Anti-inflammatory activity of argan oil and its minor components

[a]Hanane Ben Menni, [a]Meriem Belarbi, [a]Dounia Ben Menni, [b]Hadjer Bendiab, [c]Yamina Kherraf , [d]Riadh Ksouri, [b]Noureddine Djebli; [e,f]Francesco Visioli

[a]Laboratoire de Produits Naturels (LAPRONA), Département de Biologie, Université de Tlemcen (Algeria); [b]Laboratoire de Pharmacognosie et Phytothérapie, Université de Mostaganeme (Algeria); [c]Laboratoire d'Histologie Embryologie et Génétique Clinique CHU de Tlemcen (Algeria); [d]Laboratoire des Plantes et Médicinales (LPAM), Centre de Biotechnologie de Borj-Cédria (Tunisia); [e]IMDEA-Food, CEI UAM+CSIC, Madrid (Spain) and [f]Department of Molecular Medicine, University of Padova (Italy).

Correspondence to:

Francesco Visioli

Department of Molecular Medicine

University of Padova

Viale G. Colombo 3

35121 Padova, Italy

Email: francesco.visioli@unipd.it

Abstract

Argan oil is thought to be the most expensive edible oil worldwide. It is difficult to produce and the argan tree only grows in a limited geographical area, notably Morocco and Algeria. Because it is produced by mechanical means, argan oil contains “minor” components that might be endowed with healthful effects. We investigated in vivo the anti-inflammatory activities of argan oil and its unsaponifiable fraction, using diclofenac as the control, in a carrageenan-induced rat model of inflammation. Rats were given different amounts of argan oil or its unsaponifiable fraction, by gavage. We report that argan oil and its “minor” components effectively lessen the inflammatory actions of carrageenan. Far from being “pharmacological” the actions of argan oil are comparable with those of diclofenac in the short, i.e. 4 h term. Sustained consumption of argan oil might, therefore, contribute to lessen the burden of degenerative diseases associated with higher inflammatory status.

Keywords: argan oil; inflammation; phytosterols; tocopherols; atherosclerosis.

Introduction

Inflammation, especially the low-grade/chronic one can potentially trigger or facilitate the onset of several diseases, such as atherosclerosis and other cardiovascular diseases; metabolic syndrome, type 2 diabetes and obesity; sarcopenia and osteoporosis; neurodegeneration; major depression and impaired mental wellbeing; and cancer (Calder et al. 2017). This becomes especially important during aging. Indeed, aspirin or ibuprofen extend longevity in different organisms e.g. *S. cerevisiae, C. elegans and D. melanogaster*. However, the use of non-steroidal anti-inflammatory drugs (NSAIDs) is associated with untoward effects such as increased GI bleeding (Lanas 2016). An alternative, more viable approach is that of a proper diet, rich in anti-inflammatory compounds such as (poly)phenols, prebiotics, and polyunsaturated fatty acids (Calder et al. 2017). Healthy eating patterns are indeed associated with lower circulating concentrations of inflammatory markers including C-reactive protein and several cytokines (Calder et al. 2017).

Argan (*Argania spinosa* L.) is a tropical tree that belongs to the sapotaceae family. In 1998, the United Nations Educational, Scientific and Cultural Organization (UNESCO) designated the Argan forest in South-Western Morocco a UNESCO biosphere reserve because of its ecological and socioeconomic benefits (www.unesco.org). This plant mostly grows in Morocco and Southwestern Algeria (Tindouf area), where it is the second most common tree after *Acacia radianna*. Other trees are successfully grown in various parts of the country, particularly in the North-West (Stidia in the region of Mostaganem) (El Abbassi et al. 2014).

The argan tree produces oleaginous fruits, whose oil has nutritional and pharma-nutritional properties that are being explored (Sour et al. 2012; Sour et al. 2015; Ursoniu et al. 2018). Edible argan oil is prepared from roasted kernels, whereas unroasted kernels are used in the production of cosmetic argan oil (Harhar et al. 2010). In addition to being

employed in cosmetics, in fact, argan oil is consumed by humans as part of their diet or as folk medicine (Charrouf and Guillaume 2010).

