide Adenine Dinucleotide Phosphate
eNOS	endothelial Nitric Oxide Synthase
CARDIA	Coronary Artery Risk Development in Young Adults
YALTA	Young Adult Longitudinal Trends in Antioxidants
HPLC	High Performance Liquid Chromatography
NHANES	National Health and Nutrition Examination Survey
ACL	total liposoluble antioxidants from serum
ACW	total hidrosoluble antioxidants from serum
TC	Total cholesterol
TG	Triglyceride
CHD	Coronary heart disease
MUFA	Monounsaturated Fatty Acid
SOD1	Superoxide dismutase 1
GPx1	Glutathione peroxidase 1
EPIC	European Prospective Investigation into Cancer and Nutrition Study

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