Argan oil improves dyslipidemia of metabolic syndrome: Human interventional study.

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Abstract

This study aims to evaluate the effect of argan oil on the metabolic syndrome parameters. For that, 29 patients have been selected from a group of hypertensive patients visiting the cardiology department of the University Hospital Ibn Rochd in Casablanca Morocco to participate in a nutritional intervention study with alimentary argan oil. The patients selected were randomized into 2 groups: one group was consuming 25 ml of argan oil daily for a period of 3 weeks of intervention, and the other group as control group did not consume argan oil. The average age of these patients in both groups is between 57 and 63 years. A detailed analysis of dietary intake was carried out before, during, and after the argan oil intervention phase. This dietary intake consists of lowering calorie-intake of lipids and carbohydrates, and of increasing proteins without reaching significance. Accordingly, the analysis of the plasma lipid parameters before and after the nutritional intervention with argan oil showed an improvement of the following parameters: a significant decrease in plasma concentration of triglycerides ($p<0.001$) from 246 ± 112 mg/dl to 126 ± 56 mg/dl) and a significant increase ($p=0.01$) in the plasma concentration of HDL cholesterol (from 35 ± 11 mg/dl to 54 ± 27 mg/dl) after the argan oil intervention. Nevertheless, the plasma concentrations of total cholesterol and LDL-cholesterol were not significantly altered. This study concludes that argan oil can prevent the cardiovascular complications in patients suffering from metabolic syndrome.

Keywords: Argan oil, Metabolic syndrome, Prevention, Cardiovascular diseases, Lipids.

Introduction

The metabolic syndrome encompasses a set of metabolic disorders of carbohydrate, lipid, and vascular disorders [1-3]. The combination of all these factors multiplies by ten times the risk of type II diabetes [4] and by three or four times the onset of cerebrovascular accident (AVC) and heart disease [4-14].

There are currently at least six definitions of the metabolic syndrome that are all based on consensus rather than on scientific evidence. The three most common definitions are those proposed by the World Organization (WHO), the National Cholesterol Education Program - Adult Treatment Panel III (NCEP-ATPIII) and the International Diabetes Federation (IDF), the criteria were released in April 2005 [1,2,15-20]. The risk factors include abdominal obesity [waist circumference of the high >102 cm in men and >88 cm in women, high triglycerides level >150 mg/dl and low HDL level <40 mg/dl in men and <50 mg/dl in women, fasting hyperglycaemia ≥ 110 mg/dl and hypertension (BP systolic ≥ 130 mm Hg and/or diastolic BP ≥ 85 mm Hg). The presence of at least three elements of these factors greatly increases the risk of developing cardiovascular disease [21], type II diabetes, non-alcoholic fatty liver disease and polycystic ovaries [10].

The epidemic obesity especially abdominal one, physical inactivity and insulin resistance, make of the metabolic syndrome a real public health problem [22], affecting both the developed countries and less developed ones. The prevalence is generally higher in men than in women and it increases with age. [2,7,23]. Overall, it is estimated that approximately 20 to 27% [6,24] adult subjects in the world have a more or less

severe metabolic syndrome. The progression of the epidemic prevalence of the metabolic syndrome constitutes a challenge for the coming years, due to health costs incurred.

Therefore, the need to implement prevention strategies at a larger scale should be considered as a priority since there is no specific medication until the present because of the multiplicity of the factors involved. The only recourse and the first line is a change in the dietary lifestyle with an engaging lifestyle management [2,25]. In this context, argan oil is recognized for centuries for its many virtues such as culinary, cosmetic and medical, which seems very interesting in lifestyle changes. It is extracted from the kernels of the fruit of an endemic tree growing in south-western Morocco called Argania Spinoza.

Given the demonstrated metabolic actions of argan oil on the lipid profile in dyslipidemic and diabetics patients, it was proposed to carry out an argan oil intervention study to assess the benefits of this oil on the lipid risk factors of metabolic syndrome. Indeed, Argan oil, as an unsaturated vegetable oil has a specific chemical composition that makes it appropriate for cardiovascular health especially its glyceride part composed of about 80% of unsaturated fatty acids [oleic acid 44.8% and 35.7% linoleic acid] and its minority unsaponifiable portion rich in antioxidants mainly polyphenols, sterols, tocopherols and squalene [26,27].