In addition to fatty acids (mostly polyunsaturated), argan oil contains approximately 1% of “minor components” such as tocopherols, (poly)phenols, sterols, carotenoids, and xanthophylls (Harhar et al. 2010). This is due to the fact that argan oil is obtained by physical means, similarly to olive oil, without the use of solvents. Therefore, most of the unsaponifiable components of the seeds are transferred to the final product. Argan oil’s quality and composition, hence, depend on numerous parameters, namely genetic and environmental factors (climate and altitude), but also the oil extraction process, soil type, temperature, climate during harvest (e.g. rain vs. drought), fruit maturity, and harvest timing (Chakhchar et al. 2017).

We aimed at studying the anti-inflammatory activity of a well-characterized edible argan oil and its unsaponifiable fraction, in a mouse model.

Materials and methods

Mature fruits of *Argania spinosa* were collected during July 2016 from trees of the Tindouf areas (South-Western Algeria).

Argan oil was obtained via traditional methods of pulping, crushing, roasting, trituration, kneading, and conditioning (Harhar et al. 2011). The resulting oil was analyzed as follows.

Density index

It is the ratio of the mass of a given volume of argan oil at 20 °C and the mass of an equal volume of water distributed at the same temperature. We used a pycnometer with a graduated thermometer and calibrated at 20 °C. The relative density d_{20} is given by the following formula: $d_{20}= (m_2-m_0)/(m_1-m_0)$, where m_0 is the mass of the empty pycnometer; m_1

is the mass of the pycnometer filled with distilled water; and m_2 is the mass of the pycnometer filled with oil ((AFNOR) 1984).

Refractive index (n_d^t)

We measured the oil's refractive index using a refractometer at 20 °C. The refractive index was calculated by the following formula: $n_d^{20} = n_d^t + 0.00035\ (t-20)$, where n_d^t is the temperature at which the determination was made; n_d^{20}: refractive index at 20 °C; t: temperature at which the determination was made ((AFNOR) 1984)

Acidity index (I_A)

Argan oil (0.5 g) was dissolved in 20 ml of ethanol/n-butanol solution (60:40; v/v). A control container was put in parallel with the same amount of solvent used. Each test was titrated with KOH (0.1 N) in the presence of phenolphthalein as the detector.

We calculated acidity by the following formula: $I_A = ((V_1-V_2) \times M \times N) /m$, where V_1 is the volume (ml) of KOH used for the test sample; V_2 is the volume (ml) of KOH used for the control; M: the molecular weight of KOH (56.11 g / mol); N: the normality of KOH solution (0,1 N); m: the weight (g) of the oil sample ((AFNOR) 1985).

Saponification index (I_S)

We saponified 1 g of oil under reflux with 25 ml of ethanolic KOH (0.5 N) for 1 hour. The sample was titrated with 0.5N HCl, in the presence of phenolphthalein the detector. Controls did not contain the oil.

We calculated the saponification index by the following formula: $I_S= ((V_1-V_2) \times M \times N) /m$, where V_1 is the volume (ml) of HCL used for the control; V_2 the volume (ml) of KOH used for the test sample; M the KOH molecular weight (56.11 g/mol); N the normality of KOH solution (0.5 N); m the weight (g) of the oil sample ((AFNOR) 1990).

Fatty acid analysis

Total fatty acids were derivatized into their corresponding methyl esters as described by Cecchi et al. (Cecchi et al. 1985). Transmethylation was performed by the addition of 2 mL of hexane, 0.5 mL of 3% sodium methylate, 0.2 mL of 1 N H_2SO_4 and 1.5 mL of 10% sodium chloride. The hexanic phase, containing fatty acid methyl esters (FAME), was recovered and its volume reduced using a stream of nitrogen, prior to analysis. We analysed FAMEs by gas chromatography (GC) using a Hewlett–Packard 6890 apparatus equipped with a flame ionization detector (FID) and an electronic pressure control (EPC) injector (Agilent Technologies, Palo Alto, CA). A HP–Innowax capillary column (polyethylene glycol: 30 m 0.25 mm i.d., 0.25mm film thickness; Agilent Technologies, Hewlett– Packard) was used; the flow of the carrier gas (N_2) was 1.6 mL/min and the split ratio 60:1. Analyses were performed by using an oven temperature of 150 °C for 1 min, followed by an increase from 150 °C to 200 °C at a rate of 15 °C/min, and then from 200 to 225 °C at a rate of 2 °C/min and finally held as such for an additional 2 min period. The detector and injector temperatures were set at 275 and 250 °C, respectively.

