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Review

# Argan oil: Which benefits on cardiovascular diseases?

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**Abstract**

*Aim:* The argan oil, extracted from argan-tree fruits, has been known for its various pharmacological properties and used as a natural remedy since several centuries. In this review, we present a summary of the results obtained from a survey of the literature on argan oil.
*Data synthesis:* Various studies conducted in vitro or on human and animal models suggest that argan oil could play a beneficial role in cardiovascular diseases prevention and its consumption could protect against atherosclerosis and cancer via a variety of biological mechanisms.
*Conclusion:* Argan oil reduces cardiovascular risk and may be used as anti-atherogenic oil.


*Keywords:* Argan oil; Cardiovascular diseases; Blood pressure; Lipids; Oxidation

## Contents



## 1. Introduction

The link between diet and the development of some pathologies such as arterial hypertension, diabetes, cardiovascular diseases (CVD) and cancer has been the subject of various studies [1,2]. As far as food lipids are concerned, the influence of the ingested quantities and quality in human and animal models was often highlighted [3,4]. Several recommendations based on experimental, epidemiological or nutritional data have shown that the incidence of CVD is positively correlated with saturated fatty acids intake and negatively correlated with unsaturated fatty acids intake, which are abundant but unequally distributed in vegetable oils such as olive, sunflower and linseed oils [3,5]. Indeed, many studies have shown that products rich in components such as tocopherols and phenolic compounds reduce the susceptibility of lipoproteins to lipid peroxidation, which play a crucial role in the development of the atherosclerosis process [6,7]. In addition, virgin olive oil which is rich in oleic acid, decreases the CVD incidence by improving its major risk factors, such as the lipoprotein profile, blood pressure, glucose metabolism and antithrombotic profile [8]. Endothelial function, inflammation and oxidative stress are also positively modulated as consequences of the olive oil consumption [9–11]. Some of these effects are attributed to minor components of virgin olive oil, mainly phenolic compounds [7].

Argan oil, obtained from the pit of *Argania spinosa*, is another vegetable oil rich in oleic acid and linoleic acid with an oleic/linoleic ratio of 1.25. Interestingly, the unsaponifiable fraction of this oil is mainly rich in antioxidant compounds such as sterols, saponin and phenolic compounds, principally

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γ-tocopherol isoform [12]. Considering its rich composition in antioxidant compounds and unsaturated fat, argan oil can be used as a nutritional intervention in the CVD and cancer disease prevention.

## 2. Argan oil

*A. spinosa* (Sapotaceae) is an endemic tree of south-western Morocco where it constitutes the third most common tree. The oleaginous fruits of argan tree furnish edible and marketable oil "argan oil" that provides up to 25% of the dweller daily lipid diet and 9% of annual oil production in Morocco [13]. Argan oil is extracted following multistep procedures from the pit of the fruit by traditional method, press- or solvent-extraction and has been used for nutritional (directly eaten on toasts or used for cooking), cosmetic and medicinal purposes [14]. Recently, it was shown that the geographical origin of the argan fruit and the extraction method used to produce the oil, considerably influence its physicochemical composition and characteristics [15]. Generally, this oil is rich in unsaturated fatty acids (80%) principally oleic and linoleic acids (44.8 and 33.7%, respectively). Interestingly, the unsaponifiable fraction (1% of the oil constituents) of argan oil is mainly rich in antioxidant compounds such as tocopherols, which is present in a higher proportion compared to olive oil (637 mg/kg versus 258 mg/kg, respectively) and especially in its γ-isoform (75%) (Table 1) [12]. Moreover, this non-glyceric fraction is rich in phenolic compounds, principally ferulic and syringic acids (3147 and 37 μg/kg, respectively), which are absent in olive oil. Also, it is rich in some sterols such as schottenol (1420 mg/kg) and spinasterol (1150 mg/kg). These two families of sterols, known for their anticancer properties, are rarely encountered in other vegetable oils [16,17]. Argan oil also contains a non-negligible proportion of squalene, anther anti-cancerous product (3140 mg/kg versus 4990 mg/kg in olive oil). These compounds prevent oxidation, contributing to the stability of the oil [18].