Materials and Methods

Patients

70 hypertensive patients were diagnosed during their consultation in the cardiology department of the University Hospital Ibn Rochd of Casablanca, and shortlisted to participate in this study. All patients underwent clinical examinations with an electrocardiogram (ECG) and Doppler Ultrasound to go along with the inclusive criteria of the study. From 70 patients enrolled in this study, only 43 met the inclusion criteria of the study. During the interventional period, 14 patients have not completed the 3 weeks of intervention of argan oil for unknown reasons. Therefore, only 29 patients have completed the study.

In addition, the enrolled patients included in this interventional study have been informed about the objectives of the study and they agree to participate in this study protocol approved by the Institutional Review Boards of Ibn Rochd Hospital Center (Casablanca) according with the ethical standards of the responsible regional committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. All participants provided informed consent prior to the start of the study.

The inclusive criteria were: Waist ≥ 94 cm in man/88 cm in woman Hypertriglyceridemia (TG ≥ 150 mg/dl), Low plasma HDL (HDL<40 mg/dl) hypertension (BP ≥ 130/85 mm Hg), hyperglycemia (glucose ≥ 110 mg/dl) or type-2 diabetes.

The exclusive criteria were the presence of a liver or kidney disease or HIV, the intake of hormone therapy in the previous six months, the treatment with statins and anti-diabetic medication as well as smokers.

Design study

Before the nutritional intervention with argan oil, a listing of clinical information has been prepared containing information on cardiovascular risk factors for patients (dyslipidaemia, diabetes, obesity, smoking, etc.) and eventual family previous history (Figure 1).

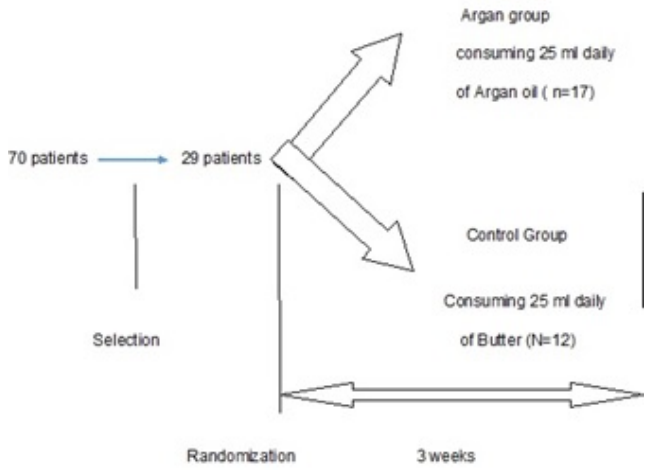

Figure 1. Study design.

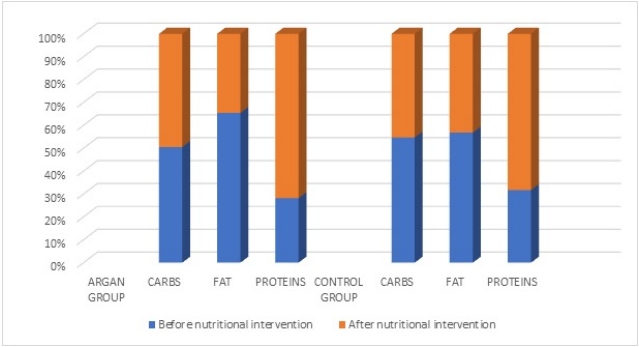

Figure 2. Carbohydrates, fats and proteins intake expressed as percentage of the total daily energy intake of both groups of the study.

On one hand, a food record was completed by the nutritional data on each patient before, during and after the intervention as a food questionnaire. This questionnaire is based on a booster 24 and a food frequency questionnaire. The analysis of the nutritional data and averages thus obtained were carried out using nutrition software (Nutrilog).

On the other hand, the patients under study followed a proper diet for 3 weeks according to the WHO recommendations:

Proteins intake at the rate of 1 to 12 g/kg/day or 12 to 15% mainly composed of (PHVB) High Proteins Biological Value of marine origin and Vegetable Proteins (PV). Animal Proteins (PA) should be avoided. Lipids intake at the rate of 1 g/kg/day or 30 to 35% favouring polyunsaturated fatty acids PUFA intake and monounsaturated fatty acids MUFA, omega acid 3 (ω3) and omega acid 6 (ω6). Carbohydrates intake at the rate of 3 to 5 g/kg/ day or 50-55% reducing the consumption of rapid sugars.