FAMEs were identified by comparison of their retention times with those of pure reference standards (Sigma–Aldrich, Steinheim, Germany). The GC apparatus was connected to a HP Chemstation (Rev.A.0401) software for peak area and fatty acid percentage calculation.

Unsaponifiable fraction

The unsaponifiable fraction was extracted and determined according to the AFNOR NF t 60-205 method ((AFNOR) 1984)

Five g of oil were saponified with an ethanolic solution of potassium hydroxide (2 N) by refluxing for 20 minutes. After cooling and addition of 50 ml of distilled water, the

unsaponifiable fraction was extracted with diethyl ether and then washed with water until neutral pH was reached. The extract was then filtered through anhydrous sodium sulphate and evaporated under vacuum using a rotary evaporator. The residue was dried and allowed to cool.

The content of unsaponifiable compounds was determined as: Unsaponifiables (%) = (m_1/m_0) ×100, where m_1 is the mass (g) of the dried residue and m_0 the mass (g) of the test sample.

Analysis of tocopherols

We quantified α-, β-, γ-, and δ-tocopherols according to the method described by the ISO 9936:2016 publication (9936:2016 2016). For this, 0.2 g of oil was dissolved in 4 ml of hexane. Tocopherols' separation was carried out by a Waters HPLC equipped with a UV-Visible detector and a 25 cm long C_{18} column. Elution was performed with 0.5% isopropanol in hexane at a flow rate of 1.5 ml/min. Wavelength: 292 nm and injection loop 20 µl.

All analyses were carried out in triplicate. Values are expressed as means ± SD.

Analysis of phytosterols

Sterols have been identified according to Sanchez-Machado et al. (Sanchez-Machado et al. 2004)**.** After saponification and removal of unsaponifiables with hexane, sterols were measured by a Waters HPLC equipped with a UV-Visible detector and a 25 cm long C_{18} column. Elution was performed with a mixture of methanol/acetonitrile (30/70; V/V). Wavelength: 205 nm, an injection loop: 20 µl.

In Vivo Potential Anti-Inflammatory Activity

The experimental procedures and protocols used in this study were approved by the Institutional Animal Ethics Committee (1205/c/08/ CPCSEA, on 21.04.08). The animals

were obtained from the laboratory animal service of the Pasteur Institute of Algeria. We used female NMRI mice weighing 24-30 g. Mice were housed in polypropylene cages and maintained under standard laboratory conditions, i.e. 20 ± 2 °C and relative humidity of 60%-70%. All animals had free access to water and standard diet. They were acclimatized for least one week before the experiments started. All experiments were conducted after an overnight fast (water was available).

Acute toxicity

Argan oil (5 and 8 g/kg) and its unsaponifiable fraction (10 and 15 g/Kg) were administered to six mice by gavage. All animals were observed for 15 days after administration.

Inflammatory paw edema test

We used the method of Trovato et al. (Trovato et al. 2001). Eighteen mice were divided into six groups of three animals each. Two groups (H1) and (H2) received argan oil, orally, at doses of 5 and 8 g/kg, respectively. The unsaponifiable extract of argan oil was dissolved and dispersed in Tween 80 (15%) and administered to the (EX1) and (EX2) groups of mice at doses of 10 and 15 g/kg, respectively. The same amount of Tween 80 (15%) was administered to the control group (C). The anti-inflammatory activity of argan oil and its unsaponifiable fraction was compared to that of a reference group (Std) that was given 50 g/kg of diclofenac. One hour after oral administration, edema was induced by the injection of 0.1 mL of carrageenan solution (0.5%) into the sub-plantar region of the right hind paw of all mice. The size of the edema was measured by a plethysmometer from 1 to 6 h after injection.

The percentage increase and inhibition of edema was calculated from the formula: Percentage of edema increase (%) = $(V_1 - V_0/V_0) \times 100$ and Percentage of edema inhibition

(%) = (E_c - E_t/E_c) x 100, where V_1 is the paw volume of the rat after carrageenan injection; V_0 the paw volume of the rat before carrageenin injection; E_c the edema rate of the control group; E_t the edema rate of the treated group.

Histological study

Mice were anesthetized with chloroform six hours after the injection of carrageenan and their legs were removed, fixed in 10% neutral buffered formalin, and incased in paraffin. Four-micrometer sections were cut, stained with hematoxylin-eosin, and observed for histopathological changes under an optical microscope.

