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Therapeutic potential of argan oil – A review

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1 **ABSTRACT**

2
3 Even though the therapeutic benefits of argan oil consumption have been claimed by Morocco
4 natives and explorers for more than 8 centuries, argan oil has mostly remained strictly
5 confidential for a long time. Recently, drastic improvements in argan oil preparative process have
6 allowed the production of large quantities of argan oil whose quality now fits the international
7 standard. As a direct consequence, these last ten years argan oil has spread over the world and it
8 is now currently purchased in Japan, North America or Western Europe despite its elevated price.
9 Argan oil composition principally includes mono-unsaturated (up to 80%) and saturated (up to
10 20%) fatty acids. As minor components, argan oil contains polyphenols, tocopherols, sterols,
11 squalene, and triterpene alcohols. Together with the mono-unsaturated fatty acids, these four
12 types of minor compounds are also likely responsible for the global beneficial effects of argan oil
13 on human health. The antiproliferative, normoglycemic, and cardiovascular-protective effects of
14 argan oil have been actively evaluated these last five years. This review is aimed at presenting an
15 overview of the known pharmacological properties of argan oil and its still expanding therapeutic
16 potential.

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19 Keywords: *Argania spinosa*, Morocco, fatty acid, phenol, human health

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1. Introduction

Edible argan oil is prepared by cold-pressing the slightly roasted kernels of the argan tree [*Argania spinosa* (L.) Skeels] fruit. This tree is only endemic in South-western Morocco where it covers an area of 320,000 square miles. There, it constitutes a unique biotope, named “the argan forest” that has been classified by UNESCO as a Biosphere Reserve since 1998. In south-western Morocco, the argan tree supports the rural domestic economy by shading family-scale agricultural crops, maintaining the fertility of soil, protecting the soil against erosion, providing its hard and dense wood for fuel or tool making, offering its nuts, fruit pulp and leaves as cattle fodder. Finally, and may be more importantly in this subtropical area, its very strong ability of drought-resistance makes of the argan tree a powerful weapon for slowing down the desert progression.¹

The sustainable development of the argan forest was initiated fifteen years ago.² The first step of this ambitious program consisted in the search of argan tree produces possessing an economic value.

Cell wall polymers of plants constitute the functional matrix that controls plant growth, development, and interactions with (a)biotic environments. Some of these polymers have a cosmetic or nutraceutic value. Cell wall polymers of *A. spinosa* leaves and fruit pulp include potentially valuable xyloglucans, galacturonans and pectins.³⁻⁵ Nevertheless, those compounds have not been industrially exploited, yet. Early phytochemical studies have led to the identification of several saponins from *A. spinosa*.⁶ The tree global high content in saponins has been confirmed more recently.⁷⁻⁹ Some of these saponins present promising antiviral¹⁰ or antioxidant¹¹ properties. Their introduction in cosmetic creams is also industrially investigated.¹² Other metabolites from *Argania spinosa* have a valuable potential in the cosmetic domain and their industrial use is also actively investigated. Particularly, its press-cake is a rich source of

valuable proteins,¹³ and its leaves contain high level of flavonoids (mainly quercetin and myricetin derivatives) presenting a cosmetic potential.¹⁴ Finally, *A. spinosa* triterpenes are also industrially evaluated.¹⁵

However, argan oil is by far the noblest produce derived from the argan tree. Its dietary and medicinal qualities are responsible for argan oil specific place on the oil market. Today, not only is argan oil quoted as “ the world’s most expensive oil” but it was also ranked number one cosmetic ingredient in 2009. For long, argan forest dwellers have claimed that argan oil is hepatoprotective, choleric, prevents diabetes, has anti-inflammatory properties, revitalizes the skin, cures acne, hydrates dry skin, makes hair shining... This review presents an overview of argan oil medicinal properties presently investigated.

2. Argan oil, the chemical constituents and bioactive components

Glycerides are, by far, the main chemical constituents of argan oil (up to 99%). Triglycerides compose not less than 95% of this fraction. The main fatty acids in these triglycerides are oleic and linoleic acids (47±1% and 33±3%; respectively), two n-6 (omega-6) fatty acids. Small amounts of saturated fatty acids also compose the triglycerides of argan oil: stearic acid (4 to 7%) and palmitic acid (12 to 15%).¹⁶ For comparison purpose, the fatty acid content of some common and “less common” oils is reported Table 1.