Table 1
Chemical composition of argan oil and olive oil [12]

| | Argan oil | Olive oil |
|---|---|---|
| Tocophérols (mg/kg oil) | | |
| γ-tocopherols | 480 ± 7 | 26 ± 1 |
| α-tocopherol | 35 ± 1 | 190 ± 1 |
| δ-tocopherol | 122 ± 10 | 42 ± 2 |
| Total | 637 ± 18 | 258 ± 3 |
| Sterols (mg/100 g oil) | | |
| Schottenol | 142 ± 11 | nd |
| Spinasterol | 115 ± 7 | nd |
| $\delta^{8-22}$ stigmastadiene-3β-ol | 9 ± 1 | nd |
| β-sitosterol | nd | 156 ± 3 |
| Campesterol | nd | 12 ± 1 |
| Stigmasterol | nd | nd |
| Others | 29 ± 1 | 151 ± 10 |
| Total | 295 ± 20 | 319 ± 14 |
| Phenolic compounds (μg/kg oil) | | |
| Vanillic acid | 67 ± 3 | 359 ± 7 |
| Syringic acid | 37 ± 5 | 0 |
| Ferulic acid | 3147 ± 20 | 51 ± 2 |
| Tyrosol | 12 ± 1 | 19,573 ± 37 |
| Others | 0 | 773,000 ± 53 |
| Total | 3263 ± 29 | 792,983 ± 99 |
| Squalene (mg/100 g oil) | 314 ± 1 | 499 |

Data expressed mean ± S.E.M.; nd, not detected.

## 3. Biological activity of argan oil

The quality of fatty acids contained in argan oil and the abundance of the antioxidant compounds in the unsaponifiable fraction, suggests a putative use for this oil in nutritional prevention against some pathologies such as CVD. However, only few studies have reported the pharmacological effects of this oil and its compounds as anti-hypertensive, hypolipemiant and presenting antioxidant activities in human and animal models [19–23].

It has been known for many years that the unsaturated fatty acid-rich diet could regulate blood pressure, plasma lipids and blood pressure lipoproteins profiles and, consequently, reduce the risk of the development of atherosclerosis and the incidence of CVD [3–5]. This has been exemplified by the beneficial effect of Mediterranean diet attributed to its richness in olive oil [24]. This oil constitutes an important source of monounsaturated fatty acid (MUFA) (73% of oleic acid), while sunflower oil presents a high content in polyunsaturated fatty acids (PUFA) (61.6% of linoleic acid). Interestingly, argan oil presents an equilibrated proportion in MUFA and PUFA (44.8% of oleic acid and 33.7% of linoleic acid). Linoleic acid (C18: $2n-6$) is an essential fatty acid and serves as a precursor for the biosynthesis of arachidonic acid (C20: $4n-6$), which is a precursor of prostaglandin E1 (PGE1), prostacyclin (PGI2) and PGI3 and thromboxane (TXA 2) that are known for there platelet anti-aggregator and vasodilator activities [25]. Kumar and Das [26] suggested that the anti-hypertensive effect of linoleic acid acted by the inhibition of the PUFA on the angiotensin-converting enzyme (ACE) that is known as a powerful vasoactive agent. Also, arachidonic acid has a hypocholesterolemic effect [27]. Indeed, arachidonic-derived fatty acids, particularly γ-linolenic acid, reduced the total cholesterol, VLDL, IDL and LDL-cholesterol concentrations within human and rat sera [28,29]. Those studies pointed out that vegetable oils rich in PUFA decrease the VLDL and LDL-cholesterol and increase the HDL-cholesterol levels in the plasma. Richard et al. [30] also reported that a daily dietary intake of 3–8 mmol γ-linolenic acid reduces serum total cholesterol and LDL-cholesterol levels. It has been suggested that a high-MUFA diet may reduce the risk of CVD by producing LDL particles that are enriched in oleic acid and more resistant to oxidative modifications [4,31]. Hence, this group of fatty acid is not easily oxidizable and is involved in the modulation of the HDL fluidity, which increases their capacity to promote cholesterol efflux [32].