Statistical analysis

Statistical analyses were performed using the XLSTAT 2018 software, a one-way ANOVA, and a Student's *t*-test. The results are expressed as mean ± SEM (n= 3). Values of $p < 0.05$; $p < 0.01$ were considered significant (*) and very significant (**), respectively.

Results

Physicochemical indexes

The oil we used had density of 0.91, a refractive index of 1.47, an acidity of 1.12, and a saponification index of 192.7 (Table 1).

Fatty Acids Profile

The fatty acid composition of the argan oil we studied is shown in Table 1. Unsaturated fatty acids are the predominant components and account for more than 80% of the total. The most abundant fatty acids were oleic and linoleic acid, (45.06 ±1.54 and 35.87 ±1.17%, respectively), followed by the saturated palmitic (11.99 ± 0.12%) and stearic (6.17

± 0.39%) fatty acids. Argan oil is not a good source of omega 3 acids and, indeed, we only recorded traces of α-linoleic acid.

Unsaponifiable fraction

The unsaponifiable fraction represented 1.1% of the oil and was composed as follows (Table 1).

Schottenol is the predominant (46.86 ± 0.19%) sterol, followed by spinasterol, stigmasta 8-22-dien-3b-ol and Delta7 avenasterol (39.78 ± 0.14, 8.76 ± 1.03, and 4.26 ± 0.84%, respectively).

Tocopherol analysis (Table 1) shows that the predominant (576.29 ± 30.67) tocopherol is γ-tocopherol, followed by δ-tocopherol (99.41 ± 7.95) and α-tocopherol (66.65 ± 15.76).

Acute toxicity

After oral administration of either oil (5 and 8 g/kg) or its unsaponifiable fraction (10 and 15 g/Kg), no behavioral change and no mortality were recorded for any animal observed 15 days after treatment.

Anti-inflammatory activity of whole argan oil

The carrageenan-induced increase of paw volume was significantly reduced at 4 h, as compared with controls, in groups of mice that received argan oil (both 5 and 8 g/kg) and was very significantly at 5 and 6 h in the three groups treated (Table 2).

Argan oil (H1) was significantly more efficacious than diclofenac 4 h from the injection of carrageenan. At that time point, there was no significant difference between the effect of the argan oil tested (H1 and H2) and that of the reference product, with better efficacy for oil at a dose of 5 g/kg than 8 g/kg.

Anti-inflammatory activity of the unsaponifiable fraction

After 5 h from the injection of carrageenan, the paw volume was very significantly reduced in the group treated with the unsaponifiable extract of argan oil (EX2, 15 g/Kg), compared with controls (C) (Table 2).

The unsaponifiable fraction of argan oil at the dose of 10 g/kg reached its maximum activity 4 h after the injection of carrageenan and was more effective at 15 g/kg. Indeed, at the 5th hour, its effects on paw edema were slightly stronger than those of diclofenac given at 50 g/kg; no significant difference was observed compared to the standard group after the fourth hour, when the anti-inflammatory effects of diclofenac peaked.

Histological study of mouse paws

The results obtained in the histological study (Figure 1) confirm – at the tissutal level - those (percentage increase and inhibition of edema) recorded with the plethysmometer. In particular, we evaluated edema, congestion, and inflammatory infiltrates. We recorded that carrageenan-induced inflammation was greater in the untreated, control mice (group) than in the treated groups (H2 and EX1). Groups Std, H1, and EX2 exhibited the lowest degree of inflammation.

Discussion

Argan oil is thought to be the most expensive edible oil worldwide. It is difficult to produce and the argan tree only grows in a limited geographical area, notably Morocco and Algeria. Yet, argan trees are important to the ecosystem and protect local land from desertification, as acknowledged by the UNESCO. Because it is produced manually without the use of solvents, argan oil retains most of the components found in kernels. In this respect, argan oil is similar to olive oil, also exclusively produced by mechanical means. In

particular, argan oil is more than fatty acids and contain “minor” components that might be endowed with healthful effects. It is important to study edible argan oil because it provides a substantial portion of energy and essential fat to several indigenous people, which is in line with the UN Sustainable Development Goals.

In this study, we investigated the anti-inflammatory activities of argan oil and its unsaponifiable fraction, by administering low, physiological doses and using diclofenac as a representative NSAID control. We report that argan oil and its “minor” components effectively lessen the inflammatory actions of carrageenan.