The control group followed the dietary recommendations suggested by the study.

For Argan group, the substitution of their daily fat intake by 25 ml of argan oil was followed during 3 weeks of intervention. Argan oil consumed comes from the same original production (provided by argan oil Company, Casablanca) packed in bottles of 250 ml. The chemical composition of argan oil described in Table 1, meets the production standards of argan oil.

Table 1. Detailed chemical composition of Argan oil [26-29].

Glyceride saponifiable part (99% of total mass)	**Unsaponifiable part (1% of total mass)**
Saturated Fatty Acid	
• Myristic acid (C14: 0) 0.2%	Carotenes 37.5%
• Pentadecanoic acid (C15: 0) 0.1%	Tocopherols 7.5%
• Palmitic acid (C16: 0) from 11.5 to 15%	620 mg/kg
• Heptadecanoic acid (C17: 0) tracks	• γ-Tocopherol 69%
• Stearic acid (C18: 0) from 4.3 to 7.2%	• β-Tocopherol 16%
• Arachidonic acid (C20: 0) 0.5%	• χ-Tocopherol 13%
• Gadoleic acid (C20: 1 n-11) 0.5%	• δ-Tocopherol 2%
• Behenic acid (C22: 0) 0.2%	Triterpene alcohols 20%
	Tirucallol 27.9%, β-amyrin 27.3%, 18.1% butyrospermol
Unsaturated Fatty Acid	Fraction stéroloique=Methyl- sterols and sterol 20%
→ Monounsaturated fatty acids	• Spinasterol=α - stigmastadiene 7.22 (E)-dien-3β-ol 41.5 to 44%
• Palmitoleic acid (C16: 1) 0.2%	• Shotténol=5α-stigmasta-7-en-3β-ol 47.5 to 48%
• Omega 9 or Oleic acid (C18: 1 n-9) from 43 to 49.1%	• Stigmasterol [25,26] 4%
→ Polyunsaturated fatty acids	• D7-avenasterol stigmastadiene 7.24 to 28-dien-3β -ol 4%
• Omega 6 or Linoleic acid (C18: 2 n-6) from 29.3 to 36%	Xanthophylls 6.5%
• α-linolenic acid (C18: 3 n -3) 0.3%	Phenols=<5 mg/kg

Table 2. Anthropometric data of included.

	Age (years)	**Weight (kg)**	**Size (m)**	**BMI (kg/m²)**	**WS Men**	**WS Women**	**HC Man**	**HC Women**
Argan group	63.76 ± 10.49	71.98 ± 13.23	1.60 ± 0.07	28.19 ± 5.37	98 ± 10.82	103.71 ± 11.44	97.66 ± 3.34	103.50 ± 22.50
Control group	57.75 ± 12.93	76,68 ± 14.58	1.60 ± 5.88	29,47 ± 5.88	92.33 ± 4.62	106.33 ± 13.88	94.66 ± 3.34	110.55 ± 14.45

BMI: Body Mass Index; WS: Waist Size (in cm); HC: Hip Circumference (in cm)

At the end of this period of nutritional intervention, a second blood sample and a second food survey was made in the cardiology department of the University Hospital Ibn Rochd of Casablanca.

Blood samples were taken after 12 h of fasting in the cardiology department of the University Hospital Ibn Rochd of Casablanca. The blood was collected in EDTA and dry tubes then centrifuged at a speed of 4,000 rpm for a period of 15 min.

The serum obtained from dry tubes and the plasma obtained from EDTA tubes were distributed in Eppendorf tubes before being stored at -20°C until use.

Statistical analyses were done using STATA software comparing the means of two matched samples. Differences are considered significant when the p-value is less than 0.05.

Biological assays

Serum concentrations of total cholesterol, triglycerides, LDL-cholesterol and HDL-cholesterol were determined from the non-haemolysed serum. The free cholesterol and esterified cholesterol present in the sample give the coupled reactions as described above and reveals a quantifiable colored complex spectrophotometrically at 510 nm.

Triglycerides present in the sample generate according to the reactions described below a quantifiable colored complex spectrophotometrically at 510 nm.

The very low-density lipoprotein (VLDL) and the low-density lipoprotein (LDL) in the sample, precipitate in the presence of phosphotungstate and magnesium ions. The floating liquid from the centrifugation containing high-density lipoprotein

cholesterol (HDL) is quantified spectrophotometrically at 500 nm.