Minor components of argan oil include other organic derivatives such as (poly)phenols. Among those, vanillic acid, syringic acid, ferulic acid, tyrosol, catechol, resorcinol, (-)-epicatechin, (+)-catechin have been unambiguously identified.^{17,18} The presence of caffeic acid and oleuropein that was reported once¹⁹ has never been confirmed. Squalene, carotens, triterpene alcohols (butyrospermol, tirucallol, β-amyrine, lupeol, 24-methylene cycloartanol, citrostadienol,

1 and cycloeucalenol), sterols (spinasterol, schottenol, stigma-8,22-dien-3 β -ol (22*E*, 24*Z*),
2 stigmasta-7,24-28-dien-3 β -ol (24*Z*)), and α -, β -, γ -, and δ -tocopherols (13%, 16%, 69%, and 2%;
3 respectively)^{17, 20} are other minor organic components of argan oil together with traces of
4 inorganic elements (iron, copper, manganese, and lead).²¹ The chemical composition of most of
5 the edible vegetable oils is responsible for their favorable pharmacological profile.²² The
6 particularly beneficial and healthful properties of argan oil have mainly been attributed to its
7 specific polyphenol, squalene, and tocopherol content.¹⁷

8 Unsaturated fatty acids are involved several metabolic processes including chronic
9 inflammation which also represents a causative factor in a variety of cancers.²³ Although fatty
10 acids belonging to the n-3 series are sometimes presented as the most efficient cardioprotectors,
11 n-6 fatty acids are also essential in the composition of an equilibrated lipid diet.²⁴ Indeed, oleic
12 acid is directly responsible for the reduction in blood pressure through regulation of membrane
13 lipid structure²⁵ and inhibits gelatinase A (MMP-2) activity,²⁶ an enzyme involved in cancer
14 proliferation and Alzheimer's disease. Moreover, linoleic acid, the second major fatty acid of
15 argan oil, is the metabolic precursor of arachidonic acid and multiple bioactive eicosanoids
16 derived from arachidonic acid.

17 Because of their free radical scavenging and anti-oxidant properties phenolic compounds and
18 tocopherols also dramatically contribute to the beneficial pharmacological properties of argan oil.
19 γ -Tocopherol is also known for its role in the primary prevention of heart disease²⁷ and possibly
20 prostate cancer.²⁸

22 **3. Argan oil, various types**

23 *Traditional argan oil*

1 It is the oil as it has been -and still is- prepared for centuries by Moroccan women. Its extraction
2 process has already been reported in details.²⁰ Traditionally prepared argan oil chemical
3 composition is poorly reproducible and frequently of low quality resulting in short preservation
4 time.²⁹ It is mainly used on a family scale but sometimes sold to tourists along the roads of
5 Morocco. In this later case, adulterations are frequent.³⁰ For a single person, from 100 kg of dry
6 fruit, 2 to 2.5 liters of oil are obtained after 58 hours of work. See Table 2.

8 *Cold press edible argan oil (virgin argan oil)*

9 To produce large quantities of argan oil of high quality, implantation of woman cooperatives
10 has been encouraged in South-western Morocco. Because fruit origin and its processing influence
11 argan oil quality,³¹ in these cooperatives strict preparation rules, which include the use of
12 mechanical presses in place of hand-pressing, have been implemented. Also, the use of goat-
13 digested argan nuts has been strictly declared outlaw, even though such picking method should
14 never be considered as a general practice as sometimes stated.³² In these cooperatives, from 100
15 kg of dry fruit, 4 to 6 liters of oil are obtained after 13 hours of work by a single person.

17 *Cold press cosmetic argan oil*

18 It is also produced in woman cooperatives but it is prepared from non-roasted kernels.
19 Collected argan nuts must satisfy the same quality rules as for edible argan oil. Because the
20 kernels are not roasted, cosmetic argan oil content in volatile components is lower than in edible
21 argan oil.³³ Cold press cosmetic argan oil does not have the hazelnut taste of edible argan oil and
22 its preservation time is shorter than that of edible oil. It is directly used for skin application or as
23 hair lotion.

Industrial cosmetic argan

Industrial argan oil results from the solvent extraction of crunched argan kernels coming from mostly not selected argan nuts. Such extraction method is exclusively used by some cosmetic companies. Solvent-extracted oil is also sometimes flash distilled and deodorized. Industrial cosmetic argan oil exclusively enters in the composition of creams, shampoos, body lotions and added preservatives compensate the loss of the naturally protecting agents (tocopherols, polyphenols...).