In terms of fatty acids, linoleic acid (of which argan oil is quite rich) is being scrutinized by the scientific community because of its theoretical pro-inflammatory effects, being it the precursor of arachidonic acid and, in turn, eicosanoids. However, the results of human epidemiological studies and some intervention trials argue against this hypothesis and actually show that the intake of linoleic acid results in anti- rather than pro-inflammatory actions (Marklund et al. 2019). Notable examples come from observation and intervention trials, whose pooled data clearly indicate that linoleic acid counterintuitively lowers systemic inflammation (Poli and Visioli 2015). In addition, for every 5%en increase in polyunsaturated fatty acids replacing saturated ones, the effects on the total:HDL-C ratio would predict a 9% lower risk of CHD. For the same 5%en replacement, prospective cohort studies have observed a 13% lower risk of CHD. The pooled analysis of randomized trials also indicates that for the same 5%en shift, a 10% lower risk of CHD could be expected (Mozaffarian et al. 2010).

Worth of discussion is the anti-inflammatory effect of the unsaponifiable fraction.

(Poly)phenols are anti-inflammatory products of plants’ secondary metabolism (Del Rio et al. 2013). Argan oil does not contain (poly)phenols in relevant amounts (4 - 50 mg/kg and Table 1). Even though some of them, e.g. hydroxytyrosol are effective anti-inflammatory agents (Crespo et al. 2018), the true contribution of argan oil’s (poly)phenols to the observed

effects requires ad-hoc investigations. Tocopherols, namely γ-tocopherol are abundant in argan oil. Even though the true effects of tocopherols, especially α-tocopherol on the cardiovascular system are equivocal, basic evidence indicates that these molecules modulate signal transduction and might play anti-inflammatory roles in disorders such as allergy (Galli et al. 2017).

Finally, part of the anti-inflammatory effects might be consequent to the actions of phytosterols. Whereas there is sufficient basic science evidence that these compounds are anti-inflammatory in arrange of conditions, human evidence is inconclusive (Vilahur et al. 2018). Therefore, we think it unlikely that argan oil's phytosterols are chiefly responsible for the anti-inflammatory actions we report.

In conclusion, we report that argan oil (sourced from Algeria) and its unsaponifiable fraction have anti-inflammatory actions at nutritionally relevant doses. These effects, far from being "pharmacological" are comparable with those of diclofenac in the short, i.e. 4 h term. Sustained consumption of argan oil (alone or in combination with, e.g. the more affordable virgin olive oil) might, therefore, contribute to lessen the burden of degenerative diseases associated with higher inflammatory status and further studies should be directed to identify its most active components.

Acknowledgments

Supported in part by POR FESR 3S4H

Conflict of Interest

The Authors declare no conflict of interest.

Figure Legend

Hematoxylin-eosin staining of mouse paws. Representative images are shown. (a) edema; (b) congestion, (c) inflammatory infiltrate. A) Control; B) diclofenac; C) Argan oil 5

g/Kg; D) Argan oil 8 g/Kg; E) Argan oil's unsaponifiable extract 10 mg/Kg; F) Argan oil's unsaponifiable extract 15 mg/Kg.

References

AFNOR. 1984. Recueil de normes françaises des corps gras, graines oléagineuses produits dérivés. 3rd. Edition. Paris, France.

AFNOR. 1985. Détermination de l'indice d'acide et de l'acidité (méthodes titrimétriques). Paris, France.

AFNOR. 1990. Détermination de l'indice de saponification. Paris, France.

Calder PC, Bosco N, Bourdet-Sicard R, Capuron L, Delzenne N, Dore J, Franceschi C, Lehtinen MJ, Recker T, Salvioli S et al. 2017. Health relevance of the modification of low grade inflammation in ageing (inflammageing) and the role of nutrition. Ageing Res Rev. 40:95-119.

Cecchi G, Biasini S, Castano J. 1985. Méthanolyse rapide des huiles en solvant. Note de laboratoire. Rev Franç Corps Gras. 4:163–164.

Chakhchar A, Haworth M, El Modafar C, Lauteri M, Mattioni C, Wahbi S, Centritto M. 2017. An assessment of genetic diversity and drought tolerance in argan tree (argania spinosa) populations: Potential for the development of improved drought tolerance. Front Plant Sci. 8:276.

Charrouf Z, Guillaume D. 2010. Should the amazigh diet (regular and moderate argan-oil consumption) have a beneficial impact on human health? Crit Rev Food Sci Nutr. 50(5):473-477.