Plasma LDL concentration was determined according to the Friedewald formula LDL-C (g/l)=Total cholesterol-(HDL +TG/5), which is reliable only if the plasma level of triglycerides is less than 400 mg/dl, which is the case for all samples.

Table 3. Waist/hip circumference medium Ratio in patients from the argan and control groups.

	Medium Waist in cm	Medium hip Circumference in cm	Waist/hip Circumference Ratio
Argan group	102.70 ± 11.22	102.70 ± 11.90	1 ± 0.92
Control group	102.83 ± 13.56	106.58 ± 12.56	0.97 ± 1.08

Results

Analysis of anthropometric data

As summarized in Table 2, the anthropometric data showed that patients in the control group had an average waist size of 92.33 ± 4.62 for men and 106.33 ± 13.88 for women. While patients Argan group had a waist circumference average for men of 98 ± 10,82cm and 103.71 ± 11.44 for women.

These waistline values are high according the IDF 2005 for both sexes in the 2 groups.

The average waist circumference in the Argan group is 102.7 ± 11.22 and 102.83 ± 13.56 in the control group. The Waist/Hips circumference ratio TT/TH is about 1 in both groups (Table 3). The distribution of adiposity is android type; therefore, the risk of cardiovascular disease is high. Table 4 explain the evolution of body weight before and after nutritional intervention. During the three weeks of nutritional intervention and after the diet, the patients of both groups did not lose any significant weight.

Analysis of clinical data

From the clinical point of view, the 29 patients in the study had a high blood pressure and were under antihypertensive drugs. Approximately 59% of Argan group is under monotherapy (Furosemide) against 75% for the control group. Good adherence was observed in all patients (stable blood pressure 140/90 mm Hg).

All the patients have a primary hypertension called symptomatic hypertension, which is not derived from any kidney, thyroid or hormonal or cardiovascular causes. They all have metabolic syndrome without apparent complications. In addition, they are non-smokers, which explains the absence of COPD (chronic obstructive pulmonary disease) and non-practicing any kind of physical activity (Table 5).

The ultrasound DOPPLER did not detect any fatty deposits or venous thrombosis among the Argan group patients. However, 18% of them have a coronary heredity and are likely to develop atherosclerosis in the long run.

Table 4. Changes of body weight before and after nutritional intervention with 25 ml of argan oil.

Group	Body weight before intervention in Kg	Body weight after intervention in Kg
Argan group	71.98 ± 13.23	70.02 ± 13.01
Control group	76.68 ± 14.58	73.30 ± 13.80

Table 5. Clinical data in both groups of the nutritional intervention with 25 ml of argan oil (in percent).

Group	Physical Activity	Treatment	Compliance	Self-Measurement	Secondary Hypertension	Complications
Argan group	0	Monotherapy 58.82	94	47	0	0
Control group	0	Monotherapy 75	100	42	0	0

Analysis of nutritional data

Before nutritional intervention, the total daily energy intake of (AET) carbohydrates, lipids and proteins for Argan group is 49%, 36% and 11%, respectively. Whereas for the control group, it is 58%, 25% and 13% (Figure 2). According to WHO data [30], the distribution of food intake shows that the Argan group have a normoglucidique (50 to 55% of the AET) normolipidique (30-40% of the AET) and high protein (12-16% of the AET) type of diet. 47% of the patients in this group are dyslipidemic despite of a normal lipid diet, this shows a significant consumption of saturated or trans fatty acids. Furthermore, 65% of this population is diabetic without thereby following a diet low in sugar. This promotes obesity and therefore the metabolic syndrome.

The control group has a food distribution slightly hyperglucidic (50% are obese), low fat (17% have dyslipidaemia) and normoproteique.

After the nutritional intervention, we note a decrease in the total daily energy intake of fat and carbohydrates with an increase in proteins in both groups but non-statistically significant.

Effect of the argan oil on plasma lipids

After the nutritional intervention, plasma concentrations of total cholesterol decreased significantly for Argan group from 167 mg/dl ± 30 mg/dl to 155 ± 30 mg/dl, however, this sharp decrease remains insignificant. For the control group, total cholesterol increased slightly despite good adherence to the

diet imposed by the dietician (low in saturated and trans fatty acids) (Figure 3).