The polyphenol and tocopherol content of traditional or cold press argan oils is similar. Their different preservation time is mainly due to the selection of the argan nuts and the use of water (sometimes of poor bacteriological quality) during the traditional process.

Edible argan oil is also the major constituent of “*Amlou*”, a highly nutritive preparation whose composition also includes large quantities of crunched almonds and honey.

4. Human being health and argan oil consumption

In addition to traditional claims, the benefits of argan oil consumption on human health have been evidenced by several epidemiologic or clinical studies. The general benefit indicated by the results of those studies has already triggered the preparation of argan oil-based emulsions for parenteral nutrition.³⁴

Has cancer chemoprotective effects

Because argan and olive oils share a very quite similar composition, initially, the cancer chemoprotective effect attributed to olive oil has also been attributed to argan oil. The high level

1 of γ -tocopherol, by far the most potent tocopherol as antioxidant, in argan oil conjugated to its
2 high content in squalene have even led to attribute a higher chemoprotective effect to argan oil
3 than to olive oil. Indeed, for olive oil, some minor component content depends on the oil
4 geographic origin and large variations can be observed. Because argan oil chemical composition
5 is more homogenous than that of olive oil, its consumption is frequently cited as highly valuable
6 for cancer prevention.³⁵ Antioxidants present in argan oil³⁶ are believed to prevent or delay the
7 onset of reactive oxygen species consecutively to lipid peroxidation.¹⁷ More specific
8 investigations on prostatic cells have shown that argan oil tocopherols possess a cytotoxic
9 activity and exert an inhibitory effect on the proliferation of hormone-independent (DU145 and
10 PC3) as well as hormone-dependent (LNCaP) prostatic cell lines, this later being the most
11 sensitive. A cell cycle arrest mediated by up-regulation of the P27 cell cycle regulatory protein
12 could explain the observed physiological activity of the tocopherols.³⁷ Large scale
13 epidemiologic studies using a γ -tocopherol enriched diet have confirmed benefit of γ -tocopherol
14 for prostate cancer prevention.²⁸ These results have encouraged the study of the antiproliferative
15 effect of the polyphenol and sterol fraction of argan oil. The PC3 cell lines were found to be the
16 most sensitive to argan oil polyphenols. Inhibition of ornithin decarboxylase, an enzyme strongly
17 expressed in prostate cancer, or of the autophosphorylation of the epithelial growth factor
18 receptor could explain this activity. Argan oil was found to have a strong antiproliferative activity
19 against prostate cancer cell lines. More specifically, argan oil sterol fraction displayed a strong
20 antiproliferative activity against human DU145 cell line whose metastatic potential is moderate,³⁸
21 whereas argan oil polyphenol fraction exhibited a dose-dependant antiproliferative effect against
22 DPC1 (dog prostate cancer) and human PC3 cell line, whose proliferative potential is high.³⁹ In
23 an independent study, the antiproliferative effect of the squalene and polyphenol-rich

unsaponifiable extract of argan oil on two cell lines (human HT-1080 fibrosarcoma and the transformed and invasive MSV-MDCK-inv cells) was clearly evidenced. Using hepatoma tissue culture cells, it was shown that the squalene and polyphenol-rich extract of argan oil reduces the ability of extracellular signal-regulated kinases 1 and 2 (ERK1/2) to respond to increasing doses of insulin. Conversely, the response of the serine/threonine kinase (Akt), whose major function is to promote growth-factor-mediated cell survival and to block apoptosis response, remained undisturbed. Further studies showed that argan oil polyphenols specifically interrupt the insulin-signaling cascades at the MEK1/2-ERK1/2 interface.⁴⁰