Crespo MC, Tome-Carneiro J, Davalos A, Visioli F. 2018. Pharma-nutritional properties of olive oil phenols. Transfer of new findings to human nutrition. Foods. 7(6).

Del Rio D, Rodriguez-Mateos A, Spencer JP, Tognolini M, Borges G, Crozier A. 2013. Dietary (poly)phenolics in human health: Structures, bioavailability, and evidence of protective effects against chronic diseases. Antioxid Redox Signal. 18(14):1818-1892.

El Abbassi A, Khalid N, Zbakh H, Ahmad A. 2014. Physicochemical characteristics, nutritional properties, and health benefits of argan oil: A review. Crit Rev Food Sci Nutr. 54(11):1401-1414.

Galli F, Azzi A, Birringer M, Cook-Mills JM, Eggersdorfer M, Frank J, Cruciani G, Lorkowski S, Ozer NK. 2017. Vitamin e: Emerging aspects and new directions. Free Radic Biol Med. 102:16-36.

Harhar H, Gharby S, Ghanmi M, El Monfalouti H, Guillaume D, Charrouf Z. 2010. Composition of the essential oil of argania spinosa (sapotaceae) fruit pulp. Nat Prod Commun. 5(6):935-936.

Harhar H, Gharby S, Kartah B, El Monfalouti H, Guillaume D, Charrouf Z. 2011. Influence of argan kernel roasting-time on virgin argan oil composition and oxidative stability. Plant Foods Hum Nutr. 66(2):163-168.

ISO 9936:2016. 2016. Animal and vegetable fats and oils -- determination of tocopherol and tocotrienol contents by high-performance liquid chromatography. Geneva, Switzerland

Lanas A. 2016. Advances in gastrointestinal bleeding. Gastroenterol Hepatol. 39 Suppl 1:53-61.

Marklund M, Wu JHY, Imamura F, Del Gobbo LC, Fretts A, de Goede J, Shi P, Tintle N, Wennberg M, Aslibekyan S et al. 2019. Biomarkers of dietary omega-6 fatty acids and incident cardiovascular disease and mortality: An individual-level pooled analysis of 30 cohort studies. Circulation.

Mozaffarian D, Micha R, Wallace S. 2010. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: A systematic review and meta-analysis of randomized controlled trials. PLoS Med. 7(3):e1000252.

Poli A, Visioli F. 2015. Recent evidence on omega 6 fatty acids and cardiovascular risk. Eur J Lipid Sci Technol. 117:1847-1852.

Sanchez-Machado DI, Lopez-Hernandez J, Paseiro-Losada P, Lopez-Cervantes J. 2004. An hplc method for the quantification of sterols in edible seaweeds. Biomed Chromatogr. 18(3):183-190.

Sour S, Belarbi M, Khaldi D, Benmansour N, Sari N, Nani A, Chemat F, Visioli F. 2012. Argan oil improves surrogate markers of cvd in humans. Br J Nutr. 107(12):1800-1805.