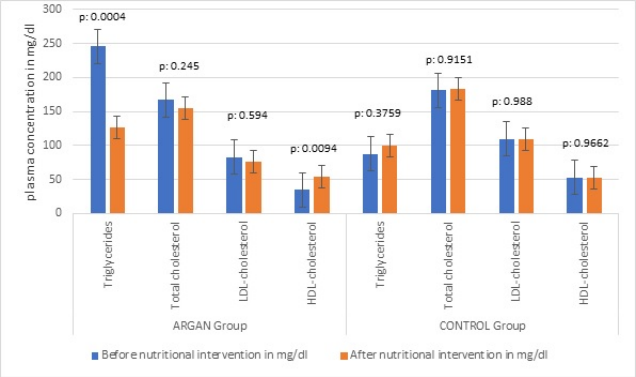

Figure 3. Plasma lipid concentrations of the two groups of patients before and after the nutritional intervention with 25 ml of argan oil.

This fully shows that the diet alone has no effect on total cholesterol. The argan oil has again demonstrated its effectiveness.

After the nutritional intervention, the plasma concentration of HDL-cholesterol increased significantly (p=0.01) in the consumer group of argan oil from 35 ± 11 mg/dl to 54 ± 27 mg/dl.

The Argan oil has divided the risk occurring from cardiovascular diseases by 2 (>55 mg/dl) for patients in this group compared with the major risk that was awaiting them (<40 mg/dl) [31].

The control group did not show any significant change in its plasma concentration of HDL-C (Figure 3).

After three weeks of nutritional intervention, Argan group noted a non-significant decrease in plasma concentration of LDL-C (p=0.01), which decreased from 83 ± 43 mg/dl to 76 ± 37 mg/dl. No change in the plasma concentration of LDL-C was observed for the control group (Figure 3).

After three weeks of nutritional intervention, Argan group showed a significant decrease in triglycerides (p<0.001), which decreased from 246 ± 112 mg/dl to 126 ± 56 mg/dl. While for the control group, a non-significant increase in triglycerides was notified from 89 ± 30 mg/dl to 100 ± 30 mg/dl.

Evaluation of cardiovascular risk

The cardiovascular risk is assessed by calculating the ratio of total cholesterol/HDL-cholesterol (TC/HDL-C) [32,33]. This risk is also known as an atherogenic index. Its normal value is less than five (<5) according to recent European consensus. The atherogenic index is proportional to the increasing cardiovascular risk. The Table 5 shows the evolution of the average ratio TC/HDL-cholesterol in both groups of patients before and after nutritional intervention.

The increase in body mass index does not always leads to an increase of the atherogenic index measured by biochemical parameters. Indeed, there is no correlation between the AI and obesity [34]. However, it depends on dyslipidemia.

The cardiovascular risk in the Argan group was decreased from 5.33 to 3.42, whereas in the control group it remains unchanged, despite the diet. This shows once again that the argan oil with its high MUFA and PUFA, is able to decrease the risk occurring from cardiovascular complications.

Discussion

Cardiovascular diseases by atherosclerosis are the leading cause of death in industrialized countries [35]. Many studies have highlighted the close link between atherosclerosis and eating habits, lifestyle and some aspects of economic development [36]. In this study, we wanted to assess the effectiveness of Argan oil on the lipid profile and to prevent complications of metabolic syndrome. The causes of these complications include original dyslipidaemia and can lead to atherosclerosis.

These dyslipidemias are influenced by the nature of dietary fatty acids. The choice of Argan oil food as a source of fatty acids is important nutritionally since that this oil has a high percentage of unsaturated fatty acids (oleic, linoleic).

Nutritionally, the analysis of the food survey data showed that the two groups of diets differ in terms of fatty acids. The diet of Argan group is associated with a higher consumption of MUFA and PUFA, with a lower consumption of saturated fatty acids. This is due to the rich argan oil uptake in MUFA and PUFA. These are unsaturated fatty acids that have improved the clinical condition of patients. The established diet has reduced the total daily energy by 564 kcal and by 992 kcal in the Argan group and the control group respectively. This decrease did not change the body weight of the patients during the study.

Nutritional intervention studies on humans [28,37] and even with laboratory rats [38] led to interesting results. The consumption of argan oil improves the lipid profile in healthy, diabetic and dyslipidemic subjects [28]. Rich in unsaturated fatty acids (80%), argan oil is richer than olive oil in polyunsaturated linoleic fatty acids (35%) It is this fatty acid that is prized for its ability to reduce cholesterol levels in the blood.