Prevents obesity and adverse cardiovascular outcomes

Hypercholesterolemia and platelet hyperactivity are associated with increased risk of adverse cardiovascular outcomes (coronary artery disease, hypertension...). Phenolic compounds, phytosterols, and tocopherols are known efficient hypocholesterolemic agents. Not surprisingly, argan oil phenolic fraction is also able to prevent LDL oxidation. These chemicals also enhance reverse cholesterol transport by increasing HDL-lipid-bilayer fluidity. Therefore, these derivatives ensure the anti-atherogenic potential of argan oil.⁴¹ Initially evidenced on rats,^{42, 43} the hypolipidemic and hypocholesterolemic potency of argan oil itself in humans via a paraoxonase-related improvement of the plasma oxidative status has been demonstrated in 2005.⁴⁴ Other complex pathways initially resulting from an intracellular accumulation of squalene and ultimately triggering a LXR (liver X receptor) stimulation⁴⁵ could also explain the anti-atherogenic potential of argan oil. Argan oil also induces a lowering of LDL cholesterol and has antioxidant properties as shown by a study on 96 persons. Subjects consuming argan oil on a regular basis presented significantly lower levels of plasma LDL cholesterol and lipoprotein (a) and lower concentration of plasma lipoperoxides.⁴⁶ Argan oil also increases HDL cholesterol

1 levels and lowers triglyceride levels in men.⁴⁷ Therefore, and expectedly, regular argan oil
2 consumption prevents obesity.⁴⁸ Argan oil also inhibits platelet aggregation without causing
3 neither a prolongation of the bleeding time nor a change in the platelet amount. Therefore, argan
4 oil may act on the attachment of fibrinogen to GPIIb/IIIa platelet receptor without affecting
5 platelet adhesiveness to the vascular endothelium.⁴⁹ All together, these studies indicate that argan
6 oil reduces cardiovasuclar risk, prevent obesity and can be used as anti-atherogenic oil
7 confirming the traditionally claimed properties of the oil.⁵⁰

8 9 *4.3 Has no influence on the thyroid hormone profile*

10 Thyroid hormones and fatty acid metabolism are strongly intercorrelated. Unsaturated fatty
11 acids have been shown to possibly prevent hypothyroidism.⁵¹ Therefore, the hypothyroidic
12 activity of argan oil has been evaluated. A study performed on 149 volunteers has evidenced that
13 argan oil supplementation has no activity on hypothyroidism.⁵²

14 15 *4.4 Has an antidiabetic activity*

16 The cardiovascular protective and antidiabetic effects of argan oil are likely to be the most
17 anciently claimed pharmacological effects of argan oil. So far, the only scientific demonstration
18 of the possible antidiabetic activity of argan oil has been performed on rats. In healthy or diabetic
19 rats, administration of argan induced a significant glycemia reduction that lasted for 3 hours.
20 Argan oil also reduced significantly the amount of absorbed glucose in perfused jejunum
21 segment.⁵³ Even though the antidiabetic effect of argan oil was claimed for a long time, the
22 intimate mechanism linking argan oil consumption and blood glucose level regulation is still
23 unknown.

4.5 *Has no influence on the immune system*

Recent biochemical studies have shown that fatty acids could modify immune responses.⁵⁴ Indeed, lymphocyte proliferation, lymphocyte-derived cytokine production, or cell-mediated immunity can be influenced by dietary lipids. The effect of dietary argan oil on the immune system has been evaluated on rats. Those studies have shown that argan oil effect on immune cells is similar to that of olive oil, a widely consumed oil, and that argan oil has no marked effects on immune cell function.⁵⁵

4.5 *May trigger anaphylaxis*

The first, an so far unique, case of allergy to argan oil has been recently presented.⁵⁶ Allergen was characterized as a 10kDa protein likely belonging to the family of oleosins that is also encountered in peanut and sesame.

5. Argan oil vs other edible oils

The quality of an edible oil can be reflected by different factors. Among those, the most important are its sensory quality, its nutritional quality, and its pharmacological quality... If the sensory quality is important to get the consumer acceptance and hence to occupy a reasonable market share, nutritional and pharmacological qualities are essential on a dietary standpoint.

In evaluating the nutritional quality of oil, fatty acid composition occupies a special place. More specially, (poly)unsaturated fatty acids are essential nutrients for they are the biological precursors of leukotrienes and prostaglandins, two types of compounds acting as hormone-like cell messengers. However the simple presence of a high amount of linoleic acid does not necessary lead to an oil of high nutritional value, as reported for grape seed oil.⁵⁷

Olive oil is oleic acid-rich (Table 1). It is a world-wide used edible oil that is considered to