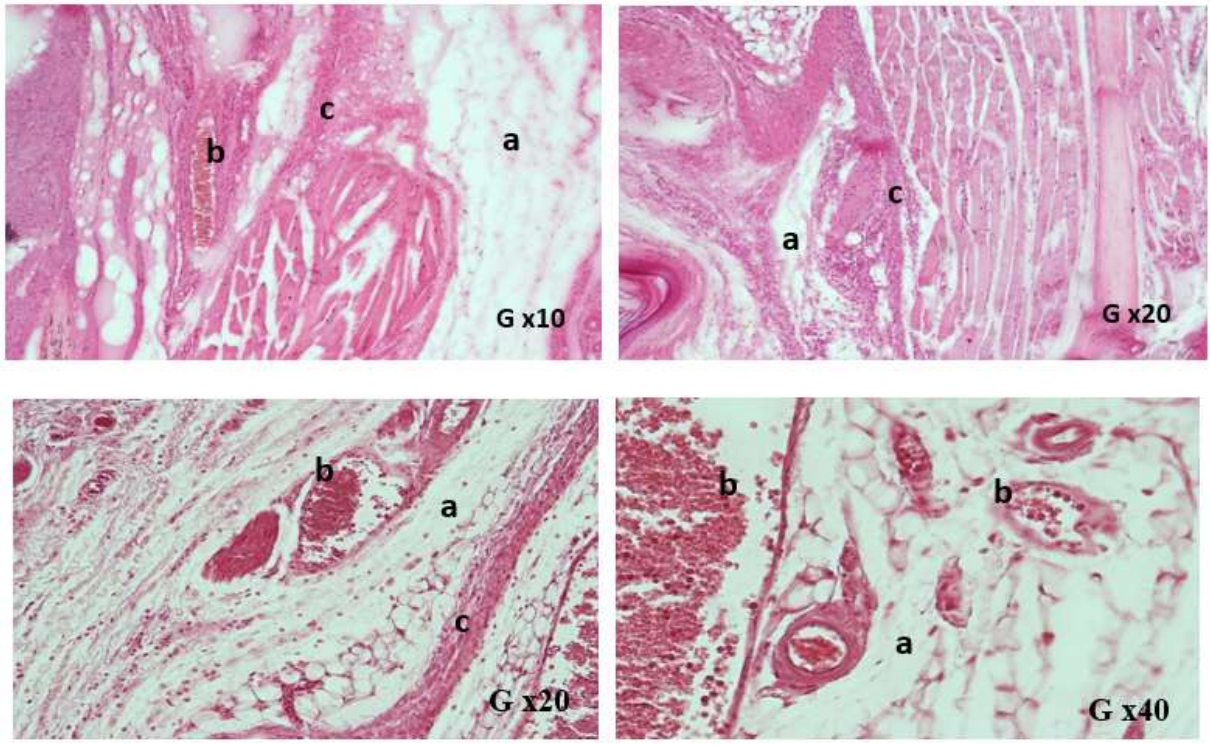
Sour S, Belarbi M, Sari N, Benammar CH, Baghdad CH, Visioli F. 2015. Argan oil reduces, in rats, the high fat diet-induced metabolic effects of obesity. Nutr Metab Cardiovasc Dis. 25(4):382-387.

Trovato A, Raneri E, Kouladis M, Tzakou O, Taviano MF, Galati EM. 2001. Anti-inflammatory and analgesic activity of hypericum empetrifolium willd. (guttiferae). Farmaco. 56(5-7):455-457.

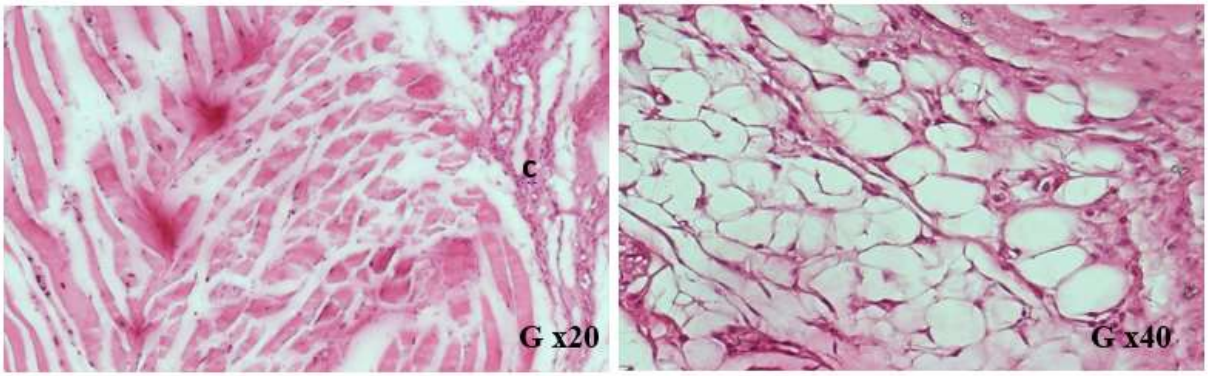
Ursoniu S, Sahebkar A, Serban MC, Banach M, Lipid, Blood Pressure Meta-analysis Collaboration G. 2018. The impact of argan oil on plasma lipids in humans: Systematic review and meta-analysis of randomized controlled trials. Phytother Res. 32(3):377-383.

Vilahur G, Ben-Aicha S, Diaz E, Badimon L, Padro T. 2018. Phytosterols and inflammation. Curr Med Chem.