The minor compounds of argan oil, such as plant sterols, may also be implicated in the hypocholesterolemic effect of argan oil [12]. Indeed, the molecular structure of those plant sterols is very similar to that of human cholesterol and thus, plant sterol intake reduces cholesterol absorption by competing with endogenous cholesterol [33,34]. Controlled clinical trials

have proven that increasing the amount of sterols in the diet modulates positively the blood lipid profile [35]. Supplementation with 2–3 g of plant sterol (stanol–sterol/day) has been shown to reduce 10–15% of LDL-cholesterol [36]. Berrada et al. [19] and Berrougui et al. [20] have shown an improvement of lipid profile in hyperlipaemia-induced rats by chronic treatment with argan oil. In these two studies, significant decreases in total cholesterol, LDL and body weight were observed, whereas the increased of HDL concentration was not significant [19,20]. These data were also confirmed in human [22,23]. Drissi et al. [22] have demonstrated, in healthy adult subjects living in the south-western of Morocco, that regularly consumption of argan oil is associated with significantly low levels of plasma LDL-cholesterol and lipoprotein(a) compared with healthy subjects living in the same area but are not argan oil consumers. More recently, the first interventional trial on human reported interesting data [23]. In a randomized controlled study, 60 healthy adult men receiving 25 ml/day of argan oil during 3 weeks were compared to a group receiving the same quantity of virgin olive oil. Analyses of the lipid intake showed a reduction in saturated fatty acids with both regimens as compared with the stabilization period. Moreover, serum lipid profile showed a significant increase in HDL-cholesterol and apolipoprotein Al (apo-Al) in both groups. However, LDL-cholesterol and apo-B decreased significantly only in olive oil group as compared with the stabilization period, while triglycerides decreased significantly by 17.5% only in argan oil group. Thus, these results confirm some data obtained previously from rat studies and indicate the triglyceride-lowering effect of argan oil in men.

In the aim to investigate the anti-hypertensive effect of argan oil and its mechanism of action, Berrougui et al. [21] have recently conducted a preventive intervention study of argan oil-rich diet (10 ml/kg) in non-developed hypertensive young SHR rats (4-weeks-old). After 7 weeks of treatment, argan oil administration reduced significantly blood pressure in SHR rats by increasing endothelial response, decreasing thromboxane A2 release, and oxidative stress markers [21]. Thus, these results show the beneficial effect of argan oil in the treatment of hypertension and hyperlipidemia, that is attributed to the PUFA, sterols as well as to other constituents contained in argan oil [21].

In spite of the high content of antioxidants in argan oil, little is known about its action. Recently, some laboratories have investigated in vitro the effect of argan oil minor compounds (tocopherols, sterols and polyphenols) at different concentrations on human-oxidized LDL by incubation with $CuSO_4$ [22,37]. LDL lipid peroxidation was evaluated by conjugated diene and malondialdehyde (MDA) formation as well as Vitamin E disappearance. In both studies, results showed that incubation of LDL with tocopherol, sterol and phenolic extracts of argan oil significantly prolonged the lag-phase of LDL peroxidation. Also, the phenolic extracts lowered the rate of lipid peroxidation and reduced the disappearance of Vitamin E in a concentration-dependent manner [22,37]. Incubation of HDL with phenolic extract significantly increased the fluidity of the HDL phospholipidic bilayer and the HDL-mediated cholesterol efflux from THP-1 macrophages. Cherki et al. [38] have also observed an increase (3.7%) of the HDL fluidity of subjects consuming argan oil for 7 weeks without being significant [38].

In parallel, other interesting ex-vivo studies have investigated whether the consumption of argan oil could improve antioxidant status in healthy men [22,39]. The first study showed that a regular consumption of argan oil significantly decreases plasma lipid peroxides (58.3%) and increases significantly the molar ratio of α-tocopherol/total cholesterol (21.6%) as well as α-tocopherol concentration (13.4%) when compared to a non-consumer group [22]. In the second study, the results showed that 25 ml/day of argan oil during 3 weeks in healthy men induces a significant increase in the paraoxonase 1 (PON1) activities (29–45%) and Vitamin E concentration (16%) and decrease significantly the lipid peroxides and conjugated diene formation (18 and 8%, respectively) compared to the baseline values. Susceptibility of LDL to lipid peroxidation as well as the maximum diene production (MDP) were significantly reduced (8 and 13%, respectively). These findings confirm the beneficial effect of argan oil on plasma antioxidant status in vitro and show the same effect for argan oil supplementation in men. Thus, argan oil offers an additional natural food supplement to reduce cardiovascular risk.