Concerning patients in the control group, no improvement in lipid parameters was observed after 3 weeks of intervention. This proves that the diet does not affect lipid metabolism.

The results from the Argan group showed improved lipid parameters. Argan oil reduces triglyceride levels in dyslipidemia involved in the metabolic syndrome. It even allows the increase of the level of HDL-C, which has a protective role, and an anti-atherogenic effect.

In addition, the level of LDL-C and total cholesterol decreased but not significantly. Therefore, regular consumption of argan oil helps to prevent the formation of atheroma plaque and cardiovascular diseases. The obtained results added the value of argan oil in the prevention of cardio-metabolic diseases. Therefore we demonstrated through this study that the prevention of complications of metabolic syndrome depends on essentially improving lipid parameters (triglycerides, HDL-

C) and this by taking daily 25 ml of argan oil. The molecular mechanisms that could explain these results may be different.

A recent study has demonstrated that the argan oil enriched diet prevents hyperlipidaemia effect by stimulating nuclear receptors PPARα, ERRα and co-activators PGC-1α and lipin-1 by increasing the beta-oxidation in the mitochondria (ACADS, ACADM, ACADVL) and in the peroxysome (ACOX1 genes) [36]. Indeed, the polyunsaturated fatty acids are known to be activators of PPAR [39], a nuclear receptor that regulates the metabolism of lipids and fatty acid oxidation [32,40]. Thus, these nuclear receptors could be the basis of future discovery of new therapies for lipid disorders even going to the treatment of hepatic steatosis [41]. Typically, the stimulation of the nuclear receptor PPARα, decreases the synthesis of VLDL, increases lipolysis and increases the plasma concentration of HDL-C by increasing reverse cholesterol transport [36,42].

A second mechanism of action of the Argan oil at the molecular level was also raised by a study on mice. It showed that phytosterols (schottenol and spinasterol) contained in the Argan oil in majority proportions of (49% and 44%, respectively) [27] act by modulating the expression of the gene promoters of two hepatic nuclear receptors LXRα and LXRβ (liver X receptors). The stimulation of these sterols LXRs induces the expression of target genes cholesterol carriers ABCA1 and ABCG1 [43]. Thus, schottenol and spinasterol can be considered as new LXRs agonists, through their chemical structures similar to cholesterol [27].

These sterols can play a protective role in limiting atherosclerosis via regulation of lipid and carbohydrate metabolisms [44] by controlling the transfer of cholesterol from peripheral cells to the liver for excretion as a form of biliary salts.

A metabolic syndrome-patient should always be considered to have at least a moderate risk of developing cardiovascular disease. This increased risk has been well shown in a Finnish study on patients with and without the metabolic syndrome for 12 years to check the incidence of cardiovascular mortality in both groups. Indeed, the relative risk of cardiovascular death was 3.55 times higher in patients with metabolic syndrome than in those who were without metabolic syndrome [3,31].

Indeed, the reduction in LDL-C concentrations depletes the risk of cerebral vascular accidents by 30%. Yet low, a residual risk remains. This residual risk is due to a low rate of HDL-C [17].

This may reinforce the importance of HDL-C via its various clinical effects as anti-atherogenic [45], anti-thrombotic, anti-oxidant and anti-inflammatory actions against atherothrombosis [46]. Thus, the increase of plasma HDL-C concentration in the blood will act favourably against the atherosclerosis progression, and therefore, on all cardiovascular complications [47]. These data are in accordance with the results we obtained in this study on argan oil.

Consequently, this study confirms the benefit of MUFA and PUFA that should be introduced in our daily diet to prevent and reduce the mortality rate from cardiovascular diseases.

Conclusion

Through this nutritional intervention study with argan oil, we conclude that the improvement of dyslipidaemia as a risk factor of the metabolic syndrome by reducing triglyceridemia (48 %) and increasing HDL-cholesterol (35 %) could be efficient against metabolic syndrome development and then contribute to prevent cardiovascular complications. In addition, the argan oil remains the unique nutritional oil that has markedly benefits on the cardiovascular diseases prevention. These results with those from previous studies reinforce the high value of argan oil in the nutritional prevention of the cardiovascular diseases.

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