1 be a key ingredient in the mediterranean diet. Hence, its nutritional quality is recognized as high⁵⁸
2 as are its unique biological properties.⁵⁹ As olive oil, argan oil also contains a high level of oleic
3 acid and, once again as olive oil, its second major unsaturated fatty acid is linoleic acid.
4 Additionally, the saturated fatty acids of both argan and olive oils are palmitic and stearic acids.
5 Therefore, the general nutritional qualities of olive and argan oils are likely to be identical. If
6 only average values are considered, olive oil contains statistically higher values of
7 monounsaturated fatty acid than argan oil that would be nutritionally close to peanut oil even
8 though this latter contains small amounts of arachidic and behenic acids, two saturated fatty acid
9 that are not found in argan oil.⁶⁰ Nevertheless, this type of classification relies only on statistical
10 analysis and the major difference between argan and olive oils is the large chemical variability
11 tolerated for olive oil. Indeed, olive oil is produced in the whole Mediterranean basin and,
12 because of its multiple geographic origins, olive oil fatty acid composition can fluctuate.
13 Consequently, and for example, its composition in linoleic acid can possibly be either 3.5 or
14 21%. Since consumers are not necessarily aware of the geographical origin of the purchased olive
15 oil, the precise nutritional value of their olive oil is uncertain. On the opposite, argan oil fatty acid
16 composition is much more homogenous and its nutritional value is less fluctuant.

17 Variation in the geographic origin of edible oils also dramatically affects the composition in
18 oil minor components that are responsible for the pharmacological quality of the oil. Several of
19 the minor olive oil compounds (polyphenols, sterols, tocopherols...) have been presented as
20 responsible for the pharmacological effects of the oil⁵⁸ but large variations have been observed in
21 term of concentration evidencing that all olive oils do not present the same pharmacological
22 potential.⁶¹ Compared to olive oil, the reproducible minor components chemical composition of
23 argan oil is likely to be responsible for a more homogenous pharmacological profile.

6. Conclusions

Argan oil specific taste and pharmacological properties justify the culinary and medicinal interest devoted to this oil during these last ten years. Benefits of argan oil eating for women at menopause stage and argan oil induced DNA UV-protection are two of the most advanced research projects currently going on argan oil pharmacology.

These last years, analytical methods have been designed⁶² and have led to new, easy to apply, and efficient anti-fraud measures. The very recently granted geographic indication of argan oil is also going to be an efficient mean to control the sensory, nutritional and pharmacological quality of argan oil. This will not only ascertain the authenticity of argan oil, that is still sometimes questioned, but also will avoid the geographic variation problem faced by olive oil. Preparative parameters (fruit drying time, kernel preservation time...) influencing the oil quality are currently actively investigated and optimum parameters will become mandatory after inclusion in the geographic indication file.

Finally, consumption of high quality argan oil will improve the quality of life of its consumers but it also actively 1) supports the sustainable development of South western Morocco,⁶³ that has been one of the poorest part of the world, 2) helps to stop desert progression, 3) brings a regular income to the argan forest dwellers, and 4) permits the survival of the argan tree, the chemical content study of which still deserving a special attention.⁶⁴

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Table 1

Percentage of oleic, linoleic, stearic, and palmitic acid in common (corn, olive, soybean, sunflower, and peanut) and less common (grape seed, argan) oilss.

Fatty acid	Corn oil	Olive oil	Soybean oil	Sunflower oil	Peanut oil ^a	Grape seed oil	Argan oil
Oleic ac.	20-42.2	55-83	17.7-28	14-39.4	35-69	12-28	43-49.1
Linoleic ac.	34-65.6	3.5-21	49.8-59	48.3-74	12-43	58-78	29.3-36
Stearic ac.	<3.3	<5	2-5.4	2.7-6.5	1-4.5	<3.3	4.3-7.2
Palmitic ac.	8.6-16.5	7.5-20	8-13.5	5-7.6	8-14	8.6-16.5	11.5-15

^a. Contains also behenic ac., arachidic ac., and eicosenoic ac. (1.5-4.5%, 1-2%, and 0.7-1.7%; respectively).

Table 2

Differences between the four argan oil types.

	Traditional oil	Cold press edible oil	Cold press cosmetic oil	Industrial cosmetic oil
Material	Uncontrolled fruit	Hand-picked fruit	Hand-picked fruit	Uncontrolled fruit
Process	Hand malaxing	Press	Press	Solvent
Preservation	One to two weeks	Several months	Up to one month	Several months
Color	Yellow to brown	Copper like	Gold like	No color
Taste	Not reproducible	Hazelnut like	Bitter	Not suitable as food
Quality	Low	Very high	Very high	Very high
Moisture	Variable	Low	Some amount	None
Antioxidants	Variable	High	High	None