The protective effect of argan oil is probably due to its high contents of powerful antioxidants, particularly polyphenols, tocopherols and sterols, which are known as powerful antioxidants [10]. These products act by several mechanisms: (1) scavenging of peroxy radicals, which break the peroxidation chain reaction; (2) chelating free $Cu^{2+}$ to form redox-inactive complexes and thus reducing metal-catalyzed oxidation of LDL; and (3) inhibiting the binding of $Cu^{2+}$ to apolipoproteins and subsequently preventing the modification of amino acid-apo-B protein residue. These hypotheses are also supported by the extended lag-phase and the reduction in the maximum diene production. Thus, LDL may be enriched with different antioxidants of argan oil, which might reduce their susceptibility to lipid peroxidation [40,41]. Gimeno et al. [42] showed that an intake of 25 ml/day of olive oil could increase the resistance of LDL to oxidation. Similarly, several in vitro and in vivo studies in humans as well as in animals have demonstrated that Vitamin E and phenolic compounds extracted from olive oil inhibited oxidation of LDL [6,11,43]. In the case of argan oil, the diminution of LDL susceptibility to lipid peroxidation, could be explained partially by an enrichment with oleic acid that reduce the oxidation potential [44]. In the same time, the marked increase of plasma Vitamin E may be due to abundance of tocopherols in argan oil (636 mg/kg), although the main tocopherol present in this oil is the γ-tocopherol form [12]. The increase of plasma α-tocopherol levels with argan oil could be consequence of an eventual conversion from γ- to α-tocopherol because of the close similarity between chemical structures of both molecules [45]. Indeed, γ-tocopherol supplementation simultaneously increases γ- and α-tocopherol levels. Recent epidemiological, experimental and mechanistic evidences suggest that γ-tocopherol may be a more potent antioxidant and cancer chemopreventive agent than α-tocopherol [46–48]. For example, it was found that γ-tocopherol have more potent interaction to reactive nitrogen

oxide species than α-tocopherol [49]. In addition, because Vitamin E is the major natural antioxidant among those present in LDL, it is considered as the first line of defence against lipid peroxidation [6]. This was confirmed by the finding of Nigdikar et al. [50] which showed that the increase in lag-phase with Vitamin E was four- to five-fold greater than with red wine polyphenols.

Also, the antioxidant activity of argan oil could be attributed to its capacity to induce a significant increase in the PON1 activities [39]. Indeed, dietary habits with a high content of vegetable oil could affect paraoxonase and arylesterase activities [51–53]. Nguyen and Sok [54] have demonstrated that the increase of PON1 activities is associated with the unsaturated fatty acid content. Indeed, they showed that monoenoic acids or their phospholipid derivatives play a beneficial role in protecting PON1 from oxidative inactivation as well as in stabilizing PON1 [54]. On the other hand, atherogenic diets have been demonstrated to reduce PON1 activities [51]. Shih et al. [51] showed that C57BL/6J mice fed with a high saturated fat, cholesterol (1.25% (w/w)), and cholate (0.5% (w/w)) diet exhibited reduced serum PON1 activities and hepatic PON1-mRNA levels.

Furthermore, antioxidant substances such as flavonoid quercetin, were shown to reduce the amount of lipoprotein-associated lipid peroxides and preserved PON1 activity [55]. Also, polygonatum extract and Vitamin E reduced oxidative stress and increased serum PON1 activity, but had no effect on PON1-mRNA expression in rabbit fed a high-cholesterol diet [56]. Similarly, Vitamin E supplementation in rats with propylthiouracil-induced hypothyroidism resulted in decreased lipid peroxide levels in plasma and significantly increased serum PON1 activity compared with propylthiouracil alone [57]. The minor polar components of argan oil could also be involved in this change. Thus, increasing plasma PON1 activities potentiate the anti-atherogenic effect of argan oil.

## 4. Conclusion

This review summarizes the principal findings obtained from argan oil and its beneficial effect as hypolipemiant, hypotensive and antioxidant activities. Indeed, the protective effect of argan oil could be attributed to its interesting chemical composition. It is essentially characterized by the presence of unsaturated fatty acids and antioxidant compounds such as Vitamin E family in which γ-tocopherol account for 70%. With regard to this chemical composition, evidences from observational and experimental studies and interventional trials, suggest that consumption of argan oil may reduce cardiovascular risk by a variety of biological mechanisms including effects on blood pressure, plasma lipid profile and antioxidant status. However, only a few studies have specifically investigated the benefit of a dietary intake of argan oil on CVD. Hence, more investigations are needed to elucidate the bonafide beneficial effects towards CVD as well as its anticancer properties.

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