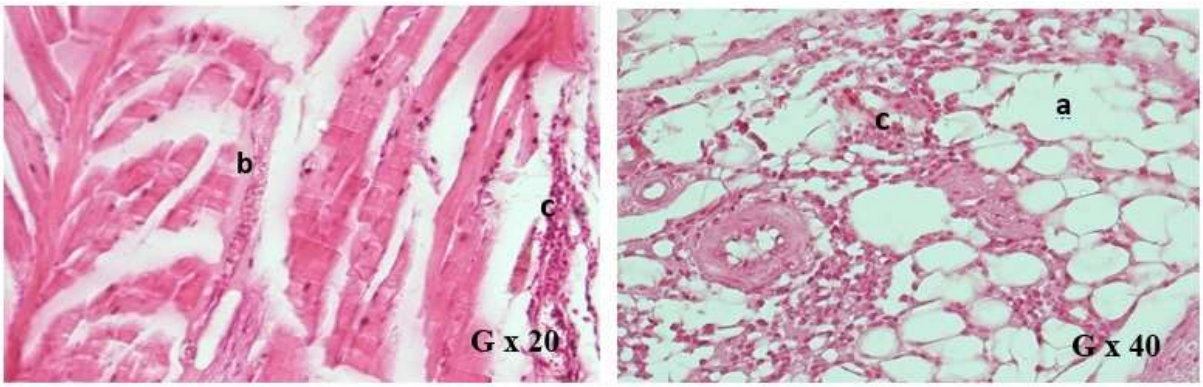
A



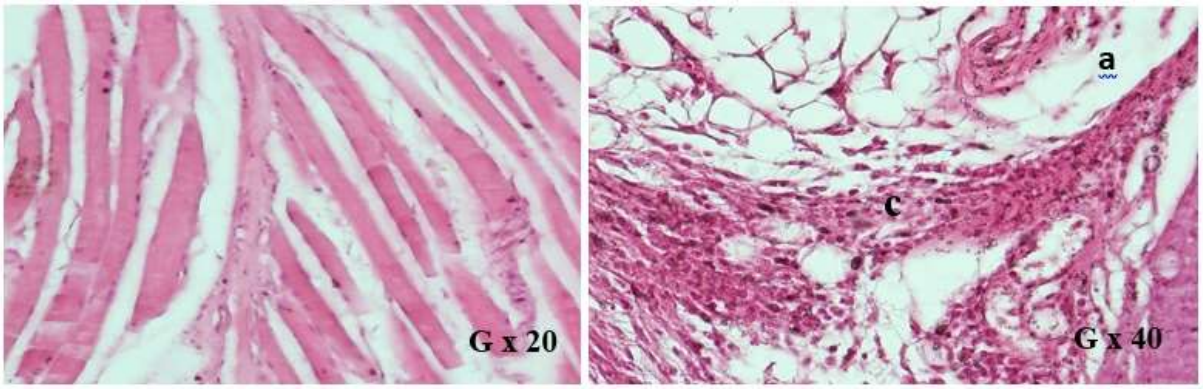
B



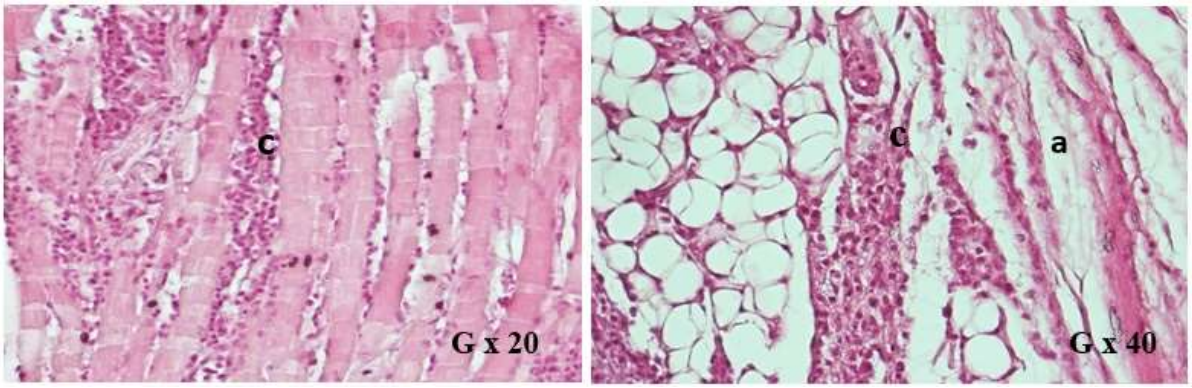
C



D



E



F